Breaking Boundaries of Science, Technology, Medicine, Art and Healthcare Policy

Annual world Congress of SBMT on Brain, Cord Mapping and 10th

Society for Brain Mapping and Therapeutics - SBMT

THEME: NANO-BIO-ELECTRONICS

Baltimore Convention Center,
Baltimore, Maryland
United States of America

May 12, 13, 14, 2013

www.worldbrainmapping.org

Annual world Congress of SBMT on Brain, Cord Mapping and

10th

Breaking Boundaries of Science, Technology, Medicine, Art and Healthcare Policy

Society for Brain Mapping and Therapeutics - SBMT

Contents

INFO

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CME ACCREDITATION

Accreditation/designation Statement:

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the International Society for Magnetic Resonace in Medicine (ISMRM) and the Society for Brain Mapping & Therapeutics (SBMT). The ISMRM) is accredited by the ACCME to provide continuing medical education for physicians.

The International Society for Magnetic Resonance in Medicine (ISMRM) designates this live activity for a maximum of 9.50 *AMA PRA Category 1 Credit*(s)™. Physicians should claim only the credit commensurate with the extent of

SBMT Mission Statement

SBMT is a non-profit society organized for the purpose of encouraging basic and clinical scientists who are interested in areas of Brain Mapping, engineering, stem cell, nanotechnology, imaging and medical device to improve the diagnosis, treatment and rehabilitation of patients afflicted with neurological disorders.

This society promotes the public welfare and improves patient care through the translation of new technologies/therapies into life saving diagnostic and therapeutic procedures. The society is committed to excellence in education, and scientific discovery. The society achieves its mission through multi-disciplinary collaborations with government agencies, patient advocacy groups, educational institutes and industry as well as philanthropic organization.

Educational Objectives

Upon completion of the scientific meeting, participants should be able to:

- Identify new findings in brain mapping (BM) & intraoperative surgical planning (ISP) most relevant to their own sub field (i.e. molecular imaging and or biophotonics);
- Describe the effect of the newly developed methods in medical imaging, medical devices, nanotechnology, stem cell/cellular therapy;
- Discuss and design the possible future research and developments in BM, ISP and Nano-Bio-Electronics and assess the possible impact of such research and development on their own clinical and scientific work in the future;
- Describe and assess the latest cutting-edge technological advancement in BM & ISP such as emerging field of nano-bio-electronics (integration of nanotechnology with stem cell/cellular therapy, medical imaging and medical devices);
- Explain ways to build a bridge amongst multiple disciplines;
- Educate the audience about the advancements in other disciplines and explain how such advancements could help them formulate new diagnostics and treatment modalities;
- Discuss and describe governmental agencies, foundations, and industry roles in research and development of the field.

CONGRESS CHAIRS
Babak Kateb
Michael J. Roy
Rafat Ansari
Yu Chen
James M. Ecklund
Rao P. Gullapalli
James McDonald

ANNUAL SBMT WORLD CONGRESS

The Annual World Congress is a multi-disciplinary forum designed to facilitate cross-pollination and dissemination of technological and medical advances and scientific discovery.

The attendees are a mixture of neurosurgeons, radiologists, neurologists, psychiatrists, rehabilitation medicine, cardiologists, oncologists, bioethicists, policy makers, government officials, engineers, physicists, neuroscience, stem cell scientists, Bio-technologists, nano technolo-

CHARTER of SBMT

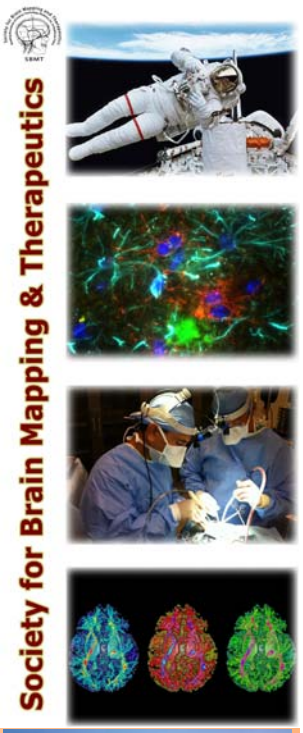
The Society for Brain Mapping and Therapeutics (SBMT) was founded in 2004 to break boundaries in healthcare. The society promotes policies that support rapid, safe, and cost-effective translation of new technology into medicine.

The SBMT globally promotes interdisciplinary research to improve the diagnosis, treatment, and rehabilitation of patients with central nervous system diseases regardless of race, creed, color, national origin, gender, or age.

The SBMT catalyzes interactions between clinical, biological, physical and engineering sciences. The Society builds transdisciplinary and translational consortia which break down traditional barriers that impede application of new technology to medical problems.

Translational research applies cutting edge basic science and advanced technologies to clinical neurosciences. The Society examines emerging disciplines such as nanotechnology, image-guided therapy, stem cell therapy, multi-modality imaging, biophotonics, and biomaterial and tissue engineering for their application to the diagnosis, treatment, and rehabilitation from neurological diseases. The Society seeks to apply these technologies to clinical problems such as brain tumors, stroke, epilepsy, neurodegenerative diseases (Parkinson, Alzheimer, multiple sclerosis and ALS), traumatic brain and spinal cord injuries, autism, post traumatic stress disorder and other psychiatric illnesses.

The Society achieves its goals through meetings, fellowships, publications, international collaborations, consortiums, and policy forums. The SBMT is a nonprofit society which has obtained support from many government agencies (USA, EU and Asia), foundations, and multi-national corporations. The Society maintains its headquarters in West Hollywood, California.



CONTINUING MEDICAL EDUCATION

In recent years astonishing advances have contributed to amazing discoveries and breakthroughs in fields of neurology, neuroscience, neurosurgery, radiology, engineering, computer science, nanotechnology, medical imaging, medical devices and cellular/stem cell therapy.

These scientific advances also have contributed to the large gap of knowledge amongst the scientists in different disciplines. One of the major challenges of 21st century for the scientific community is how to close such gaps of knowledge amongst multiple disciplines.
We have designed the annual meeting of SBMT to address such challenge by bringing together world class experts across multiple disciplines.

Moreover, we have identified a need for progressive integration of nanotechnology, cellular therapy with medical devices and imaging. This is why we have chosen “Nano-Bio-Electronics” as the theme of the 10th Annual world Congress of SBMT in Baltimore, Maryland, USA.

The purpose of the annual meeting is to create an interactive environment, which foster cross-pollination of ideas and pave the way for birth of new treatment and diagnostic modalities in the field..

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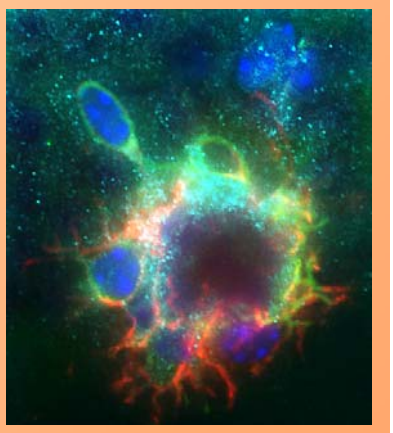

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Those who have disclosed a relationship* with commercial interests are listed below:

Name	Type of Disclosures - What was Disclosed
Allyson Rosen	University Grants/Research Support - NINDS R21NS081416; Pending VA Merit 1I01CX000604-01, France-Stanford Grant
Andreia Vaconcellos Faria	GOVERNMENT FUNDING
Christopher J. Wheeler	University Grants/Research Support Maxine Dunitz Neurosurgical Inst., Cedars-Sinai Medical Center, Dept. of Neurosurgery; Joseph Drown Foundation Grant
Cynthia Roberts	Consultant Fee - Ziemer Ophthalmic Systems AG
David F. Tate	University Granst/Research Support: Telemedicinr and Advnaced Technology Research Center (TATRC) Consultant Fee: Brigham and Wmoen';s Hospital Employee: contractor for Henry M. Foundation for the Advancement of Military Medicine
David Fiorella	CONSULTANT -Codman & Shurtleff, Covidian ev3, NFocus Medical, Cordis, Micrus Endovascular. Stock/Shareholder: Vascular Simulators LLC
Dawn S. Eliashiv	Consultant/Advisor & Lecture fee - UCB and Lundbech
Donald J. Zack	Alcon/Novartis - Consultant/Advisor Merck - Grant support Allergan - Consultant/Advisor Johns Hopkins - Patents/Royalty
E. Mark Haacke	University Grants/Research Support - NIH and DOD Industry Grant Support - Siemens Medical Solution
Edward Herskovits	Grant Support: NIH and Microsoft, Consultant/Advisor: Bioclinca,

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Ejaz Shamim	Grant Support: Allergan Equity/Owner: Medtronic Inc (own some stock)
Elizabeth Hillman	Other Financial or Material Support - Royalty payments related to 'DYCE' dynamic imaging method from MGH / PerkinElmer
Gerard Gioia	Other Financial or Material Support: Psychological Assessment Resources (PASR) Inc. (Patents/Royality), Impact Application Inc. (test author)
J. Wesson Ashford	University Grants/Research Support - VA Merit Review Grant Award Consultant Fee Grifols, Inc., Neurotez, Inc.
James Leiphart	University Grant/Research Support - NEUROPACE Employee - INOVA
James M Ecklund	University Grant/Research Support: Neuren Other Financial Support: President of a consulting company for government and military relevant neurotrauma
James Pekar	Industry Grant Support: Phillips HealthCare, Inc.
James Welsh	Other Financial or Material Support - None financially but I am co-founder of Radion Global, a board member of Coqui
Jane Tavyev Asher	Research Support: Muscular Dystrophy Association
Joseph Culver	Other Financial or Material Support - J.P.C and Washington University have financial interests in Cephalogics LLC based on a license of related optical imaging technology by the University to Cephalogics LLC.
Joshua Medow	BHR Pharma Project Trial Grant.
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Maya Koronyo-Hamaoui	Stock or Shareholder - Founding member and Shareholder in NeuroVision Imaging LLC (NVI) Speaker's Bureau - NVI
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Mohan Vemuri	Owns stock from the company (Life Tech)

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Pedro Cavaleiro Miranda	Consultant, Neuroelectrics Barcelona. This company produces toes devices.
Peter van Zijl	Industry Grant Support: Philips Healthcare
Pieter Gaillard	Stock or Shareholder - to-BBB holding BV (founder shares and stock options) Employee [any industry] - to-BBB technologies BV (salary)
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Thomas Webster	Industry Grant Support: Stryker, Audax, Consultant Fee: Nanovis Stock or Shareholder: Nanovis, Audax Honorarium: International Journal of Nanomedicine
Xingde Li	Other Financial Support: Rotality payment from LightLab Imaging LLC
Zachary T. Levine	Consultant/Advisor and Employee: Medtronic Inc.
Zoltan Mari	Consultant/Advisor: Medtronic, IPSEN, MERZ, US World Meds Grant Support: Allergin, ABBOTT

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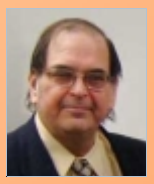

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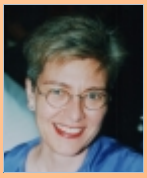

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7. Discuss and describe governmental agencies, foundations, and industry roles in research and development of the field.

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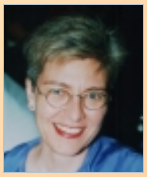

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LETTER FROM THE FOUNDER

I am very proud to oversee the progress of our organization in the last 10 years. It is amazing how SBMT and Brian Mapping Foundation (BMF) changed the dialogue in the field and even contributed to the BRAIN initiative introduced by President Barak Obama this year.

SBMT/IBMISPS started from a unique collaboration between me and Dr. Shouleh Nikzad from NASA/JPL (President Elect of the Society) back in 2003. We established this partnership through series of projects out of NASA/JPL and started series of meetings with engineers, physicians, surgeons and scientists across disciplines. The meetings just kept growing to the level that we had to come up with a plan to take this vision to a different level; this is how the Society for Brain Mapping and Therapeutics and Brain Mapping Foundation really started.

We started our first meeting with just 28 invited speakers over a day event in a small conference room at the Zilkha Institute at Keck School of Medicine of USC. We went from a small conference room to a larger hotel space to a conference centers in France, UCLA, Harvard and UCSF to a large world class convention centers such as Toronto Metro Convention Center and Baltimore Convention Center this year with near 370 speakers over 3 days. Our meetings are jointly sponsored by American Association of Neurological Surgeons (AANS) and International Society for Magnetic Resonance Imaging in Medicine (ISMRM).

The foundation has also been successful in holding 3 Brain Mapping Days at the US Congress (2) and Canadian Parliament in order to educate policymakers and impact neuroscience. These events are now jointly sponsored by Congressional Neuroscience Caucus and going to be held at the Australian and Polish Parliaments. I was personally involved in President Obama's BRAIN initiative, and was at the White House when President Obama

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announced the initiative. SBMT and Brain Mapping Foundation Board members were also involved in drafting a whitepaper to the White House.

The foundation and the Society have teamed up in order to introduce the first textbook of Nanoneuroscience and Nanoneurosurgery ever published. The textbook include 41 chapters, which is a review of more than 3000 references, is co-authored by more than 120 scientists and edited by John Heiss and myself. The Society has established a new publication in collaboration with PloSOne (world's largest open access publisher) called NeuroMapping & Therapeutics. The collection is now accepting papers online at www.PloSOne.org

The past 10 years, SBMT has successfully brought together a diverse scientific, medical, and engineering community to tackle complex neurological disorders such as brain cancer, brain and spinal cord trauma, Alzheimer's Disease, and Parkinson's disease. These efforts strived to close the gap of knowledge across disciplines. The society has successfully facilitated unprecedented cross-disciplinary interactions amongst scientific fields. This unique approach has spurred interest in the organization and its growth from the USA to include Canada, Japan, India, France, China, Brazil, Spain, Republic of Georgia, Iran, Israel, Russia, South Korea, Taiwan, Hong Kong, Germany, Sweden, Netherland, Lithuania, Italy and the UK.

BMF, is pleased to award pioneers of the field as well as policymakers and leading industry. In the last 10 years, we have recognized and awarded 63 individuals across the board including top scientists, lawmakers, community leaders, leading organizations/industry as well as students. This year was no exception and I congratulate all of our award recipients: Drs. Shouleh Nikzad, Margie Homer, Rafat Ansari, Yosef Koronyo, Maya Koronyo-Hamaoui, Yosef Koronyo, Robert Kraus, Eric Bailey, Wieslaw L. Nowinski, Reese S. Terry Jr., Ming Hsieh and Ms. Beth Nielsen Chapman as well as Congressman Earl Blumenauer, Congresswoman Cathy McMorris Rodgers and Congressman James Moran.

I commend all members of the Society for their visionary approach to translational neuroscience and truly look forward to seeing you all at the 11th Annual World Brain Mapping and Therapeutics in Sydney Australia, March 17-19, 2014!

Respectfully

SBMT - President's Letter

Medicine
Centre for Healthy Brain Ageing

Monday, April 29, 2013

On behalf of the Society for Brain Mapping and Therapeutics (SBMT) local chapter, it is our pleasure to extend our warm welcome to you all to Sydney, Australia for 2014, 11th Annual World Congress of the SBMT – Bringing Together Engineering, Science and Medicine. Australia as a multicultural society is also the home for multidisciplinary neuroscience research and has a worldwide recognition.

Brain Sciences UNSW Sydney provides a strong platform for such meetings to facilitate collaborative research and access to relevant technologies and expertise. It encompasses an inter-disciplinary approach drawing together researchers with diverse backgrounds like engineering, science and medicine from the various schools, hospitals and Institutes nationally and internationally with a collective interest in various aspects of the function and structure of the brain in both a normal and dysfunction state.

Similarly the Melbourne Brain Centre employing over 700 scientists/researchers working side-by-side in state-of-the-art laboratories next to world class clinical facilities is one of the top five centres for brain research internationally. This power-house of intellectual capacity and research strength is enabling the development of more effective diagnostic tools, treatments and ultimately cures for brain and mind disorders. The Queensland Brain Institute (QBI) in Brisbane, Brain and Mind Institute (BMI) in Sydney, The Australian Neuro-muscular Research Institute (ANRI) in Perth, Australian Brain Bank Network (ABBN) are other icons in Australia creating specific niche in neurosciences.

The Australian Society for Medical Research (ASMR) is the peak professional society representing Australian Health and Medical Research representing over 18,000 people actively involved in health and medical research through fifty-six affiliated professional societies and Medical Colleges also focussing on neurosciences. The corporate and disease related foundation memberships, patient interest groups bring a further 100,000 Australians with an interest in health and medical research into the ASMR network. The Society has a long established role in public, political and scientific advocacy.

We are looking forward to this meeting in Sydney. This harbour city is the state capital of New South Wales and the most populous city in Australia with population just over 4.6 million and is considered as the most model city in the world. It offers spectacular beauty, landscape and variety of tourist attractions. The Four Seasons Hotel, the venue for this meeting is just close to the Harbour Bridge and with an unmatched ambience.

Sincerely,

Convenor

A/Prof Kuldip S Sidhu, BSC (Med), PhD,
Stem Cells, CHeBA, UNSW Medicine
President, SBMT Local Chapter

SBMT Program

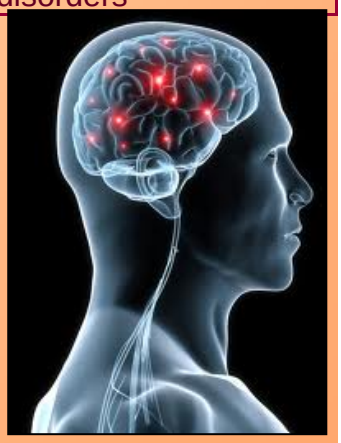
Nano-Bio-Electronics Consortium (NBEC): The Purpose of the NBEC is to facilitate integration of nanotechnology, Stem cell and cellular therapy with Medical Devices and imaging. This consortium will impact global biomedical science and healthcare delivery through national and international partnerships with governments, universities and leading industry. The following are elements of the Consortium:

1 - Scientific Meetings

This includes national meetings, international meetings, and world congress. The world congress is the society's annual meeting that invites prominent scientists and clinicians from all

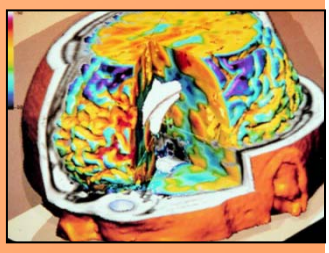
SCIENTIFIC EXHIBITS & POSTERS	SPECIAL FOCUS SESSIONS	STUDENT FUNDING OPPORTUNITIES
Basic and Clinical Research in image guided therapy. Novel research and development in brain mapping and intra-operative surgical planning. Clinical trials Bio-Ethics	Governmental Regulation Government Education Patient Advocacy Healthcare Policy Funding Opportunities	Graduate and Post Graduate Interdisciplinary Fellowships Student Travel awards University Student chapters mentorship programs Scholarships for undergraduate students studying neurological disorders

2 – Student Chapters



The student chapters are organized to promote and encourage multi-disciplinary research across disciplines. Universities with Student Chapters qualify for student travel award starting 2012.

3 – Fellowships



SBMT fellowships are focused on interdisciplinary training of neurosurgeons, neurologists, radiologists and rehabilitation physicians, neuroscientists and engineers on diseases that has major Social impact such as Traumatic brain and spinal cord injuries, neuro-oncology and neurodegenerative diseases. The fellowships are design to apply state-of-the-art research through the study of biomedical science and cutting edge technologies to clinical problems. These scholarship are awarded to masters students, pre-doctoral, and post-doctoral fellows.

4 – Visiting Scholars Program

Visiting scholars program facilitates exchange of scientific investigators and policy experts with other countries and institutions through participating SBMT centers.The goal of the visiting scholar program

5 - World Congresses

is to develop collaborations between physical and biological sciences and address major policy issues relevant to the society.

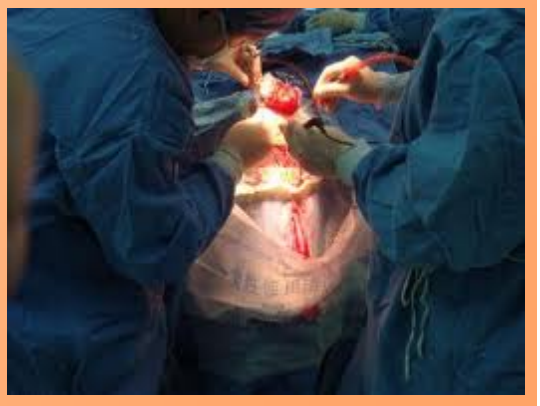
- 2012 - Toronto, Ontario, Canada
- 2011 - San Francisco, CA, USA
- 2010 - USUHS, Bethesda, Maryland, USA
- 2009 - HARVARD Medical School, Boston, MA, USA
- 2008 - UCLA California Nano-system Institute, Los Angeles, CA, USA
- 2007 - Washington DC, USA
- 2006 - Clairmont-Ferrand, France
- 2005 - Pasadena, CA, USA
- 2004 - USC Keck School of Medicine, CA, USA

SBMT Annual Meeting Organizers Encourage Cross-Disciplinary Subjects:

- Image guided systems
- Neurovascular coupling and Perfusion imaging
- ISP & Image guided surgery (OR of the future)
- BM and ISP in Stereotactic Radiosurgery (proton Therapy, Novalis, Tomo-therapy, Varian system, Xknife, gamma knife and cyberknife technologies will be compared and contrasted)
- Molecular and cellular imaging including: the use of nanoparticles for stem cell and T-cell imaging
- Neuro Anatomy and histopathology in brain mapping
- Nanoscience, genomics, computational informatics genetics in brain mapping
- Rehabilitation Medicine (e.g. TBI, Stroke, Spinal Cord Injury)
- Novel imaging techniques for TBI and PTSD (eg. DTI, PET,SPECT)
- NeuroImaging for Psychiatric Diseases (eg. PTSD, Autism,Schizophrenia)
- Nanoscience, genomics, computational informatics geneticsin brain mapping
- Neurophysiology (EEG, MEG, Evoked Potentials, EMG/NCS,ESM)
- Functional brain mapping (fMRI, PET, SPECT, Intrinsic Signal Optical Imaging)
- Brain Mapping and Intra-operative Surgical Planning using Endoscopy
- Biophotonic techniques for Brain Mapping
- Multi-modality imaging techniques
- Ultrasound Imaging
- Magnetic Resonance Spectroscopic Imaging
- High-field and low-field magnetic resonance
- High-field and low-field MRI, MR Spectroscopic Imaging, micro MRI
- Magneto encephalographic
- Transcranial Magnetic Stimulation
- Cerebral White Matter Mapping and Imaging, (eg. Diffusion Tensor Imaging) Neural Prosthesis & Robotics (Human Brain machine Interface technology)
- Minimally invasive therapy for traumatic brain injury (TBI) maging modalities for detecting mild/mod TBI, micro-TBI
- Socioeconomic, Ethical, and Healthcare issues related to the brain mapping and intra-operative surgical planning

6 – Seed Grants

SBMT, in partnership with Brain mapping Foundation and other foundationsis planning to provide seed grants to encourage cross-disciplinary collaboration. The purpose of these grants is to bridge physical and biological sciences and encourage cross disciplinary collaboration.

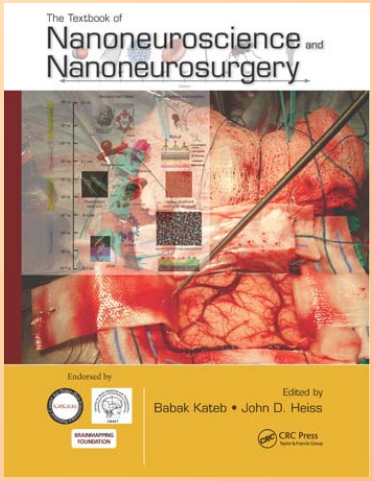


7 – Industry Partners

SBMT encourages support from private industry and provides industry with a forum to present their latest advances. The society recognizes the role of industry in translating cutting-edge research and technology into the market. SBMT is currently partnering with more than 100 multi-national corporations.

8 – Society Publications.

The Society has successfully published 3 special issues with NeuroImage. We have reached out to more than 50,000 scientists worldwide through our partnership with Elsevier in the last several years. Recently, SBMT partnered with PloSOne publishing giant to launch special Collection /publication called: NeuroMapping and Therapeutics (www.PloSOne.org <http://www.plosone.org/>) PloSOne is one of the largest Open access Publishers in the world. This partnership has enabled SBMT to reach out to a larger audience of scientists.



SBMT also published its first Textbook, which is "THE" first textbook of Nanoneuroscience and Nanoneurosurgery ever published. This textbook made possible through partnership with Taylor & Francis/CRC Publishing giant, Brain Mapping Foundation, SBMT and National Center for NanoBioElectronic (NCNBE). The textbook is edited by Babak Kateb and John Heiss and co-authored by more than 120 leading scientists in the field. The textbook is consist of 41 chapters, 600+ pages of scientific review of more than 3000 references.

9 – Government Relationships

The society works actively with the representatives of various governments In order to leverage its resources and focus attention on healthcare issues through interdisciplinary collaborations. In this regard, SBMT has partnered with Brain Mapping Foundation (BMF) and held Annual Brain Mapping Days at the US Congress and Canadian Parliament. SBMT is planning to hold a Brain Mapping Day at the Australian Parliament in 2014.

10 - Healthcare Policy

The first healthcare policy advocacy of SBMT was done in 2004 when the organization pushed for funding for a collaborative network through the office of the Honorable Barbara Boxer and Dian Feinstein of California.

In 2008 SBMT introduced formation of Science, Technology, Medicine and Law-Healthcare Policy (STML-Hub) to the US Congress and house of representative in order to establish a center for introducing technological and scientific advancements to the policy makers. The organization hoped that through this hub we could educate policymakers about the state-of-the-art science. This could help policy

In 2012 with the help and support of Congressman Moran and Congressional Neuroscience Caucus SBMT advocated report language on "Multidisciplinary Brain Research". The report language passed through the House and Senate with significant and overwhelming bipartisan support. This legislation may enable DoD to better focused on integrating nanotechnology, stem cell and cellular therapy and medical imaging/devices in order to rapidly provide solutions for the wounded warriors and civilians with neurological disorders such as PTSD and TBI.

11 – Outreach Program

Outreach programs including woman and minority in sciences and community awareness of new technology, science and medical advancements. This includes high school and college educational programs run through student chapters worldwide.

12 – Global Physician and Scientists (GPS)

GPS is a humanitarian program, which is focused on mobilizing hysicians, scientist and surgeons to serve for few weeks in the poor and rural areas of the United States and abroad. This program will collaborate with industry and government officials and will use the national and international SBMT centers as bases of operations. The program is designed to not only help alleviate healthcare disparities by bringing world class physicians to the

KEYNOTE SPEAKERS

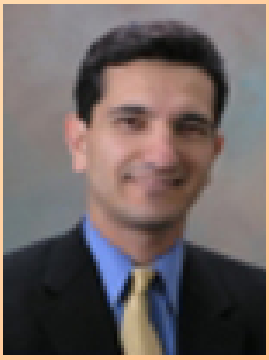
Founding Chairman of the Board of SBMT and Brain Mapping Foundation, Scientific Director of SBMT and Brain Mapping Foundation, Director of National Center for Nano-Bio-Electronics, Senior Editor of SBMT-NeuroMapping & Therapeutics, Research Scientist, Department of Neurosurgery, Cedars-Sinai Medical Center.

Babak Kateb is a neuroscientist with more than 17 years of research experience. His research has been focused on peripheral neuropathy, stroke, epilepsy, fetal cell transplant into the brain, pancreatic islet xenotrasplantation, human brain computer interface and brain implants, effect of hypothermia in traumatic brain injury patients with low Glasgow Coma Score, image guided surgery using NASA's thermal and UV imaging technology, optical imaging and laser spectroscopy, microwave ablation, stem cell research, nanoneurosurgery and virtual reality neurosurgical simulation.

Babak's pioneering work on "Internalization of NASA's Multi-Wall Carbon Nanotubes by Microglia: Possible Application in Immunotherapy of Brain Tumors (in vivo and In Vitro)" is published in NeuroImage and Journal of NeuroImmunology. He also discovered that brain cancers smell differently by using NASA's electronic nose. He was awarded NASA's Tech Brief award in 2008 for his discovery. The result of this Pilot study is published in the 2009 IBMISPS-NeuroImage issue.

Babak has been serving as the founding chairman of the board of directors for SBMT and the Brain Mapping Foundation, as well as Chief Executive Officer and Scientific Director of SBMT and the Brain Mapping Foundation since 2004 as well as Director of National Center for Nano-Bio-Electronics. He chairs the publication committee of SBMT, as editor in chief. He has established a new publication with PLoSOne called: Neuro-Mapping & Therapeutics collections and was the force behind 3 successful IBMISPS-NeuroImage special issues with high impact factors. He is editor of "Nanoneurosurgery" Text book, which is scheduled for release by Taylor & Francis Publisher by 2012.

Babak has been trained and employed at the Department of Neurology at the West Los Angeles VA Medical Center, UCLA Department of Neurosurgery, the Dumont-UCLA Transplant center, Cedars-Sinai Medical Center transplant Center, Maxine Dunitz Neurosurgical Institute at Cedars Si-



Babak Kateb
Chairman/CEO
SBMT & President of Brain Mapping Foundation

KEYNOTE SPEAKERS

Vice Admiral Nathan is the 37th surgeon general of the Navy and chief of the Navy's Bureau of Medicine and Surgery.

Nathan received his Bachelors of Science from Georgia Tech and his M.D. from The Medical College of Georgia in 1981. He completed Internal Medicine specialty training in 1984 at the University of South Florida before serving as the Internal Medicine Dept Head at Naval Hospital Guantanamo Bay, Cuba. In 1985 Nathan transferred to Naval Hospital, Groton, Connecticut as leader of the Medical Mobilization Amphibious Surgical Support Team. In 1987, Nathan transferred to Naval Medical Center San Diego as Head, Division of Internal Medicine with additional duty to the Marine Corps, 1st Marine Division.

In 1990 he served as a Department Head, Naval Hospital Beaufort, South Carolina before reporting to Naval Clinics Command, London, U.K. where he participated in military-to-military engagements with post-Soviet Eastern European countries. In 1995, he was assigned as specialist assignment officer at the Bureau of Naval Personnel, providing guidance to over 1,500 U.S. Navy Medical Corps officers. In 1998 he accepted a seat at the Joint Industrial College of the Armed Forces located in Washington, D.C., graduating in 1999 with a Masters in “Resourcing the National Strategy.” Nathan went on to serve as the Fleet Surgeon, Forward Deployed Naval Forces, Commander, U.S. 7th Fleet, aboard the flagship USS Blue Ridge (LCC 19), out of Yokosuka, Japan. In 2001, he transferred as Deputy Commander, Navy Medical Center Portsmouth, Va.

In 2004 Nathan assumed command of Naval Hospital Pensacola with additional oversight of 12 clinics in 4 states where he oversaw Navy medical relief efforts following hurricanes Ivan, Dennis, and Katrina. Despite all facilities receiving crippling blows; his command still garnered the TRICARE/DOD award for “highest patient satisfaction in a medium sized facility”. In June 2006, he transferred as the Fleet Surgeon to the commander, U.S. Fleet Forces Command, instrumental in organizing the Fleet Health Domain integration with the Fleet Readiness Enterprise while providing medical global force management. In 2007, Nathan was assigned as Commander, Naval Medical Center Portsmouth and Navy Medicine Region East with command of over 18,000 personnel and an operating budget exceeding $1.2 billion.

Nathan also served as Commander, Walter Reed National Military Medical Center and Navy Medicine, National Capital Area where he

Vice Admiral
Matthew L. Nathan
Surgeon General,
US Navy;
Chief, US Navy Bureau
of
Medicine and Surgery

KEYNOTE SPEAKERS

A lifelong resident of Portland, Oregon, Congressman Earl Blumenauer (OR-3) has devoted his entire career to public service.

While still a student at Lewis and Clark College, he spearheaded the effort to lower the voting age both in Oregon and at the national level. He was elected to the Oregon Legislature in 1972, where he served three terms and Chaired the House Education and Revenue Committee in 1977-78. In 1978, he was elected to the Multnomah County Commission, where he served for eight years before being elected to the Portland City Council in 1986. There, his 10-year tenure as the Commissioner of Public Works demonstrated his leadership on the innovative accomplishments in transportation, planning, environmental programs and public participation that have helped Portland earn an international reputation as one of America's most livable cities.

Elected to the US House of Representatives in 1996, Mr. Blumenauer has created a unique role as Congress' chief spokesperson for Livable Communities: places where people are safe, healthy and economically secure. From 1996 to 2007, he served on the Transportation and Infrastructure Committee, where he was a strong advocate for federal policies that address transportation alternatives, provide housing choices, support sustainable economies and improve the environment. He was a member of the Foreign Affairs Committee from 2001 to 2007, and vice-chair of the Select Committee on Energy Independence and Global Warming from 2007 to 2010. He is currently a member of the Budget Committee and Ways and Means Committee and the subcommittees on Health and Trade.

These committee assignments give Mr. Blumenauer a unique platform from which to initiate and further legislation that addresses and mitigates the effects of global warming. His priorities also include healthcare reform, honest trade, financing critical infrastructure, building livable communities in a global economy, and ensuring economic security for working families

A leading environmental advocate both in Oregon and Congress, Congressman Blumenauer has authored and co-sponsored legislation to preserve and protect public lands, shift the nation's energy policy towards renewable energy and energy efficiency, curb global warming, clean our nation's water bodies, and many others.

Earl Blumenauer
U.S. Representative
for Oregon's
3rd Congressional
District

KEYNOTE SPEAKERS

Howard J. Federoff, M.D., Ph.D., Executive Vice President for Health Sciences and Executive Dean of the School of Medicine, oversees a biomedical research organization with an estimated $274 million in external research funding in 2011. Dr. Federoff is responsible for advancing the educational and research missions of Georgetown University Medical Center (GUMC), and working effectively with the leadership of MedStar Health, its clinical partner.

GUMC consists of the School of Medicine (founded in 1851), the School of Nursing & Health Studies, the Biomedical Graduate Research Organization (BGRO), and Georgetown Lombardi Comprehensive Cancer Center (LCCC).

Dr. Federoff is committed to having GUMC focused on four key areas that will advance its strategic goals and define the mission of Georgetown medicine in the University's current capital campaign, *For Generations to Come*. GUMC's campaign priorities include the increase of financial aid for students, the preparation of physician-scientists and medical students to be in the vanguard in the emerging field of systems medicine, the advancement of scientific understanding and human health through biomedical research, and the improvement of access to quality health care for all patient populations both at home and around the world.

Dr. Federoff received his M.S., Ph.D., and M.D. degrees from the Albert Einstein College of Medicine, and completed his internship, residency, and clinical and research fellowships at Massachusetts General Hospital/ Harvard Medical School.

Dr. Federoff's research interests include gene therapy and neurodegenerative diseases such as Parkinson's, Alzheimer's, and prion diseases. He holds a number of medical patents with a number of other patents pending. His research has received support from the National Science Foundation, the National Institutes of Health (NIH), and the U.S. Department of Defense, among other sources. Dr. Federoff has published widely in peer-reviewed journals and served as a reviewer for many of these journals.

Howard J. Federoff
Executive Vice President for Health Sciences, Executive Dean of the School of Medicine, Georgetown

KEYNOTE SPEAKERS

Capt. Paul S. Hammer is the director of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE).

He is responsible for the work of DCoE headquarters and centers, the Defense and Veterans Brain Injury Center, the Deployment Health Clinical Center and the National Center for Telehealth and Technology, and a combined mission to improve the lives of our nation's service members, families and veterans by advancing excellence in psychological health and traumatic brain injury (TBI) prevention and care.

He leads a groundbreaking collaborative effort that includes the Department of Veterans Affairs, civilian agencies, community leaders, advocacy groups, clinical experts and academic institutions dedicated to expanding the psychological health and TBI state of knowledge.

Hammer received his Bachelor of Science degree in chemistry from the University of San Francisco and his medical doctorate from the Uniformed Services University of the Health Sciences. He completed his psychiatry residency at Naval Medical Center in San Diego and is board certified in psychiatry.

His career has largely focused on psychological trauma following a disaster. He led the Navy's west coast Special Psychiatric Rapid Intervention Team providing numerous interventions to deliver immediate, on-the-ground psychological health support following suicides, training accidents and natural and man-made disasters.

Hammer led international and high-profile disaster response, most notably in the Korean Air Lines crash in Guam in 1997 and the Joint Task Force Mental Health interventions following Hurricane Mitch in 1998. In his various assignments, he has educated thousands of service members on operational stress control, psychological health and traumatic brain injury care.

CAPTAIN
Paul S. Hammer
Director, Defense Centers of Excellence for Psychological Health and Traumatic Brain

Timetable

Day 1

Sunday

May 12,

	Day 1 (Sunday May 12, 2013)			
7:00 AM	*Opening Registration Desk*			
8:00 AM - 8:10 AM	Welcome & Introduction (Room 314-317) Mike Roy, 2012 SBMT President			
8:10 AM - 8:20 AM	Welcome & Introduction (Room 314-317) Kuldip Sidhu, 2013 SBMT President Elect			
8:20 AM - 8:55 AM	*Key Note* Babak Kateb, Founder/Chairman/CEO of SBMT & President of Brain Mapping Foundation (Room 314-317)			
8:55 AM - 9:10 AM	Coffee Break & Poster Viewing			
9:10 AM - 10:55 AM	1 - Military Medicine: Improving Identification and Management of PTSD & TBI (CME) (Room 310) Co-Chairs: J Grimes and M. Roy		2 - Image Guided Interventions (Room 301) Chair: R. P Gullapalli	
9:10 AM	1. M. Roy		1. J. Desai	
9:25 AM	2. R. D-Arristia		2. G. Woodworth	
9:40 AM	3. D. Perl		3. J. Elias	
9:55 AM	4. J. Smirniotopoulos		4. Ming Li	
10:10 AM	5. G. Ling		5. K. Chaichana	
10:25 AM	Q&A		6. R. Kraus (2013 Awardee)	
10:40 AM			Q&A	
10:55 AM - 11:10 AM	Coffee Break & Poster Viewing			
11:10 AM - 12:20 PM	3 - Frontiers in iPSC: Technology, Translation and Regulatory Frame work (Room 310) Chair: K. Sidhu	4 - Veteran Session 1: Evaluating multiple illnesses and their long-term sequelae at the WRIISCs (CME) (Room 301) Chair: D. Helmer	5 - Synchrotron-generated Microbeam Radiosurgery (Room 303) Chair: P. Romanelli	
11:10 AM	1. K. Sidhu	1. J. Chapman	1. A. Bravin	
11:25 AM	2. J. Kehler	2. J. Serrador	2. P. Coan	
11:40 AM	3. M. Vemuri	3. M. Adamson	3. P. Romanelli	
11:55 AM	4. G. Stacey	Q&A	4. E. Schültke	
12:10 AM	5. M. Homer (2013 Awardee)		5. M. Wright	
12:15 PM	Q&A		Q&A	
12:20 PM - 1:00 PM	Lunch Break & Poster Viewing			
1:00 PM - 2:30 PM	6 - Controversies in TBI Management (CME) (Room 310) Chair: N. Vyas	7 - Deep Brain Stimulation (CME) (Room 301) Chair: E.Shamim	8 - NanoNeurosurgery and NanoBioElectronics (1) (CME) (Room 303) Co-Chairs: B. Kateb and K. Jain	1:00 PM - 4:00 PM *Medtronic Workshop (Room 305)* Introduction to Medtronic StealthViz(tm) Advanced Visualization and Planning Software
1:00 PM	1. L. Altaweel	1. E. Shamim	1. M. Zhang	
1:15 PM	2. P. Raksin	2. C. Lungu	2. P. Gaillard	
1:30 PM	3. M. Stippler	3. K. Zaghloul	3. T. Lu Lowe	
1:45 PM	4. J. Medow	4. Z. Levine	4. R. Yin	
2:00 PM	5. H. Eisenberg	5. Z. Mari	Q&A	
2:15 PM	Q&A	Q&A		
2:30 PM - 2:45 PM	Coffee Break & Poster Viewing			
2:45 PM - 4:30 PM	12 - VA session 2: long-term effect of TBI and its co-occurring conditions (CME) (Room 301) Chair: M. Adamson	10 - Bio-Photonic session: Near-infrared Spectroscopy (NIRS) and Imaging for Clinical Translation (CME) (Room 310) Chair: X. Li	11 - NanoNeurosurgery and NanoBioElectronics (2) (CME) (Room 303) Co-Chairs: B. Kateb and K. Jain	Oral Posters 6 (Room 310)
2:45 PM	1. K. Main	1. H. Liu	1. M. Malhotra	2:45 B. Guthikonda
3:00 PM	2. S. Soman	2. A. H. Gandjbakhche	2. N. Kotov	2:55 T. E. Reid
3:15 PM	3. J. Ashford	3.A. Medvedev	3. K. Jain	3:10 H. North
3:30 PM	Q&A	4.K. Pourrezaei	4. X. Wang	3:20 J. Xia
3:45 PM		5. J. Culver	Q&A	3:30 L. Reece
4:00 AM		6. M. Angela Franceschini		3:40 J. Chodakiewitz
4:15 PM		Q&A		3:50 Q&A
	BLACK TIE ONLY Cocktail event (6-8PM) Hilton Hotel in Baltimore GALA 8-11pm Hilton Hotel in Baltimore			

Timetable

Day 2

Monday

May 13,

	Day 2 (Monday, May 13, 2013)				
7:00 AM - 8:00 AM	*Opening Registration Desk*		*Nextim Workshop (Room 305)* Pre-surgical Mapping of Eloquent Cortex with Navigated Brain Stimulation		
8:00 AM - 8:15 AM	*Welcome & Introduction (Room 314 - 317)*				
8:15 AM - 8:50 AM	*Key Note* Howard Federoff, Dean of School of Medicine, Georgetown University School of Medicine (Room 314-317)				
8:50 AM - 9:25 AM	*Key Note* Vice Admiral Mathew Nathan Surgeon General of the US Navy (Room 314-317)				
9:25 AM - 9:40 AM	Coffee Break & Poster Viewing				
9:40 - 11:25 AM	13 - Neuro-Ophtalmology: Innovations in Visual Neuroscience (CME) (Room 302) Chair: V. Patel	14 - Aviation and Space Medicine (Room 301) Chair: R. Ansari	15 - Future of Human Assisted Devices Impacting TBI Rehabilitation (CME) (Room 303) Chair: J. Leiphart		16 - Inflammation and Alzheimer's Disease (CME) (Room 310) Chair: M. Koronyo-Hamaoui
9:40 AM 9:55 AM 10:10 AM 10:25 AM 10:40 AM 10:55 AM 11:10 AM	1. P. Subramanian 2. A. Kassam 3. V. Patel Q&A	1. C. Roberts 2. D. E. Callan 3. M. B. Datiles III 4. R. Ansari (2013 Awardee) 5. K. Pourrezaei Q&A	1. A. Ganjei 2. P. Pasquina 3. M. Boninger 4. E. M. Haacke Q&A		1. TBD 2. M. Koronyo-Hamaoui (2013 Awardee) 3. D. Lee 4. C. Wheeler 5. C. Miller Q&A
11:25 AM - 12:10 PM	Lunch Break & Poster Viewing				
12:10 PM - 1:55 PM	17 - Sports Concussion (CME) (Room 301) Co-Chairs: J. Ecklund and K. Green	18 - Pediatric Neuro-Oncology (Room 303) Chair: R. Packer	19 - Functional Neuroimaging (Room 310) Chair: J. Greenspan		20 - Autism (Room 302) Co-Chairs: C. Wheeler and P. Patterson
12:10 PM 12:25 PM 12:40 PM 12:55 PM 1:10 PM 1:25 PM 1:40 PM	1. T. A. Mayer 2. G. Gioia 3. K. Crutchfield 4. R. Stern Q&A	1. R. Fernandes 2.R. Lonser 3.K . Warren 4.G. Vezina 5.P. Vyas 6. R. Packer Q&A	1. J. Pekar 2. Y. Yang 3. D. Seminowicz 4. C. Smith 5. C. Sour Q&A		1. C. Pardo 2. P. Patterson 3. C. Wheeler 4. J. Asher 5. S. Mostofsky Q&A
1:55 PM - 2:10 PM	Coffee Break & Poster Viewing				
2:10 PM - 3:45 PM	21 - VNS use in Epilepsy, Psychiatric Disorders and Autism (CME) (Room 301) Chair: E. Tsimerinov	22 - BioPhotonics: Emerging Technologies for Neuroimaging (CME) (Room 303) Chair: A. Dunn	23 - EpiGenetics (CME) (Room 310) Chair: J. McDonald		24 - Multi-Modal TBI Imaging and Diffusion MRI Tractography: uses, strengths, and limitations (CME) (Room 302) Chair: M. Budde / P. Defina
2:10 PM 2:25 PM 2:40 PM 2:55 PM 3:05 PM 3:20 PM 3:35 PM	1.E. Tsimerinov 2.J. Chung 3. J. Hopp 4. W. IsHak 5. D. Eliashiv Q&A	1. X. Li 2. Y. Chen 3. C. Min Tang 4. S. Hu 5. Q Luo Q&A	1. J. W. McDonald 2.V. Belegu 3. Y. Su 4. Y. Gao 5. L. Martin 6. S. Merbs Q&A		1. K. Oishi 2. M. Komlosh 3. M. Budde 4. P. Defina Q&A
3:50 PM - 4:10 PM	Coffee Break & Poster Viewing				
4:10 PM - 5:40 PM	25 - Stem Cell and Brain Diseases (Room 301) Co-Chairs: R. Chaudhry and K. Sidhu	26 - Neuro-Immunology and Vaccine Therapy (Room 302) Chair: D. Irvin	27 - Optical Imaging of Brain Function (CME) (Room 303) Chair: Y. Chen	28 - NeuroOncology (Room 310) Co-Chairs: S. Prabhu and C. Teo	29 - Multimodality imaging (1) (Room 305) Co-Chair: A. Filler
4:10 PM 4:25 PM 4:40 PM 4:55 PM 5:10 PM 5:25 PM	1. M. Rao 2. O. Cooper 3. C. Atwood 4. E. Feigal 5. V. Yamamoto Q&A	1. D. Griffin 2. G. Lynn 3. J. Tiegler 4. D. Barouch 5. D. Woodland 6. D. Clever	1. C. Du, N. Volkow, Y. Pan 2. V. Tsytsarev 3. R. Wang 4. A. Dunn 5. E. Hillman Q&A	1. C. Teo 2. S. Prabhu 3. M.Lim 4.S. Nikzad (2013 Awardee) Q&A	1. A. Filler 2. Z. Nadareishvili 3. A. Degnan Q&A

Timetable

Day 3

Tuesday

May 14,

	Day 3 (Tuesday, May 14, 2013)				
8:00 AM	*Opening Registration Desk*				
8:15 AM - 8:30 AM	*Welcome & Introduction (Room 314 - 317)*				
8:30 AM - 9:05 AM	*Key Note –* Captain Paul S. Hammer, MC, USN, Director of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) (Room 314-317)				
9:05 AM - 10:35 AM	30 - Image Analysis in the Era of Big Data (CME) (Room 301) Chair: E. Herskovits	31 - The efficacy and mechanisms of robot-assisted therapy in neurorehabilitation (CME) (Room 310) Chair: L. Forrester	32 - Contemporary Management of Penetrating Brain Injuries (Room 302) Chair: J. Ecklund and K. Green	33 - Translational research institutes (Room 303) Chair: D. Ford	Oral Posters 1 (Room 305)
9:05 AM	1. A. Varshney	1. S. Conroy	1. B. C. Walters	1. D. Ford	9:05 A. Worth
9:20 AM	2. E. Herskovits	2. S. Kantak	2. A. Potapov	2. G. Smith	9:15 R. Yadav
9:35 AM	3.E. Siegel	3. L. Forrester	3. P. Sioutos	3. J. Prince	9:25 D. Zelinsky
9:50 AM	4.P. Kochunov	4. R. Goodman	4. B. Aarabi		9:35 J. Zhuo
10:05 AM	5. S. Chen	5. A. Roy			9:45 G. Pasinetti 9:55 J. Rose 10:05 M. Janowski
10:20 AM	Q&A	Q&A	Q&A	Q&A	10:15 M. Okon 10:25 Q&A
10:35 AM - 10:50 AM	Coffee Break & Poster Viewing				
10:50 AM - 11:50 AM	34 - Stereotactic Radiosurgery and IMRT (Room 301) Chair: J. Welsh	39 - Computational Modeling using MRI Data to Enhance Diagnosis or Therapy (Room 303) Co-Chairs: P. Basser and M. Sarntinoranont	42 - NIH Funding of Grants in Brain Imaging (Room 302) Co-Chairs: G. Farber and G. Liu	44 - Stem Cells Towards Opthalmology/ Malignancy/ Osteoarthritis (Room 310) Co-Chairs: R Chaudhry and K. Sidhu	Oral Posters 3 (Room 305)
10:50 AM	1. J. Rockhill	1. P. C. Miranda	1. G. Farber	1. J. Goldberg	10:50 J. Pavon
11:05 AM	2. J. Welsh	2. M. Sarntinoranont	2. M. Weinrich	2. H. Lazarus	11:00 J. Rose 11:10 J. Rosenberg
11:20 AM	3. S. Goetsch	3. K.T. Ramesh	3. G. Liu	3. R Chaudhry	11:20 R. Rotta 11:30 C. Sharma
11:35 AM	Q&A	4. W. Nowinski (2013 Awardee)	Q&A	Q&A	11:40 Q&A
11:50 AM - 12:10 PM	Lunch Break & Poster Viewing with Keynote Speaker				
12:10 PM - 12:45 PM	*Key Note* *Congressman Earl Blumenauer, Co-Chair of the Congressional Neuroscience Caucus (Room 314-317)*				
12:45 PM - 2:15 PM	38 - Genetic and Epigenetic Biomarkers for TBI (Room 302) Chair: R. Lipsky	35 - New MRI Contrasts for Brain Imaging: (Room 301) Co-Chairs: P. Basser and P. Van Zijl	36 - Advanced Materials and Neuroscience: (Room 303) Chair: J.P. Allain	37 - Brain Tissue Banks (Room 310) Chair: B. Daly	Oral Posters 2 (Room 305)
12:45 PM	1. D. Seo	1. J. Duyn	1. J. Planell	1. R. Little	12:45 A. Toma
1:00 PM	2. J. Rusiecki	2. C. Liu	2. T. Webster	2. R. Zielke	12:55 O. Toukolehto 1:05 S. Vadera
1:15 PM	3.R. Lipsky	3. E. Ozarslan	3. J.J. Pavon	3. E. Shen	1:15 J.A. Verhoog 1:25 X. Wang
1:30 PM	Q&A	4. R. Freidlin	4. Z. Chen	4. L. Li	1:35 A. Marshall
1:45 PM		5. P. Van Zijl	5. D. Fiorella	5. A. Jaffe	1:45 C. Liang 1:55 N. Naseer
2:00 PM		Q&A	Q&A	Q&A	2:05 Q&A
2:15 PM - 2:30 PM	Coffee Break & Poster Viewing				
2:30 PM - 4:15 PM	41 - Brain Mapping & Psychological Disorders and TBI (Room 302) Chair: J Grimes	40 - Neuro-Ophthalmology: Glaucoma as a model for chronic CNS disease (CME) (Room 301) Chair: R. Nickells	43 - High Definition Fiber Tracking, Mapping Brain Tracts and Brain Trauma and Surgical Procedures (Room 303) Chair: W.Schneider	47 - Pathology and Imaging in Aging and Dementia (Room 310) Co-Chairs: A. Rosen and L. Beason-Held	Oral Posters 4 (Room 305)
2:30 PM	1.J. Grimes	1.O. Sundin	1. W. Schneider	1. J. Troncoso	2:30 T. Stoica
2:45 PM	2. L. French	2. D. J. Zack	2. J. Fernadez Maranda	2. A. Faria	2:40 A. Toma
3:00 PM	3.D. F. Tate	3. J. Goldberg	3.D. Okonkwo	3. S. Resnick	2:50 J. Ciurea 3:00 E. Goncalves
3:15 PM	4.M. MacDonald	4. S. McKinnon	4.H. Hetherington	4. Thambisetty	3:10 H. Guo 3:20 J. Pavon
3:30 PM		5. L. Levin	5.J. Mountz	5. L. Beason-Held	3:30 M. Kirsch 3:40 K. Koulitchenkova
3:45 PM	Q&A	6. R. Nickells	Q&A	6. A. Rosen	3:50 C. Liang
4:00 PM		Q&A		Q&A	4:00 Q&A
4:20 PM - 4:35 PM	Coffee Break & Poster Viewing				
4:35 PM - 6:05 PM	46 - Translation and Commercialization (Room 314-317) Co-Chairs: C. Rogers, G. Cross, A. Martinez-Coll				Oral Posters 5 (Room 305)
4:35 PM	1. W. Grundfest				4:35 E. B. Tinoco
4:50 PM	2. S. Baral				4:45 M. Budde
5:05 PM	3. E. Bailey				4:55 N. Butingan
5:20 PM	4. R. Terry				5:05 Y. Chang
5:35 PM	5. B. Borson				5:15 Y. Chodakiewitz
5:50 PM	Q&A				5:25 E. Goncalves 5:35 Q&A
6:05 PM	*CLOSING COMMENTS (Room 314 - 317)*				

SCIENTIFIC PROGRAM

	Day 1 (Sunday May 12, 2013)
7:00 AM	***Opening Registration Desk***
8:00 AM - 8:10 AM	**Welcome & Introduction (Room 314-317)** **Mike Roy, 2012 SBMT President**
8:10 AM - 8:20 AM	**Welcome & Introduction (Room 314-317)** **Kuldip Sidhu, 2013 SBMT President Elect**
8:20 AM - 8:55 AM	***Key Note*** **Babak Kateb,** **Founder/Chairman/CEO of SBMT** **& President of Brain Mapping Foundation** **(Room 314-317)**
8:55 AM - 9:10 AM	Coffee Break & Poster Viewing
9:10 AM - 10:55 AM	**1 - Military Medicine: Improving Identification and Management of PTSD & TBI (CME)** **(Room 310)** **Co-Chairs: J Grimes and M. Roy**
9:10 AM	1.1 **Advances in the Early Identification and Treatment of PTSD and TBI** Michael J. Roy, Director, Division of Military Internal Medicine, Professor of Medicine Uniformed Services University
9:25 AM	1.2 **Interventions to Improve the Course of TBI** Ramon Diaz-Arrastia, Clinical Director, Center for Neuroscience and Regenerative Medicine, Professor of Neurology Uniformed Services University
9:40 AM	1.3 **The Neuropathology of TBI: Similarities and Differences vs. Neurodegenerative Disorders** Daniel Perl, Director, Neuropathology, Center for Neuroscience and Regenerative Medicine Uniformed Services University
9:55 AM	1.4 **Imaging TBI: What We Know ... and What We Don't Know** Jim Smirniotopoulos, Program Leader, Diagnostics and Imaging Center for Neuroscience and Regenerative Medicine, Professor of Radiology, Neurology, and Biomedical Informatics, Uniformed Services University of the Health Sciences
10:10 AM	1.5 **U.S. Military System of Care for TBI** Geoff Ling, Professor of Neurology, USUHS Program Manager, DARPA
10:25 AM	**Q&A**

	Day 1 (Sunday May 12, 2013)
9:10 AM - 10:55 AM	**2 - Image Guided Interventions (Room 301)** **Chair: R. P Gullapalli**
9:10 AM	2.1 **Deep Brain Stimulation: History and clinical application** Jaydev Desai, Associate Professor & Director - Robotics, Automation, and Medical Systems (RAMS) Laboratory University of Maryland, College Park, MD
9:25 AM	2.2 **Neuro-oncology Applications of MR-guided Focused Ultrasound** Graeme Woodworth, Assistant Professor, Department of Neurosurgery University of Maryland School of Medicine, Baltimore
9:40 AM	2.4 **MRI Guided Internventions** Ming Li, Chief, Bioengineering Section, Cardiothoracic Surgery Research Program National Heart, Lung, and Blood Institute, Bethesda, MD
9:55 AM	2.5 **The Survival Effect of Volumetric Extent of Resection for Eloquent Glioblastoma and the Use of Intraoperative Ojemann Stimulation, OCT, and Intraoperative MRI in Maximizing Resection Abstract** Kaisorn L. Chaichana, Neurosurgery Resident Johns Hopkins Univ. School of Medicine
10:10 AM	2.6 **A New MRI: Ultra-Low Field MRI** Robert H. Kraus, Chief Scientist, Director of Operations Samitaur Medical Technologies
10:25 AM	**2.6 A New MRI: Ultra-Low Field MRI** Robert H. Kraus, Chief Scientist, Director of Operations
10:40 AM	**Q&A**
10:55 AM - 11:10 AM	**Coffee Break & Poster Viewing**
11:10 AM - 12:20 PM	**3 - Frontiers in iPSC: Technology, Translation and Regulatory Frame work (Room 310)** **Chair: K. Sidhu**
11:10 AM	3.1 **Patient-derived Stem Cells as Model for Alzheimer's disease.** Kuldip Sidhu, Associate Professor, Stem Cell Research, University of New South Wales
11:25 AM	3.2 **Manipulating Cell Fate with mRNA** James Kehler, Application Development Scientist Stemgent
11:40 AM	3.3 **Novel Tools for Human iPSC Technolgy and Differentiation to Neural lineages** Mohan Vemuri, Director, Stem Cells Life Technologies,Inc
11:55 AM	3.4 **Banking Stem Cell Lines** Glyn Stacey, The UK Stem Cell Bank, National Institute for Biological Standards and Control, MHPRA, UK
12:10 AM	3.5 **JPL Electronic Nose: From Sniffing Brain Cancer to Trouble in Space** Margie L. Homer, Senior Engineer NASA/JPL
12:15 PM	**Q&A**

	Day 1 (Sunday May 12, 2013)
11:10 AM - 12:20 PM	**4 - Veteran Session 1: Evaluating multiple illnesses and their long-term sequelae at the WRIISCs (CME)** **(Room 301)** **Chair: D. Helmer**
11:10 AM	4.1 **A Model of Anisotropy and Diffusivity in Chronic Mild Blast-related Brain Injury** Julie Chapman, Director of Neuroscience War Related Illness and Injury Study Center (WRIISC) Veterans Affairs, Washington DC
11:25 AM	4.2 **Blast Exposure is associated with Impaired Cerebral Blood Flow Regulation in US Veterans** Jorge M. Serrador, Associate Director of Research War Related Illness and Injury Study Center (WRIISC) Veterans Affairs, New Jersey
11:40 AM	4.3 **Effect of age on fiber integrity in Veterans deployed to various combat zones** Maheen Mausoof Adamson, Clinical Assistant Professor (affiliated), Psychiatry & Behavioral Sciences, Stanford School of Medicine, Stanford CA, Acting Director of Research, Director, PhD Fellowship Program War Related Illness and Injury Study Center (WRIISC), Veterans Affairs
11:55 AM	**Q&A**
11:10 AM - 12:20 PM	**5 - Synchrotron-generated Microbeam Radiosurgery** **(Room 303)** **Chair: P. Romanelli**
11:10 AM	5.1 **Radiobiology and emerging medical applications of synchrotron radiation** Alberto Bravin, Chief of the Biomedical Beamline, European Synchrotron Radiation Facility(ESRF),Grenoble,FR
11:25 AM	5.2 **Synchrotron Radiation Microimaging** Paola Coan, Associate Professor Of Physics, University Ludwig Maxilimians,Munich,DE
11:40 AM	5.3 **Synchrotron-generated Microbeams for Cellular-scale Radiosurgery** Pantaleo Romanelli, Chief Medical Officer, AB Medica,Milan,IT; Scientific Director,Brain Radiosurgery,CDI,Milan,IT; Visiting Scientist,ESRF,Grenoble,FR
11:55 AM	5.4 **Applications of microbeam radiosurgery to the treatment of brain tumors** Elisabeth Schultke, Department of Neurosurgery,Freiburg University,DE
12:10 AM	5.5 **Microbeam radiation: an industrial point of view** Michael Wright, Senior Scientist Varian Medical Systems, Palo Alto, CA
12:15 PM	**Q&A**
12:20 PM - 1:00 PM	Lunch Break & Poster Viewing

	Day 1 (Sunday May 12, 2013)
12:20 PM - 1:00 PM	**Lunch Break & Poster Viewing**
1:00 PM - 2:30 PM	**6 - Controversies in TBI Management (CME)** **(Room 310)** **Chair: N. Vyas**
1:00 PM	6.1 **Controversies in Traumatic Brain Injury Management : Induced Hypothermia** Laith Altaweel, Associate Professor of Neuroscience Inova Fairfax Medical Campus
1:15 PM	6.2 **The use of Hypertonic Saline in TBI Management** Patricia Raksin, John H. Stroger Hospital of Cook County
1:30 PM	6.3 **Decompressive Craniectomy for TBI** Martina Stippler, Director of Neurotrauma University of New Mexico School of Medicine
1:45 PM	6.4 **Quality Improvement Initiatives in the NeuroICU** Joshua Medow, Asst Professor of Neurosurgery University of Wisconsin, Madison
2:00 PM	6.5 **Decompressive Craniotomy - Role in the Management of TBI** Howard M. Eisenberg, Professor of Neurosurgery University of Maryland School of Medicine
2:15 PM	**Q&A**
1:00 PM - 2:30 PM	**7 - Deep Brain Stimulation (CME)** **(Room 301)** **Chair: E.Shamim**
1:00 PM	7.1 **Deep Brain Stimulation: History and clinical application** Ejaz Shamim, NIH/NINDS
1:15 PM	7.2 **DBS: Using Physiology for Mapping and Targeting** Codrin Ion Lungu, Chief, National Institutes of Health Parkinson Clinic, NIH, Staff Clinician, NINDS, NIH, Clinic Director, Botulinum Toxin Clinic, NINDS, NIH
1:30 PM	7.3 **Neuronal Activity in the Human Subthalamic Nucleus Encodes Decision Conflict during Action Selection.** Kareem A. Zaghloul, Staff Clinician, Surgical Neurology Branch, National Institutes of Neurological Disorders and Stroke National Institutes of Health, Bethesda, MD
1:45 PM	7.4 - Zachary T. Levine, Director of Neurosurgery and Movement Disorders Holy Cross Hospital, Silver Spring, MD
2:00 PM	7.5 **Essential Tremor: One Disease? What Can Thalamic Microelectrode Mapping Teach Us About the Heterogeneity of ET?** Zoltan Mari, Assistant Professor of Neurology The Johns Hopkins Hospital, Department of Neurology
2:15 PM	**Q&A**

	Day 1 (Sunday May 12, 2013)
1:00 PM - 2:30 PM	**8 - NanoNeurosurgery and NanoBioElectronics (1) (CME)** **(Room 303)** **Co-Chairs: B. Kateb and K. Jain**
1:00 PM	8.1 - Miqin Zhang, Professor, Dept of Materials Science and Engineering, University of Washington, Seattle, WA, Adjunct Professor, Dept of Orthopaedics and Sports Medicine, UW School of Medicine, Adjunct Professor, Dept of Radiology, UW School of Medicine, Adjunct Professor
1:15 PM	8.2 **THE G-TECHNOLOGY, GLUTATHIONE PEGYLATED LIPOSOMES, TO SAFELY ENHANCE THE DELIVERY OF DRUGS TO THE BRAIN** Pieter Gaillard, CSO to-BBB technologies BV
1:30 PM	8.3 **Nanomaterials for Controlled Drug Delivery across Blood Brain/Retinal Barriers** Tao Lu Lowe,
1:45 PM	8.4 **Improvement of Paclitaxel's Antineoplastic Efficacy in vivo Using PEOX Polymer Nanoencapsulation** Ray Yin, ANP Technologies®, Inc.
2:00 PM	**Q&A**
1:00 PM - 4:00 PM	**1:00 PM - 4:00 PM** ***Medtronic Workshop*** ***(Room 305)*** ***Introduction to Medtronic StealthViz(tm)*** ***Advanced Visualization and Planning Software***
2:30 PM - 2:45 PM	**Coffee Break & Poster Viewing**

	Day 1 (Sunday May 12, 2013)
2:30 PM - 2:45 PM	**Coffee Break & Poster Viewing**
2:45 PM - 4:30 PM	**10 - Bio-Photonic session: Near-infrared Spectroscopy (NIRS) and Imaging for Clinical Translation (CME)** **(Room 310)** **Chair: X. Li**
2:45 PM	10.1 **Opportunities and Challenges of NIRS to study cognitive functions** Hanli Liu, Professor University of Texas, Arlington
3:00 PM	10.2 **Imaging cognitive function with near infrared spectroscopy for TBI and ASD patients** Amir H. Gandjbakhche, Senior Investigator National Institutes of Health
3:15 PM	10.3 **Shedding near-infrared light on brain networks** Andrei Medvedev, Assistant Professor Georgetown University
3:30 PM	10.4 **Applications of Near Infra Red Spectroscopy (NIRS) in Monitoring Blood Flow and Oxygen Consumption in the Brain Due to Cognitive and Physiological Stimuli** Kambiz Pourrezaei, Department of Biomedical Engineering, Drexel University Philadelphia
3:45 PM	10.5 **Optical Imaging of Spontaneous Brain Activity** Joseph Culver, Associate Professor Washington University at St. Louis
4:00 AM	10.6 **Application of NIRS and Diffuse Correlation Spectroscopy (DCS) on neonates** Maria Angela Franceschini, Assistant Professor Harvard Medical School
4:15 PM	**10.6 Application of NIRS and Diffuse Correlation Spectroscopy (DCS) on neonates** Maria Angela Franceschini, Assistant Professor Harvard Medical School
4:15 PM	**Q&A**

	Day 1 (Sunday May 12, 2013)
2:45 PM - 4:30 PM	**11 - NanoNeurosurgery and NanoBioElectronics (2) (CME)** **(Room 303)** **Co-Chairs: B. Kateb and K. Jain**
2:45 PM	11.1 **Nanoparticles-based siRNA delivery for neurodegenerative diseases** Meenakshi Malhotra, Department of Biomedical Engineering McGill University, Montreal, Canada
3:00 PM	11.2 **Nanotechnology for Neurotechnology** Nicholas A. Kotov,
3:15 PM	11.3 **Applications of nanobiotechnology to research in neurosciences** Kewal Jain,
3:30 PM	11.4 **Bio-Imaging and Cell Recognition Based on New Nano-Scaled Molecules and Nanocomposites** Xuemei Wang, State Key Lab of Bioelectronics, Chien Shiung WU Laboratory, Southeast University, People s Republic of China
3:45 PM	**Q&A**
2:45 PM - 4:30 PM	**12 - VA session 2: long-term effect of TBI and its co-occurring conditions (CME)** **(Room 301)** **Chair: M. Adamson**
2:45 PM	12.1 **Probabilistic fiber tractography aids mild TBI and PTSD diagnoses in US Veterans** Keith Main, Postdoctoral Fellow, Psychiatry & Behavioral Sciences, Stanford School of Medicine, Stanford CA, Postdoctoral Fellow, War Related Illness and Injury Study Center (WRIISC), Veterans Affairs, Palo Alto Health Care
3:00 PM	12.2 **Emerging Advanced Neuroimaging Techniques for Evaluating Traumatic Brain Injury (TBI)** Salil Soman, Palo Alto VA, CA WRIISC Fellow, Stanford Radiological Sciences Laboratory Postdoctoral Fellow, Palo Alto VA Neuroradiology Attending
3:15 PM	12.3 **Clinical Review of Neuroimaging Findings in Veterans Evaluated at the California WRIISC, including TBI Patients and First Gulf War Combatants** J. Wesson Ashford, Stanford University, VA Alzheimer's Center
3:30 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
7:00 AM - 8:00 AM	***Opening Registration Desk***
7:00 AM - 8:00 AM	***Nextim Workshop (Room 305)*** ***Pre-surgical Mapping of Eloquent Cortex with Navigated Brain Stimulation***
8:00 AM - 8:15 AM	***Welcome & Introduction (Room 314 - 317)***
8:15 AM - 8:50 AM	***Key Note*** **Howard Federoff, Dean of School of Medicine, Georgetown University School of Medicine** **(Room 314-317)**
8:50 AM - 9:25 AM	***Key Note*** **Vice Admiral Mathew Nathan** **Surgeon General of the US Navy** **(Room 314-317)**
9:25 AM - 9:40 AM	**Coffee Break & Poster Viewing**
9:40 - 11:25 AM	**13 - Neuro-Ophtalmology: Innovations in Visual Neuroscience (CME)** **(Room 302)** **Chair: V. Patel**
9:55 AM	13.2 - Amin Kassam, Department of Ophthalmology, University of Ottawa The Ottawa Hospital – Civic Campus
10:10 AM	13.3 **Intracranial Hypertension -- imaging guiding management** Vivek Patel, Associate Professor of Neuro-ophthalmology and Adult Strabismus University of Ottawa, Canada
10:25 AM	13.4 - Benjamin Burt, Assistant professor of Oculoplastic and Orbitofacial Surgery Texas Tech University
10:40 AM	**Q&A**

	Day 2 (Monday, May 13, 2013)
9:40 - 11:25 AM	**14 - Aviation and Space Medicine (Room 301)** **Chair: R. Ansari**
9:40 AM	14.1 **Noninvastive Prediction of Changes in Intracranial Pressure in Patients with Idiopathic Intracranial Hypertension** Cynthia Roberts, Professor of Ophthalmology and Biomedical Engineering Martha G. and Milton Staub Chair for Research in Ophthalmology, The Ohio State University, Columbus
9:55 AM	14.2 **Aviation Cerebral Experimental Sciences (ACES): Neuroergonomic Approach to Investigating Perceptual, Motor, and Cognitive Processes** Daniel E. Callan, Brain Networks and Communication Laboratory, Center for Information and Neural Networks (CiNet), National Institute of Information and Communication Sciences, Osaka University, Japan
10:10 AM	14.3 **From Outer Space to the Eye Clinic: Use of Dynamic Light Scattering (DLS) technology to detect and study early cataracts and neuro-degenerative changes** Manuel B. Datiles, Medical Officer and Senior Investigator, Senior Attending Ophthalmologist National Eye Institute, National Institutes of Health
10:25 AM	14.4 **Study of Vision Impairment and Intracranial Pressure in Astronauts via Choroidal Blood Flow** Rafat Ansari, Human Research Program, NASA/ GRC
10:40 AM	14.5 **Use of Near Infra Red Technology in the Area of Aviation** Kambiz Pourrezaei, Department of Biomedical Engineering, Drexel Univ. Philadelphia
10:55 AM	**Q&A**
9:40 - 11:25 AM	**15 - Future of Human Assisted Devices Impacting TBI Rehabilitation (CME) (Room 303)** **Chair: J. Leiphart**
9:40 AM	15.1 **Burden of the TBI Disease: Health Care Costs & Related Disability** Ali Ganjei, Medical Director, Inova Rehabilitation Services
9:55 AM	15.2 **Current and Emerging Treatment Strategies in the Rehab Setting** Paul Pasquina, Colonel, U.S. Army Medical Corps Chief, Dept of Orthopaedics & Rehabilitation
10:10 AM	15.3 **Brain Computer Interfaces: Results, Lessons Learned, and New Applications** Mike Boninger, Professor and Chair, Department of Physical Medicine and Rehabilitation University of Pittsburgh School of Medicine
10:25 AM	15.4 **Development of MRI Biomarkers for Improved Diagnosis of TBI** E. Mark Haacke, Director MR Research Facility of Wayne State Univ. at Harper Hospital
10:40 AM	**Q&A**

	Day 2 (Monday, May 13, 2013)
9:40 - 11:25 AM	**16 - Inflammation and Alzheimer's Disease (CME)** **(Room 310)** **Chair: M. Koronyo-Hamaoui**
9:40 AM	16.2 **ACE overexpression in monocytic cells alleviates AD-like pathology and symptoms** Maya Koronyo-Hamaoui, Assistant Professor of Neurosurgery and Biomedical Sciences Neuroimmunology and Retinal Imaging laboratory, Maxine-Dunitz Neurosurgical Institute, Cedars-Sinai Medical Center
9:55 AM	**16.3 Manipulations of Microglia During Aging and The Impact on Alzheimer's disease Pathology** Daniel C. Lee, Assistant Professor USF College of Pharmacy,USF Health Byrd Alzheimer's Institute
10:10 AM	**16.4 Age-related CD8+ T cell clonal expansions enter brain and induce amyloidopathy, neurodegeneration, and severe cognitive decline** Christopher J. Wheeler, Associate Professor, Dept. of Neurosurgery, Immunology Program Head, Maxine Dunitz Neurosurgical Inst.,Cedars-Sinai Medical Ctr
10:25 AM	**16.5 Alzheimer's Disease - In The Beginning...** Carol A. Miller, Professor, Departments of Pathology and Neurology, Co-Director of Alzheimer's Disease Research Center, Director of Neuropathology Core Chief, Neuropathology, Los Angeles County USC Medical Center Keck School of Medicine of USC, Department of Pathology
10:40 AM	**Q&A**
11:25 AM - 12:10 PM	**Lunch Break & Poster Viewing**
12:10 PM - 1:55 PM	**17 - Sports Concussion (CME)** **(Room 301)** **Co-Chairs: J. Ecklund and K. Green**
12:10 PM	**17.1 The History and Initiatives in the NFL** Thom A. Mayer, Medical Director
12:25 PM	**17.2 Neuropsychological Testing** Gerard Gioia, Director, Neuropsychology
12:40 PM	**17.3 Return to Play Guidelines** Kevin Crutchfield, Director, Comprehensive Sports Concussion Program
12:55 PM	**17.4 Clinical Presentation and Diagnosis of Chronic Traumatic Encephalopathy** Robert Stern, Professor of Neurology and Neurosurgery, Co-Founder, Center for the Study of Traumatic Encephalopathy Director,
1:10 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
12:10 PM - 1:55 PM	**18 - Pediatric Neuro-Oncology (Room 303)** **Chair: R. Packer**
12:10 PM	18.1 **MULTIFUNCTIONAL NANOPARTICLES FOR THERANOSTICS OF PEDIATRIC BRAINSTEM GLIOMAS** Rohan Fernandes, Principal Investigator Children's National Medical Center
12:25 PM	18.2 **Convection Delivery; Distribution** Russel Lonser, Senior Investigator Chief, Surgical Neurology Branch in NINDS
12:40 PM	18.3 **Spectroscopy** Katherine Warren, Head, Pediatric Neuro-Oncology Section Investigator Center for Cancer Research, National Cancer Institute
12:55 PM	18.4 **MR: Diffusion, Perfusion and Trachtography** Gilbert Vezina, Faculty, Diagnostic Imaging and Radiology Principal Investigator, Children's Research Institute (CRI), Center
1:10 PM	18.5 **Use of PET in Pediatric Brain Tumors** Pranav Vyas, Assistant Professor of Radiology and Pediatrics Director,PET/CT, George Washington University School of Medicine and Health Sciences, Children's National Medical Center
1:25 PM	18.6 **Clinical Imaging Challenges** Roger Packer, Senior Vice President, Center for Neuroscience and Behavioral Medicine
1:40 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
12:10 PM - 1:55 PM	**19 - Functional Neuroimaging (Room 310)** **Chair: J. Greenspan**
12:10 PM	19.1 **Brain Functional Connectivity in Recovery from Chronic Spinal Cord Injury** Chair: James Pekar, Associate Professor & Manager F.M. Kirby Research Center, Johns Hopkins School of Medicine
12:25 PM	19.2 **Resting-state brain activities: Mechanisms and potential clinical applications** Yihong Yang, Senior Investigator & Chief, Functional MRI Section National Institute of Drug Abuse – Intramural Research Program, Baltimore, MD
12:40 PM	19.3 **Functional and structural MRI studies of chronic pain mechanisms and treatment** David Seminowicz, Assistant Professor, Department of Neural and Pain Sciences University of Maryland School of Dentistry, Baltimore, MD
12:55 PM	19.4 **The Neuro-Protective Effects of Exercise in Older Adults at Increased for Alzheimer's Disease** Carson Smith, Assistant Professor, Department of Kinesiology School of Public Health, University of Maryland, College Park, MD
1:10 PM	19.5 **Default Mode Interference Hypothesis & its application to TBI** Chandler Sours, Department of Diagnostic Radiology & Nuclear Medicine UM, Baltimore, MD
1:25 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
12:10 PM - 1:55 PM	**20 - Autism** **(Room 302)** **Co-Chairs: C. Wheeler and P. Patterson**
12:10 PM	20.1 **Neuroglia and the Innate Neuroimmune System in Autism** Carlos Pardo, Psychiatry and Biobehavioral Sciences Johns Hopkins
12:25 PM	20.2 **Brain-Gut-Immune Connections in Autism** Paul Patterson, Principal Investigator California Institute of Technology
12:40 PM	20.3 **CD103-deficient mice exhibit a sex-dependent phenotype suggestive of autism spectrum disorder** Christopher J. Wheeler, Associate Professor, Dept. of Neurosurgery Maxine Dunitz Neurosurgical Inst,Cedars-Sinai Medical Center
12:55 PM	20.4 **A Yoga Intervention for Autism** Jane Tavyev Asher, Child Neurology/ Neurodevelopmental Disabilities, Cedars-Sinai – Depts of Pediatrics, Neurology Assistant Professor – UCLA – Depts of Pediatrics, Cedars-Sinai Medical Center
1:10 PM	20.5 **Autism: Moving to Connect Brain to Behavior** Stewart H. Mostofsky, M.D., Director, Laboratory for Neurocognitive and Imaging Research (LNIR) Kennedy Krieger Institute
1:25 PM	**Q&A**
1:55 PM - 2:10 PM	**Coffee Break & Poster Viewing**

	Day 2 (Monday, May 13, 2013)
1:55 PM - 2:10 PM	**Coffee Break & Poster Viewing**
2:10 PM - 3:45 PM	**21 - VNS use in Epilepsy, Psychiatric Disorders and Autism (CME)** **(Room 301)** **Chair: E. Tsimerinov**
2:10 PM	21.1 **VAGUS NERVE STIMULATION USE IN PATIENTS with REFRACTORY EPILEPSY and DEVELOPMENTAL DELAY and/or AUTISM** Evgeny Tsimerinov, Associate Director Clinical Neurophysiology Laboratory at Cedars-Sinai
2:25 PM	21.2 **Brain Stimulation and Epilepsy: VNS in Children with Medically Refractory Epilepsy** Jeffrey Chung, Interim Director, Epilepsy Program, Interim Director, Neurophysiology Department of Neurology, Cedars-Sinai Medical Center
2:40 PM	21.3 **Vagus Nerve Stimulation for Adults: A Summary and Update** Jennifer L. Hopp, Associate Professor, Neurology, Director, Epilepsy Monitoring Unit Department of Neurology, University of Maryland School of Medicine, Baltimore, MD
2:55 PM	21.4 **QUALITY OF LIFE IN POSTTRAUMATIC STRESS DISORDER** Waguih W. IsHak, Director of the Psychiatry Residency Training Program and Director of Medical Student Education in Psychiatry Cedars-Sinai Medical Center
3:05 PM	21.5 **Neurostimulation history and current trends** Dawn S. Eliashiv, Professor of Neurology David Geffen SOM UCLA
3:20 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
2:10 PM - 3:45 PM	**22 - BioPhotonics: Emerging Technologies for Neuroimaging (CME)** **(Room 303)** **Chair: A. Dunn**
2:10 PM	22.1 **Optical Microimaging Technology and Its Potential for Brain Function Assessment and Surgical Guidance** Xingde Li, Professor Johns Hopkins University
2:25 PM	22.2 **Intra-operative Optical Guidance for Neurosurgery** Yu Chen, Assistant Professor University of Maryland at College Park
2:40 PM	22.3 **Novel scattering anisotropy based method for tractography: a new atlas of the human brain** Cha-Min Tang, Professor University of Maryland at Baltimore
2:55 PM	22.4 **Neurovascular PhotoacousticMicroscopy** Song Hu, Assistant Professor University of Virginia
3:05 PM	22.5 **Visible Brainwide Networks at Single-neuron Resolution with Micro-Optical Sectioning Tomography** QingmingLuo, Director, Britton Chance Center for Biomedical Photonics
3:20 PM	**Q&A**
2:10 PM - 3:45 PM	**23 - EpiGenetics (CME)** **(Room 310)** **Chair: J. McDonald**
2:10 PM	23.1 **Role of Epigenetic Mechanisms in Neurologic Disease** John W. McDonald, International Center for Spinal Cord Injury Kennedy Krieger Institute
2:25 PM	23.2 **The Role of Epigenetic Mechanisms in activity-dependent neurological recovery following spinal cord injury** Visar Belegu, Research Scientist, International Center for Spinal Cord Injury, Kennedy Krieger Institute
2:40 PM	23.3 **Neuronal Activity-Induced Changes of DNA Methylation Landscape in the Adult Brain** Yijing Su, Institute for Cell Engineering, Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD
2:55 PM	23.4 **Neuronal activity modifies the DNA CpG and non- CpG methylation landscape in the adult brain** Yuan(Gary) Gao, Associate Professor, Methylomics, transcriptomics and bioinformatics big data analytics and visualization, Department of Biomedical Engineering, The Whitaker Institute at Johns Hopkins
3:05 PM	23.5 **ALS and Epigenetic Regulation of Motor Neuron Cell Death and Skeletal Muscle Mitochondria** Lee Martin, Professor, Departments of Pathology, Division of Neuropathology, and Neuroscience Johns Hopkins University
3:20 PM	23.6 **DNA Methylation and Expression of Retina-Specific Genes** Shattnath Merbs, Associate Professor of Ophthalmology & Oncology, Ophthalmic Plastic and Reconstructive Surgery, The Wilmer Eye Institute, The Johns Hopkins School of Medicine
3:35 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
2:10 PM - 3:45 PM	**24 - Multi-Modal TBI Imaging and Diffusion MRI Tractography: uses, strengths, and limitations (CME)** **(Room 302)** **Chair: M. Budde / P. Defina**
2:10 PM	24.1 **Diffusion MRI Tractography: Uses for Group Analysis** Kenichi Oishi, Assistant Professor, Department of Radiology Johns Hopkins University School of Medicine
2:25 PM	24.2 **Anatomic & Functional Connectivity Using MRI/DTI to Differentiate Minimally Conscious, Vegetative and Locked-In States** Philip A. Defina, International Brain Research Foundation, Inc.
2:40 PM	24.3 **Optical imaging and DTI of Animal Models of Brain Injury** Matthew Budde, Assistant Professor, Department of Neurosurgery Zablocki VA Medical Center, Neuroscience Research Labs, Milwaukee, WI
2:55 PM	24.4 **Sensitive detection of changes in CNS and PNS microstructure using double pulsed-field gradient MRI** Michal Komlosh, CNRM and Henry Jackson Foundation, Bethesda, MD
3:05 PM	**Q&A**
3:50 PM - 4:10 PM	**Coffee Break & Poster Viewing**
4:10 PM - 5:40 PM	**25 - Stem Cell and Brain Diseases** **(Room 301)** **Co-Chairs: R. Chaudhry and K. Sidhu**
4:10 PM	25.1 **Surgery for Recurrent GBM** Mahendra Rao, Senior Investigator, The National Institutes of Health, Bethesda, MD
4:25 PM	25.2 **Using induced pluripotent stem cells to discover new treatments for Parkinson's disease** Oliver Cooper, Director, Stem Cell Facility, Neuroregeneration Research Institute, Harvard Medical School, USA
4:40 PM	25.3 **Amyloid-Precursor Protein and the Regulation of Neurogenesis: Implications for the Treatment of Alzheimer's Disease and Traumatic Brain Injury** Craig Atwood, Research Director, Wisconsin Alzheimer's Institute and Wisconsin Comprehensive Memory Program, Associate Professor of Medicine, University of Wisconsin-Madison
4:55 PM	25.4 **Advancing Stem Cell Science Towards Therapies for Patients: CIRM's Initiatives and Funding Opportunities** Ellen Feigal, Senior Vice President, Research and Development, California Institute for Regenerative Medicine (CIRM)
5:10 PM	25.5 **Wnt signaling in neurogenesis** Vicky Yamamoto, Fellow, Department of Head and Neck, Keck School of Medicine University of Southern California
5:25 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
4:10 PM - 5:40 PM	**26 - Neuro-Immunology and Vaccine Therapy (Room 302)** **Chair: D. Irvin**
4:10 PM	26.1 **Viral encephalitis and the immune response** Diane Griffin, Professor,Alfred and Jill Sommer Professor and Chair in Molecular Microbiology and Immunology The Johns Hopkins University
4:25 PM	26.2 **Controlling the magnitude and duration of local innate immune responses with polymer carriers of Toll-like receptor 7/8 agonists** Geoffrey Lynn, National Institutes of Health, Vaccine Research Center
4:40 PM	26.3 **Adenovirus Vectors From Various Serotypes Induce Distinct Cytokine Profiles** Jeff Teigler, Graduate Student Harvard Medical School, Division of Vaccine Research, Beth Israel Deaconess Medical Center
4:55 PM	26.4 **Novel HIV Vaccine Strategies** Dan Barouch, Associate Professor of Medicine Chief, Division of Vaccine Research Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center
5:10 PM	26.6 **Paths to Stemness: Building the ultimate anti-tumor T cell for adoptive immunotherapy** David Clever, NIH Fellow National Institutes of Health
5:25 PM	**Q&A**
4:10 PM - 5:40 PM	**27 - Optical Imaging of Brain Function (CME) (Room 303)** **Chair: Y. Chen**
4:10 PM	27.1 **Optical imaging of brain functional changes in cocaine mice** Congwu Du, Department of Biomedical Engineering Stony Brook University
4:25 PM	27.2 **In Vivo Brain Optical Imaging for the Study of Normal Brain Function and Disease** Vassiliy Tsytsarev, Research Assistant Professor University of Maryland at Baltimore
4:40 PM	27.3 **Non-invasive 3D optical imaging of cerebral blood flow in vivo** Ruikang K Wang, Professor University of Washington
4:55 PM	27.4 **Optical Tools for High Resolution Imaging of Cerebral Hemodynamics** Andrew Dunn, Associate Professor University of Texas at Austin
5:10 PM	27.5 **Exposed-cortex optical mapping of brain function: From animal to man** Elizabeth Hillman, Associate Professor, Department of Biomedical Engineering and Radiology, Columbia University
5:25 PM	**Q&A**

	Day 2 (Monday, May 13, 2013)
4:10 PM - 5:40 PM	**28 - NeuroOncology (Room 310)** **Co-Chairs: S. Prabhu and C. Teo**
4:10 PM	28.1 **Surgery for Recurrent GBM** Charles Teo, Director, The Centre for Minimally Invasive Neurosurgery
4:25 PM	28.2 **Surgery for eloquent area tumors: Integration of New Imaging Modalities** Sujit Prabhu, Associate Professor, Department of Neurosurgery The University of Texas MD Anderson Cancer Center
4:40 PM	28.3 **Combining Stereotactic Radiosurgey with Anti-pd-1 Therapy to Create a Durable Immunotherapy Against GBM** Michael Lim, Associate Professor, Department of Neurosurgery Johns Hopkins University School of Medicine
4:55 PM	28.4 **From Nebulae to Neurons: Using Nanoengineered Material and Bandengineered Devices for Space Astrophysics, Planetary Studies, Brain Studies, Medicine and More** Shouleh Nikzad, Senior Research Scientist, NASA/JPL
5:10 PM	**Q&A**
4:10 PM - 5:40 PM	**29 - Multimodality imaging (1) (Room 305)** **Co-Chair: A. Filler**
4:10 PM	29.1 **Advances in Diffusion Anisotropy Imaging – New Mathematical Models** Aaron Filler, Director, Institute for Nerve Medicine Santa Monica, CA
4:25 PM	29.2 **Neuroimaging of acute stroke** Zurab Nadareishvili, Assistant Professor of Neurology, Department of Neurology, Medical Faculty Associates, George Washington University, Assistant Director, NIH Stroke Program at Suburban Hospital/Johns Hopkins Medicine, Bethesda, MD
4:40 PM	29.3 **Applications of nanoparticles in imaging carotid atherosclerosis with MRI** Andrew Degnan, Research Associate, University of Cambridge, Radiology Resident, UPMC
4:55 PM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
8:00 AM	***Opening Registration Desk***
8:15 AM - 8:30 AM	***Welcome & Introduction (Room 314 - 317)***
8:30 AM - 9:05 AM	***Key Note –*** **Captain Paul S. Hammer, MC, USN, Director of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE)** **(Room 314-317)**
9:05 AM - 10:35 AM	**30 - Image Analysis in the Era of Big Data (CME)** **(Room 301)** **Chair: E. Herskovits**
9:05 AM	30.1 **High-performance Visual Computing for Medical Imaging** Amitabh Varshney, Director, University of Maryland Institute for Advanced Computer Studies, Professor, Department of Computer Science. University of Maryland, College Park, MD
9:20 AM	30.2 **Bayesian Mining of Image Data** Edward Herskovits, Associate Professor, Department of Diagnostic Radiology & Nuclear Medicine University of Maryland School of Medicine, Baltimore, MD
9:35 AM	30.3 **-** Eliot Siegel, Chief of Imaging Services Maryland Veterans Affairs (VA) Healthcare System at Baltimore, MD
9:50 AM	30.4 **Neuroimaging biomarkers as genetic endophenotypes for neurodegenerative aging and mental disorders** Peter Kochunov, Associate Professor Maryland Psychiatric Research Center, University of Maryland Baltimore, MD
10:05 AM	30.5 **Novel Statistical Frameworks for Brain Connectivity and Network Analysis** Shuo Chen, Assistant Professor, Dept of Epidemiology & Biostatiscts University of Maryland, College Park
10:20 AM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
9:05 AM - 10:35 AM	**31 - The efficacy and mechanisms of robot-assisted therapy in neurorehabilitation (CME) (Room 310)** **Chair: L. Forrester**
9:05 AM	31.1 **The efficacy of upper extremity robot-assisted rehabilitation in hemiparetic stroke** Susan Conroy, Adjunct Instructor, Physical Therapy and Rehabilitation Science University of Maryland School of Medicine
9:20 AM	31.2 **Use of TMS to demonstrate cortical plasticity in stroke patients undergoing robot-assisted neurorehabilitation.** Shailesh Kantak, Academic Fellow, Physical Therapy and Rehabilitation Science University of Maryland School of Medicine
9:35 AM	31.3 **The efficacy of robot-assisted ankle rehabilitation in hemiparetic stroke.** Larry Forrester, Associate Professor, Physical Therapy and Rehabilitation Science and Neurology University of Maryland School of Medicine
9:50 AM	31.4 **Use of EEG coherence to study cortical changes in robot-assisted ankle neurorehabilitation in hemiparetic stroke.** Ronald Goodman, Fellow VA Maryland Exercise and Robotics Center of Excellence (MERCE)
10:05 AM	31.5 **The efficacy and mechanisms of robot-assisted gait training in hemiparetic stroke.** Anindo Roy, Assistant Professor University of Maryland School of Medicine
10:20 AM	**Q&A**
9:05 AM - 10:35 AM	**32 - Contemporary Management of Penetrating Brain Injuries (Room 302)** **Chair: J. Ecklund and K. Green**
9:05 AM	32.1 **Guidelines Update for the Management of PBI** Beverly C. Walters, Professor of Neurosurgery, VCU School of Medicine-Inova Campus Inova Health Systems
9:20 AM	32.2 **Penetrating Brain Injury In the Soviet Union** Alexander Potapov, Professor of Neurosurgery Burdenko Neurological Institute, Moscow
9:35 AM	32.3 **Unique Features of Blast Induced PBI** Panayiotis Sioutos, Neurosurgery Fellow, Department of Neurosciences, Inova Fairfax Hospital
9:50 AM	32.4 **Vascular injuries in PBI** Bizhan Aarabi, Professor of Neurosurgery University of Maryland
10:05 AM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
9:05 AM - 10:35 AM	**33 - Translational research institutes (Room 303)** **Chair: D. Ford**
9:05 AM	33.1 **Advancing Translational Research at American Academic Medical Centers** Daniel Ford, Professor of Medicine and Vice Dean for Clinical Investigation Johns Hopkins University
9:20 AM	33.2 **PET Molecular Imaging in Traumatic Brain Injury** Gwenn Smith, Professor Geriatric and Neuropsychiatry Johns Hopkins University
9:35 AM	33.3 **Mapping Human Brain with MRI** Jerry Prince, Professor of Electrical and Computer Engineering Johns Hopkins University
9:50 AM	**Q&A**
10:35 AM - 10:50 AM	**Coffee Break & Poster Viewing**
10:50 AM - 11:50 AM	**34 - Stereotactic Radiosurgery and IMRT (Room 301)** **Chair: J. Welsh**
10:50 AM	**34.1 Irradiating CNS Tumors – We've Personalized Targeting, Can We Personalize Dose?** Jason K. Rockhill, Associate Professor, Radiation Oncology, University of Washington, School of Medicine
11:05 AM	**34.2 Stereotactic radiosurgery with charged particle beams** James Welsh, NIU Institute for Neutron Therapy at Fermilab, Batavia
11:20 AM	**34.3 -** Steven J. Goetsch, Chief Physicist, San Diego Gamma Knife Center La Jolla, CA
11:35 AM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
10:50 AM - 11:50 AM	**39 - Computational Modeling using MRI Data to Enhance Diagnosis or Therapy (Room 303)** **Co-Chairs: P. Basser and M. Sarntinorinant**
10:50 AM	39.1 **Using MRI data and computational modeling for directing Tumor Treating Fields (TTF) in GBM** Pedro Cavaleiro Miranda, Faculty of Sciences, Institute of Biophysics and Biomedical Engineering, University of Lisbon
11:05 AM	39.2 **Using MRI and Transport modeling to predict efficacy of Convection Enhanced Delivery (CED) of Chemotherapeutic Agents** Malisa Sarntinoranont, Associate Professor, Mechanical & Aerospace Engineering University of Florida
11:20 AM	39.3 **A Multiscale Computational Approach to Estimating Axonal Damage under Inertial Loading of the Head.** K. T. Ramesh, Alonzo G. Decker Jr. Professor of Science & Engineering, Director, Hopkins Extreme Materials Institute (HEMI), Professor, Department of Mechanical Engineering Johns Hopkins University
11:35 AM	39.4 **Brain atlases of anatomy and vascular disorders for the SBMT** Wieslaw L. Nowinski, Principal Scientist, Lab Director, Biomedical Imaging Lab Agency for Science, Technology and Research, Singapore **Q&A**
10:50 AM - 11:50 AM	**42 - NIH Funding of Grants in Brain Imaging (Room 302)** **Co-Chairs: G. Farber and G. Liu**
10:50 AM	42.1 **NIH 101** Gregory Farber, Director Office of Technology Development and Coordination, Bethesda, MD
11:05 AM	42.2**NICHD Support for Neuroimaging Research** Michael Weinrich, Director National Center for Medical Rehabilitation Research (NCMRR)
11:20 AM	42.3 **NIBIB and Brain Imaging** Guoying Liu, Program Director Division of Applied Science and Technology
11:35 AM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
10:50 AM - 11:50 AM	**44 - Stem Cells Towards Opthalmology/ Malignancy/ Osteoarthritis (Room 310)** **Co-Chairs: R Chaudhry and K. Sidhu**
10:50 AM	44.1 **Retinal Ganglion Cell Differentiation and Transplantation** Jeff Goldberg, Bascom Palmer Eye Institute University of Miami
11:05 AM	44.2 **MESENCHYMAL STROMAL CELL THERAPY FOR MULTIPLE SCLEROSIS** Hillard Lazarus, Professor of Medicine, Case Western Reserve University Director, Novel Cell Therapy The George & Edith Richman Professor and Distinguished Scientist in Cancer Research
11:20 AM	44.3 **Stem Cell Therapies for Neural Degenerative Diseases** Rasul Chaudhry, Professor of Molecular Biology, Department of Biological Sciences, Co-Director OU-WB Institute for Stem Cell and Regenerative Medicine, Oakland University
11:35 AM	**Q&A**
11:50 AM - 12:10 PM	**Lunch Break & Poster Viewing with Keynote Speaker**
12:10 PM - 12:45 PM	***Key Note*** ***Congressman Earl Blumanauer, Co-Chair of the Congressional Neuroscience Caucus (Room 314-317)***
12:45 PM - 2:15 PM	**35 - New MRI Contrasts for Brain Imaging: (Room 301)** **Co-Chairs: P. Basser and P. Van Zijl**
12:45 PM	35.1 **SWI** Jeff Duyn, Investigator NINDS, NIH
1:00 PM	35.2 **Susceptibility Tensor Imaging** Chunlei Liu, Assistant Professor, Radiology, Medical Physics Brain Image and Analysis Center, Duke UNC
1:15 PM	35.3 **Average Propagator MRI** Evren Ozarslan, Department of Radiology Harvard University
1:30 PM	35.4 **Axon Diameter Distribution (ADD) MRI Mapping** Raisa Freidlin, CIT (Center for Information Technology), NIH
1:45 PM	35.5 **CEST/APT imaging** Peter van Zijl, Director F. M. Kirby Research Center, Kennedy Krieger Institute Research Scientist , Depart of Radiology, Johns Hopkins University School of Medicine
2:00 PM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
12:45 PM - 2:15 PM	**36 - Advanced Materials and Neuroscience: (Room 303)** **Chair: J.P. Allain**
12:45 PM	36.1 **3D Instructive Nanofibers Scaffolds Mimic Neural Progenitor Niches** Josep A. Planell, Director Institute for Bioengineering of Catalonia, Barcelona, Spain
1:00 PM 1:15 PM	36.2 **Novel Neural Devices Based on Nano Technologies: The Future Is Here** Thomas Webster, Chair & Professor Department of Chemical Engineering Northeastern University
1:30 PM	36.3 **New Nanostructured Multifunctional Surfaces of Titanium Alloys Obtained by Directed Irradiation Synthesis (DIS) for Treatments of Spinal Cord Damages** Juan Jose Pavon Palacio,
1:45 PM	36.4 **Graphene Platform for Bio-sensing and Neuro-electronic Interface Applications** Zhihong Chen, Associate Professor of Electrical and Computer Engineering Purdue University, West Lafayette, Indiana
2:00 PM	36.5 **The Treatment of Brain Aneurysms with Flow Diversion** David Fiorella, Head of Dept. of Neurosurgery Stony Brook's Cerebrovascular Ctr
12:45 PM - 2:15 PM	**37 - Brain Tissue Banks (Room 310)** **Chair: B. Daly**
12:45 PM	37.1 **The NIH Neurobiobank Initiative** Roger Little, Senior Advisor, Science Coordination, Office of Science Policy, Planning, and Communications, NIMH
1:00 PM	37.2 **Overview of the HICHD National Brain and Tissue Bank** H. Ronald Zielke, Professor, Division of Pediatric Research, Department of Pediatrics University of Maryland School of Medicine, Baltimore, MD
1:15 PM	37.3**Mapping the Human Brain Transcriptome** Elaine Shen, Scientific Program Manager Allen Institute for Brain Science
1:30 PM	37.4 **The Medical Examiners role in Facilitating the Donation of Brain Tissue for Research** Ling Li, Assistant Medical Examiner OCME, State of Maryland
1:45 PM	37.5 **Genomic measurements in post-mortem brain tissue and its relevance to development and psychiatric illness** Andrew Jaffe, Investigator, Genome Informatics Lieber Institute, Johns Hopkins, Baltimore, MD
2:00 PM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
12:45 PM - 2:15 PM	**38 - Genetic and Epigenetic Biomarkers for TBI (Room 302)** **Chair: R. Lipsky**
12:45 PM	38.1 **The Genetics of Stress** Dongju Seo, Associate Research Scientist Yale Stress Center, Yale University School of Medicine, New Haven, CT
1:00 PM	38.2 **Epigenetic Biomarkers in TBI** Jennifer Rusiecki, Associate Professor of Epidemiology
1:15 PM	38.3 **Genetic and Epigenetic Biomarkers for TBI** Robert Lipsky, Director of Neuroscience Translational Research, Inova Fairfax Medical Campus Professor of Neurosciences, Virginia Commonwealth University-Inova Campus
1:30 PM	**Q&A**
2:15 PM - 2:30 PM	**Coffee Break & Poster Viewing**
2:30 PM - 4:15 PM	**40 - Neuro-Ophthalmology: Glaucoma as a model for chronic CNS disease (CME) (Room 301)** **Chair: R. Nickells**
2:30 PM	40.1 **-** Olof H. Sundin, Department of Ophthalmology Texas Tech University
2:45 PM	40.2 **USE OF HIGH CONTENT SCREENING TO IDENTIFY NOVEL NEUROPROTECTIVE AGENTS** Donald J. Zack, Wilmer Eye Institute Johns Hopkins University School of Medicine
3:00 PM	40.3 **Optic Nerve Regeneration: Regulation by Kruppel-Like Factors** Jeff Goldberg, Bascom Palmer Eye Institute University of Miami
3:15 PM	40.4 **Similarities Between Glaucoma and Alzheimer's Disease** Stuart McKinnon, Department of Ophthalmology Duke University Eye Center
3:30 PM	40.5 **Interrupting Redox Signaling: Novel Therapies for Axonal Degenerative Disease** Leonard A. Levin, Professor and Chair of Ophthalmology McGill University Professor of Ophthalmology, University of Wisconsin, Adjunct Professor University of Montreal
3:45 PM	40.6 **Genetic control of susceptibility to optic nerve damage: a protective role for autophagy?** Robert W. Nickells, Department of Ophthalmology and Visual Sciences New Haven, CT
4:00 PM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
2:30 PM - 4:15 PM	**41 - Brain Mapping & Psychological Disorders and TBI (Room 302)** **Chair: J Grimes**
2:30 PM	41.1 **Overview and Missions of the Defense and Veterans Brain Injury Center** Jamie Grimes, COL, MC, National Director, DVBIC, OTSG Neurology Consultant
2:45 PM	41.2 **Longitudinal Studies on Traumatic Brain Injury Incurred by Members of the Armed Forces in Operation Iraqi Freedom and Operation Enduring Freedom** Louis French, Chief, TBI Services, Department of Orthopeadics and Rehabilitation Walter Reed National Medical Military Center (WRNMMC)
3:00 PM	41.3 **Multimodal MRI at Baseline, Rehab, and Recovery in mTBI: the iSCORE Project** David F. Tate, Co-Director Center for Neurological Imaging, Boston, MA
3:15 PM	41.4 **Evidence from a Clinical Rehabilitation Trial Demonstrating Neuroplastic Change Following Blast-related TBI** Margaret MacDonald, Clinical Researcher DVBIC Fort Carson
3:30 PM	**Q&A**
2:30 PM - 4:15 PM	**43 - High Definition Fiber Tracking, Mapping Brain Tracts and Brain Trauma and Surgical Procedures (Room 303)** **Chair: W.Schneider**
2:30 PM	43.1 **HDFT creating accurate personalized circuit diagrams** Walter Schneider, Professor Psychology, Neurosurgery & Radiology U. Pittsburgh PhD
2:45 PM	43.2 **HDFT in neurosurgery HDFT in neurosurgery** Juan Fernadez Maranda, Assist. Professor Neurosurgery MD, PhD Univ. Pittsburgh Med. Ctr
3:00 PM	43.3 **HDFT in TBI Seeing and Quantifying TBI** David Okonkwo, Assoc. Professor MD, PhD Univ. Pittsburgh Med. Ctr
3:15 PM	43.4 **MRSI & HDFT in TBI** HoBby Hetherington, Professor Radiology PhD Univ. Pittsburgh Med. Ctr
3:30 PM	43.5 **PET & HDFT in CTE early Alzheimer's** James Mountz, Professor Radiology MD, PhD Univ. Pittsburgh Med. Ctr
3:45 PM	**Q&A**

	Day 3 (Tuesday, May 14, 2013)
2:30 PM - 4:15 PM	**47 - Pathology and Imaging in Aging and Dementia (Room 310)** **Co-Chairs: A. Rosen and L. Beason-Held**
2:30 PM	47.1 **Asymptomatic Alzheimer's Disease: Morphological And Gene Expression Changes** Juan Troncoso, Department of Pathology, Johns Hopkins University School of Medicine
2:45 PM	47.2 **Brain Quantification by MRI in Primary Progressive Aphasia** Andreia Vaconcellos Faria, Department of Radiology, Johns Hopkins School of Medicine
3:00 PM	47.3 **Tracking Alzheimer's Neuropathology In Vivo With Imaging** Susan Resnick, Laboratory of Behavioral Neuroscience, National Institute on Aging, NIH
3:15 PM	47.4 **Plasma Biomarkers and Risk Variants in Alzheimer's Disease** Madhav Thambisetty, Laboratory of Behavioral Neuroscience, National Institute on Aging, NIH
3:30 PM	47.5 **Changes in Brain Function Are Seen Before Cognitive Impairment Begins** Lori Beason-Held, Laboratory of Behavioral Neuroscience, National Institute on Aging, NIH
3:45 PM	47.6 **Applying Imaging to Improve Treatments of Brain Disorders in Older Adults** Allyson Rosen, Assistant Professor of Psychology, VA Palo Alto Health Care System, Stanford University
4:00 PM	**Q&A**
4:20 PM - 4:35 PM	**Coffee Break & Poster Viewing**
4:35 PM - 6:05 PM	**46 - Translation and Commercialization (Room 314-317)** **Co-Chairs: C. Rogers, G. Cross, A. Martinez-Coll**
4:35 PM	**1. W. Grundfest**
4:50 PM	**2. S. Baral**
5:05 PM	**3. E. Bailey**
5:20 PM	**4. R. Terry**
5:35 PM	**5. B. Borson**
5:50 PM	**Q&A**
6:05 PM	***CLOSING COMMENTS (Room 314 - 317)***

Day 1 (Sunday, May 12, 2013)

Oral Posters 6 (Room 305)

2:45 - B. Guthikonda - Minimally Invasive Placement of Spinal Cord Stimulators with Bone Cement: An Effective Option for Refractory Pain While Minimizing the Risk of Lead Migration

2:55 - J. Xia - Invivo Diffusion Kurtosis and MR Spectroscopy Changes Following a Novel Direct Cranial Blast Injury Model

3:05- L. Reece - Cellular Studies in the Development of a Bioactive Stent Prototype to Close Aneurysm/ Pseudoaneurysm Neck Orifices

3:15 - J. Chodakiewitz- Ibu2TEG Nanoprodrug Vehicle of Paclitaxel for Glioblastoma Treatment

3:25 - Q&A

Day 3 (Tuesday, May 14, 2013)

Oral Posters 1 (Room 305)

9:05 - Andrew Worth - An ever-improving model of the structure of the living human brain

9:15 - Rohtas Yadav - Magnetic Resonance Imaging (MRI) in Tuberculosis of the Spine

9:25 - Deborah Zelinsky - Unexpected Effects of Selective Retinal Stimulation on Metabolism and Quality of Life After Brain Injury

9:35 - Jiachen Zhuo - Invivo Diffusion Kurtosis and MR Spectroscopy Changes Following a Novel Direct Cranial Blast Injury Model

9:45 - Giulio Pasinetti - Molecular Mapping of Spreading Neurodegeneration as a Novel Strategy for Treatment of Neurodegenerative Disorders

9:55 - Jessica Rose - Identification of early white matter tracts in the neonatal brain: atlas-based segmentation parameters influence DTI measurements

10:05 - Miroslaw Janowski - Stem Cell Transplantation to the Central Nervous System under the Guidance of Ultra-Fast Real-Time MR Imaging

10:15 - Monica Okon - An Electrical Analog Model of Intracranial Pressure

10:25 - Q&A

Coffee Break & Poster Viewing

Oral Posters 3 (Room 305)

10:50 - Juan Pavon - Development of a New Treatment for Penetrating Brain Injury (PBI) Aneurysms: Magnetic Bacterial Nano-Cellulose (MNBC) and Nanostructured NiTi by Directed Irradiation Synthesis (DIS)

11:00 - Jessica Rose - Brain microstructural development at near-term age in very low birth weight preterm infants: an atlas-based diffusion imaging study.

11:10 - Joseph Rosenberg - Neuropsychological Performance and DTI in the Corpus Callosum of Mild TBI Patients with and without Memory Problems

11:20 - Roger Rotta - Preoperative nTMS generated motor maps correlate well with Direct cortical stimulation â€“ initial experience with 14 patients

11:30 - Q&A

Oral Posters

Day 3 (Tuesday, May 14, 2013)

Oral Posters 2 (Room 305)

1:25 - Xuemei Wang - Target bio-molecular probes for effective biomedical imaging through the design of multifunctional gold nanostructure

1:35 - Andrew Marshall - Sex-linked difference of metabolic concentrations in hippocampus in Sprague-Dawley rats: a high resolution in vivo proton MRS study at 7 Tesla

1:45 - Chia-Pin Liang - Coherence-gated Doppler (CGD): a Fiber Sensor for Avoiding Hemorrhage in Neurosurgery

1:55 - Noman Naseer - Functional Near-Infrared Spectroscopy based Classification of Prefrontal Activity for Development of a Brain-Computer Interface

2:05 - Q&A

Coffee Break & Poster Viewing

Oral Posters 4 (Room 305)

2:30 - Teodora Stoica - Temporal changes of cerebral blood perfusion following mild Traumatic Brain Injury

2:40 - Alexander Toma - Differetiated Approach of Puncture Kypho- and Vertebroplasty in Compression Fractures of Vertebral Bodies

2:50 - Jan Ciurea - A METHOD OF ELECTRICAL STIMULATION IN PROLONGED DISTURBANCES OF CONSCIOUSNESS

3:00 - Eduardo Manuel Goncalves - HIGH FREQUENCY HEART RATE VARIABILITY EVOKED BY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION OVER THE MEDIAL PREFRONTAL CORTEX: A PRELIMINAR INVESTIGATION ON BRAIN PROCESSING OF ACUTE

3:10 - Hengchang Guo - Two-photon Fluorescence Imaging of Intracellular Reactive Oxygen Species H2O2

3:20 - Juan Pavon - Development of a New Treatment for Penetrating Brain Injury (PBI) Aneurysms: Magnetic Bacterial Nano-Cellulose (MNBC) and Nanostructured NiTi by Directed Irradiation Synthesis (DIS)

3:30 - Matthias Kirsch - Multimodal, optical, label-free spectroscopic imaging of spinal cord injury

3:40 - Ksenia Koulitchenkova - MRI study of structural changes in brain of adult Wag/Rij rats after febrile seizures at early postnatal age

3:50 - Chia-Pin Liang - Concurrent Multi-scale Imaging with Magnetic Resonance Imaging (MRI) and Optical Coherence Tomography (OCT) for Neurosurgery Guidance

4:00 - Q&A

Coffee Break & Poster Viewing

Oral Posters

Day 3 (Tuesday, May 14, 2013)

Oral Posters 5 (Room 305)

4:35 - Erika Breceda Tinoco - Behavioral and neuro-physiological effects of chronic unilateral arm amputation: a preliminary analysis

4:45 - Matthew Budde - Neurological Consequences of Primary Blast Traumatic Brain Injury in the Rat: Relating Diffusion Tensor Imaging and Behavior

4:55 - Nina Butingan - High-Sensitivity and High-Specificity of Mild Traumatic Brain Injury Diagnostic Method Using White Matter Tractography from Diffusion Tensor Imaging

5:05 - Yau-Zen Chang - Efficient Registration between CT/MRI Multi-Slices and 3D Face Data for Frameless Brain Surgery

5:15 - Yosef Chodakiewitz - Ibu2TEG Nanoprodrug Vehicle of Paclitaxel for Glioblastoma Treatment

5:25 - Eduardo Manuel Goncalves - TRANSCRANIAL ALTERNATING CURRENT STIMULATION (tACS) ENHANCEMENT OF ELECTROENCEPHALOGRAPHIC (EEG) ALPHA WAVES POWER AND ASSOCIATED HEART RATE VARIABILITY (HRV) ALTERATIONS: AN EXPLORATORY INVESTIGATION ON THE INFLUENCE OF tACS-ENHANCED ALPHA WAVES ON AUTONOMOUS NERVOUS SYSTEM IMBALANCE, AND ITS RELEVANCE IN STRESS SCIENCE

5:35 - Q&A

FACULTY

Bizhan Aarabi	- Professor of Neurosurgery University of Maryland
Maheen Mausoof Adamson	- Clinical Assistant Professor (affiliated), Psychiatry & Behavioral Sciences, Stanford School of Medicine, Stanford CA, Acting Director of Research, Director, PhD Fellowship Program War Related Illness and Injury Study Center (WRIISC), Veterans Affairs, Palo Alto Health Care System, Palo Alto, CA
Jean Paul Allain	- Associate Professor of Nuclear Engineering, Associate Professor of Materials Engineering, Affiliate Faculty of the Birck Nanotechnology Center, Director, Radiation and Surface Science and Engineering Laboratory Purdue University
Laith Altaweel	- Associate Professor of Neuroscience Inova Fairfax Medical Campus
Rafat Ansari	- Human Research Program, NASA/ GRC
J. Wesson Ashford	- Stanford University, VA Alzheimer's Center
Craig Atwood	- Research Director, Wisconsin Alzheimer's Institute and Wisconsin Comprehensive Memory Program, Associate Professor of Medicine, University of Wisconsin-Madison School of Medicine and Public Health
Dan Barouch	- Associate Professor of Medicine Chief, Division of Vaccine Research Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center

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Barry Daly	- Professor of Radiology, Vice Chair for Research, Department of Diagnostic, Radiology University of Maryland School of Medicine
Manuel B. Datiles	- Medical Officer and Senior Investigator, Senior Attending Ophthalmologist National Eye Institute, National Institutes of Health
Philip A. Defina	- International Brain Research Foundation, Inc.
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Chandler Sours	- Department of Diagnostic Radiology & Nuclear Medicine University of Maryland, Baltimore, MD
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Martina Stippler	- Director of Neurotrauma University of New Mexico School of Medicine
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Olof H. Sundin	- Department of Ophthalmology Texas Tech University
Cha-Min Tang	- Professor University of Maryland at Baltimore
David F. Tate	- Co-Director Center for Neurological Imaging, Boston, MA
Jane Tavyev Asher	- Child Neurology/ Neurodevelopmental Disabilities, Neurology Assistant Professor – UCLA – Depts of Pediatrics, Cedars-Sinai Medical Center
Jeff Teigler	- Graduate Student Harvard Medical School, Division of Vaccine Research, Beth Israel Deaconess Medical Center

Charles Teo	- *Director, Centre for Minimally Invasive Neurosurgery, Prince of Wales Private Hospital Associate Professor, University of New South Wales*
Madhav Thambisetty	- Laboratory of Behavioral Neuroscience, National Institute on Aging, NIH
Juan Troncoso	- Department of Pathology, Johns Hopkins University School of Medicine
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Evgeny Tsimerinov	- Associate Director Clinical Neurophysiology Laboratory at Cedars-Sinai
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Amitabh Varshney	- Director, University of Maryland Institute for Advanced Computer Studies, Professor, Department of Computer Science. University of Maryland, College Park, MD
Mohan Vemuri	- Director, Stem Cells Life Technologies,Inc
Gilbert Vezina	- Faculty, Diagnostic Imaging and Radiology Principal Investigator, Children's Research Institute (CRI), Center
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Xuemei Wang	- State Key Lab of Bioelectronics, Chien Shiung WU Laboratory, Southeast University, People s Republic of China
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H. Ronald Zielke	- Professor, Division of Pediatric Research, Department of Pediatrics University of Maryland School of Medicine, Baltimore, MD

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Gala Reception

AWARDS:

BEACON OF COURAGE AND DEDICATION AWARD

The Beacon Award *is presented to individuals who have demonstrated extraordinary courage and dedication for increasing awareness about neurological diseases, and for patients and their families who have exceeded expectations in fighting a neurological disorder with unprecedented courage. The Beacon Award identifies remarkable individuals who set the highest standards for increasing awareness of, and fighting, neurological diseases.*

Past Award Recipients:

2013 Beth Nielsen Chapman, Brain Tumor Survivor, Singer/Songwriter
2011 Drs. Minoru Freund, Gabrielle Giffords
2010 The Honorable Tammy Duckworth
2009 SGM Colin R. Rich and ABC News Anchor Bob Woodruff
2008 Dustin Hoffman (Two time Oscar Winner)
2007 Dr. Behnam Badie
2005 Dr. Soraya Khalilian
2004 Dr. Jennifer Neale

PIONEER IN MEDICINE AWARD

The Pioneer in Medicine Award *is presented to individuals who have significantly contributed to the scientific advancement in the fields of medicine and image guided therapy through a multidisciplinary approach. Their groundbreaking contributions have made development of state-of-the-art technology and scientific discovery a reality.*

Past Award Recipients:

2013 Drs. Maya Koronyo-Hamaoui, Yosef Koronyo, Robert H. Kraus, Jr., Margie L. Homer, Shouleh Nikzad, Rafat Ansari, Wieslaw L. Nowinski
2012 Drs. Andres Lozano, Antonio DeSalles, George Paxinos
2011 Patrick Soon Shiong
2010 Drs. Andrew Schwartz, Jonathan Wolpaw and John Donoghue
2009 Drs. Peter Black and Keith L. Black
2008 Dr. Ron Kikinis
2007 Drs. Richard Frakowiack, Arthur W. Toga and John Mazziotta
2006 Drs. Alim Louis Benabid and Warren Grundfest
2005 Drs. Ferenc Jolesz and Ken Curley
2004 Dr. Peter Gruen

Gala Reception

AWARDS:

PIONEER IN HEALTHCARE POLICY AWARD

The Pioneer in Healthcare Policy Award is presented to lawmakers who have demonstrated visionary and cross-disciplinary approaches to introducing laws that have contributed to the advancement of science, technology, education, and medicine. They have paved the way to better integration of such advancements in other fields, like medicine and neuroscience. These lawmakers champion better healthcare for all.

Past Award Recipients:

2013 US President Barak Obama, US Representatives Cathy McMorris Rodgers, Earl Blumenauer, James Moran
2012 Member of Parliament Kirsty Duncan
2010 Senator Harry Reid
2009 Senator John Kerry
2008 Governor Arnold Schwarzenegger
2007 Madam Speaker Nancy Pelosi and Senator Edward Kennedy
2005 Senator Barbara Boxer

PIONEER IN TECHNOLOGY AWARD

The Pioneer in Technology Award is presented to the trail blazing companies and their CEOs/presidents who have facilitated the development of pioneering technologies through interdisciplinary approaches that have impacted diagnostics, treatment, and healthcare delivery in unprecedented ways.

Past Award Recipients:

2013 Eric M. Bailey, President, CEO, Founder, Neurologica
Reese S. Terry Jr., Co-founder and former CEO of Cyberonics
2012 Kevin Lobo, Group President, Orthopaedics Stryker Corporation
2009 William A Hawkins, Chairman and CEO of Medtronic
2008 Mark L. Vachon, GE Healthcare
2007 Steve Rusckowski, Philips Healthcare
2006 Carl O'Connell, CEO of Carl Zeiss Inc.

Gala Reception

AWARDS:

GOLDEN AXON AWARD

The Golden Axon Award is presented to individuals outside of the medical community who inspire with good will and an enthusiastic interest in science, technology and medicine. Named for the neuron cell fiber that carries outgoing messages to other target cells, the founding principle of the Axon Award is to recognize a highly regarded individual in the public sector who helps raise awareness and funding of SBMT and its mission in the community via fundraising event (s) and activities.

Past Award Recipients:

2012 Michael Chen, Cheryl Rogers
2010 Dr. Michael Fehlings
2010 Joel Ross (CEO/Cofounder ORLive),
Peter Gailey (President/Cofounder ORLive)

HUMANITARIAN AWARD

Humanitarian Award *is given to physicians and scientists who have contributed significantly to survival and quality of life of patients across the Globe.*

Past Award Recipients:

2013 Ming Hsieh, Founder of Cogent Inc.
2012 Geoffrey Ling
2011 Drs. Henry Marsh and Rocco Armonda

YOUNG INVESTIGATOR AWARD

Past Award Recipients:

2009 Vicky Yamamoto (Stem cell Research- USC Broad Stem Cell Center)

STUDENT RESEARCH AWARD

Past Award Recipients:

2010 Joseph Yetto (USUHS)
2009 Josh Neman (UCLA student Chapter)
2007 Amir Goodarzi (UCLA student chapter)

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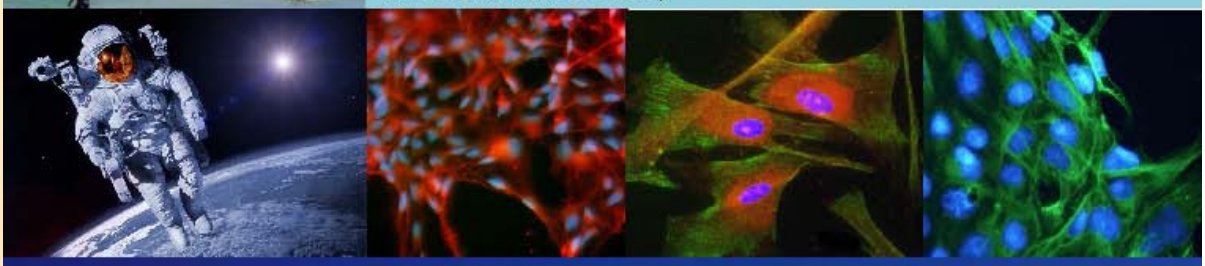

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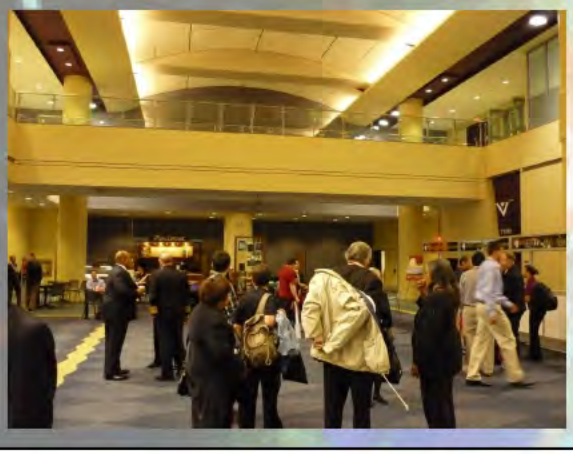
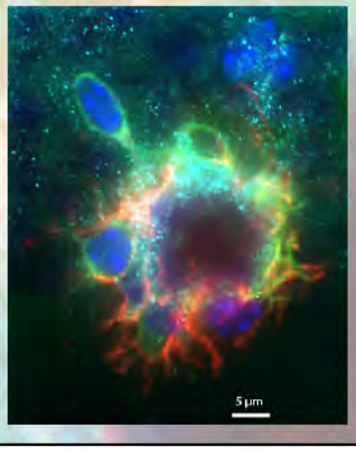
Breaking Boundaries of Science, Technology, Medicine, Art, and Healthcare Policy





Abstracts of Session Speakers

Baltimore Convention Center
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The Baltimore Convention Center

(Use the Search feature of your acrobat reader to find a specific speakers abstract)
This file contains the abstracts for those who submitted their abstracts prior to the submission deadline

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Subthreshold PTSD in Military Service Members Returning from Iraq and Afghanistan

Background: Posttraumatic stress disorder (PTSD) is a signature injury of the Iraq and Afghanistan wars. There is evidence that subthreshold PTSD is both functionally impairing and far more common than full PTSD, rendering it responsible for greater overall impairment in the community. It is therefore important to better understand and characterize subthreshold PTSD.

Methods: We enrolled 81 U.S. military service members in this prospective cohort study within 2 months after return from deployment, who did not initially meet criteria for PTSD. Each completed a comprehensive 2-day evaluation including psychophysiologic measures, functional MRI and diffusion tensor imaging. We are now completing 12 month follow-up assessments for the subsequent development of PTSD. In this report, we compare the baseline assessments for those with and without subthreshold PTSD symptoms: PTSD Checklist (PCL) score 28-49 versus PCL < 28.

Results: The 2 groups did not differ in age, gender, branch of service or alcohol use, but those with subthreshold symptoms were more likely to have experienced TBI during deployment (10% vs. 4%), and had greater symptoms of depression (PHQ-9 mean score 4.3 vs. 1.5) and anxiety (GAD-7 mean 4.3 vs. 1.6). The SF-36 assessment of functional status discerned no difference in general health, but did in social functioning (mean 94 vs. 83) and vitality (76 vs. 67). Our initial analyses identify significant differences in psychophysiologic responses to both fear acquisition and fear extinction, with subthreshold PTSD symptoms being associated with generally greater responses in heart rate, eye blink, and galvanic skin response to both danger and safety cues. In addition, we also report differences between those with and without subthreshold symptoms on functional MRI (fMRI).

Conclusions: Psychophysiologic stimuli elicit heightened responses, as well as generalization of fear conditioning, in military service members who recently returned from combat with subthreshold PTSD. FMRI also documents consistently greater efforts required to perform tasks in the face of emotional distractors in those with subthreshold symptoms. This supports the significance of subthreshold symptoms, and supports efforts to target those with subthreshold PTSD for intervention.

My Talk Title: "**Imaging TBI: What We Know ... and What We Don't Know**"
Abstract:
"**New Imaging techniques are providing an "embarrassment of riches" in revealing previously unseen lesions caused by head trauma. Microbleeds, linear hemorrhages, and dural enhancement are frequent - often with seemingly loose correlation to clinical status. Much more work is needed to understand the pathophysiology and significance of these findings.**"

JGS

Title: U.S. Military System of Care for TBI
Presenter: Geoffrey S. F. Ling, M.D., Ph.D., FAAN, FANA

Traumatic brain injury (TBI) is common and especially with military service. In Iraq and Afghanistan, explosive blast related TBI has become prominent and is mainly from improvised explosive devices (IED). Civilian standard of care clinical practice guidelines (CPG) were appropriate has been applied to the combat setting. When such CPGs do not exist or are not applicable, new practice standards for the military are created, as for TBI. Thus, CPGs for prehospital care of combat TBI CPG and mild TBI/concussion were introduced as was a DoD system-wide clinical care program, the first large scale system wide effort to address all severities of TBI in a comprehensive organized way. As TBI remains incompletely understood, substantial research is underway. For the DoD, leading this effort are The Defense and Veterans Brain Injury Center, National Intrepid Center of Excellence and the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury. This program is a beginning, a work in progress ready to leverage advances made scientifically and always with the intent of providing the best care to its military beneficiaries.

Brain tumors are among the most feared complications of cancer occurring in 20–40% of adult cancer patients. Though there have been significant advances in treatment, the prognosis for these patients is poor. Whether there is a primary malignancy or a secondary malignancy, whenever the brain of the cancer patient is involved in treatment, there is a significant impact on their overall quality of life. While the most optimal treatment currently for most brain tumors involves primary surgical resection, many patients may not be able to undergo that treatment plan due to either their poor general health or an unfavorable location (either deep inside the brain or inaccessibility of the tumor) of the lesion.

Magnetic resonance imaging (MRI) provides excellent soft tissue contrast and has become a standard imaging modality for physicians in several image-guided interventions. However, the nature of MR imaging imposes several constraints on the development of a robotic system. These challenges include actuator choice, sensor choice, material choice, size of the robot, etc., to name a few.

In this talk, we will discuss our progress on the development of MINIR: Minimally Invasive Neurosurgical Intracranial Robot, and identify the challenges in the development of this meso-scale robotic system operated under MRI guidance.

The title talk will be: "Neuro-oncology Applications of MR-guided Focused Ultrasound"

Objectives:
1. Highlight the clinical needs in neuro-oncology relevant to MRgFUS
2. Understand the pre-clinical research opportunities for MRgFUS in Neuro-oncology
3. Explore ongoing neuro-oncology research using MRgFUS
3. Discuss the potential for the MRgFUS technology in Clinical Neuro-oncology practice

MRI guided Intervention

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MRI provides excellent visualization particularly in its ability to provide high-resolution images of blood filled structures. MRI permits 3D cardiac imaging with high soft tissue contrast. Vascular as well as soft tissue visualization can easily be performed simultaneously. New generations of open, wide and short bore MR scanners and real time sequences made not only cardiovascular diagnostics but also cardiovascular intervention possible. One of the strengths of real time MRI (rtMRI) is the ability to interactively adjust image acquisition, reconstruction and display parameters during the scan. These interactive features accommodate image contrast, image plane orientations, acquisition speed, spatial resolution, temporal resolution, 3D rendering and device tracking.

A series of applications have been developed with rtMRI guidance. In the NHLBI, rtMRI was used to guide percutaneous transcatheter myocardial injections of gadolinium contrast, and to target delivery of mesenchymal stem cells labeled with micron-scale iron-oxide particles to myocardial infarct borders. MRI provides visualization of catheter navigation, myocardial function, infarct borders, and labeled cells after injection. With rtMRI guidance the transfemoral guiding catheter traversed the aorta, navigating away from the cephalic vessels and across the aortic valve, using intrinsic blood and tissue contrast. Another rtMRI guided percutaneous procedure has been investigated is stenting of aortic coarctation in an animal model. Pre-operatively, the margins of the coarctation lesion and the ostium of the subclavian artery were determined with MRI scanning and digitally marked on the 3D-rendered image. The stent-mounted balloon was introduced through the sheath over the active guidewire. The interactive acquisition of multiple planes combined with online 3D rendering provided the physician visualization of the anatomy and the device position.

Our group has investigated the use of rtMRI to guide transapical aortic valve implantation in an animal model. MRI was used to precisely identify the anatomic landmarks of the aortic annulus, coronary artery ostia, and the mitral valve leaflets. Multiple oblique planes were prescribed to delineate the anatomy of the native aortic valve and left ventricular outflow tract. Enhanced by the use of an active marker wire, this imaging allowed correct placement and orientation of the valve to avoid coronary obstruction or impingement on the mitral valve. Via a transapical approach a series of bioprosthetic aortic valves were inserted. The average implantation time was less than ninety seconds. In addition to anatomic confirmation of adequate placement of the prosthetic valve, functional confirmation of the valve and left ventricle was also obtained with MR imaging. Intraoperative perfusion scanning can be used to confirm adequacy of myocardial blood flow after valve placement. Phase contrast imaging can be used to identify intra- or para-valvular leaks. Cine imaging can be used to assess mitral valve function and myocardial function as well.

MRI provides better image quality and allows procedure planning, device tracking and direct functional assessments prior to, during, and immediately after an intervention. Real-time noninvasive imaging that can provide both anatomic details and functional assessments will enable minimally invasive beating-heart, cardiac surgery without cardiopulmonary bypass and facilitate other cardiovascular therapies.

The Survival Effect of Volumetric Extent of Resection for Eloquent Glioblastoma and the Use of Intraoperative Ojemann Stimulation, OCT, and Intraoperative MRI in Maximizing Resection Abstract

Kaisorn L. Chaichana, M.D.

Objective: There is an increasing body of evidence supporting an association between increased extent of resection (EOR) and survival for patients with glioblastoma (GB). These studies, however, are primarily comprised of patients with non-eloquent GB. The role of EOR and survival for patients with eloquent GB remains unclear since surgery for these lesions has a higher risk of neurological deficits. The goals of this study were to evaluate if there is an association between EOR and survival, and if direct brain Ojemann stimulation, optical coherence tomography (OCT), and intraoperative magnetic resonance imaging (MRI) could each enhance EOR for eloquent GB.

Methods: Adult patient who underwent surgery for an intracranial primary GB at an academic tertiary-care institution between 2007 and 2011 were retrospectively reviewed. The pre and postoperative volumes were measured in a semi-automated fashion using MRI with gadolinium obtained prior to and within 48 hours after surgery. Multivariate proportional hazards regression analysis was used to identify if an association existed survival and recurrence with volumetric EOR. Student's *t*-test was used to compare EOR between patients who underwent resection with and without brain Ojemann stimulation. OCT and intraoperative MRI evaluations are ongoing.

Results: 193 patients underwent surgery for an eloquent GB during the reviewed period [64 (33%) somatosensory cortex, 19 (10%) supplementary motor cortex, and 110 (57%) language cortex. 55 (28%) patients underwent direct brain Ojemann stimulation. The median [IQR] pre and postoperative tumor volumes were 29.2 [11.3-53.6] and 4.7 (0.4-13.9) cm^3, respectively. The mean percent resection was 70.8 ± 2.3%. In multivariate analysis, EOR was independently associated with prolonged survival [HR(95%CI); 0.406 (0.240-0.700), **p=0.001**] and delayed recurrence [HR(95%CI); 0.321 (0.168-0.634), **p=0.001**]. The minimum percent resection associated with prolonged survival and delayed recurrence was 65%. In matched-pair analysis, after matching patients for age, KPS, and preoperative tumor volume, patients who underwent resection with direct brain Ojemann stimulation had an increased EOR as compared to patients without stimulation (78.3 ± 3.4% vs. 62.4 ± 5.1%**, p=0.01)**.

Conclusions: The optimal treatment of eloquent GB requires establishing a fine balance between extensive resection and avoiding iatrogenic deficits. The present study shows that achieving an increased EOR is associated with improved survival and prolonged recurrence, where a minimum of 65% (measured volumetrically) needs to be achieved. The use of direct Ojemann brain stimulation can facilitate more extensive resection for eloquent GB without an increased risk of neurological deficit. Studies on OCT and intraoperative MRI are ongoing.

A New MRI: Ultra-Low Field MRI

R.H. Kraus, Jr., Ph.D.; Samitaur Medical Technologies

This presentation will review the development of ultra-low field (ULF) magnetic resonance imaging (MRI) at Los Alamos National Laboratory (LANL). The LANL “SQUID Team” developed ULF-MRI as an integral part of the magnetoencephalography (MEG) instrumentation for functional brain imaging. While the ULF-MRI was developed to complement and address a long-standing drawback of MEG, we found that ULF-MRI has numerous unique benefits and applications that could representgame changers for health care in the United States and around the world. The presentation will quickly review ULF-MRI development, some of its uniquedifferences from traditional MRI, and one or two novel applications.

Patient-derived Stem Cells as Model for Alzheimer's disease.

K. S. Sidhu*, H. Chung, and P.S. Sachdev***
**UNSW Medicine, Stem Cells, Centre for Healthy Brain Ageing, Sydney, Australia*
**Children Medical Research Institute, University of Sydney, Westmead, Australia

Alzheimer's disease (AD) is a neurodegenerative disorder and represents the most common form of dementia, affecting over 35.6 million people worldwide. AD is characterized by the progressive loss of specific neurons in the brain, which leads to gradual loss of bodily functions, long term memory loss and eventually death. The pathology of AD remains elusive due to the lack of appropriate animal and/or *in vitro* models, which recapitulate the human AD. The induced pluripotent stem (iPS) cells derived from patient's somatic cells and thus patient-specific and disease-specific iPS cells offer great potential in regenerative medicine, in drug discovery and modelling disease processes *in vitro*. Here we report the first generation of feeder-free iPS cells from Alzheimer's patient with an early onset of disease using a polycistronic lentiviral vector containing four pluripotent genes, Oct4, Sox2, Klf4 and cMyc. These iPS cells are pluripotent as demonstrated by both the *in vitro* and in *vivo assays* i.e. stem cell surface markers, gene expressions and teratomas formation after injecting these cells into the SCID mice. These iPS cells from patients that are predisposed to Alzheimer's disease have been analyzed by using the microarray chip and the computation of data is assisting in developing the *in vitro* models for this disease and for future regenerative medicine. Genome-wide microarray analysis revealed that AD-iPS cells are similar to control iPS cells and hESC lines, however, eight candidate genes differentially expressed between familial iPS cells and sporadic iPS cells. Some Alzheimer's specific genes and pathways were overrepresented in these cells hence *in vitro* disease modelling possible.

Company Name: Stemgent

Presenter Name: James Kehler

Talk Title: Manipulating Cell Fate with mRNA

The development of an accelerated RNA reprogramming system enables the generation induced Pluripotent Stem Cells (iPSCs) from patient samples in under two-weeks in a xeno-free system without the risk of integration. This clinically relevant technology is available to investigators as a proven system or as a custom reprogramming service for the successful generation of multiple iPSC models including neurodegenerative diseases. As an extension of this powerful platform, mRNA's for specific neural transcription factors can be used to develop faster and more efficient, defined differentiation protocols. In addition, mRNA's for a deficient protein can be precisely delivered to neuronal iPSC-derivatives to test whether the disease phenotype can be rescued or ameliorated. When combined with genome editing technologies such as TALEN's, investigators can rapidly perform gain and loss of gene function experiments in human iPSC-derivatives, ushering in a new era of functional human genetics for modeling human neurodegenerative disorders in a dish.

Novel Tools for Human iPSC Technolgy and Differentiation to Neural lineages

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Pluripotent stem cells are excellent candidates for cell replacement therapy and tissue engineering. In order to efficiently expand and differentiate pluripotent stem cells, reliable reagents that are defined, qualified, and preferably prepared from animal origin–free raw materials are desirable. The presentation will focus on: a) Novel reagents for the derivation and culture of hESC and hiPSC in different culture options b) Molecular methods for pluripotent stem cell characterization and c) Differentiation to neural lineage from pluripotent stem cells.

The combination of these reagents offers the stem cell researcher a novel cell culture platform for a serum-free and feeder-free environment that can be adapted for large scale manufacture. Together with the ability to transfer hiPSCs directly into this GMP reagents for large scale expansion, this set of tools helps move us one step closer to a GMP'able process to manufacture pluripotent stem cells in large scale and use them in a wide variety of regenerative applications

Banking Stem Cell Lines

Glyn Stacey

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The UK was established to support the permissive regulation for the derivation and use of human embryonic stem cells (hESCs) for therapeutic applications.

A number of centres have also been sponsored to derive hESC lines suitable for use in humans under the EU Tissues and Cells Directive (EUTCD) and the UKSCB as facilities to produce qualified seed stocks of these cells ready for supply to clinical trials.

The UK regulatory framework for the clinical application of human stem cell lines has now matured with the implementation of the EUTCD under a regulatory Code of Practice (Quality and Safety (human application) Regulations (2007)), overseen by the Human Tissues Authority. This is coordinated with the Human Fertilisation and Embryology Authority which licenses all uses of human embryos and gametes. This regulatory oversight is complimented by a non-statutory high level Steering Committee, which oversees the use of human stem cell lines, and has also involved the establishment of a physical resource centre or 'Bank' called the 'UK Stem Cell Bank' (www.ukstemcellbank.org.uk). The Bank produces high quality stocks of human stem cell lines, both embryonic and adult, which have been subjected to quality control and characterisation, and are traceable to fully informed consent. The Bank has clinical grade laboratories that are licensed for the provision of cells for clinical use. This presentation will outline the approaches used by the Bank to deliver cells for clinical application and the safety and efficacy issues that may need to be addressed before the use of human stem cell lines will be considered acceptable.

G Stacey , UKSCB, NIBSC/MHPRA, May 2013

A Model of Anisotropy and Diffusivity in Chronic Mild Blast-related Brain Injury

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Introduction

The global incidence of traumatic brain injury (TBI) is approximately 10 million cases annually. Among Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) veterans, incidence rates as high as 23% have been estimated, with mild TBI (mTBI) being the most common. Findings from DTI studies have bolstered objective evidence of brain abnormalities subsequent to mild TBI (mTBI), generally showing differences between those with and without brain injury. However, these results have been inconsistent with respect to tract involvement and type of anomaly, yielding no consistent marker. The heterogeneity of brain injury as well as differences in patient selection/definition, phase of recovery, level of severity, and presence and type of co-morbidities also contribute to the variability of findings.

Methods

To better understand the long-term effects of mild blast-related TBI (mbTBI), we undertook a DTI study with a design focus on internal validity. DTI metrics and psychosocial outcomes were compared between OEF/OIF veterans with mild blast-related TBI (mbTBI) (n=15) and uninjured control veterans (n=15). Cases were at least 1 year post-injury at evaluation. Measures of Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD) and Radial Diffusivity (RD) were assessed for a set of white matter tracts using DTI Studio. To convert images to MNI space, AIR was used to perform an affine trilinear alignment on all images using FA to drive the transformation. Subsequently, Large Deformation Diffeomorphic Metric Mapping was run using FA and Trace. Standard Regions of Interest (ROIs) for each participant were selected from the Johns Hopkins University (JHU) MNI template Type III White Matter Parcellation Map (WMPM).

Results

Due to a significant group difference in age (controls higher) and the known impact of age upon DTI results, ROI comparisons were calculated using Univariate ANCOVAs holding age constant. Numerous group differences in widespread tracts revealed a repeated pattern in measures of anisotropy and diffusivity. Significant FA differences emerged in 14 disparate tracts, 79% of which conformed to the pattern of lower anisotropy for cases versus controls. In all but one (97%) of the significant differences in measures of AD (7 tracts), RD (14 tracts), and MD (12 tracts), case values were higher than controls. Both the number and the distribution of these differences varied substantially from what would be expected by chance. Psychosocial variables did not account for any variance among DTI results.

Conclusions

We demonstrated a consistent pattern of diffusion metrics in our sample comparing veterans with and without mbTBI. Our design focus on internal validity likely increased the accuracy of our results. We propose a physiologic model to explain the observed pattern of data. These results support the presence of lasting structural abnormalities following mbTBI. Although this pattern must be replicated with a larger sample, refinement of a predictable model for mbTBI could assist in diagnosis and monitoring of this injury.

Keywords: Diffusion tensor imaging, blast, traumatic brain injury, anisotropy, diffusivity, veterans

Blast Exposure is associated with Impaired Cerebral Blood Flow Regulation in US Veterans

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Blast exposure is a significant problem for the current and recent military conflicts, however, data remains limited on the effects of a pressure wave on cerebral blood flow regulation. The goal of this work was to determine if veterans with a blast exposure demonstrate impaired cerebral autoregulation.

Ten veterans (males, 35.1 ± 9.3 years) participated. All ten endorsed blast exposure; seven reported a previous head injury. To assess autoregulation in both the anterior (ACA) and middle cerebral arteries (MCA) we had participants perform three sit to stand maneuvers while continuously monitoring beat-by-beat TCD and blood pressure. We also measured end tidal CO_2 via nasal cannula. Examining veterans who had reported previous head injury, we found they had lower autoregulatory index values in both the ACA (Blast: 4.4±0.6; Blast+Head Injury: 3.8±0.6) and MCA (Blast: 5.3±0.7; Blast+Head Injury: 3.8±0.7). While blood pressure decreases when standing was similar between groups (Blast: -19.9±2.5; Blast+Head Injury: -21.2±1.6 mmHg), decreases in cerebral flow velocity were significantly greater in the Blast+Head Injury group (ACA: -22.1±3.2% ; MCA: -17.9±2.7%) compared to Blast only (ACA: : -13.7±4.1% ; MCA: -11.9±4.1%).

These data indicate that veterans with blast exposure and previous head injury are more likely to show impaired cerebral autoregulation. This is consistent with our recent findings in which veterans with blast exposure and head injury demonstrated unilateral vestibular damage. However, further work is needed to confirm this initial finding. Supported by the War Related Illness & Injury Study Center, Veterans Administration and NIH grant R21DC009900 (Serrador).

Ankle robotics therapy during sub-acute hospitalization after hemiparetic stroke

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Introduction: Approximately 800,000 Americans are diagnosed with stroke each year, making it the greatest source of chronic physical disability in the U.S. There is wide agreement that functional deficits from residual hemiparesis can be partially offset through experience-dependent plasticity in the neural networks that control movement. Modern robotic devices offer a means to shape these emergent networks by engaging the affected limb(s) with high volumes of goal-directed motor practice during therapy. Thus modular lower extremity (LE) robotics may offer a valuable avenue for restoring neuromotor control in stroke survivors with hemiparetic gait. Prior results with chronic stroke suggest that intensive seated visuomotor training with an ankle robot (Anklebot) may enhance paretic ankle motor control and carry over to gait function; however this approach has not been tested in the earliest phases of rehabilitation, when natural recovery is underway. Question: What are the feasibility and efficacy of daily training with the Anklebot during early sub-acute hospitalization post-stroke?

Methods: Inpatients from a stroke rehabilitation unit were randomly assigned to either an Anklebot group or a passive stretching-mobilization group. After regular daily therapies, seated Anklebot training employed an â€œassist-as-neededâ€ approach during > 200 volitional target movements in the plantar-dorsiflexion and inversion-eversion ranges. The activity consisted of playing a videogame by attempting to move a cursor through moving gates that crossed the screen at different spatial levels, thereby stimulating volitional effort in multiple directions. Training difficulty was adjusted to each participantâ€™s active range of motion and target success rate. The stretching group received >200 daily mobilizations of the paretic ankle delivered in these same ranges of motion by the trained research team. All sessions lasted about 1 hour.

Results: As expected both groups walked overground significantly faster at discharge, however the robot group improved more in interlimb symmetry. Greater gains in paretic ankle motor control also were observed in the robot group, seen as increased peak and mean angular speeds, and increased smoothness of movement trajectories. There were no study-related adverse events.

Conclusions: Intensive LE robotic therapy is feasible for use during sub-acute phase hospitalization post-stroke without compromising usual inpatient care. Ankle robotics in this early phase may improve the rate of decreasing paretic ankle impairments, with potential to accelerate restoration of gait and complement traditional pre-gait activities. Future imaging studies with electroencephalography and/or functional near-infrared spectroscopy over the course of Anklebot therapy will help discern cortical network changes associated with motor learning and brain plasticity.

Radiobiology and emerging medical applications of synchrotron radiation

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Synchrotron radiation facilities are laboratories where the most intense and collimated X-ray beams on Earth are made available to researchers for a wide range of scientific and biomedical applications. In medicine, synchrotron X-rays are used to develop new imaging, radiation therapy and surgery techniques, using in-vitro and in-vivo models. Clinical trials on patients are also carried out when the specific characteristics of the source cannot be reproduced yet in a hospital. The European Synchrotron Radiation Facility (ESRF, Grenoble, France) is probably the leading place in the world for biomedical research with synchrotron X-rays. An experimental station fully dedicated to high resolution imaging and the development of innovative radiotherapy protocols and techniques is installed. The platforms for stereotactic radiation therapy clinical trials targeting brain tumours and the station for preclinical investigations in brain cancer therapy and radiation surgery using microbeams are accessible to the international users' community.
At the ESRF, highly intense, monochromatic and quasi parallel X-ray beams can be selected with continuity in the range 10 - 200 keV allowing performing high resolution computed tomography imaging over several scales, from the single neuron up to a human being. These beams can also be delivered stereotactically to a tumour previously loaded with a contrast agent that allows to locally enhancing the dose deposition. In microbeam radiation therapy (MRT) multienergy X-rays are spatially fractionated in arrays of microscopic beams (from 25 to 600 microns) and delivered with submillimetric precision to the central nervous system (CNS). Doses up to hundreds of Grays, delivered in a fraction of a second, can be very well tolerated by the CNS as shown in several small and large animal models. The basic concepts of the imaging and radiation therapy techniques developed and used at the ESRF will be here introduced.

Keywords:

Synchrotron radiation, X-ray imaging, radiation therapy, radiation surgery, microbeams

Educational Objectives:

1. Introducing the audience to synchrotron radiation facilities, their distribution around the world, and accessibility
2. Present the possibilities and tools offered by synchrotron radiation laboratories for developing preclinical and clinical research in neuroimaging, radiation therapy and brain radiosurgery using intense X-ray beams

3. Providing an introduction of the microbeam radiation therapy technique developed at synchrotrons and an overview of the preclinical application of microbeams in the treatment of central nervous system diseases.

Synchrotron Radiation Microimaging

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The advent of modern neuroimaging with computed tomography (CT) and magnetic resonance (MR) imaging has allowed for a better diagnosis and characterization of brain abnormalities and diseases. Despite the deep insights offered by these imaging methods, their sensitivity and/or spatial resolution are insufficient to study at the cell level the structures of this very complex tissue.

Synchrotron radiation (SR) may provide the opportunity to overcome many of the limitations affecting current diagnostic methods at hospitals. Pre-clinical imaging on the micro- and nano-scale with multidimensional resolution (spatial, temporal and chemical) is made possible by the high intensity, energy selectivity and collimation of the SR beam. The unique features of SR allow exploiting both absorption and phase information in addition to scattering techniques with X-ray energy discrimination. Over the last decade, an increasing number of works have been dedicated to the application of these high contrast and resolution SR imaging modalities in neuroimaging showing important advantages with respect to conventional imaging.

SR-CT imaging has shown unique capabilities for brain perfusion studies, as it permits to obtain quantitative measurements of contrast elements within the tissue and vasculature. High resolution images of parameters as the cerebral blood volume and the permeability coefficients can be obtained with X-ray doses compatible with in-vivo imaging.

Studies employing SR X-ray chemical nano-imaging have highlighted the role of trace elements in neurodegenerative disease like, for instance, Parkinson and Alzheimers' disease, and the pathophysiological significance of metals in brain cells.

X-ray phase sensitive imaging methods have been used for investigating excised rat and human cerebella without the application of any stain or contrast agent. Images clearly depict the hippocampus and cerebellum regions (with white and gray matter) and the substantia nigra structure. Normal and tumor tissues are also effectively discriminated. Another important

application regards the detection of core pathological features of Alzheimer's disease (AD). Proof of principle studies in phase contrast micro-CT were performed on the brains of AD-model mice, demonstrating the ability of the method in visualizing the amyloid plaques as small nodules in the cortex and hippocampus.

This presentation will give a concise introduction to the principle imaging methods used at SR facilities for neuroimaging investigations and will show how these techniques can supplement conventional imaging. A short overview of the recent results produced in pre-clinical research is offered as well as a discussion of the possible translation of the methods in the clinical practice.

Keywords:
Synchrotron radiation, high spatial resolution, high sensitive imaging

Educational Objectives:

1. Introducing the audience to synchrotron radiation based imaging as a powerful pre-clinical concept for high resolution and high sensitive investigation methods in neuroimaging at cell level.
2. Providing an overview of the main results of synchrotron radiation based neuroimaging.
3. Enable the audience to ask questions on the possibilities offered by the novel synchrotron radiation based imaging techniques.

Synchrotron-generated microbeams for cellular-scale radiosurgery

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Synchrotron-generated microplanar beams (microbeams) provide an extremely selective irradiation modality characterized by the ability to restrict the delivery of high-dose x-ray radiation to microscopic volumes . Microbeam irradiation can deliver doses in the order of hundreds to thousands Gy to tissue slices going from 25 to 600 μm,inducing irreversible tissue damage spatially restricted to the irradiated volume while the adjacent cells are not damaged. Microbeams have been used to generate microscopic cortical cuts similar to Multiple Subpial Transections(MST), a surgical technique used for the treatment of epileptic foci located over eloquent cortex. Microbeam transections replicate the ability of MST to modulate the cortex without functional injury while providing the ability to generate microscopic cortical incisions of the wanted thickness and spacing in a non invasive way .

This novel experimental approach has been used to induce sensorimotor cortex and hippocampal transections in normal and epileptic rats . Microbeam sensorimotor cortex transections generated no motor deficit in normal rats while markedly reduced convulsive seizure duration in rats with status epilepticus induced by focal injection of kainic acid . Hippocampal transections induced no evident MR and behavioral abnormalities. 7 T MR imaging revealed no sign of radio-induced edema or radionecrosis and no distortion or atrophy of the transected hippocampus .Clear-cut hippocampal transections remained stable over time, as demonstrated by long-term immunohistology . Viability of hippocampal neural progenitors was not affected.

Microbeam transections provide a novel tool to study the functions of the cortex and hippocampus and pave the way for the development of new therapeutic strategies for epilepsy and other functional brain disorders.

The potential of microbeam radiosurgery for the treatment of brain tumors.

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The concept of microbeam radiation therapy (MRT) has mainly been developed during the last two decades at the NSLS of the Brookhaven Laboratories and at the European Synchrotron Radiation Facility in France. MRT uses the high photon flux generated by synchrotron light sources to deposit high doses of X-ray energies in the tissue. Aiming for spatial fractionation of the synchrotron beam, the insertion of a specially designed collimator produces an array of quasi-parallel microbeams. Several work groups have developed irradiation protocols, with and without adjuvant therapy, which have been successfully used to significantly increase survival in small animal models of malignant brain tumors. While the successful protocols may differ in applied dose and beam geometry, there also seem to be common denominators such as the ratio between the width of and the center-to-center distance between the microbeams.

From a medical physics point of view, the foremost challenges are to understand whether the typical dose profile of MRT that has been advantageously used in small animal models can be reproduced in the significantly larger and more deeply seated human tumors and how the size differences between animal and human tumor affect dose planning.

Thus, technical challenges in the transition phase from pre-clinical to clinical applications include the development of a treatment planning system as well as the design of redundant patient safety systems.

Biomedical scientists use the present stage of methods development to focus on the understanding of various pathomechanisms that make MRT potentially such a powerful treatment concept for patients with malignant brain tumors. Morphological differences between the vascular anatomy of normal blood vessels and tumor-associated blood vessels might contribute just as importantly to the therapeutic potential of MRT as the dissimilarities between tumor and healthy tissue in the generation of radiation-induced bystander effects.

This presentation will give a short introduction to the concept of MRT and a compact overview into past and present pre-clinical experiments. The challenges in the transition phase between bench and bedside are briefly discussed

Keywords: Animal model, Malignant brain tumor, Microbeam radiation, Synchrotron, Therapy

Microbeam Radiosurgery: An Industrial Perspective

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Abstract

A number of scientific studies on small animals over the past two decades have demonstrated the astonishing fact that healthy biological tissue can tolerate an enormous amount of dose (>500 Gy) when delivered in an array of thin planes of radiation (<500 um), termed microbeam radiation. Although cells in the direct path of the microbeam radiation are killed, the adjacent non-irradiated tissues mount a healing response. Studies have also demonstrated that diseased tissue, such as cancerous tumors, can be destroyed by microbeam radiation via cross-firing from several directions. Thus, microbeam radiosurgery (MBRS) appears to have tremendous potential to control internal disease with zero toxicity to surrounding healthy tissue.

In spite of its long demonstrated potential, MBRS has yet to become a clinical tool. This presentation examines the problems associated with MBRS, and potential solutions. It is shown that a path to a clinically useful device is emerging.

Key Words: Minimally invasive therapy.

Controversies in the Management of Traumatic Brain Injury: Induced Hypothermia

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Severe traumatic brain injury (TBI) affects 10,000 Americans per year and is associated with a high rate of disability and death. The initial injury can result in contusions or diffuse injury, followed by cerebral edema over the coming days. Cerebral edema can raise intracranial pressure (ICP), causing additional brain injury. The management of ICP is a two tier approach. First tier therapies consist of supportive measures, pain control, hyperosmolar therapy, etc. If these measures fail to control ICP, remaining treatment options include surgical evacuation or decompression, barbiturate coma, and induced hypothermia(IH), or second tier therapies. Of particular interest is the use of IH.

IH involves actively cooling the core body temperature to 33-35^{o}C, which is thought to have neuroprotective benefits. IH for 12-24 hours soon after cardiac arrest has been shown to improve neurological outcomes while reducing mortality. In TBI, IH has been in use for than two decades. Several series have shown IH to effectively control refractory ICP, presumably by minimizing cerebral edema. More recent studies have focused on IT soon after TBI, or prophylactic IH(PIH), rather than when ICP becomes refractory. While initial trials of PIH were promising, three well done multicenter randomized control studies in both pediatric and adult TBI patients found no benefit with PIH sustained for 24 or 48 hours versus normothermia. In these studies, IH reduced ICP initially, which paradoxically increased with rewarming due to rebound cerebral edema, perhaps negating any early benefits of IH. Post-hoc analysis suggested that some of effects of rebound edema might be mitigated by clot evacuation, but additional studies are needed to confirm this finding. Smaller studies of lesser quality, utilizing a longer IH period with a slower rewarming rate, have shown good results with IH versus normothermia. However, longer IH likely increases complications, such as infection and bleeding. In addition, the role of IH and co-interventions with other second tier therapies has yet to be determined and complicates any future study designs.

Nonetheless, at least two RCT are ongoing to assess the benefit of longer IH versus normothermia after severe TBI. In the POLAR study, the efficacy of PIH for 3-7 days with ICP driven rewarming will be determined. On the other hand, the Eurotherm3235 study will assess the efficacy of IH for refractory ICP. As with the POLAR study, IH will be for at least 48 hours and guided by ICP levels. Thus, in spite of the negative results and shortcomings of initial studies, interest in defining the efficacy of IH in TBI continues.

The Use of Hypertonic Saline in TBI Management
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May 12, 2013

Objectives:

1. To define the role of hyperosmolar therapy in the management of TBI
2. To understand the physiologic effect of hyperosmolar therapy
3. To assess the available evidence regarding the relative clinical efficacy of mannitol and hypertonic saline

Abstract:
Uncontrolled, raised intracranial pressure (ICP) is a frequent cause of morbidity and mortality in the setting of severe traumatic brain injury (TBI). While there is little controversy regarding the appropriateness of surgical intervention when a mass lesion is present, optimal management is less clear when the pathology is global and diffuse. Hyperosmolar therapy is an integral component of medical therapy for increased ICP; yet, no class I data exist to support clinical practice.

The ideal osmotic agent would be one that creates a favorable osmotic gradient, is inert, is nontoxic, and has few side effects. The reflection coefficient describes permeability of the intact blood-brain barrier. An osmotic agent with a reflection coefficient that approaches one should be excluded by an intact blood brain barrier and, therefore, less likely to induce rebound edema. It follows that sodium has a reflection coefficient of 1. That of mannitol is slightly lower (0.9).

An intact blood brain barrier is necessary to optimize the hyperosmolar effect. Hyperosmolarity reduces ICP proportionate to the volume of remaining normal tissue in an injured brain. The peak decrease in brain volume coincides with maximal osmolarity after infusion. Sustaining this decrease requires maintaining the hyperosmolar effect. The hyperosmolar state must be maintained until the underlying mass decreases in size or another intervention occurs. Otherwise, the gradient for water transfer eventually reverses, leading to rebound increases in ICP.

The 3rd edition of *Guidelines for the Management of Severe Traumatic Brain Injury*[i] provides a level II recommendation for the use of mannitol in the management of increased ICP but stops short of making a similar recommendation for hypertonic saline, citing insufficient strength of evidence. The effect of mannitol likely is governed by multiple factors. Osmotic and rheologic mechanisms have been posited. Whether administered as a single bolus dose or as part of a repeated, "maintenance" regimen, the efficacy of mannitol ultimately is limited by a tendency to reduce perfusion, by inducing hypotension and reducing cerebral perfusion pressure.

Hypertonic saline, on the other hand, offers the opportunity for ICP reduction without volume depletion. The primary effect of hypertonic saline is likely osmotic.

Several secondary effects – rheologic, hemodynamic, vasoregulatory, neurochemical, and immunologic – have been proposed. Bolus dosing is most common. Continuous infusion has been suggested as "prophylaxis" for ICP crises.

Studies comparing the efficacy of mannitol and hypertonic saline have varied with respect to the concentration of hypertonic saline, method of administration, use of isovolume versus equimolar dosing, timing of intervention relative to injury, duration of therapy, and interpretation of what constitutes a positive response. Taken together, these studies suggest a trend toward equivalence to slight superiority of hypertonic saline for ICP reduction in the acute setting, though the benefit with respect to outcomes is less certain.

In summary, hyperosmolar therapy is an essential, though incompletely understood component of therapy for raised ICP in the setting of TBI. Future studies are needed to address optimal concentrations for dosing, method of administration, and relative clinical efficacy in a prospective, randomized fashion.

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[i] Brain Trauma Foundation. Guidelines for the Management of Severe Traumatic Brain Injury, 3rd ed. Journal of Neurotrauma, volume 24, supplement 1, 2007. (DOI: 10.1089/neu.2007.9999)

The purpose of the presentation is to focus on those areas of critical care that can lead to significant quality improvement and cost reduction. As an example, a neurocritical care ICU is reviewed with a series of multidisciplinary quality improvement initiatives and their relevance to medical practice, patient and employee satisfaction, cost, and mortality. Mortality in the most ill patients was reduced by 44% and direct hospital costs were concomitantly reduced by over $2.5 million.

THE G-TECHNOLOGY, GLUTATHIONE PEGYLATED LIPOSOMES, TO SAFELY ENHANCE THE DELIVERY OF DRUGS TO THE BRAIN

Pieter Gaillard – *to-BBB technologies BV, Leiden, the Netherlands*

Many CNS diseases remain insufficiently treated due to poor drug efficiency and/or insufficient concentrations of the drug in relevant brain tissues. While several promising drug candidates are available for various CNS disorders there is a need to increase their ability to effectively cross the blood-brain barrier (BBB) to make them useful in clinical practice. The endogenous tripeptide glutathione (GSH) is found at high levels in the brain and is actively transported across the blood-brain barrier [1]. Therefore, glutathione PEGylated liposomes (G-Technology®) were developed to mediate safe targeting and enhanced delivery of encapsulated drugs to the brain [2].

to-BBB's lead product, glutathione PEGylated liposomal doxorubicin (2B3-101), is based on PEGylated liposomal doxorubicin (Doxil®/ Caelyx®) and was developed as brain-targeted chemotherapy [3]. In preclinical studies, 2B3-101 showed a 5-fold enhanced delivery of doxorubicin to the brain compared to Doxil/Caelyx, and an improved survival of mice with experimental glioblastoma. Furthermore, the GLP toxicity studies showed no major differences between 2B3-101 and Doxil; no cardiotoxicity and neurotoxicity was observed. The ongoing clinical trial is designed to determine the safety, tolerability and pharmacokinetics of 2B3-101 in patients with solid tumors and brain metastases or recurrent malignant glioma. Currently, the dose-escalation part is almost completed, and the phase IIa part of the study to determine preliminary antitumor efficacy at the maximum tolerated dose will start soon after.

to-BBB's second product in development is glutathione PEGylated liposomal methylprednisolone (2B3-201) for the treatment of patients with acute and chronic neuroinflammation. Methylprednisolone (MP) has beneficial therapeutic properties, yet its use is limited by several (severe) acute and chronic side effects or invasive local delivery routes. Systemic administrations of 2B3-201 have recently resulted in superior efficacy and reduced side effects compared to the free MP in several rodent models with neuroinflammation [4]. 2B3-201 was subsequently investigated in a pharmacokinetic and biodistribution study and compared to free MP, showing a dramatically enhanced plasma circulation half life, and higher sustained levels of 2B3-201 in brain and spinal cord. Furthermore, therapeutic doses of 2B3-201 did not result in psychotic-like behavioral effects in rats, as were clearly demonstrated by free MP. Also, repeated weekly administrations of 2B3-201 were well tolerated in rats, while the same weekly doses of free MP were causing side effects.

The mechanistic *in vitro* and *in vivo* studies performed to date have demonstrated that glutathione PEGylated liposomes (G-Technology®) offer a promising platform that could be used to safely enhance the delivery of drugs to the brain.

References

1. Gaillard, P.J. et al. *Drug Discov. Today: Technol.* 2011, doi:10.1016/j.ddtec.2011.12.002.
2. Rip, J. et al. Presented at: *Pharmacology and Toxicology of the Blood-Brain Barrier: State of the Art, Needs for Future Research and Expected Benefits for the EU*. Brussels, Belgium. 11-12 February, 2010.
3. Gaillard, P. J. et al. Presented at*: the 103rd Annual Meeting of the American Association for Cancer Research;* Chicago, USA, Mar 31-Apr 4, 2012.
4. Gaillard P.J. et al. *J Control Release* 2012, 164: 364-369

Opportunities and Challenges of NIRS to study cognitive functions

Hanli Liu

Functional near-infrared spectroscopy (fNIRS) is a non-invasive imaging technique which can measure cerebral oxygenation changes induced by brain activations. Diffuse optical tomography (DOT), a variant of fNIRS with multi-channel measurements, has demonstrated the ability to image or map human brain activities on to a 3D standard human brain atlas. The spatial resolution and image accuracy of 3D DOT are significantly enhanced by using a voxel-based general linear model. Consequently, this emerging neuroimage tool provides researchers with unique opportunities to study human cognitive functions that may reveal particular cognitive deficits associated with specific neurological disorders. In this talk, we will report our recent development on implementing brain-atlas-based 3D DOT, followed by volume-rendered brain activation images of the prefrontal cortex (PFC) in response to several neuropsychological tests (Digit Span and Stroop test) and an established risk-decision making paradigm. The study with the latter paradigm allows us to conclude that the dorsal lateral prefrontal cortex acts differently between genders when they make risk decisions. While the results show a great promise of using 3D DOT to shed light on human cognitive functions, it is also of challenge since PFC is very complex and involves many cognitive and affective functions. It is difficult to isolate a particular cortical region when performing a given cognitive task. Also, interplay or interconnection between the PFC and other parts of the cortical areas may need to be carefully considered when we interpret the underlying meanings of the observed DOT images.

Shedding near-infrared light on brain networks

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Key words: Near-infrared spectroscopy, Brain hemodynamics, Functional connectivity, Resting state, Prefrontal cortex, Hemispheric asymmetry

Introduction. Near-infrared spectroscopy (NIRS) provides a cost effective tool for noninvasive brain imaging especially well-suited for vulnerable populations such as newborns, children and elderly patients. Recent advances in brain functional network analysis allow for new approaches to study functional architecture of the brain. Evidence is emerging that this architecture is relatively stable during various cognitive tasks as well as the resting state. Numerous fMRI studies have confirmed that resting state networks (RSN) reflect interactions in cognitively relevant functional networks. Recent studies also demonstrate that NIRS can be used to detect spontaneous hemodynamic fluctuations and assess regional connectivity through functionally relevant correlations within those fluctuations. The current state of the field of functional connectivity is briefly reviewed here and the original results are presented demonstrating that functional connectivity can be successfully studied by NIRS with the advantage of high temporal resolution, less sensitivity to motion, portability and low cost.

Methods: Hemodynamic signals were recorded at rest in 13 right-handed (RH) and 2 left-handed (LH) healthy subjects using a continuous-wave instrument (CW5, TechEn, Milford, MA) with two probes placed bilaterally over the prefrontal areas including the inferior frontal gyrus (IFG) and the middle frontal gyrus (MFG) using anatomical 10-20 landmarks. Cardiac and respiratory oscillations were removed using Independent Component Analysis and signals were passband filtered between 0.01-0.1 Hz to target slow spontaneous oscillations of the resting state networks. Correlation coefficients between all channels were calculated for changes in oxygenated (HbO) and deoxygenated (HbR) hemoglobin as well as time-frequency decomposition of signals was performed with the Morlet wavelets and power/coherence as well as Granger Causality were calculated for all pairwise channel combinations.

Results: Both coherence and correlation matrices showed qualitatively similar patterns of regional connectivity. Connectivity values were higher within each anatomical region (IFG and MFG) and between homologous areas in different hemispheres (e.g., left IFG <-> right LFG) than between those regions in the same hemisphere (e.g., left IFG <-> left MFG) thus revealing â€˜clusteringâ€™ evident in the connectivity matrices. Laterality indexes were calculated as t-values for the â€˜left > rightâ€™ comparisons of intrinsic connectivity within each regional group of channels in each subject. Regardless of handedness, the group average laterality indexes were negative thus revealing significantly higher connectivity in the right hemisphere in the majority of RH subjects and in both LH subjects. The analysis of Granger Causality between homologous areas in two hemispheres also showed a greater flow of information from the right to the left hemisphere.

Conclusions: These data further demonstrate the feasibility of using NIRS for the analysis of resting state functional networks. NIRS-based connectivity patterns correspond well to the anatomical and functional compartmentalization of the prefrontal cortex (e.g., inferior and middle frontal gyri). Furthermore, the results provide evidence on the hemispheric asymmetry of the resting state connectivity and point to an important role of the right hemisphere in the functional architecture of the resting state. These data encourage further exploration of connectivity by optical imaging and its application for the analysis of hemispheric relationships in neurological disorders.

Investigation of the Applicability of the Near Infrared Spectroscopy (NIRS) in the general area of Pain Management.

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The overall physiological, anatomical and psychological system that manages pain in human being is very complicated and to a large extent not reasonably understood. This lack of understanding has created great suffering for patients, economic costs for the society. One culprit hindering the progress toward the better understanding of this aspect of human overall defense system is the lack of objective methods to assess an individual suffering. Presently self report is the main piece of information provided to the clinician and care givers involved with treatment of individuals suffering from acute or chronic pain.

Today various methods have been used as a way of monitoring pain to provide care giver potentially a more objective assessment of the patient pain suffering. Some of these methods include laser Doppler flowmetry (LDF) , skin response , EEG and in the research environments fMRI and PET . While these methods have been very useful to increase the body of knowledge about the overall pain system. however none of these approaches have found wide spread clinical usage. In this talk I will briefly discuss the pros and cons of each of these methods.

Also several investigators have studied the use of NIRS for monitoring a subject psychological and physiological response to painful stimuli. In a recent review article by Manon Ranger et al,of McGill University (1)the authors give a thorough overview and evaluation of the various research involving NIRS in the area of pain study and make good recommendations for further development.

For the last several years we , at Drexel University, have also investigated the potential use of NIRS in a pain management clinic. In particular we have used a continuous wave (CW) NIRS to monitor a subject hemodynamic response to repeated and continuous cold painful stimuli. We have used various protocols for creating nociceptive cold stimuli in subjects with no acute or chronic pain as well as with patient suffering from chronic pains. In this talk I will briefly discuss our results. Based on these studies by us and others we are cautiously optimistic that a simple NIRS system may have a reasonable chance for use in a regular clinical settings and more sophisticated NIRS system may play a positive role in the area of pain research and identifying the so called " pain network).

Innovating in Pain Assessment of the Critically Ill: Exploring Cerebral Near-Infrared Spectroscopy as a Bedside Approach

• Manon Ranger, RN, PhD Céline Gélinas, RN, PhD
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published online 19 April 2012.

Title of talk:
Optical imaging of spontaneous brain activity

Abstract
Optical neuroimaging has never lacked clinical potential, due to its ability to longitudinally and non-invasively monitor brain function. However, progress towards the bedside practice of methods to map brain function, such as functional near infrared spectroscopy (fNIRS), has been hindered by conceptual and technical limitations. One obstacle is that task-based neuroimaging, which is standard in cognitive neuroscience research, is generally ill-suited to clinical populations since they may be unable to perform any task. Recently in functional magnetic resonance imaging (fMRI), it was discovered that even during the absence of overt tasks, fluctuations in brain activity are correlated across functionally-related cortical regions. Thus, the spatial and temporal evaluation of spontaneous neuronal activity has allowed mapping of these resting-state networks (RSNs). Translating these advances to optical techniques would enable new clinical and developmental studies. Yet, mapping spontaneous activity with fNIRS measurements presents significant challenges due to the obscuring influences of superficial signals, systemic physiology, and auto-regulation. In this talk, we will demonstrate the feasibility of functional connectivity DOT (fc-DOT). These fc-DOT methods provide a task-less approach to mapping brain function in populations that were previously difficult to research. Our advances may permit new studies of early childhood development and of unconscious patients. We also will present a new technique combining resting-state functional connectivity mapping and optical intrinsic signal (OIS) in mice. Highly detailed mapping of functional networks is achieved across most of the cerebral cortex. Synthesis of these multiple network maps through iterative parcellation and clustering provides a comprehensive map of the functional neuroarchitecture that is in agreement with histologic literature (e.g., the Paxinos atlas). In principle, fcOIS allows new paradigms linking cognitive neuroscience and mouse models where manipulations of disease, metabolism, and development are possible.

Peptide-tagged nanoparticle formulation for intranasal siRNA delivery to the brain

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Neurodegeneration is characterized by a progressive loss of neuron structure and function[1]. Current neurodegenerative disease therapeutic strategies include catheter implantation, intra-carotid infusions, surgery and chemotherapy, all of which are invasive in nature and pose a risk of post-surgical complications and fatal side-effects[2]. It has been estimated that up to 98% of newly developed small molecules cannot successfully cross the blood-brain barrier[2]. RNA interference provides a novel class of therapeutic drugs, wherein double-stranded RNA (dsRNA) triggers the catalytic degradation of the targeted gene's mRNA, effectively and selectively silencing the expression of the diseased gene[3,4]. However, the application of siRNA as a novel therapeutic has limitations with regards to stability, off-target effects and the need to cross the blood-brain barrier. Thus, a need exists for the development of a novel non-invasive and targeted therapeutic delivery system for successful siRNA delivery. Here we investigate the use of a peptide-tagged nanoparticle formulation capable of effectively delivering siRNA to the brain (cerebral cortex and cerebellum) via intranasal administration, following olfactory pathway. The study also investigates the formulation's biodistribution, toxicity and efficacy. Results indicate the delivery of siRNA, after 4 hrs of intranasal administration at an optimal dose of 0.5 mg/kg of animal weight, with minimal toxicity and biodistribution to other organs. The study shows great potential for the peptide-tagged nanoparticles carrying siRNA as a therapeutic modality for the treatment/prevention of neurodegenerative diseases.

References

1. Przedborski, S., Vila, M., & Jackson-Lewis, V. Neurodegeneration: what is it and where are we? *J.Clin. Invest.* **111,** 3-10 (2003).
2. Pardridge, W. M. Blood-brain barrier drug targeting: the future of brain drug development. *Mol Interv.* **3,** 90-105 (2003).
3. Gonzalez-Alegre, P. Therapeutic RNA interference for neurodegenerative diseases: from promise to progress. *Pharmacol Ther.* **114,** 34-55 (2007).
4. Malhotra, M., Nambiar, S., Rengaswamy, V., & Prakash, S. Small interfering ribonucleic acid design strategies for effective targeting and gene silencing. *Expert Opin Drug Discov.* **6,** 269-89 (2011).

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Abstract: SBMT session on nanobiotechnology, 12 May 2013

Title: Applications of nanobiotechnology to research in neurosciences
Presenter: K. K. Jain MD, Jain PharmaBiotech, Basel, Switzerland

This presentation is an extension of the applications of nanobiotechnology in neurology and neurosurgery presented by preceding speakers with focus on investigative aspects. It will consider wider use of nanobiotechnology beyond nanoparticles to cover nanoscale devices[1] and integration of nanobiotechnology with other biotechnologies for application in neurology and neurosurgery[2]. It will include:

- Use of nanoelectrodes for electrophysiological studies and brain mapping.
- Novel applications of nanoparticle-enhanced imaging for cerebrovascular disorders, e.g. early aneurysm detection and to guide endovascular interventions.
- Nanomotors as basis for treatment of neurodegenerative disorders.
- Role of nanotechnology in approaches to regeneration/repair of the CNS.
- Nanobiotechnology as adjunct to cell therapy of CNS disorders.
- Role of nanobiotechnology for the development of personalized neurology.
- Future prospects of nanoneurology and nanoneurosurgery including use of nanorobotics and nanolasers.

References:
1. Jain KK Handbook of Nanomedicine, 2nd ed, Springer, 2012.
2. Jain KK. Applications of Biotechnology in Neurology, Springer, 2013.

Probabilistic fiber tractography aids mild TBI and PTSD diagnoses in US Veterans

Keith Main[1,2], Sally Pierce[1,3], Salil Soman[1,2], Wes Ashford[1,2], Maheen Adamson[1,2]

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INTRODUCTION: Traumatic Brain Injury (TBI) affects almost 1.6 million people in the United States each year (Rutland-Brown, et al., 2006 & Selassie et al., 2008). Nearly two-thirds of injured US soldiers sent from Iraq to Walter Reed Army Medical Center were diagnosed with TBI (Warden, 2006). Many of these servicemen and women are also diagnosed with posttraumatic stress disorder (PTSD). The co-occurrence of mild (mTBI) and PTSD is of great scientific interest given the number OEF/OIF veterans returning to civilian life. Sustained efforts in this domain will likely reveal neurological similarities and differences that contribute to an understanding of their comorbidity. The following case study investigated the co-occurrence of TBI and PTSD in a veteran seen at The War Related Illness and Injury Study Center (WRIISC) at the VA Palo Alto Health Care System. The goal was to leverage new neuroimaging analysis techniques to better diagnose brain states associated with the patient's behavioral and cognitive sequelae. We believe the current case study presents a model of "bench to bedside" implementation.

METHODS: WJ is a middle aged, Asian, married, veteran male with 12 years of education who came to the WRIISC with a history of significant head trauma, complaints of chronic back and knee pain, a diagnosis of PTSD, and cognitive complaints. During his military service in the Navy he reported that he hit his head on a metal valve while fighting a fire on-ship. He experienced post-concussive symptoms but no loss of consciousness. He also reported traumatic experiences in the Navy involving death and sexual assault.

JW was scanned in a 3T GE MRI (high-resolution T1 Anatomical scan and a 30 direction DTI sequence) and completed a battery of neuropsychological tests focusing on PTSD, TBI and memory. DTI data were analyzed with custom software for the creation of tensor maps and white matter tractography providing fractional anisotropy (FA) values, mean diffusivity (MD) and fiber tracking.

RESULTS: There was a significant difference between the left superior longitudinal fasciculus in WJ compared to a control group , $t = -3.9$, $p = 0.005$. FA values for the SLF were lower for WJ indicating the fiber tract is compromised. In contrast, there was no difference between WJ and the Controls for the right superior longitudinal fasciculus, $t = 1.7$, $p = .07$. FA values were not significantly different for the right SLF.

CONCLUSIONS: The executive functioning deficits and emotional dysregulation WJ exhibits are consistent with a diagnosis of PTSD. Diffusion Tensor Imaging (DTI) demonstrated abnormal frontal fiber tracts in the left superior longitudinal fasciculus, which has been implicated in emotional dysregulation. Therefore, it is suggested that WJ's presentation may be related to frontal lobe injury in addition to his PTSD. As the symptoms of PTSD and TBI can be very similar and difficult to disentangle, our case presents potential neuroimaging and neurocognitive testing approaches that may aid in the diagnosis and management of patients with both conditions.

While a large proportion of TBI patients have negative traditional neuroimaging, growing recognition of potentially subtle injuries like Diffuse Axonal Injury (DAI) secondary to TBI has spurred the development of alternative neuroimaging methods for evaluating the sequelae of TBI. This session will review emerging advanced neuroimaging techniques for the evaluation of traumatic brain injury.

Clinical Review of Neuroimaging Findings in Veterans Evaluated at the California WRIISC, including TBI Patients and First Gulf War Combatants

J. Wesson Ashford, M.D., Ph.D., War Related Illness and Injury Study Center, VA Palo Alto Health Care System, and Department of Psychiatry & Behavioral Sciences, Stanford University School of Medicine

The WRIISC (War Related Illness and Injury Study Center) programs, based at the Washington, DC VA, the East Orange, NJ VA, and the Palo Alto, CA VA, see predominantly Veterans who have been deployed to combat situations. About half of the Veterans who come to the California WRIISC program have had traumatic brain injuries (TBIs), some in combat and others in many diverse situations. Another half of the Veterans served in the First Gulf War (GWI). Those Veterans with a history of TBI usually have some obvious or subtle pathology on 3T-MRI brain scans. The most common findings are white matter changes that are not in regions typically seen with vascular dementia: the lesions are more lateral and frequently near a gray-white matter boundary. On DTI analyses, disruption of fiber passages can be seen. The abnormalities are frequently associated with specific and probably related neuro-cognitive or behavioral changes. Similar changes are frequently seen in Veterans of GWI. Radiologists usually say little of ventricular asymmetry, but the asymmetry seen in Veterans with TBI is usually consistent with the pattern of neuropsychological deficits. Mild diffuse atrophy in Veterans below 50 years of age is more suggestive of late sequelae of TBI or another insult rather than age-related neurodegeneration. Many of the Veterans with a history of TBI have chronic headache. While no specific pathological processes explaining the headaches have been found, many of these individuals have larger than expected pineal glands, which could cause intermittent increases of intraventricular pressure.

Future concerns: There are 5 areas for further development: 1) The WRIISC programs have not been assessing APOE genotype, but there is concern about the role of the epsilon4 allele in predisposing to cognitive and behavioral impairment and chronic traumatic encephalopathy. In fact, there should be higher level DOD consideration for APOE genotyping of individuals before deployment for avoidance of exposure to blasts in individuals with an APOE-epsilon4 gene. 2) Better assessment of brain tracks may clarify more specific pathways that are disrupted by TBI. Further, examination of the brain stem, which mediates many of the functions commonly found to be disordered, chronic fatigue, chronic pain, PTSD, depression, may help further understand the problems faced by individuals who have had TBI. 3) Careful measurement, quantitation of brain structures, including hippocampus and pineal, may help to understand chronic memory deficits and headaches, as well as other disorders. 4) Assessment of perfusion, usually using SPECT in the past, but arterial spin labeling (ASL) in the future, could provide better information of brain tissue integrity. 5) Neuropsychological and behavioral measures need to be integrated with brain image information. Computerized cognitive assessment should provide a better and better indication of brain pathology.

Noninvasive Prediction of Changes in Intracranial Pressure in Patients with Idiopathic Intracranial Hypertension

Presenter: Professor Cynthia J. Roberts, PhD[1,2]

Co-Authors: Monica Okon[1], Keerthana Bolisetty[3], Robert H. Small, MD[1,4], and Steven E Katz, MD[2]

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Introduction

Ocular Pulse Amplitude (OPA) has been reported to be affected by ocular blood flow and ocular rigidity.[1] An electrical analog model was previously constructed and validated to predict OPA based on measured blood pressure and heart rate,[2] as well as to predict changes in OPA based on change in subject position between sitting, supine and Trendelenburg with head-down tilt.[3] The purpose of the current study was to test the hypothesis that elevated intracranial pressure (ICP) is also reflected in the OPA signal.

Method

A total of 10 right eyes of 10 subjects with signs and symptoms of Idiopathic Intracranial Hypertension (IIH) based on the modified Dandy criteria[4] were prospectively enrolled. In addition to the standard work-up for IIH, PASCAL Dynamic Contour Tonometry (DCT) was performed to measure intraocular pressure (IOP) and OPA. Systemic blood pressure was also acquired and pulse pressure (PP) was calculated as the difference between systolic and diastolic pressure. Treatment consisted of shunt placement or medication, followed by a second DCT measurement an average of 107 days after treatment. In a separate set of subjects (n=7), ocular pulse pressure waveforms were obtained in the supine position immediately before and after the lumbar puncture (LP). Both opening pressure (OP) and closing pressure (CP) were recorded, as well as volume of cerebrospinal fluid (CSF) removed, blood pressure and heart rate. For all 17 subjects, IOP, OPA, IOP/OPA, and PP were compared before and after treatment, or before and after LP, with a student t-test. Linear regression was performed between ΔICP and ΔIOP/OPA in the subjects with both OP and CP after LP. An electrical analog model was used to predict the change in ICP after LP in one subject.

Results

A significant change ($p=0.05$) in IOP/OPA was found after treatment for IIH, with no change in PP. A significant relationship between ΔICP and ΔIOP/OPA ($r^2= 0.7588$; $p= 0.0107$) was found after LP. The electrical analog model successfully predicted the change in ICP after LP.

Conclusions

Changes in ICP are related to changes in OPA. It is hypothesized that integrating a model of CSF pressure with the previous validated model of OPA may allow prediction of changes in ICP based on changes in measured OPA, with the input of measured subject data included blood pressure. This would allow noninvasive monitoring of changes in ICP.

1. Perkins, E. S., The Ocular Pulse. *Current Eye Research*, 1981. 1(1): 19-23.
2. Karol HJ, Roberts CJ, Small RH. "Electrical Analog Model of Ocular Pulse Amplitude as a Function of Systemic Pulse Pressure and Ocular Rigidity." ARVO 2007; 4946.

3. Roberts, CJ, Mahmoud AM, Small RH. The response of Ocular Pulse Amplitude (OPA) to an Increase in Intraocular Pressure (IOP) Generated by Changing Subject Position in order to Investigate Ocular Blood Flow and Validate a Novel Electrical Analog Model. ARVO 2010: 565.
4. Digre KB, Corbett JJ (2001). "Idiopathic intracranial hypertension (pseudotumor cerebri): A reappraisal". *Neurologist* **7**: 2–67.

Abstract

Aviation Cerebral Experimental Sciences (ACES) Neuroergonomic Approach to Investigating Perceptual, Motor, and Cognitive Processes

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The goal of aviation cerebral experimental sciences (ACES) is to investigate neural processes underlying various perceptual, motor, and cognitive tasks utilizing very rich ecologically valid conditions such that what we learn about the brain in the laboratory can be directly applied to real-world situations (Neuroergonomics). It is likely that in order to investigate complex real world behavior it is necessary to understand the processes within the context of the underlying interacting brain networks rather than under reduced isolated conditions that only occur in the laboratory. Utilizing multiple brain imaging methods the objective is to determine neural correlates of perceptual and motor processing as well as cognitive/mental states including alertness, fatigue, workload, and anxiety that are difficult to quantify behaviorally. By understanding the underlying neural processes in the context of complex real-world tasks such as flight operations, machine-learning decoding techniques can be used to control adaptive automation and give feedback to modulate brain activity and behavior to facilitate learning, situational awareness, and decision making to enhance performance, safety, and efficiency.

In several studies I have demonstrated that it is possible to use robust interactive visual presentation and manipulation of multiple controls to investigate perceptual motor and cognitive processes under real-world conditions. For example, in an fMRI study using a glider-landing task, performance is related to increased activity in brain regions involved with action planning. Relevant to issues involving resting state networks, a decrease in spontaneous activity in action planning regions starting 25 seconds prior to initiation of the task predicts future landing performance. In another piloting task study, adaptive automation, based on an MEG brain-machine-interface, is utilized to recover from an unpredicted perturbation in flight attitude faster than can be initiated by hand. In moving toward application in real-world situations I have developed a vehicle simulator that provides an engaging interactive environment by presentation of multimodal stimuli (6 Degrees-of-Freedom motion platform, full field dome projection, force-feedback), allows for recording of simultaneous control responses, and is integrated with a real-time EEG brain-machine-interface system. While one application of this system is in flight simulation, another application is for controlling unmanned aerial vehicles UAVs utilizing immersive environmental feedback by projecting the onboard video to the full-field dome and the accelerations to the motion platform. This form of embodied remote vehicle operation will allow for development of neuroergonomic technology to optimize performance by utilizing multiple sources of information from sensory stimulation, motor responses, and decoded brain activity. The Cognionics dry-wireless EEG system has been used to test the feasibility of recording brain activity in extreme environments. Independent component analysis could extract clear auditory evoked potentials (AEP experiment) and brain activity during various flight maneuvers within an open cockpit biplane in the presence of extensive physiological and environmental artifacts. The proposed research has far reaching implications for advancement in knowledge of brain processes involved with complex real world tasks as well as development of neuroergonomic technology that can be used in a wide variety of applications such as vehicle/machine operation, medical/psychological diagnosis, and rehabilitation/treatment.

Abstract for SBMT- Datiles et al May 13 11 am Session in Space and Aviation (Ansari R, Moderator-Chair)

Title: From Outer Space to the Eye Clinic: Use of Dynamic Light Scattering (DLS) technology to detect and study early cataracts and neuro-degenerative changes

Authors: Datiles MB [1], Ansari RR[2], King JF[2], Zigler JS[3], Ferris F[1], Stark WJ[3]. [1]National Eye Institute, National Institutes of Health, Bethesda, MD,[2] John Glenn Research Institute, NASA, Cleveland, OH, [3]Wilmer Eye Institute, Johns Hopkins University Hospital, Baltimore, MD.

In a NASA-NIH Collaborative Study, we modified a Dynamic or Quasi-elastic Light Scattering (DLS) device being used by one of the authors in the NASA Flight Station in outer space for crystallization experiments, into an ophthalmologic tool to study the ocular lens in vivo in the Eye Clinic at NIH. The DLS probe was mounted inside a Keratron corneal mapping device which had a 3 dimensional aiming system, to allow us to measure the crystallin proteins of the ocular lens in normal clear lenses as well as in cataracts (cloudy lenses) reliably and repeatedly.

With the clinical DLS device, we successfully identified and measured the alpha crystallin lens protein species, which has recently been discovered to have molecular chaperone properties. This gives alpha crystallins the ability to prevent cataracts by protecting the other lens proteins from sticking together, aggregating and forming larger protein complexes which scatter light, leading to age related nuclear cataracts. Therefore, alpha crystallins are the built in anti cataract proteins in the lens, and once a person's supply of the protein is used up, protein aggregation and cataract can then proceed in an uncontrolled manner.

We then conducted at NIH a large cross sectional study of 380 normal and cataractous lenses from patients aged 7 to 86 years and showed that the DLS detected and measured the loss of the anti cataract lens protein alpha crystallins as cataracts formed. Hence the DLS will allow eye physicians to detect the earliest lens changes leading to cataract formation in patients safely and non-invasively. The physicians can then give patients advance warning to change their lifestyle as well as take anti oxidants to prevent further lens deterioration and formation of blinding age related cataracts.

We are currently undertaking a longitudinal study at Johns Hopkins on 66 eyes on patients aged 34 to 79 years being followed for cataract formation every 6 months. Analysis of data at 18 months showed that the DLS detected significant loss of alpha crystallins as a cataract formed and progressed, versus slower loss of alpha crystallins in lenses that had only aging lens changes. This shows the usefulness of the DLS device in monitoring the loss of alpha crystallins which then lead to cataract formation and progression. It also shows its potential usefulness as a monitoring device in the future testing of anti cataract drugs that are being developed in various laboratories, and also in helping determine the role of various risk factors in causing cataracts.

These studies also serve to open the role of alpha crystallins as biomarkers for tracking the effects of oxidative damage to proteins which occur in aging as well as in neuro-degenerative disorders such as Alzheimer's disease and Parkinson's disease.

This series of studies shows how scientific studies can be successfully undertaken when 2 government agencies collaborate and use specialized talents in their respective agencies, and that public-private collaborations can then further propel development of projects to benefit the american public.

Study of Vision Impairment and Intracranial Pressure in Astronauts via Choroidal Blood Flow

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ABSTRACT

An experimental study of choroidal microcirculation on 25 volunteer subjects while flying parabolic trajectories is reported. A compact head-mounted non-invasive laser Doppler flowmetry apparatus was used to evaluate if the ocular blood flow is altered at “zero” gravity (0G). The red blood cell speed, choroidal blood volume, and choroidal blood flow increased during “zero” gravity periods. The results point in the direction of the hypothesis that the choroidal engorgement may play a role in changing vision in astronauts due to increased intracranial pressure in space flight.

To be presented at the 10th SBMT Annual Congress, May 13th, 2013, Baltimore, MD

Use of Near Infra Red Technology in the Area of Aviation

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In the last decade by support from ONR, DARPA and FAAA we, at Drexel University, have used a simple CW Near Infra Red Spectroscopy(NIRS) system to monitor the operator cognitive load dealing with mission sensitive operations. These operations have been involved with flight controllers as well as with UAV operators.

It is well known that cognitive workload can greatly impact the situational awareness of operators. It is well documented that many catastrophic incidents have happened when the operators were sleep deprived or cognitively overloaded.

The new frontiers in human –machine interface and the design of the cockpit for the radar operators, pilots, etc, are, to the extend possible, monitor the operator cognitive load and use various modality of communications, visual, verbal to provide an minimize the cognitive workload. Further it is essential that in future systems using wearable and simple technologies such as NIR to predict the operator fatigue to avoid any catastrophic events such as airplane crash's, nuclear reactor disasters, etc.

In this talk I will present the work that we at Drexel uUniversity have done using NIRS to monitor the cognitive workload and strategies to improve the process. NIRS accomplishes this goal by monitoring the relative changes in the oxygenated and deoxygenated hemoglobin in the pre-frontal cortex.

1. NIR Spectroscopy Measurements of Cognitive Load Elicited by GKT and Target Categorization.
In: HICSS, 2003

Kurtulus Izzetoglu, Gunay Yurtsever, Alper Bozkurt, Birsen Yazici, Scott C. Bunce, Kambiz Pourrezaei, Banu Onaral

2. Functional Near Infra Red Neuroimaging, IEEE Trans Neural Syst Rehabil Eng 13, 153-159 (2005)

Izzetoglu M., Izzetoglu, K., Bunce, S., Ayaz, H. , Devaraj, A. , Onaral, B, Pourrezaei, K.

Brain Computer Interfaces: Results, Lessons Learned, and New Applications

Michael Boninger, Jennifer Collinger, Robert Gaunt, Andrew Schwartz, Wei Wang, Doug Weber

Brain Computer Interfaces (BCI) have great potential to impact the lives of individuals with disabilities. By interfacing directly with the brain it is possible to obtain a control signal that allows for multiple degrees of freedom and for natural movement. Recent work at the University of Pittsburgh has shown that individuals with high-level tetraplegia can learn to use a BCI to control a prosthetic arm for functional tasks. In addition, in animal models we have shown the ability to decode and reproduce sensory information in the central nervous system. While these advances have obvious implications in both spinal cord injury and amputation, they also have promise in the area of traumatic brain injury. Indeed, the BCI work provides amazing insight into the function of the brain that is consistent with the new brain mapping initiative announced by President Obama. BCI work has provided insight into learning, neuroplasticity and the integration of sensory and motor learning. BCI likely also has a role in the application of regenerative medicine, as BCI may be able to provide critical stimulus that enables appropriate differentiating of stem cells or enhances other reparative strategies.

Development of MRI Biomarkers for Improved Diagnosis of TBI

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Abstract

Imaging plays a key role in the diagnosis and longitudinal follow up of traumatic brain injury (TBI). Among injury pathologies, vascular injury is associated with diffuse axonal injury (DAI) and traumatic axonal injury (TAI). The vascular network is ubiquitous and is an integral part of the tissue structure. In this talk, we focus on angiographic and venographic-related imaging methods and their role in assessing mild, moderate, and severe TBI. We begin with an introduction to susceptibility weighted imaging (SWI) and magnetic resonance angiography (MRA) and then provide evidence of different types of vascular damage. We give clinical examples of microbleeds and perfusion deficits in stroke and microbleeds in dementia, since these are not unrelated to TBI. This discussion is followed by examples of TBI-induced microbleeds are presented along with the concept of low-impact medullary vein damage (MVD). This MVD has been seen even for so-called mild TBI cases and blast injury as well.

Vascular damage can also manifest as a reduction in local perfusion even when no clear macroscopic vessel damage is seen. To further understand the role of vascular abnormalities, we then introduce the different perfusion weighted imaging (PWI) techniques available and their application in TBI. The combination of SWI and PWI should make it possible to differentiate the role of local thrombus versus changes in oxygen saturation in MVD, for example. We conclude with recommendations related to the use of perfusion with MRA, SWI, and oxygen saturation measurements to obtain a complete picture of the hemodynamics of the brain.

ACE overexpression in monocytic cells alleviates AD-like pathology and symptoms

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Alzheimer's disease (AD) neuropathology is tightly associated with accumulation of toxic forms of amyloid-β protein (Aβ) in the brain. Studies have shown that the peptidase angiotensin-converting enzyme (ACE) can degrade Aβ, converting neurotoxic $A\beta_{1\text{-}42}$ alloforms to the less pathogenic forms ($A\beta_{X\text{-}40}$). Our group has demonstrated a direct role for innate immune cells, especially bone marrow (BM)-derived monocytes and macrophages, in the clearance of Aβ plaques and in mediating various tissue-healing processes. Introducing targeted ACE-overexpression to microglia, monocytes and macrophages in the double-transgenic $APP_{SWE}/PS1_{dE9}$ (ADtg) mouse model resulted in a striking reduction of AD-related pathology and near complete restoration of cognitive functions. We have found that these mice exhibit far more potent innate immune responses, with increased cerebral infiltration of ACE-overexpressing monocytes strongly involved in Aβ plaque removal, along with reduced harmful inflammation (i.e. cytotoxic microglia and reactive astrocytes) and lower levels of soluble $A\beta_{1\text{-}42}$. To explore how high-levels of ACE in monocytes alter their capacity to resist Aβ toxicity, we further assessed *in vitro* monocytic survival and uptake capacity in response to fibrillar $A\beta_{1\text{-}42}$. We found that BM-derived ACE-overexpressing monocytes/macrophages as compared to their WT counterparts have increased viability after exposure to toxic $A\beta_{1\text{-}42}$ fibrils. Further, their immediate capacity to uptake and clear $A\beta_{1\text{-}42}$ fibrils was greater. These changes in monocytic phenotype were directly induced by ACE overexpression since they substantially reversed by inhibition of ACE catalytic domains. Also, the immunological profiles of ACE-overexpressing microglia after LPS treatment were substantially altered (i.e. TNFα, IL-1β). To investigate the therapeutic efficacy of these cells in murine ADtg models, we performed BM transplantation of ACE-overexpressing, or WT, or ADtg marrow. We observed attenuation of AD-associated pathology, with reduced Aβ burden and astrocytosis, and increased infiltration of monocytes exhibiting a local anti-inflammatory phenotype (reduced TNFα). Importantly, adoptive transfer of ACE-overexpressing $CD115^{+}$ monocytes to the peripheral blood of symptomatic

ADtg mice, once a month for three months, restored cognitive function as assessed by Barnes maze test. Altogether, these results demonstrate a key role for peripheral monocytes and the peptidase ACE in resisting AD and present a very promising immune based approach for the treatment of AD by harnessing monocytes with targeted overexpression of ACE.

Keywords: Alzheimer's disease, angiotensin-converting enzyme, Aβ-degrading peptidase, immunotherapy, phagocytosis, innate immunity, monocyte, macrophage, microglia,

Manipulations of Microglia During Aging and The Impact on Alzheimer's disease Pathology

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Microglial activation in Alzheimer's disease (AD) remains controversial due to reports showing therapeutic benefits based on treatments that activate the immune response to drugs that suppress activation. Some manipulations cause both a reduction in pathology, and a reduction in microglial activation. Several reports and data presented here suggest that either classical or alternative activation of microglia can lead to enhanced amyloid clearance. However, similar treatments can exacerbate pathology in tau depositing mice. Treatments that benefit amyloid-beta pathology seem to accelerate tau pathology. Evidence shows at least two polarized states of microglia/ macrophages consisting of a classical activation state, coupled with proinflammatory cytokine profiles referred to as M1 activation, or an alternative (M2) activation state, associated with dampened proinflammatory cytokine signaling and healing responses. Several reports argue for the existence of both M1 and M2 states (a hybrid state or continuum) during chronic neuroinflammatory diseases such as AD. The impact of aging likely influences the activation state and alters AD pathology. Herein, we performed intraparenchymal injections into hippocampus with stimulator cocktails M1-activating cocktail (TNF-α/ IL-1β/ IL-12) or an M2-activating cocktail (IL-4/ IL-13) designed to elicit either an M1 or an M2 bias at different ages in mice. We used microarray analysis and qrtPCR to identify novel signatures of inflammatory profiles in the CNS in regards to aging. We show age-related changes in classical and alternative activation responses in the mouse CNS and that M1 and M2 markers can be expressed in different cell populations during an M1 response. Furthermore the M2 response significantly declines with age suggesting an exaggerated or prolong proinflammatory response with age. One product activated by both stimulator cocktails was arginase-1 typically associated with the M2 phenotype. Arginase 1 (Arg1) and nitric oxide synthases increase during certain inflammatory events and both compete for L-arginine to produce either polyamines or nitric oxide, respectively. Our preliminary results indicate that Arg1 overexpression in the mouse CNS modifies tau pathology. We postulate that therapeutics aimed toward targets such as Arg1 and polyamines could modify amyloid beta and tau pathology.

Age-related CD8+ T cell clonal expansions infiltrate brain and induce neurodegenerative pathology similar to spontaneous Alzheimerâ€™s Disease.

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Introduction: Alzheimerâ€™s Disease (AD), the most common form of age-related dementia, currently afflicts 5.4 million individuals domestically, and is projected to afflict 15 million by mid-century. Patients with mutations in genes that promote toxic amyloid beta (Abeta) accumulation in brain develop rare familial forms of AD. Experimental treatments have thus aimed to curtail toxic Abeta accumulation, but this approach has been clinically disappointing. One reason may be that >90% of AD patients have spontaneous rather than familial AD, and the two may begin and progress quite differently. Recent evidence suggests that age-related immune defects impact spontaneous AD, but this has not been rigorously tested. Clonal expansions of CD8+ T cells (TCEs) represent the most common age-related immune defect. CD8+ T cells can be induced to expand by injecting them into T cell-deficient mice, but their relationship to age-related TCEs and neurodegeneration remain unknown.

Methods: We injected purified wild-type, IFNgamma-deficient, or Perforin-deficient donor T cells into young wild-type or T cell-deficient B6.Foxn1 mice and characterized donor cell expansions using age-related TCE markers, as well as pathologic and cognitive hallmarks of AD. Behavioral tests were performed on cell-injected and age-matched control cohorts at various times post-injection (Open Field, 12 wks, 6 and 15 months; Fear Conditioning, 6 mos; Y-maze/Spontaneous Alternation, 10 months; Barnes Maze, 15 months). T cell infiltration and Abeta accumulation in brain was assessed early and late, along with astrogliosis, plaque formation, neuronal/synaptic marker levels, and brain mass.

Results: CD8+ cells from all donors elicited expansions that were phenotypically similar to age-related TCEs when injected into B6.Foxn1 hosts, 3-4 wk post-injection (up-regulated CD122, CD127 & KLRG1; oligoclonal TCR Vbeta; down-regulated CD8). Donor CD8+ and Abeta accumulation in brain were simultaneously detected by Western blot in B6.Foxn1 brains within 3 weeks of injection. No difference in overall activity of CD8+-injected relative to age-matched controls was detected at any time point. Fear Conditioning indicated low responsiveness of CD8+-injected relative to CD4+- or control-injected B6.Foxn1 6 months after injection, and persistent memory deficits were detected at 10 months by Y-maze. Profound hippocampal learning defects were detected by Barnes Maze at 15 months. Significant accumulation of soluble Abeta1-40, immature Abeta plaques, and astrogliosis in entorhinal cortex, hippocampus, and cingulate cortex was seen in CD8+-injected B6.Foxn1 by 15 months, together with progressive loss of brain mass (5 and 10% at 6 and 15 months, respectively). Notably, B6.Foxn1 mice treated with Perforin-deficient CD8+ T cells exhibited no neuropathology and lacked cognitive deficits, whereas those treated with IFNgamma-deficient CD8+ T cells were cognitively intact, yet exhibited significantly elevated plaques within hippocampus, elevated neuronal and synaptic markers, and increased brain mass.

Conclusions: CD8+ T cell expansions identical to age-related TCEs are readily induced in young B6.Foxn1 mice, where they enter brain and cause function-dependent neurodegenerative and cognitive pathology. Notably, lytic and pro-inflammatory CD8+ T cell functions may independently impact development of this neuropathology. This non-transgenic model uniquely recapitulates multiple aspects of spontaneous AD and may thus be useful in clarifying the etiology, biology, and treatment of this disease. \ This work has not yet been submitted for publication elsewhere. \

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EDUCATIONAL OBJECTIVES: 1) To learn about molecular approaches to Alzheimer's disease, 2) be able to define the search for relevant gene expression in selectively vulnerable neurons in Alzheimer's disease. 3) To understand roles of tissues from flies, mice and humans in defining experimental models of disease.

INTRODUCTION: The three neuropathological hallmarks of Alzheimer's disease (AD) include selective vulnerability of neurons, accumulation of A-beta peptide and of tau protein. Each of the latter two aberrantly assemble into highly insoluble, fibrillar aggregates. To date, least is understood about the first hallmark. Our laboratory initially approached this question, by application of monoclonal antibodies (MAbs) generated using *Drosophila* heads as immunogen. Over 50% crossreacted immunohistochemically with human CNS tissues, many on functional domains encoding protein homologues in flies and mice. Several showed increased reactivity in AD tissue with neurons vulnerable in the disease compared with normal age-matched controls. Probing a human cDNA library, one MAb identified JNK3, which is a major signaling molecule in a cell death cascade. Next, JNK3 cDNA was used to define interacting proteins in a yeast two-hybrid system. One, DENN encodes a family of proteins over 200kDa that are phylogenetically broadly expressed in neurons including in the human CNS and other somatic tissues. DENN also has an inflammatory role binding TNF-alpha, and in neurons is a Rab3 GDP-GTP exchange protein, binding to synaptic vesicles in the axon. This binding region also serves as a "death-domain".

METHODS: Human CNS tissues obtained at autopsy, and SH-SY5Y cells were compared on gels for mRNA splice isoforms. Immunofluorescence microscopy was used for distribution of relevant neuronal proteins.

RESULTS: Using differentiated human neural tumor cells (SH-SY5Y), the largest mRNA isoform, IG20, functions in cell death, the smallest, DENN-SV is neuroprotective. Functional mapping reveals both nuclear import and export signals as well as a JNK-binding domain. When SH-SY5Y cells are exposed to toxic levels of oligomeric A-beta peptide, an initial response is a relative increase of the DENN-SV and relatively less of the IG20 mRNA. Later, by 24 h. exposure to toxic levels of oligomeric A-beta peptide, an initial response is a relative increase of the DENN-SV and relatively less of the IG20 mRNA. Later, by 24h. exposure, there is a reversal of this DENN-SV/IG ratio and progression to cell death. Over the long, many years course of AD, a similar profile of DENN-SV/IG20 is seen in AD-affected regions and mirrors the dementia progression and A-beta accumulation. Further, introduction into cells *in vitro* of siRNA specific for suppression of these variants reveals that IG20 enhances cell death while DENN-SV reduces cell loss.

CONCLUSIONS: Significantly, recent bioinformatics studies have revealed that the C90RF72 gene product is homologous to members of the DENN protein family and interacts with TDP43, an RNA-binding protein which regulates mRNA splicing, transport, trafficking and translation. TDP43 is also aggregated in AD, FTLD-ALS and other FTLD syndromes.

Neuropsychological testing in Sport-Related Concussion

Gerard A. Gioia, Ph.D.

Objectives

1. Describe the role of neuropsychological assessment and management of concussion
2. Identify methods of neuropsychological assessment, specific testing batteries

Description

This workshop will review the role of a brain-behavior model, neuropsychological testing and complementary assessment methods in the management of sport related concussion. The clinical condition of concussion is defined, including the key signs and symptoms, and the ways that neuropsychological testing can assist in understanding and managing the injury. Participants will also learn about the clinical presentation of children and adolescents and a unique developmentally-relevant assessment and management approach. Strengths and limitations of neuropsychological testing will be reviewed, as well as its role in research.

MULTIFUNCTIONAL NANOPARTICLES FOR THERANOSTICS OF PEDIATRIC BRAINSTEM GLIOMAS

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Pediatric brainstem glioma (BSG) is an aggressive cancer of the brainstem and constitutes 15-20 % of all brain tumors in children. BSGs remain one of the hardest cancers to treat with less than 10 % of patients surviving more than 2 years post diagnosis. The failure of various treatment strategies in appreciably improving overall survival is because drug penetration into and distribution within BSG tumor tissue is poor. This is because BSG patients typically have intact blood-brain barriers (BBB). The intact BBBs make it difficult to estimate drug concentrations within BSG tumors and have resulted in drugs being administered at the maximum tolerated dose instead of the effective dose. Further, the historic lack of BSG biopsies performed because of their perceived morbidities has resulted in a lower number of BSG biomarkers being identified. Therefore there is an urgent need to devise new strategies for treating BSGs that overcome these shortcomings. Nanotechnology allows the synthesis of versatile nanoparticles that can be used for targeted drug delivery to the brain. Nanoparticles generally feature 1) small sizes (1 – 200 nm) that enable penetration of the body barriers, 2) high surface area to volume ratios that enable attachment of ligands that facilitate crossing the BBB and target tumor-specific biomarkers, 3) the ability to be imaged (via medical imaging technologies such as MRI or CT), therefore, their concentrations can be estimated *in vivo* and 4) the ability to carry therapeutic agents to the tumor sites. This utility of the nanoparticles to simultaneously perform therapy and diagnostics is referred to as theranostics. In this work, we describe multifunctional Prussian blue (PB) nanoparticles (NPs) for theranostics of BSGs. Our non-toxic PB NPs enable multimodal molecular imaging of BSGs (via MRI and fluorescence) by molecularly targeting the biomarker neuroglia-2 overexpressed in BSGs identified from post-mortem tissue proteomic analysis. Further out PB NPs perform tumor site-selective synthesis of a cytotoxic reactive oxygen species inducing cell death. We present successful preliminary studies conducted *in vitro* with BSG cells that suggest the potential of clinically translating our multifunctional, theranostic PB NPs for improved prognosis of children with BSG.

Title:

Brain Tumors in Children: Diffusion, Perfusion, Tractography

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Department of Diagnostic Imaging and Radiology

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Abstract:

Diffusion Imaging (DI)

Diffusion imaging (DI) investigates the molecular translational movements (i.e. the Brownian motion) of water molecules. Brownian motion produces signal loss proportional to the degree of molecular translation/diffusion. Within the cerebral milieu, cellular membranes and other macromolecular structures restrict water diffusion, which results in increased signal on DI (less diffusion means less signal loss secondary to spin dephasing). Thus signal on DI can reflect cellular density and microarchitecture. The apparent diffusion coefficient (ADC) is a measure of the ability of tissue to restrict water diffusion – higher ADC values mean greater (facilitated) diffusion, lower ADC values imply lower (restricted) diffusion. ADC is significantly lower in high-grade than in low-grade tumors.

DTI tractography is used to plan the surgical approach of CNS tumors: important association pathways (e.g. pyramidal, optic tracts…) can be localized in relation to a tumor; this helps the surgeon to avoid injury to these tracts. DTI is also useful to evaluate for the presence and extent of tumoral invasion: whereas focal (well-marginated) tumors should displace but not disrupt axons outside of their borders, the microscopic tumor extension of infiltrative tumors disrupts local axonal structures.

Perfusion Weighted Imaging (PWI)

Perfusion weighted imaging (PWI) measures cerebral hemodynamics at the microcirculation level. Three different techniques are available: dynamic susceptibility contrast imaging, dynamic contrast-enhanced imaging and arterial spin labeling. PWI is helpful in the evaluation of tumor grade and in targeting a lesion for biopsy by identifying the regions with greatest capillary

density (highest grade). PWI can differentiate hypervascular tumors from tissue necrosis or from pseudoprogression

Positron Emission Tomography (PET) is an important imaging assessment tool in a variety of pediatric neoplasm. Technical aspects of performance of PET using a variety of radiopharmaceuticals will be discussed along with current indications for evaluation of various types of pediatric brain tumors. Potential new uses for PET in this patient population will also be explored.

Abstract for Clinical Imaging Challenges

Clinical Imaging Challenges

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Washington, DC

Childhood brain tumors are an extremely challenging group of lesions to both diagnose and treat. In total, although infrequent, they are the most common form of solid pediatric brain tumor, second only to leukemia in incidence of all pediatric cancers and the leading cause of death relating to pediatric malignancies. Treatment of childhood brain tumors is limited by the immaturity and vulnerability of the developing brain and treatment sequelae are common. Outcome is impacted by exactness of diagnosis and treatment is dependent on the extent of the tumor at the time of diagnosis. Childhood brain tumors also have significant challenges as compared to brain tumors occurring in adults. Childhood brain tumors may be congenital or developmental lesions, and separation of a tumor from dysplastic areas of the brain can be difficult, especially in genetic symptoms such as neurofibromatosis type 1. Unlike the situation in adults, approximately one-third to one-half of lesions occur in the posterior fossa. Childhood brain tumors have a higher propensity to disseminate the neuro-axis, making evaluation of extent of disease critical. In additional, many pediatric brain tumors are low-grade and infiltrating and enhancement patterns cannot be utilized to determine extent of disease. Confounding factors in the evaluation of children with central nervous system tumors is the need to limit x-ray exposure in the very young and the requirement of many of these children for sedation.

There may be a poor correlation between neuro-imagining finding and functional outcomes in these patients and function can be very difficult to assess in a very young child. RAPNO is a international attempt to standardize the neuro-radiographic assessment of pediatric brain tumors, as well as the standardization of functional outcomes. Standard neuro-imaging requires assessment/measurement of both the enhancing and non-enhancing images. Bidirectional area measurements have been the gold

standard for evaluation in response in pediatric brain tumor therapeutic trials, but are difficult in tumors with irregular shapes and infiltrating natures. Volumetric analysis, although considered optimal, is still not uniformly utilized and is not automated. Techniques such as MR diffusion, perfusion and tractography are likely to be increasingly utilized. PET scanning has a limited role by means that are presently utilized, but will likely have increasing importance as different isotopes become available. Spectroscopy is often obtained at the time of imaging, but has yet to been shown to be consistently associated with outcome and is still under study. There is great hope that nanotechnology and tumor painting will help in assessments. Finally, as new delivery systems are utilized for agents to hone to the tumor, a better understanding of the extent of distribution of the agents will be needed.

Brain Functional Connectivity in Recovery from Chronic Spinal Cord Injury

James J. Pekar, Ph.D.
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In this brief talk, I will introduce methods used to acquire and analyze magnetic resonance imaging data reporting on brain functional connectivity, and show how such measures promise to inform assessment of individuals with chronic spinal cord injury.

Resting-state brain activities: Mechanisms and potential clinical applications

Yihong Yang, Ph.D.

Neuroimaging Branch, National Institute on Drug Abuse, National Institutes of Health

There has been growing interest in intrinsic brain activity “at rest” that may be used to reveal circuit-level information of brain functions. Alterations of resting-state brain activity have been implicated in various neurological and psychiatric disorders. In this seminar, the underlying neural mechanisms of intrinsic brain activity and the characteristics of resting-state fMRI signal will be discussed. Applications of functional connectivity in substance addiction, such as searching for “addiction circuits” will be demonstrated.

How acute and chronic pain affect brain function and structure: neuroimaging evidence in humans and rats

Neuroimaging research in the past two decades has vastly improved our understanding of the brain circuitry involved in experimental and chronic pain conditions. Two new challenges for pain neuroimagers include understanding the effects of treatment on abnormal brain structure and function and developing reverse-translational models for testing new therapies. This talk provide attendees an overview of the state of the pain imaging field, with specific focus on these new challenges. Data will be presented from studies of functional and structural MRI in chronic low back pain, migraine, and burning mouth syndrome in humans, and in models of neuropathic pain in rodents. The ultimate goal of these lines of work is to identify brain targets – either single regions or networks – for novel chronic pain interventions.

The neuro-protective effects of exercise in older adults at increased risk for Alzheimer's disease

J. Carson Smith, PhD, FACSM
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University of Maryland, College Park, MD

Significance: The prevalence of cognitive impairment among older adults in the U.S. is estimated to be over 20 percent and, with an aging U.S. population, cognitive impairment and Alzheimer's disease constitutes an alarming public health problem. Despite the known risk factors and primary neuropathology of Alzheimer's disease, a NIH panel recently concluded that there is insufficient evidence to support the use of any pharmaceutical agents or dietary supplements to prevent cognitive decline or Alzheimer's disease. Physical exercise, however, was noted as one behavioral intervention that shows promise in the fight against Alzheimer's disease.

Presentation Summary: Despite popular views regarding the effects of exercise on cognition and brain function, the question of whether physical activity and exercise interventions may differentially impact cognitive trajectory, clinical outcomes, and brain structure and function among individuals at the greatest risk for Alzheimer's disease has not yet been answered. Some studies suggest that the protective effects of physical activity on the future diagnosis of dementia appear to be larger in those at increased genetic risk for Alzheimer's disease. There is also limited evidence that exercise training may be effective at helping to promote stable cognitive function in older adults diagnosed with mild cognitive impairment, and greater cardiorespiratory fitness is associated with greater brain volume in early-stage Alzheimer's disease patients. In APOE-ε4 allele carriers compared to non-carriers, greater levels of physical activity may be more effective in reducing amyloid burden and are associated with greater activation of semantic memory-related neural circuits.

Learning Objectives: This talk will advance the knowledge of attendees by providing a review of the literature that addresses the question of whether or not physical activity is more or less effective at preserving cognitive function and/or brain function in those at increased risk for AD, with particular emphasis on recent functional neuroimaging studies.

Neuroglia and the Innate Neuroimmune System in Autism

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Autism spectrum disorders (ASD) are part of neurodevelopmental abnormalities that have produced an important impact on the magnitude of neurological and developmental problems that affect the overall health of the pediatric population. Most of the neurobiological studies demonstrate that the main core of neuropathological abnormalities in ASD are characterized by disturbances in neuronal organization, such as an excessive number of neurons, simplification of dendritic organization and disorganization of cortical lamination. Studies from our laboratory and others have disclosed the role of neuroglia as well as immune mediators (e.g., cytokine/chemokines) in brain tissues from patients with ASD in which an increased activity of microglia and astroglia coincide with changes in the profiles of innate neuroimmune responses such as those from Toll-like receptors (TLR) signaling pathways and oxidative stress. Interestingly, the pattern of neuroglial and innate immune activation follows a pattern of selective involvement of areas of the cerebral cortex known to be dysfunctional in ASD such as the frontal and anterior cingulate gyri as well as cerebellum. In addition, studies in blood and cerebrospinal fluid from patients with ASD also show that a process of activation of innate immune pathways occur in patients with ASD. These findings support the view that activation of neuroglia cells and neuroimmune mediators such as cytokines, chemokines and signaling pathways such as Toll-like receptors may influence neuronal and synaptic function and contribute to the pathobiological mechanisms and neurobehavioral processes present in ASD.

CD103-deficient mice exhibit a sex-dependent phenotype suggestive of autism spectrum disorder

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Introduction: Autism spectrum disorders (ASD) are pervasive neurodevelopmental disorders characterized by social and communication deficits, restricted repetitive interests and behaviors appearing in early childhood. The causes of ASD remain unknown, and immunological, neurological, and environmental etiologies have all been postulated. This uncertainty is in large part due to the absence of biologically informative animal models for ASD. Core ASD symptoms can be reproduced in animals lacking neuro-active genes or by administering high doses of neurotoxins, but such models may only help illuminate the biochemical underpinnings of ASD within brain, without illuminating the mechanisms whereby brain alterations are initiated. The development of mechanistically informative models of ASD is thus critical to determine the clinical causes, course, and treatment approaches for ASD. Recent studies suggest the involvement of cytolytic immune cell dysfunction in ASD etiology. The largest subpopulation of newly-produced cytolytic immune cells in the general circulation (CD8+ T cells), are highly sensitive to environmental stress, and constitutively express the integrin, CD103. CD103 is a ligand for E-cadherin that regulates CD8+ T cell and dendritic cell (DC) homing to gut and brain. CD103 deficiency in mice also alters immune tolerance, gut autoimmunity, and inflammation, which parallel common co-morbidities in ASD. Thus, decreased levels of CD103+, particularly on DCs and/or CD8+ T cells, could represent a potential link between environmental stress, gut, brain, and immune co-morbidities in ASD.

Methods: We analyzed immune cell content in brain and behavior in wild-type C57BL/6 and/or CD103-deficient from ages 2-10 months of age, using Open Field, Repetitive Grooming, Spontaneous Alternation, Barnes Maze, and Social Approach tests. All tests were performed on males and females separately, and at identical ages.

Results: Female mice deficient for the CD103 gene exhibited identical overall activity, with increased self-grooming, decreased spontaneous alternation, and accelerated learning times in the Barnes Maze test. Importantly, these mice also exhibited a complete absence of the novel socialization preference observed in age- and sex-matched wild-type mice. Male CD103-deficient mice exhibited general hyperactivity, and initially delayed learning in the Barnes Maze test, with no propensity for either increased grooming or decreased spontaneous alternation.

Conclusions: These findings suggest that CD103-deficiency mediates increased repetitive behavior, preference for sameness, and social disturbance, with unimpaired learning and memory, specifically in females. By contrast, males exhibited hyperactivity with altered learning characteristics. The female phenotype closely parallels discrete ASD symptoms, and may thus represent a unique mechanistically informative model for gender-dependent ASD. Determining the immune and brain parameters contributing to each of the differences observed in CD103-deficient mice may aid the identification of discrete targets to treat ASD and/or associated cognitive symptoms.

This work has not been submitted for publication or presentation elsewhere.

VAGUS NERVE STIMULATION USE IN PATIENTS with REFRACTORY EPILEPSY and DEVELOPMENTAL DELAY and/or AUTISM

Target audience: health care providers and alien professionals
Outcome/objectives: Vagus nerve stimulation (VNS) plays a crucial role in the management of medically intractable epilepsy. Along with seizure reduction, VNS treatment has been responsible for improvements in the attention, mood, behavior and quality of life of autistic patient with epilepsy. It is important to recognize that Autism is the third most common developmental disability in the United States [(1)]. These patients suffer from a debilitating range of emotional and behavioral problems including social isolation, poor verbal communication, mood swings and temper tantrums. In addition, 12-39% of these patients have epilepsy [(2, 3)]. Studies have shown an important relationship between behavioral problems and seizure occurrence. Behavioral regression correlated with worsening control seizures in autistic patients [(4)], while improvement of behavior and quality of life coincided with seizure reduction.
Purpose: Vagus nerve stimulation (VNS) has proved an invaluable tool in treating patients with medically intractable epilepsy. VNS reduces the frequency and duration of seizures, but can also improve alertness and behavior. Behavioral regression correlated with worsening control seizures in autistic patients [(4)], while improvement of behavior and quality of life coincided with seizure reduction.
Method: Peer reviewed Clinical Trials and scientific literature review.
Results: The beneficial effect of VNS treatment on mood, alertness, behavior and quality of life has been observed in patient with autism and refractory epilepsy independently from seizure control.
Discussion: Our findings are consistent with previous VNS studies by Harder et al [(6)] showing positive effects on mood and behavior in epileptic patients. Parker et al [(7)] described the VNS treatment of 16 children with epileptic encephalopathies who showed improvement in verbal performance that was independent of seizure reduction. In a study by Huf et al [(5)], VNS therapy of 40 young adults with refractory epilepsy and mental retardation (IQ <70) produced marked improvement in alertness, mood changes and verbal performance after 1 and 2 years of treatment. In two larger retrospective studies, based on data from the VNS patient outcome registry maintained by Cyberonics, Inc., Park [(9)] and Levy [(10)] et al. reported improvement in several quality-of-life areas in patients with intractable epilepsy and autism. The neurochemical basis for the effects of VNS on mood and behavior may be explained by its effect on central adrenergic pathways. These divergent pathways innervate multiple brain regions, including the locus ceruleus, amygdala, hypothalamus, cingulate gyrus, hippocampus, and orbito-frontal cortex, areas known to play a role in behavior [(11)].
Conclusion: The majority of our autistic patients with intractable epilepsy showed sustained behavior improvements in alertness, behavior, and quality of life during VNS therapy. These improvements were noted earlier in the course of VNS therapy and being independent from seizure frequency control. If these observational findings can be replicated in a larger, prospective study on VNS in patients with autism and medically intractable seizures, utilizing neuropsychometric assessments pre- and post-VNS implantation, then VNS therapy in autistic patients, with-out co-morbid seizures, may prove to be a valuable and effective treatment option.

References:

1. Blackwell J. Clinical practice guideline: screening and diagnosing autism. J Am Acad Nurse Pract. 2001;13:534-6
2. Hitoshi Harra. Autism and epilepsy: A retrospective follow-up study. Brain & Develop 2007;10:1016
3. Susanna Danielson. Carina Gillberg, Eva Billstedt, Christopher Gilberg, and Ingrid Olson. Epilepsy in young adults with autism: a prospective polulation-based follow-up study of 120 individuals diagnosed in childhood.
4. Tanya C. Warwick, James Griffith, Bernardo Reyes, Benalfew Legesse, Melanie Evans. Effects of vagus nerve stimulation in patient with temporal lobe epilepsy and Asperger syndrome: Case report and review of the literature. Epilepsy & Behavior 2007;10:344-347
5. Roger L. Huf, Adam Mamelak, Kara Kneedy-Cayem. Vagus nerve stimulation therapy: 2-year prospective open-label study of 40 subjects with refractory epilepsy and low IQ who are living in long-term care facilities. Epilepsy & Behav 2005;6:417-423
6. Harder CL, Pulver MC, Ravdin LD, Nikolov B, Halper JP, Labar DR. A pilot study of mood in epilepsy patient treated with vagus nerve stimulation. Epilepsy Behav 2000;1:93-9
7. Parker AP, Polkey CE, Binnie CD, Madigan C, Ferrie CD, Robinson RO. Vagal nerve stimulation in epileptic encephalopathies. Pediatrics 1999;103:778-782
8. Murphy JV, Wheless JW, Schmoll CM. Left vagal nerve stimulation in six patients with hypothalamic hamartomas. Pediatr Neurol 2000;30:485-489

9. Yong D. Park. The effects of vagus nerve stimulation therapy on patients with intractable seizures and either Landau-Kleffner syndrome or autism. Epilepsy & Behav 2003;4:286-290
10. Michael L. Levy, M.D., Ph.D., Karen M. Levy, R.N., B.S.N., Dayna Hoff, M.B.A., Arun Paul Amar, M.D., Min S. Park, M.D., Jordan M. Conklin, B.S., Lissa Baird, M.D., and Michael L.J. Apuzzo, M.D. Vagus nerve stimulation therapy in patients with autism spectrum disorder and intractable seizures: results from the vagus nerve stimulation therapy patient outcome registry. J Neurosurgery Pediatrics 5:595-602, 2010
11. George MS, Sackeim HA, Rush AJ, et al. Vagus nerve stimulation: a new tool for brain research and therapy. Biol Psychiatry 2000;47:287-95
12. Hassert DL, Myashita T, Williams CL. The effects of peripheral vagal nerve stimulation at memory-modulating intensity on norepineprine output in the basolateral amygdala. Behov Neuroscience 2004;118:79-88
13. Roosevelt RW, Smith DC, Clough RW, Jensen RA, Browning RA. Increased ex-tracellular concentration of norepinephrine in cortex and hippocampus following vagal nerve stimulation in the rat. Brain Research 2006;1119:124-132
14. Sackeim HA, Keilp JG, Rush AJ, et al. The effect of vagus nerve stimulation on cognitive performance in patients with treatment-resistant depression. Neuropsychiatry Neuropsychology Behav Neurol 2001;14:53-62
15. A. John Rush, Harold A. Sackeim, Lauren B. Marangell, Mark S. George and et al. Effects of 12 Months of Vagus Nerve Stimulation in Treatment-Resistant Depression: A Naturalistic Study. Biol Psychiatry 2005; 5H:355-363

16. Malek Bajbouj, MD, Angela Merkl, MD, Thomas E. Schlaepfer, MD, Caroline Frick, MD et al. Two-Year Outcome of Vagus Nerve Stimulation in Treatment-Resistant Depression. Journal of Clinical Psychopharmacology 30, 3:273-281, 2010
17. Wang H, Chen X, Lin Z, Shao Z, Sun B, Shen H, Liu L. Long-term effect of vagus nerve stimulation on interictal epileptiform discharges in refractory epilepsy. J Neurol Sci. 2009 Sep 15;284(1-2):96-102. doi: 10.1016/j.jns.2009.04.012. Epub 2009 May 8.
18. Kawai K, Shimizu H, Maehara T, Murakami H Outcome of long-term vagus nerve stimulation for intractable epilepsy. Neurol Med Chir (Tokyo). 2002 Nov;42(11):481-9;

Brain Stimulation and Epilepsy: VNS in Children with Medically Refractory Epilepsy

Jeffrey M Chung, MD

About 467,711 children between the ages 0 and 17 carry the diagnosis of epilepsy in the United States, with 150,000 new cases being diagnosed each year. Despite the addition of new medications and re-introduction of efficacious medications into the U.S., 20-40% of these patients' seizures remain intractable. Some of the characteristics of medically refractory epilepsy syndromes in the pediatric population such as Lennox Gastatut, West, and Dravet syndromes are less commonly seen in adults, and these patients are often not candidates for resective surgical treatment. For them, other management options such as dietary and device-oriented therapy may provide reduction in seizure frequency and improvement of quality of life. Vagus Nerve Stimulator (VNS) is a FDA-approved device-oriented therapy for treatment of medically refractory epilepsy. To date, the data on safety, efficacy, and changes in quality of life of VNS in children and adolescents are similar to those in adults. Secondary benefits such as decrease in the number of anti-epileptic medications use, emergency room visits, and the incidence of status epilepticus have also been demonstrated in some studies. Overall, VNS presents a viable option to the treatment of children and adolescents with medically refractory epilepsy.

Vagus Nerve Stimulation for Adults: A Summary and Update

Jennifer Hopp, MD
Associate Professor of Neurology

University of Maryland School of Medicine

We will review a summary of the history of Vagus Nerve Stimulation (VNS) in the adult epilepsy population with updates of clinical and scientific understanding in the field of neurostimulation in epilepsy. The review will include the basics of external neurostimulation, efficacy of VNS in the adult epilepsy population, and updates in labeling, new models of VNS and in clinical understanding of the use of this device in the treatment of refractory epilepsy.

SBMT 2013 Congress

Submission # 201

QUALITY OF LIFE IN POSTTRAUMATIC STRESS DISORDER

Waguih William IsHak - Cedars-Sinai Medical Center and UCLA
Konstantin Balayan - Cedars-Sinai Medical Center
Gabriel Tobia - Cedars-Sinai Medical Center

Abstract: INTRODUCTION:Quality of life (QOL) refers to an individual's overall sense of wellbeing and subjective physical, psychological, and social functioning. QOL is significantly affected in patients with Post-Traumatic Stress Disorder (PTSD). This is a systematic review of the relevant literature on QOL impairment in PTSD subgroups and the impact of treatment interventions on QOL.

METHODS: A systematic database search from 1970-2011 was conducted using Medline, PsycINFO, and Cochrane Database of Systematic Reviews using the key words: “PTSD”, “post traumatic stress disorder”, “stress disorders”, “quality of life”, “QOL”, and “health-related quality of life.” Two reviewers applied pre-defined selection criteria independently and reached consensus on the inclusion of 22 studies that focused on QOL in PTSD.

RESULTS: The findings revealed that QOL is gravely impaired in PTSD subgroups, such as veterans, refugees, survivors of terrorist attacks, natural disaster survivors, rescue personnel, and survivors of violence. Research shows that PTSD is an independent predictor of QOL impairment, and that various psychotherapeutic and pharmacological treatment modalities have a positive effect on QOL in PTSD. However, their ability to improve QOL to community norm levels is unclear.

CONCLUSIONS: This review also highlights the importance of including QOL as an essential outcome measure in PTSD clinical and research work.

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Waguih William IsHak, MD, FAPA, Konstantin Balayan, M.D., and Gabriel Tobia, M.D. (Cedars-Sinai Medical Center)

INTRODUCTION:Quality of life (QOL) refers to an individual's overall sense of wellbeing and subjective physical, psychological, and social functioning. QOL is significantly affected in patients with Post-Traumatic Stress Disorder (PTSD). This is a systematic review of the relevant literature on QOL impairment in PTSD subgroups and the impact of treatment interventions on QOL.

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CONCLUSIONS: This review also highlights the importance of including QOL as an essential outcome measure in PTSD clinical and research work.

The work is not being submitted for publication or presentation elsewhere.

Educational Objectives

1. Appreciate the magnitude of QOL impairments in PTSD. 2. Understand the impact of PTSD treatment on QOL. 3. Learn about various psychotherapeutic and pharmacological treatments that could improve QOL in PTSD.

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Optical Microimaging and Its Potential for Brain Function Assessment and Surgical Guidance

Carment Kut [1], Jiefeng Xi [1], Jessica Mavadia [1], Kaisorn Chaichana [2], Wenxuan Liang [1], John Issa [1], Gunnstein Hall [1], Fausto Rodriguez [3], Alfredo Quinones-Hinojosa [2], and Xingde Li [1]

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Abstract: Optical coherence tomography (OCT) and multiphoton endomicroscopy are two representative emerging high-resolution optical micro imaging technologies. OCT can be envisioned as an optical analog of ultrasound B-mode imaging except that it utilizes near-infrared low coherence light rather than sound where no coupling medium is required. OCT imaging contrast is from the optical scattering and absorption properties of biological tissues. In addition to structural imaging at the tissue architectural level, OCT can also image blood flow with a few microns spatial and a few tens of um/second temporal resolution. Multiphoton imaging technology utilizes simultaneous absorption of multiple photons to excite fluorescent molecules (such as NADH, FAD, or exogenous dyes) or structural proteins (such as collagen) to generate fluorescence or harmonics signals, from which high-resolution molecular, biochemical, physiological or metabolic, and fine structural information can be obtained. Recently we have explored the feasibility of OCT for assessing brain tumor, aiming to provide more objective intra-operative guidance during brain tumor surgery. Brain tumor is one area where precision tumor removal is most critical for improving patient survival while not comprising motor and sensory functions. Blinded ex vivo human tissue OCT imaging studies have shown that a better than 91% specificity in identifying tumor infiltrated zone can be achieved, which is significantly better than the 50% specificity currently available in the operating room. A reasonable sensitivity about 70% was also achieved. A portable OCT system with ultrahigh resolution (of ~3-7 um) and high speed (of ~100 – 400 frames per second) is being developed suitable for clinical use. In addition to structural imaging, such an OCT system is also capable of imaging blood flow and blood vessels in real time, which can potentially be used to study brain function or tumor models. Some results will be presented during the talk. Comparing with OCT, multiphoton endomicroscopy is a much newer technology. Our group has developed the first, ultracompact, fully integrated and all-fiber-optic endomicroscope of a diameter about 2 mm, capable of two-photon fluorescence and second harmonic generation (SHG) imaging of biological tissues without the need for tissue staining. This talk will briefly review the key technological aspects of nonlinear optical endomicroscopy. Ex vivo and in vivo subcellular imaging results with the technology will be presented, including some preliminary in vivo mouse braining imaging. The potential of multimodal imaging technologies that integrate OCT (for morphological imaging) and single or two-photon fluorescence endomicroscopy (for molecular or redox imaging) will also be discussed.

Intra-operative Optical Guidance for Neurosurgery

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We developed an MRI-compatible optical coherence tomography (OCT) imaging probe for neurosurgery guidance. MRI/OCT multi-scale imaging integrates micro-resolution optical imaging with wide-field MRI imaging, and has potential to further improve the targeting accuracy. In this study, we developed the first MRI-compatible OCT imaging system. Also, we demonstrated that a thin OCT fiber probe (0.3 mm) integrated within MRI surgical tools can provide microstructure information from the ROI obscured by MRI artifacts. The concurrent MRI/OCT dynamic images on sheep brain ex vivo demonstrated that OCT can reveal many MRI occult structures. The large-scale MRI image can be used to plan the trajectory and monitor the coarse instrument position relative to the target and real-time, while high-resolution OCT image can detect the micro-landmarks for high-precision targeting.

In addition, we present a low-cost blood vessel sensing probe (0.3 mm in diameter) using a coherence-gated Doppler (CGD) technology that can integrate with microelectrode to detect the blood vessels lying ahead to improve the safety of this procedure. CGD probe can provide real-time audio feedbacks to the motion of moving scatters within a well-defined sample volume. The thin and flexible optical probe can be integrated within surgical tools for blood vessel detection. Instead of imaging, we fixed the path length of reference arm and tailored the sample volume to acquire the ensemble information from ROI (0.1-1 mm) by using the light source with appropriate coherent length. The interference fringe (~ kHz) reflecting the flow speed of moving scatters was directly converted to audio signal after amplification and frequency filtering. By placing CGD fiber probe on top of exposed rat femoral vessels, the distinctive audio feedbacks from artery, vein and surrounding tissues can be clearly differentiated. Results of CGD detection of blood vessels in deep sheep brain in vivo under ultrasound guidance will be presented

Title: Photoacoustic Microscopy of Ischemic Stroke

Leading author: Song Hu, Assistant Professor of Biomedical Engineering, University of Virginia

Co-authors: Brian Soetikno, Ernie Gonzales, Jin-Moo Lee, and Lihong V. Wang, Washington University in St. Louis

Abstract:

Studying cerebrovascular responses to brain ischemia has been limited by imaging modalities that have either good tissue penetration but inadequate spatial resolution, or high resolution but invasive preparations (e.g., open-skull windows).

To address this outstanding challenge, we have developed neurovascular photoacoustic microscopy (PAM) with micron-level resolution. Multiple hemodynamic parameters—including vessel diameter, oxygen saturation of hemoglobin (sO_2), and oxygen extraction fraction (OEF)—were longitudinally monitored through intact skulls of adult Swiss Webster mice, before, during, and up to 72 hours after a 60-minute intraluminal transient middle cerebral artery occlusion (MCAO). The cerebral vasculature was imaged using dual-wavelength PAM to quantify sO_2, based on which OEF was computed. Further, two-dimensional segmentation algorithms were developed to enable multi-parameter analysis at the single vessel level, and an unbiased cluster analysis was utilized to predict tissue fate. Seventy-two hours after ischemia, animals were intravascularly perfused with carbon black ink and then sacrificed. Whole brains were stained with triphenyltetrazolium chloride and to delineate infarct and vasculature at the cortical surface.

According to our experimental results, arteries/arterioles were easily distinguished from veins/venules in baseline PAM images, based on the distinct sO_2 values (the mean arterial and venous sO_2 values are 87% and 76%, respectively). During MCAO, no significant changes in the mean arterial sO_2 value were observed; however, the venous sO_2 decreased precipitously, more significantly in regions that went on to infarct (45%) compared to surrounding peri-infarct regions (52%). Three and 7 hours after reperfusion, the venous sO_2 recovered but not back to the baseline level. Twenty-four and 72 hours after reperfusion, the venous sO_2 in regions of infarction (83%) increased above baseline, approaching the mean arterial sO_2 value of 90%, while the venous sO_2 in peri-infarct regions (71%) returned near the baseline level. The OEF of infarct regions rose from 21% (baseline) to 52% (during MCAO) and declined to below baseline values (12%) 72 hours after the onset of occlusion, indicating tissue death. In contrast, the OEF of peri-infarct regions increased to 45% during the occlusion and returned to the baseline level after 72 hours. Taking advantage of the high spatial resolution of PAM and vessel segmentation technique, we also observed bimodal sO_2 distributions within veins that crossed the infarct and peri-infarct regions. It was due to the convergence of the venous blood with distinct sO_2 from infarct and peri-infarct regions.

Our findings demonstrate that PAM is capable of longitudinally measuring cerebral oxygen metabolism during focal ischemia, with minimal invasiveness and high resolution. Unbiased cluster analysis of OEF during ischemia has successfully predicted tissue fate (dead or alive), suggesting that an OEF threshold exists.

Visible Brainwide Networks at Single-neuron Resolution with Micro-Optical Sectioning Tomography

Qingming Luo

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Revealing neural circuit mechanisms is critical for understanding brain functions. Significant progress in dissecting neural connections has been made using optical imaging with fluorescence labels, especially in dissecting local connections. However, acquiring and tracing brain-wide, long-distance neural circuits at the neurite level remains a substantial challenge. We obtained a three-dimensional structural data set of a Golgi-stained whole mouse brain at the neurite level with our developed Micro-Optical Sectioning Tomography (MOST) system, which directly demonstrates the whole-brain structural connectivity at the neurite level in a standard format. In this talk, we will clarify the unique features of the MOST, which is a novel microscopic optical imaging technique aiming at providing a submicron resolution by sectioning. We will demonstrate the most recent results with the new protocol combining a novel resin-embedding method for maintaining fluorescence, an automated fluorescence MOST system for long-term stable imaging, and a digital reconstruction-registration-annotation pipeline for tracing the axonal pathways in the mouse brain. We also discuss the potential optical techniques and methods and present the challenges to be urgently solved for neuroscientists and information scientists.

[1] A. Li, H. Gong, B. Zhang, Q. Wang, C. Yan, J. Wu, Q. Liu, S. Zeng, and Q. Luo, "Micro-optical sectioning tomography to obtain a high-resolution atlas of the mouse brain," *Science*, 330(6009):1404-8 (2010).

[2] B. Zhang, A. Li, Z. Yang, J. Wu, Q. Luo, and H. Gong, "Modified Golgi-Cox method for micrometer scale sectioning of the whole mouse brain," *J Neurosci Meth*, 197(1): 1-5(2011).

[3] Q. Wang, A. Li, H. Gong, D. Xu, and Q. Luo, "Quantitative study on the hygroscopic expansion of spurr resin to obtain a high-resolution atlas of the mouse brain", *Exp Bio Med* 237:1134-1141 (2012)

[4] H. Gong, S. Zeng, C. Yan, X. Lv, Z. Yang, T. Xu, Z. Feng, W. Ding, X. Qi, A. Li, J. Wu, Q. Luo, "Continuously tracing brain-wide long-distance axonal projections in mice at a one-micron voxel resolution", *NeuroImage* 74 (2013) 87-98

[5] T. Zheng, Z. Yang, A. Li, X. Lv, Z. Zhou, X. Wang, X. Qi, S. Li, Q. Luo, H. Gong, and S. Zeng, "Visualization of brain circuits using two-photon fluorescence micro-optical sectioning tomography", *Optics Express*, 21(8): 9839-9850 (2013)

[6] T. Quan, T. Zheng, Z. Yang, W. Ding, S. Li, J. Li, H. Zhou, Q. Luo, H. Gong, and S. Zeng, "NeuroGPS: automated localization of neurons for brain circuits using L1 minimization model", *Scientific Reports*, 3: 1414, DOI: 10.1038/srep01414

[7] C Yan, A Li, B Zhang, W Ding, Q Luo, H Gong, "Automated and Accurate Detection of Soma Location and Surface Morphology in Large-Scale 3D Neuron Images", *PloS ONE* 8 (4), e62579

[8] Z Yang, B Hu, Y Zhang, Q Luo, H Gong, "Development of a Plastic Embedding Method for Large-Volume and Fluorescent-Protein-Expressing Tissues", *PloS ONE* 8 (4), e60877

Title

Role of epigenetic mechanisms in activity-dependent neurological recovery following spinal cord injury

Abstract

Spinal cord injury (SCI) is a devastating condition that imposes major individual and societal costs. The extent of the neurological impairment following SCI varies but the factors that limit the subsequent neurological recovery are not well understood. Activity-Based Restorative Therapy is a unique and personalized therapeutic intervention for individuals with SCI. We have developed animal and cell-based models of ABRT and have shown that induction of remyelination is a potential mechanism for neurological recovery in this therapeutic intervention. While we understand that such remyelination requires neuronal activation and induction of gene expression, how these changes lead to induction of remyelination remains unclear. DNA methylation in CpG islands as well as in gene enhancer and promoter regions is a key mechanism that regulates gene expression. DNA methylation has been shown to be involved in regulation of activity-dependent developmental process such as neurogenesis, memory formation as well psychiatric disorders its role in oligodendrocyte differentiation and myelination has not been sufficiently examined. The discovery that DNA methylation is regulated by activity, even after short-term stimulation (1 hr) opens up the possibilities that DNA methylation in neurons or oligodendrocytes can regulate remyelination. We are using inhibitors of epigenetic mechanisms (DNA methylation and histone acetylation) to examine, *in vitro*, whether epigenetic mechanisms play a role in regulating myelination in an activity-dependent system.

Neuronal Activity-Induced Changes of DNA Methylation Landscape in the Adult Brain

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Epigenetic modifications of chromatin molecules, including the genomic DNA and histone proteins, play critical roles in orchestrating transcriptomes of all cell types and their developmental potentials. Emerging evidence suggests important roles for epigenetic regulation in activity-dependent brain functions, including synaptic plasticity, learning and memory, circadian rhythm, drug addiction, and adult neurogenesis. Recent studies have further implicated critical roles of DNA methylation changes in neural plasticity. Our early studies have shown that neuronal stimulation induces DNA demethylation at specific promoters of brain-derived neurotrophic factor and fibroblast growth factor 1 in a Gadd45b- and TET1-dependent fashion in the adult mouse dentate gyrus (Ma et al. Science 2009; Guo et al. Cell 2011). Using a next-generation sequencing-based method for genome-wide analysis at a single-nucleotide resolution, we recently showed that 1.4% of all CpGs measured exhibit rapid active demethylation or de novo methylation in adult mouse dentate granule neurons in vivo before and after synchronous neuronal activation (Guo et al. Nat. Neurosci. 2011). These activity-modified CpGs exhibit a broad genomic distribution with significant enrichment in low-CpG density regions, and are associated with brain-specific genes related to neuronal plasticity. Our study implicates modification of the neuronal DNA methylome as a previously under-appreciated mechanism for activity-dependent epigenetic regulation in the adult nervous system. I will present our latest progress on molecular mechanisms regulating DNA methylation dynamics in the adult brain, genome-wide analysis of DNA modifications, and implication of active DNA demethylation in brain disorders.

Abstract

Neuronal activity modifies the DNA CpG and non- CpG methylation landscape in the adult brain

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DNA methylation, a critical regulator for brain function and dysfunction, has been traditionally viewed as a highly stable epigenetic mark in postmitotic cells, and has been believed to be restricted to CpG dinucleotides in metazoan genomes. How extensively the neuronal DNA CpG and non CpG methylation is regulated by neuronal activity is unknown. Using a next-generation sequencing–based method for genome-wide analysis at single-nucleotide resolution, we quantitatively compared the CpG and non CpG methylation landscape of adult mouse dentate granule neurons *in vivo* before and after synchronous neuronal activation, and we show that neuronal DNA from adult mouse dentate gyrus harbors a significant amount of non-CpG methylation (mCpH, H = A/C/T). Neuronal CpH methylation is conserved in human brains, depleted at protein-DNA interaction sites, and anti-correlates with gene expression. Both mCpG and mCpH repress transcription in vitro. The presence of CpH methylation significantly expands the proportion of neuronal genome under cytosine methylation regulation; our findings

thus provide a new perspective on this key epigenetic modification in neuronal identity, plasticity and disorders.

ALS and Epigenetic Regulation of Motor Neuron Cell Death and Skeletal Muscle Mitochondria

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DNA methylation is an epigenetic mechanism for gene silencing engaged by DNA methyltransferase (Dnmt)-catalyzed methyl group transfer to carbon-5 in cytosine residues in gene regulatory and nonpromoter regions. Dnmt3a can also function as a DNA demethylase. It is unknown if aberrant DNA methylation can cause neurodegeneration. We tested the hypothesis that Dnmts can mediate neuronal cell death. During apoptosis of motor neuron-like NSC34 cells induced by the DNA damaging agent camptothecin, levels of Dnmt1 and Dnmt3a increased five-fold and two-fold, respectively, and 5-methylcytosine accumulated in nuclei. Enforced expression of Dnmt3a induced degeneration of cultured NSC34 cells. Truncation mutation of the Dnmt3a catalytic domain and Dnmt3a RNAi blocked apoptosis of cultured neurons. Inhibition of Dnmt catalytic activity with RG108 and procainamide protected cultured neurons from excessive DNA methylation and apoptosis. In vivo, Dnmt1 and Dnmt3a are expressed differentially during mouse brain and spinal cord maturation and in adulthood when Dnmt3a is abundant in synapses and mitochondria. The presence of Dnmt3a in mitochondria suggests an epigenetic regulation of mitochondrial DNA (mtDNA). By immunoblotting Dnmt3a was present in highly pure mitochondria of adult mouse CNS and skeletal muscle and adult human cerebral cortex. Dnmt1 was not detected in mouse CNS or muscle mitochondria. Immunofluorescence confirmed the mitochondrial localization of Dnmt3a and showed 5-methylcytosine in mitochondria. Because mitochondria are implicated in amyotrophic lateral sclerosis (ALS) pathogenesis, we evaluated Dnmt3a and 5-methylcytosine levels in ALS mice. In *superoxide dismutase-1* (SOD1) transgenic mouse models of ALS, Dnmt3a protein levels were reduced at presymptomatic or early disease in skeletal muscle and spinal cord. By DNA pyrosequencing and ELISA, 5-methycytosine was present in mtDNA of CNS and muscle. ALS mice had aberrant mtDNA methylation. Mitochondria with extensively methylated DNA were found sequestered into autophagosomes, and mitophagy was increased and mitochondrial content was decreased in skeletal muscle of SOD1 mice. In human ALS, motor neurons showed significant abnormalities in Dnmt1, Dnmt3a, and 5-methylcytosine. Thus, motor neurons can engage epigenetic mechanisms to drive apoptosis, involving Dnmts and increased DNA methylation. Furthermore, we demonstrate a mitochondrial localization of Dnmt3a and a tissue-preferential cytosine methylation of mtDNA. This work reveals new aspects of mitochondrial biology involving epigenetics and suggests that aberrant epigenetic modification of skeletal muscle and CNS mtDNA and nuclear DNA in ALS could be a possible disease mechanism.

DNA Methylation and Expression of Retina-Specific Genes

The retina is a highly organized tissue with specialized cells types that develop from a common retinal progenitor cell type. Our previous studies have shown that in the adult mouse, genes that are preferentially expressed in photoreceptors (PRs) from the retinal outer nuclear layer (ONL) are unmethylated in PRs but are methylated in non-expressing, non-PR cells from the retinal inner nuclear layer (INL). To understand when these differential DNA methylation patterns are established and to begin to understand their significance to retinal development, we are investigating the methylation status of PR-specific genes in the developing mouse retina. We have identified a region of hypomethylation near the transcription start sites of *Rbp3* and *Rho* that precedes expression at time points as early as E11.5 and hypothesize that this differential methylation could be involved in mediating the retinal lineage determination process. In parallel, we have completed a genome-wide identification of differentially methylated regions, comparing adult retina to brain and have correlated these regions with tissue-specific expression.

Diffusion MRI Tractography: Uses for Group Analysis

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Diffusion tensor imaging (DTI) can provide rich anatomical information about the brain white matter. Various white matter tracts, which are not visible on T1- and T2-weighted anatomical scans, can be clearly delineated on DTI-derived maps. Group analysis of the white matter is based on the hypothesis that there are changes in white matter anatomy related to development and aging, degeneration and regeneration, or reorganization of the microstructures. For the statistical analysis to identify differences between groups, quantification of the white matter anatomy is essential. While voxel-based statistical analysis, which is performed after image normalization to the template space, carries maximum information about localization of the difference between groups, the statistical power to detect such a difference is not necessarily high, because of the low signal-to-noise ratio of each voxel, and the difficulty in identifying the corresponding voxel across subjects. To increase the signal-to-noise ratio and to ameliorate the effect of inaccurate image normalization, voxel grouping, such as defining regions of interest (ROI) to obtain the average value of the voxels inside the region, is often used. The statistical power is maximized when the size and shape of the ROI exactly follow the locations of the "true" difference, where the difference is seen histologically. If we have an *a priori* hypothesis that the difference can be seen in the entire trajectory of specific fiber tracts, using tractography to define ROIs—which is often called a "tract-of-interest" (TOI) approach—is a logical choice. Although a TOI approach is suitable for sensitively detecting small but widespread changes within a white matter tract, there are several drawbacks. Since a limited number of fiber tracts can be reproducibly identified across individuals, many brain areas and fiber tracts remain unexamined. Tractography results are also known to be highly sensitive to the choice of algorithm and parameters. A large degree of cross-subject variability of reconstructed tracts has also been reported. These limitations should be considered thoroughly when using a TOI approach for white matter exploration.

Introduction: Sensitive detection of changes in tissue microstructure in the CNS and PNS may lead us to better ways to detect and diagnose pathology, such as mild TBI (mTBI). The beaded morphology axons exhibit following mechanical, chemical, or metabolic insults1,2 may accompany mTBI, but Diffusion weighted MRI (DWI) methods like DTI may not be sensitive or specific enough to detect these subtle changes. New methods, like the Double Pulsed Field Gradient (d-PFG) MR multiple scattering techniques3,4, which provide microstructural information, such as average cell size, cell shape, and microscopic anisotropy, may be able to â€œdrill into the voxelâ€ and detect these microscopic changes. In these studies d-PFG MRI was used to tease microstructural features of axons by measurements of pore diameters in CNS white matter and beading in a PNS injury model.

Material & Methods: Fixed samples of porcine spinal cord and rat brain were used for mapping the fiber diameter. Fixed rat sciatic nerve which was subjected to axial tension sufficient to induce beading or minimal tension to straighten out their macroscopic undulation (control) was used for the mTBI model. 7T and 14T vertical bore magnets equipped with micro-2.5 gradient set (Bruker Biospin) were used. D-PFG filtered MRI sequences were applied. A bi-compartmental model (free and restricted diffusion) was used to fit the data5

Results & Discussion: The calculated fiber diameter distributions are in the range expected for spinal cord white matter and rat corpus callosum. The injured sciatic nerve showed clear evidence of beading.

Conclusion: dPFG MRI shows promise for characterizing tissue microstructural features, which could serve as a novel contrast in several CNS and PNS pathologies. \ Methods like dPFG MRI should allow us to learn more about tissue microstructure to be able to perform in situ and in vivo histology.

References: 1. Markin V. S. et al., Biophys. J., Volume 76 (1999), 2852-2860, 2. Budde M. D., Frank J. A., Proc. Natl. Acad. Sci., Volume 107 (2010), 14472-14477, 3. Mitra P. P., Phys. Rev. B, Volume 51 (1995), 15074-15078, 4. Komlosh M. E. et al., J. Magn. Reson. Volume 208 (2011), 1168-1177, 5. E. Ã–sarslan J. Magn. Reson. Volume 199 (2009), 56-67 \

Optical imaging and DTI of Animal Models of Brain Injury

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Animal models of traumatic brain injury (TBI) have been essential to understand the consequences and mechanisms of injury. Compared to the abrupt and heterogeneous nature of human TBI, animal models investigated under well-controlled laboratory conditions have enabled the characterization of injury starting from the moment of initial trauma. However, recent work has indicated that TBI, including mild TBI, may lead to chronic neurodegenerative disorders that manifest many years or decades after the initial insults, such as chronic traumatic encephalopathy (CTE). Currently, CTE can only be diagnosed in post-mortem brain sections. A renewed effort is underway to understand the connection between head trauma and chronic neurological dysfunction and identify biomarkers capable of assessing disease activity in living individuals. Advanced magnetic resonance imaging techniques, including diffusion tensor imaging, offer improved sensitivity to subtle injury and it is believed that DTI may play a role in diagnosis of mild TBI and CTE. In this talk, I will highlight work applying DTI to animal models of TBI in order to understand the pathology underlying the DTI changes. Moreover, current efforts to apply DTI to animal models that more closely mimic human mild TBI will be discussed in the context of identifying the relathipship between TBI and chronic neurodegeneration.

Anatomic & Functional Connectivity Using MRI/DTI to Differentiate Minimally Conscious, Vegetative and Locked-In States

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Abstract

This lecture will focus on the anatomical differentiation and white matter changes that identify minimally conscious, vegetative and locked-in states. MRI data is extremely relevant in understanding and identifying the neural substrates in various states of disordered consciousness. While there are diffuse metabolic changes throughout the brain, the anatomical lesions that are critical in differentiation of these states lies in midbrain and brain stem structures. Anatomical and functional brain mapping is more precise in identifying and differentiating these disordered states of consciousness. The current standard in labeling disorders of consciousness utilizes coma scales lacks validity, reliability and specificity of these states.

Using induced pluripotent stem cells to discover new treatments for Parkinson's disease

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Induced pluripotent stem cells (iPSCs) can individualize cell therapy and the modeling of neurodegenerative diseases, such as Parkinson's disease (PD). Since lineage restriction limits the clinical applications of adult neural stem cells for treating PD, human pluripotent stem cells have emerged as the ethical and scalable source of safe and functional nigral type dopaminergic neurons for synaptic restoration. We propose that ongoing preclinical studies are essential for making informed decisions regarding the transplantation of either isogenic or HLA-matched human nigral dopaminergic neurons in future clinical trials. Cellular reprogramming technology has also provided a unique tool that can interpret the genetic basis for an individual's risk of developing PD into clinically meaningful information. Recent in vitro studies highlight the convergence of cell biological pathways that lead to neurodegeneration in different familial forms of PD. Such phenotypic convergence may be used to interpret the cell biological signatures of iPSC-derived neural cells from an individual with sporadic PD. Along these lines of investigation, iPSCs are enabling research for new treatments in PD.

Amyloid-β Precursor Protein and the Regulation of Neurogenesis: Implications for the Treatment of Alzheimer's Disease and Traumatic Brain Injury

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Alzheimer's disease (AD) is a neurodegenerative disease characterized by the reactivation of the cell cycle in post-mitotic, terminally differentiated, neurons in the neocortex and hippocampus of the AD brain. This is evidenced by 1) the ectopic expression of cell cycle proteins, 2) chromosomal replication (endoreduplication), 3) elevated mitochondrial DNA and COX-1 expression, suggestive of *de novo* mitochondrion synthesis, 4) upregulated growth factor signal transduction pathways, 5) attempted microtubule dissociation (tau hyperphosphorylation) and 6) amyloid-β precursor protein (AβPP) processing towards the amyloidogenic pathway, in differentiated neurons in those regions of the brain affected by AD. To determine the role of AβPP in the regulation of cell cycle dynamics, we examined AβPP expression and processing in human embryonic stem cells, a developmental model. AβPP and all the enzymatic machinery to process AβPP via the amyloidogenic (β-secretase and γ-secretase components) and non-amyloidogenic (α-secretase) pathways were expressed in hESC, and this expression changed with their differentiation into neural precursor cells (NPC). The differential processing of AβPP via secretase enzymes was found to regulate the proliferation and differentiation of hESC. hESC's endogenously produce Aβ, which when added exogenously in soluble and fibrillar forms but not oligomeric forms, markedly increased hESC proliferation. The inhibition of AβPP cleavage by β-secretase inhibitors significantly suppressed hESC proliferation and promoted nestin expression, an early marker of NPC formation. The induction of NPC differentiation via the non-amyloidogenic pathway was confirmed by the addition of secreted AβPPα, which suppresses hESC proliferation and promotes the formation of NPC. Together, these data indicate that the early expression and differential processing of AβPP is normally required for embryonic neurogenesis. We have further discovered that AβPP expression and processing are under the control of the reproductive hormones human chorionic gonadotropin/luteinizing hormone (hCG/LH) and the sex steroids progesterone and 17β-estradiol, such that when the ratio of hCG/sex steroid is low, AβPP is processed towards the non-amyloidogenic pathway that drives neural differentiation. However, when the hCG/sex steroid ratio is high, such as occurs following menopause/andropause, AβPP is processed towards the amyloidogenic pathway which drives NPC proliferation. With respect to AD, these results indicate that the hormonal dysregulation associated with aging may promote amyloidogenic AβPP processing and the aberrant reactivation of the cell cycle in post-mitotic neurons, as observed in the AD brain. Moreover, these results indicate hESC as a useful model system for understanding not only neurogenesis, but also neurodegeneration and neuroregeneration. These results have important implications for current therapeutic strategies aimed at stem cell replacement and the modulation of Aβ production for the treatment of neurodegenerative diseases and head trauma.

Advancing Stem Cell Science Towards Therapies for Patients: CIRM's Initiatives and Funding Opportunities

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Advancing science into therapies for patients is a complex and expensive path to travel, and the uncertainty of success, particularly for innovative technologies, makes the funding of the translational steps towards and into the clinic, particularly challenging. This talk will address the role the California Institute for Regenerative Medicine (CIRM) is playing in advancing stem cell science into the clinic, providing information on the scope of programs, initiatives, and funding opportunities to help investigators from academia and companies make progress in their research.

Created in 2004 through the passage of Proposition 71 by voters in California, CIRM's funding began in late 2006, focusing on CIRM's mission to advance stem cell science towards therapies for patients with chronic disease and injuries. CIRM's first 5 years set priorities based on establishing a strong foundation for leadership in stem cell research, seeding the entire field with discoveries using a variety of stem cell-based platforms, resulting in over $1.7 billion in 600 awards to 60 institutions/companies, publication of more than 1,200 journal articles, construction of 12 dedicated stem cell facilities, recruitment of more than 130 stem cell researchers to the state, and 77 translational projects in more than 30 therapeutic areas.

The focus for the next 5 years is on driving the science to clinical trials to generate evidence of therapeutic benefit for patients, engaging industry in strategic partnerships to facilitate commercialization of therapies, while maintaining a pipeline of discovery including the basic science, which has the potential to fundamentally transform the field and medicine.

Controlling the magnitude and duration of local innate immune responses with polymer carriers of Toll-like receptor 7/8 agonists

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The capacity of Toll-like receptor 7/8 agonists (TLR 7/8a) to directly activate all major human dendritic cell subsets, as well as B-cells and monocytes, make these agents particularly attractive for use as both direct immunotherapeutic agents and vaccine adjuvants. Despite their potential, small molecule TLR 7/8a undergo rapid clearance following injection leading to transient (< 24 hours) and weak immune cell activation at target sites (e.g., tumor and draining lymphatics). To address these limitations and improve local activation, we have developed chemical strategies for linking multiple TLR 7/8a to biocompatible polymer carriers, referred to as Poly-TLR 7/8a, to retain the agonist within the tumor and proximal draining lymphatics following intratumoral injection. Combinatorial synthesis was used to prepare a number of unique Poly-TLR 7/8a. These were fluorescently labeled to facilitate tracking *in vivo* and administered into the footpads of mice. At serial time points, proximal draining lymph nodes were isolated and evaluated for polymer persistence and local innate immune stimulation using flow cytometry. We show that Poly-TLR 7/8a is retained in the proximal draining lymphatics for up to 23 days and is taken up by ~ 20-40% of all dendritic cells at peak response (~ 96 hr). Poly-TLR 7/8a enhanced local dendritic cell recruitment (> 50 fold, relative to the small molecule TLR 7/8a), upregulated CD80 and CD86 co-stimulatory molecule expression and induced high levels of Th1-polarizing cytokines (IFN-gamma and IL-12p40). No systemic toxicity was observed, as serum cytokines (IL-6, IL-12p40, etc.) were undetectable in mice that received Poly-TLR-7/8a. Finally, we have shown that the persistence (from 2 days to > 4 weeks) and magnitude of local innate immune responses can be modulated by varying precisely defined chemical parameters. In summary, Poly-TLR 7/8a is more potent and less toxic than currently available small molecule TLR 7/8a and offers a chemically tunable delivery scaffold for modulating immune responses at target sites. Our current efforts are focused on evaluating whether persistence of local innate immune stimulation by Poly-TLR 7/8a can reverse immunosuppression and promote tumor clearance in mice.

Adenovirus Vectors From Various Serotypes Induce Distinct Cytokine Profiles

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Multiple Adenovirus (Ad) vectors which differ markedly in their basic biology are being pursued for HIV vaccine development. Despite the known importance of innate immune activation on adaptive response formation, differences in innate responses to Ads remain poorly characterized. We thus evaluated cytokine responses to Ad vector stimulation both post-vaccination of rhesus monkeys *in vivo* and in human PBMC *in vitro*.

Rhesus monkeys were immunized with $3x10^{10}$vp Ad5, 35, 26, 48, or Ad5HVR48 and human PBMC were stimulated *in vitro* with 10^3vp/cell Ad5, 35, 26, 48, or Ad5/35 chimeric vectors. In certain experiments, human PBMC were pre-incubated with anti-Ad receptor monoclonal antibodies or were depleted of specific PBMC cellular subsets by magnetic separation. Supernatant and serum cytokines were measured by luminex and ELISA.

Monkeys vaccinated with the CD46-using vectors Ad35 and Ad26 displayed higher induction of antiviral and proinflammatory (e.g. IFNγ, IP-10, IL-6) cytokines compared to Ad5 which uses CAR on d1 post-vaccination ($p<0.05$, Mann-Whitney U test). Vectors containing Ad48 HVR's (Ad48 and Ad5HVR48) produced a temporally

separate cytokine response at d7 post-vaccination. In human PBMC, Ad35 and Ad26 induced higher levels of anti-viral and proinflammatory cytokines (e.g. IFNα2, IFNγ, IL-1β) compared to Ad5 ($p<0.01$, Kruskal-Wallis test; Dunn's correction). Replacement of Ad5 fiber with that of Ad35 (Ad5f35) increased Ad5 cytokine induction ($p<0.05$), while Ad35f5 displayed decreased stimulation relative to Ad35. Blockade of CD46, but not CAR, by mAb decreased interferon induction by Ad35 and Ad26 ($p<0.05$). Depletion of pDC from PBMC resulted decreased IFNα2 ($p<0.05$) and TNFα ($p<0.05$), depletion of T cells reduced IFNγ ($p<0.05$), and depletion of monocytes/macrophages decreased inflammatory marker IL-1RA ($p<0.01$) induction.

These data demonstrate that CD46-uilizing Ad35 and Ad26 vectors induce profoundly different innate immune responses as compared to CAR-utilizing Ad5 vectors both *in vitro* and *in vivo*. These responses are influenced by both the primary receptor usage of the vector as well as other virus capsid components. The cytokine milieu elicited by these vectors depends on the input from several PBMC cellular subsets and may depend on cellular cross-talk between them. These findings confirm that major biologic differences exist among Ad vectors and may help explain their different adaptive immune phenotypes.

Exposed-cortex optical mapping of brain function: From animal to man

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Brain imaging using light can provide functional contrast based on the differing absorption properties of oxy- and deoxy-hemoglobin in blood. Additional contrast can be generated by endogenous and exogenous fluorescence, such as from metabolites NADH and FAD, or in animals, from genetically targeted fluorescent proteins and calcium sensitive fluorophores. Since light is strongly scattered in tissue, high resolution imaging of the brain's cells and vasculature requires exposure the cortex via a craniotomy, allowing direct visualization and the use of techniques such as in-vivo two-photon microscopy. Commonly performed in rodent models, optical imaging and in-vivo microscopy of the exposed cortex has provided myriad insights into neuronal activity and organization, disease states, brain development and neurovascular coupling; the relationship between neuronal activity and blood flow. In this talk, optical techniques and related results exploring physiology and functional mapping using light in rodent models will be described. Additional studies will also be shown where these same techniques were translated for acquisition of data on exposed human cortex during surgical resection of benign and malignant lesions.

Title:

Surgery for eloquent area tumors: Integration of New Imaging Modalities

Abstract:

The goals of surgery for tumors in eloquent areas of the brain are to maximize tumor resection yet preserving the functional status of the patient. Integration of new imaging modalities and brain mapping techniques play a large role during resection. Identifying and preserving areas of function during awake craniotomy procedures is the “gold standard” during neurosurgical operations. We have recently integrated newer anatomical tools using digital atlas based strategies to better define areas of function and measuring areas of resectability in “real-time” using the intraoperative MRI (iMRI). Here we discuss newer imaging strategies and pitfalls during glioma resection in eloquent brain areas.

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Real time Open MRI Guidance for Percutaneous Nerve Decompression

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Keywords: Interventional MRI, Open MRI, Nerve decompression, Minimally invasive surgery

Introduction

Real time Open MRI provides an opportunity for surgical manipulation of tissue on a percutaneous basis. However, it has never been possible to carry out actual decompression of nerve entrapments in this fashion. Interventional MRI has been used to carry out diagnostic and therapeutic treatment of nerve entrapments in large scale formal outcome trials involving anti-inflammatory or muscle spasm reduction methods. In this case, the images revealed that the serial administration of the treatment agents resulted in relieving the mechanical entrapment. This methodology provides a model for further study of the use of MRI for percutaneous minimally invasive surgery.

Methods

FLASH sequences in 0.25T Philips Open interventional system were used to obtain images at 12 second intervals in a patient with a symptomatic adhesive entrapment of the distal sciatic nerve in the lower thigh. Preoperative MR Neurography at 1.5T demonstrated a focal adhesion of the nerve to adjacent semi-membranosus muscle with associated nerve hyperintensity in the area of the adhesion. Pain and Tinel's sign were appreciated at the site during "exam under MRI." A 10 centimeter titanium needle was used to apply Hylenex human recombinant hyaluronidase during a series of images. The Hylenex included 600 units in 3 cc. In addition, 0.5 cc of celestone 6 mg/ml and 3 cc of 0.75 marcaine without epinephrine were applied.

The procedure involved advancing the titanium needle to a position at the interface between the nerve and the muscle and injecting the medication agents in sequence in volumes of 0.1 to 0.5 cc. The device was advanced as the adhesion separated and was also moved to different areas of the adhesion during the procedure.

Results

At the start of the procedure, the distal sciatic nerve was visualized and the clinical relevance of the abnormality observed on MR Neurography was confirmed by exam under MRI revealing sensitivity at the point of adhesion and Tinel's into the area of radiating pain perceived by the patient.

The introduction of treatment agents resulted in an MRI guided hydro-dissection effect. This progressed steadily until the nerve was mostly surrounded by the injected agent. The result of the procedure was the relief of the adhesive nerve entrapment.

Conclusion

Although angiography provides for interventional work inside blood vessels and endoscopy provides for percutaneous surgery in various spaces susceptible to illumination and video visualization, Open MRI is particularly well suited for the development of a surgical armamentarium for percutaneous work in solid spaces adjacent to delicate tissues such as peripheral nerves.

This report reveals a methodological basis for using MRI with controlled fluid percussion augmented with hyaluronidase to separate tissues subject to pathologic and symptomatic adhesions.

Note: This work had not been submitted for publication in any other journal, website or format.

Title: Advances in Atherosclerosis Imaging: Is multimodal carotid imaging the path to improved stroke prediction?

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One of the greatest challenges in stroke prevention involves determining which patients may benefit from early interventions. Despite advances in therapy and improved healthcare delivery, stroke remains the second leading cause of death worldwide. One major contributing risk factor is carotid atherosclerosis, which confers a greater annual stroke risk to individuals with significant plaque build-up causing arterial stenosis. Earlier studies have identified a benefit for carotid endarterectomy to surgically remove substantial artery-narrowing plaque in individuals with symptomatic disease. The application of endarterectomy to those with less severe and asymptomatic disease is still unclear. Nevertheless, individuals with asymptomatic carotid atherosclerosis constitute the bulk of patients who will develop potentially disabling strokes. A means of telling which patients with asymptomatic disease have vulnerable plaque prone to rupture that will cause stroke is the challenge that needs to be answered.

Imaging methods for the carotid arteries looking at plaque properties have advanced greatly with magnetic resonance imaging able to accurately identify high-risk plaque components such as a lipid-rich necrotic core or intra-plaque hemorrhage. However, additional gains in assessing plaque vulnerability may be obtained by looking at plaque inflammation, as atherosclerosis is a fundamentally inflammatory process. Other imaging modalities including FDG-PET and specialized molecular imaging approaches can potentially better inform clinicians as to the individual stroke risk of patients with carotid stenosis. One method explored by this presentation in greater depth is the use of ultrasmall superparamagnetic iron oxide particles (USPIO) – these nanoparticles are taken up by key inflammatory macrophages within plaque that can be visualized as signal loss with MRI. Promising evidence from earlier studies showed differences between USPIO activity and those with recently symptomatic carotid plaque as well as USPIO uptake reduction with statin therapy in the ATHEROMA trial. The recent study presented here offers a suggestion that USPIO

uptake may approach significance in predicting recurrent cardiovascular and cerebrovascular events within a year of follow-up from the USPIO-enhanced MRI study. This presentation additionally explores future avenues of research including multimodal methods that incorporate morphological, functional and even therapeutic attributes. The importance of an encompassing approach that looks at multiple means of analysis including biomechanical properties and looks at systemic atherosclerosis may better inform clinicians as to an individual's stroke risk. With further research in these promising technologies, it may be finally possible to personalize the treatment and prevention of stroke.

Abstract:

Despite the importance and high level of reliance on medical images in the practice of medicine, there have been major challenges associated with their inclusion in "big databases" in medical research. Medical images represent major challenges with regard to their size, the inherent difficulties with searching for and indexing medical image content, and the lack of a standard for "tagging" the images and the features within the images as well as many others. This topic is highly significant to the area of brain imaging and mapping and addressing these challenges is critical in order for medical images to play a significant role in the large data mining that will be essential for personalized medicine and to facilitate and enable scientific discovery on a large scale.

In neuroimaging, brain connectivity generally refers to associations between neural units from distinct brain locations. In this talk, we focus on several statistical modeling strategies to address current challenges for brain connectivity analysis. First, we introduce a multilevel model to summarize region level brain connectivity based on voxel level connectivity, and then make group level inferences. Second, we apply modern machine learning and statistical methods to investigate the spatial correlation between networks and then identify network based connectivity biomarkers for neural diseases. At last, we combine multimodal neuroimaging to gain additional information for brain connectivity analysis.

Title: The Efficacy of Upper Extremity Robot-Assisted Rehabilitation in Hemiparetic Stroke

Authors/Institutions: Susan S. Conroy, VA Maryland Health Care Systems, University of Maryland School of Medicine.

Presentation Type: Oral (Symposium on robot assisted rehabilitation)

Keywords: stroke, hemiparesis, therapeutic robots

Introduction: Stroke is the leading cause of disability among adults in the United States occurring in over 795,000 people each year. Hemiparesis affecting the arm and hand is a common impairment and insufficient recovery has a lasting negative impact on quality of life. Technological advances in engineering and neurological science have led to the development of innovative robotic tools for neurological rehabilitation. Determining the therapeutic effectiveness of upper extremity robotics to augment therapy and improve motor control through automated, interactive, and intensive repetitive training has been the focus of recent investigations.

Hypothesis: Scientific evidence supporting the efficacy of robot-assisted therapy in the rehabilitation of upper extremity motor deficits in patients with stroke is improving.

Methods: Recent randomized controlled studies and systematic reviews of robot-assisted training for the upper extremity will be presented and discussed.

Results/Conclusions: Evidence supporting robot-assisted upper extremity training is increasing. The Veterans Administration/Department of Defense and the American Heart Association 2010 guidelines for stroke care both recognize and endorse robot-assisted intervention for upper extremity training in patients with stroke.

Ankle robotics therapy during sub-acute hospitalization after hemiparetic stroke

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Introduction: Approximately 800,000 Americans are diagnosed with stroke each year, making it the greatest source of chronic physical disability in the U.S. There is wide agreement that functional deficits from residual hemiparesis can be partially offset through experience-dependent plasticity in the neural networks that control movement. Modern robotic devices offer a means to shape these emergent networks by engaging the affected limb(s) with high volumes of goal-directed motor practice during therapy. Thus modular lower extremity (LE) robotics may offer a valuable avenue for restoring neuromotor control in stroke survivors with hemiparetic gait. Prior results with chronic stroke suggest that intensive seated visuomotor training with an ankle robot (Anklebot) may enhance paretic ankle motor control and carry over to gait function; however this approach has not been tested in the earliest phases of rehabilitation, when natural recovery is underway. Question: What are the feasibility and efficacy of daily training with the Anklebot during early sub-acute hospitalization post-stroke?

Methods: Inpatients from a stroke rehabilitation unit were randomly assigned to either an Anklebot group or a passive stretching-mobilization group. After regular daily therapies, seated Anklebot training employed an â€œassist-as-neededâ€ approach during > 200 volitional targeted paretic ankle movements in the plantar-dorsiflexion and inversion-eversion ranges. The activity consisted of playing a videogame by attempting to move a cursor through moving gates that crossed the screen at different spatial levels, thereby stimulating volitional effort in multiple directions. Training difficulty was adjusted to each participantâ€™s active range of motion and target success rate. The stretching group received >200 daily mobilizations of the paretic ankle delivered in these same ranges of motion by the trained research team. All sessions lasted about 1 hour.

Results: As expected both groups walked overground significantly faster at discharge, however the robot group improved more in interlimb symmetry. Greater gains in paretic ankle motor control also were observed in the robot group, seen as increased peak and mean angular speeds, and increased smoothness of movement trajectories. There were no study-related adverse events.

Conclusions: Intensive LE robotic therapy is feasible for use during sub-acute phase hospitalization post-stroke without compromising usual inpatient care. Ankle robotics in this early phase may improve the rate of decreasing paretic ankle impairments, with potential to accelerate restoration of gait and complement traditional pre-gait activities. Future imaging studies with electroencephalography and/or functional near-infrared spectroscopy over the course of Anklebot therapy will help discern cortical network changes associated with motor learning and brain plasticity.

Introduction: The impact of stroke on walking function is often significant, negatively affecting an individualâ€™s mobility and ability to perform everyday activities. Many individuals have residual deficits even after completion of all conventional rehabilitation therapy. Moreover, increasing evidence suggests that conventional rehabilitation does not provide adequate task-repetitive practice to optimize motor learning and recovery across the continuum of care. Robotics may offer a promising avenue for gait therapy by providing a customizable motor learning platform. The Baltimore VA Medical Center has developed a 2 degree-of-freedom â€œassist-as-neededâ€ ankle robot (â€œAnklebotâ€ [illegible] stroke. The Anklebot is capable of functions post independently modulating specific sub-tasks within the gait cycle to better address the heterogeneity of hemiparetic stroke recovery. In this study, we investigate whether a modular, deficit-adjusted approach to using the Anklebot for locomotor training can lead to sustainable gains in selected aspects of gait function in chronic stroke. Here, we describe and present preliminary data from a single chronic stroke survivor.

Methods: A novel sub event-triggered control system was used, which enables precise timing of robotic assistance to key functional deficits of hemiparetic gait, thereby affording the opportunity to customize robotic support to individual gait deficit profiles. Training was adaptive in that, training parameters were adjusted across the intervention based on subject performance, and tolerance. The case subject entered the program with pronounced foot drop (<2Â° volitional dorsiflexion) making it a logical target for intervention. Training was conducted during 3xweekly visits with 48 hours between visits. On each visit, the session began with TM walking at self-selected speed (visit 1: 30 cm/s, visit 18: 36 cm/s) with the robot in a â€œrecord-onlyâ€ mode. This was followed by two 20-min trials of Anklebot-assisted walking during which the Anklebot provided dorsiflexion assistance, commencing immediately following toe-off and peaking during mid-swing.

Results: We compared the peak dorsiflexion angle during unassisted walking at admission, discharge, and 6-week follow-up. There was a marked increase in the peak dorsiflexion angle at discharge (2.5Â°Â±1.1Â° vs. 7Â°Â±0.5Â°), and this improvement was durably retained at 6 weeks follow-up (8Â°Â±0.8Â°). Notably, patient reported permanent discard of her assistive device (AFO) in her activities of daily life. The patientâ€™s independent floor walking speed also increased durably (47.4Â±6.1 cm/s vs. 76.5Â±2.4 cm/s vs. 81.9Â±10.2 cm/s) that may be attributed to improved volitional control at the paretic ankle.

Conclusions: Six weeks of Anklebot-assisted gait training eliminated drop foot and increased overground gait speed in a single stroke subject. We are currently using the approach in subjects with impaired push-off propulsion. We anticipate that this modular, deficit-adjusted approach will, over time, â€œteachâ€ the central nervous system to take over from gradual withdrawal of robotic support in order to supplant the robot with volitional movements at the paretic ankle.

COOMPARISON OF PENETRATING BRAIN INJURIES IN RUSSIA AND TAJIKISTAN DURING PEACE TIME AND LOCAL MILITARY CONFLICTS

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Introduction. We analyzed the structure of gunshot penetrating brain injury (PBI) and its outcome in Russia and Tajikistan in peace-time and local military conflicts (based on the experience of Burdenko neurosurgery Institute and the Republican hospital in Dushanbe).

Material and methods. We analyzed 113 patients with PBI treated at Burdenko Institute from 1993 to 2010 and 116 pts with PBI got in local military conflicts in Tajikistan and treated in Dushanbe hospital from 1992 to 2000. Patients from Burdenko Institute included 98 male (87%) and 15 female, with a mean age of 31,9 years. The majority of the injured were admitted to Burdenko Institute from different hospitals of Moscow and other regions of Russia. After admission to Burdenko Institute all patients underwent CT scanning in dynamics. Patients in Dushanbe Hospital included 88 male (76%) and 28 female, with a mean age of 25,6 years; of them 16 (14%) were children aged 6-15 years. The majority of patients (93%) got to a neurosurgical department directly from the scene and only 7% were transferred from other hospitals. Of all the admitted to Dushanbe hospital only 20 pts (17%) underwent CT, the rest underwent craniography.

Results. Burdenko Group included the following types of missile: bullets (pistol, rifle, Kalashnokov sub-machine-gun in some cases) - 81 pts (71,7%), shotgun bullets - 8 pts (7,1%), shrapnel/shell fragments - 19 pts (16,8%) and home-made missile - 5 pts (4,4%) while Dushanbe hospital Group included: bullets - 90 pts (77,6%): of them - Kalashnikov submachine-gun - 59 pts (66%), pistol or rifle - 31 pts (34%); shrapnel/shell fragments - 26 pts (22,4%).

The number of perforating (through and through) injuries was significantly higher in Dushanbe Group compared to Burdenko Group - 43,1% against 8,9%, and 39 (78%) of 50 perforating injuries (Dushanbe Group) were caused by the Kalashnikov submachine-gun.

Only 34 (30%) of 113 injured patients were in coma in Burdenko Group, while the percent of the injured in coma in Dushanbe Group was more than twice higher (68%; $p<0,01$).

Surgical procedures included: craniotomy or craniectomy, debridement, lobectomy, ventriculostomy, vascular injury repair, dural closure. Duroplasty was performed with pericranium and in some cases with temporal muscle or aponeurosis. Postoperative period was characterized by CSF leaks and cranio-cerebral infectious complications in 35 (15,3%) of 229 cases with the former (CSF leak) being a significant risk factor ($p<0,01$) for development of cranio-cerebral infectious complications.

The majority of died patients had GCS score raging 3-8, multilobar brain damage, transventricular and brain stem injuries. Outcomes were marked as follows: dead - 58 (25,3%): vegetative state + severe disability - 26 (11,4 %), moderate disability + good recovery - 145 (63,3 %). Massive brain damage was the main cause of mortality (35%) in Dushanbe Group compared to Burdenko Group (16%).

Conclusions

Gunshot injury in civilian situations is usually caused by a low-velocity missile compared to that of in military situations. Perforating injuries are not so frequent thus explaining a lower mortality rate, especially within the first 24 hours of injury.

Irradiating CNS Tumors – We've Personalized Targeting, Can We Personalize Dose?

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Ionizing radiation therapy plays a key role in the management of primary and metastatic brain tumors. Advanced techniques including 3-D Conformal Radiation, Intensity Modulated Radiation Therapy (IMRT), and Stereotactic Radiosurgery (SRS) are utilized to deliver dose to a personalized target. The challenge remains as to what total dose, fractionation, and timing may be best for each patient with his or her specific clinical disease. Personalized models of treatment response to radiation are necessary to create individualized dose plans. In addition to tumor response factors, host response factors are important. Our current research effort has been involved in developing such models for primary brain tumors and metastatic disease.

Susceptibility Tensor Imaging

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Introduction: Magnetic response of biologic tissue is a fundamental process of MRI. Until very recently, however, B0-field induced magnetic field perturbation within tissues has largely been regarded as a source of image artifacts. Recent methodological developments have produced unparalleled anatomical details of the brain based on magnetic susceptibility effect. Susceptibility has also been found to be an excellent indicator of iron stores in certain brain regions and a measure of myelination in brain white matter. Susceptibility anisotropy measured by susceptibility tensor imaging (STI) offers a new window into white matter architecture and brain connectivity at a spatial resolution higher than that is currently available (1).

Methods: The interactions between biological tissues and the strong magnetic field generated by an MRI scanner produce a heterogeneous and complex field pattern around biomolecules, cells and organelles. Within an image voxel, the distribution of the field can be characterized by a set of multipole tensors in the spatial frequency domain (p-space) (2). The first term is called monopole; the second term is called dipole; the third term is called quadrupole and so on (Eq. [1]). For a given applied magnetic field, these multipoles can be measured by sampling the p-space which is accomplished by either applying a set of encoding gradients before data acquisition or equivalently by shifting k-space data in 3D. While the anisotropy of the dipole and quadrupole tensors can be measured with this strategy, the anisotropy of the monopole has been measured by varying the orientations of the brain within the magnet (Eq. [2]).

$$\Phi(\mathbf{p}) = \Phi_0 + \gamma B_0 t\, \hat{\mathbf{p}}^{\mathrm{T}} \boldsymbol{\chi}_d \hat{\mathbf{p}}\, p + \gamma B_0 t\, \hat{\mathbf{p}}^{\mathrm{T}} \boldsymbol{\chi}_q \hat{\mathbf{p}}\, p^2 \quad [1]$$

$$\Phi_0(\mathbf{k}) = \mu_0 \left(\frac{1}{3} \hat{\mathbf{H}}^{\mathrm{T}} \boldsymbol{\chi}(\mathbf{k}) \hat{\mathbf{H}} - \hat{\mathbf{H}} \bullet \mathbf{k} \frac{\mathbf{k}^{\mathrm{T}} \boldsymbol{\chi}(\mathbf{k}) \hat{\mathbf{H}}}{k^2} \right) \gamma H t \quad [2]$$

Results: The anisotropy in the monopole has been demonstrated in mouse brains *ex vivo* (1), human brain specimens (3) and human brains *in vivo* (4, 5). Monopole susceptibility tensors have been measured in mouse brains, kidneys and human brains. It has been shown that fiber tracts can be reconstructed by following the eigenvectors of the tensor (6). Dipole and quadrupole tensors can be measured without any rotation by performing a p-space analysis. By sampling the p-space from a single volume of gradient echo images, these tensors have been measured in simulated axon bundles, mouse brains and human brains. In the simulated axons, the orientation of the minor eigenvector agreed with the axon orientation. In the brain experiments, similarity between the eigenvector orientation and underlying fiber orientation was observed.

Discussions and Conclusions: Susceptibility tensor imaging is a new non-invasive MRI technique for studying brain microstructure and connectivity. The principle of STI is based on the interaction between brain tissues and the strong magnetic field provided by MRI scanners. The interaction is stronger at higher field strength. STI may provide an alternative method for studying brain connectivity at a spatial resolution exceeding current capability.

References: **1**. C. Liu, Magn Reson Med 2010; 63: 1471–1477. **2**. C. Liu & W. Li, NeuroImage 2013; 67: 193-202. **3**. J. Lee et al, PNAS 2010; 107: 5130-5135. **4**. W. Li et al, NeuroImage 2012 ; 59 : 2088-2097. **5**. X. Li, et al, NueroImage 2012 ; 62 : 314-330. **6**. C. Liu, et al, NeuroImage 2012 ; 59 : 1290-1298.

INTRODUCTION: Diffusion-weighted magnetic resonance (MR) signals reflect information about underlying tissue microstructure and architecture. We propose a quantitative, efficient, and robust mathematical and physical framework for representing diffusion-weighted MR imaging (MRI) data obtained in "q-space," and the corresponding "mean apparent propagator (MAP)" describing molecular displacements in "r-space." We also define and map novel quantitative descriptors of diffusion, which can be computed robustly using this framework.

METHODS: The technique is based on the idea of expressing the three-dimensional q-space MR signal in terms of the Hermite functions, which provide rapid convergence in both real and Fourier spaces that make them ideally suited to problems of q-space signal analysis and MAP estimation. This representation is an extension of its one-dimensional (1D) counterpart (Ozarslan et al., in Proc Intl Soc Mag Reson Med, vol. 16, 2008, p. 35.), which was shown to accurately represent the signal decay originating from very different environments (from free to restricted) (Ozarslan et al., in Excursions in Harmonic Analysis: The February Fourier Talks at the Norbert Wiener Center, New York: Springer Science + Business Media, 2013, vol. 2, pp. 373â€“400.). Employing a suitable metric that quantifies the dissimilarity between two MAPs, we devised several new quantitative parameters, or MRI "stains," derived from the entire MAP that capture distinct novel features about nervous tissue microstructure. Among these, propagator anisotropy (PA) measures the dissimilarity between the full MAP and its isotropic counterpart. Similarly, its dissimilarity to DTI's Gaussian propagator led to the definition of the non-Gaussianity (NG) index. Finally, the return-to-the origin probability (RTOP) can be computed, which is shown to be related to the average volume of an ensemble of isolated pores irrespective of their shape, orientation, and coherence.

RESULTS: MR images of an excised marmoset brain were acquired at 7T using a diffusion-weighted EPI sequence. A total of 489 acquisitions were performed by sampling q-space on 7 different shells defined by b-values ranging from 200 to 9800 s/mm2. MAP-MRI technique provided accurate resolution of complex tissue cytoarchitecture in regions with orientational complexity. The introduced indices provided several new contrasts, which could be sensitive to changes associated with numerous cerebral diseases. MAP-MRI reconstructions obtained using a small fraction of the entire data set (b-value up to 3200 s/mm2) suggested the ability of the technique to overcome the technical limitations of q-space MRI acquisitions in human subjects.

CONCLUSION: MAP-MRI is a new method that extends diffusion tensor imaging (DTI) to generate a true and proper propagator or MAP in each voxel. By quantifying the non-Gaussian character of the diffusion process, this method more completely characterizes diffusion anisotropy.

Axon Diameter Distribution (ADD) MRI

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Abstract: INTRODUCTION: Myelinated axons transmit signals at a speed proportional to their diameter. The axon diameter distribution (ADD) provides information about how much information can be transmitted along a fascicle. Here we present an integrated and general experimental and theoretical framework for using diffusion MRI data to measure the ADD in brain white matter throughout the entire Central Nervous System (CNS).

3D DWI (q-space) data analysis: We obtain estimates of the ADD for fascicles in any orientation, anywhere within a brain volume. We first determined the direction of maximum diffusivity and then estimate the DW signal attenuation profile, E(qâŠ¥) vs. qâŠ¥, perpendicular to the fascicleâ€™s main axis. This data is then used with models of diffusion in impermeable tubes to estimate the E(qâŠ¥) that would be produced by a pack of axons with a particular ADD. The estimated ADD is obtained by minimizing the residual errors between the predicted signals and measured E(qâŠ¥) vs. qâŠ¥ data. Our calculation of E(qâŠ¥) also corrects for the motional narrowing artifact caused by using finite-width diffusion gradient pulses without which, the ADD would be artifactually skewed towards having smaller diameter axons.

ADD models: We use a novel statistical models to fit ADD data. This is a parametric probability density function (pdf) developed by maximizing the information transmitted along fascicles subject to anatomical and energetic constraints. This pdf was found to be more robust than the lognormal, Î³.

METHODS: Marmoset brains obtained after necropsy were fixed in 4% formaldahyde, then rehydrated and packed in Fomblin. They were scanned with a Bruker 7T (Avance III) microimager. The q-space MRI protocol consisted of 496 DWI acquisitions on 7 shells (q-values between 13 and 93 mm-1) with Î´=2.85 ms with diffusion times (Î”) of 20 and 40 ms.

RESULTS: Multivariate k-means clustering was performed using a set consisting of the hindered compartment fractions, diffusion coefficients, and two parameters of the estimated ADD in each voxel within white matter pathways.

CONCLUSION: The ADD is a high-value histological feature that is now accessible in all brain white matter pathways. The need for a nonparametric ADD model is acute in both developmental biology and in pathological applications where one has no a priori knowledge about how skewed or heavy tailed the ADD is or even whether it is mono or multi-modal. Because of the relatively low overhead of estimating average propagators in each voxel now, this new MRI approach has the potential to be translated in vivo to both animal and humans with current DWI hardware.

Keywords	*Diffusion Tensor Imaging (primary keyword)*
Abstract Topics	Diffusion Tensor Imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	To present a novel technique for using diffusion MRI data to measure the Axonal Diameter Distribution in brain white matter throughout the entire Central Nervous System (CNS).

3D INSTRUCTIVE NANOFIBERS SCAFFOLDS MIMIC NEURAL PROGENITOR NICHES

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Keywords: Biomaterials; PLA Electrospun nanofibers; glial and neuronal progenitors.

Regenerative medicine is probably one of the most scientific promises and challenges in this first part of the 21st Century. Different strategies of cell therapy or tissue engineering are being developed and scaffolds able to deliver signals to the biological environment play a leading role. The question arising is whether the biological functionality of the scaffolds depends directly upon the properties their constitutive biomaterials. This ability to produce signals and stimuli able to control cell fate is what is generally understood as the role of smart biomaterials. The requirements on the scaffolds depend on the specific tissue application and this means that constraints on the scaffold design will need to be considered (geometry, handability, suturability, mechanical properties, etc). The present talk tries to show how physico-chemical properties of biomaterials are relevant issues in scaffold production fabrication and processing and play a leading role in mimicking neural progenitor niches.

To develop tissue engineering strategies useful for repairing damage in the central nervous system (CNS) it is essential to design scaffolds that emulate the NSC niche and its tight control of neural cell genesis, growth, and differentiation. The aim of this study is to develop an artificial scaffold of polylactic acid (PLA) nanofibers to induce an environment that mimic embryonic radial glia organization and favors neuronal migration after a brain injury. For this purpose uncoated 3D electrospun random and aligned PLA nanofibers were used to study the behavior of neural cells from mice cerebral cortices in vitro and in vivo. Both, random and aligned fibers supported neural cells growth, but only aligned fibers permit neural cells invasion. Moreover, aligned fibers induce immature phenotypes in neuronal and glial cell cultures. Glial cells grown in aligned fibers showed bipolar shape and expressed the radial glia markers Nestin and BLbP, and the progenitor marker Pax6. On the other hand, neurons grown in aligned fibers were characterized by a decrease in the expression of Î²-III Tubullin, and an increase of neuron restricted progenitor marker, Tbr2 and the stem cell marker Sox2.

In the in vivo model, aligned PLA nanofibers implanted in the somatosensory cortex, were not encapsulated by a scar and did not seem to have elicited a foreign body reaction. It was also discovered that immature glial cells stained with Nestin, progenitorâ€™s cells and blood vessels could penetrate into the aligned nanofibers after 7 days of implantation, indicating that the topography of the scaffold is playing a role in the migration of neural cells inside the injury.

Our results suggest that aligned PLA nanofibres may mimic some of the physical and biochemical characteristics of the NSC niche. Its mechanical and surface properties may act synergistically in the modulation of bipotential and glial restricted progenitor and neuronal progenitorâ€™s phenotypes, while topography may play an important role in angiogenesis in vivo.

Novel Neural Devices Based on Nano Technologies: The Future Is Here

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Inspired from biological systems, nanotechnology is beginning to revolutionize medicine including improved prevention, diagnosis, and treatment of numerous diseases. This talk will summarize efforts over the past decade that have synthesized novel nanoparticles, nanotubes, and other nanomaterials to improve medicine. Efforts focused on the use of nanomaterials to minimize immune cell interactions, inhibit infection, and increase tissue growth will be especially emphasized. Tissue systems covered will include the nervous system, specifically treating stroke-induced neural tissue damage and paralysis. Due to complications translating in vitro to in vivo results, only in vivo studies will be emphasized here. Materials to be covered will include carbon nanotubes, ceramics, metals, polymers, and composites thereof. Self-assembled nano-chemistries will also be emphasized. As the US FDA has now approved several nanomaterials for medical applications, recent results from FDA trials will also be discussed. In summary, this talk will provide the latest information concerning the design and use of numerous nanomaterials in neural regenerative medicine while highlighting what is necessary for this field to continue to grow.

New Nanostructured Multifunctional Surfaces of Titanium Alloys Obtained by Directed Irradiation Synthesis (DIS) for Treatments of Spinal Cord Damages

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ABSTRACT \ \ Spinal cord has a determinant role in locomotion of the muscle-skeletal system and its relationship with brain functions is also crucial for human movement achievements; any kind of disease or trauma can have a severe detrimental effect in life quality of patients. Some clinical treatments for spinal pathologies like Anterior Cervical Diskectomy (ACD), Posterior Cervicothoracic Osteotomy (PCO), Anterior Lumbar Interbody Fusion (ALIF), Lumbar Disk Arthroplasty (LDA) and some others, can affect not only spine bone and discs, but also spinal cord. On the other hand, some focused spinal cord treatments like Spinal Cord Arteriovenous Malformations (AVMs) and Intramedullary Spinal Cord Cavernous Malformation (ISCCM) can involve also bone and discs of the surrounded areas. Most of the conventional treatments to these pathologies imply using medical grade of titanium (Ti) and its alloys as plates, screws, wires, porous implants, etc. Despite using these materials have proved to have a high clinical success, it is also recognized their limitation because this practice belongs to first and second generation of biomaterials: both the material itself and its surface only act at micro-scale level. Regeneration and tissue growth medicine practices require third generation biomaterials which are those designed to stimulate both cells and biological environment at molecular (nano) scale level. In that sense, nanotechnology and nanomaterial cutting-edge developments have emerged as the unique alternative to successfully addressed any critical damage of tissues as those above mentioned. Some authors like Dalby et al. (2009), McNnamara et al. (2010) and Wheeldon et al. (2010) have recently showed that stem cells adhesion, differentiation, proliferation and gene expression can be enhanced when cells are in contact with nano-structured biomaterials surfaces. In our research, we have developed new nano-structured surfaces on commercially pure titanium (CP Ti) and Ti6Al4V alloy by using Directed Irradiation Synthesis (DIS) technique. These materials are surface modified with multifunctional purposes: different nano-structuring parameters are expected to generate different tissue growth stimulation for bone, discs and spinal cord tissues. Evaluated processing conditions have been reasonable repeatable to control nano-structuring of both kind of Ti materials. Contact angle testing of Ti nano-structuring samples obtained by DIS enabled measurement of decreasing of hydrophobicity (between 40-50%). DIS technique have proved to be suitable to reproduce these multifunctional surfaces and the biological testing of these new surfaces with different cells lines showed promising results with respect to previous hypothesis established for every involved tissue for future complex and complete treatment of spinal cord damages and tissues associated. \

Graphene Platform for Bio-sensing and Neuro-electronic Interface Applications

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ABSTRACT

Graphene has become a rising star in the physics and electronics community due to its excellent transport properties, including high carrier mobilities and transconductance values and its ultra-thin body nature allowing for ultimate device scaling. Working with chemical vapor deposition (CVD) grown graphene adds another level of flexibility to device fabrication and integration – we will show in detail later that CVD graphene can be transferred to any desirable substrate and is proposed here to be easily integrated with other materials like protein. Using this new material as the channel of our field-effect transistor device offers excellent mechanical, chemical, electrical and bio-compatible properties.

Electrolyte-gated graphene field-effect transistors have been demonstrated as chemical and bio-sensors. We are exploring graphene as a material for detecting food-borne pathogens like E.coli O157:H7 and Salmonella in various saline media. Electronic charge in membranes of these captured bacteria modifies the conductance of graphene via electrostatic interaction. Simultaneous fluorescence and electrical results show sensitivity of 3-4 bacteria cells per sensor and high selectivity towards pathogenic strain. Electrical signal readout of conductance change after bacteria attachment to antibodies allows us to integrate the sensor with existing state of the art data acquisition circuits. Our goal is to enable single cell bacteria detection using these sensors. Also, parallel detection of various forms of pathogens on same chip via functionalizing different antibodies on graphene is possible. This scalable pathway for fabricating functionalized graphene sensors can also be used in detection of neuron spiking activity. We propose a novel electrolyte-gated graphene-protein FET for noninvasive extracellular stimulation and recording of electrical activities of neural stem cells. Benefiting from the excellent electronic and optical properties of graphene and its easy and flexible processing nature, we expect an in depth study of neural activities with higher spatial resolution and larger signal-to-noise ratio to allow for a general application in neurobiology, biosensories and neural prostheses research.

Overview of the NICHD Brain and Tissue Bank: Potential Contributions to Brain Mapping

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The NICHD Brain and Tissue Bank for Developmental Disorders (NICHD BTB) has been funded since 1991 to further research that will improve the lives of patients in the developmentally disabled community and lead to prevention or effective treatments for the hundreds of disorders that affect humanity. The research has focused on biochemical, histological, genetic, structural and imaging analyses of tissue collected at autopsy. The NICHD BTB works closely with researchers to ensure that the tissue collected meets the requirement for specific research projects.

The NICHD BTB is prepared to work with researchers in the brain imaging field to enhance their research. Brain banks are in the unique position in that they have obtained IRB approval to obtain brain donations for research through prior arrangements with multiple sources of human tissue. In our particular case the NICHD BTB works with national support groups for various disorders as well as with Medical Examiner's Offices. The NICHD BTB has the means to collect, process and distribute the tissue. Tissue is stored both in formalin and frozen at -80^{o}C. Over 3,500 donor families have donated brain and systemic tissue for research. Over 900 researchers in 23 countries have utilized the tissue to publish over 600 scientific publications. Research performed on living patients or animal models requires verification of results at the cellular or tissue level. For these verifications, access to post-mortem human tissue is a necessity. Post mortem tissue has been shown to be invaluable for research purposes.

ABSTRACT FOR 10TH ANNUAL CONGRESS OF THE SOCIETY FOR BRAIN MAPPING AND THERAPEUTICS

Brain Tissue Banks Session
Day 3, Tuesday, May 14, 2013
Chair: B. Daly

Speaker: Elaine Shen, Scientific Program Manager, Allen Institute for Brain Science, Seattle, WA

Title:
Mapping the Human Brain Transcriptome

Authors:
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Abstract:
The Allen Human Brain Atlas is a publicly available online atlas of the adult human brain that integrates anatomic and genomic information with visualization and data mining tools, thus providing a resource for scientists investigating links between brain anatomy, gene expression and brain function. Primary components of the resource are (1) an 'all genes-all structures' dataset of genome-wide microarray-based gene expression profiles from anatomically discrete and defined cortical, subcortical, cerebellar and brainstem structures across multiple (n = 6) brains; and (2) a portfolio of *in situ* hybridization-based gene expression studies in targeted gene sets and brain regions. Basic functionality includes the abilities to search anatomic structures to view and compare gene expression and to search for a specific gene or genes in various data representations. Normalized array data are viewable graphically across multiple structures and multiple gene probes in heat map format or in colorized human brain representations, whereas ISH data are viewable as primary images. Magnetic resonance image (MRI) data provides the infrastructure for two- and three-dimensional spatial visualization of gene expression in its anatomic context. Brain banks, tissue repositories, medical examiner offices and MRI collaborators were essential partners and subject matter experts in the creation of the Atlas, which depended on postmortem tissue that met inclusionary and exclusionary criteria and was of high quality for histology and gene expression data generation and analyses. A standardized pipeline of tissue dissection, MR imaging, preservation and tracking processes was implemented at distinct tissue bank or collection sites. At each site, multiple groups and individuals coordinated activities at each step of the pipeline to ensure

completion in a timely manner with the highest tissue and MRI data quality possible. These intra- and inter-institution collaborative partnerships were a fundamental component of the Allen Human Brain Atlas project.

The Medical Examiners Role in Facilitating the Donation of Brain and Tissue for Research

Ling Li, M.D., David R. Fowler, M.D.

Office of the Chief Medical Examiner, State of Maryland

The Office of the Chief Medical Examiner (OCME) is responsible for the medicolegal death investigation in the State of Maryland. Traditionally, the work done by medical examiners has been viewed mainly as serving the criminal justice system. During the last several decades, however, the role of medical examiners has evolved from criminal justice service focus to a broader involvement that now significantly benefit the public health, public safety, education and research in medicine, and the development of strategies to prevent injury, disease, and death. Medical examiners are part of decision makers for tissue recovery and organ transplantations in the United States. The medical examiners at the OCME have also plaid a significant role in facilitating the donation of brain and tissue for medical research. Since many potential brain and tissue donors, especially normal control tissues donors fall under medicolegal jurisdiction, the medical examiners bear responsibility to authorize or deny the recovery of autopsy tissues on a case-by-case basis. The medical examiners make decision that the brain and tissue recovery for medical research can be done in all potential cases, without detriment to evidence collection, postmortem examination, and determination of cause and manner of death.

The legal and ethical issues regarding the use of human tissues for medical research have received great public attention. To protect the deceased's organs and tissues from being used for postmortem research that is incompatible with the deceased or their families' wishes and values, the medical examiners make sure that informed consent is obtained for all tissue donations.

In the past two decades, the OCME at the State of Maryland has been working closely with the Brain and Tissue Bank for Developmental Disorders of the National Institute of Child Health and Human Development (NICHD), the Allen Institute for Brain Science, the Maryland Psychiatric Research Center (MPRC), and the Lieber Institute for Brain Development (LIBD) to obtain donation of autopsy brains and tissues from more than 1000 donors. The OCME has provided invaluable source of human brain and tissues for medical research

Title: Genomic measurements in post-mortem brain tissue and its relevance to development and psychiatric illness

Andrew E Jaffe, Thomas M. Hyde, Daniel R. Weinberger, Joel E. Kleinman

Post-mortem human brain tissue has the ability to identify novel neurobiology of illness, including discovering new gene transcripts associated both directly with illness and though genetic variation associated with clinical risk. We review key findings using post-mortem brain tissue over the last five years, including molecular "switches" - genes that have different transcriptional preferences in fetal versus adult life periods. Lastly we discuss integrating genomic measurements from different applications, including genetic variation, gene expression, and DNA methylation in the dorsolateral prefrontal cortex in hundreds of non-psychiatric controls and patients diagnosed with schizophrenia. This work highlights the importance of large and well-characterized post-mortem human brain collections for the study of brain development and psychiatric illness.

"The Genetics of Stress"
: Sensitized limbic response to stress is associated with life trauma and genetic influence underlying the link between stress and addiction.

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Life trauma increases allostatic load in the limbic circuit involved in stress and reward-related response. Sensitized limbic regions from repeated trauma enhances susceptibility to stress-related illnesses and addictive behaviors. Research also indicated that the influence of certain genetic variations on stress-related brain response could underlie the relationship between stress and addiction. Specifically, the limbic circuit may represent a key region of epigenetic changes underlying stress-related neuronal adaptations that promote the risk of addictive disorders. However, few studies examined the genetic influences on neural substrate underlying life trauma and addiction. In order to understand neural substrates underlying trauma-related neuroadaptions and genetic variations related to stress and addiction, we conducted two neuroimaging studies using functional magnetic resonance imaging (fMRI) in healthy and cocaine-dependent individuals.

First, in order to understand the effect of life trauma on neural response, brain activity was examined in 73 healthy individuals (24 women; age M=27.52, SD=7.8), while participants were engaged in brief guided imagery of individualized stress and neutral-relaxing situations. Life trauma subscale of Cumulative Adversity Interview (CAI; Turner et al., 1995) was used to measure traumatic experience. Fasting morning cortisol response was also collected. Results indicated that life trauma was significantly associated with blunted, fasting morning cortisol level ($r = -31$, $p<0.01$). Trauma score was also positively correlated with stress-induced brain activity in the left lateral PFC, right amygdala, hippocampus, medial temporal lobe and cerebellum. Additionally, blunted morning cortisol level was associated with hyperactive response to stress in the right amygdala and medial temporal lobe, suggesting the important role of limbic function in life trauma and disrupted hypothalamic-pituitary-adrenal axis reactivity.

Second, to understand genetic influences on the stress-related neural responses, drug craving, and cocaine relapse risk, we examined the role of the kappa opioid receptor gene (OPRK1), which has been frequently associated with stress reactivity. Specifically, we examined the effects of the OPRK1 rs6989350 C>G on cocaine craving and its association with relapse outcome using combined fMRI and clinical outcome design in cocaine-dependent patients (CG: N=10; CC: N=57). The CG patients displayed higher stress-induced cocaine craving ($p=.019$) and greater relapse rate ($p=0.0075$) than the CC patients. In addition, in a subgroup of patients who underwent fMRI (N=13), the CG group showed hyperactivity in the limbic-mid brain regions during stress and cocaine-cue compared with the neutral condition. Increased activity in the right amygdala and hippocampus was also evident during stress exposure in CG vs. CC group.

To summarize, the current study indicate that hyperactive limbic response to stress is associated with trauma-related neuronal adaptations in healthy individuals. In addition, increased limbic activity was also associated with variations in stress-related OPRK1 rs6989350 C>G gene (CG/CC), suggesting its importance in the link between stress and addiction. The limbic region is a key brain region associated with trauma-related neuroadaptations and stress genes such as the OPRK that plays a role in mediating stress effects on addictive processes. The current study also support an emerging view that an interaction among gene, environmental stress, and drug abuse influence neuroadaptations and behavioral outcome in stress-related addictive behaviors.

TBI and DNA methylation in select immune function gene promoter regions and repetitive elements: a repeated measures case-control study of U.S. military service members

Background and Objectives: Human and animal traumatic brain injury (TBI) studies have demonstrated that a profound inflammatory response is initiated immediately following TBI and is characterized by the expression of several cytokines with both pro- and anti-inflammatory functions. An epigenetic mechanism, DNA methylation is intrinsically linked to regulation of gene expression and is modifiable. We evaluated temporal changes in DNA methylation in select promoter regions of immune system-related genes in U.S. military service members with a TBI diagnosis, pre- and post-diagnosis, and in controls. **Methods:** TBI cases were identified via the Defense and Veterans Brain Injury Center (DVBIC) TBI Surveillance Database and identifiers linked with existing serum samples housed at the Department of Defense Serum Repository (DoDSR). From this eligible pool of cases, we randomly selected service members less than 40 years of age, with an injury date occurring after the start of their first OEF/OIF deployment but before any subsequent deployment, resulting in 93 mild, 38 moderate, and 13 severe cases in our study population. Controls (n=50) were randomly selected from all service members meeting the same criteria as cases without a diagnosis of TBI via the DVBIC database or Defense Medical Surveillance System. For each TBI case and control, one serum sample drawn within one year of first OIF/OEF deployment and one drawn after that deployment were identified. DNA was extracted from each sample and DNA methylation was measured via pyrosequencing, following bisulfite conversion. Percent methylated cytosine (%5-mC) was quantified in the promoter regions of interleukin (IL)1α, IL1β, IL6, IL8, IL10, IL13, NGF, TGFβ1, and TNFβ and in long interspersed nucleotide elements, LINE-1 and Alu. We used multivariate analysis of variance and generalized linear models to make temporal comparisons of %5-mC for cases (pre- to post-deployment) versus controls (pre- to post-deployment). An α of ≤0.05 indicated statistical significant. **Results**: Mild TBI cases had significantly higher IL1β promoter %5-mC post-deployment compared with cases pre-deployment. Moderate TBI cases had significantly higher %5-mC compared with controls, post-deployment. Although there were only 13 severe TBI cases in the study, we found a consistent pattern of reduced IL-8 methylation in severe cases compared with controls, post-deployment. **Discussion:** IL-1β, TNFβ, and IL-8 have been described as pro-inflammatory cytokines, which typically are over expressed after TBI. The patterns of methylation found in our study – ie, higher methylation in cases post- vs. pre-deployment and in cases vs. controls, post deployment – would likely be associated with decreased cytokine expression. Mechanistic studies are needed to understand the implications of these types of methylation changes with respect to RNA/protein expression. Studying the role of DNA methylation in the disease process of TBI has the potential to transform our understanding about the molecular etiology of this complex disease and could fuel novel therapeutic approaches, particularly since modifications in DNA methylation can potentially be reversed.

Traumatic brain injury (TBI) has acute and chronic outcomes for those who survive. Our understanding of the how genomic responses intersect with these processes is just beginning to take shape. Management of the TBI patient will take a multidisciplinary approach, incorporating gene-based, protein, and metabolic profiling into a clinical framework, drawing from the specialties of neurosurgery, neuroradiology, neurology, and psychiatry in order to advance our ability to more effectively treat brain injury and to predict outcome. From a molecular perspective I will examine possible mechanisms of response and methodological issues in correlating how genetic and epigenetic mechanisms may modify outcomes in TBI patient populations. Because study population sizes have been generally limited, I will discuss results on genes that have been the focus of independent studies. I also present a justification for testing more speculative candidate genes in recovery from TBI, to outline the importance of prioritizing functional variants.

Electric fields for the treatment of Glioblastomas: a sensitivity analysis

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Oscillating electric fields are being investigated as an adjunct and even an alternative to chemotherapy in the treatment of glioblastoma multiforme (GBM). The magnitude and direction of the electric field in the tumor are important determinants of treatment efficacy. We used computational methods to investigate the effect of variations in the dielectric properties of head tissues and in their thickness on the magnitude of the electric field in the brain. The effect of the tissues' complex geometry on the electric field distribution was also examined using a realistic head model.

We reviewed the literature to select average values and ranges for the electrical conductivity and relative permittivity of head tissues at 200 kHz. This range of values probably reflects experimental uncertainty in the measurements but may also include inter-subject variability. The range of thicknesses for the scalp, skull and CSF was intended to cover both normal and pathological cases. We used the finite element method to calculate the electric field in a 4-layer spherical model and one realistic model of the head. The electrode arrays and the current intensity used in the models mimicked as closely as possible a commercial device specifically designed for the treatment of tumors (www.novocure.com).

The results obtained with the spherical head model show that variations in the tissue permittivities have little effect on the magnitude of the electric field, mainly because capacitive currents are smaller than resistive currents. Variations in tissue conductivities within the published range can increase the magnitude of the electric field in the brain by up to 60% or decrease it by up to 40%, with the conductivities of the skull and the brain having the largest effect. Variations in layer thickness produce similar changes. Changes in the electric field magnitude are largest in more superficial brain regions. In the realistic head model, the electric field did not decrease slowly and smoothly with distance from the electrodes. Instead, local maxima were observed in the white matter at tissue boundaries approximately perpendicular to the direction of the current. In both models, the magnitude of the electric field was greater than 1 V/cm over large regions of the brain.

These calculations indicate that the electric field magnitude predicted in the brain is sufficiently high to arrest cell proliferation based upon in vitro experiments. Variations in tissue dielectric properties or in layer thickness could affect estimates of the magnitude of the electric field in the brain by up to about 50%. In the realistic head model, the complex geometry of tissue boundaries led to localized maxima in the white matter. The inclusion of anisotropy in the electrical conductivity of white matter in future models is expected to increase the observed shunting and spatial non-uniformity of the tumor treating electric fields. Improved patient specific models could provide a means to estimate the electric field in the tumor and to optimize its delivery. This new tool could be used in treatment planning, as well as to understand outcomes when using TTF therapy.

Abstract topics: Minimally invasive therapy

Keywords: Minimally invasive therapy

Educational objectives:

1) to understand the variability of outcomes in the use of alternating electric fields to treat glioblastomas. 2) to predict the electric field in the brain using computational models. 3) to propose methods to optimize the delivery of the electric field.

MR-Based Biotransport Models of the Brain and Solid Tumors

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Local drug delivery methods such as direct infusion, e.g. convection-enhanced delivery, are being used to improve targeting and increase uptake of drugs in the central nervous system and tumors. Rational design of such regional therapies requires new tools to evaluate drug transport issues specific to nervous tissue and tumor micro-environments. For instance, drug distributions are influenced by infusion parameters as well as underlying tissue microstructure and physiologic flows. To account for these factors, we are developing 3D models of the brain and tumors from high resolution magnetic resonance imaging (MRI) data.

Brain models incorporate diffusion tensor imaging (DTI) data, and uniquely account for the effects of embedded white matter fibers on extracellular transport. These models are being validated in rodent and primate brains. Flow fields and tracer distributions are predicted following direct infusions, e.g. convection-enhanced delivery, into injured brain regions and compared with MR measures of distribution.

Also, data from dynamic contrast enhanced-MRI (DCE-MRI) is used to account for the effect of heterogeneous leaky vasculature on tumor drug transport. These DCE-MRI based models account for elevated interstitial fluid pressure and abnormal extracellular flow patterns within the tumor interior. The effect on systemic and infusion delivery is then predicted.

Development of validated computational transport models will aid researchers in determining the potential of new drug compounds and designing effective treatment regimes. Research in extracellular transport is emerging as an increasingly important area of research in drug delivery, since the vast majority of therapeutic agents must traverse this space before reaching their targets. The need for this research has only increased with improved engineering and functionalization of therapeutic agents such as viral vectors and nanoparticles.

Similarities Between Glaucoma and Alzheimer's Disease

Stuart J. McKinnon - Duke Eye Center

Contact: Stuart McKinnon (stuart.mckinnon@duke.edu)

Abstract: Chronic neurodegenerations such as Alzheimerâ€™s disease (AD) manifest in the later decades of life, as does glaucoma, one of the leading causes of vision loss in the world. We have shown that molecular events that are seen in the brains of AD patients are also seen in the retinas and optic nerves in rodent glaucoma models and in human glaucoma patients. In addition, glaucoma is diagnosed more frequently in patients with AD than in patients without AD, and loss of peripheral vision is more rapid in glaucoma patients with AD than those without AD.

The retinal ganglion cell (RGC) is the primary retinal cell type damaged in glaucoma, and investigations into death mechanisms have determined that RGCs die by apoptosis, or programmed cell death. Central to apoptosis is the activation of specific proteases, termed caspases. Caspases are important in cellular execution and are activated not only in chronic neurodegenerations such as AD but also in RGCs after optic nerve axotomy. Caspases have been shown in our lab to be activated in rodent models of glaucoma. Our work has also shown that caspase-3, a major effector of the apoptotic cascade, is activated in RGCs and also cleaves amyloid precursor protein (APP, a major protein also involved with AD), to produce neurotoxic protein fragments that include amyloid-beta. We have also shown activation of caspase-8, which initiates apoptosis after activation of receptors of the tumor necrosis factor (TNF) superfamily. This suggests a new hypothesis for RGC death in glaucoma involving chronic amyloid-beta neurotoxicity, in a manner that mimics AD at the molecular level. With the loss of the protective effect of APP and the upregulation of toxic APP fragments that include amyloid-beta, RGCs ultimately die from chronic caspase activation, loss of synaptic homeostasis, amyloid-beta cytotoxicity and neuroinflammatory events.

The potential benefits from this work are that treatments contemplated for AD could be used to treat glaucoma. Conversely, novel neuroprotective strategies developed to treat glaucoma could be used to treat other chronic neurodegenerations as well.

Keywords	*General issues (primary keyword)* Anatomy Histopathology
Abstract Topics	Basic Neuroscience
The abstarct book's publications additonal Information summary	
Educational Objectives	1. Understand the similarities in molecular mechanisms between glaucoma and Alzheimerâ€™s disease. 2. Understand the roles of neuroinflammation in glaucoma. 3. Understand that the eyes can be potentially used as a paired model of chronic neurodegenerations such as Alzheimerâ€™s disease.

Society for Brain Mapping and Therapeutics
10th Annual World Congress
D. Benjamin Borson, M.A., J.D., Ph.D.
Borson Law Group, PC

Title: Bringing Inventions to the Wider World: Protection Strategies and Commercialization

Abstract:

Bringing improvements in health care to patients requires substantial investment in ideas, development of systems and methods, and refinements of diagnostic and therapeutic interventions. Investments are unlikely to be made unless returns on those investments can be realized. Return on investments is made possible through licensing. Licensing of patented inventions and other intellectual properties (IP) is well recognized as a primary tool for realizing return on investment. Patents provide exclusive rights to their owners. Successfully bringing innovations to the wider world requires coordinating business opportunities, scientific considerations, and legal realities. Implementing a world-wide strategy for protecting intellectual property requires knowledge of different countries' laws and procedures. Patent laws are changing, and recent court decisions on diagnosis and treatment patents provide ongoing challenges to understand how intellectual property laws are interpreted and enforced, both currently and into the future. All countries now use a form of a "first to file" regime that severely penalizes inventors for disclosing inventions before filing a patent application. With proper strategies combining business, science, and the law, commercializing important innovations results in improved patient care, recognition of innovators' contributions, and business success, all of which can lead to further innovation and improvements in health care.

ABSTRACTS

ASYMPTOMATIC ALZHEIMER'S DISEASE: MORPHOLOGICAL AND GENE EXPRESSION CHANGES

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It has been known for long time that the autopsy brains of normal older individuals can have amyloid neuritic plaques and neurofibrillary tangles characteristic of Alzheimer's disease (AD) and several prospective autopsy studies have corroborated these observations Our observations in the Baltimore Longitudinal Study of Aging (BLSA) indicate that approximately 50 % of the autopsy brains of cognitively normal subjects older than 80 years of age bear substantial amyloid neuritic plaques and neurofibrillary tangles, a state that we call asymptomatic Alzheimer's disease (ASYMAD) and others call preclinical AD, high pathology controls or high plaque non-demented subjects. In other prospective autopsy studies the frequency of ASYMAD ranges from 30% to 50 % The notion of ASYMAD is also supported by the detection of Aβ-amyloid in vivo by positron emission tomography (PET) scanning in the brains of ~ 50% of cognitively normal individuals older than 70 years. Our studies of ASYMAD have documented that this group of subjects has distinctive changes in cerebral blood flow many years before death.

In two studies of subjects in their 80s, we have observed significant hypertrophy of cerebral neurons, particularly in the CA1 region of the hippocampus, in ASYMAD subjects. We have interpreted this hypertrophy as a manifestation of brain plasticity and compensation that allows preservation of cognition in the presence of substantial AD pathology. In one of the studies, ASYMAD appeared strongly correlated with years of education and ApoE status. Preliminary studies of gene expression in ASYMAD subjects reveal changes in several genes relevant to AD, i.e., RAB5A, ABCA1, and IL-6.

Understanding the mechanism that allows some individuals to remain functionally normal despite the development of substantial AD pathology is very important as it can illuminate the pathogenesis of the disease and provide clues for its prevention and treatment.

TRACKING ALZHEIMER'S NEUROPATHOLOGY IN VIVO WITH IMAGING

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Through serial neuroimaging and neuropsychological evaluations of participants in the Baltimore Longitudinal Study of Aging (BLSA), we are examining changes in brain structure and function as predictors of cognitive decline and resilience. Since 1994, magnetic resonance imaging (MRI), positron emission tomography (PET) blood flow scans, and neuropsychological testing have been performed for participants, aged 55 and older. PET imaging of β-amyloid deposition using 11-C-Pittsburgh Compound B (PiB) was added in 2005, allowing for the assessment of Alzheimer's-related pathology in the living brain. Consistent with autopsy data from BLSA and other studies, approximately 30% of cognitively normal individuals have detectable amyloid deposition in the brain on *in vivo* imaging. Individuals with higher levels of β-amyloid are older, have greater longitudinal decline in memory and other cognitive functions, and show greater longitudinal increase in amyloid deposition. We are continuing to follow these individuals and are examining modifiers of both structural and functional brain changes and their associations with cognitive function. Neuroimaging biomarkers are contributing to the early detection of pathology and diagnosis of Alzheimer's disease (AD), to the selection and therapeutic monitoring of patients in clinical trials, and to differential diagnosis among dementia subtypes. Early prediction of cognitive impairment and factors that promote cognitive resilience in the face of pathology will be essential as new therapies are developed.

PLASMA PROTEOMICS AND RISK VARIANTS IN ALZHEIMER'S DISEASE

Madhav Thambisetty, MD, PhD
Laboratory of Behavioral Neuroscience, National Institute on Aging, NIH

There is a critical unmet need for peripheral biomarkers of Alzheimer's disease (AD) that accurately reflect neuropathology and are sensitive to heterogeneity in clinical progression. The identification of such "biologically relevant" biomarkers is likely to greatly enhance the development of effective disease-modifying treatments for AD. Until recently however, biomarker studies in AD relied upon a 'case versus control' approach that largely ignored two important and well-established observations:

1) A large proportion of non-demented elderly control subjects have significant Alzheimer's neuropathology in their brains
2) Patients with a clinical diagnosis of AD differ considerably in the severity of cognitive impairment and rates of clinical progression

We have overcome some of the important limitations of traditional biomarker studies by aiming to identify plasma proteins associated with specific endophenotypes of AD pathology such as amyloid deposition and brain atrophy as well as those related to clinical heterogeneity including disease severity and rate of clinical progression.
In parallel with our biomarker studies, independent large-scale Genome Wide Association Studies (GWAS) have identified several novel risk variants for AD. These novel AD risk genes however, occur commonly in the general population and exert small effects on disease risk, making it unlikely that they will be of utility as stand-alone predictors of disease risk. Nevertheless, they may offer important clues about mechanisms underlying disease pathogenesis.
It is striking that both our biomarker studies as well as recent GWAS offer independent converging lines of evidence implicating two biological pathways in AD pathogenesis i.e.

1) Complement modulation, and
2) Lipoprotein transport

We have applied multi-modal neuroimaging to ask how these novel AD risk variants in the complement and lipoprotein-related pathways influence brain function and amyloid deposition. In this presentation, I will discuss both our proteomic studies in plasma aimed at the discovery of biologically relevant AD biomarkers as well as present results on our studies relating AD-risk genes to endophenotypes of AD pathology.

CHANGES IN BRAIN FUNCTION ARE SEEN BEFORE COGNITIVE IMPAIRMENT BEGINS

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It is estimated that 16 million individuals in the U.S. alone will be diagnosed with dementia by the year 2050. There is an increasing need to identify early markers of brain change that occur prior to the onset of cognitive impairment in order to develop targeted intervention strategies. Here, we examine changes in resting-state brain function in participants from the Baltimore Longitudinal Study of Aging (BLSA). Using annual ^{15}O-water positron emission tomography (PET) scans with baseline collection beginning an average of 11 years prior to impairment, longitudinal changes in regional cerebral blood flow (rCBF) over a 7 year period were compared between participants who eventually developed cognitive impairment (n=22) and those who remained cognitively normal (n=99). Significant differences in rCBF change were seen prior to the onset of symptoms in those who subsequently developed impairment. These changes included greater longitudinal rCBF increases in orbitofrontal, medial frontal and anterior cingulate regions, and greater longitudinal decreases in parietal, occipital and thalamic regions. Whereas some studies have shown that increased activity occurs in posterior brain regions in the early stages of impairment, we show that anterior regions increase activity prior to the onset of symptoms. Our results suggest that functional changes can be detected many years prior to development of cognitive impairment, and that these changes occur in regions that develop early pathologic changes in Alzheimer's disease.

BRAIN QUANTIFICATION BY MRI IN PRIMARY PROGRESSIVE APHASIA

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Although the atrophy patterns associated with Primary Progressive Aphasia (PPA) have been described, because of the anatomic variability within the population, qualitative examination of the structural imaging has not always been useful to diagnose individual cases. A quantitative image analysis could allow the objective assessment of the atrophy, assisting the diagnosis and classifications. One of the most widely used quantitative analyses, normalization-based whole brain analysis, is largely dependent on the accuracy of the image transformation, which is a significant issue for PPA subjects that exhibit a large and variable degree of brain atrophy. To overcome these challenges, we used a state-of-the-art normalization algorithm and an automated 3D segmentation to quantify anatomic features in a population of 50 PPA patients and 27 age-matched normal controls.

In an exploratory analysis with Principal Component Analysis (PCA), using the volumes of 211 structures, we found the most similar participants in terms of anatomical features. Then, we created and tested predictive models to classify participants as control or as PPA, and into the three PPA variants. The ability to generalize this approach to an automated method for individual classification that could be applied to routine clinical practice has a great potential to assist the diagnosis of PPA and other neurodegenerative diseases.

We used the same approach to explore anatomical-functional correlations in diverse language domains. We found that participants who make predominantly phonologically plausible errors have greater atrophy in the left uncinate, inferior fronto-occipital fasciculus, and other deep grey and white matter structures, compared to participants with impairments in phonology-to-orthography conversion mechanisms. We also investigated the relationship between deficits in naming and areas of focal atrophy. Across all tasks, error rates were correlated with focal atrophy in the left anterior temporal and most of them with the posterior-inferior part of left temporal gyrus. These imaging data directly complement the imaging obtained from chronic stroke participants and furthers our understanding of the role of different brain regions involved in the language process.

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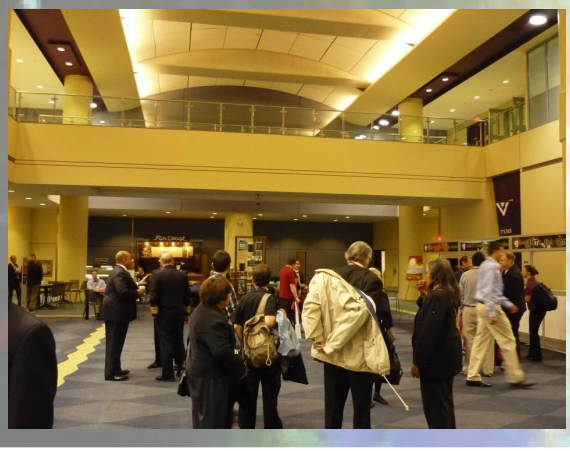
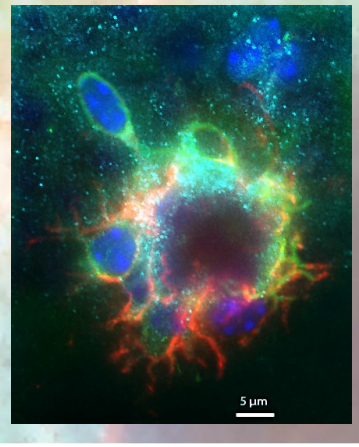
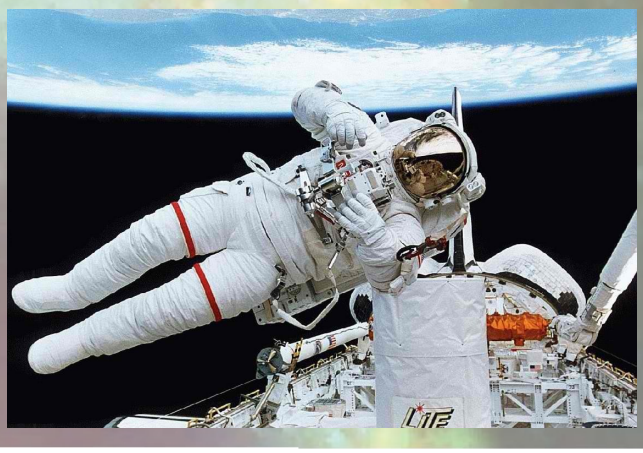
Breaking Boundaries of Science, Technology, Medicine, Art, and Healthcare Policy







Abstracts of Oral Presenters & Posters

Baltimore Convention Center
One West Pratt Street | Baltimore, Maryland 21201

May 12 - 14, 2013

The Baltimore Convention Center

(Use the Search feature of your acrobat reader to find a specific speakers abstract)
This file contains the abstracts for those who submitted their abstracts prior to the submission deadline

Revised 5/29/13

Unexpected Effects of Selective Retinal Stimulation on Metabolism and Quality of Life After Brain Injury

Deborah Zelinsky - The Mind-Eye Connection

Contact: Deborah Zelinsky (mindeyeconnection@msn.com)

Abstract: After brain injury, quality of life is often affected by disruptions between sensory, motor, cognitive, perceptual and emotional systems. Typically, people who have suffered brain injuries develop dysfunctional filtering mechanisms, exhibiting either unusually acute or reduced awareness to subtle environmental changes. In some cases, it is possible to address brain injury through selective retinal stimulation to influence neural pathways, and affect metabolic processes.

Neuro-ophthalmologists often monitor changes in retinal structures, since visual impairments can reflect systemic conditions. An often overlooked concept in rehabilitation is the converse -- selective stimulation of retinal pathways used to induce positive changes in physiological functions. Optometrists, whose work emphasizes neuro-optometric concepts, activate those retinal pathways to help people with brain injuries readapt to environmental changes more easily. These improvements can occur even if patients have 20/20 eyesight and no visual field impairments.

This premise argues for an unconventional use of eyeglasses. When glasses are designed to alter incoming light, they can affect biochemical and neurological processes through the retinal pathways. The mechanisms involve both visual and non-image-forming retinal circuitry. Impact on brain networks through stimulation of four main retinal pathways can be quantified, and used to assess and modify internal tolerance to external changes.

Keywords

Rehabilitation Medicine (neural repair and regeneration) (primary keyword)
Psychiatry (PTSD,?)
Brain mapping/functional imaging for rehab medicine and PTSD
Minimally invasive therapy

Abstract Topics

Vascular & Blood flow imaging
Nanoscience, genomics, genetics
Functional brain mapping (fMRI, PETâ€¦)
Psychiatry (PTSD,â€¦)
Brain mapping/functional imaging for rehab medicine

Minimally invasive therapy
Rehabilitation Medicine (neural repair and regeneration
Basic Neuroscience

The abstarct book's publications additonal Information summary

TITLE: Unexpected Effects of Selective Retinal Stimulation on Metabolism and Quality of Life After Brain Injury

Deborah Zelinsky, O.D., F.N.O.R.A.
The Mind-Eye Connection
1414 Techny Road
Northbrook,IL 60062
mindeyeconnection@msn.com

ABSTRACT:
After brain injury, quality of life is often affected by disruptions between sensory, motor, cognitive, perceptual and emotional systems. Typically, people who have suffered

brain injuries develop dysfunctional filtering mechanisms, exhibiting either unusually acute or reduced awareness to subtle environmental changes. In some cases, it is possible to address brain injury through selective retinal stimulation to influence neural pathways, and affect metabolic processes.

Neuro-ophthalmologists often monitor changes in retinal structures, since visual impairments can reflect systemic conditions. An often overlooked concept in rehabilitation is the converse -- selective stimulation of retinal pathways used to induce positive changes in physiological functions. Optometrists, whose work emphasizes neuro-optometric concepts, activate those retinal pathways to help people with brain injuries readapt to environmental changes more easily. These improvements can occur even if patients have 20/20 eyesight and no visual field impairments.

This premise argues for an unconventional use of eyeglasses. When glasses are designed to alter incoming light, they can affect biochemical and neurological processes through the retinal pathways. The mechanisms involve both visual and non-image-forming retinal circuitry. Impact on brain networks through stimulation of four main retinal pathways can be quantified, and used to assess and modify internal tolerance to external changes.

KEYWORDS:
Neuro-optometric rehabilitation, retinal circuitry, non-visual perception, retinal pathways, retinal ganglion cell, koniocellular

Introduction: Three photoreceptors in the retina each influence internal functions, integrating external sensory signals with internal biochemical cycles. After brain injury, sensory and motor pathways are often disrupted. As a result, patients are sometimes unable to adapt to environmental changes. This signal integration occurs in sensory receptors, as well as in sub-cortical and cortical structures.

Methods: Specialized eyeglasses were individually designed to enhance sensory integration in patients with post-concussive syndromes.

Results: Patients were able to tolerate changes in their environment more easily. Their sense of being â€œoverwhelmedâ€ by environmental changes diminished.

Conclusions: When specialized glasses were customized for individual patients, other rehabilitation techniques had more impact, and quality of life was improved.

EDUCATIONAL OBJECTIVES:
1) To demonstrate that using specialized eyeglasses on patients with brain injuries can help them readapt to environmental changes more easily. This use of eyeglasses is unconventional, in the sense that it does not necessarily improve vision. Nevertheless, it is effective.

2) To develop awareness in the scientific community that retinal stimulation can have significant impacts on physiological systems. The mechanisms involve biological cycles within the body, such as sleep.

Educational Objectives 1) To demonstrate that using specialized eyeglasses on patients with brain injuries can help them readapt to environmental changes more easily. This use of eyeglasses is unconventional, in the sense that it does not necessarily improve vision. Nevertheless, it is effective. 2) To develop awareness in the scientific community that retinal stimulation can have significant impacts on physiological systems. The mechanisms involve biological cycles within the body, such as sleep.

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Inducing modularity to brain; Using temporary stimuli to trigger new inter-neuron connections containing permanent data of brain functionally induced structural subdivisions

Meraj Zolghadrpour - none

Contact: meraj zolghadrpour (paracentrallobule@gmail.com)

Abstract: Background and aims: teaching a brain for modularity acquisition was not a goal for the educational institutions to be methodologically and of course widely refined as a curriculum to handle all its end-products and by-products.

Method: each new experiment triggers new connections in the brain so theoretically itâ€™s possible to teach a brain to acquire some sort of active modular self-consciousness via scheduled short and long term environmental exposure to temporary brain functioning stimuli (brain images, PET, fMRI, etc.) and other precise and approximate instruments and information based on empirical and theoretic databases to become at least permanently self-conscious of the modularity(functional divisions) of itself.

Results: first, the unprecedented result in my research was the metamorphosis of the brain functionally instrumentally evaluated hierarchy into brain structurally pedagogically acquired hierarchy.Second, after three years of exposing my own brain to the all available scientific tools (images, brain waves, etc.) I accomplished the stage that my brain acquired a permanent active self-conscious map of its structural divisions as end-product with measurable reactions to different waves of different wavelengths and so many incredible and diverse but scientific by-products which necessitates examination in advanced laboratories, A fully modularized brain particularly in higher levels of brainâ€™s structural hierarchy (the cerebral cortex subdivisions and main lobes of the deep brain to Brodmannâ€™s areas) based on simple brain maps besides some newly induced brain highways engaged in the coordinate and/or subordinate procedures of yet unspecified sequential and/or parallel operation but responsive to waves. In addition I should mention the diversity of the by-products of a modularized brain for those individuals who reach this level fully or partially. Based on the quantity and quality of rewiring and the vicinity of particular brain site in which this rewiring is developing, there are different by-products which could be measured, be regulated and be drummed up methodologically. I present all my experiments with an unrivaled concrete data attachment in all over the brain research history, my own brain.

Conclusions: if the most profound aim of this era in science is to solve the brain problem and our technological achievements are not powerful enough to handle it, one solution is to insert another permanent refined course about brain in the education curriculum of different levels of our educational system to have more and more consciously modularized human brains for analysis in the laboratories.

Keywords: brain modularity, brain lobes, cerebral cortex, hemispheres, end-products and by-products, individual by-products diversity, upper levels of brainâ€™s structural hierarchy, Brodmannâ€™s areas

Keywords *Anatomy (primary keyword)*
General issues
Functional brain mapping (fMRI, PET?)
Brain mapping/functional imaging for rehab medicine and PTSD

Abstract Topics
General issues
Anatomy
Functional brain mapping (fMRI, PETâ€¦)
Basic Neuroscience

The

abstarct

of brain functionally induced structural subdivisions

book's publications

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additonal Information

summary

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methodologically and of course widely refined as a curriculum to handle all its end-products and by-products.

Methods: each new experiment triggers new connections in the brain so theoretically itâ€™s possible to teach a brain to acquire some sort of active modular self-consciousness via scheduled short and long term environmental exposure to temporary brain functioning stimuli (brain images, PET, fMRI, etc.) and other precise and approximate instruments and information based on empirical and theoretic databases to become at least permanently self-conscious of the modularity(functional divisions) of itself.

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Keywords: brain modularity, brain lobes, cerebral cortex, hemispheres, end-products and by-products, individual by-products diversity, upper levels of brainâ€™s structural hierarchy, Brodmannâ€™s areas

Educational Objectives

introducing my accomplishments, providing more advanced opportunitis to study and improve my brain functions through team works,achieving a good basis for my future education,

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

On emerging advances in neural information processing and space time physiologic calculations.

Cartik Sharma - STM

Contact: Cartik Sharma (cartik.sharma@gmail.com)

Abstract: We present a quantum theoretical framework to explain neural decision making from first principles. Neuronal firing and activation is studies in the context of real world settings in the normal activation, stimulus and response experimental setup. Aggregators for data patterns specific to a certain lobe are initiated to collect and observe neuronal responses. A series of microstates is identified with each neural activation and numerical estimates pertaining to these data patterns are calculated in space time coordinates.

The physics of underlying computation involve measure of entropy of individual microstates, an underlying premise for measure of randomness. Entropy measurements over time directed towards reducing values will give predictors of arriving at a decision. Expectation of reward from a set of cues is directly proportional to bias from prior contexts and information content or entropy. { E(r) = bi x Î¦ , Expectation of reward proportional to ith bias at entropy phi specific to to contextual state}

The formal assumption is to model information interpretation by estimates of entropy measures during the neural decision making task. We identify a mapping between original activation, episodic memory and relational response tied to specific reward centers. Entropy as a measure of information content in the conventional sense is applied to monotonic convergence towards specific decision making. This is motivated from the quantum principles of measurement, the observation of measurement and striking an implicit interconnectedness between simultaneous measurements explained with the mechanism of quantum entanglement (Bell et al). Predictable neuronal pathways are identified for solid decision making and critical reasoning. This allows for an elegant explanation of neuronal firing in the space time context. This is in agreement from findings of neuronal firing and avalanches (Plenz, et al). We further explore the governing equations for the quantum theoretic framework proposed to control such firing in the non traditional sense. The reduced form of cognitive measurements gives us a tangible predictor in the sense of cognitive reserve and directional neuronal output. We also measure the resultant energy spectrum at various stages of the decision making process to arrive at the most effective decision making route.

Implied applications include restoration of neuronal pathways in the sense of a training task towards rehabilitation and recovery. These predicates will allow and explain for stimulated neuronal firing with improved gradient calculations for entropy measures and faster neuronal processing. This work involves modeling our neural correlates with sporadic variability to explain neuronal raison d' etre in higher order cognitive tasks. The ergodicity of measurement gives an ensemble average for neurons accurate to function and context.

Keywords *Brain mapping/functional imaging for rehab medicine and PTSD (primary keyword)*
4D, Neuro-mathematics and bio-informatics
Neurophysiology (EEG, MEG, ?)
Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration)

Abstract Topics
Neurophysiology (EEG, MEG,â€¦)
Functional brain mapping (fMRI, PETâ€¦)
Neural Prosthesis & Robotics
Imaging modalities for detecting mild/mod TBI, micro-TBI
Brain mapping/functional imaging for rehab medicine

The abstarct book's publications additonal
On emerging advances in neural information processing and space time physiologic calculations.
Cartik Sharma
Cartik.sharma@gmail.com

On Emerging advances in neural information processing and space time physiologic

Information summary

calculations.

We present a quantum theoretical framework to explain neural decision making from first principles. Neuronal firing and activation is studies in the context of real world settings in the normal activation, stimulus and response experimental setup. Aggregators for data patterns specific to a certain lobe are initiated to collect and observe neuronal responses. A series of microstates is identified with each neural activation and numerical estimates pertaining to these data patterns are calculated in space time coordinates. The physics of underlying computation involve measure of entropy of individual microstates, an underlying premise for measure of randomness. Entropy measurements over time directed towards reducing values will give predictors of arriving at a decision.

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Implied applications include restoration of neuronal pathways in the sense of a training task towards rehabilitation and recovery. These predicates will allow and explain for stimulated neuronal firing with improved gradient calculations for entropy measures and faster neuronal processing. This work involves modeling our neural correlates with sporadic variability to explain neuronal raison d' etre in higher order cognitive tasks. The ergodicity of measurement gives an ensemble average for neurons accurate to function and context.

Keywords: Neural ensembles, Quantum entaglement,ergodicity

Educational Objectives

Neural circuitry, neural information processing, rehabilitation and training

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Use of diffusion tractography integrated into neuronavigation during surgery of intra-axial brain tumors located in close proximity to the corticospinal tract

Eduard Neuman - University Hospital Brno
Martin Smrcka - University Hospital Brno
Milos Kerkovsky - University Hospital Brno
Tomas Svoboda - University Hospital Brno
Pavel Fadrus - University Hospital Brno

Contact: Eduard Neuman (eneuman@volny.cz)

Abstract: Poster type of presentation is prefered.

Objective: This study was conducted to assess the benefit of the integration of the corticospinal tract diffusion tractography into the neuronavigation during operations of intra-axial brain tumors located close to the corticospinal tract.

Methods: The diffusion tractography was used along with the subcortical electric stimulation to locate the corticospinal tract. Motor evoked potentials elicited by the stimulation were recorded. The method was used in 10 patients with an intra-axial brain tumor (astrocytoma gr. II-IV).

Results: The corticospinal tract was succesfully confirmed by the electrostimulation in the approximate location predicted by the diffusion tractography in all patients. Resection of the tumor was terminated when the motor evoked potentials were elicited by the stimulus current of 10 mA (monopolar stimulation, train of 4 pulses at frequency of 500 Hz and pulse duration of 400 Âµs). No patient has suffered from a new permanent neurological deficit.

Conclusion: Although we are convinced that due to brain shift that occurs during tumor resection it is not enough to rely solely on the projections of the corticospinal tract in neuronavigation without electrophysiological validation of the tract course, the diffusion tractography integrated into neuronavigation appears to be a valuable guidance for the identification of the corticospinal tract in the surgical field.

Keywords Neuronavigation, Diffusion tractography, Corticospinal tract, Motor evoked potentials, Brain tumors, Diffusion tensor imaging

Abstract Topics Image guided systems

The abstarct book's publications additonal Information summary	
Educational Objectives	to introduce experience with use of diffusion tractography intraoperatively, to introduce simple method of integration of diffusion tractography into neuronavigation
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Multimodal, optical, label-free spectroscopic imaging of spinal cord injury

Matthias Kirsch - Neurosurgery, UniversitÃ¤tsklinikum Dresden
Roberta Galli - Clinical Sensoring and Monitoring, UniversitÃ¤tsklinikum Dresden
Ortrud Uckermann - Neurosurgery, UniversitÃ¤tsklinikum Dresden
Martin G. Winterhalder - Dept. of Chemistry, University of Konstanz
Kerim H. Sitoci-Ficici - Neurosurgery, UniversitÃ¤tsklinikum Dresden
Kathrin D. Geiger - Neuropathology, UniversitÃ¤tsklinikum Dresden
Edmund Koch - Clinical Sensoring and Monitoring, UniversitÃ¤tsklinikum Dresden
Gabriele Schackert - Neurosurgery, UniversitÃ¤tsklinikum Dresden
Andreas Zumbusch - Dept. of Chemistry, University of Konstanz
Gerald Steiner - Clinical Sensoring and Monitoring, UniversitÃ¤tsklinikum Dresden

Contact: Matthias Kirsch (matthias.kirsch@tu-dresden.de)

Abstract: Spinal cord injury triggers a series of complex biochemical alterations of nervous tissue. Up to now, such cellular events cannot be studied without conventional tissue staining. The development of optical, label free imaging techniques could provide powerful monitoring tools with the potential to be applied in vivo. In this work, we assess the ability of vibrational spectroscopy to generate contrast at molecular level between normal and altered regions in a rat model of spinal cord injury.

Materials and Methods: Adult rats underwent laminectomy of thoracic vertebrae 9 and 10 followed by a hemimyelonectomy to generate a defined one-sided spinal cord lesion. Several treatment arms using gene-activated adipose tissue transplant were used as an autologous graft. The animals were observed for 7 or 21 days. Then, the spinal cord was harvested and several imaging modalities were used to analyse the tissue, namely 2-photon microscopy, second harmonic generation microscopy, Fourier-transformed vibrational optical spectroscopy, Raman spectroscopy and coherent anti-Stokes Raman spectroscopy on unstained samples, as well as conventional immunofluorescence staining using confocal microscopy.

Results: Using tissue sections, we demonstrate that Fourier-transform infrared spectroscopy and spontaneous Raman spectroscopy are able to identify the lesion, the surrounding scar and unharmed normal tissue, delivering insight into the biochemical events induced by the injury and allowing mapping of tissue degeneration. The FT-IR and Raman spectroscopic imaging provides the basis for fast multimodal non-linear optical microscopy (coherent anti-Stokes Raman scattering, autogenous 2-photon fluorescence and second harmonic generation). The latter proves to be a fast tool for

imaging of the lesion on unstained tissue samples, based on the alteration in lipids content, extracellular matrix composition and microglia/macrophages distribution pattern. The combination of the three modalities revealed rapid (within seconds) high resolution imaging of nervous system structures including fiber tracts, infiltrating reactive cells, extend of the lesion on a cellular level, as well as to identify morphological changes upon scar formation and therapy induced changes.

Conclusion: The current set of label-free optical imaging technologies allow for a high resolution, fast and reproducible analysis of the biochemical and morphological composition of CNS tissue exemplary demonstrated using a rat model of spinal cord injury. These results establish these technologies in the field of regeneration in central nervous system, with the long term goal to extend them to intravital use, where fast and non-harmful, label-free imaging is required.

Abstract Topics	Molecular and cellular imaging Histopathology Multimodality imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	Experimental cellular imaging, SCI model, regeneration
Files	*Submission exists, but was not archived (suffix)*

Reviews

Magnetic Resonance Imaging (MRI) in Tuberculosis of the Spine

Rohtas Yadav - PGIMS, Rohtak,India

Contact: Rohtas Yadav (rohtaskryadav@gmail.com)

Abstract: Purpose: To see the profile of various MRI findings in patients of Tuberculosis of the spine.

Method and Materials: 50 patients with clinical diagnosis and / or suspected on plain radiographs to be suffering from Tuberculosis of spine were included in the study. All the patients were subjected to detailed clinical history, physical examination and relevant lab investigations. MRI was done on Philips Gyroscan Nova 1.5 Tesla consisting of multislice acquisitions in coronal plane as screening procedure, followed by sequences in sagittal planes using spin echo sequences, dominated by T1 and T2 relaxation effects. Axial multislice sequences dominated by T1 and T2 weighed images were performed in the area of interest. Gadolinium enhanced T1 weighed images and Fat suppressed images were also acquired, if required. The diagnosis of Tuberculosis of the spine was confirmed on culture and / or histopathology in all cases.

Results: 26 male and 24 female patients between 6-90 years of age; on plain radiography showed vertebral body involvement in 44, posterior elements in 5 and gibbous deformity in 3. Dorsal spine was most commonly involved (44%), followed by lumber (20%), dorsolumber (18%), lumbosacral (10%) and cervicodorsal spine (8%). Single vertebra was involved in 2, two in 21, three in 8, four in 7 and more than four in rest of the patients. The lesion was seen as hypointense signal intensity on T1 weighted images and hyperintense signal intensity on T2 weighted & STIR images. Most common pattern of involvement was paradiscal (72%), followed by body (24%) and intervertebral disc only (4%). Posterior elements signal intensity changes were seen in 33 patients with structural alteration in 8 patients. Pre & Para vertebral soft tissue lesion was seen in 37, subligamentous extension in 4 and epidural collection in 39 patients. Spinal cord signal intensity changes were seen in 27 patients. Gadolinium administrated in 36 patients showed peripheral enhancement of soft tissue lesion in 34 and bone lesion enhancement in all the patients.

Conclusion: The anatomical pattern of involvement, particularly of the soft tissues and the discs, is specific for Tuberculosis of the spine. The ability of MRI to detect Tuberculosis of the spine earlier than any other diagnostic modality could reduce bone destruction and deformity and also avoid the need for surgical intervention.

Keywords *Spinal Cord Imaging and Diagnostics (primary keyword)*
Imaging modalities for detecting mild/mod TBI, micro-TBI

Abstract Topics Spinal Cord Imaging and Diagnostics

The abstarct book's publications additonal Information summary

Magnetic Resonance Imaging (MRI) in Tuberculosis of the Spine.
Rohtas K. Yadav, Professor & HOD Radio-diagnosis,
Pt. B D Sharma PGIMS, Rohtak, INDIA, 124001.

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Educational Objectives To see the profile of various MRI findings in patients of Tuberculosis of the spine.

Files *Submission exists, but was not archived (suffix)*

Reviews

Functional Near-Infrared Spectroscopy based Classification of Prefrontal Activity for Development of a Brain-Computer Interface

Noman Naseer - Department of Cogno-Mechatronics Engineering, Pusan National University, Busan, Korea
Keum-Shik Hong - Department of Cogno-Mechatronics Engineering, Pusan National University, Busan, Korea

Contact: Noman Naseer (noman@pusan.ac.kr)

Abstract: Functional near-infrared spectroscopy (fNIRS) is a novel brain signal acquisition tool for brain-computer interface (BCI). It is an optical technique to measure localized cortical brain activity. The main advantages of using this technique are relatively low cost, safety, portability and wearability. In the present research we propose to apply fNIRS to measure the brain activity during mental arithmetic and discriminate it from the rest state, which could potentially lead to on/off BCI application. Five healthy subjects are asked to solve simple arithmetic calculations during the activity period. Continuous-wave imaging system (DYNOT: dynamic near-infrared optical tomography) is used to acquire brain signals during the arithmetic task and rest. Two emitters and six detectors are placed on the prefrontal cortex of the subjects. Only eight channels with emitter-detector distance of 3 cm are considered for the analysis. The signals acquired are first normalized and then filtered to remove low frequency noise. Linear discriminant analysis (LDA) is then used as the classifier and the values of concentration changes in oxy and deoxy hemoglobins, from the selected channels for specific time points, are fed to the classifier. Using LDA we are able to distinguish clearly between the activity (mental arithmetic) and rest states with an average accuracy, averaged over all channels and for all subjects, of above 83%. These classified signals can be translated into control commands for on/off control of an external device or a two-choice BCI. The results show fNIRS to be a potential candidate for BCI by using mental arithmetic.

Keywords Operational issues
Functional brain mapping (fMRI, PET?)
Brain mapping/functional imaging for rehab medicine and PTSD

Abstract Topics Functional brain mapping (fMRI, PETâ€¦)
Brain mapping/functional imaging for rehab medicine

The abstarct book's publications additonal Information summary

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Two pages of supplementary material (that contains details, figures and a table) has been
attached with the main file.

We would prefer to give a poster presentation.

This work has not been submitted for publication or presentation elsewhere.
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Educational Objectives Functional near-infrared spectroscopy based classification of prefrontal activity is presented. It has been shown that the activity and rest states are clearly distinguishable from each other using linear discriminant analysis. The classified signals can be translated into control commands for a two-choice BCI

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

MRI study of structural changes in brain of adult Wag/Rij rats after febrile seizures at early postnatal age

Ksenia Kulichenkova - Human and Animal Physiology Department, Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia
Mikhail Gulyaev - Centre for Magnetic Tomography and Spectroscopy, Lomonosov Moscow State University, Moscow, Russia
Valery Petuchov - Centre for Magnetic Tomography and Spectroscopy, Lomonosov Moscow State University, Moscow, Russia
Sergey Titov - Russian State University for the Humanities
Kenul Abbasova - Human and Animal Physiology Department, Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia

Contact: Ksenia Koulitchenkova (koulitchenkova@gmail.com)

Abstract: The aim of our study was to examine structural changes in brains of Wag/Rij and Wistar strain rats exposed to febrile seizures (hereinafter FS) in early postnatal period. Wag/Rij strain rats have genetically determined absence seizures.

Methods. We used 9 and 12 days old Wag/Rij and Wistar rat pups, 28 pups altogether. We applied the model of febrile seizures on the rat pups according to Mccaugharan, Edwards, Sechechter., (1984). Overheating the pups was carried out in mild conditions with light (using 200Wt filament bulb) from the appropriate distance to provide +41ÂºÐ¡ in the experimental chamber. Pups underwent overheating for no less than 15 minutes at the age of 9 and 12 days. Every minute we fixed the severity of seizures according to the special scale. Before and after hyperthermic seizures rectal temperature was fixed. MRI study of the ratsâ€™ brain was carried out in 30 and 60 days after FS. MRI was conducted using Brucker BioSpin 70/30 plant (Germany) at the MSU Centre for Magnetic Tomography and Spectroscopy. We measured T2 signal intensity in several structures and also the volume of hippocampus. After that we made an EEG study using intracranial electrodes in frontal cortex, thalamus and hippocampus.

Results. Our research showed that both rat stains had similar sensitivity to FS at the age of 9 and 12 days. Both Wag/Rij and Wistar strains had reliable reduction of hippocampal volume in 3 and 6 months after FS as compared to the control groups that had no FS. See Table 1 in an attached file for a reliable increase in T2 signal as compared to the control groups. The EEG study showed that Wag/Rij rats demonstrate more frequent and prolonged spike wave discharges after FS. It also showed abnormal high-amplitude activity in Wistar ratsâ€™ hippocampi.

Conclusions. According to our results, limbic structures are vulnerable to the initial damaging action of FS in both rat strains. However, in Wistar strain rats it was not only the limbic structures that were damaged, but also other cortex regions. Consequently, we can assert that in case of Wistar strain rats, the epileptogenesis involves more structures. These data conform to the electrophysiological researches demonstrating that Wag/Rij strain rats are more resistant to the secondary generalization.

Keywords *Neurophysiology (EEG, MEG, ?) (primary keyword)*
Anatomy
Histopathology

Abstract Topics Anatomy
Neurophysiology (EEG, MEG,â€¦)

The abstarct book's publications additonal Information summary

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Title: MRI study of structural changes in brain of adult Wag/Rij rats after febrile
seizures at early postnatal age.
Authors: Ksenia Kulichenkova1, Mikhail Gulyaev2, Valery Petuchov2, Kenul Abbasova1
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e-mail: koulitchenkova@gmail.com
Abstract:
The aim of our study was to examine structural changes in brains of Wag/Rij and Wistar
strain rats exposed to febrile seizures (hereinafter FS) in early postnatal period. Wag/Rij
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strain rats have genetically determined absence seizures.
Methods. We used 9 and 12 days old Wag/Rij and Wistar rat pups, 28 pups altogether. We applied the model of febrile seizures on the rat pups according to Mccaugharan, Edwards, Sechechter., (1984). Overheating the pups was carried out in mild conditions with light (using 200Wt filament bulb) from the appropriate distance to provide +41Â°Ð¡ in the experimental chamber. Pups underwent overheating for no less than 15 minutes at the age of 9 and 12 days. Every minute we fixed the severity of seizures according to the special scale. Before and after hyperthermic seizures rectal temperature was fixed.
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Table 1. Reliable increase in T2 signal in Wag/Rij and Wistar strain rats as compared to the control groups.

	Wag/Rij in 3 months	Wag/Rij in 6 months	Wistar in 3 months	Wistar in 6 months
Ventral hippocampus	+/-	+	+	+
Amygdala	+	+	+	
Entorhinal cortex				+
Somatosensory cortex				+

Conclusions. According to our results, limbic structures are vulnerable to the initial damaging action of FS in both rat strains. However, in Wistar strain rats it was not only the limbic structures that were damaged, but also other cortex regions. Consequently, we can assert that in case of Wistar strain rats, the epileptogenesis involves more structures. These data conform to the electrophysiological researches demonstrating that Wag/Rij strain rats are more resistant to the secondary generalization.

Keywords: MRI, EEG, febrile seizures, limbic structures, Wag/Rij

The first part of this study was demonstrated as a poster on 16th World Congress of Psychophysiology in Pisa, Italy. Now we added to it an EEG study. This new data coordinates our previous results and also shows some interesting and unexpected EEG activity.

Educational Objectives This appears to be the first study on the relationship between childhood febrile seizures and absence epilepsy using an animal model. Weâ€™ve taken a state-of-the-art approach to the problem of epilepsy. The study also touches upon the problem of relationship between childhood febrile seizures and temporal lobe epilepsy.

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Differetiated Approach of Puncture Kypho- and Vertebroplasty in Compression Fractures of Vertebral Bodies

Alexander Toma - SarNIITO
Ilya Toma - Saratov State Medical University
Svetlana Gramma - SarNIITO
Anna Golubeva - SarNIITO
Svetlana Toma - Municipal Hospital â„–1

Contact: Alexander Toma (al_toma@mail.ru)

Abstract: Introduction. The research objective is to determine therapeutic approach and improve the results of surgical treatment of patients with stenotic complicated degenerative damages of the lumbar part of spine according to the degree of spinal canal lumen deficiency (SCLD) and lumen deficiency of intervertebral foramina (LDIF).

Methods. Results of surgical treatment of 51 patients aged from 35 up to 65 are analysed. Anterior form of the spinal canal deformity has been diagnosed in 23 patients. Circular stenosis is determined in 17 patients. In 11 patients stenosis of intervertebral foramina is revealed. Maximal SCLD up to 85% is revealed in two patients with circular stenosis of the spinal canal. Maximal LDIF up to 75% is revealed in 3 patients. Transligamentary and intralaminar discectomy was performed in 19 of 23 patients with the anterior form of the spinal canal deformity. Surgical intervention with the use of endoscopic equipment was performed in 9 patients. Osteoplastic laminectomy was performed in four patients. Among 17 patients with circular stenosis of the spinal canal osteoplastic laminectomy was performed in 14 patients with SCLD from 60 % up to 80 %, in 6 patients with SCLD over 80 %, additionally, transpedicular fixation (TF) of the damaged vertebral segment with correction of height of intervertebral space was used as well. The resection of osseous overgrowths of external surface of joints was carried out in 11 patients with LDIF up to 60 % with the use of endoscopic equipment. Among 51 patients osteoplasty of the defect of osteoligamentous apparatus was performed in 36 patients.

Results. The excellent result was received in 24 patients, good result - in 18 patients and satisfactory one - in 9 patients. Among 36 patients who underwent osteoplasty of osteoligamental defect, musculotunicary cicatrix formation was not revealed in anyone of them.

Conclusion. Preferable choice of surgical technique in decompression of the spinal canal in patients with circular stenosis with SCLD over 60% can serve osteoplastic laminectomy. When there is stenosis of intervertebral foramina with LDIF up to 60 % it is expedient to carry out the decompression by means of the intralaminar approach with the use of endoscopic equipment if possible, and when there is LDIF over 60% it is expedient to perform osteoplastic laminectomy with supplemental correction of height of intervertebral spaces and TF. Application of osteoplasty of osteoligamental defect allows to prevent the development of musculotunicary cicatrices.

Keywords *Minimally invasive therapy (primary keyword)*
Intraoperative Surgical Planning
Spinal Cord, Trauma Repair and regeneration

Abstract Topics
Intraoperative Surgical Planning
Minimally invasive therapy
Spinal Cord, Trauma Repair and regeneration

The abstarct

Differetiated Approach of Puncture Kypho- and Vertebroplasty in Compression Fractures of Vertebral Bodies
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book's publications additonal Information summary

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Methods. Results of surgical treatment of 51 patients aged from 35 up to 65 are analysed. Anterior form of the spinal canal deformity has been diagnosed in 23 patients. Circular stenosis is determined in 17 patients. In 11 patients stenosis of intervertebral foramina is revealed. Maximal SCLD up to 85% is revealed in two patients with circular stenosis of the spinal canal. Maximal LDIF up to 75% is revealed in 3 patients. Transligamentary and intralaminar discectomy was performed in 19 of 23 patients with the anterior form of the spinal canal deformity. Surgical intervention with the use of endoscopic equipment was performed in 9 patients. Osteoplastic laminectomy was performed in four patients. Among 17 patients with circular stenosis of the spinal canal osteoplastic laminectomy was performed in 14 patients with SCLD from 60 % up to 80 %, in 6 patients with SCLD over 80 %, additionally, transpedicular fixation (TF) of the damaged vertebral segment with correction of height of intervertebral space was used as well. The resection of osseous overgrowths of external surface of joints was carried out in 11 patients with LDIF up to 60 % with the use of endoscopic equipment. Among 51 patients osteoplasty of the defect of osteoligamentous apparatus was performed in 36 patients.

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Educational Objectives 1.Experimental Research.2.Bone Tissue Regeneration.3.Support Ability Restoration

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

An ever-improving model of the structure of the living human brain

Andrew Worth - Neuromorphometrics, Inc.
Jason Tourville - Boston University

Contact: Andrew Worth (SBMT@Neuromorphometrics.com)

Abstract: In a traditional brain atlas the anatomist aggregates experience of many individuals and presents it as a single brain. This establishes what is normal, but individuals differ from each other, to a greater or lesser extent, in each neuroanatomical region. We are building a model of brain structure by labeling each voxel in a large number of individual MRI scans. Our goal is to continuously improve the model, not only by adding more scans, increasing the number of anatomical regions, and by parcellating regions into more specific sub-regions, but also by iteratively reviewing the results in the context of the whole model to find and fix errors.

Magnetic resonance can provide only an imperfect representation of the highly detailed â€œtrueâ€ neuroanatomy. Beyond noise and artifacts, MR signals have only macroscopic resolution and mainly indicate myelin content. But because MRI is non-invasive, it is clinically relevant: we are building a model of the living human brain. And the significance of this model is that it provides quantitative information about normal variation as a result of individually labeling a large number of scans.

The model was created by specifying neuroanatomical boundaries and extents and using in-house software, â€œNVMâ€ to comprehensively label each brain voxel in every scan. Raw MRI scans were preprocessed (for example, positional and intensity normalization), and labeled scans were added to a probabilistic atlas and normative statistics on volume, location, shape, and intensities were compiled into a database. All structures in each individual scan were then compared to the atlas and statistics in a â€œbootstrappingâ€ process to check, correct, and refine the boundaries and voxel labels.

Protocols defining 157 ROIs were used to manually label 64 T1-weighted MRI scans. A probabilistic atlas and normative statistics were generated to refine the labeling and then the atlas and statistics were re-created. We show example structures from the atlas and give examples of the neuroanatomical variation by showing typically different gyral and sulcal configurations.

Even beyond the multi-decade effort needed to develop the system and train technicians, the amount of work necessary to get to this point was enormous. The total

technician time needed was more than 2 years. The initial time required to label every structure in every slice of a single scan started out at about a week and decreased to 2-3 days. While ongoing improvements in automation will lower the cost, it is still high enough to be unjustifiable. The only way to increase the number of labeled scans is to spread out both the funding for the work and also the use of the results. We provide academic researchers with access to all scans in the database for less than the cost of adding a single scan to that database. As multiple researchers contribute, the database can continue to grow.

Releasing the model will help in creating automation and provide a database to mine, which will lead to the discovery of biomarkers and to an understanding of the variation of brain structure.

Keywords	*Anatomy (primary keyword)* Stereotactic Radiosurgery
Abstract Topics	Image guided systems Intraoperative Surgical Planning Stereotactic Radiosurgery Anatomy Functional brain mapping (fMRI, PETâ€¦) Diffusion Tensor Imaging Multimodality imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	To better understand the variation in the structure of the living human brain
Files	*Submission exists, but was not archived (suffix)*

Reviews

BOLD fMRI: Development of a Metabolic Approach to the Diagnosis and Monitoring of Brain Pathology

Susan C Feldman - UMDNJ-NJMS Radiology
Maureen Barry - UMDNJ-NJMS Radiology
Brian Lee - UMDNJ-NJMS
Helene Hill - UMDNJ-NJMS Radiology
Stuart Cook - UMDNJ-NJMS Neurology

Contact: Susan C. Feldman (sufeldma@umdnj.edu)

Abstract: BOLD fMRI: Development of a Metabolic Approach to the Diagnosis and Monitoring of Brain Pathology Feldman, Susan C, PhD, Dept. Radiology, UMDNJ-New Jersey Medical School, Newark, NJ, 07103; sufeldma@umdnj.edu,; Barry, Maureen, MD, Dept. Radiology UMDNJ-New Jersey Medical School, Newark, NJ, 07103; barryma@umdnj.edu; Lee, Brian BS1, UMDNJ-New Jersey Medical School, Newark, NJ, 07103, leebw@umdnj.edu; Hill, Helene, PhD1, Dept. Radiology, UMDNJ-New Jersey Medical School, Newark, NJ, 07103; hill@umdnj.edu; Cook, Stuart, MD2 , Dept. Neurology and Neuroscience, UMDNJ-New Jersey Medical School, Newark, NJ, 07103;cooksd@umdnj.edu Introduction: Development of metabolically relevant indices of brain pathology is of increased importance as adjuncts to clinical practice. These approaches have the potential to give the clinician a more up-to-date picture of changes in the patientsâ€™ condition than more â€˜staticâ€™ imaging and measurement techniques.

We have been exploring the use of resting state BOLD fmri for the characterization brain of lesions, specifically of brain tumors and plaque in Multiple Sclerosis. The BOLD fmri signal reflects the concentrations of oxy/de-oxy hemoglobin in the selected voxel/structure/region. In these studies we are exploring issues of specificity, sensitivity and reproducibility using both patients and normal subjects.

Methods: Subjects are scanned at either 3.5 or 1.5 T at the time of their scheduled MRI. For the BOLD study they were asked to remain quietly in the scanner with their eyes closed for 5 minutes. The BOLD images were overlaid onto 3mm T1images. BOLD signal data in voxels of interest (VOI) was analyzed using SPN and AFNI.

Results: In a study of the visual system we noted that individual parts of the visual system exhibit a BOLD signal that is functionally related more closely to other parts of the system than to outside points. Within the visual system, the cortex and optic radiations were consistently the most closely related parts. This was so even when comparing the data from tumor vs. normal and resting state vs. finger-tapping.

In MS patients, the BOLD fMRI signal identified plaque as different and distinguishable from the rest of the brain. The signal from an identified MS plaque frequently, but not always, identified (i.e., was highly correlated with) other plaque, suggesting relationships between these discrete lesions. Several large plaques, which on standard FLAIR images appeared homogeneous, actually had several discrete signals: upon further investigation, these individual signals could usually be correlated to other plaque VOIs, in other areas of the CNS. By comparing the heterogeneous signals with previous FLAIR images, we could distinguish â€˜oldâ€™ from â€˜newâ€™ plaque.

In tumors there is clear definition of the tumor borders without edema, which is important in neurosurgery. Do different types/grades, etc. elicit different signals, and can these be used to identify and/or grade them?

In MS, is there a unique MS â€˜plaque signalâ€™ or is the signal not statistically different from myelin lesions in other disorders? Conclusions: Our studies indicate that the BOLD signal relates to an intrinsic quality of the system/tissue/lesion as opposed to the activity being performed. This suggests the utility of this approach for monitoring disease progression and treatment.

Keywords *Functional brain mapping (fMRI, PET?) (primary keyword)*
Molecular and cellular imaging

Abstract Topics

General issues
Functional brain mapping (fMRI, PETâ€¦)

The abstarct book's publications additonal Information summary

BOLD fMRI: Development of a Metabolic Approach to the Diagnosis and Monitoring of Brain Pathology

Feldman, Susan C, PhD, Dept. Radiology, UMDNJ-New Jersey Medical School, Newark, NJ, 07103; sufeldma@umdnj.edu,; Barry, Maureen, MD, Dept. Radiology UMDNJ-New Jersey Medical School, Newark, NJ, 07103; barryma@umdnj.edu; Lee, Brian BS1, UMDNJ-New Jersey Medical School, Newark, NJ, 07103, leebw@umdnj.edu; Hill, Helene, PhD1, Dept. Radiology, UMDNJ-New Jersey Medical School, Newark, NJ, 07103; hill@umdnj.edu; Cook, Stuart, MD2 , Dept. Neurology and Neuroscience, UMDNJ-New Jersey Medical School, Newark, NJ, 07103;cooksd@umdnj.edu

Introduction: Development of metabolically relevant indices of brain pathology is of increased importance as adjuncts to clinical practice. These approaches have the potential to give the clinician a more up-to-date picture of changes in the patientsâ€™ condition than more â€˜staticâ€™ imaging and measurement techniques.
We have been exploring the use of resting state BOLD fmri for the characterization brain of lesions, specifically of brain tumors and plaque in Multiple Sclerosis. The BOLD fmri signal reflects the concentrations of oxy/de-oxy hemoglobin in the selected voxel/structure/region. In these studies we are exploring issues of specificity, sensitivity and reproducibility using both patients and normal subjects.
Methods: Subjects are scanned at either 3.5 or 1.5 T at the time of their scheduled MRI. For the BOLD study they were asked to remain quietly in the scanner with their eyes closed for 5 minutes. The BOLD images were overlaid onto 3mm T1images. BOLD signal data in voxels of interest (VOI) was analyzed using SPN and AFNI.
Results: In a study of the visual system involving tumor patients and normal volunteers, we noted that individual parts of the visual system exhibit a BOLD signal that is functionally related more closely to other parts of the system than to outside points.
Within the components of the visual system, the cortex and optic radiations were consistently the most closely related parts. This was so even when comparing the data from tumor vs. normal and resting state vs. finger-tapping.
In MS patients, the BOLD fMRI signal identified plaque as different and distinguishable from the rest of the brain. The signal from an identified MS plaque frequently, but not always, identified (i.e., was highly correlated with) other plaque, suggesting relationships between these discrete lesions. Several large plaques, which on standard FLAIR images appeared homogeneous, actually had several discrete signals: upon further investigation, these individual signals could usually be correlated to other plaque VOIs, in other areas of the CNS. By comparing the heterogeneous signals with previous FLAIR images, we could distinguish â€˜oldâ€™ from â€˜newâ€™ plaque.
In tumors there is clear definition of the tumor borders without edema, which is important in neurosurgery. Do different types/grades, etc. elicit different signals, and can these be used to identify and/or grade them?
In MS, is there a unique MS â€˜plaque signalâ€™ or is the signal not statistically different from myelin lesions in other disorders?
Conclusions: Our studies indicate that the BOLD signal relates to an intrinsic quality of the system/tissue/lesion as opposed to the activity being performed. This suggests the utility of this approach for monitoring disease progression and treatment.

(This submission is a summation and evaluation of our work to date.Portions of this work have been published previously (Feldman etal, AJNR,2009) or presented as individual studies at various meetings.)

Educational Objectives

1. Present evidence that the BOLD fMRI signal is a useful tool in clinical evaluations. 2 Present issues that still need clarification. Present evidence that in neurosurgery there is a change in practice to identify tumor borders for neurosurgical planning.

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Identification of early white matter tracts in the neonatal brain: atlas-based segmentation parameters influence DTI measurements

Rachel Vassar - Department of Orthopedic Surgery, Stanford University
Naama Barnea-Goraly - Center for Interdisciplinary Brain Sciences Research, Stanford University
Jessica Rose - Department of Orthopaedic Surgery, Stanford University

Contact: Jessica Rose (jessica.rose@stanford.edu)

Abstract: Introduction: This study investigates the effects of segmentation parameters for semi-automated, atlas-based analysis of neonatal white matter (WM) development in very-low-birth-weight (VLBW) preterm infants at near-term age. Preterm children have an elevated risk of neurological impairments that can lead to motor and cognitive deficits. Diffusion tensor imaging (DTI) is a sensitive tool for measuring water diffusion along WM tracts and can be used to study brain development in infants. Previous studies indicate neonatal DTI may be a sensitive predictor of neurodevelopmental outcomes in preterm children.

Semi-automated, atlas-based DTI analysis is a time-efficient tool for investigation of WM structure and holds promise for clinical implementation. However, threshold levels used for analysis of WM tracts in adults may not be applicable to the neonatal population, in which WM tracts are less developed and undergoing rapid structural changes and myelination. The effect of segmentation parameters on atlas-based diffusion measurements in neonates is not well documented, yet may significantly affect results.

Methods: DTI scans were obtained from neonates (n=46) within a cohort of 102 VLBW (BWâ‰¤1500g, GAâ‰¤32weeks) infants admitted to the NICU, scheduled for routine near-term brain-MRI (3T GE-Discovery-MR750) between 1/1/10â€“12/31/12 at mean GA-at-scan of 36.6Â±1.4wks. Parental consent was obtained for this IRB-approved prospective study. 68/102 had successful DTI, 46/68 had no evidence of brain injury at near-term-MRI.

This study compares four diffusion thresholds: one based on overall diffusivity (trace<0.006mm2s-1) to eliminate CSF and three based on fractional anisotropy (FA) (FA>0.15, FA>0.20, FA>0.25) for WM identification. Relative brain region volumes, FA and radial diffusivity (RD) values were compared in ten subcortical WM regions (Figure 1) selected with DiffeoMap neonatal brain atlas. Paired t-tests were performed to determine significance of threshold effects on FA and RD values,using p<0.0125, corrected for multiple comparisons.

Results: Application of higher diffusion thresholds resulted in significant reduction of all 10 brain region volumes selected. The FA threshold of FA>0.15 was most inclusive, selecting 79.1%(51.7-99.1%) of atlas-defined regions, compared to 55.3%(23.8-93.6%) using the threshold FA>0.20, and 34.7%(5.5-79.8%) using the threshold FA>0.25 (Figure 1a). Higher thresholds resulted in significantly increased FA (Figure 1b), and decreased RD (Figure 1c), in all regions except the posterior limb of the internal capsule. Inferior aspects of the corticospinal tract demonstrated the smallest change in volume, FA, and RD value; the corona radiata and external capsule demonstrated the largest FA value changes with application of different thresholds.

Conclusion: The optimal threshold application for neonatal WM segmentation is currently unknown but may differ from those recommended in adults due to inherent differences in WM structure and myelination. Application of different FA thresholds in our study resulted in significant changes in the volume selected and in DTI values. These differences may partly stem from inclusion of grey matter and less developed WM when applying lower FA thresholds; however, the low volumes selected with standard adult FA threshold values suggest that lower FA thresholds should be used to investigate neonatal WM structure. Further

investigation is needed to determine underlying histology and its relation to DTI values in newborn brains.

Keywords	*Diffusion Tensor Imaging (primary keyword)* Anatomy
Abstract Topics	Anatomy Diffusion Tensor Imaging
The abstarct book's publications additonal Information summary	See uploaded document for full abstract with supplementary figures. This work has not been previously submitted for publication, and we are interested in submitting a full paper along with this abstract for the 2013 conference edition of NeuroImage.
Educational Objectives	publication, clinical applications
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

ELECTRIC LASER NEUROSTIMULATION USE IN PATIENTS WITH VERTEBRAL CEREBRO-SPINAL INJURIES

Alexander Toma - SarNIITO
Ilya Toma - Saratov State Medical University
Svetlana Gramma - SarNIITO
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Abstract: ELECTRIC LASER NEUROSTIMULATION USE IN PATIENTS WITH VERTEBRAL CEREBRO-SPINAL INJURIES

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Introduction The objective of the work consists in the demonstration of the capability of epidural electric laser stimulation in complex treatment of victims of vertebral cerebro-spinal trauma.

Methods In the work the analysis of the results of treatment of 35 victims of vertebral cerbro-spinal trauma aged from 16 up to 48 is represented. Among injured persons damages in the cervical part of spine were registered in 11 (31,4%), damages in the thoracic part of spine were observed in 8 (22,9%), damages in the thoracicolumbar part of spine (ThXI-ThXII and LI-LII) were found in 16 (45,7%). The assessment of neurologic disorders was studied according to the scale ASIA/IMSOP. In 5 (14,3 %) patients rough neurologic disorders were observed - group "ÐÐ'". 16 (45,7 %) patients formed group "C ". The remaining patients were included into group "D" - 14 (40,0 %) persons. Besides conventional investigations and complex of necessary surgical interventions epidural lightguide-electrodes were implanted in all the 35 patients capturing the area above and below the level of the spinal cord lesion. Electrostimulation parameters for the whole period of treatment were improving according to the results of electroneuromyographic monitoring and the degree of spinal cord lesion. Laser irradiation was carried out immediately after every electrostimulation session. It was performed by the influence of the low-intensive electromagnetic radiation by sessions with time duration 1-10 minutes every 4-12 hours. Results As the result of the conducted electropulse influence on the spinal cord in the acute period of the trauma we succeeded in achieving positive outcomes in 28 (80,0 %) of victims that allowed us to restore lost functions of the spinal cord more completely.

Conclusion Electric laser neurostimulation influence gives a hopeful perspective in treatment of patients with injuries of the spinal cord.

Keywords *Spinal Cord, Trauma Repair and regeneration (primary keyword)*
Neurophysiology (EEG, MEG, ?)
Minimally invasive therapy

Abstract Topics Neurophysiology (EEG, MEG,â€¦)
Spinal Cord, Trauma Repair and regeneration

The abstarct

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ELECTRIC LASER NEUROSTIMULATION USE IN PATIENTS WITH VERTEBRAL CEREBRO-SPINAL INJURIES
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summary

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In the work the analysis of the results of treatment of 35 victims of vertebral cerbro-spinal trauma aged from 16 up to 48 is represented. Among injured persons damages in the cervical part of spine were registered in 11 (31,4%), damages in the thoracic part of spine were observed in 8 (22,9%), damages in the thoracicolumbar part of spine (ThXI-ThXII and LI-LII) were found in 16 (45,7%). The assessment of neurologic disorders was studied according to the scale ASIA/IMSOP. In 5 (14,3 %) patients rough neurologic disorders were observed - group "ÐÐ'". 16 (45,7 %) patients formed group "C ". The remaining patients were included into group "D" - 14 (40,0 %) persons. Besides conventional investigations and complex of necessary surgical interventions epidural lightguide-electrodes were implanted in all the 35 patients capturing the area above and below the level of the spinal cord lesion. Electrostimulation parameters for the whole period of treatment were improving according to the results of electroneuromyographic monitoring and the degree of spinal cord lesion. Laser irradiation was carried out immediately after every electrostimulation session. It was performed by the influence of the low-intensive electromagnetic radiation by sessions with time duration 1-10 minutes every 4-12 hours.

Results
As the result of the conducted electropulse influence on the spinal cord in the acute period of the trauma we succeeded in achieving positive outcomes in 28 (80,0 %) of victims that allowed us to restore lost functions of the spinal cord more completely.

Conclusion
Electric laser neurostimulation influence gives a hopeful perspective in treatment of patients with injuries of the spinal cord.

Key Words: electric laser neurostimulation, spinal cord injury

Educational Objectives 1.Spinal Cord Regeneration. 2.Restoration of Spinal Cord Functions. 3.Spinal Cord Electric Laser Stimulation Technique

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Resting-state functional connectivity in fNIRS signal revealed by wavelet analysis

Xiao-Su Hu - Department of Cogno-Mechatronics Engineering, Pusan National University, Busan, Koera
Keum-Shik Hong - Department of Cogno-Mechatronics Engineering, Pusan National University, Busan, Koera
Shuzhi Ge - Department of Cogno-Mechatronics Engineering, Pusan National University, Busan, Koera

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Abstract: In this work, we investigated the feasibility of using wavelet analysis to reveal the resting-state functional connectivity (RSFC) in functional near-infrared spectroscopy (fNIRS) signal. fNIRS is a non-invasive neuroimaging technique that recently has been developed to measure the changes of cerebral blood oxygenation associated with brain activities. fNIRS has the advantages that: It is low cost, insensitivity to the motion artifactsï¼Œand its equipment is portable. Spontaneous low-frequency hemodynamic fluctuations in distant regions in a human brain exhibit some correlation even in the absence of tasks or stimuli. This phenomenon (easily observable by fMRI) is termed the RSFC. The RSFC is believed to reflect neural interactions among distant brain regions, thereby providing information on the default brain network. The RSFC has thus become a powerful measure for the study of brain integration, brain working network, and brain diseases. Notably, researchers recently have reported that the RSFC can be detected using fNIRS: its validity, further, has been confirmed. Seed correlation and ICA based method have been proposed for revealing RSFC in fNIRS signal. In this work, a wavelet analysis based framework was proposed to reveal RSFC. The data were acquired with a continuous-wave NIRS imaging system (DYNOT) at a sampling rate of 1.8 Hz from motor cortex area. In the experiment, the subject was asked to complete two sessions. The first session consisted of an 8-min resting period. After session 1, the subject was asked to have a short break and then to begin session 2. Session 2 consisted of seven task blocks and seven rest blocks. Wavelet analysis was applied to the resting-state fNIRS signal in the current work. Daubechies 4 (DB4) wavelet with 8 scales was used as the wavelet basis function. We selected coefficients corresponding to the wavelet scale with frequency band 0.01-0.1 Hz. These coefficients are compared along their time courses to form RSFC maps. Only oxy-hemoglobin (HbO) signal is considered in this work. Correlations in both ipsilateral and contralateral hemisphere could be found in resting-state fNIRS signal. The RSFC pattern variation against the time course could be also reflected by the proposed method.

Keywords *Functional brain mapping (fMRI, PET?) (primary keyword)*

Abstract Topics Functional brain mapping (fMRI, PETâ€¦)

The abstarct book's publications additonal Information summary

Resting-state functional connectivity in fNIRS signal revealed by wavelet analysis

Xiao-Su Hu(a), Keum-Shik Hong(a,*), Shuzhi Sam Ge(a,b)
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Introduction
In this work, we investigated the feasibility of using wavelet analysis to reveal the resting-state functional connectivity (RSFC) in functional near-infrared spectroscopy (fNIRS) signal. fNIRS is a non-invasive neuroimaging technique that recently has been developed to measure the changes of cerebral blood oxygenation associated with brain activities (Obrig & Villringer, 2003; Boas et al., 2004; Hu et al., 2010; Hu et al., 2011; Ferrari & Quaresima, 2012; Hu et al., 2012). fNIRS has the advantages that: It is low cost, insensitivity to the motion artifactsï¼Œand its equipment is portable. Spontaneous low-frequency hemodynamic fluctuations in distant regions in a human brain exhibit some correlation even in the absence of tasks or stimuli. This phenomenon (easily observable by fMRI) is termed the RSFC. The RSFC is believed to reflect neural interactions among distant brain regions, thereby providing information on the default brain network. The RSFC has

thus become a powerful measure for the study of brain integration, brain working network, and brain diseases (Fox & Raichle, 2007). Notably, researchers recently have reported that the RSFC can be detected using fNIRS:(White et al., 2009; Lu et al., 2010) its validity, further, has been confirmed. Seed correlation and ICA based method have been proposed for revealing RSFC in fNIRS signal.

Method
The data were acquired with a continuous-wave NIRS imaging system (DYNOT) at a sampling rate of 1.8 Hz from motor cortex area. Fig.1 shows the channel distribution and measurement location. In the experiment, the subject was asked to complete two sessions. The first session consisted of an 8-min resting period. After session 1, the subject was asked to have a short break and then to begin session 2. Session 2 consisted of seven task blocks and seven rest blocks. Wavelet analysis was applied to the resting-state fNIRS signal in the current work. Daubechies 4 (DB4) wavelet with 8 scales was used as the wavelet basis function. We selected coefficients corresponding to the wavelet scale with frequency band 0.01-0.1 Hz. These coefficients are compared along their time courses to form RSFC maps. Only HbO signal is considered in this work.

Results
Correlations in both ipsilateral and contralateral hemisphere could be found in resting-state fNIRS signal. The RSFC pattern variation against the time course could be also reflected by the proposed method. Fig. 2 shows the representative wavelet decomposition (8 levels) of fNIRS signal. Fig. 3 shows the RSFC pattern variation time course at representative time points.

Conclusion
In this study, we propose a wavelet analysis based method for identifying the RSFC in fNIRS signal. This method could reveal the RSFC as well as its variation against time.

The figures could be found in uploaded Hu_SBMT2013.pdf.

References

Boas, D.A., Dale, A.M., & Franceschini, M.A. (2004). Diffuse optical imaging of brain activation: approaches to optimizing image sensitivity, resolution, and accuracy. NeuroImage, 23, S275-S288.
Ferrari, M., & Quaresima, V. (2012). A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application. NeuroImage, 63(2), 921-935.
Fox, M.D., & Raichle, M.E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nature Reviews Neuroscience, 8(9), 700-711.
Hu, X.S., Hong, K.S., & Ge, S.S. (2011). Recognition of stimulus-evoked neuronal optical response by identifying chaos levels of near-infrared spectroscopy time series. Neurosci Lett, 504(2), 115-120.
Hu, X.S., Hong, K.S., & Ge, S.S. (2012). fNIRS-based online deception decoding. J Neural Eng, 9(2), 026012.
Hu, X.S., Hong, K.S., Ge, S.S., & Jeong, M.Y. (2010). Kalman estimator- and general linear model-based on-line brain activation mapping by near-infrared spectroscopy. Biomed Eng Online, 9(1), 82.
Lu, C.M., Zhang, Y.J., Biswal, B.B., Zang, Y.F., Peng, D.L., & Zhu, C.Z. (2010). Use of fNIRS to assess resting state functional connectivity. Journal of Neuroscience Methods, 186(2), 242-249.
Obrig, H., & Villringer, A. (2003). Beyond the visible--imaging the human brain with light. J Cereb Blood Flow Metab, 23(1), 1-18.
White, B.R., Snyder, A.Z., Cohen, A.L., Petersen, S.E., Raichle, M.E., Schlaggar, B.L., & Culver, J.P. (2009). Resting-state functional connectivity in the human brain revealed with diffuse optical tomography. NeuroImage, 47(1), 148-156.

Educational Objectives a new method for identifying RSFC; RSFC pattern variation time course; studying the resting-state brain

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Behavioral and neuro-physiological effects of chronic unilateral arm amputation: a preliminary analysis

Erika Breceda Tinoco - Washington DC Veterans Affairs Medical Center
Alexander Dromerick - Medstar National Rehabilitation Hospital
Evan Chan - Medstar Health Research Institute
Friedhelm Sandbrink - Washington DC Veterans Affairs Medical Center
Sambit Mohapatra - Medstar Health Research Institute
Peter Lum - The Catholic Unversity of America
Raquel Silva - Medstar National Rehabilitation Hospital
Michelle Harris-Love - Medstar National Rehabilitation Hospital

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Abstract: Title: Behavioral and neuro-physiological effects of chronic unilateral arm amputation: a preliminary analysis.

Introduction: The substantial reorganization of the affected motor cortex after unilateral arm amputation is well known. A recent study showed disrupted intact arm function when compared to age-matched controls, suggesting changes in the intact motor cortex may also occur after amputation.

Objective: We investigated the intra- and inter-hemispheric physiological effects of chronic arm amputation and their relationship to intact and affected limb motor performance in a convenience sample of chronic (>1 yr) below the elbow amputees (n=4) and age matched healthy controls (n=3).

Methods: A randomized eight-target center-out paradigm was used to quantify motor performance and adaption in each arm. Participants were asked to produce planar shoulder and elbow movements to move their intact or prosthetic hand while attached to the robot. Participants observed a monitor displaying hand and target position. For motor performance testing, participants were asked to perform these movements with no vision of their hand and no forces applied by the robot (i.e. null field) for 10 trials per target. To test motor adaptation, participants performed the same movement with visual feedback of hand position, but a novel, velocity-dependent force field was applied to the hand during the movement for 60 trials per target. After 40 trials of reaching in the force field, 5 â€œcatchâ€ trials were randomly introduced in which the force field was unexpectedly removed, providing an indication of the â€œafter effectâ€ of motor adaptation. In separate sessions, transcranial magnetic stimulation was used to measure paired-pulse interhemispheric inhibition (IHI) targeting proximal muscle representations in each cortical hemisphere at interstimulus intervals of 10 and 40 ms. IHI targeting the distal representation of the intact arm/hemisphere was measured as well. In addition, the size and location of the brain area representing the proximal muscles was estimated by applying TMS over a 9 x 9 grid with 10 mm spacing using stereotactic neuro-navigation and the sizes and locations of these motor areas in the affected and intact hemispheres were compared.

Results: Participants performed the movements successfully with both the intact and prosthetic arms. For motor performance, the majority of participants tested thus far have shown between-limb differences in maximal directional error and endpoint error of their reaching movements, with about half of them showing greater error in the intact than the prosthetic arm. For motor adaptation, approximately half of the participants demonstrate between-limb differences in motor adaptation to an imposed force field. These differences may be related to physiological imbalances between the two cortical hemispheres, a possibility that is currently under investigation.

Conclusion: These findings suggest that, similar to the deficits that have been shown in the â€œunaffectedâ€ arm after stroke, there may be deficits in the intact arm after amputation. These deficits may be related in part to the profound cortical reorganization that occurs after arm amputation, a possibility that bears further investigation.

Keywords *Transcranial Magnetic Stimulation (primary keyword)*

Neurophysiology (EEG, MEG, ?)
Rehabilitation Medicine (neural repair and regeneration)

Abstract Topics

Neurophysiology (EEG, MEG,â€¦)
Transcranial Magnetic Stimulation
Brain mapping/functional imaging for rehab medicine
Rehabilitation Medicine (neural repair and regeneration
Basic Neuroscience

The abstarct book's publications additonal Information summary

Behavioral and neuro-physiological effects of chronic unilateral arm amputation: a preliminary analysis.

Erika Breceda Tinoco (1,2), Alexander W. Dromerick (1,3,5), Evan Chan (1,5), Friedhelm Sandbrink (2), Sambit Mohapatra (1,5), Peter S. Lum (1,4), Raquel Silva (1), Michelle Harris-Love (1,3).
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Introduction: The substantial reorganization of the affected motor cortex after unilateral arm amputation is well known. A recent study showed disrupted intact arm function when compared to age-matched controls, suggesting changes in the intact motor cortex may also occur after amputation.
Objective: We investigated the intra- and inter-hemispheric physiological effects of chronic arm amputation and their relationship to intact and affected limb motor performance in a convenience sample of chronic (>1 yr) below the elbow amputees (n=4) and age matched healthy controls (n=3).
Methods: A randomized eight-target center-out paradigm was used to quantify motor performance and adaption in each arm. Participants were asked to produce planar shoulder and elbow movements to move their intact or prosthetic hand while attached to the robot. Participants observed a monitor displaying hand and target position. For motor performance testing, participants were asked to perform these movements with no vision of their hand and no forces applied by the robot (i.e. null field) for 10 trials per target. To test motor adaptation, participants performed the same movement with visual feedback of hand position, but a novel, velocity-dependent force field was applied to the hand during the movement for 60 trials per target. After 40 trials of reaching in the force field, 5 â€œcatchâ€ trials were randomly introduced in which the force field was unexpectedly removed, providing an indication of the â€œafter effectâ€ of motor adaptation. In separate sessions, transcranial magnetic stimulation was used to measure paired-pulse interhemispheric inhibition (IHI) targeting proximal muscle representations in each cortical hemisphere at interstimulus intervals of 10 and 40 ms. IHI targeting the distal representation of the intact arm/hemisphere was measured as well. In addition, the size and location of the brain area representing the proximal muscles was estimated by applying TMS over a 9 x 9 grid with 10 mm spacing using stereotactic neuro-navigation and the sizes and locations of these motor areas in the affected and intact hemispheres were compared.
Results: Participants performed the movements successfully with both the intact and

prosthetic arms. For motor performance, the majority of participants tested thus far have shown between-limb differences in maximal directional error and endpoint error of their reaching movements, with about half of them showing greater error in the intact than the prosthetic arm. For motor adaptation, approximately half of the participants demonstrate between-limb differences in motor adaptation to an imposed force field. These differences may be related to physiological imbalances between the two cortical hemispheres, a possibility that is currently under investigation.
Conclusion: These findings suggest that, similar to the deficits that have been shown in the â€œunaffectedâ€ arm after stroke, there may be deficits in the intact arm after amputation. These deficits may be related in part to the profound cortical reorganization that occurs after arm amputation, a possibility that bears further investigation.

Key words: amputation, upper extremity, transcranial magnetic stimulation, motor control

This work has not been previously submitted for publication or presentation.

Educational Objectives 1. Guide active discussion on motor performance and adaptation differences that occur post amputation in the intact and amputated limb. 2.Participants will be able to relate interhemispheric inhibition and its effect on motor performance post amputation. 3. Participants will be able to visualize size and location of motor areas in the affected and intact hemispheres. Prior to 2009 (Schabowsky et al), the intact arm was thought to be normal following amputation. This study aims at increasing our understanding behind these changes and possible underlying neurophysiological mechanism to help improve rehabilitation approaches.

Files *Submission exists, but was not archived (suffix)*

Reviews

Cellular Studies in the Development of a Bioactive Stent Prototype to Close Aneurysm/Pseudoaneurysm Neck Orifices

Lisa M. Reece - Dept. of Basic Medical Sciences, College of Veterinary Medicine, Purdue University, West Lafayette, IN USA

Ravindra Kempaiah - School of Materials Engineering, College of Engineering, Purdue University

Sandra Arias Suarez - School of Nuclear Engineering, College of Engineering, Purdue University

Milad Alucozai - College of Health and Human Sciences, Purdue University

Emily K. Walker - School of Materials Engineering, College of Engineering, Purdue University

Juan Jose Pavon Palacio - School of Nuclear Engineering, College of Engineering, Purdue University

Jean Paul Allain - School of Nuclear Engineering, College of Engineering, Purdue University

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Abstract: Current treatments for aneurysms/pseudoaneurysms incorporate clipping and coil embolization, including stent-assisted coiling. While these procedures can be effective, it would be highly advantageous to the patient for a biologically active stent to be employed that would allow stem cells to be manipulated to heal the arterial lining. However, cell behavior is influenced by surface chemistry and topography where changes in nanotopography can result in alterations in cell proliferation, adhesion, differentiation, and gene expression. A first step to realizing a bioactive stent device is to assess how well cells can positively interact with the particular biomaterial that may constitute the stent itself. One particular type of biomaterial known as nanobacterial cellulose (NBC) has been used extensively in tissue implants for skin, subcutaneous tissue, and digestive tract organs. NBC has also been used to improve the healing process of burns and chronic wounds and is therefore known to be very biocompatible and thus a good candidate for the bioactive stent device model. It is understood that cells can sense substrate texture by changing their morphology, cytoskeleton configuration, and intra- and extracellular signaling. This is important because NBC possesses a unique surface roughness due to the fibril lattice and porous nature of the arrangement of the strings of polymer that make up this substance. NBC can act as a framework to which cells can attach, grow, proliferate and ultimately begin to close the aneurysm neck in vivo. The problem is how to recruit cells to the stent location. It was determined that magnetically labeled cells could be attracted to the NBC nidus if the bacterial cellulose held ferromagnetic properties. We therefore generated ferromagnetic iron oxide nanoparticles (FION) using a basic standard chemical thermal process. NBC was rendered magnetic through the impregnation of the newly

synthesized FION in the same reaction, producing magnetic nanobacterial cellulose (MNBC). Of great importance is that the iron oxide nanoparticles are not by themselves biocompatible; thus to render them so, different coatings (dextran and citrate) in several diverse concentrations were used to cover the FION surface before adding to the magnetization reaction. To test the newly synthesized MNBC, two different cell types, Human Umbilical Vein Endothelial Cells (HUVEC), and Human Aortic Smooth Muscle Cells (HASMC), were grown in the presence of the MNBC samples until they were harvested and cytotoxicity was measured using the single cell gel electrophoresis assay (Comet Assay) to analyze DNA damage. Also, magnetically enhanced HUVEC and HASMC were tested to see if they were attracted to the magnetic field generated by the MNBC by simple visual observations. In summary, this study shows that the different varieties of MNBC successfully attracted the magnetic cells to itself. Cytotoxicity results relate that the non-magnetic NBC for both cell types is biocompatible while various concentrations of the coated iron oxide nanoparticles and the resultant MNBC yielded growth results ranging from cell death (necrosis) to cell proliferation with decent viability. Taken together, it seems that the MNBC is a good candidate for the tissue nidus of a bioactive stent device.

Keywords	*Minimally invasive therapy (primary keyword)* Vascular & Blood flow imaging Molecular and cellular imaging
Abstract Topics	Vascular & Blood flow imaging Molecular and cellular imaging Nanoscience, genomics, genetics
The abstarct book's publications additonal Information summary	
Educational Objectives	The educational objective of the presentation is to provide basic and clinical researchers an opportunity to discover an alternative to existing treatments for aneurysm therapies. While the research is in its infancy, its impact is far reaching: from military personnel to the general public. The research has been funded by the DoD for a three year period.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Enhancement of Brain Rehabilitation by use of the Verhoog Screening & Remediation Program (VSRP)

Jo Ann Verhoog - Verhoog Music Institute for Neuroscience Research

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Abstract: JoAnn Verhoog, Owner, Director Verhoog Institute of Music for Neuroscience Research 1305 Forest Ave. Evanston, IL 60201 joann_vmi@yahoo.com

Brain injury affects more than simply structural components of gray and white matter. It often has functional manifestations including deficiencies in three main areas. 1) intake of information though sensory pathways (i.e. visual, auditory and pathways used respectively in such activities as reading , listening), 2) overall processing of sensory information needed in filtering out distractions, maintaining attention, and organizing details within larger concepts, and 3) output of motor reactions and responses, used in balance, walking, navigating through surrounding space, etc.

By measuring the challenges and limitations in those three main functional systems, remediation of physiological barriers compounding those symptoms can often be achieved by addressing underlying causes. Over the past thirty years, the Verhoog Screening and Remediation Program (VSRP) has amassed a normative database of findings, providing an easy method to determine and remediate faulty sensory/motor channels.

The simple, brief screening portion identifies damaged circuits, and the remediation program can selectively activate brain pathways in a carefully planned, hierarchical order. This remediation employs neuroplasticity and allows for enhancement in quality of life while developing new neural pathways in an enjoyable manner. Those patients with brain injuries told that they were incapable of continuing their professional lives were able to return to work within eighteen months of the Verhoog remediation, some in as little as six months. KEYWORDS: Music, Cognitive Skills, Auditory processing, Visual Processing, Brain Injury

Keywords

Rehabilitation Medicine (neural repair and regeneration) (primary keyword)
Brain mapping/functional imaging for rehab medicine and PTSD
Minimally invasive therapy

Abstract Topics

Neurophysiology (EEG, MEG,â€¦)
Psychiatry (PTSD,â€¦)

Brain mapping/functional imaging for rehab medicine
Minimally invasive therapy
Basic Neuroscience

The abstarct book's publications additonal Information summary

TITLE: Enhancement of Brain Rehabilitation by use of the Verhoog Screening & Remediation Program (VSRP)

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Abstract: Brain injury affects more than simply structural components of gray and white matter. It often has functional manifestations including deficiencies in three main areas. 1) intake of information though sensory pathways (i.e. visual, auditory and pathways used respectively in such activities as reading , listening), 2) overall processing of sensory information needed in filtering out distractions, maintaining attention, and organizing

details within larger concepts, and 3) output of motor reactions and responses, used in balance, walking, navigating through surrounding space, etc.

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The simple, brief screening portion identifies damaged circuits, and the remediation program can selectively activate brain pathways in a carefully planned, hierarchical order. This remediation employs neuroplasticity and allows for enhancement in quality of life while developing new neural pathways in an enjoyable manner. Those patients with brain injuries told that they were incapable of continuing their professional lives were able to return to work within eighteen months of the Verhoog remediation, some in as little as six months.

KEYWORDS:
Music, Cognitive Skills, Auditory processing, Visual Processing, Brain Injury

SUPPLEMENT:
Introduction: After brain injury, there are often many residual processing problems. Patients present with such diagnoses as attention deficit disorder, acquired dyslexia, aggressive behavior, etc. The challenges and limitations associated with these complex mental conditions are lessened by changing physiological barriers and developing new neural pathways.

The Verhoog Program has two portions. The first portion (a brief screening) identifies dysfunctional conditions such as reading, listening, staying mentally focused, or having inefficient information processing. The second portion (rehabilitation) rebuilds damaged brain functions by activating processing pathways by using visual and auditory signaling as inputs and motor reactions and responses as a way to monitor changes.

In addition to assessments of visual and auditory intake obstacles, two other types of obstacles evaluated are 1) filtering distractions from the auditory and visual intake channels and 2) which of thirteen processing styles of thinking are efficiently used, based on three overarching processing modes (Analytical, Conceptual and Experimental).

The screening identifies how each of the above four areas (visual, auditory, filtering distractions or processing methods) is obstructing normal function. Upon completion of all four tests, the Verhoog Program gives specific details, providing information about which area(s) negatively impact their ability to learn. Analysis of the data establishes guidelines so that individualized rehabilitation programs can be designed to address each area(s) needing activation.

Methods: By modifying visual and auditory intake techniques, the brief screening determines which of thirteen processing styles are habitually used for accurate interaction with the surrounding environment and efficiency in learning. Remediation is individually designed to develop functional circuitry necessary to stimulate alternate processing areas, if habitual ones are damaged.

Modifications to visual and auditory intake ability is performed by varying visual and auditory components such as target size, style, color, target location, eye position and varying vocal features of gender, pitch, speed or tone of voice. Another skill assessed is the ability to pull a selected target (figure) out of a distracting background while maintaining attention on that target.

Intake modifications include visual and auditory distractions variables, such as changes in lighting and background noises, and also subjectively measuring personal discomfort. Active coaching is applied during the remediation portion to enable the brain to develop faster connections.

Results: The screening determines which pathways create the most obstacles for each patient. Thirty years of data shows that 70% of people demonstrate limited styles of processing, 20% are color sensitive and 40% have a visual intake dysfunction.
After rehabilitation, 80% of participants experienced new professional insights & skills that included:

- â€¢ Increased speed of work with less effort
- â€¢ Fewer mistakes
- â€¢ Better organization
- â€¢ Creativity to see and solve a problems before it occurred

â€¢ Thinking outside the box
â€¢ Improved problem solving
â€¢ Clearer & expanded interpersonal communications
â€¢ Shift thinking and see from new perspectives
â€¢ Reduced stress
â€¢ Increased enjoyment in work
â€¢ Increased self-confidence
â€¢ Clear and easy employment of analytical abilities

The Verhoog Program has greatly increased cognitive abilities, allowing faster learning and increased enthusiasm. It provides students with the ability to process analytically, conceptualize, problem solve, use intuition and expand communication skills. They comfortably move from the perspective of Observer, Participant and Teacher roles while learning or relearning skills that transfer to their work, introspection and their personal life.

Conclusions: After the structures of the brain are disrupted by either injury or surgery, it is important to thoroughly assess brain function and remediate processing. The Verhoog Screening and Remedial Processing accomplishes both with a minimal amount of time and effort. Its thirty years of normative data provide excellent guidelines in development of new functional pathways and its screening portion should be included in general testing of brain injured patients to determine specific intake and processing obstacles. The program portion will allow for remediation to enhance quality of life.

The Verhoog Screening Remediation Program (VSRP) has positively impacted hundreds of adults over the past thirty years. Its screening process provides the ability to identify specific learning obstaclesâ€™ that more than 40% of non - brain injured adults face. The data collected identifies which area(s) is affecting an adultâ€™s ability to reach their highest potential. The Program then remediates the dysfunctional area(s), providing adults with the tools needed to have new successes that occur with clarity of the situation and ease in working. Adults with brain trauma and brain damage resulting from surgical operations regain a professional life that would have been lost without the remediation.

Educational Objectives 1) To demonstrate that music can be used in a non-invasive way to assess functional damage and remediate dysfunctional circuitry after brain injury, by accelerating learning. 2) To develop awareness in the scientific community that music can be used in a specific hierarchical order during remediation of brain function. 3) To provide a simple, enjoyable method for enhancing quality of life after brain injury

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Target bio-molecular probes for effective biomedical imaging through the design of multifunctional gold nanostructure

Jianling Wang - State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University

Yuanyuan Zhang - State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University

Qiwei Li - State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University

Hui Jiang - State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University

Xuemei Wang - State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University

Contact: Xuemei Wang (xuewang@seu.edu.cn)

Abstract: Target bio-molecular probes for effective biomedical imaging through the design of multifunctional gold nanostructure Jianling Wang,1 Yuanyuan Zhang,1 Qiwei Li,1 Hui Jiang,1 Xuemei Wang*,1 1 State Key Laboratory of Bioelectronics (Chien-Shiung Wu Lab), School of Biological Science and Medical Engineering, Southeast University, Nanjing, 210096, China Corresponding author: xuewang@seu.edu.cn Gold-based nanomaterials have been focused owing to their attractive nanostructures as contrast agent, delivery vehicles, or therapeutics for improving the diagnosis and treatment of some important disease like tumors. In this contribution, we have explored the possibility to design multifunctional gold nanostructure as well as bio-friendly nano-interface/probes for tumor targeting treatment and biomedical imaging of cancer cells /and related tissues. The results of confocal fluorescence/Raman spectroscopy and scanning electrochemical microscopy study demonstrate that the relevant nanostructure based bio-molecular probes could be utilized as sensitive biomarkers and therapy agents for the targeted cells/tissues. To further explore the mechanism and interaction between the multifunctional gold nano-interface/probes and the biological tissues, the in vivo bio-imaging analysis has been explored by construction of the xenograft tumors model in nude mice. Moreover, the molecular mechanism of the interaction between the nano-interface/probes and target cells/tissues is demanding to be testified by experiments, which are being designed in our research. Through the confocal Raman/fluorescence spectroscopy and scanning electrochemical microscopy study, effective biomedical imaging could be obtained by target bio-molecular probes, just due to the acquiescence of multifunctional gold nanostructural probes in the focus of infections. The related nano-probes could essentially fulfill specific and sensitive biomedical imaging and therapy, realizing the effective disease diagnostics and

treatments as well as point of care testing. Key wards: Gold Nanomaterials, Biomedical Image, Multifunctional Nanointerface, Nanoscaled Probes
Acknowledgements: This work is supported by the National Basic Research Program of China (No.2010CB732404) and National Natural Science Foundation of China (21175020, 90713023). Reference: [1] Wang C.; Li J.; Amatore C.; Chen Y.; Jiang H.; Wang X. Angew. Chem. Int. Ed. 2011, 50: 11644 [2] de la Rica, R.; Matsui, H. Chem. Soc. Rev. 2010, 39 : 3499 [3] Wu D, Zhang X., Liu P., Zhang L., Fan F., Guo M. Curr. Nanosci. 2011;7:110.

Keywords	*Molecular and cellular imaging (primary keyword)* Image guided systems Imaging modalities for detecting mild/mod TBI, micro-TBI Multimodality imaging
Abstract Topics	Molecular and cellular imaging Multimodality imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	Molecular and cellular imaging,Multimodality imaging,Image guided systems
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

3-dimensional positioning of motor tract during brain tumor surgery

Fumio Yamaguchi - Nippon Medical School, Neurosurgery
Hadashi Higuchi - Nippon Medical School, Neurosurgery
Hirotomo Ten - Nippon Medical School, Neurosurgery
Tomoko Omura - Nippon Medical School, Neurosurgery
Yudo Ishii - Nippon Medical School, Neurosurgery
Koji Adachi - Nippon Medical School, Neurosurgery
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Abstract: 3-dimensional positioning of motor tract during brain tumor surgery

Fumio Yamaguchi, Hadashi Higuchi, Hirotomo Ten, Tomoko Omura, Yudo Ishii, Koji Adachi, Takayuki Kitamura, Akira Teramoto

Department of Neurosurgery, Nippon Medical School

Introduction: The difficulty of 3 dimensional recognition of deep brain structure often makes surgeons to lose their way during subcortical resection of tumors. The advanced technology such as fiber tracking information integrated in navigation system gives us important information; however intraoperative brain shift and discrepancy between calculated anatomical information and actual functioning structure degrade the precision of location of motor tracts.

Methods: NY Tract Finder (NYTF), an electrode designed for navigation-assisted subcortical brain mapping, was used during the resection of 33 brain tumors adjacent to motor tract. 25mm-long plastic 16-gauge (G) needleâ €™s sheaths were inserted into the point of 5mm short of the motor tracts along with this electrode. The timing of the stop of electrode insertion was noticed by the evoked EMG recording. Neuronavigational information was used as a reference for the determination of electrode direction. Multiple plastic needle sheaths were placed to track the motor tract for surgical guidance.

Results: The tracking of motor fibers was practicable in surgical field. Inserted plastic sheaths enabled the recognition of the location of under-passing motor pathways even if they were not exposed. The direction and depth of motor tracts were known by watching those plastic tube inserted into white matter. Plastic sheaths could guide safe resection of tumors without the injury of functioning motor fibers.

Conclusion: Three-dimensional positioning of motor pathways is feasible by this method. It is important to know the advantage and disadvantage of neuronavigation system for its efficient use. The neurophysiological detection of motor fibers is indispensable for the safe and maximal resection of subcortical tumors. 3-dimensional positioning of motor tract is a good guide during brain tumor surgery.

Keywords
Intraoperative Surgical Planning (primary keyword)
Operational issues
Image guided systems
Diffusion Tensor Imaging

Abstract Topics
Operational issues
Image guided systems
Intraoperative Surgical Planning
Neurophysiology (EEG, MEG,â€¦)

Multi-modality imaging and ultrasound
Diffusion Tensor Imaging

The abstarct book's publications additonal Information summary

Title:
3-dimensional positioning of motor tract during brain tumor surgery

Authors:
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Introduction:
The difficulty of 3 dimensional recognition of deep brain structure often makes surgeons to lose their way during subcortical resection of tumors. The advanced technology such as fiber tracking information integrated in navigation system gives us important information; however intraoperative brain shift and discrepancy between calculated anatomical information and actual functioning structure degrade the precision of location of motor tracts.

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NY Tract Finder (NYTF), an electrode designed for navigation-assisted subcortical brain mapping, was used during the resection of 33 brain tumors adjacent to motor tract. 25mm-long plastic 16-gauge (G) needleâ€™s sheaths were inserted into the point of 5mm short of the motor tracts along with this electrode. The timing of the stop of electrode insertion was noticed by the evoked EMG recording. Neuronavigational information was used as a reference for the determination of electrode direction. Multiple plastic needle sheaths were placed to track the motor tract for surgical guidance.

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Three-dimensional positioning of motor pathways is feasible by this method. It is important to know the advantage and disadvantage of neuronavigation system for its efficient use. The neurophysiological detection of motor fibers is indispensable for the safe and maximal resection of subcortical tumors. 3-dimensional positioning of motor tract is a good guide during brain tumor surgery.

Key words:
Subcortical brain mapping, Tractography, Neuronavigation, 3D positioning

Educational Objectives change of practice (surgical procedure)

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Engineering the Abio-to-Bio Interface to Enable Next-generation Neural Prostheses

Anthony Guiseppi-Elie - Clemson University

Contact: Anthony Guiseppi-Elie (guiseppi@clemson.edu)

Abstract: The need for a low impedance, biocompatible, abio-to-bio interface suitable for implantable bioactive devices has led to the development of electroconductive hydrogels. Conductive electroactive polymers (CEPs) are one dimensional organic semiconductors synthesized from aromatic monomers into extended pi-conjugated polymers. The synthesis of CEPâ€™s, in conjunction with highly hydrated hydrogels, produces a class of hybrid materials with the conductivity of the CEPs and the inherent biocompatibility of the hydrogel. In addition, CEPs provide a biofabrication route for the additive electrodeposition of biorecognition molecules to specific nano- and micron-dimensioned metallic and semiconducting sites on microfabricated metallic or semiconductor MEMS devices. Through judicious engineering of repeat unit chemistry, polymer architecture, crosslink density and microstructure, the mechanical, transport and surface properties of these interpenetrating co-networks may be controlled. When implanted, these materials enable: i) programmed low voltage electro-release of factors suitable for mitigating the inflammatory response, ii) hosting of molecular recognition agents such as enzymes and peptides and iii) accommodation of supramolecular assemblies of CNTs and enzymes supporting direct electron transfer for generation-3 biosensors and implantable biofuel cells.

Keywords	*Neural Prosthesis & Robotics (primary keyword)*
Abstract Topics	Neural Prosthesis & Robotics
The abstarct book's publications additonal Information summary	
Educational Objectives	1) Publication 2) Failure modes of DBSD3)Possible solutions involvng materials engineering

Files	*Submission exists, but was not archived (suffix)*

Reviews

Spinal Cord Mapping for Chronic Pain Treatment

Nicolae Iftimia - Brandeis University
Kris Carlson - Beth Israel Deaconess Medical Center
Longzhi Mei - Beth Israel Deaconess Medical Center
Jay Shils - Lahey Clinic
Jeffrey Arle - Beth Israel Deaconess Medical Center

Contact: Nicolae Adrian Iftimia (nickiftimia@gmail.com)

Abstract: Spinal Cord Stimulation (SCS) is a neurosurgical technique currently used in treating chronic pain disorders caused by spinal cord injury or disease â€“ conditions affecting millions of patients worldwide and costing billions of dollars per year. SCS involves surgical placement of paddle stimulator leads onto the dorsal side of the spinal cord, adjacent to the dura mater; thus, electrical signals are sent to axons within the dorsal columns, modulating neural activity. The paddle electrodes are connected to a pulse generator implanted in the lower back. Although SCS is generally a safe procedure, several complications can occur â€“ many due to improper electrode placement. These include hematomas, scarring, infection, cerebrospinal fluid leak, and paralysis. Mapping of the spinal cord neural circuitry, in conjunction with computational modeling, could be used to inform the placement of electrodes for SCS, thereby increasing efficacy and therapeutic value while reducing the occurrence and gravity of these complications. This may also aid in illuminating certain aspects of the mechanism by which SCS achieves its analgesic effects. Using neural modeling software (Universal Neural Circuitry Simulator or UNCuS), we have created a dynamic yet robust computational model of the neural circuitry in a generic spinal cord segment. Our software optimizes biological accuracy and computational efficiency towards clinical purposes, and allows for key parameters to be modified to fit each individual. Neurons are based on a modified MacGregor spiking model, incorporating a â€˜lumpedâ€™ conductance term that accounts for any additional conductances which may contribute to a cellâ€™s current-voltage curve. Through accurate simulation of this current-voltage relationship, the model captures the essential characteristics and input-output transfer function of any particular neuron. Currently, the model comprises approximately 360,000 neurons and 60 million synaptic connections. Only intrinsic cell characteristics were incorporated; the model itself is agnostic to any proposed pain theories and emergent higher-order behaviors. The finite element method was used to model electrodes and associated 3-D potential fields and simulate their interaction with the neural circuitry. Calibration was performed by reproducing the H-reflex. A â€˜painâ€™ signal was then created in silico by stimulating specific afferent C-fiber

inputs to the circuit, which activated the â€˜wide dynamic rangeâ€™ (WDR) projection cells to send this noxious information to the brain. Subsequently, electrodes were used to stimulate the axons of the dorsal columns, resulting in retrograde inhibition of the WDR neurons â€“ effectively causing â€˜pain relief.â€™ The mechanisms of this neuromodulation were investigated. We also tested how electrically resistive scar tissue interferes with SCS as a function of scar geometry. Several hypotheses regarding optimal electrode placement were derived from these simulations. Incidentally, these hypotheses bear certain similarities to the classic gate control theory of pain. Clinical testing of these hypotheses revealed that novel stimulation paradigms could be used in certain patients to achieve superior treatment results. Data derived from the clinical trials and the clinical literature further corroborated the model. In conclusion, we have enumerated multiple potential mechanisms for the blockade of pain that map onto our model of the spinal cord and may benefit SCS.

Keywords	*Spinal cord instrumentation and implants (primary keyword)* Neural Prosthesis & Robotics Rehabilitation Medicine (neural repair and regeneration) Spinal Cord, Trauma Repair and regeneration
Abstract Topics	Neural Prosthesis & Robotics Rehabilitation Medicine (neural repair and regeneration Spinal Cord, Trauma Repair and regeneration Spinal cord instrumentation and implants
The abstarct book's publications additonal Information summary	
Educational Objectives	1. spread awareness of spinal cord injury; 2. inform the audience about new advances in spinal cord stimulation and mapping; 3. talk about the clinical relevance of this research
Files	*Submission exists, but was not archived (suffix)*

Reviews

Efficient Registration between CT/MRI Multi-Slices and 3D Face Data for Frameless Brain Surgery

Yau-Zen Chang - Chang Gung University
Jung-Fu Hou - Chang Gung University
Shih-Tseng Lee - Chang Gung Memorial Hospital

Contact: Yau-Zen Chang (zen@mail.cgu.edu.tw)

Abstract: During frameless neurosurgery, the 3D surface data of patientâ€™s face must be aligned with CT/MR images to reference patients to a navigation system. Among the methods to register the CT/MR images with 3D face data, the Iterative Closest Point algorithm, together with building a k-D tree, has been the dominant method. Although these approaches are fast enough for practical applications, however, they are extremely sensitive to initial pose and require multiple trials to find a reliable solution. Alternatively, these two 3D data sets can be registered by the use of computationally demanding 3D chamfer distance transform (CDT). This work presents an efficient procedure without resort to GPU-based systems for real-time operation. We propose to use 2D chamfer distance transform on the contour of each image slice to assign distance quantities at each CT image layer to measure its degree of alignment with the patientâ€™s 3D face data. With this transform, degree of match can be directly estimated by direct indexing without calculation of distances between closest points. And a parallel version of Particle Swarm Optimization algorithm is applied to find the best coordinate transformation for the alignment. Major improvement in performance of the approach comes from the benefit that the distance transform has to be executed only once for the layers.

A plastic CT-compatible phantom was made using the iPro 8000 SLA Center, 3D Systems Inc., for accuracy assessment. The phantom has 24 artificial targets located on the head surface and 35 inside the skull; all are accurately designed using the Pro/ENGINEER Wildfire 5.0. The targets are 10 mm in diameter and 2 mm high with 1.5 mm wide pinholes at the center. The target registration error (TRE) is defined as the deviation between the coordinates estimated by the system and the CAD data. Experimental results show that the TRE is 2.72 Â± 0.735 mm.

Keywords

Image guided systems (primary keyword)
Intraoperative Surgical Planning

Abstract Topics

Image guided systems
47

The abstarct book's publications additonal Information summary

Educational Objectives	To introduce an alternative way to register the CT/MR images with 3D face data.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Correlation Between Magnetoencephalography â€œClusterectomyâ€ and Postoperative Seizure-Free Outcomes

Sumeet Vadera - Cleveland Clinic
Lara Jehi - Cleveland Clinic
Richard Burgess - Cleveland Clinic
Andreas Alexopoulous - Cleveland Clinic
John Mosher - Cleveland Clinic
Jorge Gonzalez-Martinez - Cleveland Clinic
William Bingaman - Cleveland Clinic

Contact: Sumeet Vadera (svadera@gmail.com)

Abstract: Introduction - During the presurgical evaluation of patients with medically intractable focal epilepsy, a variety of noninvasive studies are performed to localize the hypothetical epileptogenic zone (EZ) and guide the resection. Magnetoencephalography (MEG) is becoming increasingly utilized in the clinical realm for this purpose. To date, no studies have performed coregisteration of MEG clusters with postoperative resection cavities to evaluate whether complete â€œclusterectomyâ€ was performed and then compared this with postoperative seizure free outcomes.

Methods â€“ We retrospectively reviewed the charts and imaging studies of 65 patients undergoing MEG followed by resective epilepsy surgery from 2009 until 2012 at the Cleveland Clinic. Preoperative MEG studies were fused with postoperative MRIs to evaluate whether clusters were within the resected area. These data were then correlated with postoperative seizure-freedom.

Results â€“ Sixty-five patients were included in this study. The average follow-up was 13.9 months, mean age at surgery was 23.1 years, and mean epilepsy duration was 13.7 years. In 29 patients, the main cluster was located completely within the resection cavity, in 28 it was completely outside the resection cavity and in 7 it was partially within the resection cavity. Seventy-four percent of patients were seizure-free at 12 months, which decreased to 60% seizure-free at 24 months and onwards. Improved likelihood of seizure-freedom was seen with complete cluster resection in patients with extra-temporal lobe epilepsy (p = 0.04)

Conclusions â€“ In patients with preoperative MEG studies that show clusters in surgically accessible areas outside the temporal lobe, we suggest aggressive resection to improve the chances for seizure freedom. When the cluster is found within the temporal lobe, further diagnostic testing may be required to better localize the EZ.

Keywords
Neurophysiology (EEG, MEG, ?) (primary keyword)
Image guided systems
Intraoperative Surgical Planning
Multi-modality imaging and ultrasound

Abstract Topics
General issues
Image guided systems
Intraoperative Surgical Planning
Neurophysiology (EEG, MEG,â€¦)
Functional brain mapping (fMRI, PETâ€¦)
Multi-modality imaging and ultrasound
Multimodality imaging

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summary

Sumeet Vadera MD*, Lara Jehi MDâ€¡, Richard Burgess MD PhDâ€¡, Katherine Sheaâ€¡, Andreas Alexopoulos MDâ€¡, John Mosher PhDâ€¡, Jorge Gonzalez-Martinez MD PhD*, William Bingaman MD*

*Department of Neurosurgery; and â€¡Epilepsy Center, Cleveland Clinic Foundation, Cleveland, Ohio

Abstract
Introduction -
During the presurgical evaluation of patients with medically intractable focal epilepsy, a variety of noninvasive studies are performed to localize the hypothetical epileptogenic zone (EZ) and guide the resection. Magnetoencephalography (MEG) is becoming increasingly utilized in the clinical realm for this purpose. To date, no studies have performed coregisteration of MEG clusters with postoperative resection cavities to evaluate whether complete â€œclusterectomyâ€ was performed and then compared this with postoperative seizure free outcomes.
Methods â€"
We retrospectively reviewed the charts and imaging studies of 65 patients undergoing MEG followed by resective epilepsy surgery from 2009 until 2012 at the Cleveland Clinic. Preoperative MEG studies were fused with postoperative MRIs to evaluate whether clusters were within the resected area. These data were then correlated with postoperative seizure-freedom.
Results â€"
Sixty-five patients were included in this study. The average follow-up was 13.9 months, mean age at surgery was 23.1 years, and mean epilepsy duration was 13.7 years. In 29 patients, the main cluster was located completely within the resection cavity, in 28 it was completely outside the resection cavity and in 7 it was partially within the resection cavity. Seventy-four percent of patients were seizure-free at 12 months, which decreased to 60% seizure-free at 24 months and onwards. Improved likelihood of seizure-freedom was seen with complete cluster resection in patients with extra-temporal lobe epilepsy ($p = 0.04$)
Conclusions â€"
In patients with preoperative MEG studies that show clusters in surgically accessible areas outside the temporal lobe, we suggest aggressive resection to improve the chances for seizure freedom. When the cluster is found within the temporal lobe, further diagnostic testing may be required to better localize the EZ.

Keywords: Magnetoencephalography, Seizure-free outcomes, cluster resection, dipoles.

Educational Objectives 1) Learn when MEG clusterectomy has the highest likelihood of obtaining seizure freedom. 2) This research will improve preoperative patient workup for seizure monitoring.

Files *Submission exists, but was not archived (suffix)*

Reviews

Ibu2TEG Nanoprodrug Vehicle of Paclitaxel for Glioblastoma Treatment

Yosef Chodakiewitz - Alpert Medical School of Brown University
Amith Subhash - University of Utah School of Medicine
Allen Yen - Boston University
Bong Seop Lee - Cedars Sinai Medical Center
John Yu - Cedars Sinai Medical Center

Contact: Yosef Chodakiewitz (yosef_chodakiewitz@brown.edu)

Abstract: Glioblastoma multiforme (GBM) is the most common primary brain tumor in adults. After diagnosis, median survival is 3 months without treatment. With combination treatment involving surgery, radiation, and chemotherapy, median survival is extended to just 15 months. Current chemotherapeutic formulations have poor efficacy, and the tumors invariably recur.

Paclitaxel (PTX), which kills mitotically active cells, might be a promising agent for use in GBM treatment. Ideally, PTX would be delivered systemically so that cancer pockets could be attacked wherever they might be in the body. However, PTX is a nonpolar compound, which makes the aqueous environment of the plasma an obstacle for its systemic delivery. Furthermore, the blood-brain-barrier (BBB) strongly limits the ability of systemically delivered therapeutic substances to cross from the vascular compartment into actual brain tissue at the brainâ€™s capillaries. Thus, non-modified PTX would require higher dosages and/or dissolution in potentially toxic co-solvents to be able to carry out its anticancer activity in the body. This is not a clinically viable solution, as side-effects and overall toxicity quickly become intolerable and outweigh potential therapeutic benefits.

In the present study, we investigate the potential role of a nanoprodrugâ€”a novel type of nanoparticleâ€”as a delivery vehicle of PTX (an NPD-PTX) for GBM treatment. We will discuss the general concept, strategy, and design of an NPD-PTX, as well as present some preliminary results from this early stage of our investigation. Using Ibu2TEG as the prodrug matrix for the NPD-PTX, we have so far observed that a potent cytotoxic effect is maintained on GBM cells treated in vitro with the NPD-PTX formulation. We have also begun to demonstrate the strong brain tumor targeting ability of NPD-PTX in vivo, using the Xenogen IVIS 200 imaging system to view bio-distribution of fluorescently tagged NPD-PTX particles injected into mice with intracranial GBM.

Keywords *Nanoscience, genomics, computational informatics genetics (primary*

	keyword) Perfusion imaging, micromagnetic resonance imaging
Abstract Topics	Nanoscience, genomics, genetics
The abstarct book's publications additonal Information summary	
Educational Objectives	1. Explain the clinical challenge to efficacious use of chemotherapy for treating brain cancer. 2) Explain the concept and design of a nanoprodrug--a novel type of nano particle--as a drug delivery system for chemotherapy to improve its efficacy in brain cancer treatment. 3) Present early results in our study of an Ibu2TEG nanoprodrug formulation of PTX for Glioblastoma treatment.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

High-Sensitivity and High-Specificity of Mild Traumatic Brain Injury Diagnostic Method Using White Matter Tractography from Diffusion Tensor Imaging

Nina Butingan - University of California, Irvine College of Medicine
Kirk Shin - University of California, Irvine College of Medicine
Pauline Phan - University of California, Irvine College of Medicine
Vivian To - University of California, Irvine College of Medicine
Angela Wei - University of California, Irvine College of Medicine
Eric Chang - University of California, Irvine College of Medicine
Joseph Wu - University of California, Irvine College of Medicine

Contact: Nina Butingan (nbutingan@gmail.com)

Abstract: Traumatic brain injury (TBI) is a leading cause of death, injury, and disability in the United States, affecting nearly 1.7 million Americans each year. While the severity of TBIs can range from mild to severe, most cases of TBI are of the milder concussive form. Because of the ambiguity in the clinical diagnosis of chronic, post-concussive mild TBI (mTBI) using neuropsychological evaluation alone, a more concrete, biological, and evidence-based approach is necessary to corroborate the neuropsychological findings in patients suspected of having mTBI. Recent advances in neuroimaging have guided physiciansâ€™ diagnoses of psychiatric ailments like mTBI. Differences in brain anatomy and physiology can be detected through sensitive techniques like Flourodeoxyglucose-Positron Emission Tomography (FDG-PET) and magnetic resonance diffusion tensor imaging (DTI). Diffusion tensor imaging measures the restricted diffusion of water in various body tissues to produce neural tract images. Since damage to structural connections in the brain is a common feature of TBI, we propose the use of white matter tract dissections derived from DTI scan data as a method for differentiating mTBI patients from normal controls without TBI. We hypothesize that raters will be able to determine with high-sensitivity and high-specificity differences in white matter tractography of mTBI patients versus normal controls. For this study, 60 subjects total were screened neuropsychologically (30 mTBI patients and 30 normal controls) prior to the acquisition of brain scans using DTI. The mean age and gender ratio for the mTBI group was 37.4 years Â± 15.3, 14 male, 16 female, and the mean age and gender ratio for the control group was 34.4 Â± 11.4, 20 male, 10 female. The 30 patients with mTBI were clinical referrals for brain injury who had documented neuropsychological deficits several months post-trauma. MRI diffusion tensor imaging was performed on all 60 subjects. Tractographies were analyzed using Diffusion Toolkit and visualized using TrackVis. Five raters, familiar with white matter tractographies, were shown examples of white matter tract corpus callosum dissections of 10 normal controls and 10 patients with confirmed mTBI. After the initial example stage, the raters were asked to evaluate the remaining 40 subjects as either â€œTBIâ€ or â€œControlâ€ under blind experimental conditions. The 20 subjects used in the example stage were different from the 40 subjects used in the blind evaluation stage. Sensitivity and specificity were calculated from the results using standard binary classification measures of true-positives, true-negatives, false-positives, and false-negatives. Our average sensitivity in ratings was 89.5% Â± 7.6% and our average specificity was 93.5% Â± 1.8%. We can conclude from our analysis that white matter tract dissections provide a highly-specific and highly-sensitive measure for diagnosing patients with mTBI. While the results from this study suggest the usefulness of white matter tract dissections in the diagnosis of mTBI, previous studies conducted similarly in our lab have shown that statistical fractional anisotropy (FA) Z-maps derived from DTI show an even higher degree of sensitivity and specificity (94.5% and 98.1%, respectively). Both methods, however, seem to provide promising supplemental evidence for the clinical diagnosis of the disease.

Keywords *Imaging modalities for detecting mild/mod TBI, micro-TBI (primary keyword)*
Diffusion Tensor Imaging
Psychiatry (PTSD,?)

Abstract Topics Diffusion Tensor Imaging
Psychiatry (PTSD,â€¦)

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HIGH-SENSITIVITY AND HIGH-SPECIFICITY OF MILD TRAUMATIC BRAIN INJURY DIAGNOSTIC METHOD USING WHITE MATTER TRACTOGRAPHY FROM DIFFUSION TENSOR IMAGING

Nina Butingan1, Kirk Shin1, Pauline Phan1, Vivian To1, Angela Wei1, Eric Chang1, Joseph Wu1

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INTRODUCTION
Traumatic brain injury (TBI) is a leading cause of death, injury, and disability in the United States, affecting nearly 1.7 million Americans each year. While the severity of TBIs can range from mild to severe, most cases of TBI are of the milder concussive form. Because of the ambiguity in the clinical diagnosis of chronic, post-concussive mild TBI (mTBI) using neuropsychological evaluation alone, a more concrete, biological, and evidence-based approach is necessary to corroborate the neuropsychological findings in patients suspected of having mTBI. Recent advances in neuroimaging have guided physiciansâ€™ diagnoses of psychiatric ailments like mTBI. Differences in brain anatomy and physiology can be detected through sensitive techniques like Flourodeoxyglucose-Positron Emission Tomography (FDG-PET) and magnetic resonance diffusion tensor imaging (DTI). Diffusion tensor imaging measures the restricted diffusion of water in various body tissues to produce neural tract images. Since damage to structural connections in the brain is a common feature of TBI, we propose the use of white matter tract dissections derived from DTI scan data as a method for differentiating mTBI patients from normal controls without TBI. We hypothesize that raters will be able to determine with high-sensitivity and high-specificity differences in white matter tractography of mTBI patients versus normal controls.

METHODS
For this study, 60 subjects in total were screened neuropsychologically (30 mTBI patients and 30 normal controls) prior to the acquisition of brain scans using DTI. The mean age and gender ratio for the mTBI group was 37.4 years Â± 15.3, 14 male, 16 female, and the mean age and gender ratio for the control group was 34.4 Â± 11.4, 20 male, 10 female. The 30 patients with mTBI were clinical referrals for brain injury who had documented neuropsychological deficits several months post-trauma. MRI diffusion tensor imaging was performed on all 60 subjects. Tractographies were analyzed using Diffusion Toolkit and visualized using TrackVis. Five raters, familiar with white matter tractographies, were shown examples of white matter tract corpus callosum dissections of 10 normal controls and 10 patients with confirmed mTBI. After the initial example stage, the raters were asked to evaluate the remaining 40 subjects as either â€œTBIâ€ or â€œControlâ€ under blind experimental conditions. The 20 subjects used in the example stage were different from the 40 subjects used in the blind evaluation stage. Sensitivity and specificity were calculated from the results using standard binary classification measures of true-positives, true-negatives, false-positives, and false-negatives.

RESULTS
Our average sensitivity in ratings was 89.5% Â± 7.6% and our average specificity was 93.5% Â± 1.8%.

CONCLUSIONS
We can conclude from our analysis that white matter tract dissections provide a highly-specific and highly-sensitive measure for diagnosing patients with mTBI. While the results from this study suggest the usefulness of white matter tract dissections in the diagnosis of mTBI, previous studies conducted similarly in our lab have shown that statistical fractional anisotropy (FA) Z-maps derived from DTI show an even higher degree of sensitivity and specificity (94.5% and 98.1%, respectively). Both methods, however, seem to provide promising supplemental evidence for the clinical diagnosis of the disease.

Key words: traumatic brain injury, diffusion tensor imaging, sensitivity, specificity, diagnosis

Educational Objectives To improve the clinical diagnosis of mTBI, to expand the use of DTI tractography dissections in a clinical setting by providing evidence that it is a highly accurate method, and publication.

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Optical imaging of whisker frequency sensitivity in the mouse barrel cortex

Vassiliy Tsytsarev - Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore
Qinggong Tang - Department of Bioengineering, University of Maryland, College Park
Cha-Wei Chen - Department of Bioengineering, University of Maryland, College Park
Yu Chen - Department of Bioengineering, University of Maryland, College Park
Reha Erzurumlu - Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore

Contact: Vassiliy Tsytsarev (tsytsarev@umaryland.edu)

Abstract: We studied the cortical maps of frequency selectivity of the mystacial vibrissae using voltage-sensitive dye optical imaging (VSDi) at high spatial and temporal resolution. We developed low amplitude, high frequency range whisker stimulator and used it for VSDi in four adult mice (B6, bodyweight 20â€“30g) under urethane anesthesia. The voltage-sensitive dye RH-1691 (Optical Imaging, 1.0 mg/ml in artificial cerebrospinal fluid â€“ACSF), was applied to the exposed dura mater for approximately 1 h then the unbound dye was washed out and the surface was covered with silicone oil and cover glass. The algorithm of each experiment was as follows: different frequency stimulus was generated by the MiCAM-02 imaging system (SciMedia Inc, 2012) every 10 s. This stimulus starts the recording session is 100 trials and each trial contains 500 frames of 5 ms duration. The whisker stimulation started during the 300th frame. After the first frame analysis, the activated areas were identified by the number of activated pixels exhibiting a change in fluorescence (Î”F/F) greater than half of the maximum change in signal, and the pseudocolor maps of the neural activity have been obtained. The results showed that differences between responses to the single pulse and 100, 200, 333 and 500 Hz mechanical stimulation frequencies within 60 ms were indicated by a change in the voltage-sensitive dye optical signal. We found that whiskers stimuli with different frequencies led to different activation patterns in the barrel field. Our results provide preliminary evidence that the different neural pools of the barrel cortex have different frequency preferences, supporting recent electrophysiological studies (Andermann et al, Neuron, 2004; Neimark et al, J Neurosci, 2003). To our knowledge this is the first demonstration of whisker frequency sensitivity and selectivity of barrel cortex neurons with optical imaging methods. Supported by NIH NS039050 (RE).

Keywords
Functional brain mapping (fMRI, PET?) (primary keyword)
4D, Neuro-mathematics and bio-informatics
Brain mapping/functional imaging for rehab medicine and PTSD

Abstract Topics
Functional brain mapping (fMRI, PETâ€¦)
Brain mapping/functional imaging for rehab medicine
Basic Neuroscience

The abstarct book's publications additonal Information summary

Optical imaging of whisker frequency sensitivity in the mouse barrel cortex

Vassiliy Tsytsarev (1), Qinggong Tang (2), Cha-Wei Chen (2) Yu Chen (2) and Reha Erzurumlu (1)
1 â€“ Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore. 2 - Department of Bioengineering, University of Maryland, College Park.
E-mail (1): Tsytsarev@umaryland.edu
Key words: whiskers, barrel field, somatosensory cortex, voltage-sensitive dye.

We studied the cortical maps of frequency selectivity of the mystacial vibrissae using voltage-sensitive dye optical imaging (VSDi) at high spatial and temporal resolution. We developed low amplitude, high frequency range whisker stimulator and used it for VSDi in four adult mice (B6, bodyweight 20â€“30g) under urethane anesthesia. The voltage-sensitive dye RH-1691 (Optical Imaging, 1.0 mg/ml in artificial cerebrospinal fluid â€“ACSF), was applied to the exposed dura mater for approximately 1 h then the unbound dye was washed out and the surface was covered with silicone oil and cover glass. The algorithm of each experiment was as follows: different frequency stimulus was generated by the MiCAM-02

imaging system (SciMedia Inc, 2012) every 10 s. This stimulus starts the recording session is 100 trials and each trial contains 500 frames of 5 ms duration. The whisker stimulation started during the 300th frame. After the first frame analysis, the activated areas were identified by the number of activated pixels exhibiting a change in fluorescence (Î”F/F) greater than half of the maximum change in signal, and the pseudocolor maps of the neural activity have been obtained. The results showed that differences between responses to the single pulse and 100, 200, 333 and 500 Hz mechanical stimulation frequencies within 60 ms were indicated by a change in the voltage-sensitive dye optical signal. We found that whiskers stimuli with different frequencies led to different activation patterns in the barrel field. Our results provide preliminary evidence that the different neural pools of the barrel cortex have different frequency preferences, supporting recent electrophysiological studies (Andermann et al, Neuron, 2004; Neimark et al, J Neurosci, 2003). To our knowledge this is the first demonstration of whisker frequency sensitivity and selectivity of barrel cortex neurons with optical imaging methods.
Supported by NIH NS039050 (RE).

Educational Objectives voltage-sensitive dye brain optical imaging; somatosensory cortex

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Neuropsychological Performance and DTI in the Corpus Callosum of Mild TBI Patients with and without Memory Problems

Joseph Rosenberg - University of Maryland School of Medicine
Jiachen Zhuo - University of Maryland School of Medicine
Teodora Stoica - University of Maryland School of Medicine
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Rao Gullapalli - University of Maryland School of Medicine

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Abstract: Introduction: Many mild traumatic brain injury mTBI patients report persistent symptoms and demonstrate reduced cognitive functioning, often in the absence of clinical CT or MRI findings. Studies using alternative MR techniques such as MR spectroscopy, diffusion tensor imaging (DTI), and functional MRI have noted metabolic and structural alterations in the corpus callosum (CC) following mTBI. These alterations can disrupt hemispheric connectivity, and may contribute to cognitive deficits such as memory impairment. To further investigate mechanisms underlying impairment, we assessed DTI measures in the CC of mTBI patients with and without memory complaints, and compared results with neuropsychological performance. We hypothesize that mTBI patients reporting memory problems will demonstrate DTI alterations in the CC, and will perform worse on neuropsychological assessments of memory, compared to controls and patients not reporting memory problems.

Methods: As part of the MagNeT (Magnetic Resonance Imaging of NeuroTrauma) Study, mTBI patients (Glasgow Coma Scale score=13-15) received an MRI evaluation in the acute (â‰¤10 days) and sub-acute (1 month) stages of injury. Patients also completed the Military Acute Concussion Evaluation (MACE), which includes the Standard Assessment of Concussion as an objective measure of neurocognitive functioning. The MACE includes 4 sub-tests: Orientation, Immediate Memory, Concentration, and Delayed Recall, as well as a summed MACE Total score. The presence of memory problems was determined at the acute stage by a self-reported score of >0 for the â€œMemory Problemsâ€ item of the Rivermead Post-Concussion Symptoms Questionnaire. Twenty-one patients (9 with memory problems, 12 without) with DTI and MACE data at both the acute and sub-acute visits were compared to 31 healthy controls. Neither age nor years of education differed significantly among groups.

Diffusion weighted images were obtained, and fractional anisotropy (FA) and mean, radial, and axial diffusivity (MD, RD, AD) were measured regionally in the corpus callosum genu (CCG), body (CCB), and splenium (CCS).

Results: At the acute stage, mTBI patients in both groups scored significantly worse than controls on Delayed Recall, though the deficit was greater and more significant in patients with memory problems (p=0.006) than in those without (p=0.040). Only patients reporting memory complaints scored significantly worse than controls on the MACE Total (p=0.016). At this stage patients reporting memory problems demonstrated decreased FA (p=0.006) and increased MD (p=0.001) and RD (p=0.001) in the CCG, as well as increased MD (p=0.012) and RD (p=0.012) in the CCB. Similar differences were present between patients with and without memory problems.

At the sub-acute stage, patients with memory problems scored significantly worse on Delayed Recall than both controls (p=0.003) and those without memory problems (p=0.018). No differences in DTI were significant at this stage.

Conclusions: Our results suggest that mTBI patients reporting memory problems demonstrate DTI alterations in the CC, as well as reduce neuropsychological performance, at the acute stage. These DTI alterations appear to normalize by the sub-acute stage, though neuropsychological performance on a memory task remains reduced. Acute DTI alterations in the CC may be a contributing factor to the persistent impairments noted following mTBI.

Keywords *Diffusion Tensor Imaging (primary keyword)*
Imaging modalities for detecting mild/mod TBI, micro-TBI

Abstract Topics

Diffusion Tensor Imaging
Imaging modalities for detecting mild/mod TBI, micro-TBI

The abstarct book's publications additonal Information summary

Neuropsychological Performance and DTI in the Corpus Callosum of Mild TBI Patients with and without Memory Problems

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Introduction: Many mild traumatic brain injury mTBI patients report persistent symptoms and demonstrate reduced cognitive functioning, often in the absence of clinical CT or MRI findings. Studies using alternative MR techniques such as MR spectroscopy, diffusion tensor imaging (DTI), and functional MRI have noted metabolic and structural alterations in the corpus callosum (CC) following mTBI. These alterations can disrupt hemispheric connectivity, and may contribute to cognitive deficits such as memory impairment. To further investigate mechanisms underlying impairment, we assessed DTI measures in the CC of mTBI patients with and without memory complaints, and compared results with neuropsychological performance. We hypothesize that mTBI patients reporting memory problems will demonstrate DTI alterations in the CC, and will perform worse on neuropsychological assessments of memory, compared to controls and patients not reporting memory problems.

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At the sub-acute stage, patients with memory problems scored significantly worse on Delayed Recall than both controls (p=0.003) and those without memory problems. (p=0.018). No differences in DTI were significant at this stage.

Conclusions: Our results suggest that mTBI patients reporting memory problems demonstrate DTI alterations in the CC, as well as reduce neuropsychological performance, at the acute stage. These DTI alterations appear to normalize by the sub-acute stage, though neuropsychological performance on a memory task remains reduced. Acute DTI alterations in the CC may be a contributing factor to the persistent impairments noted following mTBI.

Keywords: Diffusion Tensor Imaging (DTI), Mild Traumatic Brain Injury (mTBI), Military Acute Concussion Evaluation (MACE)

Educational Objectives	Novel Imaging Markers of TBI, Clinical Assessment and Outcomes Following TBI, Mechanisms of Injury and Recovery Following TBI
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Sex-linked difference of metabolic concentrations in hippocampus in Sprague-Dawley rats: a high resolution in vivo proton MRS study at 7 Tesla

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Rao Gullapalli - University of Maryland
Su Xu - University of Maryland

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Abstract: Although significant in vivo imaging research relies on the rodent model, very little has been reported on the gender based differences in neurometabolites among healthy rodents. The purpose of this study was to compare the metabolic concentrations obtained from normal age-matched male, virgin female, and post-weaning female Sprague-Dawley rats in the hippocampus. We demonstrated a sex-linked difference of metabolic Taurine concentration. The findings in our present study emphases the importance of gender-matching for studies investigating differences in neurometabolic concentrations, and the potential significance of gender based medication for neurological pathologies.

Keywords	Magnetic resonance Spectroscopic Imaging
Abstract Topics	Magnetic resonance Spectroscopy
The abstarct book's publications additonal Information summary	This work has not been submitted for presentation elsewhere
Educational Objectives	The importance of gender matched studies were observed in this experiment. The concentration of neurometabolities are affected by gender. The effectiveness of medication for neuropathologies may rely on gender.

Files	*Submission exists, but was not archived (suffix)*

Reviews

Two-photon Fluorescence Imaging of Intracellular Reactive Oxygen Species H2O2

Hengchang Guo - Fischell Department of Bioengineering, University of Maryland
Hossein Aleyasin - Burke Medical Research Institute, Weill Medical College of Cornell University
Scott Howard - School of Applied Engineering & Physics, Cornell University
Bryan Dickinson - Department of Chemistry and Chemical Biology, Harvard University
Vivian Lin - Department of Chemistry, University of California, Berkeley
Renee Haskew-Layton - Burke Medical Research Institute, Weill Medical College of Cornell University
Jianting Wang - Fischell Department of Bioengineering, University of Maryland
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Contact: Hengchang Guo (hcguo@umd.edu)

Abstract: Hydrogen peroxide (H2O2), a common reactive oxygen species (ROS) found in biological systems, is now recognized as an intracellular second messenger for cellular signaling that exerts diverse physiological and pathological effects. It is also an oxidative stress indicator related to cancer, diabetes, and neurodegenerative diseases such as Alzheimerâ€™s, Parkinsonâ€™s and Huntingtonâ€™s diseases, as well as stroke. In addition, H2O2 is involved in therapeutic processes such as wound healing and an adaptive response in astrocytes leading to neuronal protection.

To monitor the production of intracellular H2O2 in situ, we developed a biophotonic technique including a two-photon fluorescence (TPF) microscope and chemoselective fluorescent probes such as Peroxyfluor-6 acetoxymethyl ester (PF6-AM) and Mitochondria Peroxy Yellow 1 (MitoPY1). We developed these fluorescent probes based on boronate-switch mechanism for selective detection of intracellular H2O2 with improved sensitivity. PF6-AM was designed with the intracellular acetoxymethyl ester functionalities allowing for cell membrane-permeability. MitoPY1 was designed with a mitochondrial-targeting phosphonium moiety for detection of H2O2 localized to cellular mitochondria. Two-photon absorption (TPA) spectra of the chemoselective fluorescent probes were measured with a mode-locked Ti:sapphire laser in the wavelength range of 740-1040 nm. The peak TPA cross section values of these probes are comparable to that of fluorescein, which is sufficiently large for the TPF imaging to detect localized endogenous H2O2 production in living cells.

To characterize this technique, we present the application of TPF imaging to monitor intracellular hydrogen peroxide (H_2O_2) production in the HT22 cell line and in rat astrocytes. TPF imaging was demonstrated in these brain cells to monitor cytoplasmic H_2O_2 production and localized mitochondrial H_2O_2 production. The probe Peroxyfluor-6 acetoxymethyl ester (PF6AM) shows high membrane permeability and Mitochondria Peroxy Yellow 1 (MitoPY1) shows targeted labeling to cellular mitochondria. This study demonstrates that TPF imaging provides a novel opportunity for real-time monitoring of H_2O_2 detection and oxidative stress evaluation in live cells and in vivo.

Keywords	*Molecular and cellular imaging (primary keyword)* Biophotonics
Abstract Topics	Molecular and cellular imaging Biophotonics Basic Neuroscience
The abstarct book's publications additonal Information summary	
Educational Objectives	publication,clinical trial, change of practice
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Concurrent Multi-scale Imaging with Magnetic Resonance Imaging (MRI) and Optical Coherence Tomography (OCT) for Neurosurgery Guidance

Chia-Pin Liang - Department of Bioengineering, University of Maryland, College Park

Il Kyoon Kim - Department of Bioengineering, University of Maryland, College Park

Bo Yang - Department of Mechanical Engineering, University of Maryland, College Park

George Makris - Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, Baltimore

Jaydev Desai - Department of Mechanical Engineering, University of Maryland, College Park

Rao Gullapalli - Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, Baltimore

Yu Chen - Department of Bioengineering, University of Maryland, College Park

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Abstract: We developed a novel platform based on a teleoperated robot to perform high-resolution optical coherence tomography (OCT) imaging under continuous MRI guidance. The superior soft tissue contrast and versatile imaging protocols of intra-operative MRI make it a promising guidance tool for high-precision functional neurosurgical interventions. However, MRI alone may not have the resolution or contrast to detect micro-anatomical landmarks surrounding the targets. Microscopic OCT imaging on the other hand can visualize these landmarks and has been used to guide deep brain surgeries in small rodents in vivo and target human brain nuclei ex vivo. The limited field of view of OCT however necessitates that the OCT be selectively transported to the specific site of interest under MRI guidance. The combination of large-scale MRI tissue morphology and high-resolution OCT micro-anatomy in a concurrent and co-registered manner has great potential to improve the accuracy and efficiency of various neurosurgery. In this first ever development of MRI-compatible OCT imaging system, we integrated the OCT probe into a titanium cannula and navigated toward the target using a MRI-compatible robot under MRI guidance. The concurrent MRI/OCT system (imaging speed 0.25 frames/s for MRI and 15 frames/s for OCT) was used to image sheep brain ex vivo, and human basal ganglia ex vivo. The results demonstrated that OCT clearly distinguishes gray matter and white matter transitions with ultra high resolution (30 um), which enables us to target specific neural tracts with unprecedented accuracy. Moreover, OCT provides different contrast based on optical scattering, which is great complimentary to the MRI contrast. We demonstrated that OCT can easily resolve a gray matter nucleus with densely packed

white matter fibers (thalamus) from the surrounding white mater capsule (internal capsule) based on the scattering analysis. On the other hand, MRI has low contrast in the same region. We demonstrate that the large-scale MRI image can be used to plan the trajectory and monitor the coarse instrument position relative to the target, and real-time, high resolution OCT image can be used to detect the important micro-landmarks for precise targeting and monitoring of surrounding tissues.

Keywords	*Multimodality imaging (primary keyword)* Image guided systems Intraoperative Surgical Planning Biophotonics
Abstract Topics	Image guided systems Intraoperative Surgical Planning Endoscopy Biophotonics Magnetic resonance Spectroscopy Multimodality imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	publication, award, change of practice
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Ovulation is associated with increased functional connectivity in amygdala and attention networks in the healthy female brain

Timothy Meeker - Univ. of Maryland
Dieuwke Veldhuijzen - Utrecht Univ. Medical Center
Michael Keaser - Univ. of Maryland
Rao Gullapalli - Univ. of Maryland
Joel Greenspan - Univ. of Maryland

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Abstract: Introduction Several recent studies have reported consistent variation in BOLD responses to arousing stimuli across the menstrual cycle, particularly in the amygdala (Goldstein, et al, J. Neurosci., 2005, Dreher, et al., PNAS, 2007, Derntl, et al., Psychoneuroendocrinology, 2008, Andreano and Cahill, NeuroImage, 2010, Ossewaarde, et al., Psychoneuroendocrinology 2010 and Frank, et al., Brain Res., 2010). Additionally, menstrual cycle variations may explain the observation of greater variability in functional connectivity (FC) for brain networks in women compared to men (Tomasi and Volkow, Hum Brain Mapp, 2012). In this study, we evaluated menstrual cycle variations in FC as they relate to the amygdalaâ€™s connectivity to the rest of the brain, with particular interest in regions associated with emotion and arousal. Additionally, we evaluated menstrual cycle variation in the FC of the cognitive dorsal attention network (DAN).

Methods Functional MRI sessions of thirteen normally cycling, healthy women were analyzed for this study. Participants underwent four fMRI sessions during each of their menstrual, follicular, ovulation and luteal phases. Menstrual cycle phases were verified by serum hormone analysis. Resting state fMRI scans consisted of 171 volumes collected with a TR of 2 seconds using echo planar imaging with a 3.594 x 3.594 x 6 mm resolution. Functional MRI data were analyzed using AFNI. To perform seed-based FC analysis we defined seeds, extracted the mean time series and regressed that time series to the whole brain on a voxel-wise basis. Within-subject analyses were performed on whole brain correlation coefficients for each seed using one-way RM-ANOVA for phase. We controlled for multiple comparisons using a Monte Carlo simulation to determine minimum cluster size.

Results Menstrual cycle phase had a significant effect on seed-based FC in the right and left-seeded amygdala network, as well as the left and right DANs. In the right and left amygdala network, RM-ANOVA revealed regions of significant phase effect including right dorsolateral prefrontal cortex, right inferior and superior parietal lobule,

and right anterior insula. In the left and right DANs, widespread phase effect was discovered including bilateral thalamus, periaqueductal gray and bilateral dorsolateral prefrontal cortex. Almost exclusively, amygdala network and DAN FC was strongest during the ovulation phase.

Conclusions We found that the FC or at least one arousal/emotional network and one cognitive network varied significantly across the menstrual cycle in healthy females, with peak FC occurring during ovulation. These findings support the notion that higher variation in connectivity in females is at least partly due to menstrual cycle effects (Tomasi and Volkow, Hum Brain Mapp, 2011). These results are likely relevant to the observations that emotion recognition and amygdalar BOLD response to emotional faces and to high caloric content food is enhanced near ovulation (Derntl, et al., Psychoneuroendocrinology, 2008 and Frank, et al., Brain Res., 2010). Our findings of enhanced amygdala network connectivity to executive and integrative cortical areas during ovulation emphasize the evolutionary importance of this processing stream during times of peak fertility in healthy women.

Keywords	*Functional brain mapping (fMRI, PET?) (primary keyword)* Anatomy
Abstract Topics	Functional brain mapping (fMRI, PETâ€¦) Basic Neuroscience
The abstarct book's publications additonal Information summary	
Educational Objectives	Evaluate menstrual cycle effects upon brain network connectivity; examine brain network dependence upon gonadal hormones; recognize importance of sex differences and hormonal influences upon brain network function
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Cocaine-induced disruption of brain function: Novel insights from optical neuroimaging studies in rodents

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Contact: Congwu Du (congwu@bnl.gov)

Abstract: Background:

Deficits in prefrontal function play a crucial role in compulsive cocaine use, which is a hallmark of addiction. Dysfunction of the prefrontal cortex might result from effects of cocaine on neurons as well as from disruption of cerebral blood vessels. However, the mechanisms underlying cocaineâ€™s neurotoxic effects are not fully understood, partially due to technical limitations of current imaging techniques (PET and fMRI) to differentiate vascular from neuronal effects at sufficiently high temporal and spatial resolution. Here, we present a novel multimodel imaging platform, which allows us to simultaneously monitor hemodynamics, tissue metabolism and neuronal activity at high spatiotemporal resolutions over a large field of view (FOV). In addition, the use of transgenic mice expressing fluorescent probes on specific cell types allows us to separately image cocaine effects on the activity of D2 receptor (D2R) and D1 receptor (D1R) expressing neurons (using [Ca2+]i) in different brain area such as cortex and striatum.

Methods:

We apply our newly developed optical/ fluorescence imaging techniques (OFIs) to study the effects of acute and chronic cocaine. OFIs integrates (1) dual-wavelength laser speckle imaging for concurrent detection of cerebral blood flow (CBF), blood volume (CBV), and tissue hemoglobin oxygenation (StO2) at high spatiotemporal resolutions across a large FOV, (2) digital-frequency-ramping Doppler optical coherence tomography for in vivo 3D quantitative imaging of the neurovascular network, (3) Rhod2 fluorescence imaging to measure [Ca2+]i(marker of neuronal activity), and (4) a micro-catheter probe (uOFI) to assess striatal regions in real time and at high spatiotemporal resolution. We use transgenic mice that expressed EGFP either in D2R or D1R neurons. For the acute effects of cocaine we used an intravenous dose of 1 mg/kg and for the chronic effects we administered 20mg/kg cocaine ip daily for 2 weeks.

Results:

We show that in the cortex acute cocaine significantly decreased CBF while increasing deoxyhemoglobin and increasing [Ca2+]i and that these responses were markedly enhanced with repeated drug exposures. These sensitized responses with chronic cocaine exposures are likely to increase the vulnerability of the neuronal tissue to micro-ischemia and the consequent damage to cortical tissue from hypoxia.

Our studies with the microprobe showed that acute cocaine rapidly increases [Ca2+]i in D1R-expressing neurons in striatum, whereas it progressively decreases [Ca2+]I in D2R-expressing neurons consistent with the stimulatory and inhibitory signaling of D1R and D2R respectively. The dynamic analysis of the ratio of D1R to D2R signaling revealed that after acute cocaine there is a fast and short lasting predominance of D1R over D2 that return to baseline after 20 minutes of its administration. This suggests that cocaineâ€™s rewarding effects entail both fast D1R stimulation (resulting in abrupt activation of direct-pathway neurons) and a slower D2R stimulation (resulting in longer-lasting deactivation of indirect-pathway neurons).

These results demonstrate the values of our new imaging tools to distinguish vascular from neuronal responses in response to drugs, thus complimenting other neuroimaging modalities (e.g., PET, fMRI).

Keywords	*Biophotonics (primary keyword)* Vascular & Blood flow imaging Multimodality imaging
Abstract Topics	Biophotonics
The abstarct book's publications additonal Information summary	
Educational Objectives	This novel technique 1) will give us new insight of the extent of cocaineâ€™s toxic and damaging effects on neurons and neurovasculature; 2) will provide new imaging technology and enhance the academic education; 3) will bridge instrumentation development for neuroscience to translational research on drug abuse and addiction
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

New Nanostructured Multifunctional Surfaces of Titanium Alloys Obtained by Directed Irradiation Synthesis (DIS) for Treatments of Spinal Cord Damages

Juan PavÃ³n - Purdue University
Emily Walker - Purdue University
Sandra Arias - Purdue University
Lisa Reece - Purdue University
Jean Paul Allain - Purdue University

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Abstract: New Nanostructured Multifunctional Surfaces of Titanium Alloys Obtained by Directed Irradiation Synthesis (DIS) for Treatments of Spinal Cord Damages J. PavÃ³n1, 2, 3, E. Walker2, 4, S. Arias1, 2, 4, L. M. Reece2, 5, J. P. Allain1, 2, 4 1School of Nuclear Engineering, Purdue University, West Lafayette, IN 47907 2Birck Nanotechnology Center, Purdue University, West Lafayette, IN 47907 3Biomaterials and Biomechanics Group, Bioengineering Program, University of Antioquia, Colombia. 4School of Materials Engineering, Purdue University, West Lafayette, IN 47907 5Department of Basic Medical Sciences, College of Veterinary Medicine, Purdue University, West Lafayette, IN USA

ABSTRACT

Spinal cord has a determinant role in locomotion of the muscle-skeletal system and its relationship with brain functions is also crucial for human movement achievements; any kind of disease or trauma can have a severe detrimental effect in life quality of patients. Some clinical treatments for spinal pathologies like Anterior Cervical Diskectomy (ACD), Posterior Cervicothoracic Osteotomy (PCO), Anterior Lumbar Interbody Fusion (ALIF), Lumbar Disk Arthroplasty (LDA) and some others, can affect not only spine bone and discs, but also spinal cord. On the other hand, some focused spinal cord treatments like Spinal Cord Arteriovenous Malformations (AVMs) and Intramedullary Spinal Cord Cavernous Malformation (ISCCM) can involve also bone and discs of the surrounded areas. Most of the conventional treatments to these pathologies imply using medical grade of titanium (Ti) and its alloys as plates, screws, wires, porous implants, etc. Despite using these materials have proved to have a high clinical success, it is also recognized their limitation because this practice belongs to first and second generation of biomaterials: both the material itself and its surface only act at micro-scale level. Regeneration and tissue growth medicine practices require third generation biomaterials which are those designed to stimulate both cells and biological environment at molecular (nano) scale level. In that sense, nanotechnology

and nanomaterial cutting-edge developments have emerged as the unique alternative to successfully addressed any critical damage of tissues as those above mentioned. Some authors like Dalby et al. (2009), McNnamara et al. (2010) and Wheeldon et al. (2010) have recently showed that stem cells adhesion, differentiation, proliferation and gene expression can be enhanced when cells are in contact with nano-structured biomaterials surfaces. In our research, we have developed new nano-structured surfaces on commercially pure titanium (CP Ti) and Ti6Al4V alloy by using Directed Irradiation Synthesis (DIS) technique. These materials are surface modified with multifunctional purposes: different nano-structuring parameters are expected to generate different tissue growth stimulation for bone, discs and spinal cord tissues. Evaluated processing conditions have been reasonable repeatable to control nano-structuring of both kind of Ti materials. Contact angle testing of Ti nano-structuring samples obtained by DIS enabled measurement of decreasing of hydrophobicity (between 40-50%). DIS technique have proved to be suitable to reproduce these multifunctional surfaces and the biological testing of these new surfaces with different cells lines showed promising results with respect to previous hypothesis established for every involved tissue for future complex and complete treatment of spinal cord damages and tissues associated.

Keywords

Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration)
Spinal Cord, Trauma Repair and regeneration
Spinal cord instrumentation and implants

Abstract Topics

Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration
Spinal Cord, Trauma Repair and regeneration
Spinal cord instrumentation and implants

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Educational Objectives

1. To highlight the importance of nanotechnology in Regenerative Medicine, 2. To show nano-structured titanium as alternative for treatment of spinal cord damages; 3. Importance of cells stimulation for tissue repairing.

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Ankle robotics therapy during sub-acute hospitalization after hemiparetic stroke

Larry Forrester - University of Maryland School of Medicine
Anindo Roy - University of Maryland School of Medicine
Amanda Krywonis - Kernan Orthopaedics and Rehabilitation Hospital
Glenn Kehs - Kernan Orthopaedics and Rehabilitation Hospital
Hermano Krebs - Massachusetts Institute of Technology
Richard Macko - University of Maryland School of Medicine

Contact: Larry Forrester (lforrester@som.umaryland.edu)

Abstract: Introduction: Approximately 800,000 Americans are diagnosed with stroke each year, making it the greatest source of chronic physical disability in the U.S. There is wide agreement that functional deficits from residual hemiparesis can be partially offset through experience-dependent plasticity in the neural networks that control movement. Modern robotic devices offer a means to shape these emergent networks by engaging the affected limb(s) with high volumes of goal-directed motor practice during therapy. Thus modular lower extremity (LE) robotics may offer a valuable avenue for restoring neuromotor control in stroke survivors with hemiparetic gait. Prior results with chronic stroke suggest that intensive seated visuomotor training with an ankle robot (Anklebot) may enhance paretic ankle motor control and carry over to gait function; however this approach has not been tested in the earliest phases of rehabilitation, when natural recovery is underway. Question: What are the feasibility and efficacy of daily training with the Anklebot during early sub-acute hospitalization post-stroke?

Methods: Inpatients from a stroke rehabilitation unit were randomly assigned to either an Anklebot group or a passive stretching-mobilization group. After regular daily therapies, seated Anklebot training employed an â€œassist-as-neededâ€ approach during > 200 volitional targeted paretic ankle movements in the plantar-dorsiflexion and inversion-eversion ranges. The activity consisted of playing a videogame by attempting to move a cursor through moving gates that crossed the screen at different spatial levels, thereby stimulating volitional effort in multiple directions. Training difficulty was adjusted to each participantâ€™s active range of motion and target success rate. The stretching group received >200 daily mobilizations of the paretic ankle delivered in these same ranges of motion by the trained research team. All sessions lasted about 1 hour.

Results: As expected both groups walked overground significantly faster at discharge, however the robot group improved more in interlimb symmetry. Greater gains in paretic ankle motor control also were observed in the robot group, seen as increased peak and mean angular speeds, and increased smoothness of movement trajectories. There were no study-related adverse events.

Conclusions: Intensive LE robotic therapy is feasible for use during sub-acute phase hospitalization post-stroke without compromising usual inpatient care. Ankle robotics in this early phase may improve the rate of decreasing paretic ankle impairments, with potential to accelerate restoration of gait and complement traditional pre-gait activities. Future imaging studies with electroencephalography and/or functional near-infrared spectroscopy over the course of Anklebot therapy will help discern cortical network changes associated with motor learning and brain plasticity.

Keywords *Neural Prosthesis & Robotics (primary keyword)*
Rehabilitation Medicine (neural repair and regeneration)

Abstract Topics Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration

The abstarct

Ankle robotics therapy during sub-acute hospitalization after hemiparetic stroke

Larry W. Forrester, PhD1,2,3, Anindo Roy, PhD2,3, Amanda Krywonis, DScPT4, Glenn Kehs,

book's publications additonal Information summary

MD2,4, H. Igo Krebs, PhD2,5, Richard F. Macko, MD1,2,3

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Introduction: Approximately 800,000 Americans are diagnosed with stroke each year, making it the greatest source of chronic physical disability in the U.S. There is wide agreement that functional deficits from residual hemiparesis can be partially offset through experience-dependent plasticity in the neural networks that control movement. Modern robotic devices offer a means to shape these emergent networks by engaging the affected limb(s) with high volumes of goal-directed motor practice during therapy. Thus modular lower extremity (LE) robotics may offer a valuable avenue for restoring neuromotor control in stroke survivors with hemiparetic gait. Prior results with chronic stroke suggest that intensive seated visuomotor training with an ankle robot (Anklebot) may enhance paretic ankle motor control and carry over to gait function; however this approach has not been tested in the earliest phases of rehabilitation, when natural recovery is underway. Question: What are the feasibility and efficacy of daily training with the Anklebot during early sub-acute hospitalization post-stroke?

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Conclusions: Intensive LE robotic therapy is feasible for use during sub-acute phase hospitalization post-stroke without compromising usual inpatient care. Ankle robotics in this early phase may improve the rate of decreasing paretic ankle impairments, with potential to accelerate restoration of gait and complement traditional pre-gait activities. Future imaging studies with electroencephalography and/or functional near-infrared spectroscopy over the course of Anklebot therapy will help discern cortical network changes associated with motor learning and brain plasticity.

Educational Objectives

Learning objectives: 1) Describe the current state of rehabilitation robotics as applied to functional recovery after stroke. 2) Discuss recent advances in using robotics to enhance motor learning and lower extremity function after stroke; 3) Describe the application of EEG and neurophysiological approaches used to characterize neural plasticity and learning. Impact:This work has the potential to help advance the goal of optimizing motor recovery after neurological disease and injury.

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Development of a New Treatment for Penetrating Brain Injury (PBI) Aneurysms: Magnetic Bacterial Nano-Cellulose (MNBC) and Nanostructured NiTi by Directed Irradiation Synthesis (DIS)

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Juan PavÃ³n - **Purdue University**

Sandra L. Arias - **Purdue University**

Milad Alucozai - **Purdue University**

Emily Walker - **Purdue University**

Fernando Pastrana - **Purdue University**

Lisa M. Reece - **Purdue University**

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Teodoro Tigno - **Neurosurgery Service, Dept. of Surgery, Walter Reed National Military Medical Center in Bethesda, MD, Washington, USA**

Rocco Armonda - **Neurosurgery Service, Dept. of Surgery, Walter Reed National Military Medical Center in Bethesda, MD, Washington, USA**

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Abstract: Penetrating Brain Injury (PBI) aneurysms are conventionally treated by surgical clipping or endovascular coiling. These well-known clinical approaches have showed limited success due to thrombus formation and rupture of aneurysm walls related to the high pressure inside the damaged blood vessels. In that sense, there is an increasing interest in neurosurgery to develop new alternatives for treatment of this kind of trauma. Our group has postulated that a stent used as a tissue scaffold with a magnetic face directed at the aneurysmal neck orifice would be the most efficient strategy to induce closure of PBI. Nanotechnology has emerged recently as a promising field to address neuro-endovascular strategies that address PBI-induced arterial damage. Authors like Dalby et al. have recently shown that stem cell adhesion, differentiation, proliferation and gene expression can be enhanced when cells are in contact with nanostructured biomaterials surfaces. In our research, we have thus developed two new nanostructured biomaterials which are candidates to be used in a project of a novel treatment of PBI: development and fabrication of a bioactive stent to induce closure of the damaged arterial wall using bacterial nano-cellulose (BNC) and nickel-titanium alloy (NiTi). First, the new nanostructured composite biomaterial

consists of a layer of a BNC matrix chemically impregnated with magnetic iron oxide nanoparticles. BNC is recognized as a suitable biomaterial due to its successful uses in tissue grafts and, once it is rendered magnetic, it can attract magnetic cells in order to begin the stimulation of tissue growth across the aneurysm neck. Characterization shows the magnetic nanobacterial cellulose (MNBC) to be full of tightly bound ferrous nanoparticles to the BNC matrix. Further, the iron oxide nanoparticles have themselves been coated with various substances (PEG, PEI, citric acid and Collagen I) to render them biocompatible. It has also been verified that the MNBC has enough high magnetic gradient to recruit magnetically-labeled Human Aortic Smooth Muscle Cells (HASMCs) to begin cellular proliferation. HASMCs were also used to test the cytotoxicity and cell viability of BNC and MBNC at 24h, 48h and 72h. We found that HASMCs were ~98% confluent on both BNC and MBNC scaffolds, thus providing evidence of cellular adhesion, migration and proliferation. Secondly, NiTi is a biomaterial that possesses unique properties like shape memory and superelasticity and has been used in cardiovascular devices for years. Our group is currently working in a surface modification (nanostructuring) of conventional NiTi stent materials by directed irradiation synthesis (DIS) techniques. This novel nano-structured surface can provide optimum attachment of recruited cells, as well as the promotion of intrinsic stimulation to these cells for tissue growth along the aneurysm neck defect. Contact angle testing of NiTi nanostructured samples enabled measurement of decreasing of hydrophobicity (between 20-40%). DIS has proven to be suitable to reproduce these multifunctional surfaces and characterization results have corroborated the previous hypothesis for the establishment of a biofunctional surface of the bioactive interfaces for novel neuro-endovascular treatment through integration between MBNC and modified NiTi.

Keywords

General issues (primary keyword)
Nanoscience, genomics, computational informatics genetics
Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration)

Abstract Topics

General issues
Nanoscience, genomics, genetics
Neural Prosthesis & Robotics
Rehabilitation Medicine (neural repair and regeneration

The abstarct book's publications additonal Information summary

Educational

1. To highlight the importance of nanotechnology in

Objectives	Regenerative Medicine, 2. To show nano-structured biomaterials as alternative for treatment of PBI aneurysms; 3. Importance of cells stimulation for blood vessel repairing.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Coherence-gated Doppler (CGD): a Fiber Sensor for Avoiding Hemorrhage in Neurosurgery

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Joe Schmitt - St. Jude Medical, Inc
Paul Bigeleisen - Department of Anesthesiology, University of Maryland School of Medicine, Baltimore
Justin Slavin - Department of Neurosurgery, University of Maryland School of Medicine, Baltimore
Samir Jafri - Department of Neurology, University of Maryland School of Medicine, Baltimore
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Abstract: Miniature optical sensors that can detect blood vessels in front of advancing instruments will significantly benefit many interventional procedures. Towards this end, we developed a thin and flexible coherence-gated Doppler (CGD) fiber probe (O.D. = 0.125 mm) that can be integrated with minimally-invasive tools to provide real-time audio feedback of blood flow at precise locations in front of the probe. Coherence-gated Doppler (CGD) is a hybrid technology with features of laser Doppler flowmetry (LDF) and Doppler optical coherence tomography (DOCT). Because of its confocal optical design and coherence-gating capabilities, CGD provides 10-100 times higher spatial resolution (< 100 um) than LDF (mm-cm). The diffuse optics design of LDF often includes high noises from surrounding tissues and thus not ideal for applications required high spatial specificity, such as pinpointing blood vessels in front of surgical instruments. And compared to DOCT imaging systems, CGD is more sensitive, simpler and less costly to produce. In vivo studies of rat femoral vessels using CGD demonstrate its ability to distinguish between artery, vein and bulk movement of the surrounding tissue based on the pulsation pattern, pitch the volume of audio feedbacks. Finally, by placing the CGD probe inside a 30-gauge needle and advancing it into the brain of an anesthetized sheep, we demonstrate that it is capable of detecting vessels in front of advancing probes during simulated stereotactic neurosurgery. With simultaneous ultrasound (US) monitoring from the surface of the brain, we show that CGD can detect at-risk blood vessels up to 3 mm in front of the advancing probe and the audio signal from the artery, vein and bulk motion in the highly scattering brain tissue can be easily differentiated by their characteristic pitch and the pulsation pattern. The improved spatial resolution afforded by coherence gating

combined with the simplicity, minute size and robustness of the CGD probe suggest it may benefit many minimally invasive procedures and enable it to be embedded into a variety of surgical instruments.

Keywords	*Intraoperative Surgical Planning (primary keyword)* Biophotonics Minimally invasive therapy
Abstract Topics	Intraoperative Surgical Planning Biophotonics Minimally invasive therapy
The abstarct book's publications additonal Information summary	
Educational Objectives	publication, award, clinical trial,
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Invivo Diffusion Kurtosis and MR Spectroscopy Changes Following a Novel Direct Cranial Blast Injury Model

Jiachen Zhuo - Diagnostic Radiology, University of Maryland School of Medicine
Su Xu - Diagnostic Radiology, University of Maryland School of Medicine
Kaspar Keledjian - Neurosurgery, University of Maryland School of Medicine
Volodymyr Gerzanich - Neurosurgery, University of Maryland School of Medicine
J. Marc Simard - Neurosurgery, University of Maryland School of Medicine
Rao Gullapalli - Diagnostic Radiology, University of Maryland School of Medicine

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Abstract: Traumatic brain injury resulting from an explosive blast (bTBI) is one of the most serious wounds suffered by warfighters. Experimental models of bTBI provide a useful tool for understanding the microstructural and metabolic changes induced by the damage. In this study we investigated brain alterations using diffusion kurtosis imaging (DKI) and proton magnetic resonance spectroscopy (1H MRS) following a rodent model of direct cranial blast injury (dcBI), in which a blast overpressure could be delivered exclusively to the head, precluding indirect brain injury via thoracic transmission of the blast wave. We investigated microstructural and metabolic changes in 10 adult male Long-Evans rats at baseline, 24hrs, 7days, 14days, and 28days after dcBI at 7 Tesla. The pressure used to cause dcBI ranges from 427kPa to 517kPa. The overpressure blast did not create any MR visible injuries using conventional sequences (e.g. T1 or T2 weighted) at any time points. However we observed significantly increased fractional anisotropy (FA) in the cerebellum, internal capsule, corpus callosum at 14 days, which continueed to increase toward 28 days. Significantly reduced mean diffusivity (MD) was observed in the cortex and corpus callosum at 14 days, which showed recovery at 28 days. Significantly increased mean kurtosis (MK) was observed in the internal capsule from 7 days; and the cerebellum, corpus callosum, pons, medulla from 14days, with the changes continued to increase toward 28 days. Metabolic changes indicated changes in the internal capsule with increased GABA and glutamine at 14 days, which showed recovery at 28days, while increased total choline at 28days. In the cerebellum, increased NAA was observed at 28days. The increased FA, reduced MD and increased MK in the cortex, cerebellum, and internal capsule, corpus callosum at 14 to 28 days post injury may be an indication of cell and axonal swelling and possible cytotoxic edema. Increased MK at 28 days may also indicate a delayed microglial activation or activation that peaks for it to be detectable through changes in MK and also through changes in key metabolites such as NAA. NAA is a neuronal osmolyte and a source of acetate for lipid and myelin

synthesis in oligodendrocytes, and its increase at 28 days suggests existence of active repair process. Taken together, the results from MRS and MRI are consistent with mTBI using the controlled bTBI model which show delayed structural changes using advanced imaging techniques on animals where conventional MRI is negative.

Keywords	*Imaging modalities for detecting mild/mod TBI, micro-TBI (primary keyword)* Magnetic resonance Spectroscopic Imaging Diffusion Tensor Imaging
Abstract Topics	Magnetic resonance Spectroscopy Diffusion Tensor Imaging Imaging modalities for detecting mild/mod TBI, micro-TBI
The abstarct book's publications additonal Information summary	
Educational Objectives	1. Brain injury caused by the direct blast wave has unique temporal profile, suggesting a delayed repair process. 2. Advanced neuroimaging markers (e.g. DKI and MRS) can reveal subtle microstructural and metabolic changes, that often times missed by conventional imaging.
Files	*Submission exists, but was not archived (suffix)*

Reviews

A METHOD OF ELECTRICAL STIMULATION IN PROLONGED DISTURBANCES OF CONSCIOUSNESS

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Abstract: Introduction Brain electrical stimulation therapy (BEST) and its clinical application in prolonged posttraumatic disturbances of consciousness is presented. Patients and method A total number of 32 post trauma patients with prolonged consciousness disturbances - eye opening without being fully aware after about 30 days since admission to the unit - in spite of standard therapy, was selected for this study. Of these 16 underwent stimulation, with a control group of 16 patients. The stimulator is a generator of biphasic currents applied through two electrodes: one electrode was placed on posterior pharyngeal wall, in front of atlanto-occipital joints and the other on the vertex. Results A favourable outcome was defined as Glasgow Outcome Scale (GOS)>3 at discharge, which was recorded in 12 stimulated patients and in 8 in the control group, which was statistically different. Conclusion The mechanisms of action of BEST are still hypothetical. It is seen as a potential preventive tool against development of the vegetative state (VS) due to functional inhibition.

Keywords *General issues (primary keyword)*

Abstract Topics General issues

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A METHOD OF ELECTRICAL STIMULATION IN PROLONGED DISTURBANCES OF CONSCIOUSNESS
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Key words: vegetative state, brain electrical stimulation therapy
ABSTRACT

Introduction
Brain electrical stimulation therapy (BEST) and its clinical application in prolonged posttraumatic disturbances of consciousness is presented.
Patients and method
A total number of 32 post trauma patients with prolonged consciousness disturbances - eye opening without being fully aware after about 30 days since admission to the unit - in spite of standard therapy, was selected for this study. Of these 16 underwent stimulation, with a control group of 16 patients.
The stimulator is a generator of biphasic currents applied through two electrodes: one electrode was placed on posterior pharyngeal wall, in front of atlanto-occipital joints and the other on the vertex.
Results
A favourable outcome was defined as Glasgow Outcome Scale (GOS)>3 at discharge, which was recorded in 12 stimulated patients and in 8 in the control group, which was statistically different.
Conclusion
The mechanisms of action of BEST are still hypothetical. It is seen as a potential preventive tool against development of the vegetative state (VS) due to functional inhibition.

Educational Objectives Due to small number of patients, the statisitcal analysis is not well grounded. Meanwhile, the method is an alternative not presented before and could give support for noninvazive brain neuromodulation

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Electric fields for the treatment of Glioblastomas: a sensitivity analysis

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Abeye Mekonnen - IBEB, Faculty of Science, University of Lisbon, Portugal
Ricardo Salvador - IBEB, Faculty of Science, University of Lisbon, Portugal
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Abstract: Oscillating electric fields are being investigated as an adjunct and even an alternative to chemotherapy in the treatment of glioblastoma multiforme (GBM). The magnitude and direction of the electric field in the tumor are important determinants of treatment efficacy. We used computational methods to investigate the effect of variations in the dielectric properties of head tissues and in their thickness on the magnitude of the electric field in the brain. The effect of the tissuesâ€™ complex geometry on the electric field distribution was also examined using a realistic head model.

We reviewed the literature to select average values and ranges for the electrical conductivity and relative permittivity of head tissues at 200 kHz. This range of values probably reflects experimental uncertainty in the measurements but may also include inter-subject variability. The range of thicknesses for the scalp, skull and CSF was intended to cover both normal and pathological cases. We used the finite element method to calculate the electric field in a 4-layer spherical model and one realistic model of the head. The electrode arrays and the current intensity used in the models mimicked as closely as possible a commercial device specifically designed for the treatment of tumors (www.novocure.com).

The results obtained with the spherical head model show that variations in the tissue permittivities have little effect on the magnitude of the electric field, mainly because capacitive currents are smaller than resistive currents. Variations in tissue conductivities within the published range can increase the magnitude of the electric field in the brain by up to 60% or decrease it by up to 40%, with the conductivities of the skull and the brain having the largest effect. Variations in layer thickness produce similar changes. Changes in the electric field magnitude are largest in more superficial brain regions. In the realistic head model, the electric field did not decrease slowly and smoothly with distance from the electrodes. Instead, local maxima were observed in the white matter at tissue boundaries approximately perpendicular to the direction of the current. In both models, the magnitude of the electric field was greater than 1 V/cm over large regions of the brain.

These calculations indicate that the electric field magnitude predicted in the brain is sufficiently high to arrest cell proliferation based upon in vitro experiments. Variations in tissue dielectric properties or in layer thickness could affect estimates of the magnitude of the electric field in the brain by up to about 50%. In the realistic head model, the complex geometry of tissue boundaries led to localized maxima in the white matter. The inclusion of anisotropy in the electrical conductivity of white matter in future models is expected to increase the observed shunting and spatial non-uniformity of the tumor treating electric fields. Improved patient specific models could provide a means to estimate the electric field in the tumor and to optimize its delivery. This new tool could be used in treatment planning, as well as to understand outcomes when using TTF therapy.

Keywords	*Minimally invasive therapy (primary keyword)*
Abstract Topics	Minimally invasive therapy
The abstarct book's publications additonal Information summary	
Educational Objectives	1) to understand the variability of outcomes in the use of alternating electric fields to treat glioblastomas. 2) to predict the electric field in the brain using computational models. 3) to propose methods to optimize the delivery of the electric field.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Ankle-robotics assisted training and cortical efficiency are enhanced by reward based motor learning

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Anindo Roy - VA RR&D Maryland Exercise and Robotics Center of Excellence, Baaltimore, MD
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Jason Diaz - VA RR&D Maryland Exercise and Robotics Center of Excellence, Baaltimore, MD
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Abstract: Title: Ankle-robotics assisted training and cortical efficiency are enhanced by reward based motor learning

Ronald N. Goodman PhD,1Jeremy C. Rietschel PhD,1 Brian Jung,1,2 Jason Diaz,1 Anindo Roy PhD,1,3 Richard F. Macko MD,1,2,3 Larry W. Forrester PhD,1,2,3

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Introduction: In the United States someone has a stroke every 45 seconds making it the leading cause of chronic disability in this country. Losses of mobility, increased risk of falling and cognitive impairment are included in its list of sequelae. Hemiparetic gait is a persistent problem for the majority of survivors. Lower extremity robotics is rapidly emerging as a practical and effective method for enhancing cognitive-motor recovery after stroke. Established principles of cognitive-motor-learning identify a positive relationship between reward and motor learning. Yet, there are no studies we are aware of that have established whether reward quantitatively improves the rate or efficacy of robotics-assisted rehabilitation, and if adaptive neurophysiologic changes are associated with these hypothesized improvements.

Question: Can reward based behavioral reinforcement enhance neuromotor outcomes in stroke survivors when added to a motor learning based, lower extremity, robotics assisted intervention?

Methods: A 3-week / 9 session (~1 hour) clinical pilot was conducted with ten chronic hemiparetic stroke survivors to determine the comparative effects of high vs. low reward incentive during ankle-robotics training. Participants were randomly assigned to a high-(HR) or low-reward (LR) group. Training entailed playing a video-game by moving the paretic-ankle to hit moving targets while wearing an impedance-controlled ankle robot (anklebot) that provided assistance â€œas needed.â€ Training challenge was individualized to each participantâ€™s active range of motion and target success rate. Outcomes included paretic-ankle motor control, learning curves, spatio-temporal parameters of gait and associated changes in cortical networking (EEG coherence) and activation (EEG spectral power) during volitional (unassisted) ankle movements. Results: The HR Group had faster learning curves, smoother movements, reduced contralesional frontoparietal coherence and reduced spectral power in the left-temporal region. Gait analysis showed the HR group increased non-paretic step-length and trended toward increased floor-walking velocity. Conclusion: This study suggests that robotics-assisted ankle rehabilitation is enhanced by reward based behavioral reinforcement. Concomitant shifts in EEG suggest that motivation may hasten motor learning and neural plasticity, even years after a disabling stroke.

Future directions: We are currently examining changes in cortical networks using Graph Theory based network analysis and have noted differences in the high vs. low reward groupsâ€™ response to this short robotics assisted intervention. Additionally because of the increased biological opportunity for improving recovery outcomes during earlier phases of stroke, we have begun to collect EEG during the subacute phase of stroke. We have initiated

studies in subacute stroke to explore brain plasticity and the cortical network changes associated with usual care vs. usual care + robotics-assisted training.

Keywords Neurophysiology (EEG, MEG, ?)
Neural Prosthesis & Robotics

Abstract Topics Neurophysiology (EEG, MEG,â€¦)
Neural Prosthesis & Robotics

The abstarct book's publications additonal Information summary

Title: Ankle-robotics assisted training and cortical efficiency are enhanced by reward based motor learning

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Introduction: In the United States someone has a stroke every 45 seconds making it the leading cause of chronic disability in this country. Losses of mobility, increased risk of falling and cognitive impairment are included in its list of sequelae. Hemiparetic gait is a persistent problem for the majority of survivors. Lower extremity robotics is rapidly emerging as a practical and effective method for enhancing cognitive-motor recovery after stroke. Established principles of cognitive-motor-learning identify a positive relationship between reward and motor learning. Yet, there are no studies we are aware of that have established whether reward quantitatively improves the rate or efficacy of robotics-assisted rehabilitation, and if adaptive neurophysiologic changes are associated with these hypothesized improvements.

Question: Can reward based behavioral reinforcement enhance neuromotor outcomes in stroke survivors when added to a motor learning based, lower extremity, robotics assisted intervention?

Methods: A 3-week / 9 session (~1 hour) clinical pilot was conducted with ten chronic hemiparetic stroke survivors to determine the comparative effects of high vs. low reward incentive during ankle-robotics training. Participants were randomly assigned to a high-(HR) or low-reward (LR) group. Training entailed playing a video-game by moving the paretic-ankle to hit moving targets while wearing an impedance-controlled ankle robot (anklebot) that provided assistance â€œas needed.â€ Training challenge was individualized to each participantâ€™s active range of motion and target success rate. Outcomes included paretic-ankle motor control, learning curves, spatio-temporal parameters of gait and associated changes in cortical networking (EEG coherence) and activation (EEG spectral power) during volitional (unassisted) ankle movements.

Results: The HR Group had faster learning curves, smoother movements, reduced contralesional frontoparietal coherence and reduced spectral power in the left-temporal region. Gait analysis showed the HR group increased non-paretic step-length and trended toward increased floor-walking velocity.

Conclusion: This study suggests that robotics-assisted ankle rehabilitation is enhanced by reward based behavioral reinforcement. Concomitant shifts in EEG suggest that motivation may hasten motor learning and neural plasticity, even years after a disabling stroke.

Future directions: We are currently examining changes in cortical networks using Graph Theory based network analysis and have noted differences in the high vs. low reward groupsâ€™ response to this short robotics assisted intervention. Additionally because of the increased biological opportunity for improving recovery outcomes during earlier phases of stroke, we have begun to collect EEG during the subacute phase of stroke. We have initiated studies in subacute stroke to explore brain plasticity and the cortical network changes associated with usual care vs. usual care + robotics-assisted training.

Learning Objectives: 1) Describe the current state of rehabilitation robotics as applied to functional recovery after stroke, 2) Discuss the potential of reward based reinforcement to adaptively modulate the state of the learner and enhance numerous applications in motor learning based neurorehabilitation, 3) Explain the ability of EEG to provide relevant high-temporal resolution data to explicate the underlying neural mechanisms engaged during motor recovery in order to design more efficacious neurorehabilitation for stroke survivors.

Impact: This work has the potential to help advance the goal of optimizing neuromotor recovery after neurological disease and injury.

Key Words: reward, motor-learning, ankle robotics, EEG, EEG coherence, EEG spectral power, hemiparetic stroke

Educational Objectives

Educational Objectives: 1) Describe the current state of rehabilitation robotics as applied to functional recovery after stroke, 2) Discuss the potential of reward based reinforcement to adaptively modulate the state of the learner and enhance numerous applications in motor learning based neurorehabilitation, 3) Explain the ability of EEG to provide relevant high-temporal resolution data to explicate the underlying neural mechanisms engaged during motor recovery in order to design more efficacious neurorehabilitation for stroke survivors.Impact: This work has the potential to help advance the goal of optimizing neuromotor recovery after neurological disease and injury.

Files

Submission exists, but was not archived (suffix .pdf)

Neurological Consequences of Primary Blast Traumatic Brain Injury in the Rat: Relating Diffusion Tensor Imaging and Behavior

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Alok Shah - Medical College of Wisconsin
Michael McCrea - Medical College of Wisconsin
Frank Pintar - Medical College of Wisconsin
Brian Stemper - Medical College of Wisconsin

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Abstract: Introduction- The incidence of traumatic brain injury (TBI) among military personnel is increasing at an alarming rate. The overwhelming majority of TBI events are categorized as mild (mTBI), and exposure to blast forces from improvised explosive devices is a major factor contributing to the unprecedented rate of mTBI. Diffusion tensor imaging (DTI) of veterans has revealed brain abnormalities following even a single blast injury. Animal models of blast have been integral in understanding the effects of blast on the brain, yet DTI has been infrequently applied to these models that permit the study of blast under well-controlled laboratory conditions. In this study, DTI was used to investigate the microstructural consequences of blast injury in a rat model.

Methods- A rat model of primary blast was employed. Blast shockwaves with peak overpressures of either 100 or 450 kPa were delivered using a highly reproducible shocktube. Body shielding and head restraint were used to limit pulmonary or acceleration-induced head trauma, respectively. Animals subsequently underwent a battery of behavioral tests to assess motor, emotional, and cognitive dysfunction. DTI was performed at 4 or 30 days post-blast. Spatial registration of images and voxel-by-voxel statistical testing permitted visualization of the spatially-dependant pattern of brain abnormalities.

Results- Blast TBI caused significant anxiety evident as less time spent in the open arms of the elevated plus maze in animals with 450 kPa blast at 4 days post-blast. The effect was more pronounced at 30 days post-blast. No learning or memory cognitive dysfunction was evident on the Morris Water Maze. DTI revealed significant brain abnormalities in blast-exposed animals that were related to the magnitude of the blast. The ipsilateral cortex and thalamus were significantly abnormal at 4 days post-blast, whereas the injury progressed to include the contralateral cortex and brainstem at 30 days post-blast. At both timepoints, the injury was more pronounced and more extensive following 450 kPa blast compared to 100 kPa. Furthermore, a significant

correlation between the DTI changes and behavioral measures of anxiety was observed in the amygdala and hippocampus, consistent with their involvement in such behaviors.

Conclusions- The results provide fundamental insight into the neurological consequences of blast TBI, particularly the spatially-dependant pattern of injury and evolution of injury during the subacute phase. The relationship between emotional dysfunction and brain abnormalities may provide insight into co-morbidities associated with blast TBI, including depression or post traumatic stress disorder. Overall, the findings and further applications will be important to aide in prevention of blast TBI and guide therapeutic and rehabilitative efforts.

Keywords	*Imaging modalities for detecting mild/mod TBI, micro-TBI (primary keyword)* Diffusion Tensor Imaging Histopathology
Abstract Topics	Diffusion Tensor Imaging Imaging modalities for detecting mild/mod TBI, micro-TBI
The abstarct book's publications additonal Information summary	
Educational Objectives	Educational objectives: The audience will learn how blast neurotrauma is used in a preclinical research setting; how DTI can be used to uncover the effects of mild TBI; how behavioral testing and MRI can reveal associations between brain trauma and outcomes
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Modular Ankle Robotics for Locomotor Training Post-Stroke: A Novel Deficit-Adjusted Approach

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Richard Macko - University of Maryland School of Medicine
Joseph Barton - University of Maryland School of Medicine
Ronald Goodman - Baltimore VA Exercise and Robotics Center of Excellence
Larry Forrester - University of Maryland School of Medicine

Contact: Anindo Roy (aroy@som.umaryland.edu)

Abstract: Introduction: The impact of stroke on walking function is often significant, negatively affecting an individualâ€™s mobility and ability to perform everyday activities. Many individuals have residual deficits even after completion of all conventional rehabilitation therapy. Moreover, increasing evidence suggests that conventional rehabilitation does not provide adequate task-repetitive practice to optimize motor learning and recovery across the continuum of care. Robotics may offer a promising avenue for gait therapy by providing a customizable motor learning platform. The Baltimore VA Medical Center has developed a 2 degree-of-freedom â€œassist-as-neededâ€ ankle robot (â€œAnklebotâ€) to improve walking and balance functions post-stroke. The Anklebot is capable of independently modulating specific sub-tasks within the gait cycle to better address the heterogeneity of hemiparetic stroke recovery. In this study, we investigate whether a modular, deficit-adjusted approach to using the Anklebot for locomotor training can lead to sustainable gains in selected aspects of gait function in chronic stroke. Here, we describe and present preliminary data from a single chronic stroke survivor.

Methods: A novel sub event-triggered control system was used, which enables precise timing of robotic assistance to key functional deficits of hemiparetic gait, thereby affording the opportunity to customize robotic support to individual gait deficit profiles. Training was adaptive in that, training parameters were adjusted across the intervention based on subject performance, and tolerance. The case subject entered the program with pronounced foot drop (<2Â° volitional dorsiflexion) making it a logical target for intervention. Training was conducted during 3xweekly visits with 48 hours between visits. On each visit, the session began with TM walking at self-selected speed (visit 1: 30 cm/s, visit 18: 36 cm/s) with the robot in a â€œrecord-onlyâ€ mode. This was followed by two 20-min trials of Anklebot-assisted walking during which the Anklebot provided dorsiflexion assistance, commencing immediately following toe-off and peaking during mid-swing.

Results: We compared the peak dorsiflexion angle during unassisted walking at admission, discharge, and 6-week follow-up. There was a marked increase in the peak dorsiflexion angle at discharge (2.5Â°Â±1.1Â° vs. 7Â°Â ±0.5Â°), and this improvement was durably retained at 6 weeks follow-up (8Â°Â±0.8Â°). Notably, patient reported permanent discard of her assistive device (AFO) in her activities of daily life. The patientâ€™s independent floor walking speed also increased durably (47.4Â±6.1 cm/s vs. 76.5Â±2.4 cm/s vs. 81.9Â±10.2 cm/s) that may be attributed to improved volitional control at the paretic ankle.

Conclusions: Six weeks of Anklebot-assisted gait training eliminated drop foot and increased overground gait speed in a single stroke subject. We are currently using the approach in subjects with impaired push-off propulsion. We anticipate that this modular, deficit-adjusted approach will, over time, â€œteachâ€ the central nervous system to take over from gradual withdrawal of robotic support in order to supplant the robot with volitional movements at the paretic ankle.

Keywords *Neural Prosthesis & Robotics (primary keyword)*
Rehabilitation Medicine (neural repair and regeneration)

Abstract Topics Neural Prosthesis & Robotics

The MODULAR ANKLE ROBOTICS FOR LOCOMOTOR TRAINING POST-STROKE:

abstarct

A NOVEL DEFICIT-ADJUSTED APPROACH

book's publications

A. Roy1,2, R.F. Macko1,2,3, J.E. Barton1,2, R.G. Goodman1, L.W. Forrester1,2,4

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2Baltimore VA Exercise and Robotics Center of Excellence
3Geriatric Research Education and Clinical Core
4Department of Physical Therapy and Rehabilitation Science, University of Maryland at Baltimore

additonal Information

summary

ABSTRACT

Introduction: The impact of stroke on walking function is often significant, negatively affecting an individualâ€™s mobility and ability to perform everyday activities. Many individuals have residual deficits even after completion of all conventional rehabilitation therapy. Moreover, increasing evidence suggests that conventional rehabilitation does not provide adequate task-repetitive practice to optimize motor learning and recovery across the continuum of care. Robotics may offer a promising avenue for gait therapy by providing a customizable motor learning platform. The Baltimore VA Medical Center has developed a 2 degree-of-freedom â€œassist-as-neededâ€ ankle robot (â€œAnklebotâ€) to improve walking and balance functions post-stroke. The Anklebot is capable of independently modulating specific sub-tasks within the gait cycle to better address the heterogeneity of hemiparetic stroke recovery. In this study, we investigate whether a modular, deficit-adjusted approach to using the Anklebot for locomotor training can lead to sustainable gains in selected aspects of gait function in chronic stroke. Here, we describe and present preliminary data from a single chronic stroke survivor.

Methods: A novel sub event-triggered control system was used, which enables precise timing of robotic assistance to key functional deficits of hemiparetic gait, thereby affording the opportunity to customize robotic support to individual gait deficit profiles. Training was adaptive in that, training parameters were adjusted across the intervention based on subject performance, and tolerance. The case subject entered the program with pronounced foot drop (<2Â° volitional dorsiflexion) making it a logical target for intervention. Training was conducted during 3xweekly visits with 48 hours between visits. On each visit, the session began with TM walking at self-selected speed (visit 1: 30 cm/s, visit 18: 36 cm/s) with the robot in a â€œrecord-onlyâ€ mode. This was followed by two 20-min trials of Anklebot-assisted walking during which the Anklebot provided dorsiflexion assistance, commencing immediately following toe-off and peaking during mid-swing.

Results: We compared the peak dorsiflexion angle during unassisted walking at admission, discharge, and 6-week follow-up. There was a marked increase in the peak dorsiflexion angle at discharge (2.5Â°Â±1.1Â° vs. 7Â°Â±0.5Â°), and this improvement was durably retained at 6 weeks follow-up (8Â°Â±0.8Â°). Notably, patient reported permanent discard of her assistive device (AFO) in her activities of daily life. The patientâ€™s independent floor walking speed also increased durably (47.4Â±6.1 cm/s vs. 76.5Â±2.4 cm/s vs. 81.9Â±10.2 cm/s) that may be attributed to improved volitional control at the paretic ankle.

Conclusions: Six weeks of Anklebot-assisted gait training eliminated drop foot and increased overground gait speed in a single stroke subject. We are currently using the approach in subjects with impaired push-off propulsion. We anticipate that this modular, deficit-adjusted approach will, over time, â€œteachâ€ the central nervous system to take over from gradual withdrawal of robotic support in order to supplant the robot with volitional movements at the paretic ankle.

Educational Objectives

Learning Objectives: 1) Describe the current state of rehabilitation robotics as applied to functional recovery after stroke. 2) Discuss recent advances in using robotics to enhance motor learning and lower extremity function after stroke; 3) Describe the application of EEG and neurophysiological approaches used to characterize neural plasticity and learning; 2) Impact: This work has the potential to help advance the goal of optimizing motor recovery after neurological disease and injury.

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Quantitative magnetic resonance imaging of tissue damage of the nucleus pulposus after diode laser treatment in ex-vivo bovine spines

Zsolt Cselik - University Of KaposvÃ¡r
Ronald A. von Jako - GE Healthcare Surgery
MihÃ¡ly Aradi - Zalaegerszeg County Hospital
Ivett JuhÃ¡sz - University Of KaposvÃ¡r
Zsolt EgyhÃ¡zi - â€œKaposi MÃ³râ€ County Teaching Hospital
Zsuzsanna Lelovics - University Of KaposvÃ¡r
Attila Schwarcz - University Of PÃ©cs
Peter Bogner - University Of PÃ©cs
Imre Repa - University Of KaposvÃ¡r

Contact: Zsolt Cselik (cselik.zsolt@yahoo.com)

Abstract: Introduction Low back pain and/or disc herniation occur in 65â€“70% of people over 40 years of age. The variety of percutaneous techniques available for addressing spinal ailments continues to grow. Percutaneous laser disc decompression (PLDD) is commonly used to lower high pressure in the nucleus pulposus in degenerative disc. Our aim was to examine the impact of PLDD administered at different wavelengths by using quantitative MRI measurements in ex-vivo bovine spine model.

Methods To model PLDD, we inserted a flexible quartz fiber by surgical navigation into the nucleus pulposus of 14 vertebrae in three freshly harvested spines. Using both 980-nm (5 discs) and 1470-nm (9 discs) wavelength diode lasers, a part of the nucleus pulposus was vaporized by heat convection. Similar energy levels were delivered with both wavelengths. Quantitative MRI measurements (T1- and T2-weighted and apparent diffusion coefficient [ADC]) were made before and after the laser procedure. To verify the morphological changes detected on the MRI scans, we did pathological evaluation of the intervertebral discs.

Results The 980-nm wavelength laser caused significant signal decrease on T1- and increase on T2-weighted imaging at the site of the quartz fiber whereas the 1470-nm wavelength laser caused no visible change on T1 and T2 maps. Pathological findings showed a wider carbonization zone and steam-bubble formation related to T1 and T2 changes. When the whole nucleus pulposus was examined, no significant ADC changes were detected for the 980-nm wavelength, but significant T1 and ADC increases were found with the 1470-nm wavelength. With the 1470-nm laser, the carbonization zone was narrower and the bubbles were smaller.

Conclusion The effect of the 1470-nm laser was detected in the whole nucleus pulposus, not only at the site of the quartz fiber because of the 40-fold greater absorption rate in water. With the 980-nm wavelength laser, the energy was absorbed in a smaller volume, but caused a greater effect (carbonization, explicit steam-bubble formation). With quantitative MRI measurements, we were able to detect the impact of the diode laser in small volume of the intervertebral disc by clinical scanner. The results and the methods are adaptable to further human examinations, which would enable clinicians to objectively measure the effectiveness of PLDD.

Keywords *Image guided systems (primary keyword)*
Stereotactic Radiosurgery
Minimally invasive therapy

Abstract Topics Minimally invasive therapy

The abstarct Quantitative magnetic resonance imaging of tissue damage of the nucleus pulposus after diode laser treatment in ex-vivo bovine spines

book's publications additonal Information summary

Zsolt Cselik MD1, Ronald A.von Jako MD, PhD 2, MihÃ¡ly Aradi MD3, Ivett JuhÃ¡sz Msc.4, Zsolt EgyhÃ¡zi MD5, Zsuzsanna Lelovics Msc, PhD 1, Attila Schwarcz MD, PhD 6, Peter Bogner MD, PHD 7, Imre Repa MD, PHD1

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Introduction
Low back pain and/or disc herniation occur in 65â€“70% of people over 40 years of age. The variety of percutaneous techniques available for addressing spinal ailments continues to grow. Percutaneous laser disc decompression (PLDD) is commonly used to lower high pressure in the nucleus pulposus in degenerative disc.
Our aim was to examine the impact of PLDD administered at different wavelengths by using quantitative MRI measurements in ex-vivo bovine spine model.

Methods
To model PLDD, we inserted a flexible quartz fiber by surgical navigation into the nucleus pulposus of 14 vertebrae in three freshly harvested spines. Using both 980-nm (5 discs) and 1470-nm (9 discs) wavelength diode lasers, a part of the nucleus pulposus was vaporized by heat convection. Similar energy levels were delivered with both wavelengths. Quantitative MRI measurements (T1- and T2-weighted and apparent diffusion coefficient [ADC]) were made before and after the laser procedure. To verify the morphological changes detected on the MRI scans, we did pathological evaluation of the intervertebral discs.

Results
The 980-nm wavelength laser caused significant signal decrease on T1- and increase on T2-weighted imaging at the site of the quartz fiber whereas the 1470-nm wavelength laser caused no visible change on T1 and T2 maps. Pathological findings showed a wider carbonization zone and steam-bubble formation related to T1 and T2 changes. When the whole nucleus pulposus was examined, no significant ADC changes were detected for the 980-nm wavelength, but significant T1 and ADC increases were found with the 1470-nm wavelength. With the 1470-nm laser, the carbonization zone was narrower and the bubbles were smaller.

Conclusion
The effect of the 1470-nm laser was detected in the whole nucleus pulposus, not only at the site of the quartz fiber because of the 40-fold greater absorption rate in water. With the 980-nm wavelength laser, the energy was absorbed in a smaller volume, but caused a greater effect (carbonization, explicit steam-bubble formation). With quantitative MRI measurements, we were able to detect the impact of the diode laser in small volume of the intervertebral disc by clinical scanner. The results and the methods are adaptable to further human examinations, which would enable clinicians to objectively measure the effectiveness of PLDD.

Educational Objectives Image guided therapy, PLDD, diode laser

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Temporal changes of cerebral blood perfusion following mild Traumatic Brain Injury

Teodora Stoica - Magnetic Resonance Research Center, Diagnostic Radiology & Nuclear Medicine, University Of Maryland School of Medicine, Baltimore, Maryland, United States

Jiachen Zhuo - Magnetic Resonance Research Center, Diagnostic Radiology & Nuclear Medicine, University Of Maryland School of Medicine, Baltimore, Maryland, United States

Steve Roys - Magnetic Resonance Research Center, Diagnostic Radiology & Nuclear Medicine, University Of Maryland School of Medicine, Baltimore, Maryland, United States

Joseph Rosenberg - Magnetic Resonance Research Center, Diagnostic Radiology & Nuclear Medicine, University Of Maryland School of Medicine, Baltimore, Maryland, United States

Chandler Sours - Magnetic Resonance Research Center, Diagnostic Radiology & Nuclear Medicine, University Of Maryland School of Medicine, Baltimore, Maryland, United States

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Contact: Teodora Stoica (tstoica@umm.edu)

Abstract: Introduction: Traumatic brain injury (TBI) accounts for 1.5 million injuries in the United States each year, and veteransâ€™ advocates believe that between 10 and 20% of Iraq veterans have some level of TBI. Novel neuroimaging tools such as arterial spin labeling (ASL) may provide insights into the subtle changes following injury and serve as an effective imaging marker to monitor novel rehabilitative efforts. Previous studies have investigated cognitive function in mTBI patients post-injury, but this studyâ€™s aim is to do so in the acute and sub-acute stage using regional CBF changes.

Methods: TBI patients were recruited in the acute stage of injury from the Adam Crawley Shock Trauma Center at the University of Maryland, Baltimore as part of the MagNeT Study (Magnetic Resonance Imaging of NeuroTrauma). 29 mTBI patients and 34 control individuals were included in this study. mTBI patients were split in two categories based on cognitive scores: Cognitive Impaired (CI) group, whose score was 1.5-2SD lower than the mean and Non-Cognitive Impaired (NCI) group, with scores comparable to the controls. Patients were scanned within 10 days of injury and approximately 1 month post injury. Participants underwent pulsed arterial spin labeling (pASL) on a 3-Tesla Siemens MRI scanner. Each mTBI patient was subject to a battery of computerized cognitive assessments out of which the weighted throughput score was extracted which measures accuracy and reaction time. This score was used to correlate with imaging measures. Repeated measures ANOVAs was carried out to test temporal changes in the frontal, occipital, parietal, temporal lobes and the thalamus, followed by independent two-tailed t-test to compare each time-point to the values obtained from the control subjects as well as its opposite group.

Results: At the 10 day period compared to controls, patients in the CI group exhibited significant lower perfusion in all lobes except the temporal. As compared to controls, patients in the NCI group had higher perfusion in the frontal and occipital lobes and lower perfusion in the thalamus. The significantly low perfusion exhibited at the 10 month time point in the CI group was also observed at the 1 month time point in the occipital and parietal lobes and thalamus. The NCI group in contrast, had significantly higher perfusion than the CI group in the same aforementioned areas, but low perfusion in the thalamus.

Conclusion: The brainâ€™s repair mechanism is complex, and investigating the results of ASL might explain how patients without cognitive impairment and high perfusion maintain a comparable cognitive score to controls despite injury. The thalamus in both groups exhibited lowered perfusion suggesting this area of the brain is sensitive to mTBI. The findings validate ASL as a viable diagnostic method and reliable marker for the therapeutic management of mTBI patients.

Keywords *Vascular & Blood flowimaging (primary keyword)*
Perfusion imaging, micromagnetic resonance imaging

Imaging modalities for detecting mild/mod TBI, micro-TBI

Abstract Topics Imaging modalities for detecting mild/mod TBI, micro-TBI

The abstarct book's publications additonal Information summary

Introduction: Novel neuroimaging tools such as arterial spin labeling (ASL) may provide insights into the subtle changes following mTBI and serve as an effective imaging marker to monitor novel rehabilitative efforts.
Methods: 29 mTBI patients and 34 control individuals were included in this study. mTBI patients were split in two categories based on cognitive scores: Cognitive Impaired (CI) group, whose score was 1.5-2SD lower than the mean and Non-Cognitive Impaired (NCI) group, with scores comparable to the controls. Patients were scanned within 10 days of injury and approximately 1 month post injury. Participants underwent pulsed arterial spin labeling (pASL) on a 3-Tesla Siemens MRI scanner. Repeated measures ANOVAs was carried out to test temporal changes in the frontal, occipital, parietal, temporal lobes and the thalamus, followed by independent two-tailed t-test to compare each time-point to the values obtained from the control subjects as well as its opposite group.
Results: Overall, the patients in the CI group had lower perfusion through the one month time point, while the NCI group had higher perfusion. The perfusion of the thalamus of both groups was significantly decreased at all time points.
Conclusion: The findings validate ASL as a viable diagnostic method and reliable marker for the therapeutic management of mTBI patients.

[This work has not been submitted for publication nor publication elsewhere]

Educational Objectives clinical care, publication, award

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Stem Cell Transplantation to the Central Nervous System under the Guidance of Ultra-Fast Real-Time MR Imaging

Miroslaw Janowski - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

Joanna Wojtkiewicz - Department of Neurology and Neurosurgery, Division of Neurosurgery, Faculty of Medical Sciences, University of Warmia and Mazury, Olsztyn, Poland

Adam Nowakowski - Dept. of NeuroRepair, Mossakowski Med. Res. Centre, Polish Acad. of Sci., Warsaw, Poland

Aleksandra Habich - Department of Neurology and Neurosurgery, Division of Neurosurgery, Faculty of Medical Sciences, University of Warmia and Mazury, Olsztyn, Poland

Monica Pearl - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

Phillipe Gailloud - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

Barbara Lukomska - Dept. of NeuroRepair, Mossakowski Med. Res. Centre, Polish Acad. of Sci., Warsaw, Poland

Wojciech Maksymowicz - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

Jeff Bulte - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

P Walczak - Radiology and Radiological Science, Johns Hopkins Univ., Baltimore, MD, USA

Contact: Miroslaw Janowski (neuroibis@gmail.com)

Abstract: Introduction: Up until now, MRI stem cell tracking has only enabled detection of cells after the transplantation was completed. We have developed a new technique that allows monitoring of cell delivery in real-time, allowing immediate intervention would cells engraft in undesired locations including the formation of life-threatening microembolisms.

Materials and Methods: Human mesenchymal stem cells were treated overnight with 20 Âµg/ml of Molday ION-Rhodamine B (BioPAL, Inc.). Immediately prior to transplantation, cells were harvested and suspended in 10 mM PBS, at 0.2-1.0x106 cells/ml. Intraarterial cell transplantation was performed in four different experimental models: rat stroke model, normal porcine brain, normal dog brain, and normal dog spinal cord. For assessment of cerebral perfusion, the labeled cell injection in the dog brain was preceded by infusion of the USPIO formulation FerahemeÂ®. For spinal delivery in dogs, cells were injected in the Adamkiewicz artery. For real-time monitoring of Feraheme and labeled cell injection, we used a standard GE-EPI sequence. For rats, a Bruker 7T horizontal bore magnet and 15 mm planar surface coil was used with TE=17 ms, TR=2000 ms, FOV=260x260mm, matrix=96x96, and

acquisition time=2 s. For dogs and pigs, a 3T Siemens Trio was used with TE=36 ms, TR=3000 ms, FOV=1080, matrix=128, and acquisition time=3 s. These fast sequences enable continuous monitoring of cell delivery. Standard T2-w and susceptibility weighted images were also acquired before and after GE-EPI.

Results: In the rat stroke model, we detected in real-time an inflow of cells into the brain characterized by a gradual, focal decrease of pixel intensities (PI) on consecutive images. Real-time GE-EPI demonstrated that cells rapidly engrafted within the stroke periphery, with a delayed inflow into the core of the infarct. At the end of the infusion, the cell distribution within the overall infarcted area was quite homogenous. The successful implementation of real-time imaging of cell delivery in rodents prompted us to test this further in a clinically relevant setting using large animals and clinical instrumentation. In dogs for spinal injections cells were infused into the Adamkiewicz artery and then monitored with GE-EPI demonstrating their broad distribution within the lumbar and thoracic spinal cord. SWI scans typically used for detection of iron labeled cells were highly affected by motion artifacts and of low quality. Perfusion imaging using FerahemeÂ® (three bolus injections of 3mg/ml, 300Âµl each) was performed to predict the cell inflow area and preservation of cerebral blood flow (CBF) following cell delivery. Three separate bolus injections resulted in a dramatic, transient drop of PI in specific regions of the ipsilateral hemisphere. Cell injection resulted in a gradual PI decrease in the region previously highlighted by FerahemeÂ® injection. To confirm that the CBF was not altered by transplanted cells, FerahemeÂ® was injected a second time (i.e., after cell delivery, three boluses), demonstrating a similar perfusion in the area containing transplanted cells.

Conclusions: GE-EPI enables monitoring of cell delivery in real-time with sufficient detail to evaluate cell engraftment and sufficient temporal resolution to discriminate early from late filling areas.

Keywords

Molecular and cellular imaging (primary keyword)
Image guided systems
Vascular & Blood flow imaging
Perfusion imaging, micromagnetic resonance imaging

Abstract Topics

Image guided systems
Vascular & Blood flow imaging
Molecular and cellular imaging
Perfusion imaging
High-field and low-field magnetic resonance
Multimodality imaging

Rehabilitation Medicine (neural repair and regeneration

Basic Neuroscience

The abstarct book's publications additonal Information summary	
Educational Objectives	stem cells, imaging, stroke
Files	*Submission exists, but was not archived (suffix)*

Reviews

Brain microstructural development at near-term age in very low birth weight preterm infants: an atlas-based diffusion imaging study.

Jessica Rose - Department of Orthopedic Surgery, Stanford University
Rachel Vassar - Department of Orthopedic Surgery, Stanford University
Katelyn Cahill-Rowley - Motion Analysis Lab, Lucile Packard Children's Hospital
Ximena Stecher Guzman - Division of Neonatology and Developmental Medicine, Stanford University
David Stevenson - Division of Neonatology and Developmental Medicine, Stanford University
Naama Barnea-Goraly - Center for Interdisciplinary Brain Sciences Research, Stanford University

Contact: Jessica Rose (jessica.rose@stanford.edu)

Abstract: Introduction: Very-low-birth-weight (VLBW) preterm infants have increased incidence of cerebral palsy (15%). Developmental coordination disorder and cognitive and language delays may affect an additional 40% of preterm infants at school age. Brain microstructural development at near-term age is not well described but has been identified as an important risk factor for neurodevelopmental problems in children born preterm. Diffusion tensor imaging (DTI) allows quantitative analysis of brain microstructure based on patterns of water diffusion and has emerged as a promising technique for early prognosis of neurodevelopmental outcome. Semi-automated, atlas-based analysis of infant brain DTI is an objective, time-efficient tool that has potential for clinical implementation. This study aims to examine neonatal white matter (WM) development on DTI in relation to gestational age (GA) at scan in order to better understand temporal-spatial trajectories of neurodevelopment and to compare relative regional development at near-term age.

Methods: DTI scans were analyzed from VLBW preterm infants (BWâ‰¤1500g, GAâ‰¤32weeks) within a cohort of 102 neonates admitted to the NICU, representing 74% of eligible infants scheduled for routine near-term brain-MRI (3T GE-Discovery-MR750) between 1/1/10â€“12/31/12. Parental consent was obtained for this IRB-approved prospective study. 68/102 had successful DTI scans; for this analysis, 46/68 met the inclusion criteria of GA-at-scan â‰¤40wks and had no evidence of brain injury at near-term-MRI.

Analysis of WM microstructure was performed in 19 subcortical and cortical regions defined by the DiffeoMap neonatal brain atlas (Fig. 1) using threshold values of trace<0.006 and FA>0.15. Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were calculated for each brain region and significant correlations (p<0.0125) with GA-at-scan were reported, corrected for multiple comparisons.

Results: Mean GA-at-scan was 36.6Â±1.4wks (34.7-38.6wks). FA values were highest in the PLIC (left=0.354Â±0.037; right=0.356Â±0.037), followed by the splenium of the corpus callosum (CC) (0.286Â±0.030). The PLIC had the lowest MD and RD values. The anterior corona radiata (ACR), superior longitudinal fasciculus (SLF) and caudate demonstrated the lowest FA, and highest MD and RD values. Posterior regions of the CC, internal capsule, and corona radiata demonstrated diffusion measurements indicative of higher development compared to anterior regions (Fig. 2).

Significant correlations with GA-at-scan were observed for FA, MD, and RD values in most regions at this near-term age. The most substantial correlations with GA-at-scan were observed in the ALIC: MD (left: R=.611, p=.000006; right: R=.635, p=.000002) and RD (left: R=.633, p=.000002; right: R=.636, p=.000002) decreased with GA-at-scan. No significant correlations with GA-at-scan were observed for FA, MD, and RD within the CC and SLF.

Conclusion: Understanding temporal-spatial development of near-term brain microstructure has important implications for identifying aberrations in developmental trajectories, which may signal future motor and cognitive deficits in preterm children. The relatively higher development in posterior regions compared to anterior regions of the CC, internal capsule, and corona radiata is consistent with anatomical findings of posterior to anterior infant brain myelination. Analysis of brain microstructure development on DTI may help identify the brain regions

that have prognostic value at near-term age.

Keywords	*Diffusion Tensor Imaging (primary keyword)* Anatomy
Abstract Topics	Anatomy Diffusion Tensor Imaging Brain mapping/functional imaging for rehab medicine
The abstarct book's publications additonal Information summary	See uploaded document for complete file with two figures attached. We can send the individual image files, if a higher resolution is needed. This work has not been submitted for publication, though we intend to publish a manuscript in Neuroimage presenting an expanded analysis of this data.
Educational Objectives	publication, clinical applications
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

TO DO OR NOT TO DO

Elangovan Duraipandian - Pandima Diagnostic Services

Contact: Elangovan Duraipandian (elangoneuro@yahoo.co.in)

Abstract: Introduction : Most of the time Masterly inactivity is the keystone in the management of Head Injury and the first 3 gold standard of treatment are: Observation â€“ Observation and Observation. No Head Injury is so trivial to ignore or so severe to despair. Minimal surgery plays a major role in saving a valuable life.

Methods: All Severe Head Injury Patients with Multiple lesions were subjected to single or double Temporal Burr Hole Craniectomy and Multiple Dural Punctures were done to let out CSF.

Most of the time Masterly inactivity is the keystone in the management of Head Injury and the first 3 gold standard of treatment are: Observation â€“ Observation and Observation. No Head Injury is so trivial to ignore or so severe to despair. Minimal surgery plays a major role in saving a valuable life. A Head Injury with Fracture skull will survive whereas One without skull Fracture may prove fatal. Do not equate Head Injury with Skull Fracture and that is why a new term already well established is emerging,that is â€˜Traumatic Brain Injuryâ€™. The role of the surgeon is very much essential at the Golden Hour 1st 6 hours and still more important in the Platinum hour of 1st 2 hours. ABC Treatment is the gold standard â€“ Airway â€“ Breathing â€“ Circulation. Look the patient as a whole, rule out associated injuries. If the CT Scan is available that will be best to rule out a space occupying lesion like Subdural or Extradural clot that requires a surgical evacuation. The oscillation is always between â€œGolden Hour Treatment and Referring the Patient to a Neurosurgical Centre. â€œ. I always advise Burr hole decompression is the first choice. Even a General surgeon can do it and then refer that patient to a Neurosurgical Centre. Aiming a better care life will be lost in the transport but only a better care can be given if patient is alive and so transported after decompression. To do or not to do, may be a pinching question to a surgeon. There wont be any complication because of a Burr Hole. So if the patient is unconscious and no CT is available a Surgeon can follow simple rules like Burr hole decompression at the Scalp Injury site or Bitemporal Burr Hole decompression. Old is Gold. Bitemporal Burr Hole decompression was the treatment of choice in the beginning of the 20th Century and still holds good today though forgotten for some few years before.

Results : Of the 42 patients 38 survived and among them atleat 30 were back to normal.

Conclusion: Unilateral or Bilateral Temporal Burr hole with Multiple Dural Punctures will save many lives in severe Head Injury.

Keywords *Minimally invasive therapy (primary keyword)*

Abstract Topics Minimally invasive therapy

The abstarct book's publications additonal Information summary

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Title : TO DO OR NOT TO DO
Author : Dr.D.Elangovan
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   Email: elangoneuro@yahoo.co.in
Abstract paper :  Introduction : Most of the time Masterly inactivity is the keystone in
the management of Head Injury and the first 3 gold standard of treatment are: Observation
â€“ Observation and Observation. No Head Injury is so trivial to ignore or so severe to
despair. Minimal surgery plays a major role in saving a valuable life.

Methods: All Severe Head Injury Patients with Multiple lesions were subjected to single or
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CSF.
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Most of the time Masterly inactivity is the keystone in the management of Head Injury and the first 3 gold standard of treatment are: Observation â€" Observation and Observation. No Head Injury is so trivial to ignore or so severe to despair. Minimal surgery plays a major role in saving a valuable life. A Head Injury with Fracture skull will survive whereas One without skull Fracture may prove fatal. Do not equate Head Injury with Skull Fracture and that is why a new term already well established is emerging,that is â€˜Traumatic Brain Injuryâ€™. The role of the surgeon is very much essential at the Golden Hour 1st 6 hours and still more important in the Platinum hour of 1st 2 hours. ABC Treatment is the gold standard â€" Airway â€" Breathing â€" Circulation. Look the patient as a whole, rule out associated injuries. If the CT Scan is available that will be best to rule out a space occupying lesion like Subdural or Extradural clot that requires a surgical evacuation. The oscillation is always between â€œGolden Hour Treatment and Referring the Patient to a Neurosurgical Centre. â€œ. I always advise Burr hole decompression is the first choice. Even a General surgeon can do it and then refer that patient to a Neurosurgical Centre. Aiming a better care life will be lost in the transport but only a better care can be given if patient is alive and so transported after decompression. To do or not to do, may be a pinching question to a surgeon. There wont be any complication because of a Burr Hole. So if the patient is unconscious and no CT is available a Surgeon can follow simple rules like Burr hole decompression at the Scalp Injury site or Bitemporal Burr Hole decompression. Old is Gold. Bitemporal Burr Hole decompression was the treatment of choice in the beginning of the 20th Century and still holds good today though forgotten for some few years before.

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This paper is not submitted for presentaion or Published any where else.There is no Financial commitment to any one.

Educational Objectives Reduce ICT; Severe Head Injury;Minimal Surgery

Files *Submission exists, but was not archived (suffix)*

Reviews

HIGH FREQUENCY HEART RATE VARIABILITY EVOKED BY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION OVER THE MEDIAL PREFRONTAL CORTEX: A PRELIMINAR INVESTIGATION ON BRAIN PROCESSING OF ACUTE STRESSOR-EVOKED CARDIOVASCULAR REACTIVITY

Eduardo GonÃ§alves - Psychiatry, Faro-Portugal

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Abstract: Introduction: Transcranial Magnetic Stimulation (TMS) is a non-invasive technique for brain stimulation. Repetitive TMS over the medial Prefrontal Cortex (mmPFC), Broadman Area 10 (BA10) may stimulate transynaptically perigenual Anterior Cingulate Cortex (pACC, BA 32), insula, amigdala, hypothalamus and connected branches of the Autonomic Nervous System (ANS) involved in stressor-evoked cardiovascular reactivity. Stressors are associated with an increase in sympathetic cardiac control, a decrease in parasympathetic control, or both, and, consequently, an increase in systolic/stroke volume, total vascular impedance/resistance and heart rate, a decrease of baroreflex sensitivity, i.e., an increase in blood pressure/arterial tension. Objectives and Aims: The present work aims, using TMS and accordingly to Gianaros modeling, based on functional neuroimaging studies and previous neuroanatomical data from animal models, to probe the connectivity of brain systems involved in stressor-evoked cardiovascular reactivity and to explore TMS potential as a tool for detection and stratification of individual differences concerning this reactivity and hemorreological risk factors correlated with the development of coronary arterial disease. Methods: Both subjects, a 52 year old male and a 40 year old female with previous increased Low Frequency (LF)/High Frequency (HF) Heart Rate Variability (HRV) ratios (respectively, 4,209/3,028) without decompensated cardiorespiratory symptomatology, gave informed consent, and ethico-legal issues have been observed. Electroencephalographic (EEG) monitoring was performed for safety purposes. Immediately after administration, over the mPFC, of 15 pulses of rTMS, during 60 second, with an inductive electrical current, at the stimulating coil, of 85,9 AmpÃ¨re per Î¼second and 66 AmpÃ¨re per Î¼second, respectively, for male and female subjects (a â€œfigure-eightâ€ coil and magnetic stimulator MagLite, Dantec/Medtronic, have been used), HRV spectrum analysis (cStress software) has been performed (during 5 minutes, in supine position). Results: In both subjects, LF power, HF power and LF/HF ratio results, before and after rTMS administration, pointed towards sympathetic attenuation and parasympathetic augmentation (respectively, in male/female subject: decreased LF power - 65,1 nu/69,3 nu, before; 56,1 nu/41,6 nu, after; increased HF power - 15,5 nu/22,9 nu, before; 30,9 nu/45,5 nu, after). Conclusions: In this preliminary investigation, the existence of a link between â€œmindâ€ and heartâ€™s function has been put in evidence, through a reversible â€œvirtualâ€ lesion, of brain systems involved in cardiovascular control, caused by TMS: rTMS over mPFC decreased brain function involved in stressor-evoked cardiovascular reactivity, suggesting the importance of TMS in the management of stress-related cardiovascular disorders.

Keywords
Anatomy
Transcranial Magnetic Stimulation
Psychiatry (PTSD,?)

Abstract Topics
Anatomy
Transcranial Magnetic Stimulation
Psychiatry (PTSD,â€¦)

The abstarct book's publications additonal

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Information summary

impedance/resistance and heart rate, a decrease of baroreflex sensitivity, i.e., an increase in blood pressure/arterial tension. Objectives and Aims: The present work aims, using TMS and accordingly to Gianaros modeling, based on functional neuroimaging studies and previous neuroanatomical data from animal models, to probe the connectivity of brain systems involved in stressor-evoked cardiovascular reactivity and to explore TMS potential as a tool for detection and stratification of individual differences concerning this reactivity and hemorreological risk factors correlated with the development of coronary arterial disease. Methods: Both subjects, a 52 year old male and a 40 year old female with previous increased Low Frequency (LF)/High Frequency (HF) Heart Rate Variability (HRV) ratios (respectively, 4,209/3,028) without decompensated cardiorespiratory symptomatology, gave informed consent, and ethico-legal issues have been observed. Electroencephalographic (EEG) monitoring was performed for safety purposes. Immediately after administration, over the mPFC, of 15 pulses of rTMS, during 60 second, with an inductive electrical current, at the stimulating coil, of 85,9 AmpÃ¨re per Î¼second and 66 AmpÃ¨re per Î¼second, respectively, for male and female subjects (a â€œfigure-eightâ€ coil and magnetic stimulator MagLite, Dantec/Medtronic, have been used), HRV spectrum analysis (cStress software) has been performed (during 5 minutes, in supine position). Results: In both subjects, LF power, HF power and LF/HF ratio results, before and after rTMS administration, pointed towards sympathetic attenuation and parasympathetic augmentation (respectively, in male/female subject: decreased LF power - 65,1 nu/69,3 nu, before; 56,1 nu/41,6 nu, after; increased HF power - 15,5 nu/22,9 nu, before; 30,9 nu/45,5 nu, after). Conclusions: In this preliminary investigation, the existence of a link between â€œmindâ€ and heartâ€™s function has been put in evidence, through a reversible â€œvirtualâ€ lesion, of brain systems involved in cardiovascular control, caused by TMS: rTMS over mPFC decreased brain function involved in stressor-evoked cardiovascular reactivity, suggesting the importance of TMS in the management of stress-related cardiovascular disorders.

Educational Objectives

Learn; Transcranial Magnetic Stimulation physical and clinical principles and applications; Brain systems involved in processing acute stressor-evoked cardiovascular reactivity; Applications of spectrum analysis of Heart Rate Variability

Files

Submission exists, but was not archived (suffix .pdf)

Reviews

Improvement of Paclitaxelâ€™s Antineoplastic Efficacy in vivo Using PEOX Polymer Nanoencapsulation

Jing Pan - ANP Technologies, Inc.
Bingsen Zhou - Fulgent Therapeutics LLC
Yubei Zhang - ANP Technologies, Inc.
Jeffrey Dougherty - ANP Technologies, Inc.
Joanna Liu - Fulgent Therapeutics LLC
Tracy Riesenberger - ANP Technologies, Inc.
Dujie Qin - ANP Technologies, Inc.
Yli Remo Vallejo - ANP Technologies, Inc.
Ray Yin - ANP Technologies, Inc.

Contact: Remo Vallejo (yli@anptinc.com)

Abstract: Introduction: Nanoencapsulation of poorly soluble drugs such as paclitaxel using polyethyloxazoline (PEOX)-based branched polymers can lower the drugâ€™s toxicity, and improve its solubility, bioavailability, and tumor-shrinking efficacy.

Methods: Paclitaxel was mixed with PEOX-based branched polymers at drug loading percentages of 11 - 17% to form nanoparticles < 90 nm in diameter. The product was purified and lyophilized as a white powder, designated FID-007. The cytotoxicity of FID-007 was tested on a normal human dermal fibroblast cell line and cell lines for human lung (A549), triple negative breast (MDA-MB-231) and ovarian (OV-90) cancers. Commercially available paclitaxel drugs, Taxol and Abraxane, were similarly tested. The single maximum tolerated dose (MTD) of FID-007, Taxol and Abraxane were determined in vivo in CD-1 mice. The multiple dose MTD for FID-007 was evaluated with CD-1 and Scid mice. The efficacy of FID-007 in controlling tumor growth was compared to the other drugs in vivo using xenograft tumor models in Scid mice with the aforementioned human cancer cell lines (20 mice per cancer). Dosages for the drugs were equitoxic based on previous MTD studies. Saline and polymer (NanoCarrier 001B) were used as negative control treatments for the xenograft studies.

Results: Cytotoxicity of FID-007 was similar to that of Taxol and Abraxane. FID-007 was cytotoxic to A549 lung cancer cells (IC50 2.8 ng/mL), to MDA-MB-231triple negative breast cancer cells (IC50 4.9 ng/mL), and to OV-90 ovarian cancer cells (IC50 5.0 ng/mL). FID-007 was over 10-fold less active in normal fibroblast cells than in tumor cells.

The single IV dose MTD in CD-1 mice was less than 30 mg/kg for Taxol, 175 mg/kg for FID-007 and >180 mg/kg for Abraxane. Multiple dose MTD of FID-007 was 100 mg/kg for CD-1 mice and 30 mg/kg for Scid mice. FID-007 exhibited significantly better efficacy in tumor growth control compared to Taxol and comparative or better efficacy than Abraxane with the three human cancer cell lines in mice. Representative results are shown in Figures 1-5.

Conclusion: Encapsulation with PEOX-based branched polymers reduced the toxicity and significantly improved the efficacy of paclitaxel in controlling tumor growth in vitro and in vivo.

Keywords *Nanoscience, genomics, computational informatics genetics (primary keyword)*
General issues

Abstract Topics General issues
Nanoscience, genomics, genetics

The abstarct `Improvement of Paclitaxelâ€™s Antineoplastic Efficacy in vivo Using PEOX Polymer Nanoencapsulation`

book's publications additonal Information summary

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Keywords: Nanoencapsulated drug, paclitaxel, tumor reduction, reduced toxicity

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The cytotoxicity of FID-007 was tested on a normal human dermal fibroblast cell line and cell lines for human lung (A549), triple negative breast (MDA-MB-231) and ovarian (OV-90) cancers. Commercially available paclitaxel drugs, Taxol and Abraxane, were similarly tested. The single maximum tolerated dose (MTD) of FID-007, Taxol and Abraxane were determined in vivo in CD-1 mice. The multiple dose MTD for FID-007 was evaluated with CD-1 and Scid mice. The efficacy of FID-007 in controlling tumor growth was compared to the other drugs in vivo using xenograft tumor models in Scid mice with the aforementioned human cancer cell lines (20 mice per cancer). Dosages for the drugs were equitoxic based on previous MTD studies. Saline and polymer (NanoCarrier 001B) were used as negative control treatments for the xenograft studies.

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Conclusion: Encapsulation with PEOX-based branched polymers reduced the toxicity and significantly improved the efficacy of paclitaxel in controlling tumor growth in vitro and in vivo.

Educational Objectives: Explain nanoencapsulation, present data demonstrating reduced toxicity and increased efficacy in tumor reduction, discuss follow-on clinical trials

Educational Objectives Explain nanoencapsulation, present data demonstrating reduced toxicity and increased efficacy in tumor reduction, discuss follow-on clinical trials

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

A Fully-Integrated Wireless System for Intracranial Direct Cortical Stimulation and Real-Time Electrocorticography Data Trasmission

Pantaleo Romanelli - **AB Medica**

Antonino Paris - **Aethra**

Stefano Marchetti - **Aethra**

Paolo Cristiani - **Aethra**

Marco Ciavarro - **Department of Human and General Physiology and Department of Pharmacy and Biotechnology University of Bologna**

Cosimo Puttilli - **AB Medica**

Contact: Pantaleo Romanelli (radiosurgery2000@yahoo.com)

Abstract: A Fully-Integrated Wireless System for Intracranial Direct Cortical Stimulation and Real-Time Electrocorticography Data Trasmission

Romanelli, P. 1; Paris, A.2; Marchetti, S.2; Cristiani, P.2.; Ciavarro, M.3, Puttilli, C.1. 1 â€“ R&D , AB Medica - Italy 2 Â¬ Aethra - Italy 3 â€“ University of Bologna, Italy

Introduction: Current techniques of cortical recording are limited by the need to transfer the signal through wires. We have developed and tested a fully implantable, externally rechargeable wireless device (ECOGIW-16E) providing a highly innovative medium for the advancement of BCI and invasive monitoring for epilepsy. Materials and methods: ECOGIW-16E is a compact device made by a single sheet of flexible polyimide support that integrates the grid of 16 electrodes, covered by a 300 Âµm layer of platinum, and an RF antenna. The casing in PEEK include a microcontroller and the transceiver module for implantable medical applications within MICS band. The device includes a triaxial accelerometer, a stimulus generator, a sensor of temperature/load current and a Li-Ion battery (3,6V 350mA/h ISO 13485). The entire device is covered with a parilene coating of 7 Âµm, to ensure maximum biocompatibility. The interface consumes 58mA (16CH @ 500SPS + TX_RF), 30mA (16CH @ 500SPS) and 7mA in standby. A dedicated cage equipped with RF coils was developed to allow seamless recharge of the device. ECOGIW-16E was implanted in a male macaque monkey (Macaca fascicularis, 6.95 kg). The animal was anesthetized and secured to a stereotaxic frame. Craniotomy was performed , placing the 16 contacts grid over the left motor cortex (M1) . The case was fixed above the skull and the wound was washed and closed.

Results: The ECoG signals of sixteen electrodes was recorded with a 512 Hz sampling rate. The frequency spectrum shows the characteristic decrease in amplitude at higher frequencies and also that there are all the characteristic frequency components of an ECoG signal (Fig 2B). We performed bipolar stimulation by pulses of rectangular shapes with anodal monophasic current pulses of 0.5 ms duration. This stimulation technique consists of a train of 5 pulses delivered at 1 Hz. Stimulus intensity was gradually increased in increments of 0.5 mA, starting at 1 mA, up to a maximum of 3 mA. During cortical stimulation of the motor cortex, movements of distinct portions of the right arm were observed with a stimulation intensity of 2 mA. Stimulation with electrode number seven and nine elicited movements of the proximal portion of the right arm, whereas the stimulation with electrodes number one generated movements of the distal portion of the right arm.

Conclusions ECOGIW-16E is a fully implantable,externally rechargeable device providing wireless real time ECoG recording and brain mapping through direct cortical stimulation. ECOGIW-16E provides much longer recording times as compared to those offered by current technology . Research and clinical applications include BCI and invasive monitoring of epilepsy. This fully-integrated system lends itself to be optimized in view of use in a closed-loop systems of electrical stimulation for aborting or blocking promptly detected seizure activity in epilepsy patients.

Keywords	*Neural Prosthesis & Robotics (primary keyword)* Neurophysiology (EEG, MEG, ?) Brain mapping/functional imaging for rehab medicine and PTSD Minimally invasive therapy
Abstract Topics	Neurophysiology (EEG, MEG,â€¦) Neural Prosthesis & Robotics Brain mapping/functional imaging for rehab medicine Minimally invasive therapy Basic Neuroscience
The abstarct book's publications additonal Information summary	
Educational Objectives	Wireless electrocorticographic monitoring and brain stimulation; Restore lost motor functions in neurological patients (BCI); ECoG signal transmission in real time through the Web.
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Molecular Mapping of Spreading Neurodegeneration as a Novel Strategy for Treatment of Neurodegenerative Disorders

Giulio Maria Pasinetti - Mount Sinai School of Medicine

Contact: Giulio Pasinetti (giulio.pasinetti@mssm.edu)

Abstract: Introduction: Abnormal folding of tau protein leads to the generation of paired helical filaments (PHFs) and neurofibrillary tangles, a key neuropathological feature in Alzheimerâ€™s disease (AD) and tauopathies. The specific anatomical pattern of pathological changes developing in the brain suggests that once tau pathology is initiated, it propagates between neighboring neuronal cells, possibly spreading along axonal networks. In other words, misfolded aggregated tau protein released by degenerating neurons can mediate and spread toxicity to neighboring cells.

Methods: We used brain molecular mapping to study whether PHFs could be taken up by cells and promote the propagation of tau pathology. Neuronal and non-neuronal cells overexpressing green-fluorescent protein tagged tau (GFP-Tau) were treated with isolated fractions of human AD-derived PHFs for 24h.

Results: We found through mapping that cells internalized PHFs through an endocytic mechanism and developed intracellular GFP-Tau aggregates with attributes of aggresomes. This was made particularly evident by the perinuclear localization of aggregates and the re-distribution of vimentin intermediate filament networks and retrograde motor protein dynein. Furthermore, the content of Sarcosyl-insoluble tau, a measure of abnormal tau aggregation, increased 3-fold in PHF-treated cells. Exosome related mechanisms did not appear to be involved in the release of GFP-Tau from untreated cells.

Conclusions: Brain mapping of the spreading of pathological tau aggregation will help therapeutic applications. The evidence that cells can internalize PHFs leading to the formation of aggresome-like bodies opens new therapeutic avenues to prevent the propagation and spreading of tau pathology. Ongoing imaging studies will help the visualization of neuropathological features.

Keywords *Molecular and cellular imaging (primary keyword)*

Abstract Topics Basic Neuroscience

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Title: Molecular Mapping of Spreading Neurodegeneration as a Novel Strategy for Treatment of Neurodegenerative Disorders

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Key Words: tau protein; aggresome; exosome; brain mapping

Educational Objectives 1) This talk will discuss how molecular tagging will help to monitor regions of susceptibility in diseases characterized by a mosaic of overlapping brain areas; 2) This talk will discuss the characterization of novel drugs that may help to identify preferential imaging pathways associated to neurodegeneration; 3) This research has impacted the field by providing new therapeutic avenues to prevent the propagation and spreading of tau pathology.

Files *Submission exists, but was not archived (suffix)*

Reviews

Preoperative nTMS generated motor maps correlate well with Direct cortical stimulation â€“ initial experience with 14 patients

Roger Rotta - University of Texas MD Anderson Cancer Center
Nicholas Levine - University of Texas MD Anderson Cancer Center
Ganesh Rao - University of Texas MD Anderson Cancer Center
Sudhakar Tummala - University of Texas MD Anderson Cancer Center
Catherine Vitela - University of Texas MD Anderson Cancer Center
Raymond Sawaya - University of Texas MD Anderson Cancer Center
Sujit Prabhu - University of Texas MD Anderson Cancer Center

Contact: Roger Rotta (rrotta@mdanderson.org)

Abstract: Introduction: The management of brain tumors in and around the eloquent areas presents a specific challenge to the neurosurgeon. The goals are to resect the lesion as much as possible, preserving the patientâ€™s existing neurological function. Functional information about the cortical and subcortical areas at risk is crucial for the avoidance of neurological deficits after tumor surgery. Although direct cortical stimulation (DCS), remains the gold standard for generating maps of motor system, non-invasive methods of motor mapping are becoming increasingly accurate and useful. Methods: We describe our initial experience with 14 patients with brain tumors located in or close to eloquent areas. All cases were performed using navigated transcranial magnetical stimulation (nTMS) and intraoperative direct cortical stimulation (DCS). Results: Of all 14 patients 36% were GBMs, 36% anaplastic gliomas, 14.2% oligodendrogliomas, 7.1% LGGs and 7% metastasis. In 92.8% of patients a positive nTMS response was achieved either in the upper or lower limb, correlating well with those generated by DCS. There were no adverse events to patients during the stimulation. The mean time for generating a preoperative nTMS map was 20 minutes. Conclusion: Navigated transcranial magnetical stimulation (nTMS) can be safely used in the presurgical mapping of the motor cortex involving either the upper or lower extremity and the results correlate well with intraoperative direct cortical stimulation (DCS).

Keywords
Transcranial Magnetic Stimulation (primary keyword)
Intraoperative Surgical Planning
Neurophysiology (EEG, MEG, ?)
Functional brain mapping (fMRI, PET?)

Abstract Topics
Intraoperative Surgical Planning
Functional brain mapping (fMRI, PETâ€¦)
Transcranial Magnetic Stimulation
Basic Neuroscience

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Abstract
Title: Preoperative nTMS generated motor maps correlate well with Direct cortical stimulation â€“ initial experience with 14 patients
Author:Roger Rotta
Co-authors:Nicholas Levine, Ganesh Rao,Sudhakar Tummala,Catherine Vitela, Raymond Sawaya,Sujit Prabhu
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Key words: nTMS, intraoperative DCS, brain mapping
Introduction:
The management of brain tumors in and around the eloquent areas presents a specific challenge to the neurosurgeon. The goals are to resect the lesion as much as possible, preserving the patientâ€™s existing neurological function. Functional information about the cortical and subcortical areas at risk is crucial for the avoidance of neurological

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Conclusion:
Navigated transcranial magnetical stimulation (nTMS) can be safely used in the presurgical mapping of the motor cortex involving either the upper or lower extremity and the results correlate well with intraoperative direct cortical stimulation (DCS).

We the authors confirm that the work presented in this manuscript is original, has not been published before and is not currently being considered for publication elsewhere. All authors have seen and approved the abstract.

Educational Objectives Presurgical mapping eloquent parts of brain before tumor resection; Prevent new neurological deficits in brain tumor surgery; Non-invasive methods of motor mapping

Files *Submission exists, but was not archived (suffix)*

Reviews

The Genomic Response to Traumatic Brain Injury

Robert Lipsky - Inova Health System

Contact: Robert Lipsky (robert.lipsky@inova.org)

Abstract: Traumatic brain injury (TBI) has acute and chronic outcomes for those who survive. Our understanding of the how genomic responses intersect with these processes is just beginning to take shape. Management of the TBI patient will take a multidisciplinary approach, incorporating gene-based, protein, and metabolic profiling into a clinical framework, drawing from the specialties of neurosurgery, neuroradiology, neurology, and psychiatry in order to advance our ability to more effectively treat brain injury and to predict outcome. From a molecular perspective I will examine possible mechanisms of response and methodological issues in correlating how genetic and epigenetic mechanisms may modify outcomes in TBI patient populations. Because study population sizes have been generally limited, I will discuss results on genes that have been the focus of independent studies. I also present a justification for testing more speculative candidate genes in recovery from TBI, to outline the importance of prioritizing functional variants.

Keywords *Nanoscience, genomics, computational informatics genetics (primary keyword)*

Abstract Topics Nanoscience, genomics, genetics

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The Genomic Response to Traumatic Brain Injury

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Email: robert.lipsky@inova.org
Key words: traumatic brain injury, genomics, epigenetics, proteomics, biomarker

Introduction: Traumatic brain injury (TBI) has acute and chronic outcomes for those who survive. Our understanding of the how genomic responses intersect with these processes is just beginning to take shape. Management of the TBI patient will take a multidisciplinary approach, incorporating gene-based, protein, and metabolic profiling into a clinical framework, drawing from the specialties of neurosurgery, neuroradiology, neurology, and psychiatry in order to advance our ability to more effectively treat brain injury and to predict outcome.
Methods: A review of human studies using the candidate gene association approach. Population-based samples of affected and unaffected individuals (case-control study) and within case comparisons were performed. A function-guided approach was used to test a hypothesis to predict the relationship between the candidate gene and the phenotype.
Results: Of all studies performed to date, functional variation of apolipoprotein E (apo E) can most influence overall patient outcome, as well as cognitive and behavioral functions following TBI.

Educational Objectives 1. Describe function guided genetic association studies. 2. Describe limitations in methodology. 3. Provide guidelines for future studies

Files *Submission exists, but was not archived (suffix)*

Reviews

QUALITY OF LIFE IN POSTTRAUMATIC STRESS DISORDER

Waguih William IsHak - Cedars-Sinai Medical Center and UCLA
Konstantin Balayan - Cedars-Sinai Medical Center
Gabriel Tobia - Cedars-Sinai Medical Center

Contact: Waguih IsHak (waguih.ishak@cshs.org)

Abstract: INTRODUCTION:Quality of life (QOL) refers to an individual's overall sense of wellbeing and subjective physical, psychological, and social functioning. QOL is significantly affected in patients with Post-Traumatic Stress Disorder (PTSD). This is a systematic review of the relevant literature on QOL impairment in PTSD subgroups and the impact of treatment interventions on QOL.

METHODS: A systematic database search from 1970-2011 was conducted using Medline, PsycINFO, and Cochrane Database of Systematic Reviews using the key words: â€œPTSDâ€, â€œpost traumatic stress disorderâ€, â€œstress disordersâ€, â€œquality of lifeâ€, â€œQOLâ€, and â€œhealth-related quality of life.â€ Two reviewers applied pre-defined selection criteria independently and reached consensus on the inclusion of 22 studies that focused on QOL in PTSD.

RESULTS: The findings revealed that QOL is gravely impaired in PTSD subgroups, such as veterans, refugees, survivors of terrorist attacks, natural disaster survivors, rescue personnel, and survivors of violence. Research shows that PTSD is an independent predictor of QOL impairment, and that various psychotherapeutic and pharmacological treatment modalities have a positive effect on QOL in PTSD. However, their ability to improve QOL to community norm levels is unclear.

CONCLUSIONS: This review also highlights the importance of including QOL as an essential outcome measure in PTSD clinical and research work.

Keywords *Psychiatry (PTSD,?) (primary keyword)*

Abstract Topics Psychiatry (PTSD,â€¦)

The abstarct book's publications additonal Information summary

QUALITY OF LIFE IN POSTTRAUMATIC STRESS DISORDER
Waguih William IsHak, MD, FAPA, Konstantin Balayan, M.D., and Gabriel Tobia, M.D. (Cedars-Sinai Medical Center)

INTRODUCTION:Quality of life (QOL) refers to an individual's overall sense of wellbeing and subjective physical, psychological, and social functioning. QOL is significantly affected in patients with Post-Traumatic Stress Disorder (PTSD). This is a systematic review of the relevant literature on QOL impairment in PTSD subgroups and the impact of treatment interventions on QOL.

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CONCLUSIONS: This review also highlights the importance of including QOL as an essential outcome measure in PTSD clinical and research work.

The work is not being submitted for publication or presentation elsewhere.

Educational Objectives 1. Appreciate the magnitude of QOL impairments in PTSD. 2. Understand the impact of PTSD treatment on QOL. 3. Learn about various psychotherapeutic and pharmacological treatments that could improve QOL in PTSD.

Files *Submission exists, but was not archived (suffix)*

Reviews

Treatment Effects of Onion (Allium cepa) and Ginger (Zingiber officinale) on Sexual Behavior of Rat after Inducing an Antiepileptic Drug (lamotrigine)

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Alireza Farnam - Department Clinical Psychiatry Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

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Abstract: Objective: The aim of the present study was to evaluate the beneficial degree of sexual behavior in male rats after inducement of onion and ginger in lamotrigine receiving groups. Material and Methods: Wistar rats (n=70) (male=35, female=35) were allocated so that males were divided into seven groups: control (n=5) and test groups (n=35). Control group used normal Saline (3 cc for each rat). Lamotrigine group were given Lamotrigine (10 mg/kg). Onion group used onion fresh juice (3 cc for each rat/daily). Ginger group was fed on ginger powder (100 mg/kg/daily). Onion & Lamotrigine group used both onion juice (3 cc fresh onion juice for each rat/day) and Lamotrigine (10 mg/kg). Ginger & Lamotrigine group used both ginger powder (100 mg/kg/day) and Lamotrigine (10 mg/kg/day). Onion, ginger & Lamortigine group jointly used ginger powder (100 mg/kg/day) and onion juice (3 cc juice for each rat) and Lamotrigine (10 mg/kg/day). All groups were given treatments orally. For sexual behaviors, Estradiolbenzoate (50 microgram) and 6 hours before test (500 microgram) progesterone was injected to the female rats subcutaneously. Then rats were viewed for erection, ejaculation and cup.

Results: There was maximum Serum total testosterone level in the onion group, there was maximum malondialdehyde (MDA) in the Lamotrigine group and there was maximum total antioxidant capacity in both the onion group and ginger group ($p<0.05$).

Conclusion: Results revealed that administration of (100 mg/kg/day) of ginger powder, and freshly prepared onion juice (3 cc for each rat), significantly lowered the adverse effects of lamotrigine, and can have beneficial effects on sexual behavior in male rat.

Keywords

General issues (primary keyword)
Histopathology

Abstract Topics

General issues
Anatomy
Neurophysiology (EEG, MEG,â€¦)

	Histopathology Basic Neuroscience
The abstarct book's publications additonal Information summary	
Educational Objectives	Anatomy-Psychiatry-Histopathology
Files	*Submission exists, but was not archived (suffix)*

Reviews

An Electrical Analog Model of Intracranial Pressure

Monica D. Okon - The Ohio State University
Steven E. Katz, MD - The Ohio State University
Cynthia J. Roberts, PhD - The Ohio State Unversity
Robert H. Small, MD PE - The Ohio State University

Contact: Monica Okon (okon.3@osu.edu)

Abstract: An Electrical Analog Model of Intracranial Pressure

Monica Okon 1, Steven E Katz, MD 2 , Cynthia J Roberts, PhD 1,2, and Robert H Small MD PE 1,3

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Introduction

According to the Intracranial Hypertension Foundation, one out of 100,000 people suffer from chronic intracranial hypertension (IIH).1 The incidence is higher for overweight women (20 out of 100,000).1 With chronic IIH, these patients have a large number of repeat lumbar punctures. Developing a non-invasive method of estimating intracranial pressure provides a new option for patients as well as relieves the burden of lumbar punctures on the health care system. The objective of the current project is to model the dynamics of intracranial pressure (ICP) change based on clinical data as a first step toward a more comprehensive model.

Methods

An electrical analog model was implemented in TopSPICE (Penzar Development, Canoga Park, CA) to represent cerebral blood flow and cerebral spinal fluid (CSF) pressure. This model was based on a model by Pasley et al.2 The driving waveform was generated from the measured blood pressure and heart rate of the subject. The parameters for the circuit were taken from literature values and then modified iteratively based on measured clinical parameters. A node analysis was conducted to determine intracranial pressure (ICP). Clinical CSF pressure waveforms were collected via an electronic transducer during a lumbar puncture, and CSF pressure was used as a surrogate for ICP. The clinical data from two subjects (one with high ICP and one with normal ICP) were used to validate the model.

Results

The clinically obtained ICP measurements validated the proposed model. Each subjectâ€™s generated blood pressure waveform was entered into the model and an ICP waveform was the output, as seen in the attached figure.

Conclusions

The proposed model has been validated using clinical data. This model can provide a foundation for more comprehensive investigations of cerebral hemo- and hydrodynamics.

1. "Incidence of Chronic IH." Intracranial Hypertension Research Foundation. The Intracranial Hypertension Research Foundation. Web.Mar. 2013 2. Pasley, R. L., Leffler, C. W., & Daley, M. L. (2003). Modeling Modulation of Intracranial Pressure by Variation of Cerebral Venous Resistance Induced by Ventilation. Annals of Biomedical Engineering, 31(10), 1238-1245.

Keywords	*4D, Neuro-mathematics and bio-informatics (primary keyword)*
Abstract Topics	4D, Neuro-mathematics and bio-informatics
The abstarct book's publications additonal Information summary	Title: An Electrical Analog Model of Intracranial Pressure Authors: Monica Okon 1, Steven E Katz, MD 2 , Cynthia J Roberts, PhD 1,2 , and Robert H Small MD PE 1,3 Author Affiliations: 1. Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio 43210 2. Department of Ophthalmology, The Ohio State University, Columbus, Ohio 43210 3. Department of Anesthesiology, The Ohio State University, Columbus, Ohio 43210 Contact Information: Monica Okon: 211 East Patterson,Columbus, Ohio, 43202 email: okon.3@osu.edu Keywords: intracranial pressure, IIH, TopSPICE, cerebral spinal fluid pressure, electrical analog model, intracranial hypertension
Educational Objectives	1. To evaluate an electrical analog model for the advancement of applications to more comprehensive models 2.To establish the model with human clinical data 3. To establish a first step to a non-invasive method of measuring intracranial pressure
Files	*Submission exists, but was not archived (suffix .pdf)*

Reviews

Acupoint Tapping in the Treatment of Post-Traumatic Stress in Veterans.

Olli Toukolehto - U.S. Army

Contact: Olli Toukolehto (olli.toukolehto@yahoo.com)

Abstract:

INTRODUCTION: A decade of war has resulted in thousands of military veterans with symptoms of post-traumatic stress (PTS). According to the Department of Veterans Affairs (VA) and the Department of Defense (DoD) Clinical Guideline for the Management of Post-Traumatic Stress, trauma-focused psychotherapies and Stress Inoculation Training are important non-pharmacological treatment interventions. The core components of these interventions include exposure, cognitive restructuring, psychoeducation, and relaxation and stress modulation techniques. Some interventions have been manualized and gained popularity, but the essential concept is that their therapeutic effect is based on these core components. In the context of treatment resistant PTS and barriers to care in the military, there exists a need for the development of alternative treatment approaches that build on these core components. "Acupoint tapping" is an alternative approach that attempts to meet this need and is the focus of this review.

METHODS: Brain imaging in acupuncture research has demonstrated that the stimulation of acupoints with acupuncture needles alters the activity of the human limbic system. Specifically, an inhibitory effect on the amygdala has been observed. It has been hypothesized that PTS therapies that utilize acupoint stimulation may reduce the negative emotional intensity experienced by the patient during treatment (presumably via the inhibition of the amygdala and possibly altering other brain areas). The observation that non-invasive electroacupuncture also has this effect is supportive of the possibility that acupoint stimulation can be achieved without the use of traditional acupuncture needles. If this finding can be generalized to stimulating acupoints with one's own fingertips, it is possible that acupoint tapping could have clinical utility in the treatment of PTS.

RESULTS: A literature review reveals preliminary findings that support this hypothesis: one recent randomized and controlled trial on PTSD demonstrated that acupoint tapping (with exposure and cognitive elements) had a strong and equal therapeutic effect when compared to EMDR. Another wait-list controlled trial involving veterans with PTSD demonstrated that 4 out of 5 veterans had subclinical symptoms (defined as a PCL-M score <50) after six hours of acupoint tapping. However, it should be noted that there is not enough evidence to currently support the use of acupoint tapping techniques outside of research settings.

CONCLUSIONS: If future research confirms these findings and acupoint tapping is identified as having an independent therapeutic effect, it could be integrated into pre-existing PTS therapies or possibly serve as a standalone intervention. Also, because it does not require technical supplies, is non-invasive, and can be self-administered, it could potentially increase resiliency and be preventive in nature. Further research in both of these areas is warranted.

Keywords *Psychiatry (PTSD,?) (primary keyword)*
Functional brain mapping (fMRI, PET?)
Minimally invasive therapy

Abstract Topics
Functional brain mapping (fMRI, PETâ€¦)
Psychiatry (PTSD,â€¦)
Minimally invasive therapy

The abstarct book's

TITLE:
Acupoint Tapping in the Treatment of Post-Traumatic Stress in Veterans.

publications additonal Information summary

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Key words: Acupoint tapping, PTSD, Emotional Freedom Techniques, EFT.

ABSTRACT

INTRODUCTION:
A decade of war has resulted in thousands of military veterans with symptoms of post-traumatic stress (PTS). According to the Department of Veterans Affairs (VA) and the Department of Defense (DoD) Clinical Guideline for the Management of Post-Traumatic Stress, trauma-focused psychotherapies and Stress Inoculation Training are important non-pharmacological treatment interventions. The core components of these interventions include exposure, cognitive restructuring, psychoeducation, and relaxation and stress modulation techniques. Some interventions have been manualized and gained popularity, but the essential concept is that their therapeutic effect is based on these core components. In the context of treatment resistant PTS and barriers to care in the military, there exists a need for the development of alternative treatment approaches that build on these core components. "Acupoint tapping" is an alternative approach that attempts to meet this need and is the focus of this review.

METHODS:
Brain imaging in acupuncture research has demonstrated that the stimulation of acupoints with acupuncture needles alters the activity of the human limbic system. Specifically, an inhibitory effect on the amygdala has been observed. It has been hypothesized that PTS therapies that utilize acupoint stimulation may reduce the negative emotional intensity experienced by the patient during treatment (presumably via the inhibition of the amygdala and possibly altering other brain areas). The observation that non-invasive electroacupuncture also has this effect is supportive of the possibility that acupoint stimulation can be achieved without the use of traditional acupuncture needles. If this finding can be generalized to stimulating acupoints with one's own fingertips, it is possible that acupoint tapping could have clinical utility in the treatment of PTS.

RESULTS:
A literature review reveals preliminary findings that support this hypothesis: one recent randomized and controlled trial on PTSD demonstrated that acupoint tapping (with exposure and cognitive elements) had a strong and equal therapeutic effect when compared to EMDR. Another wait-list controlled trial involving veterans with PTSD demonstrated that 4 out of 5 veterans had subclinical symptoms (defined as a PCL-M score <50) after six hours of acupoint tapping. However, it should be noted that there is not enough evidence to currently support the use of acupoint tapping techniques outside of research settings.

CONCLUSIONS:
If future research confirms these findings and acupoint tapping is identified as having an independent therapeutic effect, it could be integrated into pre-existing PTS therapies or possibly serve as a standalone intervention. Also, because it does not require technical supplies, is non-invasive, and can be self-administered, it could potentially increase resiliency and be preventive in nature. Further research in both of these areas is warranted.

Educational Objectives 1. Introduction to acupoint tapping in the treatment of trauma.2, Review of evidence for the use of acupoint tapping in therapy. 3. The impact that a non-invasive self-care technique could have on the psychological wellbeing of veterans.

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Integration of Neuronavigation, Neuromonitoring Electro-Physilogical Recording In Epilepsy Surgery

Qinghang Li - Neurological Surgery Department, Wayne State University
Sandeep Mittal - Neurological Surgery Department, Wayne State University
Murali Guthikonda - Neurological Surgery Department, Wayne State

Contact: Qinghang Li (qli@med.wayne.edu)

Abstract: The management of medically intractable epilepsy poses both a valuable therapeutic opportunity and a formidable technical challenge for neurosurgeons. Recent decades have produced significant developments in the capabilities and availability of adjunctive tools in epilepsy surgery. In particular, image-based neuronavigation, electrophysiological neuromonitoring and recording represent versatile and informative modalities that can assist a surgeon in performing safe and effective resections. In this paper, the authors present their experiments of last 6 years.

Methods: From April 2007 to March 2013, 114 surgeries were performed. This group of patients (63 males and 51 females) has a median age of 37 (range 17-78 years). There were 44 cases that finished two-stage surgeries. Stage 1 of surgery was designed to place two kinds of electrodes into focus area. The surface electrode is placed on the brain surface to record the cortical electrophysiological changes. The deep electrode is placed into special area of brain to record electrophysiological changes in related area. If the epileptic focus found, Stage 2 surgery are designed to resect the epileptic focus. Image-guided neuronavigation uses preoperative, intraoperative, or real-time imaging to allow the surgeon to understand spatial relationships within the brain that are not visible by line-of-sight. Accurate localization of eloquent brain regions is of critical importance during resections of nearby epileptogenic foci or lesions. Integrating preoperative image-based neuronavigation with functional imaging modalities, such as FDG-PET, fMR imaging, and MEG, can provide a wealth of information allowing preservation of eloquent brain areas and more aggressive resections without increased morbidity. Magnetoencephalography in conjunction with anatomical imaging is a powerful technique that permits the visualization of epileptic spikes within the brain. In epilepsy cases in which no offending anatomically identifiable lesion can be visualized and in which the ictal onset or irritative zone cannot be localized using conventional means, MEG can identify the anatomical location of epileptogenic spike clusters and permit an image-guided focal resection of this region. Results: Among 66 patients, 44 were performed 2 stage of surgery or more, 22 patients were performed only 1 stage which is recording and resection in one time. Neuronavigation, Neuromonitoring Electro-Physilogical

Recording were used in all cases. Conclusions: As the development of new technologies in medical images, neuronavigation, Neuromonitoring, Electro-Physilogical Recording, the integration of these new technologies with traditional epilepsy surgery will greatly improve the surgical efficiency and results

Keywords	*Functional brain mapping (fMRI, PET?) (primary keyword)*
Abstract Topics	Functional brain mapping (fMRI, PETâ€¦) Multimodality imaging
The abstarct book's publications additonal Information summary	
Educational Objectives	demonstrate modern image combined with neuronavigation technology.
Files	*Submission exists, but was not archived (suffix)*

Reviews

fMRI-Based Validation of Penfield Motor Homunculus

Gabe Oland - School of Biological and Health Systems Engineering, Arizona State University
David Frakes - School of Biological and Health Systems Engineering, Arizona State University
Peter Nakaji - Barrow Neurological Associates
Gurpreet Gandhoke - University of Pittsburgh Medical Center
Leslie Baxter - Barrow Neurological Institute

Contact: Gabe Oland (goland@asu.edu)

Abstract: Introduction: This study used positive BOLD fMRI to quantitatively determine motor function volumes and spatial relationships in order to validate and/or improve upon Wilder Penfieldâ€™s original qualitative representation of the motor homunculus from the 1950s, and to determine whether the MRI-based model can be replicated among different individuals.

Methods: Ten cognitively intact subjects underwent functional MRI using a 3 Tesla GE scanner with an 8-channel head coil. Each subject performed the same block-design â€œon-offâ€ exercise for 4 different right-sided motor tasks: toe, finger, eyebrow, and tongue movement. Blocks were 12-seconds movement/18-seconds rest, total scan time 3 minutes. Echo planar imaging (EPI) scans were obtained along with a high-resolution structural 3-D T1 sagittal image for each participant. Using SPM8, EPI scans were realigned, coregistered, and resliced to the T1 and smoothed to 2 mm^3. The difference beta maps representing â€œmotion vs. restâ€ were imported to Mimics by Materialise for segmentation using a region grow operation (50% cutoff) initiated at the beta value local maximum. The masks were exported to GeoMagic as binary STLs to record their centroid coordinates.

Results: Task volumes normalized to the Montreal Neurological Institute (MNI) coordinate space were: 1013 mm^3 for Toe, 1347 mm^3 for Finger, 832 mm^3 for Eyebrow, and 1714 mm^3 for Tongue.

Mean distances between task volume centroids in MNI space were: 37.2 mm between Toe and Finger, 53.3 mm between Toe and Eyebrow, 72.8 mm between Toe and Tongue, 17.4 mm between Finger and Eyebrow, 38.8 mm between Finger and Tongue, and 24.1 mm between Eyebrow and Tongue.

Conclusions: The mean centroid coordinates of the tasks followed Penfield's original superior-to-inferior pattern. The task separation distances in both coordinate spaces agree with Penfieldâ€™s findings, as the tasks that are farther apart on the diagram have proportionally greater separation distances, and vice versa.

However, the task activation sizes varied widely both within individuals for different tasks as well as between individuals for the same task. There does not appear to be a ratio of size comparison between tasks (for instance, finger:eyebrow or toe:finger:eyebrow:tongue) that is consistent for all individuals, as seems to be implied by the length of the bold black lines beneath relative body parts in the original homunculus.

The Penfield motor homunculus is classically understood to show not only the spatial distribution of responses, but also the relative sizes of various tasks. The fact that no volume size ratios were found to consistently describe any two particular tasks implies that this understanding based on standardized motor function volumes may be unsupported. It remains to be seen whether a different activation region segmentation methodology could lead to more consistent volume comparisons between tasks.

The Penfield diagram was supported in terms of the superior-to-inferior distribution of tasks along the precentral gyrus, as well as in terms of mean task volume sizes (finger and tongue mean volumes are larger than toe and eyebrow). Additionally, the three-dimensional representations allow for a more intuitive visualization of the mean task volumes in physical space than do standard two-dimensional projections.

Keywords *Functional brain mapping (fMRI, PET?) (primary keyword)*
Anatomy
High-field and low-field magnetic resonance

Abstract Topics

Anatomy
Functional brain mapping (fMRI, PETâ€¦)
High-field and low-field magnetic resonance
Brain mapping/functional imaging for rehab medicine
Basic Neuroscience

The abstarct book's publications additonal Information summary

fMRI-Based Validation of Penfield Motor Homunculus

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(2) David Frakes, School of Biological and Health Systems Engineering, Arizona State University, School of Electrical, Computer, and Energy Engineering, Arizona State University, 550 E. Orange St., ISTB1 281F, Tempe, AZ 85287
(3) Peter Nakaji, Barrow Neurological Associates, peter.nakaji@bnaneuro.net, 2910 N 3rd Ave Phoenix, AZ 85013
(4) Gurpreet Gandhoke, Children's Memorial Hospital, gurpreet.gandhoke@gmail.com, 2300 N Childrens Plz Suite 28, Chicago, IL 60614
(5) Leslie Baxter, Barrow Neurological Institute, 350 W Thomas Rd, Phoenix, AZ 85013

Keywords: Neurology, fMRI, somatotopy, motor cortex, homunculus

Introduction:
The motor homunculus as proposed by Canadian neuroscientist Wilder Penfield in the 1950s has been widely accepted as the standard model for the relative spatial representation of the functionality of the motor cortex. This study used positive BOLD fMRI to quantitatively determine motor function volumes and spatial relationships in order to validate and/or improve upon Penfieldâ€™s original qualitative estimations, and to determine whether the MRI-based model can be replicated among different individuals.

Methods:
Ten cognitively intact subjects underwent functional MRI using a 3 Tesla GE scanner with an 8-channel head coil. Each subject performed the same block-design â€œon-offâ€ exercise for 4 different right-sided motor tasks: toe, finger, eyebrow, and tongue movement. Blocks were 12-seconds movement/18-seconds rest, with a total scan time of 3 minutes. Echo planar imaging (EPI) scan parameters were TE = 25 ms, TR = 3000 ms, flip angle = 80Â°, FOV 24mm, and in-plane resolution 64x64, with 4-mm-thick slices covering the entire brain, along with a high-resolution structural 3-D T1 sagittal image for each participant. Using SPM8, EPI scans were realigned, coregistered, and resliced to the T1 and smoothed to 2 mm^3. The difference beta maps representing â€œmotion vs. restâ€ were imported to Mimics by Materialise for segmentation using a region grow operation (50% cutoff) initiated at the beta value local maximum. The masks were exported to GeoMagic as binary STLs to record their centroid coordinates.

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Conclusions:
The mean centroid coordinates of the tasks followed Penfield's original superior-to-inferior pattern. The task separation distances in both coordinate spaces agree with Penfieldâ€™s findings, as the tasks that are farther apart on the diagram have proportionally greater separation distances, and vice versa.

However, the task activation sizes varied widely both within individuals for different tasks as well as between individuals for the same task. There does not appear to be a ratio of size comparison between tasks (for instance, finger:eyebrow or toe:finger:eyebrow:tongue) that is consistent for all individuals, as seems to be implied by the length of the bold black lines beneath relative body parts in the original Penfield motor homunculus.

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volume size ratios were found to consistently describe any two particular tasks implies that this understanding based on standardized motor function volumes may be unsupported. It remains to be seen whether a different activation region segmentation methodology could lead to more consistent volume comparisons between tasks.

The Penfield diagram was supported in terms of the superior-to-inferior distribution of tasks along the precentral gyrus, as well as in terms of mean task volume sizes (finger and tongue mean volumes are larger than toe and eyebrow). Additionally, three-dimensional representations allow for a more intuitive visualization of the mean task volumes in physical space than do standard two-dimensional projections.

References:
[1] Penfield, W., and Rasmussen, T. The Cerebral Cortex of Man: A Clinical Study of Localization of Function. New York: Macmillan, 1950. Print.

This work has not been submitted for publication elsewhere.

Educational Objectives Analyzing Penfield motor homunculus diagram, improving functional map of motor cortex, improving pre-operative evaluations for neurosurgical patients

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews

Real time Open MRI Guidance for Percutaneous Nerve Decompression

Aaron G. Filler, MD, PhD, FRCS - Institute for Nerve Medicine

Contact: Aaron Filler (afiller@nervemed.com)

Abstract: Introduction

Real time Open MRI provides an opportunity for surgical manipulation of tissue on a percutaneous basis. However, it has never been possible to carry out actual decompression of nerve entrapments in this fashion. Interventional MRI has been used to carry out diagnostic and therapeutic treatment of nerve entrapments in large scale formal outcome trials involving anti-inflammatory or muscle spasm reduction methods. In this case, the images revealed that the serial administration of the treatment agents resulted in relieving the mechanical entrapment. This methodology provides a model for further study of the use of MRI for percutaneous minimally invasive surgery.

Methods

FLASH sequences in 0.25T Philips Open interventional system were used to obtain images at 12 second intervals in a patient with a symptomatic adhesive entrapment of the distal sciatic nerve in the lower thigh. Preoperative MR Neurography at 1.5T demonstrated a focal adhesion of the nerve to adjacent semi-membranosus muscle with associated nerve hyperintensity in the area of the adhesion. Pain and Tinel's sign were appreciated at the site during "exam under MRI." A 10 centimeter titanium needle was used to apply Hylenex human recombinant hyaluronidase during a series of images. The Hylenex included 600 units in 3 cc. In addition, 0.5 cc of celestone 6 mg/ml and 3 cc of 0.75 marcaine without epinephrine were applied.

The procedure involved advancing the titanium needle to a position at the interface between the nerve and the muscle and injecting the medication agents in sequence in volumes of 0.1 to 0.5 cc. The device was advanced as the adhesion separated and was also moved to different areas of the adhesion during the procedure.

Results

At the start of the procedure, the distal sciatic nerve was visualized and the clinical relevance of the abnormality observed on MR Neurography was confirmed by exam under MRI revealing sensitivity at the point of adhesion and Tinel's into the area of radiating pain perceived by the patient.

The introduction of treatment agents resulted in an MRI guided hydro-dissection effect. This progressed steadily until the nerve was mostly surrounded by the injected agent. The result of the procedure was the relief of the adhesive nerve entrapment.

Conclusion

Although angiography provides for interventional work inside blood vessels and endoscopy provides for percutaneous surgery in various spaces susceptible to illumination and video visualization, Open MRI is particularly well suited for the development of a surgical armamentarium for percutaneous work in solid spaces adjacent to delicate tissues such as peripheral nerves.

This report reveals a methodological basis for using MRI with controlled fluid percussion augmented with hyaluronidase to separate tissues subject to pathologic and symptomatic adhesions.

Keywords *Image guided systems (primary keyword)*
Intraoperative Surgical Planning
High-field and low-field magnetic resonance
Minimally invasive therapy

Abstract Topics

Image guided systems
Minimally invasive therapy

The abstarct book's publications additonal Information summary

Real time Open MRI Guidance for Percutaneous Nerve Decompression

Aaron G. Filler, MD, PhD, FRCS
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Keywords: Interventional MRI, Open MRI, Nerve decompression, Minimally invasive surgery

Introduction

Real time Open MRI provides an opportunity for surgical manipulation of tissue on a percutaneous basis. However, it has never been possible to carry out actual decompression of nerve entrapments in this fashion. Interventional MRI has been used to carry out diagnostic and therapeutic treatment of nerve entrapments in large scale formal outcome trials involving anti-inflammatory or muscle spasm reduction methods. In this case, the images revealed that the serial administration of the treatment agents resulted in relieving the mechanical entrapment. This methodology provides a model for further study of the use of MRI for percutaneous minimally invasive surgery.

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Although angiography provides for interventional work inside blood vessels and endoscopy provides for percutaneous surgery in various spaces susceptible to illumination and video visualization, Open MRI is particularly well suited for the development of a surgical armamentarium for percutaneous work in solid spaces adjacent to delicate tissues such as peripheral nerves.

This report reveals a methodological basis for using MRI with controlled fluid percussion augmented with hyaluronidase to separate tissues subject to pathologic and symptomatic adhesions.

Note: This work had not been submitted for publication in any other journal, website or format.

Educational Objectives Learn how Open MRI can be used to guide percutaneous surgery; understand "examination under MRI"; appreciate use of MR Neurography to support Open MRI based nerve interventions

Files *Submission exists, but was not archived (suffix)*

Reviews

TRANSCRANIAL ALTERNATING CURRENT STIMULATION (tACS) ENHANCEMENT OF ELECTROENCEPHALOGRAPHIC (EEG) ALPHA WAVES POWER AND ASSOCIATED HEART RATE VARIABILITY (HRV) ALTERATIONS: AN EXPLORATORY INVESTIGATION ON THE INFLUENCE OF tACS-ENHANCED ALPHA WAVES ON AUTONOMOUS NERVOUS SYSTEM IMBALANCE, AND ITS RELEVANCE IN STRESS SCIENCE

Eduardo GonÃ§alves - Psychiatry-Faro

Contact: Eduardo Manuel GonÃ§alves (eduar.goncalves@gmail.com)

Abstract: Introduction: In this article, it is reviewed bioengineered medical devices which interfere with brain functions â€“ including, non-invasive Brain-Computer Interfaces (BCI), used in bio-/neuro-feedback (for stress-related disorders relief) and for (â€œmind-â€œ) control of robotic prosthesis and biomimetic neural networks â€“, particularly, those designed to entrain endogenous Electroencephalographic (EEG) alpha-waves. Transcranial Alternating Current Stimulation (tACS), a non-invasive neuro-stimulation technique, providing a time-varying current strength â€“ including, an exogenous oscillatory bipolar/sinusoidal (alternating) current - imposes an oscillatory shift on the membrane potential, thereby affecting endogenous brain rhythms. Occipital stimulation through tACS enhances oscillatory activity in alpha-band, measured offline to stimulation. Aims and objectives: The present experimental setup aims to explore EEG alpha-frequency enhancement and its influence in vagal/sympathetic imbalance, as measured through Heart Rate Variability (HRV) spectral analysis [Fast Fourier Transform (FFT)]. Material and methods: The alternating current stimulus is delivered through parieto-occipital scalp (5x7 cm sponge electrodes, with impedance 24,7 KÎ©, positioned at EEG PO9 and PO10 leads) of one subject (a 40 years old female, without decompensated cardiopulmonary symptoms and not suffering from epileptic seizures, neither blindness, whom previously gives informed consent), by the Stimulator NeuroConn, Eldith (Germany), at an intensity of 500 ÂµA and frequency of 10 Hz (individual alpha frequency), during 2 minutes. Alpha-wave power is pre- and post-measured (relatively to the administration of electrical stimulation), with Emotiv wireless BCI electrodes, positioned at EEG O1,2 and P7,8 leads, during 1 minute. HRV spectral analysis (FFT) is also performed, previously and after tACS (in supine position, during 5 minutes). Results and conclusions: Endogenous parieto-occipital alpha-frequency power is slightly enhanced by tACS, at EEG O1 and P8 leads, and the HRV FFT results points towards a vagal activation (prior HF power: 45,4 nu; after stimulation HF power: 50,5 nu) and a sympathetic attenuation (prior LF power: 37,9 nu; after stimulation LF power: 33,8 nu), suggesting the utility of tACS in Stress Science. However, more research (with more subjects and control/sham designs) is needed to confirm the influence of entrained occipital alpha-rhythms on Autonomous Nervous System imbalance.

Keywords
Neurophysiology (EEG, MEG, ?)
Transcranial Magnetic Stimulation
Psychiatry (PTSD,?)

Abstract Topics
Neurophysiology (EEG, MEG,â€¦)
Transcranial Magnetic Stimulation
Psychiatry (PTSD,â€¦)
Basic Neuroscience

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Introduction: In this article, it is reviewed bioengineered medical devices which interfere with brain functions â€“ including, non-invasive Brain-Computer Interfaces (BCI), used in bio-/neuro-feedback (for stress-related disorders relief) and for (â€œmind-â€œ) control of robotic prosthesis and biomimetic neural networks â€“, particularly, those designed to entrain endogenous Electroencephalographic (EEG) alpha-waves. Transcranial Alternating Current Stimulation (tACS), a non-invasive neuro-stimulation technique, providing a time-varying current strength â€“ including, an exogenous oscillatory bipolar/sinusoidal (alternating) current - imposes an oscillatory shift on the membrane potential, thereby affecting endogenous brain rhythms. Occipital stimulation through tACS enhances oscillatory

activity in alpha-band, measured offline to stimulation. Aims and objectives: The present experimental setup aims to explore EEG alpha-frequency enhancement and its influence in vagal/sympathetic imbalance, as measured through Heart Rate Variability (HRV) spectral analysis [Fast Fourier Transform (FFT)]. Material and methods: The alternating current stimulus is delivered through parieto-occipital scalp (5x7 cm sponge electrodes, with impedance 24,7 KÎ©, positioned at EEG PO9 and PO10 leads) of one subject (a 40 years old female, without decompensated cardiopulmonary symptoms and not suffering from epileptic seizures, neither blindness, whom previously gives informed consent), by the Stimulator NeuroConn, Eldith (Germany), at an intensity of 500 ÂµA and frequency of 10 Hz (individual alpha frequency), during 2 minutes. Alpha-wave power is pre- and post-measured (relatively to the administration of electrical stimulation), with Emotiv wireless BCI electrodes, positioned at EEG O1,2 and P7,8 leads, during 1 minute. HRV spectral analysis (FFT) is also performed, previously and after tACS (in supine position, during 5 minutes). Results and conclusions: Endogenous parieto-occipital alpha-frequency power is slightly enhanced by tACS, at EEG O1 and P8 leads, and the HRV FFT results points towards a vagal activation (prior HF power: 45,4 nu; after stimulation HF power: 50,5 nu) and a sympathetic attenuation (prior LF power: 37,9 nu; after stimulation LF power: 33,8 nu), suggesting the utility of tACS in Stress Science. However, more research (with more subjects and control/sham designs) is needed to confirm the influence of entrained occipital alpha-rhythms on Autonomous Nervous System imbalance.

Educational Objectives Transcranial Alternating Current Stimulation (tACS); Entrained endogenous occipital alpha-frequencies; Heart Rate Variability; Autonomous Nervous System; Stress-related disorders

Files *Submission exists, but was not archived (suffix .pdf)*

Reviews