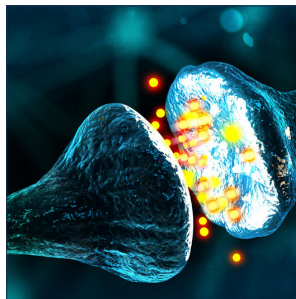
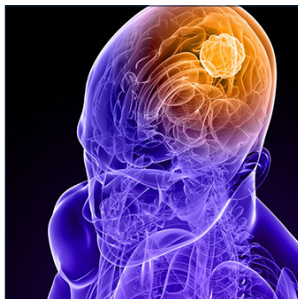
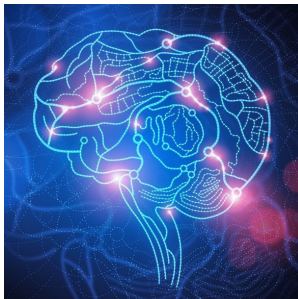

Scientific Tracks & Sessions

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The use of multi-modal imaging to discover sensitive Neuroimaging biomarkers in Huntington's disease

Nellie Georgiou-Karistianis

Monash University, Australia

A considerable effort has been underway over the last decade to establish sensitive biomarkers of disease onset and progression in Huntington's disease (HD). In particular, neuroimaging measures have been an important area for biomarker development. For example, large-scale multi-site studies (e.g., TRACK-HD, PREDICT-HD) have used structural (MRI) and microstructural (DTI) imaging methods (along with clinical/cognitive/behavioural measures) to document sensitivity of various measures in tracking progressive changes. The Melbourne based IMAGE-HD study is a biomarker development study that adopted a multi-modal approach with consideration of MRI, DTI, functional MRI (fMRI) and susceptibility weighted imaging (SWI). Importantly, across all these studies, including other smaller scale studies, volumetric changes have been shown throughout the course of disease and are observed many years prior to clinical onset. It is now well recognised that caudate volume in particular is the most sensitive marker of disease progression, with white matter changes are also seen very early on. Although there is evidence to suggest that functional deficits in multiple cortical

and subcortical regions extend well beyond the volumetric abnormalities, we are still some way from understanding whether functional changes reflect pathology or compensation, or in determining the utility of functional markers for clinical trials. This presentation will present multi-modal data from the IMAGE-HD study, as well as from other large multi-site studies, to showcase sensitive markers of disease progression in HD and will comment on the preparedness of imaging markers for therapeutic trials.

Speaker Biography

Nellie Georgiou-Karistianis completed her PhD in 1997 at Monash University, Australia. She is Professor of Psychology and currently heads an independent research group at the Monash Institute of Cognitive and Clinical Neurosciences. She leads efforts through IMAGE-HD and IMAGE-FRDA to uncover sensitive imaging and cognitive biomarkers of disease progression in rare disorders, such as Huntington's disease (HD) and Friedreich ataxia (FRDA). She also holds the position of Associate Dean (Graduate Research) in the Faculty of Medicine, Nursing and Health Sciences, Monash University, Australia, with a leadership focus on excellence and quality in graduate research training. She has over 190 peer-reviewed scientific publications, with a career total of over \$AUS12m in research funding. She is a member of the editorial board for the Journal of Huntington's Disease and serves on a number of international working groups/steering committees, including the Huntington's Disease Regulatory Science Consortium (HD-RSC), Critical Path Institute, Arizona. .

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 Notes:

Single dose does matter: An interesting case of Parkinson's Hyperpyrexia Syndrome

Raghavendra Bakki Sannegowda

Father Muller Medical College, India


Parkinsonism - hyperpyrexia syndrome (PHS) is a neurological emergency that mimics neuroleptic malignant syndrome and sepsis. Abrupt cessation of anti-Parkinson's drugs, usually levodopa is responsible for this syndrome. Relative dopamine deficiency is proposed mechanism for PHS and replacement of dopaminergic drugs is the mainstay of treatment. We report a case of Parkinson's disease who presented with manifestations of PHS after missing a single dose of levodopa. His CPK was sent which was 3000 IU favouring the diagnosis of PHS with other myriad of symptoms. Without any further delay, his anti-PD medications were re- initiated and there was

dramatic improvement in the patient's symptoms. Our case is an eye opener to show that missing even a single dose of levodopa can induce PHS, a potentially preventable and treatable condition which if untreated can mimic sepsis and is fatal.

Speaker Biography

Raghavendra Bakki Sannegowda is currently affiliated to Associate Professor, Department of Neurology, Father Muller Medical College, INDIA, continuing research in the specialized scientific area of Neurology. He is serving as an honorary author for Journal of Neurological Disorders & other reputed journals and has authored several articles along with chapters in different books related to Neurology, Neuroscience.

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 Notes:

Neuroplasticity to comprehend the scientific manifestation of shoulder pain of occupational workers

Sanjay Srivastava

Dayalbagh Educational Institute, India

The treatment of shoulder pain in overhead activities in an occupational setup has been guided by a structural-pathology paradigm where the source of dysfunctions associated with the injury is found at the site of injury. However, it raises questions like why diagnostic findings do not correlate with pain, why bilateral findings are there with unilateral shoulder injuries, why a great percentage of workers with damage to shoulder muscles are asymptomatic. The present study includes neurophysiological processes and neuroplasticity to comprehend the scientific manifestation of shoulder pain of occupational workers doing repetitive overhead activities. Neuroplasticity permits the nerve cells to compensate for injury and disease and to adjust their activities in response to changes in their environment. More recent studies have demonstrated structural as well as functional changes within the central nervous system (CNS) with chronic musculoskeletal disorders. These changes are initially favourable and help in the healing process by protecting the injured structures from further damage. Therefore, interventions targeting fundamental pathophysiological mechanisms have a much better chance of success in the rehabilitation programs. The present work studies the effects of performing

selected rehabilitation exercises while cementing neuroplastic changes by concentrating on the higher planes of consciousness. Electromyographic (EMG) activities of concerning muscles during exercises are measured using surface electrodes (Biopac MP150, Biopac System, CA). Experimentations involve 12 trained subjects who are able to concentrate on planes of higher consciousness during exercises. The results are compared with EMG activities of muscles during same set of exercises in a structural-pathology paradigm. Results support the interventions targeting fundamental pathophysiological mechanisms in the rehabilitation programs.

Speaker Biography

Sanjay Srivastava is affiliated with Industrial Kinesiology Laboratory, Dayalbagh Educational Institute (Deemed University), Dayalbagh, Agra, India. His research interests include Biomedical Engineering, Occupational Health, Consciousness Studies, and Computational Intelligence. His more recent JCR-indexed publications have appeared in *WORK: A Journal of Prevention, Assessment & Rehabilitation* (IOS Press), *International Journal of Occupational Safety and Ergonomics* (Taylor & Francis), *Journal of Back and Musculoskeletal Rehabilitation* (IOS Press), *Applied Soft Computing* (Elsevier), and *International Journal of Computational Intelligence Systems* (Atlantic Press). Dr. Srivastava has been on the review board of international conferences, JCR-indexed journals, and book-series. He has carried out an assortment of research projects funded by prestigious agencies of Government of India. He has delivered invited talks and chaired sessions in exalted national and international forums.

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 Notes:

An interesting case of Neuroacanthocytosis with head banging: A close differential of Huntington's Disease Like (HDL)

Raghavendra Bakki Sannegowda

Father Muller Medical College, India

Neuroacanthocytosis (NA) is a rare progressive degenerative disorder of the basal ganglia associated with red blood cell acanthocytes. It includes choreoacanthocytosis (ChAc) and Macleod syndrome (MLS) as core NA syndromes. SIBs are usually manifested by lip and tongue-biting and finger chewing but head scratching and head banging are also mentioned in literature. We report a case of ChAc who presented to us with head banging. A 17 year old male presented to us with 4 years history of self-injurious behaviour (SIB) in the form of repeated head banging to wall and other hard surfaces along with other self-mutilating behaviour like lip biting, tongue biting and chewing fingers. From past 2 years patient also developed other symptoms like abnormal involuntary movements, slurred speech with oro-mandibular dyskinesic movements with lingual dystonia during speech and food intake. He also had choreo-athetoid movements which were generalized involving both the upper and lower limbs. Peripheral blood Smear showed 18

% acanthocytes. MRI brain revealed significant caudate atrophy without cortical atrophy. He was treated symptomatically with tetrabenazine, anticholinergics and baclofen and advised regular follow up. Though Huntington's disease like (HDL-2), and pantothenase kinase- associated degeneration (PKAN), can present with similar neurological manifestations with acanthocytes, early presentations with autosomal recessive inheritance, significant self-injurious behaviour (SIB) and predominant caudate atrophy along with specific genetic testing differentiates ChAc from others.

Speaker Biography

Raghavendra Bakki Sannegowda is currently affiliated to Associate Professor, Department of Neurology, Father Muller Medical College, INDIA, continuing research in the specialized scientific area of Neurology. He is serving as an honorary author for Journal of Neurological Disorders & other reputed journals and has authored several articles along with chapters in different books related to Neurology, Neuroscience.

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 Notes:

Alpha synuclein impairs structural and functional integrity of mitochondria in human dopaminergic neurons

Goutham Kumar Ganjam

University of Marburg, Germany

Alpha synuclein (aSyn) is strongly linked to Parkinson's disease but the molecular targets for its toxicity remains elusive. Rapidly evolving concepts of PD pathology suggest that variants of aSyn accumulate within mitochondria leading to neuronal demise. Nevertheless, the role of aSyn in mitochondrial physiology is poorly defined. We aim to investigate the deleterious effects of mitochondrial localization of aSyn in human dopaminergic LUHMES cells. Therefore, we have generated neuron specific, adeno associated virus type 2 (AAV2) expressing cytosolic as well as mitochondrial targeting aSyn, and EGFP expressing viruses for respective controls.

Overexpression of either form of aSyn severely disrupted dendritic network, electrical activity and induced dopaminergic cell death. Both cytosolic and mitochondrial aSyn induced mitochondrial ROS formation, loss of ATP production and membrane depolarization. Real-time analysis of mitochondrial bioenergetics using Seahorse Bioscience system following AAV infection elicited a complete damage to mitochondrial respiration

capacity in dopaminergic neurons. Transmission electron microscopy illustrated a number of deformed cristae in cytosolic form and a complete loss of cristae structure and massively swollen mitochondria in mitochondrial targeted aSyn in expressing cells. Furthermore, we could show for the first time that inhibition of caspases by QVD significantly ameliorated aSyn-induced cell death and improved mitochondrial function in human dopaminergic neurons. Overall, our findings show that cytosolic as well as mitochondrial targeted expression of aSyn is detrimental to dopaminergic neurons and inhibition of caspases amended this aSyn toxicity. Thus, caspase inhibitors may provide therapeutic potential to prevent neuronal degeneration in synucleinopathies, including PD.

Speaker Biography

Goutham Kumar Ganjam is a Principal Investigator in University of Marburg, Germany. He is an expert in mitochondrial bioenergetics, neurodegeneration, inflammation, Parkinson's disease, mentoring, design, plan, execute, training graduates, etc.

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 Notes:

Activity detection and Parkinson's disease symptom monitoring at home

Dimitrios I Fotiadis

PD Neurotechnology Ltd., UK

Lately, the exploitation of advanced body sensor network technologies gains great attention tailored for the patient-centric healthcare. The synergies between the healthcare and engineering communities target the unobtrusive monitoring of patients in uncontrolled home environments to extract objective valuable knowledge for the patient's state. This allows the healthcare professionals to take healthcare back into the patient's own home and increases efficiency of consultations and care delivery. Nowadays, the management of Parkinson's disease (PD) symptoms, particularly in the early stages of the disease, shows good results. However, the long-term treatment is hampered since the available pharmacological therapy is successful only for a limited period, which results in patients developing unmanageable motor complications, which ultimately worsen the quality of life (QoL). Dosage optimization is based on the face-to-face examination of the healthcare expert during the patient's visit and the disease evaluation of day-to-day variations is difficult when relying solely upon periodic consultations. Device-based measures can be used to detect and quantify PD related motor and nonmotor impairments in specific or overall function in activities of daily living (ADLs), improving the management of the disease. Similar devices can also overcome limitations of the current clinical practice, such as low availability of expert PD practitioners or availability of expert


physicians for patients in rural or remote areas.

A system tailored to the needs of PD patients, physicians and caregivers is PDMonitorR, which is a non-invasive continuous monitoring system for PD motor symptoms. The system consists of a set of wearable monitoring devices, a mobile application, which enables patients and caregivers to record medication, nutrition and non-motor status as complementary information for the motor symptom assessment, and a physician reporting tool, which graphically presents to the healthcare professional all patient related information

Speaker Biography

Dimitrios I. Fotiadis, is a Professor of Biomedical Engineering in the Department of Materials Science and Engineering, University of Ioannina, Ioannina, Greece, where he is also the Director of the Unit of Medical Technology and Intelligent Information Systems, and is also an Affiliated Member of Foundation for Research and Technology Hellas, Institute of Molecular Biology and Biotechnology, Dept. of Biomedical Research. He is the author or coauthor of more than 250 papers in scientific journals, 450 papers in peer-reviewed conference proceedings, and more than 50 chapters in books with more than 12,000 citations (h-index = 57). He is also the editor or coeditor of 26 books. He is a fellow of IAMBES, member of IEEE Technical Committee of information Technology in Healthcare and the Editor in Chief of IEEE Journal of Biomedical and Health Informatics, and Associate Editor for Computers in Biology and Medicine. His research interests include multiscale modeling of human tissues and organs, intelligent wearable/implantable devices for automated diagnosis, processing of big medical data, sensor informatics, image informatics, and bioinformatics. He is the recipient of many scientific awards including the one by the Academy of Athens. He is the co-founder of PD Neurotechnology Ltd., based in London with focus on wearable smart systems for movement disorders.

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