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Scientific Tracks & Abstracts

Parkinson's UK - Initiatives to help connect the research community, design research and increase participation

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Before Parkinson's UK went through its rebrand in 2010, we asked our members how we were perceived. The results highlighted the need for us to communicate, collaborate and involve people affected by Parkinson's in more areas of our work. Today everything we do as an organisation includes people affected by Parkinson's. Within the research directorate we have focused on 3 key initiatives over the last decade; the Research Support Network, Research Involvement and Participation. The Parkinson's UK Research Support Network (RSN) is an online network of currently over 5,500 people affected by Parkinson's who are interested in research; getting connected to the latest research news and events and finding opportunities to take part in and shape research. Through consulting with our RSN, our other important work streams and initiatives have come about. Research Involvement has now become the cornerstone of good research. We have developed and deliver a comprehensive PPI package that teaches researchers how to do meaningful involvement and links them to our Research Involvement Volunteers. We have also created a Research Involvement Award to help support meaningful involvement. Without participation, research would not happen. In 2015 we surveyed our membership and discovered 70% of them wanted to take part in research but only 24% had. Many Parkinson's researches trials have failed to recruit participants to time and target, causing the research to go over budget and sometimes fail to reach significance. To address this, we worked with 3 key stakeholder groups; people affected by Parkinson's, Health Care Professionals and Research Professionals. From this data we developed the Participation work stream that helps researcher to connect with potential participants and people to find research in their area using our Take Part Hub. We have just published our report showing the impact of these work streams and future plans.

Biography

Amelia Hursey joined Parkinson's UK as Senior Research Participation Officer 1 July 2015 and has since been promoted to Research Participation Lead. She is responsible for initiative to increase research participation for people affected by Parkinson's, health care professionals and researchers. She is responsible for creating the innovative Parkinson's UK Take Part Hub. Before working with Parkinson's UK, Amelia obtained an MSc in Cognitive Neuropsychology from Oxford Brookes University. She worked with DeNDRoN East Anglia as a Clinical Trials Practitioner at the Norfolk and Norwich Hospital for 5 years, specialising in Parkinson's clinical research. Working with Dr Paul Worth, she supported the creation and development of an extensive Parkinson's research portfolio spanning Clinical Research Trials Phase's 2-4, observational and longitudinal research.

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Anti-Dyskinetic activity in non-human Parkinsonian primates of AV 101 a prodrug acting as a NMDA receptor glycine antagonist

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The primary deficit in Parkinson's disease (PD) is the decrease of dopamine caused by the loss of brain dopamine neurons. The most common treatment for PD is L-Dopa, the precursor of dopamine but motor complications such as dyskinesias develop with time. Glutamate is the most abundant brain excitatory neurotransmitter. Glutamatergic neurotransmission is increased in the brain in PD and L-Dopa-induced dyskinesias (LID). Antagonists of ionotropic glutamate N-methyl-D-aspartate receptors (NMDA) reduce dyskinesias in PD patients but direct acting NMDA antagonists have side effects limiting their therapeutic utility. Blockade of NMDA receptors indirectly at the glycine (GlyB) co-agonist site affords a better safety profile. We showed that increasing kynurenic acid (KYNA) levels, an endogenous GlyB inhibitor, in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) monkeys through blockade of kynurenine 3-hydroxylase, reduced LID. L-4 chlorokynurenine (4-Cl-KYN or AV-101) developed by VistaGen is a pro-drug of 7-chlorokynurenic acid (7 Cl KYNA), a potent and selective GlyB antagonist. 4-Cl-KYN, but not 7 Cl KYNA, crosses the blood-brain barrier. We hypothesize that AV-101 will decrease LID. The methodology used measures of motor behaviour in MPTP monkeys administered AV-101 with L-Dopa. Findings in a first pilot study using three MPTP monkeys showed that AV-101 reduced LID. Then a study using six other MPTP monkeys with already developed LID showed that AV-101 administration maintained their L-Dopa antiparkinsonian response measured with their locomotion (using the electronic monitoring system Vigie Primate, Viewpoint), and their antiparkinsonian score (using the Laval University Parkinson disability scale). AV-101 alone or with L-Dopa had no non-motor adverse effects in MPTP monkeys. AV-101 reduced LID in MPTP monkeys as measured with the Laval University dyskinesia scale. In conclusion, antidyskinetic activity of AV-101 comparable to amantadine was observed in nine MPTP monkeys. Better than amantadine, with its known side effects, we observed no adverse effects with AV-101. This excellent safety profile is consistent with multiple AV-101clinical studies.

Biography

Thérèse Di Paolo has research expertise in animal models of Parkinson's disease (PD) using behavioural, pharmacological and biochemical approaches. She has experience in post-mortem investigation of brains of PD patients with motor complications more specifically levodopa-induced dyskinesias (LID). She investigates LID in the MPTP monkey model the best model of this motor complication with excellent translational value for PD. She investigates the inhibition of LID in animals already displaying dyskinesias and tested numerous compounds some of which have later gone into clinical trials. She also investigates inhibition of the development of LID in de novo MPTP monkeys and the underlying biochemical correlates. She also studies the MPTP mouse model of PD to find neuroprotective compounds with a focus on repurposing drugs already in clinical use to treat endocrine conditions. Since 1986 she has published more than 122 articles with MPTP animals.

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Exercise for people with Parkinson's: A practical approach

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Statement of the problem: Public Health messaging strongly advocates physical activity, a balanced diet and the breaking of sedentary behaviour to attain as healthy a life as possible for the population. With regards physical activity, research on people with Parkinson's demonstrate short term, multiple benefits affecting motor and non-motor symptoms. Despite the evidence, the average person with Parkinson's has been shown to be at least 30% less physically active and slower than someone in the general population at diagnosis1, with many people not achieving the Department of Health's (DH) recommended 30 minutes of moderate daily activity2,3. There continues to be inconsistency in communication about what people should be doing, at what point exercise is considered suitable during the course of the Parkinson's, and what the 'best exercise' might look like. Such matters need addressing if we, as health professionals are to promote physical activity as a means by which people with Parkinson's can remain well and mobile for longer.

Session Aim: The people with Parkinson's introduced to tailored exercise report it to be an important means of controlling, even fighting symptoms of this incurable, and progressive condition (Parkinson's UK, 2017)4. There are multiple factors that influence why people engage with, and maintain participation in exercise5,6, which will be discussed in the session. Some of the wider projects currently underway across the country, and that promote inclusion of people with Parkinson's in exercise habits will also be considered. In summary, exercise has done a full turn from the 1970's when it was considered unhelpful (even harmful) for people with Parkinson's by the medical profession, to now seen as complementary to medicines management. It is now important that health professionals inform people with Parkinson's about the benefits of exercise from the point of diagnosis with the aim of directing them to valuable resources and a consistent message on the subject.

Biography

Bhanu Ramaswamy is an Independent Physiotherapy Consultant based in Sheffield, and an Honorary Visiting Fellow at Sheffield Hallam University. she practice over the past 3 decades has culminated in her specialist fields working in elder rehabilitation and neurology. A varied career includes appointment in 2004 as a Consultant Physiotherapist leading a Intermediate Care ward, becoming one of the first physiotherapists to gain a non-medical prescribing qualification in 2005. Her roles in the Health, Voluntary and Independent sectors has enabled she to contribute to qualitative research projects, co-author professional book chapters, participate in the development of international guidelines and standards of clinical practice. She has been an invited speaker to numerous (inter)national conferences, and is a Faculty member for the Allied Health section of the MDS. She has been recognised for her collaborative service to physiotherapy by receiving a Fellowship of the Chartered Society of Physiotherapy in 2014, and became an Officer of the British Empire in 2016.

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The MAO-B inhibitor Rasagiline induced Neuroprotection in PC12 Dopaminergic Neuronal model by regulation of the Akt/Nrf2 redox signaling pathway

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Parkinson's disease (PD) is a progressive, neurodegenerative disorder. One strategy for PD treatment relies on inhibition of dopamine metabolism by inhibiting the monoamine oxidase B (MAO- B). Selegiline (L-Deprenyl) and Rasagiline (Azilect) are selective MAO-B inhibitors which provide symptomatic benefit in PD treatment and found to exert neuroprotective effects. However, slowing or halting the neurodegenerative process has not yet been accomplished in PD patients using these drugs and therefore, neuroprotection is still considered an unmet clinical need. We investigated in the PC12 dopaminergic neuronal model, exposed to oxygen-glucose deprivation (OGD), the neuroprotective signalling pathways of these MAO-B inhibitors (1-3). Exposure of neurons to OGD for 3 hr followed by 18 hr of reoxygenation caused about 30-40% cell death. Rasagiline induced dose-dependent 50% neuroprotection when added either before or after the OGD insult. Clorgyline, a monoamine oxidase-A inhibitor, did not protected the neurons towards OGD-induced cell death suggesting that the neuroprotective effect of Rasagiline is independent of MAO A inhibition (4,5). Selegiline reduced OGD-induced apo-necrotic cell death by 30%. L-methamphetamine, a major Selegiline metabolite, but not 1-R-aminoindan, the major Rasagiline metabolite, enhanced OGD-induced cell death by 70%. Concomitant exposure of the cultures under OGD, to a combination of either Selegiline and L-methamphetamine or Rasagiline and 1-R-Aminoindan, indicated that L-methamphetamine, but not 1-R-Aminoindan, blocked the neuroprotective effect of the parental drug. These results suggest a neuroprotective advantage of Rasagiline over Selegiline (6). Both survival kinases phosphatidylinositol-3-kinase/protein kinase B (PI3K/Akt) and mitogen-activated protein kinase (MAPK) were activated by Rasagiline in relation to the neuroprotective effect. Rasagiline-induced nuclear shuttling of transcription factor Nrf2 and increased the expression of antioxidant heme oxygenase-1 (HO-1). Rasagiline decreased production of neurotoxic reactive oxygen species and preserved mitochondrial membrane integrity. These results indicate that Rasagiline provides neuroprotection via improving mitochondrial integrity, as well as increasing mitochondria-specific antioxidant enzymes by a mechanism involving the Akt/Nrf2 redox signaling pathway. These findings may be exploited to develop third generation of MAO-B inhibitors with improved neuroprotection in PD therapy.

Biography

Philip Lazarovici graduated in pharmacology and toxicology at the Hebrew University, post graduated on neurobiology at the Weizmann Institute of Science and conducted neurochemical and molecular research at the National Institutes of Child Health and Human Development, NIH, Bethesda, USA. He was a visiting professor in the School of Biomedical Engineering, Science and Health Systems, Drexel University and Faculty of Engineering, Temple University, Philadelphia, USA. He is a member of 15 international and national academic societies, published about 250 scientific articles and reviews and edited six books.

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Identifying the aetiology of sudden acute abnormal involuntary movements in a Primigravid

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A 20-year-old primigravid experienced sudden stiffening of the neck, upper and lower extremities and trunk associated with joint pains. she was generally well before hospital admission with no history of attacks, except for her inflammatory bowel disease that was treated more than a year ago. During physical examination, the patient manifested neck flexion deviated to the right, deviation of the eyes downward and to the right, spooning of the upper extremities, exhibition of milkmaid's grip, extension of both lower extremities and jerky speech. She also showed uncontrollable tremors of the neck and occasional flailing of upper extremities. Her preliminary laboratory tests were within normal range. It was worth noting here that her family's medical history was unremarkable. In this article, the process of arriving at the final diagnosis and treatment would be discussed.

Biography

Benjamin O Sosa is practising physician from the department of Medicine in Philippine General Hospital and also working as Professor in University of the Philippines Manila.

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