Parkinson 2017

3rd International Conference on

PARKINSON'S DISEASE AND MOVEMENT DISORDERS

September 25-26, 2017 Chicago, USA

Scientific Sessions & Abstracts

Day 1

Míra Ambrus, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Relationship between the stride length and cadence in patients with Parkinson's disease

Míra Ambrus
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Statement of the Problem: Gait disturbances are one of the principal and most incapacitating symptoms of Parkinson's disease (PD). Few studies have measured the relationship between stride length and cadence (SLCrel) in PD patient point out to a decreased stride length (SL) with a particular difficulty in its internal regulation. Therefore, improvements of SL should represent the main goal in rehabilitation and exercise interventions in PD patients. However, changes in SL must be analyzed together with changes in cadence in order to elucidate which rehabilitation approach has a specific impact in PD rather than a generalized benefit from exercise. Moreover, it is imperative to know whether the SLCrel is a reliable analysis to be used as an evaluation procedure of gait disturbances in PD patients. The purpose of this study is to explore the reliability of the SLCrel in two different sessions separated by three months in a group of PD patients.

Methodology: 35 PD patients have participated in this study. In each session, patients were asked to walk at self-selected preferred, very slow, slow, fast and very fast speeds. SL and cadence were recorded for each speed and for individual linear regression analysis were conducted over those two parameters to determine the individual slope and interception.

Findings: The slope and interception of the SLCrel showed an excellent reliability in a three months period.

Conclusion: SLC reanalysis should be implemented in order to monitor gait changes in PD patients.

Biography

Míra Ambrus has her experience in biomechanics, aging muscle strength and muscle in the field of sport science. She started to work early in research fields, during her Bachelor degree in Hungary. Then she decided to do her PhD in Spain under the supervision of Drs. Miguel Fernandezdel Olmo and Jose Andrés Sánchez Molina and started to work with patients who have Parkinson's disease (PD). Her aim is to improve the PD patients' movements, abilities, quality of life due to training and also to make the life more comfortable due to sport.

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Notes:

Azza A Ali et al., J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Impact of vinpocetine on the therapeutic effectiveness of L-DOPA using rat model of Parkinson's Disease

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Background: Parkinson's disease (PD) represents the most common movement disorder which is characterized by progressive degeneration of dopaminergic neurons as well as dysfunction of the basal ganglia. L-DOPA is still the gold standard effective therapy in PD despite the periodic increase of dosage to achieve stable therapeutic effects along with the long-term treatment side effects. Vinpocetine (Vinp) has been used for treatment of cerebrovascular disorders and may be promising as neuroprotective and PD modifier.

Objective: The objective of this study is to evaluate and compare the efficacy of Vinp and/or L-DOPA against rotenone-induced PD in rats as well as the possibility of L-DOPA dosage reduction without compromising the therapeutic effectiveness.

Methods: Rats were divided to normal group and five rotenone (RT) groups. One of RT (2.5 mg/kg) groups served as control PD model while the others were treated with either L-DOPA (10 or 25 mg/kg), Vinp (6 mg/kg) or both Vinp and L-DOPA (10 mg/kg) all for 19 days. Motor and cognitive performances were assessed using catalepsy, open-field and Y-maze tests. Striatal dopamine, norepinephrine, serotonin and acetylcholinesterase as well as mitochondrial complex I, MDA, SOD, TAC, IL-1β, TNF-α, and caspase-3 expression were measured in addition to histopathological examination of different brain regions.

Results: Concurrent treatment with Vinp and/or L-DOPA significantly ameliorated the impairments in locomotor activities and cognition as well as attenuated the depletions in monoamines and mitochondrial complex1 contents. In addition, the elevations in acetylcholinesterase activity, oxidative stress and inflammatory markers as well as caspase 3 expression induced by RT were also decreased. Combination of Vinp with low dose L-DOPA has an equivalent or almost better effect than the higher dose of L-DOPA alone.

Conclusion: Vinp has beneficial motor, cognitive, neurochemical effects and represents a promising adjuvant to L-DOPA therapy that can be translated into a serious reduction of its therapeutic doses and consequently reduction of the long-term therapy side effects. Consequently, Vinp could be recommended as a disease-modifying therapy of PD especially when given early with L-DOPA.

Biography

Azza A Ali has completed her PhD specialized in Pharmacology and Toxicology from Faculty of Pharmacy, Cairo University, Egypt. Her Postdoctoral studies included different scientific aspects especially on neurodegenerative disorders. She has also developed research line of behavioral pharmacology in Egypt. She is member of many scientific societies as (AAPS) and Alzheimer's Association (ISTAART). She is also the Editorial Board Member of many international Journals such as *Brain Disorder & Therapy, Acta Psychopathologica, EC Pharmacology and Toxicology* as well as Organizing Committee Member at the 7th International Conference on Dementia and Care Practice. She has published more than 50 papers in reputed journals, supervised and discussed more than 80 PhD and MSc thesis and actively participated by oral and posters presentations at many international conferences especially on Alzheimer's disease and Dementia as Dementia Conferences 2015, 2016 and Alzheimer's Association International Conference (AAIC 2016). She has many appreciation certificates and certificate of best presentation award at 19th International Conference on Environmental Pollution and Pollution Control (ICEPPC 2017). Currently, she is the Head of Pharmacology and Toxicology Department at Al-Azhar University, Egypt.

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Srinivas Avathvadi Venkatesan, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Srinivasan Avathvadi Venkatesan

DR.M.G.R.Medical University, India

Motor sensory stimulation (Modulation) in Parkinsonism

Parkinsonism is a neurodegenerative disorder characterized by a progressive loss of midbrain dopaminergic (DA) system. Subsequent reduction in striatal dopamine results in various clinical manifestations with Tremor, Rigidity, Bradikinesia and Postural defect. The term Motor Sensory stimulation (Modulation) encompasses a broad range of treatments, both electrical and chemical, targeting various locations in the Brain and the body to achieve the desired results. Deep brain stimulation (DBS) is a Neurosurgical treatment used in Parkinsonism and other conditions. Electrical stimulation at high frequency in precise locations of the brain results in the restoration of the balance of the circuits that are disrupted in Parkinsonism (Parkinson Disease). Stimulation in high frequency of the sub thalamic nucleus has now become a standard Neuro Surgical therapy in Parkinson disease. Transplantation of fetal dopaminergic (DA) neurons also produces symptomatic relief. The technical and ethical difficulties in obtaining sufficient and appropriate donor fetal brain tissue are the limitations in the application of this therapy. Neural precursor cells and embryonic stem (ES) cells are going to be the potential donor cells for transplantation.In the mid-1990s, creation of targeted holes in specific areas of the brain or Lesioning were the main approaches.Repalement Cell therapy was tried in some cases. Transcranial Magnetic Stimulation (TMS) is a non-invasive way of stimulating the brain, have also shown benefit in Posture and gait in some patients of Parkinson Disease. This targeted Stereotactic thalamotomy of the thalamic nucleus ventralis intermedius (VIM) is routinely used for bilateral extrapyramidal movement disorders. This targeted neuromodulator therapies can avoid the side effects. They are easily reversible if and when occurs, they can give an important degree of therapeutic effect in patients. This communication addresses the mainly Deep Brain Stimulation,Transplantaion and Stem Cell therapy and its Frontiers of the Neurophysiological basis,technical,ethical considerations and its Therapeutic effects in Parkinsonism, Tremor and Dystonia patients.

Biography

Srinivas Avathvadi Venkatesan is the President of Indian Academy of Neurology and also he is the emeritus Professor of The Tamilnadu DR.M.G.R.Medical University. Srinivas Avathvadi Venkatesan, driven by his quest for excellence and the latest discoveries on human brain related disorders, joined Madras Medical College (MMC) and received MD(General Medicine) in 1978.Later he pursued and received DM in Neurology from his alma mater.He is First Neuro physician of his state Tamil Nadu in India in government service to be conferred, the Fellow of the Royal College of Physicians (FRCP) in London in 2012, fellowship of the Indian Academy of Neurology 2004 and fellowship by the American Academy of Neurology, in 2003.He Is the First Indian to receive American Indian Neurology Award (AINA) in USA in 2001, for the best paper presentation IN STROKE during annual American Academy of Neurology meeting in 2001 in PHILADELPHIA. ByTheT-amil Nadu DR. MGR Medical University. Currently serving as a Member –in the ACADEMIC COUNCIL of National institute of Mental health and Neurosciences, Deemed University, Bangalore.

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Aimee J Nelson, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Somatosensory abnormalities in Parkinson's disease and evidence from functional neuroimaging

Aimee J Nelson
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Individuals with Parkinson's disease (PD) demonstrate abnormalities in somatosensory perception and physiology. Impairments in tactile acuity are well documented for both temporal and spatial perception, and physiological changes are also apparent. Identifying and understanding the origin of somatosensory abnormalities will aid in the treatment of PD. The present research investigates the physiological changes in primary somatosensory cortex that accompany PD, and relates these findings to alterations in brain circuits that mediate sensorimotor integration and tactile perception. Ten individuals with PD were studied on dopaminergic medications and following overnight withdrawal. Data were compared with that obtained from 10 aged-matched healthy controls. Using functional magnetic resonance imagining (fMRI) at 3T, stimulation was delivered to digits 2 and 5 of the most affected hand in PD and left hand in controls. Tactile spatial acuity was assessed using JVP domes. Somatosensory-motor integration was assessed by evoking the short- and long-latency afferent inhibition circuit using transcranial magnetic stimulation. Results indicate that PD exhibit deficient activation of somatosensory cortex, somatosensory-motor integration and impaired tacitile acuity relative to controls. Further, dopaminergic medications yield differential responses in sub-regions of the primary somatosensory cortex. These data provide support for the emerging body of literature demonstrating physiological abnormalities in somatosensory processing in PD that may contribute to the pathology of the disease. Changes in somatosensory processing may provide an explanation for sensory symptoms in PD. Activity in somatosensory cortex is modulated by dopaminergic medications and these changes may contribute to improvements in PD symptoms that occur with dopaminergic treatment.

Biography

Aimee J Nelson is an Associate Professor in the Department of Kinesiology at McMaster University. She has completed her PhD at the Institute of Medical Sciences at the University of Toronto. Her first post-doctoral appointment at the McGovern Institute for Brain Research, MIT, and second post-doctoral appointment at Toronto Western Hospital. Her academic appointment began in 2008 at the University of Waterloo and she subsequently joined McMaster University in 2012 as a Canada Research Chair, Tier 2. Her research is in basic neurophysiology and neuroimaging and her research has application in neurological injury and disease wherein hand/arm control is impaired.

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John M Baumann, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Discussing with your patients the importance of reclaiming posi-spective, uncovering your purpose and staying engaged

John M Baumann
University of Louisville, USA

My target audience is all medical personnel. The purpose of this Presentation is to encourage medical personnel who treat those diagnosed with a life-changing condition to go beyond the clinical role and discuss with their patients the importance of: Keeping or, if the disease has caused them to take on a negative attitude, reclaiming a positive perspective, uncover their purpose and staying engaged in whatever they can still do that they love to do using the twelve decide success principles.

Biography

John M Baumann inspires and helps real people to live their lives to the fullest, and even embrace their life-changing event, with the goal of uncovering their life's purpose. He is an internationally-recognized inspiring success speaker. In 2002, working as the top attorney for a public company, he was diagnosed with Parkinson's disease. From 2005 until 2014, he taught law at the College of Business at the University of Louisville to over 1,000 undergraduates. He was selected the Most Inspiring Professor. He wrote a book entitled, "*Decide Success - You Dead Yet*". He earned his Juris Doctorate degree from Cornell Law School after graduating Summa Cum Laude with a Bachelor's Degree in Business Administration from the University of Massachusetts, School of Management. As an attorney, he has passed the bar and practiced law in Texas, Louisiana and New Jersey before becoming General Counsel of a NASDAQ listed corporation headquartered in Kentucky.

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Harish C Pant, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Novel insights and therapeutics for Parkinson's disease

Harish C Pant
National Institutes of Health, USA

Besides the hallmark pathology of aggregated phosphorylated neuronal intermediate filament proteins it has been now well documented that cyclin-dependent kinase 5 (Cdk5), a critical neuronal kinase in nervous system development, function and survival, when deregulated and hyper activated induces AD, PD and ALS like phenotypes in mice. Under physiological conditions, Cdk5 activity is tightly regulated. The deregulation and hyper activation of Cdk5/p25 induces neuropathology. Thus, Cdk5/p25 becomes prime therapeutic target for AD and neurodegenerative diseases associated with the hyper activation of Cdk5. In order to prevent hyper activation of Cdk5/p25, we have designed several small peptides of p25 on the basis of Cdk5/p25 crystal structure and checked for competition with p25 and thus inhibiting selectively the hyperactivity of Cdk5, we discovered a small peptide (p5) comprising of 24 amino acids, inhibited Cdk5 hyper activation. The modification of p5 to TFP5 crosses blood brain barrier (BBB), which was tested in a transgenic AD, PD & ALS models. Post TFP5 injections in AD, PD and ALS model mice displayed significant reduction in Cdk5/p25 hyperactivity, neuroinflammation and hyperphosphorylation of cytoskeletal proteins, along with various behavioral rescues. TFP5 does not inhibit normal Cdk5/p35 activity, and therefore has no toxic side effects. In addition, treated mice rescued synaptic dysfunction and a reduction in phospho-neuronal intermediated neurofilaments and neuronal cell death. These results indicate that TFP5 and TP5 have a potential to be a therapeutic target for AD, PD and ALS neurological diseases.

Biography

Harish C Pant received his M.A. and Ph.D. degrees in Physics from Agra University, Agra, India. His postdoctoral studies were conducted on the mechanisms of electron and ion transport in model membrane systems at the Department of Biophysics at Michigan State University. He joined the Laboratory of Neurobiology in the NIMH as a senior staff fellow in 1974 with Dr. Ichiji Tasaki where he studied the function of the axonal cytoskeleton in the squid giant axon. In 1979 he moved to the NIAAA extending his studies on the neuronal cytoskeleton and the effects of alcohol on its regulation. Dr. Pant moved to the NINDS, Laboratory of Neurochemistry in 1987 where he is presently chief of the section on Cytoskeleton Regulation.

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Kohji Fukunaga, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Imparment of synaptic activity through reduced CaMKII activity in Parkinson's disease model mice

Kohji Fukunaga
Tohoku University, Japan

Parkinson's disease (PD) patients frequently reveal deficit in cognitive functions during the early stage in PD. The dopaminergic neurotoxin, MPTP-induced neurodegeneration causes an injury of the basal ganglia and is associated with PD-like behaviors. In this study, we demonstrated that deficits in cognitive functions in MPTP-treated mice were associated with reduced calcium/calmodulin-dependent protein kinase II (CaMKII) autophosphorylation and impaired long-term potentiation (LTP) induction in the hippocampal CA1 region. Mice were injected once a day for 5 days with MPTP (25mg/kg i.p.). The impaired motor coordination was observed one or two week after MPTP treatment as assessed by rota-rod and beam-walking tasks. In immunoblotting analyses, the levels of tyrosine hydroxylase protein and CaMKII autophosphorylation in the striatum were significantly decreased 1week after MPTP treatment. By contrast, deficits of cognitive functions were observed three-four weeks after MPTP treatment as assessed by novel object recognition and passive avoidance tasks but not Y-maze task. Impaired LTP in the hippocampal CA1 region was also observed in MPTP-treated mice. Concomitant with impaired LTP induction, CaMKII autophosphorylation was significantly decreased three weeks after MPTP treatment in the hippocampal CA1 region. Finally, the reduced CaMKII autophosphorylation was closely associated with reduced AMPA-type glutamate receptor subunit 1 (GluR1; Ser-831) phosphorylation in the hippocampal CA1 region of MPTP-treated mice. Taken together, decreased CaMKII activity with concomitant impaired LTP induction in the hippocampus likely account for the learning disability observed in MPTP-treated mice.

Biography

Kohji Fukunaga first discovered calcium/calmodulin-dependent protein kinase II (CaMKII) from brain. He received his PhD degrees from Kumamoto University School of Medicine in 1985. During 1988 to 1990, he worked as research fellow in Vanderbilt University (HHMI) under Professor TR Soderling. In 2002, he was appointed a Professor and Chairman in the faculty of graduate school of pharmaceutical sciences. He was Editor-in-Chief of Journal of Pharmacological Sciences (Elsevier) since 2012. He is interested in disease-modifying drug development for neurodegenerative disorders and psychiatry diseases such as autism and mental retardation.

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Day 2

Jianfeng Lu, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Reprogramming and programming of human hindbrain cells

Jianfeng Lu
Tongji University, China

Human induced pluripotent stem cells (iPSCs) are derived from somatic cells, such as skin fibroblasts, which keep the whole set of disease genome and could mimic the genetic environment. Without high efficiency of motor neuron differentiation from human iPSCs, it is hard to model motor neuron diseases in a dish using human iPSCs. By the development of a method for efficient conversion human iPSCs into motor neurons, we have successfully modeled motor neuron diseases, such as spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS) *in vitro*. This will help us understand motor neuron diseases deeply and help the development of effective treatment for the diseases.

Biography

Jianfeng Lu is a professor working in Tongji University, Shanghai, China. He has been working in the field of pluripotent stem cells and neuroscience for more than 12 years. By modulating signaling pathways, he and his colleagues are now able to efficiently convert human pluripotent stem cells into different subtypes of neural cells, which offer very useful tools for modeling diseases, for screening drugs and for cell therapy.

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Viktorija Piscalkiene, J Alzheimers Dis Parkinsonism 2017, 7:5 (Suppl)
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Improvement quality of life of people with Parkinson's disease by physical and psychosocial approach: Experience of Kaunas UAS/Kauno Kolegija project

Viktorija Piscalkiene
Kaunas University of Applied Sciences, Lithuania

Introduction: Motoric, psychical, emotional and sensory disorders determine the quality of life of people with Parkinson's disease. They burden daily life activities and influence interpersonal relationship, and increase the risk of injuries. The studies reveal that enabling or in other words the encouragement of people's abilities, motivation, learning, self-assessment and provision with target knowledge is extremely significant for persons with Parkinson' disease. It is of great importance that they would believe that they are able, have some skills and they are worth some resources, necessary for their physical and social functioning.

Aim: To improve life quality of the people with Parkinson's disease (PD) under physical and psychosocial approach. Project target group–people with PD (N=60). The interdisciplinary team that consisted of 30 lecturers and some tens of students-volunteers worked in the following project activities. Project duration-10 months (2016-2017). During the project there were delivered 1) interactive seminars under underlying issues for the people with PD and their relatives 2) there were organized camps of self-expression and healthy movement, devoted to the people with PD 3) there were conducted visits to the people, distinguishing by limited movement at their home, during which there were applied integral methods of nursing and rehabilitation.

Methodology: Applying a partially structured interview, it was sought to find out what benefits for life quality were gained through the participation in the project for the people with PD. The research was grounded on the thematic analysis.

Findings: All the people with PD, participating in the project highlighted their positive experience and positive impact on their life quality. The following experiences were reflected under cognitive approach–when people with PD, gained target knowledge in terms of self-care possibilities, being ill with this disease. Under physical approach, life quality improved due to the participation in different forums of physical activity. The researched paid the greatest value to the psychological changes, when they learnt to cognize themselves, trust themselves and assess themselves positively; to set new aims for themselves and implement them. Under social approach, positive benefit was gained through the mutual activities with students, lecturers, deeper cognition of old and new people with PD and participation in mutual integral social activities.

Conclusion & Significance: Interdisciplinary approach and application of integral techniques is very significant for the decrease of physical disorders of the people with Parkinson's disease and it aids at the improvement of emotional condition and social integration.

Biography

Viktorija Piscalkiene is cuurently working in Kaunas University of Applied Sciences, Lithuania. From 1993–2005 she worked in the Hospital of Lithuanian University of Health Sciences (LSMU) Kaunas klinikos. Her areas of scientific interests are psychosocial aspects in nursing, research of healthy ageing, evaluation of educational environment, educational evaluation of children with ADHD and opportunities for complex aid.

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Synthetic steps towards reversible chalcogen-based sensing of essential neurodegenerative disease factors

Tesla Yudhistira[1], **Sandip V Mulay**[1,2], **Youngsam Kim**[1,2] and **David G Churchill**[1,2]
[1]Korea Advanced Institute of Science and Technology, Korea
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The chemical etiology of Parkinson's disease, among other neurodegenerative diseases, is multifactorial and relates to proteins, biomolecules, as well as small soluble analytes including metal ions and ROS. The over-abundance of ROS/RNS could be an indication of Alzheimer's and Parkinson's disease (PD). Recent articles by us and other researchers have begun connecting the dots of this small molecule chemistry. There is incredible interest in preparing next-generation (e.g. ROS) probes that are reversible, sensitive, and also robust. Concentrations and the innate chemistry of selenium connect to proposed/tentative etiology of Parkinson's disease. For all of these reasons and more, we feel that the pursuit of studying organo-selenium chemistry in the context of PD will be fruitful in years to come. In this oral presentation and discussion, selenium, a key element in the redox chemistry of life and for its ability to engage in catalysis, is presented and debated in terms of diagnosis (probing) as well as potentially in therapy. To-date, the role of fluorescence and fluorescent molecules in diagnosis, treatment, as well as in biomedical research, has great current medicinal significance; this is the focus of concentrated effort across the scientific research spectrum. In particular, organo-selenium and/or organo-sulfur molecules show great promise in the detection of reactive oxygen/nitrogen species (ROS/RNS)-key factors in ageing/neurodegenerative disease in living systems. The boron dipyrromethene (BODIPY) system is a versatile class of fluorescent dye; it is commonly used in labeling, chemosensing, light-harvesting, and solar cell applications due to the many compelling characteristics, including an intense absorption profile, a sharp fluorescence emission spectrum, and high fluorescence quantum yield. As part of our ongoing effort to study chalcogenide systems, dithiomaleimide- and phenyl selenide probes (among many others) have been designed, synthesized and characterized. Commonly, fluorescence is quenched by photoinduced electron transfer (PeT) mechanism. These probes show a turn-on fluorescence response upon reaction with ONOO- (BDP-NGM) and HOCl (Mes-BOD-SePh) with significant increase in emission intensity with fast response to ROS/RNS. Live cell imaging showed that the current probes can be used for the selective detection of ROS and RNS in living systems. Time- permitting, we also like to briefly showcase other recent related fluorescent probes and studies.

Biography

Tesla Yudhistira is eagerly studying for his PhD in the Department of Chemistry at the Korea Advanced Institute of Science and Technology (KAIST) under the supervision of Prof. David G Churchill. He has obtained a bachelor's degree in Chemistry from the University of Indonesia. While pursuing science as an undergraduate, he worked in the bio electrochemistry laboratory as a student Researcher.

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If I knew then, what I know now … the definitive guide for those who do not have a chronic illness

John M Baumann
University of Louisville, USA

My target audience is all medical personnel. The purpose of this presentation is to encourage medical personnel who treat those diagnosed with a life-changing condition to go beyond the clinical role and provide a more broad perspective on the effects of the illness. Here is what I wished I knew 15 years ago, when I was diagnosed with Parkinson's disease, what I know now, and 15 years later.

Biography

John M Baumann inspires and helps real people to live their lives to the fullest, and even embrace their life-changing event, with the goal of uncovering their life's purpose (JohnBaumann.com). He is an internationally-recognized inspiring success speaker. In 2002, at 41 years old, working as the top attorney for a public company, John was diagnosed with Parkinson's disease. From 2005 until 2014, John taught law at the College of Business at the University of Louisville to over 1,000 undergraduates. John was selected the Most Inspiring Professor. John wrote a book entitled, "*Decide Success - You Dead Yet*. John earned his Juris Doctorate degree from Cornell Law School after graduating Summa Cum Laude with a Bachelor's Degree in Business Administration from the University of Massachusetts, School of Management. As an attorney, Mr. Baumann has passed the bar and practiced law in Texas, Louisiana and New Jersey before becoming General Counsel of a NASDAQ listed corporation headquartered in Kentucky.

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Kohji Fukunaga

Tohoku University, Japan

Novel disease-modifying drugs inhibiting alpha-synuclein aggregation in Parkinson's disease model mice

Backgrounds: Accumulation and aggregation of alpha-synuclein in dopaminergic neurons is one of pathogenesis of Parkinson's disease (PD), and its formation is partly regulated by long-chain polyunsaturated fatty acids (LCPUFAs) such as arachidonic acid (AA). Fatty acid binding protein 3 (FABP3, H-FABP) is critical for AA transport and metabolism in the brain. We recently demonstrated that FABP3 is highly expressed in dopaminergic neurons, especially in the substantia nigra pars compacta (SNpc). However, the pathophysiological relevance of FABP3 in PD remains unclear.

Methods: Wild and FABP3 KO mice were treated with 1-methyl-1,2,3,6-tetrahydropiridine (MPTP) and investigated its neurotoxicity in the SNpc.

Results: FABP3 KO mice were resistant to MPTP-induced dopaminergic neurodegeneration and motor deficits. Importatly, MPTP-induced alpha-synuclein accumulation in SNpc was attenuated in FABP3 KO mice compared with that in wild-type mice. In addition, we found that FABP3 overexpression promoted AA-induced alpha-synuclein oligomerization and induced cell death in PC12 cells. Over expression of FABP3 mutant protein lacking fatty-acid binding region did not promote AA-induced alpha-synuclein oligomerization and cell death. Finally, novel FABP3 ligands ameliorated MPTP-induced alpha-synuclein accumulation/aggregation and rescued dopamine neurons from degeneration in MPTP-treated mice.

Conclusion: Taken together, the formation of oligomers of alpha-synuclein is partly regulated by FABP3 through AA binding and metabolism in dopaminergic neurons, contributing to dopaminergic neuronal death seen in PD. We developed FABP ligands to develop as disease-modifying drugs for synucleinopathies in PD.

Biography

Kohji Fukunaga first discovered calcium/calmodulin-dependent protein kinase II (CaMKII) from brain in 1982. He received his PhD degrees from Kumamoto University School of Medicine in 1985. During 1988 to 1990, he worked as Research Fellow in Vanderbilt University (HHMI) under Professor TR Soderling. In 2002, he was appointed a Professor and Chairman in the faculty of graduate school of pharmaceutical sciences. He was Editor-in-Chief of Journal of Pharmacological Sciences (Elsevier) since 2012. He is interested in disease-modifying drug development for neurodegenerative disorders and psychiatry diseases such as autism and mental retardation.

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