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2nd International Conference on

Parkinson's Disease & Movement Disorders

December 05-07, 2016 Phoenix, USA

Keynote Forum

(Day 1)

Harish C Pant, J Alzheimers Dis Parkinsonism 2016, 6:6(Suppl)
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Harish C Pant

National Institute of Neurological Disorders and Stroke–NIH, USA

A small peptide derived from a neuronal cell cycle like kinase activator, P35, is a possible therapeutic candidate to reduce the phenotypes of neurodegenerative disorders like Parkinson's and Alzheimer's diseases

Our previous studies have shown that, neurofilaments, & Tau the major neuronal cytoskeletal proteins are selectively phosphorylated in axons. The phosphorylation activity is tightly regulated under physiological conditions. Under neuropathological conditions, however, phosphorylation is deregulated, occurs abnormally in perikarya and induces pathology resembling that seen in many neurodegenerative diseases (e.g. AD, ALS, PD). We identified cyclin dependent kinase 5 (Cdk5) together with its activator p35, as a major kinase regulating the topographic neuronal cytoskeleton phosphorylation. It is found that Cdk5, when deregulated by neuronal insults (A-beta, glutamate, oxidative stress, mutations and other), is hyperactivated as a stable complex with p25 (a truncated fragment of p35) and induces perikaryal hyperphosphorylated tau, synuclein and NFPs as seen in AD, PD and ALS. At autopsy, AD, PD and ALS brains display hyperactive Cdk5 (Cdk5/p25) and have confirmed that Cdk5/p25 induces neuroinflammation, tau and NF hyperphorylation along with cell death. A p25-overexpressing (P25Tg) AD model mouse displays the typical AD phenotypes. Accordingly, hyperactive Cdk5/p25 has been identified as a possible therapeutic target for neurodegeneration. All the therapeutic approaches inhibiting activities of kinases have been by interfering with ATP binding domains of the kinases that turned out to be non-specific and highly toxic. To modulate the Cdk5 activity instead of using the analogs of ATP we decided to study the effect of different truncated fragments of p35 on the regulation of Cdk5 activity. We identified a 126 amino acid (aa) truncated peptide of p35, (CIP) and smaller peptide p5 (24 aa) bind with Cdk5 with higher affinity than p25 and selectively inhibited Cdk5/p25 hyperactivity in culture, reduced tau, NFP hyperphosphorylation and cell death without toxicity and affecting endogenous Cdk5/p35 activity. The question arise, will CIP and p5 be non-toxic in vivo, in animals as in cell cultures and may prevent the phenotypes of an AD, PD and ALS transgenic mice models? Consistent with the model, we succeeded in showing that pathological and behavioral phenotypes in AD, PD and ALS model mice (over-expressing p25 transgenic) and the 5XFAD double transgenic can be alleviated after co-expression with CIP in p25 Tg and treatment with modified p5 (TFP5). We propose that CIP and TFP5 is novel therapeutic candidate to prevent Alzheimer's disease phenotypes and pathologies.

Biography

Harish C Pant received his MA and PhD 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. He moved to the NINDS, Laboratory of Neurochemistry in 1987 where he is presently the chief of the section on Cytoskeleton Regulation. His laboratory is studying the mechanisms of topographic regulation of neuronal cytoskeleton proteins by post-translational modification, including the role of kinase cascades in normal brain and during neurodegeneration.

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Yoland Smith, J Alzheimers Dis Parkinsonism 2016, 6:6(Suppl)
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Yoland Smith

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Degeneration of the Thalamostriatal System: A Potential Source of Early Cognitive Impairments in Parkinson's Disease

The existence of the thalamostriatal projection has long been known, but, until recently, the functional role of this system in normal and diseased conditions remained poorly understood. The main source of the thalamostriatal system is the centromedian/parafascicular (CM/Pf) caudal intralaminar nuclear complex, although other non-CM/Pf nuclei also contribute to this neural system. In addition to their thalamic origin, these thalamostriatal systems differ in their pattern of striatal innervation, synaptic properties, physiologic effects upon striatal neurons activity, glutamate receptors expression and extent of degeneration in Parkinson's disease and other neurodegenerative disorders. Despite direct monosynaptic excitatory connections with striatal projection neurons and interneurons, the effects of CM/Pf activation upon striatal neurons activity in vivo are complex, and likely involve intrastriatal GABAergic networks. Behaviorally, the CM/Pf-striatal system regulates attention-related cognitive processes through regulation of striatal cholinergic interneuron responses to salient stimuli. It has been suggested that the CM/Pf-striatal system plays a key role in behavioral switching and response biases for reward-oriented actions and learning. Because the CM/Pf complex heavily degenerates in Parkinson's disease, this thalamic pathology may contribute to attention-related cognitive deficits frequently seen in PD patients. The CM/Pf complex is also considered as a promising neurosurgical target for Tourette's syndrome, and possibly Parkinson's disease.

Biography

Yoland Smith got his PhD in Neuroscience from Laval University (Quebec, Canada) in 1988. After postdoctoral trainings in Oxford and Johns Hopkins University, he became Assistant professor in the Department of Anatomy at Laval University. Since 1996, he holds a faculty position at the Yerkes Primate Center of Emory University (Atlanta, GA). He has published over 250 manuscripts on the anatomy of the basal ganglia and the pathophysiology of Parkinson's disease. He is editor of prestigious journals in the field of Neuroscience, serve on NIH study sections and sit on the Advisory board of the Dystonia Medical Research Foundation. He is deeply involved in graduate education as principal investigator of various NIH training grants and previous director of the graduate neuroscience program at Emory University.

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Rudy Capildeo, J Alzheimers Dis Parkinsonism 2016, 6:6(Suppl)
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Rudy Capildeo

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Parkinson's Disease: "The First Consultation – My Approach"

The importance and value of the first consultation with your "new" patient with Parkinson's Disease (PD) cannot be overestimated. The natural anxiety of the patient, enhanced by spouse and other family members who also wish to gain entry, fuelled by information from friends, Dr Google and Dr Internet means that the consulting neurologist has to get it right – "first time". In fact, time, expertise (preferably over many years), patience and the offer "I will look after you" need to be apparent from the outset. Contrary to popular belief, diagnosis is not the main issue, nor investigations or treatment. The issues revolve around the questions, which the PD patient should be encouraged to ask, "What can you do for me?" and "What can I do to help myself?" This complex scenario will be discussed in detail from my personal perspective of looking after PD patients for more than 40 years.

Biography

Rudy Capildeo is a Consultant Neurologist who set up one of the first PD clinics in London, UK in 1973 at The Charing Cross Hospital where he also organised the first major International PD Symposium in 1979 when Sinemet Plus was first introduced by MSD (proceedings publication "Research Progress in PD, F Clifford Rose & R Capildeo, Pitman Medical). He was a Senior Investigator in the 5-year Sinemet CR First Trial (Neurology 1998, Jun; 50 (6 Suppl.6): S 15-17). A frequent presenter in national and international meetings he continues his interest in PD in his work and in his role as a teacher.

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S A Venkatesan, J Alzheimers Dis Parkinsonism 2016, 6:6(Suppl)
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Srinivas Avathvadi Venkatesan

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Clinical conundrum of neuroleptic malignant syndrome - A new look and a new AVS-CUV criterion

Statement of the Study: The research question is whether the understanding of clinical conundrum of neuroleptic malignant syndrome would become clearer when schizophrenia and affective disorders are studied separately.

Methods: Twenty schizophrenics and thirty affected disorder cases who developed NMS were studied between 1990 and 2001 prospectively. Modified criteria of Keck was used for the diagnosis of NMS. Only patients who developed fever, altered sensorium, extrapyramidal and autonomic symptoms are included standard statistical analysis of the data which included factor analysis correlation analysis and discriminate analysis were performed.

Summary of Results: Mean age of onset in schizophrenia was 32 years (18-58 yrs) and in affective disorders was 43 years (15-73 yrs). NMS developed within 9 hours of starting therapy and lasted for a mean duration of 23 days. In the affective disorder group, NMS developed over a period 17 hours and lasted for a mean duration of 11 days. Fever occurred in all the cases and earlier is schizophrenia (11.9 hours) compared to affective disorders (16.8 hours). The altered sensorium occurred within 9.6 hours in schizophrenia and 25.69 hours in affective disorder. The rigidity occurred in 38.8 hours in schizophrenia and 84.9 hours in affective disorder. Rigidity followed fever and altered sensorium in both the conditions. Autonomic symptoms occurred within 48 hours in schizophrenia and 107 hours in affective disorder. The correlation analysis showed significant correlation between NMS onset with fever and altered sensorium. Cluster analysis indicated that autonomic and extrapyramidal symptoms cause for the evolution of NMS. The factor analysis of the parameter responsible for MNS in schizophrenics are extrapyramidal symptoms 0.913, autonomic symptoms 0.858, fever 0.779, altered sensorium 0.497, whereas in affective disorders extrapyramidal symptoms 0.931, autonomous symptoms 0.955, fever 0.200, altered sensorium 0.181. Four patients died in schizophrenic group. Our discriminant analysis clearly showed the importance of the parameters with the associated probability of discrimination; autonomic symptoms (0.9), extrapyramidal symptoms (0.7), altered sensorium (0.6) and fever (0.3). The misclassification rate in the case of Schizophrenia is 15% and affective disorder is around 7%. AVS-CUV criterion can be used confidently in NMS. AVS –CUV Criterion; clinically define; autonomic symptoms and signs, extrapyramidal symptoms, altered sensorium, fever. Clinically probable: Autonomic symptoms and signs, extrapyramidal symptoms. Clinically Possible: Altered sensorium with autonomic symptoms or extrapyramidal symptoms.

Conclusion: 1. NMS developed earlier and took a longer time to resolve in schizophrenics compared with affective disorders

2. Mortality occurred only in schizophrenics

3. New AVS- CUV criteria has been added to the world literature

Biography

Srinivas Avathvadi Venkatesan serves as an Emeritus Professor at The Tamil Nadu Dr. M.G.R. Medical University; Former Adjunct Prof. IIT Madras and Visiting Professor at Cleveland – Ohio – USA; Hershey Medical College, USA. He has been rewarded with many National & international awards like AINA AWARD-Association of Indian Neurologists in America-2001, he presented more than 60 papers in national conferences and 25 in international conferences. His published works include 30 papers & 15 chapters.

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