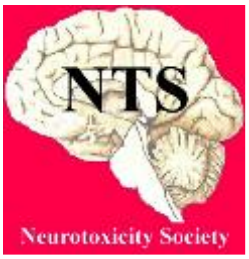

Joint Meeting
Neurotoxicity Society and
International Neurotoxicology Association
May 20-23, 2017, Florianopolis, Brazil

May 21, 13:10-14:30: NeuroInflammation and Viral Infection in the Process of Neuropathology (registration covered by ISN grant)
Organizers and Chairs: *Italo Mocchetti, Ph.D., Georgetown University, Washington, DC, USA*
G. Jean Harry, Ph.D., National Institute of Environmental Health Sciences, RTP, USA

Mechanisms of Zika infection, toxicity, and pathogenesis within the human nervous system.
Eliseo Eugenin, Ph.D., Rutgers, The State University of New Jersey, Newark, NJ, USA eugeniea@njms.rutgers.edu

Retroviruses and neurodegeneration
Joseph Steiner Ph.D., National Institute of Neurological Disorders and Stroke, Bethesda, MD, USA
steinerjp@ninds.nih.gov

Chemokines and neurodegeneration in HIV-1 infection
Marcus Kaul, Ph.D., University of California, San Diego, CA, USA mkaul@sanfordburnham.org

Neurotoxicity of HIV protein gp120
Italo Mocchetti, Ph.D., Georgetown University, Washington, DC, USA moccheti@georgetown.edu

The Symposium was featured on the first full day of the meeting as part of a day long series of 4 symposia focusing on neuroinflammation. The Symposium provided an aspect of translation of experimental studies to human disease states and new methods to address such questions. The venue for the symposium allowed for a cross-bridging of societies that take different approaches to evaluating neurotoxicity and allowed for an introduction of the ISN to those members. Total meeting attendance was 190 including a number of ISN members. The symposium was held in the larger conference room (maximum capacity of 200) of the two used for the meeting. At initial count, the attendance of the symposium was estimated at 135. The venue [Hotel Slaviero Essential Florianopolis Ingleses – Acquamar, Florianopolis, Brazil] allowed for attendance of a number of graduate students and trainees (55) from local Universities as well as the attendance of students (10) who participated in the pre-meeting school “Neuroglia in Health & Disease” sponsored by IBRO. A total of 22 countries were represented in attendance at the meeting spanning Europe, Australia, China, Japan, South America, and North America. Speakers totaled 92 with 83 posters primarily representative of trainees. Travel awards were provided to 3 trainees (USA, Chile, Hungary) and 6 poster awards were given to trainees. ISN was acknowledged as sponsor of the symposium in the final program and at the beginning of the session as well as a sponsor of the meeting on the announcement flyer and banner.

Dr. Eugenin present new work from his laboratory examining the dynamics of Zika virus (ZIKV) on neural cells. ZIKV infection-induced fever related symptoms in most people, like Dengue and West Nile virus. However, the virus can be transmitted from the pregnant mother to the fetus resulting in severe brain malformation including microcephaly and in a small population of adults the virus results in a Guillain-Barre syndrome. From examination of mechanisms by which the virus compromise the developing CNS, Dr. Eugenin presented new data identifying that ZIKV from different regions of the world have differential infectivity in human fetal mixed cultures of astrocytes and neurons. Also that cellular development is essential to support ZIKV replication and that ZIKV infects a small population of astrocytes compromising their Golgi, endoplasmic reticulum, and plasma membrane. Data was presented showing that astrocyte infection not only results in apoptosis in astrocytes and neurons but that changes in the cell to cell communication, gap junctions, and glutamatergic synapses, as well as adhesion molecules required for an efficient cortex formation.

Dr. Steiner presented his work developing screens to identify and develop neuroprotective compounds relevant to HIV-associated neurocognitive disorders (HAND). Data was presented from screening of more than 2000 compounds that included FDA approved drugs for protective efficacy against oxidative stress-mediated neurodegeneration and identified selective serotonin reuptake inhibitors (SSRIs) as potential neuroprotectants. Studies progressing from these screens to extensively evaluated identified candidates as protectants against neurotoxicity elicited by HIV Tat and gp120 and other mitochondrial toxins were presented across a range of neuronal cell features including death, mitochondrial membrane potential, and axodendritic degeneration. Sequential steps to further evaluate the robust neuroprotective actions of paroxetine were presented including *in vitro* and *in vivo* models of gp120 neurotoxicity. Findings from in vitro studies on paroxetine neuroprotection were translated to SIV infected non-human primates and progressed to an initial clinical study in HIV infected patients with HAND, a positive effect on cognitive testing was found with paroxetine treatment. The presentation demonstrated how the screen approach may identify likely candidates for further study and help to identify potential neuroprotective therapeutics to treat neurocognitive and neurodegenerative disorders resulting from HIV infection.

Dr. Kaul presented his work examining HIVgp120tg mice as a model for brain damage seen in HIV/AIDS patients. These mice express the soluble gp120 of the CXCR4-utilizing HIV-1 isolate LAV under the control of a promoter for glial fibrillary acidic protein (GFAP) in astrocytes and develop key neuropathological features observed in AIDS brains, such as decreased synaptic and dendritic density, increased numbers of activated microglia and pronounced astrocytosis. Data was presented to demonstrate that with the genetic knockout of CCR5 microglial activation was ameliorated and neuronal damage abrogated. A microarray analysis showed that brains of CCR5 wild-type (WT) and CCR5KO gp120tg mice expressed markers of an innate immune response and inflammation with upregulation of the acute phase protein lipocalin-2 (LCN2). Taking this work *in vitro*, LCN2 was found to be neurotoxic in a CCR5-dependent fashion. Inhibition of CCR5 alone failed to prevent neurotoxicity of the CXCR4-utilizing gp120 yet rescued neurons from gp120 toxicity in combination with LCN2. The overall presentation presented evidence for a coordinated pathological effect of CXCR4, CCR5 and LCN2 on microglial activation and HIVgp120-induced brain injury, and an unexpected protective effect of LCN2 that depended on the knockout or inhibition of CCR5.

Dr. Mocchetti presented work from his laboratory examining mechanisms associated with gp120 induced axonal damage and neurite pruning, similar to that observed in HIV positive subjects with neurocognitive disorders. Studies were focused on examining whether, following endocytosis, gp120 induces dynamic instability of neuronal microtubules. Data was presented to demonstrate that gp120 prevents the normal polymerization of tubulin *in vitro.* Gp120 elicited a time-dependent decrease in tubulin acetylation that was reversed by Helix-A peptide, a compound that competitively displaces the binding of gp120 to neuronal microtubules. Helix-A peptide was also able to prevent the neurotoxic effect of gp120 measured by mitochondrial damage, neurite pruning and activated caspase-3. In vivo, tubulin acetylation was observed in HIV-tg rats and in HIV positive subjects. The conclusions presented were that endocytosis of gp120 and the subsequent binding to microtubules are critical events underlying gp120 neurotoxicity.

ISN Funds Utilization - Total award $4,000.

Speaker	Eugenin	Steiner	Kaul	Mocchetti	
Registration Fee	$250.00	250.00	250.00	250.00	(exclusive of meals)
Hotel (4 nights)	360.00	360.00	360.00	360.00	
Local Transportation	50.00	50.00	50.00	50.00	
Offset Airfare	340.00	340.00	340.00	340.00	(average price $1200)

Baltimore, USA - July 9th, 2017

Dear Dr. Jean Harry and Dr. Italo Mochetti,

As an attendee of the session chaired by you, I would like to congratulate you for the very interesting session during 2017 NTS & INA Meeting. I must say that the session was filled with speakers bringing the latest information on the involvement of neuroinflammation and viral infection leading to the malfunctioning of the brain. The speakers were very enthusiastic on the importance of the translational validity of their findings, which is always motivating to the attendees. I also highlight the willingness of your speakers to discuss their researches and related topics with other attendees during coffee breaks and meals. I truly believe it greatly contributed to the success of our meeting.

Thank you very much for putting up this very illuminating session.

Best regards,

Prof. Gustavo Ferreira, PhD
Institute of Medical Biochemistry
Federal University of Rio de Janeiro, Brazil
Visiting Associate Professor
University of Maryland, Baltimore

The symposium “NeuroInflammation and Viral Infection in the Process of Neuropathology” was very interesting. The talks approached burden topics, such as Zika virus infection pathology in the Central Nervous System, a serious public health issue, especially in Brazil, in the last 2 years, and neuropathologic mechanisms of H1V infection. It was a great opportunity to deep my knowledge on this field with experienced and worldwide known professors.

Roberta de Paula Martins, PhD
Post-Doctoral Researcher, Biochemistry Department
Federal University of Santa Catarina, Brazil

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July 25, 2017

International Society for Neurochemistry
Program Support Committee

Dear Committee members:

I have been asked to provide an assessment of the ISN-supported symposium at the recent joint meeting of the Neurotoxicity Society and the International Neurotoxicology Association in Florianopolis,.Brazil that was organized by Dr. Jean Harry and chaired by Dr. Harry and Dr. Italo Mocchetti. Having attended the complete symposium, I am pleased to provide my recollections. The symposium, titled Neuroinflammation and Viral Infection in Neuropathological Processes, was well-structured to present a host of up-to-date information about the neurochemistry, neurotoxicity and neuropathogenic mechanisms of Zica virus, HIV-1 virus and other retroviruses in the nervous system. Each of the four presentations was followed by a lively question and answer session from a full audience that further highlighted the interest in this area of neuroscience. In my opinion the financial support of the ISN in this endeavor was an important factor in the success of the symposium, and indeed, the entire NTS-INA meeting.

Yours respectfully,

Michael A. Collins, Ph.D.
Professor and founding member,
Loyola Neuroscience Program
Tel: (708) 216-4560
mcollin@luc.edu

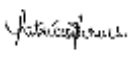
Baltimore, MD, July 12th, 2017

Dear Dr. Mochetti and Dr. Harry,

I would like to thank you for organizing the session entitled *"Neuroinflammation and Viral Infection in the Process of Neuropathology"*, which took place during the 2017 NTS & INA Joint Meeting, in Florianopolis, Brazil. As a researcher from the field of neuroinflammation, I felt very impressed by the scientific excellence of the talks. I wish the speakers had more time to show their works. The talk about Zika virus was of particular interest and delivered much more than it could be expected, including top-notch technology.

I look forward to meeting you again in the next meeting!

Best regards,



Prof. Patricia Schuck, PhD
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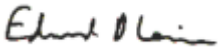
July 21, 2017

G. Jean Harry, Ph.D.
National Institute for Environmental Health Sciences
Research Triangle Park, NC, USA

Dear Jean:

I very much enjoyed the symposium "**NeuroInflammation and Viral Infection in the Process of Neuropathology,"** that you and Dr. Moccheti organized and held May 21, 2017 at the Neurotoxicity Society + International Neurotoxicology Association + convention in Florianopolis, Brazil. Processes of inflammation are key mechanisms of persisting neurobehavioral impairment after exposure to infection. The symposium presented important new data concerning the molecular mechanisms for this persisting neurotoxic damage. This timely symposium by world experts in the field provided important new information to advance the field of neurotoxicology and help avoid such damage and develop effective treatment. Thank you for your vital efforts with the convention and particularly organizing this important symposium.

Sincerely,



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NTS & INA 2017
Florianópolis / Brazil
May 20 - 23
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