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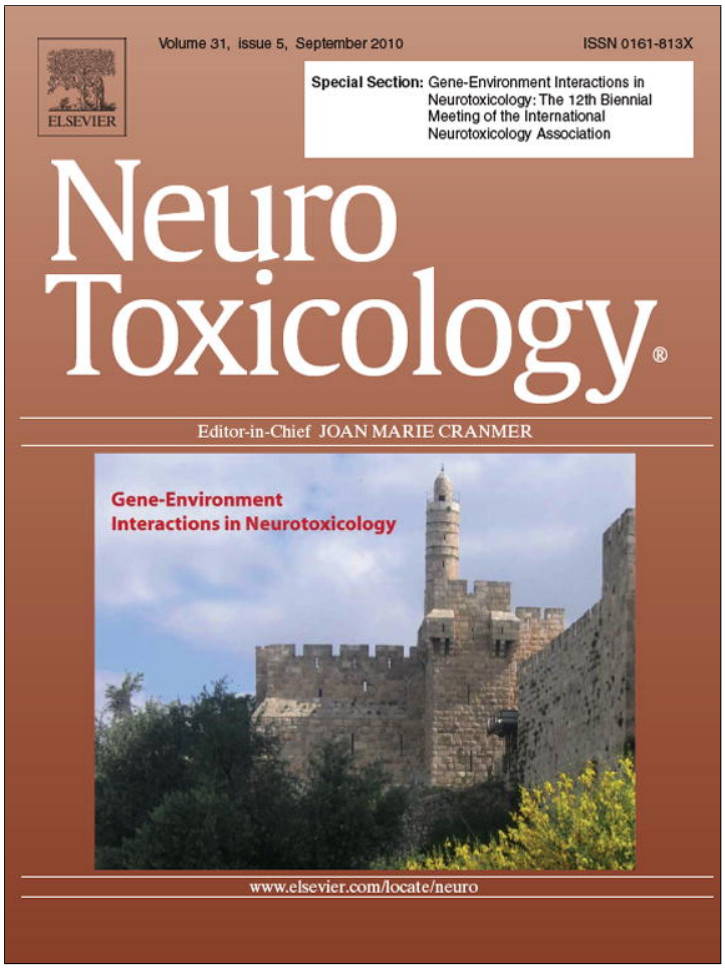

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Editorial

Gene–environment interactions in neurotoxicology: The 12th biennial meeting of the International Neurotoxicology Association

The realization that the neurotoxicity of chemicals can results from interactions between genetic inheritance and exposure to toxicants is relatively novel. The dramatic advances in research, particularly as they relate to the understanding of how external exposures interact with the genetic milieu of individuals that result in central nervous system (CNS) dysfunction, have gained great momentum in the last decade. The 5-day 12th biennial meeting of the International Neurotoxicology Association (INA) focused on this issue, namely Gene–Environment Interactions in Neurotoxicology.

To discuss the latest discoveries in this field, one hundred interdisciplinary experts from 16 countries met in June 2009 at Kibbutz Ma'aleh Hahamisha in the outskirts of Jerusalem, Israel. It was the first INA meeting in the Middle East.

The conference related basic research in the neurosciences and toxicology to major issues confronting our understanding of neurodevelopmental disorders, neurodegeneration and the impact of environmental exposures on human disease processes. The symposia featured many of the world's leading scientists in neurotoxicology and related disciplines who conduct research on the mechanisms of gene–environment interactions that result in injury to the developing and mature nervous system.

The INA-12 meeting was co-chaired by Dr. Yoram Finkelstein from Jerusalem's Shaare Zedek Medical Center, the Head of the Local Organizing Committee, and by Dr. William Boyes from the US-EPA, the President of INA. The Chairman of the Scientific Program Committee was Prof. Donald A. Fox from University of Houston in Texas.

Over 70 papers were delivered on subjects, ranging from how children's exposure to agricultural pesticides may be related to the population wide increase in attention deficit disorders to how chronic exposure to organic solvents may lead to schizophrenia and depression. The speakers also addressed policies aimed at reducing xenobiotic exposures as well as preventing and assessing health damage related to these exposures. An overall aim of INA was to promote science and communications among individuals from different countries and foster the education of medical and graduate students. A key goal of the local conference organizers was to promote greater public awareness in Israel of chemicals' adverse effects on the nervous system and to provide information to regulators in the host country. The importance of this issue was reflected by the appearance of the General Director of the Israel Environmental Protection Ministry, Dr. Yossi Inbar who gave the keynote address of the INA-12 meeting. Indeed, in his talk Dr. Inbar addressed the necessity for more legislation to protect the public from chemicals. He also expressed the expectation that individuals and institutions in Israel will become more aware of the long-term effects of low-level environmental exposure.

In keeping with the tradition of the INA meetings, the program commenced with a keynote lecture honoring the memory of Dr. Jacob Hooisma. At the INA-12 meeting, we were fortunate to have the Hooisma Lecture given by Dr. Hermona Soreq, Dean of the Faculty of Science at The Hebrew University in Jerusalem. The title of Dr. Soreq's plenary lecture was "Gene–Environment Interactions in the Mammalian Cholinergic System: Implications for Health and Disease."

The nine sessions broadly addressed current issues in neurotoxicology:

The symposium on Gene–Environment Interactions and Neurodegeneration in Non-Mammals was chaired by Dr. Michael Aschner. This symposium provided a state-of-the-art review of recent developments of non-mammalian experimental models and their utility in addressing issues pertinent to neurotoxicity, specifically identifying genes that modulate disease outcome. The symposium pointed to the power inherent to systems such as *C. elegans* and *M. drosophila* and addressed both the strengths and weaknesses of these models. This symposium also provided concrete evidence on genes and pathways that are modulated by trace metals and xenobiotics.

The symposium on Gene–Chemical Interactions in the Developing Nervous System: Proliferation, Neurogenesis and Differentiation was chaired by Dr. Donald A. Fox. This symposium provided a framework for understanding the orchestrated events of neurogenesis, the coordination of proliferation and cell fate specification by selected genes, and the effects of well-known neurotoxicants on neurogenesis in the retina, hippocampus and cerebellum. These three tissues share common developmental profiles, mediate diverse neuronal activities and function, and thus provide important substrates that mediate sensory, motor, cognitive and memory functions.

The symposium on Advances in Novel Signaling in the Expression of Neurotoxicity, chaired by Dr. Anumantha Kanthasamy and Dr. Stephen Bondy, highlighted recent studies on non-classical actions of selected neurotoxicants and their role in the expression of neurotoxic response via altered alpha-synuclein protein expression and PKC isoform signaling and amyloid beta precursor-like protein 1 (APLP1) expression.

The symposium on Strategies for In Vitro and Developmental Neurotoxicity Testing, chaired by Dr. Anna Price and Dr. Petros Lenas, provided an overview on new challenges in safety assessments for regulatory requirements. The integration of various in vitro model systems into testing strategies as well as combination of information-rich approaches with bioinformatics was discussed. Furthermore, relevant models and endpoints for developmental neurotoxicity evaluation using in vitro approach were presented.

The symposium on Endocannabinoid Signaling in Neurotoxicity and Neuroprotection was chaired by Carey Pope. Endocannabinoid

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signaling participates in a variety of neurotoxic mechanisms and serves as a viable therapeutic target for a number of neurologic disorders. An overview of endocannabinoid signaling and its potential for neuroprotection was presented, alongside with the differential role of endocannabinoid signaling in the neurochemical and behavioral correlates of drug abuse. The role of endocannabinoid signaling in anticholinesterase toxicity and its potential utility in prophylaxis and therapy also was discussed.

The symposium on Peaceful Use of Disastrous Neurotoxicants chaired by Dr. Yoram Finkelstein and Dr. Uri Wormser based on the observation that various warfare agents were used for achieving peaceful and favorable goals, and neurotoxic compounds were routinely used as drugs when the therapeutic value outweighs their adverse effects. Late effects, after more than 20 years of low-level exposure to organophosphorous (OP) pesticides, were observed in agriculture workers and residents in the Hula Valley in Israel. This presentation was complemented by addressing the effect of the OP pesticides on rat brain biochemical and cellular parameters, as measured in the pyramidal neurons of the hippocampal CA1 region. An additional lecture shed light on natural neurotoxins and showed the pharmacological properties and the angiogenic potential of these proteins isolated from snake venom, NGF and VEGF-like compounds.

A symposium, chaired by Dr. Elihu D. Richter and Dr. Philippe Grandjean addressed the question: Exposure and Susceptibility: How important are both? The participants presented two case studies from the Haifa Bay. This region is Israel's industrial center and it is an exceedingly polluted area, with industrial point source emissions and severe point source occupational health exposures for workers. Sadly, this symposium reminded us that macro-level epidemiologic studies are not able to capture such micro-level relationships as prevalent in the Haifa Bay area, or, for that matter, elsewhere in the world.

The final session was chaired by Dr. Carlos Singer. It focused on Gene–Environment Interactions in Parkinson's disease. The symposium provided an overview on the neurotoxic mechanisms underlying rarer forms of Parkinsonism and offered new insights into excitotoxicity and their interaction with genetic risk factors. The lectures presented human models of susceptibility genes and their potential interaction with known environmental risk and neuroprotective factors. An overview of the interaction between genetic susceptibility and xenobiotics (MPTP and rotenone) in the etiology of Parkinsonism was presented. The linkage between Parkinson's disease, manganese and the mitochondrial proteome also was discussed.

In the final lecture, which concluded the INA-12 meeting, Dr Walter G. Bradley reviewed the evidence of biomagnification of cyanobacterial neurotoxins and neurodegenerative disease in the Guamanian Parkinson–Dementia–ALS complex.

INA-12 organizers aimed to provoke discussions that will define questions that are of broad significance and timely experimental resolution. Therefore, these discussions have been summarized in this special issue of NeuroToxicology dedicated to INA-12 meeting. This special issue is intended to provide a framework that will propel research into new areas of neurotoxicology.

One of the traditional goals of INA is to recruit and energize young investigators to pursue careers in neurotoxicology, and therefore the program also featured a student symposium chaired by Dr. William K. Boyes, containing talks from students and postdoctoral fellows who have been selected to receive student support awards. An afternoon was dedicated to these presentations.

In addition, two poster sessions that featured more than 60 posters presented many topics of interest to neurotoxicologists. This reflected the depth and breadth of neurotoxicology research underway around the world, which provided a vibrant scientific exchange of ideas and topics.

Overall, the presentations in these symposia defined the major questions that require experimental resolution in areas that affect human neurological heath, ranging from developmental exposures to degeneration associated with the aging nervous system, as well as the interaction between the environment and genetics in precipitating neurodegeneration – the latter being chosen as the theme of INA-12 meeting.

In summary, INA-12 meeting provided a collegial setting for developing working relationships among scientists from different countries. This meeting successfully addressed major issues in human environmental health and helped uncover basic mechanisms and methodologies that will ultimately help in the development of strategies to mitigate human disease. Thus, INA-12 served as an essential component of the ''core'' meetings that have shaped the neurotoxicology research community into an interactive, international and facile research team. Following the success of INA-12 our attention turns to Xian, China, which will host INA-13 in June 2011. We are confident the next meeting will continue to build upon the momentum of INA-12 and the preceding meetings.

Conflict of interest statement

None declared.

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