Introduction

Preface: 2022 International Conference on Neuroprotective Agents

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The purpose of the International Conference on Neuroprotective Agents (ICNA) is to bring together clinical and basic science researchers from many countries and disciplines in a common forum to address various approaches to neuroprotection. These conferences and their associated summary publications provide a broad, informal, and unique forum in basic sciences as well as clinical disciplines. Clinicians learn new trends in neurochemistry and genomics, and neuropharmacologists learn new applications for their work. The atmosphere is intentionally relaxed and informal in order to foster the free exchange of ideas and concepts among the participants. Virtually all registrants give either an oral or a poster presentation, and informal discussions are an integral part of each session. The conferences have been held in relatively small venues to encourage interaction among the participants outside of the formal sessions, for example, during meals, receptions, outings, and spontaneous evening discussions.

The ICNA is generally held every 2 years, and all proceedings have been published except for the very first conference held in Rockland, ME, USA, in 1991. The focus of the first several conferences was on ischemic stroke and the potential treatments, including MK-801 and other blockers of excitatory amino acid-related insults.[1] Attention was also focused on hypothermia as a neuroprotective approach leading to the eventual successful multicenter trial of head cooling in newborns to provide protection from neurotoxicity as a result of delivery-related insults. The fifth and sixth annual ICNA publications in 2001 and 2003 emphasized several agents, including melatonin, L-carnitine, and estrogens as potential neuroprotective agents.[2,3]

With the publication of the ICNA presentations in 2005, it was evident that combinational and time-course-sensitive applications of a variety of neuroprotective agents may well be necessary to defeat neurotoxicity. New technologies including physiological monitoring, gene expression assays, and the use of endogenous agents as therapeutics were introduced.[4] By 2007, it was evident that developmental exposure to most traditional anesthetics, at the appropriate dose, duration of exposure, and developmental stage, would result in neurotoxicity and that agents such as acetyl-l-carnitine might provide neuroprotection. New approaches including neurotrophic factors and nanotechnology were also being investigated.[5]

In 2010, it was evident that neuromodulation by deep brain stimulation was gaining momentum as a treatment for movement disorders such as Parkinson's disease and refractory epilepsy. Nanotechnology continued to be of great interest, especially in achieving entry into the nervous system by aiding therapeutics to cross the blood–brain barrier.[6] During the next decade, topics ranged from new anesthetics designed to be free of nervous system insult, including xenon and steroid derivatives, to the use of omics approaches, biological pathway analysis, and biomarker development.[7]

The 13 papers that comprise this special issue of *Experimental Biology and Medicine* were part of the 15th ICNA held on September 11–14, 2022. As in special issues from previous ICNAs, the papers in this issue cover a wide range of topics in the field of neuroprotection and neurotoxicity. The use of ketamine in major depressive disorders was examined. A nonhuman primate model to evaluate the effects of ketamine and surgical stress in the developing brain was demonstrated, as well as the establishment of a new alternative method that utilized a monkey neural stem cell model to evaluate neurotoxicity. Mitochondria were shown to be a key mediator of primary and collateral effects of anesthetics. Neonatal sevoflurane exposure was shown to induce long-term changes in dendritic morphology in juvenile rats and mice. Neuroprotection after soman exposure was observed after using a glutamatergic antagonist and anticholinergic drug. Various techniques for neurotoxicity assessments were also presented, including evolving techniques for reducing phantom limb pain. It was suggested that an enriched

environment may be a viable non-invasive neuroprotective strategy. One article indicated that exposure to different sedative/hypnotic agents during a critical period of brain development may induce distinct functional changes in the subiculum that may persist into adolescence. The polyphenol ellagic acid, found in numerous fruits and vegetables, was shown to attenuate Lipopolysaccharides-induced neuroinflammation in rat brain when administered orally, and the omega-3 fatty acid alpha-linolenic acid was shown to enhance the facilitation of GABAergic neurotransmission in the hippocampus. A mini-review is also presented which indicates that down-regulation of kynurenine formation from tryptophan prolongs life span. The papers in this special issue demonstrate the breadth of topics that are typical of the ICNA.

In keeping with its "international" aspect, the 15th ICNA was held in Cluj-Napoca – a university town in the Transylvania region of Romania. Travel was facilitated by Cluj's airport being only a few kilometers from both downtown and the ICNA venue at the Grand Hotel Italia. The COVID-19 pandemic brought virtual and hybrid conferences to the center stage; the ICNA in Cluj was hybrid in format. As expected, thanks to many previous personal experiences, Professor Dafin Muresanu and his expert organizing team headed by Ovidiu Selejan and Doria Constantinescu made the entire event unfold in a well-organized manner – virtual presentations from around the world were seamlessly integrated with in-person presentations. Student participation was excellent, thanks to the extensive neuroscience research being conducted in Cluj and elsewhere.

The format was similar to previous ICNAs: a Sunday evening reception, followed by a full day of presentations on Monday plus half-day morning presentations on Tuesday and Wednesday. A brief walking tour of the historic downtown Cluj preceded dinner on Monday. The tradition of a Tuesday afternoon outing and dinner included a trip to the nearby Salina Turda – the world-famous salt mine, now a major tourist destination. At Salina Turda, one not only gains a glimpse of the history of salt mining but also enjoys an underground "theme park" complete with a panoramic (ferris) wheel, sporting activities such as miniature golf, boating on the underground lake, and a 180-seat amphitheater. "Back from the salt mines," dinner followed at the Dracula-themed Hunter Prince Castle in Turda.

Several of the 15th ICNA participants extended their stay, exploring Transylvania. Romania (like much of Eastern Europe) is becoming recognized for having natural beauty, historical sites, accommodations, and cuisine all rivaling the most notable regions of Western Europe – without the crowds of tourists and much cheaper. We are exploring the possibility of holding the 16th ICNA (likely September 2024) again in Eastern Europe, thanks to the marvelous organizational capabilities of Professor Muresanu and his colleagues.

AUTHORS' CONTRIBUTIONS

WS, TAP and RJA contributed equally to the manuscript.

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