The National Academies of SCIENCES ENGINEERING MEDICINE

Forum on NEUROSCIENCE and NERVOUS SYSTEM DISORDERS

Environmental Neuroscience: Advancing the Understanding of How Chemical Exposures Impact Brain Health and Disease—A Virtual Workshop

June 25, 2020 via Zoom

Hosted by the National Academies' Forum on Neuroscience and Nervous System Disorders
In Collaboration with the Board on Environmental Studies and Toxicology

Background

The human health impacts, on brain health and disease, of the estimated 85,000 chemicals in the environment, are largely unknown; this can be considered "the forgotten environmental risk factor." Indeed, humans are concurrently exposed to a multiplicity of chemicals during life, the sheer number of which has overwhelmed the ability to determine their individual toxicity, much less their potential interactive effects. Lifelong exposure to chemicals is known as the exposome.

Early life exposures to chemicals can result in fetal reprogramming with permanent consequences on neurodevelopment and neurodegenerative impacts. Adverse outcome pathways initiated by chemical exposure can combine with other risk factors to permit significant interactions, while persistence of some chemicals (e.g. heavy metals and PFAS) results in cumulative toxicity. As genetics alone does not fully explain neurodevelopmental disorders or neurodegenerative diseases, understanding the role of personal environmental chemical exposures becomes critical.

Key challenges in this endeavor include the need for exposure assessment using biosensors, GIS tools, and biomarkers of exposure and effect; validated high throughput screening that permit the identification of potential neurotoxicants; development of animal models that better simulate human conditions; and methods to facilitate understanding of chemical interactions, cumulative toxicity, adverse neurotoxicity pathways, and transgenerational effects. Potential tools and methods to address the knowledge gaps include functional genomics to dissect gene by environment interactions, epigenetics, in vitro approaches, alternative model organisms, functional MRI, light sheet microscopy, and connectomes.

The economic and societal costs of neurodevelopmental disorders and neurodegenerative diseases are staggering, and underscore the need to evaluate the effects of environmental exposures on brain health. This undertaking will lead to a better understanding of the adverse outcome pathways affected by these exposures for intervention, treatment, and translation of findings to parents, patients, decision makers, policy changers, and health care professionals.

Statement of Task

A planning committee of the National Academies of Sciences, Engineering, and Medicine will organize and conduct a one-day public workshop that brings together experts and key stakeholders from academia, government, industry, and non-profit organizations to explore the current knowledge landscape and future opportunities in neurotoxicology.

Invited presentations and discussions will be designed to:

- Provide an overview of what is known about neurotoxic exposures and how they lead to neurodevelopmental and neurodegenerative disorders;
- Explore how new technologies can be harnessed to identify previously-unknown neurotoxic chemicals;
- Consider whether algorithms can be developed to better predict the effects of cumulative exposures and interactions across the life-span on brain health; and
- Discuss research gaps and collaborative opportunities between neuroscientists and environmental health scientists.

The planning committee will develop the agenda for the workshop, select and invite speakers and discussants, and moderate the discussions. A proceedings of the presentations and discussions at the workshop will be prepared by a designated rapporteur in accordance with institutional guidelines.

Planning Committee

Deborah Cory-Slechta, Department of Environmental Medicine, University of Rochester Medical School, *Co-Chair*

Walter Koroshetz, National Institute of Neurological Disorders and Stroke, National Institutes of Health, *Co-Chair*

Patrick Breysse, National Center for Environmental Health / Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention

Ray Dorsey, Department of Neurology, University of Rochester Medical School

Carl Hill, Alzheimer's Association

Frances Jensen, Department of Neurology, University of Pennsylvania Perelman School of Medicine

David Jett, National Institute of Neurological Disorders and Stroke, National Institutes of Health

Cindy Lawler, National Institute of Environmental Health Sciences, National Institutes of Health

Gary Miller, Department of Environmental Health Sciences, Columbia University Mailman School of Public Health

Trevor Penning, Department of Systems Pharmacology & Translational Therapeutics, University of Pennsylvania Perelman School of Medicine

Allison Willis, Department of Neurology, University of Pennsylvania Perelman School of Medicine