MENTOR-NT: A Multiscale ENvironmental NeuroTOxicology Resource

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Life-course exposures to environmental agents are increasingly recognized as key risk factors in the pathogenesis of neurodevelopmental, neuroimmunological, and neurodegenerative disorders. These agents can be chemical (metals, pesticides, solvents), biological (viruses), or physical (radiation), and exposures may involve inhalation, ingestion and/or dermal contact. While past investigations of neurotoxic mechanisms of environmental exposures focused primarily on oxidative stress and apoptosis, recent evidence reveals the effect of neurotoxicant exposures on pathways involving epigenetic changes, protein aggregation, autophagy, deregulated kinase activation, and the gut microbiome. The consequences of these exposures are modulated by lifestage, biochemical/genetic, physiological, behavioral, socioeconomic, etc. factors. A challenge for large scale epidemiological/ecological investigations of neurological disease is assessing exposures to co-occurring environmental agents that have varying spatiotemporal distributions and intensities. Such investigations can benefit from new computational tools for retrieval, analysis and integration of information on contaminant patterns and exposure-relevant factors. A new integrative Multiscale ENvironmental NeuroTOxicology computational Resource (MENTOR) is being developed to support various aspects of neurological risk characterization: it utilizes advances in large data analytics, extant database content, and mechanistic environmental/exposure/biological modeling to support discovery-driven and hypothesis-driven analyses. Tier 1 applications focus on exposomic pattern recognition for extracting information from multidimensional data sets; higher tier applications utilize mechanistic multiscale environmental and biological models to develop neurological risk metrics for populations and individuals. Example applications of MENTOR explore identification of potentially causative associations among risk factors and health endpoints by considering publicly available demographic/socioeconomic, behavioral, environmental, biomarker and disease data.

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