

Biological Design Doctoral Defense

Applying Wastewater-Based Epidemiology to Identify Risk Factors of Neurodegenerative Diseases and Cancer at the Population Level

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Abstract

Novel means are needed to diagnose neurodegenerative diseases (NDD) and cancer, given delays in medical diagnosis and rising rates of disease incidence, prevalence, and mortality worldwide. Development of NDDs and cancer has been linked to environmental toxins. Ensuing epigenetic changes may serve as helpful biomarkers to diagnose amyotrophic lateral sclerosis (ALS), Parkinson's Disease (PD), and Alzheimer's Disease (AD) as well as various cancers sooner and more accurately. This dissertation tabulates and evaluates a spectrum of diagnostic matrixes (i.e., soil, sewage sludge, blood) and markers of disease to inform disease surveillance. A literature search using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Bradford Hill criteria implicated BMAA, formaldehyde, Mn, Hg, and Zn as environmental factors with strong association to ALS risk. Another PRISMA search identified epigenetic changes (e.g., DNA methylation) in NDD patients associated with environmental toxic exposures to air pollutants, heavy metals, and organic chemicals. Of the 180 environmental toxins hypothesized to be associated with AD, PD, or ALS, four heavy metals (As, Cd, Mn, and Hg) were common to these NDDs. Sources, as well as evidence and proxies of human exposure to these heavy metals and Pb were investigated here, namely the metal industries, and metal concentrations in topsoil, sewage sludge, and blood. Concentrations of Cd and Pb in sewage sludge were found to be significantly correlated with NDD prevalence rates in co-located populations (state-level) with odds ratios of 2.91 and 4.08, respectively. Markers of exposure and disease in urine and feces were also evaluated using PRISMA, finding 73 of 94 epigenetic biomarker panels to be valid for tracking primarily gastric and urinary cancers. In all studies, geospatial analyses indicated a preference in study cohorts located in the U.S., Europe, and the northern hemisphere, leaving underserved many populous regions particularly in the southern hemisphere. This dissertation draws attention to sewage sludge as a currently underutilized proxy matrix for assessing toxic human exposures and further identified a spectrum of particularly attractive, non-invasive biomarkers for future diagnostic use to promote early detection, survivability, and quality of life of individuals at risk of NDDs and cancer.



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