

Beyond Benzene - Identifying Toluene And Xylenes As Dominant Predictors Of Cognitive Decline

Lili Liang, MD, MSc¹, Xinyi Zhang, MA², Jenny Lin, MD, MPH³

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¹Division of Gastroenterology, The Icahn School of Medicine at Mount Sinai, New York, NY, USA

²Department of Psychiatry, The Icahn School of Medicine at Mount Sinai, New York, NY, USA

³Division of General Internal Medicine, The Icahn School of Medicine at Mount Sinai, New York, NY, USA

Toluene exhibited a pronounced threshold-like non-linear decline in processing speed, whereas its association with verbal memory followed a more gradual, linear decrease.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Early identification of modifiable environmental stressors is critical for dementia prevention. While the neurotoxicity of high-dose volatile organic compounds (VOCs) is established, the impact of contemporary, low-level mixtures remains under-characterized. We employed an explainable artificial intelligence (XAI) framework to investigate whether modern exposome VOC signatures, specially benzene, toluene, ethylbenzene and xylenes (BTEX), serve as sensitive biomarkers for early cognitive decline.	We analyzed data from the National Health and Nutrition Examination Survey (NHANES) 2011-2014 (n=1573). Extreme Gradient Boosting (XGBoost) models were developed to predict domain-specific Z-scores, integrating key demographic, socioeconomic, lifestyle, and cardiometabolic covariates. Model explainability was achieved through SHapley Additive exPlanations (SHAP) and model Gain metrics to characterize feature importance and non-linear effects. All analyses were done in R version 4.5.2.	The superior predictive performance for processing speed (DSST RMSE: 0.83) compared to memory and language domains (RMSE: 0.91-0.97). While age and education were primary drivers, blood toluene and xylenes emerged as the dominant environmental predictors across all cognitive domains. SHAP analysis revealed a robust negative directional impact for toluene and xylenes.	In modern low-exposure settings, toluene and xylenes have surpassed benzene as dominant environmental predictors of cognitive impairment. The disproportionate impact on processing speed suggests a neurotoxic progression initiated in white-matter networks before reaching hippocampal pathways. These blood VOC signatures offer high-precision, modifiable biomarkers for cognitive risk stratification and targeted public health interventions.	Güzel, B. Recent Advancements on Per- and Polyfluoroalkyl Substances (PFAS) in the Environment for Human Health: A Comprehensive Review. Water Air Soil Pollut.2025, 236, 526 Nayak, S. K.; Yamijala, S. S. R. K. C. Computing Accurate Bond Dissociation Energies of Emerging Per- and Polyfluoroalkyl Substances. J. Hazard. Mater. 2024, 468, 133804.
				CONTACT  Icahn School of Medicine at Mount Sinai Corresponding author: Lili Liang, lili.liang@mssm.edu ALZHEIMER'S ASSOCIATION 