Title: Machine Learning-Derived Ultra-Processed Food Subtypes Show Distinct Associations with Metabolic Risk and Cognitive Performance

Authors: Kate E. Worwag, Batul Yawer, Brittany DeFeis, Eric S. Porges, Aprinda I. Queen

Background: Consumption of ultra-processed foods (UPFs) is associated with increased risk for metabolic disease and cognitive decline. However, treating UPFs as one homogeneous category obscures distinct physiological mechanisms, limiting precision in behavioral interventions. This study utilized machine learning to empirically subtype the UPF supply in the USA and isolate subtype-specific impacts on metabolic and cognitive status.

Methods: The full adult sample included 11,282 adults aged ≥20 years (BMI = 28.9 kg/m²; 66.2% Non-Hispanic White; 51.9% female; 13.6% Type 2 Diabetes), and the aging subsample included 3,614 adults aged ≥60 years (BMI = 29.0 kg/m²; 77.4% Non-Hispanic White; 54.8% female; 27.1% Type 2 Diabetes); no formal cognitive screener was administered, although 14.9% reported difficulty thinking or remembering. Previously derived machine learning-based UPF subtypes (Breads/Savory Carbs, Processed Meats/Savory Meals, Sugar-Sweetened Beverages/Low-Fat Sweets, and High-Fat Sweets/Baked Goods) were applied to NHANES 2011–2014 dietary recalls to estimate subtype-specific intake. Outcomes were HbA1c, Type 2 Diabetes (adults ≥20) and a Global Cognitive Factor (adults ≥60) derived from CERAD Word Learning, CERAD Delayed Recall, Animal Fluency, and Digit Symbol Substitution. Survey-weighted regressions tested associations between UPF subtype intake and each outcome, adjusting for demographic (e.g., age, education, race, Poverty-Income-Ratio) and health covariates. Quasi-Bayesian Monte Carlo simulations (500 iterations) tested BMI as a mediator between UPF subtype and cognition.

Results: Processed Meats and High-Fat Sweets were significantly associated with higher BMI and increased odds of Type 2 Diabetes (ps < .01). High-Fat Sweets & Baked Goods were also significantly associated with lower global cognitive scores (β = -0.011, p = .030). Mediation analysis indicated that BMI did not significantly mediate this association (ACME p = .338).

Conclusion: Models revealed that UPFs are nutritionally and clinically heterogeneous. High-fat, sweet UPFs were uniquely associated with cognitive decline independent of BMI. Because this specific subtype is densely concentrated in saturated fats and refined sugars (nutrients independently linked to Alzheimer's disease and neurodegeneration), interventions might consider these in future aging research.