

Metabolomics, metagenomics and habitual diet data integration for molecular insights of diet, gut microbiome connection to brain health.

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Introduction

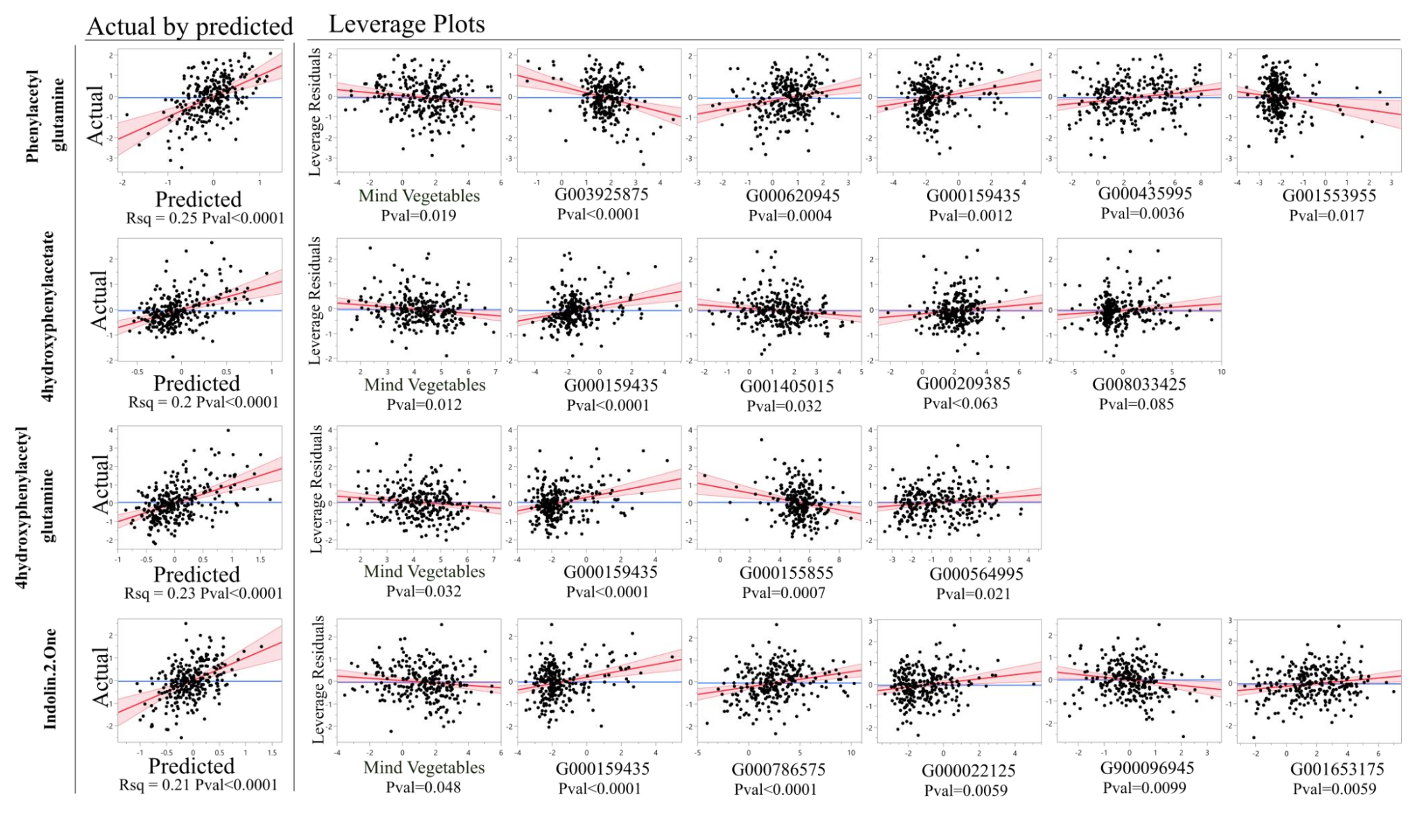
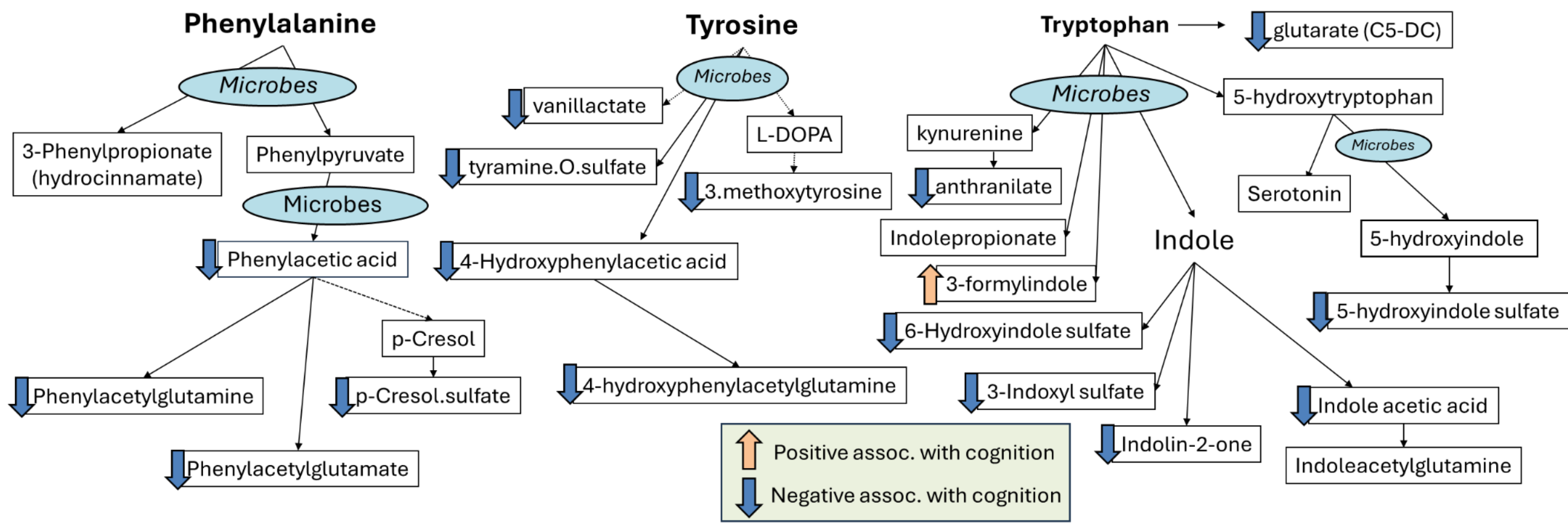
- Mounting evidence points towards exposome influences on brain health and disease including AD.
- Diet and gut microbiome were shown to influence cognition and the risk for AD development, but molecular mechanisms and the interplay between the two remain poorly understood.
- Understanding molecular processes governing this body – brain connection could help shape potential interventions, uncover metabolic pathways involved in cognition decline and help design novel interventions that targets modifiable factors in AD.

Methods

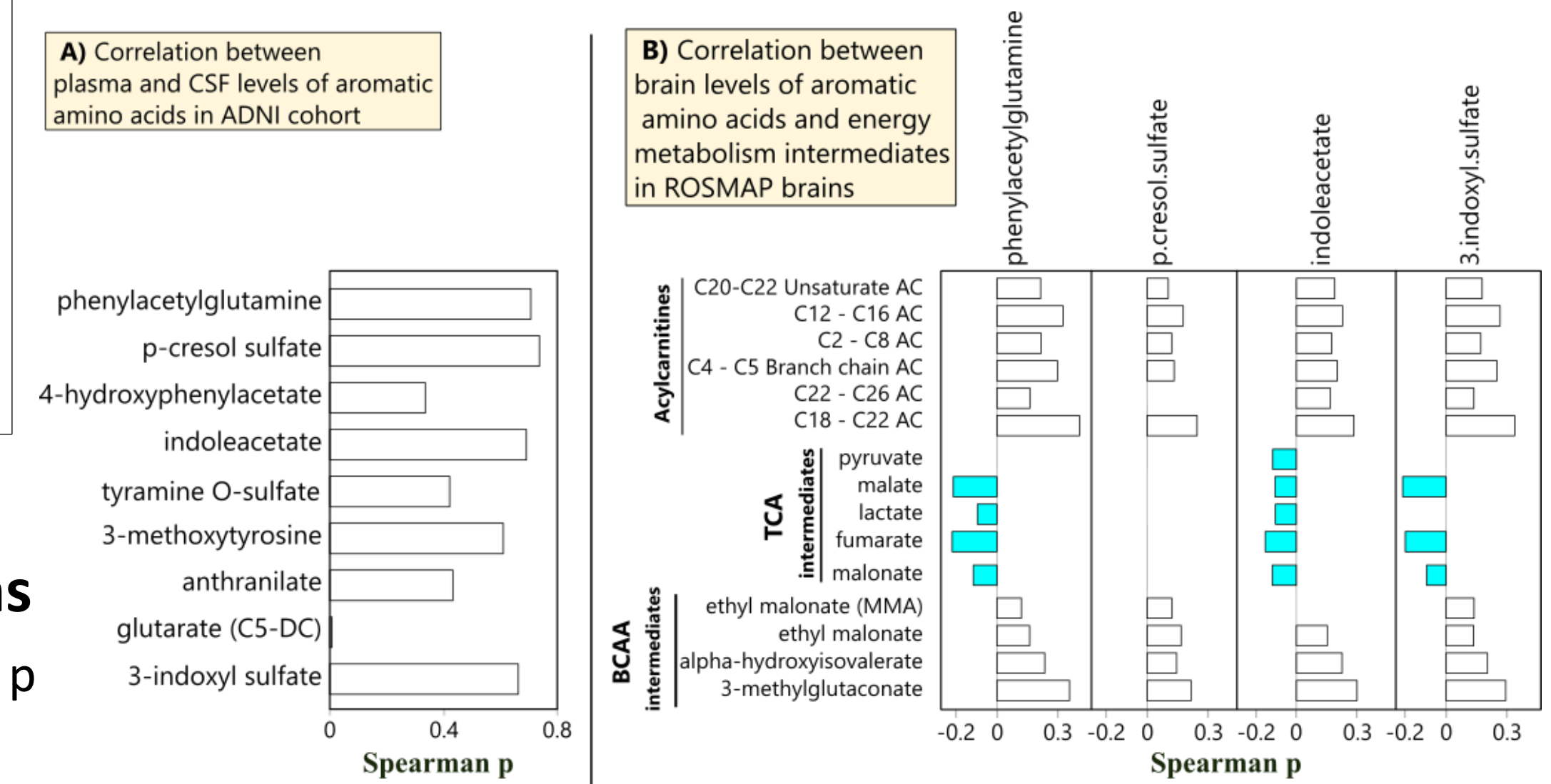
- Data from six Alzheimer’s disease (AD) research centers (ADRCs) (n=449), that includes I) food frequency questioner for habitual diet; metagenomics (n OGUs); plasma untargeted metabolomic data (~1000 metabolites); in combination with cognitive assessments and plasma AD
- The identified exposomic factors were further evaluated in terms of their presence and action in the central nervous system, utilizing 500 matched plasma and CSF samples from ADNI and 500 brain tissue of ROS-MAP participants (DLPFC).
- Combination of linear (Pearson) and non-linear (Spearman’s rank order correlation) with FDR correction was applied

Results

Pathways of human bacterial co-metabolism of aromatic amino acids is associated with cognition. Summary pathway of aromatic amino acids detected within ADRCs cohort, with indicated associations with Craft Story 21 Recall (Delayed) test (CRAFTDRE)



Diet and microbiome independently contribute to the levels of plasma aromatic amino acids metabolites. Minimal model for gut microbiome counts predicting plasma levels of selected aromatic amino acid metabolites with addition of the habitual diet



Aromatic amino acid metabolites are correlated across the blood brain barrier and show associations with brain energy metabolism markers. A) Spearman's rho between plasma and CSF levels of aromatic amino acids in ADNI cohort. B) Spearman's rho between aromatic amino acid metabolites and markers of mitochondrial energy metabolites in DLPFC brain samples from the ROS-MAP participants (n=500).

Conclusions

Big data points to influences of diet and gut microbiome on key human-bacterial co-metabolism pathways of aromatic amino acids that are associated with cognition and energy metabolism in periphery and in CNS, bringing further evidence for importance of body – brain connection in AD.

