Childhood exposure to non-persistent endocrine disrupting chemicals and multi-omic markers in a population-based child cohort

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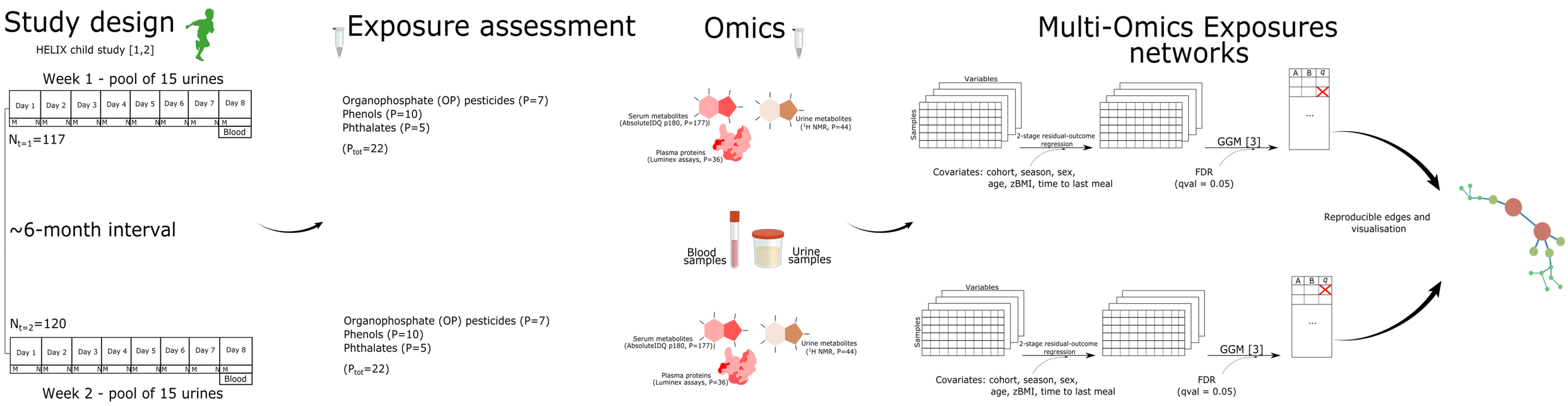
Background & Objectives

- The general population is exposed to a cocktail of chemical exposures
- Non-persistent endocrine disruptors (EDCs) are a class of chemicals that interfere with the endocrine system
- The early stages of life are particularly vulnerable to the effects of EDCs
- Multi-omic signatures might provide mechanistic insights into the effect of EDC exposure, in particular before the onset of clinical symptoms in children
- We aimed to identify multi-omic signatures associated with non-persistent EDCs using an integrative approach based on Partial Correlation Networks

Methods



Results

- The time-specific networks (N_{edges}=1,064, N_{edges}=1,109) included associations of comparable strength (ρ=0.09 (-0.09, 0.11) for both) and statistical significance (q=0.008 (0.001, 0.025), q=0.01 (0.001, 0.027)). The significant edges represented less than 3% of the possible connections
- The merged network consisted of N_{edges}=229
- Graph merging led to the exclusion of the majority of exposure-omic connections (Figure 1). Notably, none of the protein-exposure associations were reproducible
- The merged network consisted of 32 connected components, 3 of which included mixed exposure-omic connections (Figure 2)

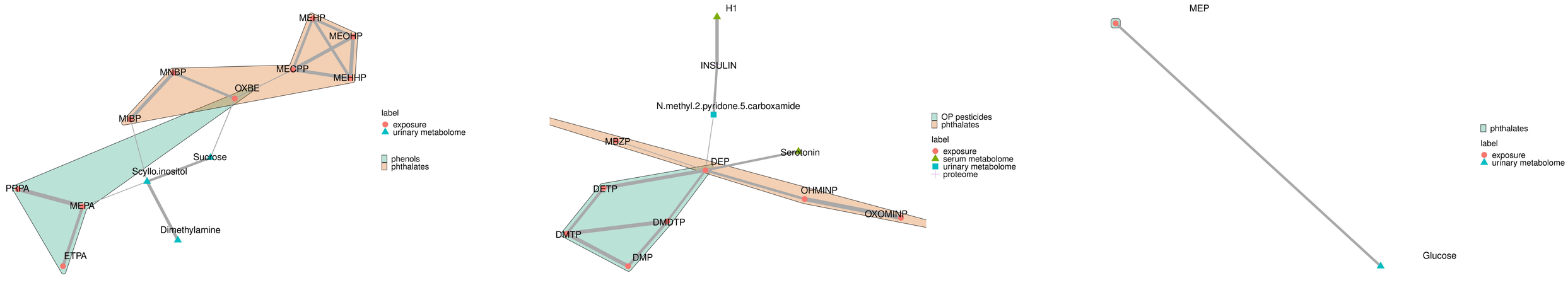


Figure 2. Clusters (i.e. connected components) of EDC exposure-omic associations.

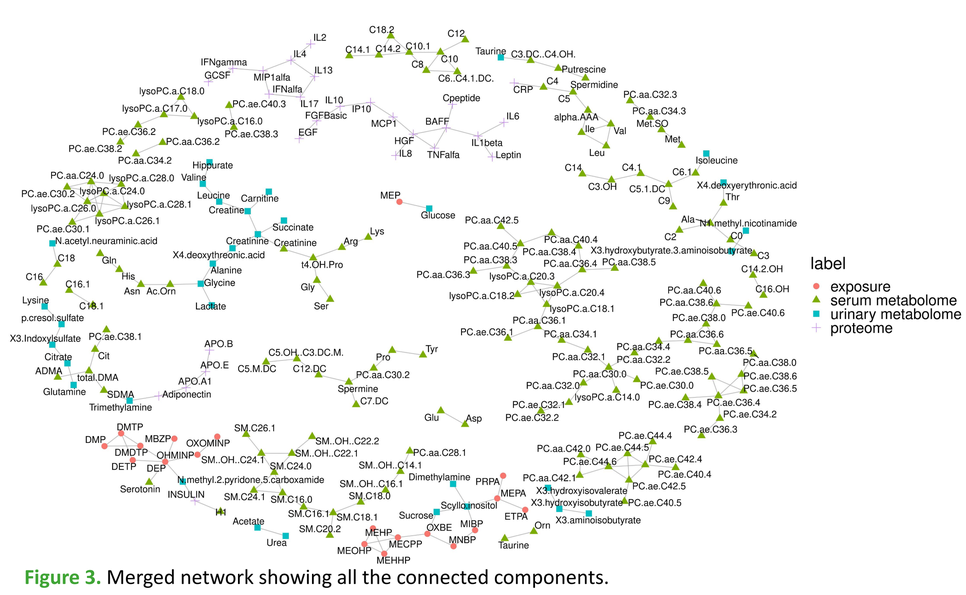


Figure 3. Merged network showing all the connected components.

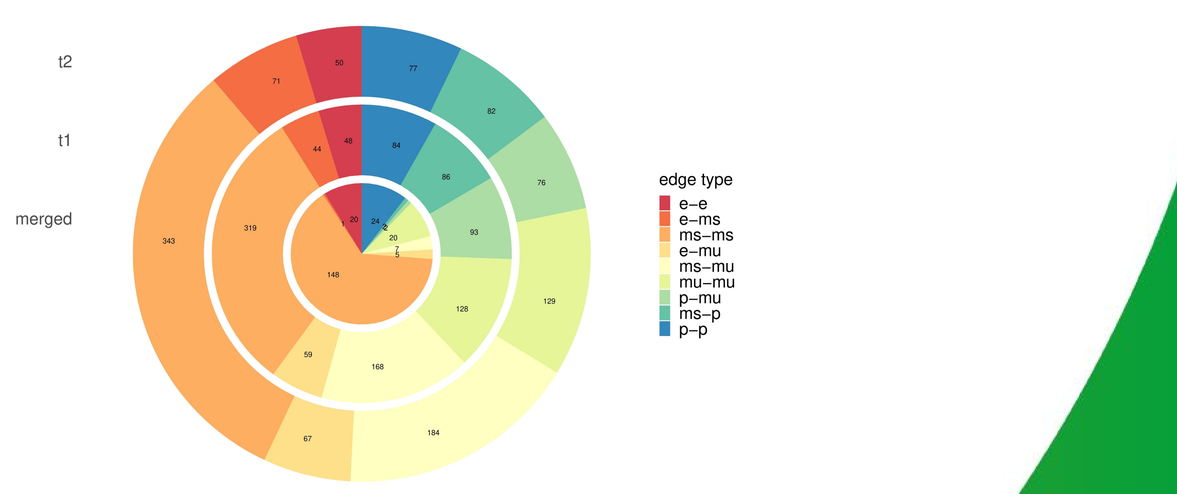


Figure 1. Multilevel pie chart showing the proportion of edge types for the time-specific and merged networks. e = exposure, ms = serum metabolite, mu = urinary metabolite, p = protein.

Conclusions

- We integrated Multi-Omic and exposure data from a child cohort using an integrative approach, and we identified associations reproducible across time points
- The association between DEP and Serotonin (ρ=0.09 for both time points) was reproducible. Exposure to Organophosphate pesticides has been linked to a variety of brain disorders [4], potentially through the serotonergic system
- In future work we plan to include methylation data

References [1] Vrijheid M, et al. "The human early-life exposome (HELIX): project rationale and design." (2014). [2] Casas M, et al. "Variability of urinary concentrations of non-persistent chemicals in pregnant women and school-aged children." (2018). [3] Schafer J, Strimmer K. "A Shrinkage Approach to Large-Scale Covariance Matrix Estimation and Implications for Functional Genomics." (2005). [4] Sarrouilhe D, et al. "Is the Exposome Involved in Brain Disorders through the Serotoninergic System?" (2021)

OBERON is a collaborative project funded by the EU Framework Programme for Research and Innovation Action (RIA), Horizon 2020, under grant agreement no 825712