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# Metabolomic and exposomic biomarkers of risk of future neurodevelopmental delay in human milk

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## Abstract

**Background:** The chemical composition of human milk has long-lasting effects on brain development. We examined the prognostic value of the human milk metabolome and exposome in children with the risk of neurodevelopmental delay (NDD).

**Methods:** This retrospective cohort study included 82 mother-infant pairs (40 male and 42 female infants). A total of 59 milk samples were from mothers with typically developing children and 23 samples were from mothers of children at risk. Milk samples were collected before 9 months of age (4.6 ± 2.5 months, mean ± SD). Neurocognitive development was assessed by maternal report at 14.2 ± 3.1 months using the Ages and Stages Questionnaires-2.

**Results:** Metabolome and exposome profiling identified 453 metabolites and 61 environmental chemicals in milk. Machine learning tools identified changes in deoxysphingolipids, phospholipids, glycosphingolipids, plasmalogens, and acylcarnitines in the milk of mothers with children at risk for future delay. A predictive classifier had a diagnostic accuracy of 0.81 (95% CI: 0.66-0.96) for females and 0.79 (95% CI: 0.62-0.94) for males.

**Conclusions:** Once validated in larger studies, the chemical analysis of human milk might be added as an option in well-baby checks to help identify children at risk of NDD before the first symptoms appear.

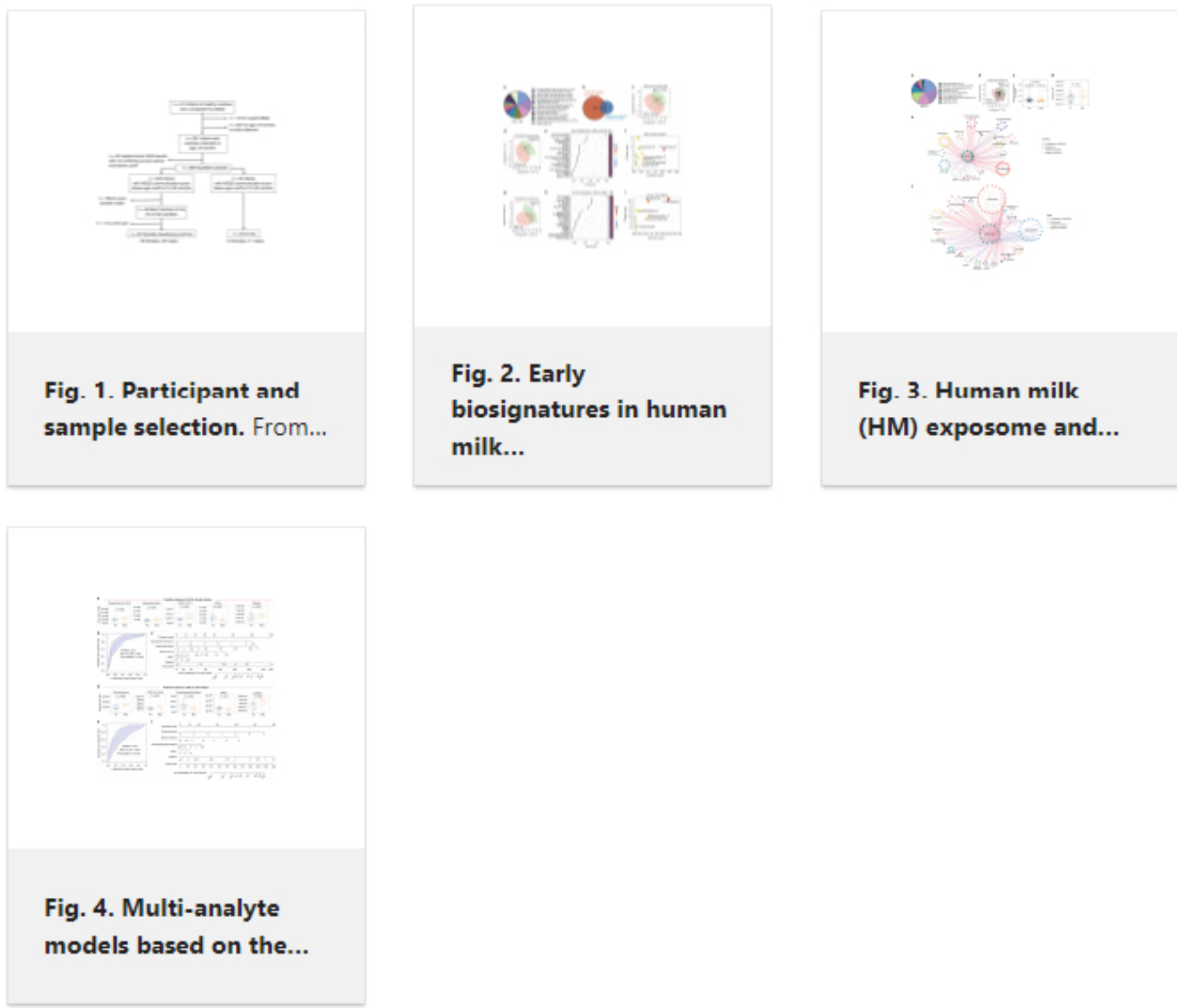
**Impact:** Maternal milk for infants sampled before 9 months of age contained sex-specific differences in deoxysphingolipids, sphingomyelins, plasmalogens, phospholipids, and acylcarnitines that predicted the risk of neurodevelopmental delay at 14.2 months of age. Once validated, this early biosignature in human milk might be incorporated into well-baby checks and help to identify infants at risk so early interventions might be instituted before the first symptoms appear.

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## Conflict of interest statement

The authors declare no competing interests.

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