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The causal effect of BMI on neurodevelopment: a within family Mendelian randomization study using MoBa

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Background: Higher BMI in childhood predicts subsequent neurodevelopmental and emotional problems, but it is unclear if associations are causal. Observational studies are vulnerable to reverse causation and confounding. Mendelian randomization (MR) studies with unrelated individuals can also suffer from familial biases, such as dynastic effects ("genetic nurture").

Methods: We apply within-family MR (WFMR) to overcome these biases. We used genetic information from 26,370 family trios in the Norwegian Mother, Father and Child Cohort Study (MoBa) to construct BMI polygenic scores in children and both parents. By using all three polygenic scores to instrument BMI, we avoided familial biases affecting previous studies.

Results: Multivariable-adjusted and conventional MR models implied an impact of children's BMI on depressive, ADHD, and autism symptoms. In conventional MR models, a 5kg/m^2 increase in BMI corresponded to depressive symptoms 0.49 SD higher (95%CI: 0.24-0.73), and ADHD symptoms 0.49 SD higher (95%CI: 0.28-0.70). WFMR estimates were less precise but gave little evidence of causal impacts of children's BMI. Maternal BMI was positively associated with children's depressive (0.16 SD per 5kg/m^2, 95%CI: 0.04-0.28) and autism symptoms, and paternal BMI with children's ADHD symptoms.

Conclusions: Compared to conventional MR models, MR models accounting for parental genotype found less evidence of causal effects of children's own BMI on emotional and neurodevelopmental symptoms. The discrepancy may suggest an influence of family or population-level effects.

Key messages: The influence of children's own BMI on emotional and neurodevelopmental problems may have been overstated. Parental BMI, familial or population level effects may influence these outcomes.

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