Prenatal Maternal Mood Influences Brain Morphological Development in the First Decade of Life

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INTRODUCTION

Prenatal Maternal Mood Linking to Brain Development

- Prenatal maternal mood disturbances—such as stress, anxiety, and depression—are key environmental exposures that influence brain development. These disturbances have been associated with structural changes in the brain, particularly in regions involved in emotion regulation (Mandl et al., 2024).

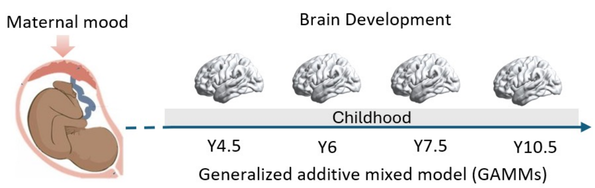
Brain Morphological Alterations

- Studies show that prenatal mood disturbances are linked to disrupted amygdala development at birth and in early childhood (Rifkin-Graboi et al., 2013; Wen et al., 2017).
- Cortical changes have also been reported, including altered gray matter volume, cortical thickness and surface area (e.g., Wei et al., 2022).
- Notably, these neurodevelopmental trajectories often differ by sex (Wen et al., 2017; Wei et al., 2022).

Research Gaps

- Most studies are cross-sectional; longitudinal data are needed to capture developmental trajectories.
- Limited research on specific mood components, such as pregnancy attitude, somatic symptoms, and positive emotions.

METHODOLOGY



Participants

- Data from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort which recruited pregnant Asian women in Singapore.
- Included children born ≥30 weeks gestation, ≥2 kg birth weight, and 5-min Apgar ≥8 to reduce confounding by birth complications.

Prenatal Maternal Mood

- Maternal mood during pregnancy was assessed at 26–28 weeks gestation using validated self-report instruments, including the State–Trait Anxiety Inventory, Beck Depression Inventory-II, Edinburgh Postnatal Depression Scale, and items from LYDON maternal health and well-being
- Confirmatory factor analysis (CFA) identified one general factor and four specific factors: depression/anxiety symptoms, somatic symptoms, pregnancy attitudes, and positive emotions.

MRI Acquisition & Processing

- T1-weighted MRI scans at ~ 4.5, 6, 7.5, 10.5 years.
- Longitudinal FreeSurfer pipeline (v7.1.1) used for segmentation.
- Extracted cortical thickness, surface area, and volume (68 regions; Desikan-Killiany atlas), and 16 subcortical volumes.

Statistical Analysis

- Generalized additive mixed models (GAMMs) were applied to examine (1) the association between maternal mood and the brain developmental trajectory and (2) their interaction with sex.
- Covariates controlled: biological sex at birth, maternal ethnicity, household income, birth weight adjusted for gestational age, and total intracranial volume
- Multiple comparisons were corrected using FDR at a $p < 0.05$ level across brain regions within each measure.

REFERENCES

[1] Mandl, S., Alexopoulos, J., Doering, S., Wildner, B., Seidl, R., & Bartha-Doering, L. (2024). The effect of prenatal maternal distress on offspring brain development: A systematic review. Early Human Development, 106009.
[2] Rifkin-Graboi, A., Bai, J., Chen, H., Hameed, W. B., Sim, L. W., Tint, M. T., Leutscher-Broekman, B., Chong, Y. S., Gluckman, P. D., Fortier, M. V., Meaney, M. J., & Qiu, A. (2013). Prenatal maternal depression associates with microstructure of right amygdala in neonates at birth. Biological psychiatry, 74(11), 837–844.
[3] Wen, D., Poh, J., Ni, S. et al. Influences of prenatal and postnatal maternal depression on amygdala volume and microstructure in young children. Transl Psychiatry 7, e1103 (2017).
[4] Wei, D., Zhang, H., Broekman, B. F., Chong, Y.-S., Shek, L. P., Yap, F., Tan, K.-H., Gluckman, P. D., Meaney, M. J., & Fortier, M. V. (2022). Cortical development mediates association of prenatal maternal depressive symptoms and child reward sensitivity: a longitudinal study. Journal of the American Academy of Child & Adolescent Psychiatry, 61(3), 392-401.

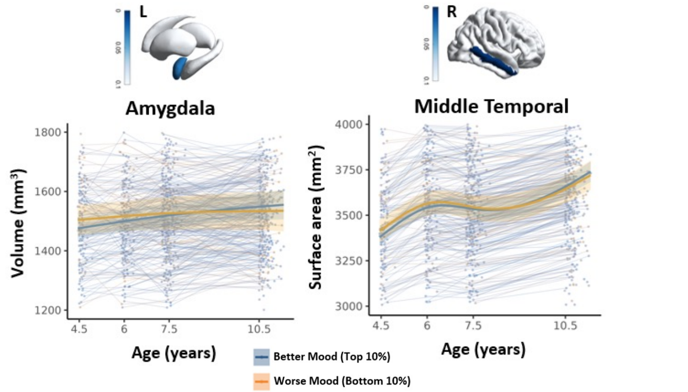
RESULTS

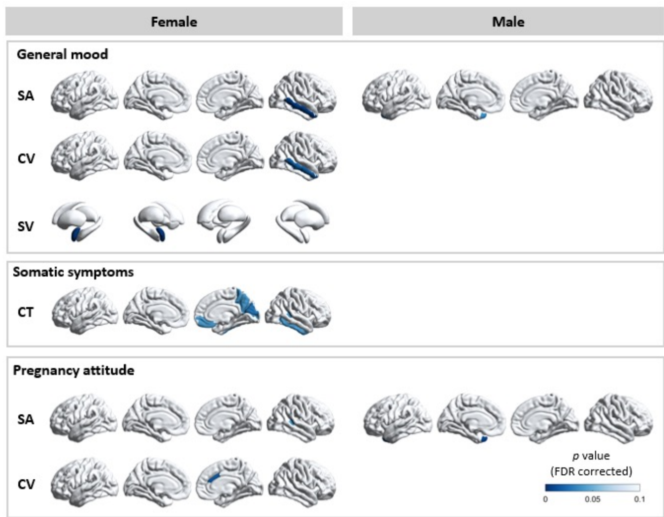
General Findings

- Worse general maternal mood during pregnancy is associated with (1) slower growth of the left amygdala, a region critical for emotional processing, and (2) reduced expansion rate of the right middle temporal gyrus (MTG), involved in social cognition and language.

Sex-Specific Effects

Girls:
(1) Worse general mood → Slower amygdala and MTG growth.
(2) More somatic symptoms → Reduced cortical thinning in visual and limbic areas.
(3) Negative pregnancy attitude → Faster growth in anterior cingulate gyrus and transverse temporal region.
Boys:
(1) Worse general mood→ Faster area expansion in the temporal pole.
(2) Negative pregnancy attitude → Slower area expansion in the temporal pole.





CONCLUSION

- Prenatal maternal mood disturbances are associated with altered structural brain development from early to middle childhood, particularly in regions involved in emotion regulation, social cognition, and sensory processing.
- The effects are region-specific and sex-dependent, highlighting the need for tailored models of neurodevelopmental risk.
- Different dimensions of mood (e.g., general mood, pregnancy attitude, somatic symptoms) show distinct associations with brain growth patterns, suggesting that prenatal distress is not a unitary construct in its impact.

Future Implications:

- Intervention strategies may benefit from targeting specific mood dimensions (e.g., sleep disturbances, negative pregnancy attitudes).
- Continued longitudinal research is essential to identify sensitive periods and developmental pathways for preventive care and early intervention.

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