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**3 JUNE 2026**

# GUSTO STUDY SUGGESTS BOYS AND GIRLS MAY DEVELOP DEPRESSIVE SYMPTOMS DIFFERENTLY, HIGHLIGHTING THE IMPORTANCE OF EARLIER PREDICTION AND MORE TAILORED SUPPORT

**SINGAPORE** – A new study led by the A*STAR Institute for Human Development and Potential (A*STAR IHDP) has found that patterns of brain development during early childhood may be linked to depressive symptoms in adolescence, and that these associations differ between boys and girls.

Published in *Molecular Psychiatry*, the study was conducted in collaboration with researchers from the KK Women's and Children's Hospital (KKH), National University Health System (NUHS), Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), and McGill University. It drew on data from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort, a longitudinal study tracking over 1,200 Singaporean mothers and their children from pregnancy through childhood.

## Different developmental pathways in early childhood

Researchers analysed 917 brain scans from 549 children, collected when they were aged 4.5, 6 and 7.5. Using longitudinal neuroimaging, they tracked changes in how different parts of the brain connect and work together over time.

Between ages 4.5 and 6, girls showed a faster rate of change in brain development than boys, suggesting that the pace of early brain development may differ by sex.

## Sex-specific links between early brain development and later depressive symptoms

The researchers then examined how the childhood brain-development patterns were associated with depressive symptoms at age 13, alongside other mental health-related measures collected between ages 10 to 12 years.

Further analysis showed that different parts of the brain were associated with different types of later depressive symptoms in boys and girls. In girls, changes in brain regions linked to emotional processing were associated with symptoms such as low mood and poor self-esteem. In boys, changes in other brain regions were associated with symptoms such as tiredness and a sense of ineffectiveness.

Together, these findings suggest that similar overall depressive symptoms in adolescence may emerge through different developmental pathways in boys and girls. They do not mean that depression can be predicted from a single brain scan, or that all boys and girls follow the same

path. Instead, they point to the need for future research to consider how risk may develop differently across sexes.

## More girls reported depressive symptoms at age 13

In addition to these developmental differences, the study observed differences in depressive symptoms during adolescence.

In total, 636 children were assessed for depressive symptoms at age 13, with girls reporting significantly higher depressive symptoms than boys. Data from the GUSTO study shows that girls at age 13 were 2.5 times more likely than boys to report clinically significant depressive symptoms, reflecting the higher prevalence of depressive symptoms among adolescent girls.

## Implications for future support strategies

Depressive symptoms often become more common during adolescence. In Singapore, adolescent mental health has become an increasing concern, with about one in three youths aged 10 to 18 reporting internalising mental health symptoms such as depression, anxiety and loneliness[1].

However, the findings from this study suggest that patterns of brain development linked to later depressive symptoms are present earlier in childhood, before symptoms typically become apparent. Moreover, these patterns are different in boys and girls.

The research highlights a potential earlier window for understanding mental health vulnerability. This underscores the need to look earlier in childhood, rather than focusing only on the adolescent years when depressive symptoms are more commonly observed.

The researchers also found that including sex-specific brain-development patterns improved the accuracy of models predicting depressive symptoms at age 13. This suggests that future prevention research should consider not only when support is introduced, but also how risk may develop differently in boys and girls.

"What excites us about these findings is that they point us to a much earlier window than we typically look. If we can better understand how the brain develops across childhood, and how that differs between boys and girls, we may be able to support children's mental health in a more timely and meaningful way," **said Dr Chan Shi Yu, senior scientist at the A*STAR IHDP and lead author of the study**.

"Because developmental pathways can differ between the sexes, these findings highlight why a one-size-fits-all approach may overlook important early signals in boys and girls. By building on

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[1] Source: Ministry of Health, Singapore. *Whole-of-society efforts to support mental health and well-being of youths in Singapore*: https://www.moh.gov.sg/newsroom/whole-of-society-efforts-to-support-mental-health-and-well-being-of-youths-in-singapore/

Singapore's GUSTO birth cohort, future research can help clarify how sex-specific developmental patterns shape later health, bringing us closer to earlier identification, prevention, and clinical strategies that are more precisely tailored to each child's developmental trajectory," **said Assistant Professor Tan Ai Peng, principal scientist at A*STAR IHDP and Department of Diagnostic Radiology at NUS Medicine**.

Together, the findings add to growing evidence that depression does not develop in the same way for everyone. A better understanding of these early developmental pathways could help researchers explore more timely and targeted ways to support children's mental health.

Study citation

Chan, S.Y., Huang, P., Ngoh, Z.M. et al. Sex-specific neurodevelopmental pathways to depressive symptoms. Mol Psychiatry (2026). https://doi.org/10.1038/s41380-026-03576-6

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## About GUSTO

Set up in 2009, GUSTO (Growing Up in Singapore Towards healthy Outcomes) is a nationwide birth cohort study involving collaborators from KK Women's and Children's Hospital (KKH), National University Health System (NUHS), National University of Singapore (NUS), and A*STAR Institute for Human Development and Potential (A*STAR IHDP). It is a longitudinal study of Singaporean mothers and their offspring. Since its inception, the study has recruited 1,247 Singaporean pregnant women as volunteers. These volunteers are studied extensively during their pregnancy, and their offspring are closely followed up as they grow up. GUSTO aims to understand how conditions during pregnancy and early childhood may affect the mothers' and children's health, growth and development, as well as metabolic, neurodevelopmental and other conditions – all of which are of major public health and economic importance in Asia and around the globe.

The research spans across four themes, where the results from monitoring both mother and child help in developing public health policies; clinically-valuable, testable interventions; reduce the burden of childhood obesity and non-communicable diseases, e.g. diabetes; and improve

neurodevelopmental outcomes in children. The study is supported by the National Research Foundation (NRF) under the Open Fund-Large Collaborative Grant (OF-LCG) administered by the Singapore Ministry of Health's National Medical Research Council (NMRC), and the Agency for Science, Technology and Research (A*STAR). In RIE2025, GUSTO is supported by funding from the NRF's Human Health and Potential (HHP) Domain, under the Human Potential Programme. Find out more at www.gusto.sg.

## About A*STAR Institute for Human Development and Potential

A*STAR Institute for Human Development and Potential (A*STAR IHDP) is host to a range of research activities that emphasise human potential and opportunities to improve health and well-being across the life course. We enable this through our research, as well as the support and participation of multiple ecosystem partners within and beyond A*STAR.

Through our work, we hope to enable communities and societies to be better versions of themselves, through opportunities to understand and access ladders for improved health and well-being. These include observational studies, pilot interventions, and evidence recommendations to practitioners and policy makers.

Our aim is to be a leading institute contributing to Singapore's vision to build human capital and potential, as part of the Human Health and Potential domain in RIE2025. Our strong foundational capabilities in translational research, renewed focus areas and commitment to supporting Singapore's needs in population health will help advance human potential, health and well-being. Find out more at www.a-star.edu.sg/ihdp.

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