

Low maternal thyroid hormone during pregnancy increases schizophrenia risk in offspring

21 June 2016

A study published in *Biological Psychiatry* reveals a new link between low levels of the thyroid hormone thyroxine during pregnancy and risk of schizophrenia in the offspring.

Low levels of free thyroxine in pregnant women, referred to as hypothyroxinemia, are associated with abnormalities in cognitive development similar to those in schizophrenia, a neurodevelopmental disorder. Hypothyroxinemia is also associated with [preterm birth](#), a risk factor for schizophrenia.

To determine if hypothyroxinemia is associated with schizophrenia, the study, led by senior author Dr. Alan Brown, Professor of Psychiatry Epidemiology at Columbia University Medical Center, the New York State Psychiatric Institute, and Columbia University's Mailman School of Public Health, examined thyroxine levels in archived serum samples from 1010 mothers of children with schizophrenia and 1010 matched control mothers. The sera were collected during the first and early second trimesters of pregnancy as part of the Finnish Maternity Cohort. Comprehensive Finnish registries of the population and psychiatric diagnoses provided information on case status (schizophrenia or control) among offspring of mothers corresponding to the prenatal serum samples.

The authors found that 11.8% of people with schizophrenia had a mother with hypothyroxinemia, compared with 8.6% of people without schizophrenia. The finding was statistically significant. This suggests that children of mothers with hypothyroxinemia during pregnancy have increased odds of developing schizophrenia. The association remained even after adjusting for variables strongly related to schizophrenia such as maternal psychiatric history and smoking.

First author of the study Dr. David Gyllenberg of the University of Turku, Finland, thinks the importance of this paper is that it "links the finding to an extensive literature on maternal hypothyroxinemia during gestation altering offspring brain development." Dr. Gyllenberg was a visiting scholar at Columbia University when much of the research was conducted.

Brown emphasized that "this work adds to a body of literature suggesting that maternal influences, both environmental and genetic, contribute to the risk of schizophrenia. Although replication in independent studies is required before firm conclusions can be drawn, the study was based on a national birth cohort with a large sample size, increasing the plausibility of the findings."

This study did not address the cause of this association, but did find that adjusting for preterm birth lessened the association between hypothyroxinemia and schizophrenia, suggesting that preterm birth may mediate some of the increased risk.

The authors note in the paper that the finding may not be specific to schizophrenia, and should be studied as a risk factor for other neurodevelopmental disorders as well, such as bipolar disorder and autism. The finding is expected to stimulate further studies examining how hypothyroxinemia causes neurodevelopmental abnormalities and ultimately contributes to risk of mental illnesses that arise during development.

"As rodent models of maternal hypothyroxinemia have been developed and schizophrenia is largely considered a disorder of brain development, I hope this paper can inform future animal studies examining molecular and cellular deviations that are relevant to schizophrenia," said Gyllenberg.

Dr. John Krystal, Editor of *Biological Psychiatry*, thinks the association has clinical potential for reducing risk in the offspring of mothers with low thyroxine levels. "This study identifies a preventable potential contributor to the risk for [schizophrenia](#). Maternal hypothyroidism can be easily diagnosed and effectively treated," said Krystal.

More information: David Gyllenberg et al, Hypothyroxinemia During Gestation and Offspring Schizophrenia in a National Birth Cohort, *Biological Psychiatry* (2016). DOI: [10.1016/j.biopsych.2015.06.014](https://doi.org/10.1016/j.biopsych.2015.06.014)

Provided by Elsevier

APA citation: Low maternal thyroid hormone during pregnancy increases schizophrenia risk in offspring (2016, June 21) retrieved 2 December 2022 from <https://medicalxpress.com/news/2016-06-maternal-thyroid-hormone-pregnancy-schizophrenia.html>

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