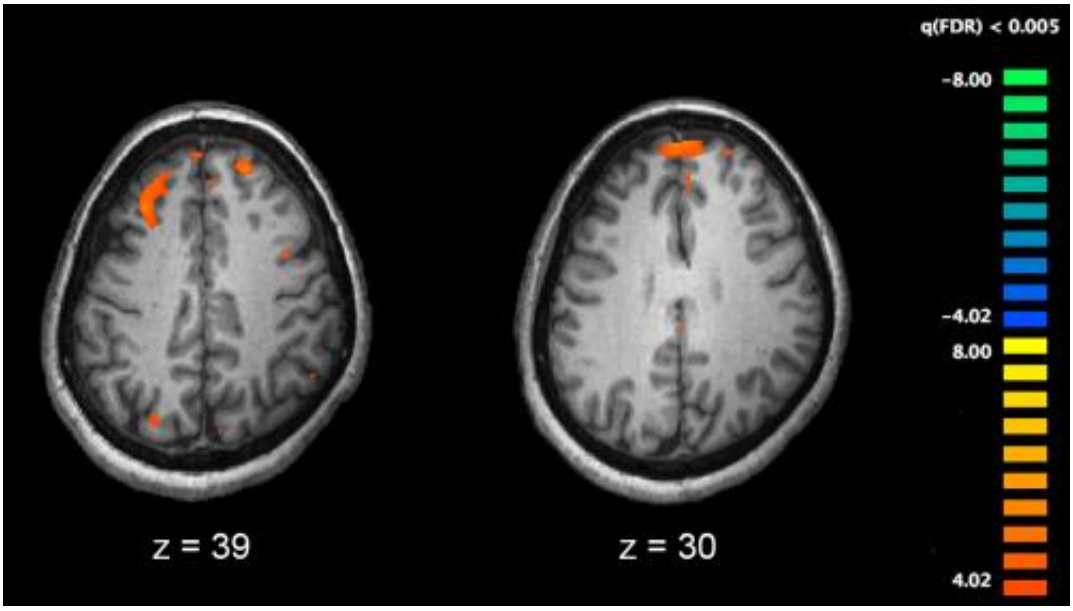
Connection found between birth size and brain disorders

September 17 2014, by Bob Yirka



Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

(Medical Xpress)—A trio of researchers has found what appears to be a clear connection between birth size and weight, and the two brain disorders, autism and schizophrenia. In their paper published in *Proceedings of the Royal Society B: Biological Sciences*, Sean Byars and

Jacobus Boomsma of the University of Copenhagen and Stephen Stearns with Yale University, describe how they found patterns in data from health records of almost 1.8 million people living in Denmark (born between 1978 and 2009) that connected the two types of brain disorders with birth weight and size.

Prior research has suggested that birth size might be somehow connected to the development of brain disorders in later life—a field of research surrounding it is known as the "Imprinted Brain Theory" where opposing outcomes in fetal development are believed to be genetically programmed by either the father or the mother to gain certain advantages. In this latest effort, the researchers sought to find concrete data that could both substantiate claims made by imprinted brain theory advocates, and the suspicion that birth weights can be correlated with brain disorders.

To find out, the team gained access to data from the medical records of 1,757,770 million people living in Denmark—they looked at baby delivery size and weight and then compared what they found to babies that grew up to develop either autism or schizophrenia. In looking at the data, the researchers report that they found a very clear correlation between high birth weight and body length, and autism. Conversely, large babies also had a lowered risk of developing schizophrenia. In a bit of a twist, they also found that the reverse was true for smaller than average babies, though not for those who were born very small (not due to an early delivery)—as a group they represent a higher risk for both disorders.

The data by the team bolsters the imprinted brain theory as it suggests male genes work to cause large babies to be born—to best carry on genes, while female genes work to suppress baby size to reduce resource needs. Also, the theory suggests that male genes work to cause the creation of autistic-like brains to take advantage of the problem solving

aspects of the disorder, while female genes work to take advantage of the types of social perceptiveness linked with schizophrenia. Furthermore, the theory suggests that autism and schizophrenia are on the opposite ends of a spectrum, and that the genes from the mother and father working against one another cause most babies to development somewhere in the middle—it's only when one or the other wins the tug-of-war, that disorders appear.

More information: Opposite risk patterns for autism and schizophrenia are associated with normal variation in birth size: phenotypic support for hypothesized diametric gene-dosage effects, *Proc. R. Soc. B* 7 November 2014 vol. 281 no. 1794 20140604, DOI: 10.1098/rspb.2014.0604

Abstract

Opposite phenotypic and behavioural traits associated with copy number variation and disruptions to imprinted genes with parent-of-origin effects have led to the hypothesis that autism and schizophrenia share molecular risk factors and pathogenic mechanisms, but a direct phenotypic comparison of how their risks covary has not been attempted. Here, we use health registry data collected on Denmark's roughly 5 million residents between 1978 and 2009 to detect opposing risks of autism and schizophrenia depending on normal variation (mean ± 1 s.d.) in adjusted birth size, which we use as a proxy for diametric gene-dosage variation in utero. Above-average-sized babies (weight, 3691–4090 g; length, 52.8–54.3 cm) had significantly higher risk for autism spectrum (AS) and significantly lower risk for schizophrenia spectrum (SS) disorders. By contrast, below-average-sized babies (2891–3290 g; 49.7–51.2 cm) had significantly lower risk for AS and significantly higher risk for SS disorders. This is the first study directly comparing autism and schizophrenia risks in the same population, and provides the first large-scale empirical support for the hypothesis that diametric gene-dosage effects contribute to these disorders. Only the kinship theory of genomic

imprinting predicts the opposing risk patterns that we discovered, suggesting that molecular research on mental disease risk would benefit from considering evolutionary theory.

Press release