New genetic evidence suggests continuum among neurodevelopmental and psychiatric disorders

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A paper published this month in the prestigious medical journal *The Lancet Neurology* suggests that a broad spectrum of developmental and psychiatric disorders, ranging from autism and intellectual disability to schizophrenia, should be conceptualized as different manifestations of a common underlying denominator, 'developmental brain dysfunction,' rather than completely independent conditions with distinct causes.

In "Developmental Brain Dysfunction: Revival and Expansion of Old Concepts Based on New Genetic Evidence," the authors make two key points:

Developmental disorders (such as autism and intellectual disability) and psychiatric disorders (such as schizophrenia and bipolar disorder), while considered clinically distinct, actually share many of the same underlying genetic causes. This is an example of 'variable expressivity'; the same genetic variant results in different clinical signs and symptoms in different individuals.

When quantitative measures of neuropsychological and neurobehavioral traits are studied instead of categorical diagnoses (which are either present or absent) and individuals are compared to their unaffected family members, it is possible to more accurately demonstrate the impact of genetic variants.

According to Andres Moreno De Luca, M.D., research scientist at the Autism and Developmental Medicine Institute at Geisinger Health System and article co-author, "Recent genetic studies conducted in thousands of individuals have shown that identical genetic mutations are shared among neurodevelopmental disorders that are thought to be clinically distinct. What we have seen over the past few years is that genetic mutations that were initially found in individuals with one disorder, such as intellectual disability or autism, are then identified in people with an apparently different condition like schizophrenia, epilepsy, or bipolar disorder".

"It turns out that the genes don't respect our diagnostic classification boundaries, but that really isn't surprising given the overlapping symptoms and frequent co-existence of neurodevelopmental disorders" said Scott M. Myers, M.D., autism specialist at Geisinger Health System and article co-author.

"We believe this study supports use of the term 'developmental brain dysfunction' or DBD, which would encompass the broad spectrum of neurodevelopmental and neuropsychiatric disorders," said David H. Ledbetter, Ph.D., executive vice president and chief scientific officer at Geisinger Health System, and article co-author. "Additionally, it is clear that diagnostic tools such as whole genome analysis for both children and their families are essential when diagnosing and treating these disorders in order to ensure the most personalized treatment."

An example used in the study was analysis of intelligence quotient (IQ) scores. The average IQ score in the general population is 100. Historically, the medical community has defined intellectual disability as an IQ of less than 70 (with concurrent deficits in adaptive functioning). But according to Dr. Ledbetter, there is little difference in the function of a child with an IQ of 69 versus 71, yet one may be diagnosed with a disability and the other may not.

"We know a variety of factors contribute to IQ score, including genetics, as a child's IQ is highly correlated with that of his or her parents and siblings. Therefore, an important factor to take into consideration when interpreting IQ is family background," said David Evans, Ph.D., professor of psychology at Bucknell University and article co-author. "Imagine if we have a child with a genetic abnormality, but the child's IQ is 85. Technically, we would not diagnose this child with a disability. However, if the family of this child has IQs around 130, we could consider that this child's genetic anomaly has 'cost' him or her 45 IQ points – a very substantial difference."

According to Dr. Myers, "One implication of this concept is that studies designed to investigate the causes and mechanisms of developmental brain dysfunction should focus on measurement of quantifiable neuropsychological and neurobehavioral traits across groups of individuals with different clinical diagnoses. Another is that whenever possible, individuals with a particular genetic variant or other risk factor should be compared to their unaffected family members, not just to population norms."

More information: www.thelancet.com/journals/lan … (13)70011-5/fulltext

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