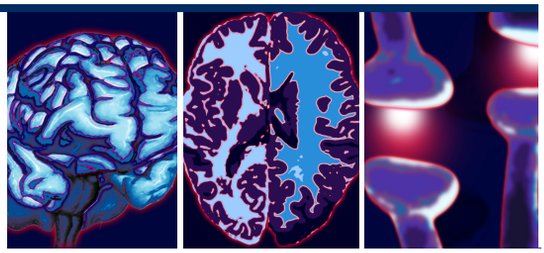
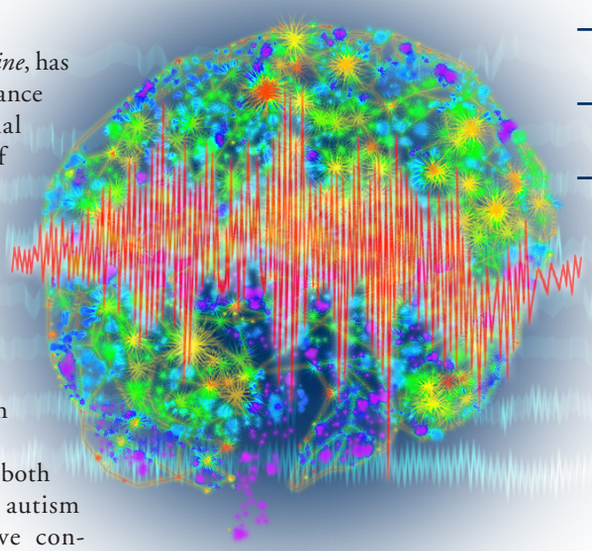


"...this joint study of tuberous sclerosis complex and autism spectrum disorder networks is described by the authors as a "unique window" to common neurobiological mechanisms in autism."

Brain connectivity differs in children with autism, EEG study suggests

Multiple redundant connections between neighboring brain areas have been found in children with autism while long-distance connections were found to be fewer in number compared with neurotypical children.



A study, published in *BMC Medicine*, has utilized network analysis to advance our understanding of functional connectivity in the brains of children with autism.

"This study 'zooms out' and looks at the brain's network performance as a whole," clarified Jurriaan Peters from the Department of Neurology at Boston Children's Hospital (MA, USA), in correspondence with *Neuropsychiatry*.

Multiple lines of evidence in both syndromic and nonsyndromic autism spectrum disorder (ASD) have converged onto a model that portrays ASD as a developmental disconnection syndrome. To help fill the gap in knowledge regarding the effects of abnormal connectivity on network properties in syndromic ASD, the investigators looked at brain functional networks of EEG connectivity and computed graphical measures, as well as conducting a resilience analysis. The researchers distinguished the effects related to ASD from those related to tuberous sclerosis complex (TSC) by applying a two-way analysis of covariance.

Sixteen children with classic autism and 14 children in whom autism is part of a genetic syndrome known as TSC were enrolled, and the team analyzed EEG recordings from each group; these were compared with readings from 46 healthy neurotypical children and 29 children with TSC but not autism, respectively.

The team found ASD- and TSC-specific differences in network properties. In TSC, the average path length was increased and this, along with other measures, indicated an altered network topology, which the authors suggest may play a role in the pathogenesis of neurological deficits.

Increased resilience, that is, the ability to find multiple ways to get between two points through redundant pathways, was seen in ASD children. "In such a network, no hub plays a specific role, and traffic may flow along many redundant routes," explained Maxime Taquet from the Boston Children's Computational Radiology Laboratory (MA, USA). This redundancy is consistent with cellular

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and molecular evidence, and indicates a brain that responds similarly to many different situations and is less able to focus on important stimuli. "It is a simpler, less specialized network that is more rigid and less able to respond to stimulation from the environment," clarified Peters, who highlighted that "altered resilience has not been described before in neurodevelopmental disorders." This resilience is thought to reflect local overconnection and reduced functional specialization. A greater proportion of short-ranging brain connections were found within one region while long-reaching connections linking disparate brain regions were less common; a pattern that is consistent with the difficulty in integrating information into higher-order concepts.

"Our findings were highly specific for ASD, regardless of etiology. This 'cross-disorder' approach both validates our findings and confirms TSC as a valid model for autism," explained Peters.

Although cautioning that the results are 'preliminary', this joint study of TSC and ASD networks is described by the authors as a "unique window" to common neurobiological mechanisms in autism. "What we found may well change the way we look at the brains of autistic children," concluded Peters optimistically. Supported by a NIH Autism Center of Excellence Grant, Peters and his colleagues are planning to repeat the analysis as part of a 'multicenter endeavor', to "collect prospective EEG, neuroimaging, genetic and neuropsychological data for better prediction of neurological outcome in TSC – and to identify early biomarkers of autism and epilepsy."

Sources: Peters JM, Taquet M, Vega C *et al.* Brain functional networks in syndromic and non-syndromic autism: a graph theoretical study of EEG connectivity. *BMC Med.* 11(1), 54 (2013); Medical News Today. Brain connections differ in kids with autism: www.medicalnewstoday.com/articles/256968.php

Researchers call for better healthcare transition services for youth with autism spectrum disorder

"However, once youth age into adulthood, we stop thinking about how to help them address their medical needs and the new challenges they are facing. Similar to educational, vocational or social transitioning, healthcare transition services are necessary to help individuals with autism spectrum disorder function independently."

Researchers from the University of Missouri (MO, USA) have conducted a study concluding that youth with autism spectrum disorder (ASD) experience disproportionately poor access to healthcare transition (HCT) services when they outgrow pediatric care. The authors recommend that the medical community develop HCT services for individuals with ASD to help ensure consistent and coordinated care, and increase their independence and quality of life.

To increase knowledge about accessibility to services for youth with ASD, the investigators examined the receipt of HCT services in youth with ASD compared with young people with other special healthcare needs (OSHCNs) by using the 2005–2006 National Survey of Children with Special Health Care Needs. Logistic regression analyses explored whether individual, family or health system factors were associated with receipt of HCT services in these young people aged 12–17 years.

"This is the first study to examine the rate in which youth with ASD receive HCT services. Our findings bring to light an important disparity in access to necessary care," explained Nancy Cheak-Zamora, lead author of the study from the Department of Health Sciences at the University of Missouri in correspondence with *Neuropsychiatry*.

In contrast to the 50% of youth with OSHCNs who received HCT

Autism spectrum disorder and four other psychiatric disorders may share genetic link

One of the largest genetic studies analyzing psychiatric illness, published recently in the *Lancet*, demonstrates that specific single nucleotide polymorphisms (SNPs) are associated with a range of psychiatric disorders. This finding, together with the variation found in calcium channel activity genes, which are thought to have pleiotropic effects on psychopathology, suggests that attempts should be made to move beyond descriptive syndromes in psychiatry.

In this study, the Cross-Disorder Group of the Psychiatric Genomics Consortium attempted to delineate the specific variants underlying genetic effects shared by several psychiatric disorders and align current diagnostic categories with recent genetic findings.

Genome-wide SNP data were analyzed in a cohort of 33,332 cases and 27,888 controls in order to characterize allelic effects on each of the five disorders: autism spectrum disorder; ADHD; bipolar disorder; major depressive disorder; and schizophrenia. Pathway analyses were used to establish the biological associations underlying genetic overlap in these disorders.

"This analysis provides the first genome-wide evidence that individual and aggregate molecular genetic risk factors are shared between five childhood- or adult-onset psychiatric disorders that are treated as distinct categories in clinical practice," highlighted Jordan Smoller, a lead author of the study from Massachusetts General Hospital (MA, USA).

Four risk gene mutation positions were found that have significant and similar associations with all five diseases mentioned previously; these include regions on chromosomes 3p21 and 10q24, as well as SNPs in two genes that help to control the flow of calcium in the brain.

"Our results provide new evidence that may inform a move beyond descriptive syndromes in psychiatry and towards classification based on underlying causes. These findings are particularly relevant in view of the imminent revision of classifications in the DSM and the International Classification of Diseases," explained Smoller.

The hope is that this study will contribute to future classification systems that may be based on biological pathogenic factors that are crucial for the identification of suitable treatments.

Source: Cross-Disorder Group of the Psychiatric Genomics Consortium. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *Lancet* doi:10.1016/S0140–6736(12)62129–1 (2013) (Epub ahead of print).

"Our results provide new evidence that may inform a move beyond descriptive syndromes in psychiatry and towards classification based on underlying causes."

services, under a quarter of youth with ASD used such services. In an attempt to explain why the discrepancy exists, it was found that only 14% of youth with ASD discussed transitioning to an adult provider with their pediatrician, under a quarter discussed health insurance retention and just under half discussed adult healthcare needs or were encouraged to take appropriate action.

"The healthcare community is doing a great job [at] getting young people with ASD into therapies," said Cheak-Zamora, who continued, "However, once youth age into adulthood, we stop thinking about how to help them address their medical needs and the new challenges they are facing. Similar to educational, vocational or social transitioning, HCT services are necessary to help individuals with ASD function independently."

Having a developmental disability or other comorbid conditions as well as ASD was found to be a strong predictor of HCT, as was as quality of healthcare. By contrast, demographic and family variables accounted for little variance. "Youth with comorbid conditions are at greatest risk for poor access to HCT services and increased quality of care has a positive effect," clarified Cheak-Zamora in correspondence with Neuropsychiatry. When asked about the most prominent findings, Cheak-Zamora explained, "We knew that on average 40% of youth with OSHCNs receive HCT services but it was very surprising to find that youth with ASD receive these services half as often as youth with other special healthcare needs."

As "our healthcare system is currently unprepared to treat" the needs of adults with ASD, "Research is needed to understand barriers to care and develop policy and practice guidelines tailored for youth with ASD," concluded Cheak-Zamora.

Source: Cheak-Zamora NC, Yang X, Farmer JE, Clark M. Disparities in transition planning for youth with autism spectrum disorder. *Pediatrics* 131(3), 447–454 (2013).

Autism risk may be reduced by maternal folic acid use

A study published in *JAMA* presents support for prenatal folic acid supplements: in the cohort studied, using prenatal folic acid supplements around the time of conception was associated with a lower risk of autistic disorder in children.

Folic acid is the synthetic form of folate, both of which play vital roles in cell production. It is known that prenatal folic acid supplements reduce the risk of neural tube defects in children; however, it is not yet known if this translates to other neurodevelopmental disorders. Such findings have lead to the obligatory fortification of flour with folic acid in several countries, and folic acid is also recommended as a supplement for women who are planning to become pregnant. The researchers examined the association between maternal use of prenatal folic acid supplements and subsequent risk of autism spectrum disorder (ASD) in their offspring.

The cohort of 85,176 children was derived from the population-based, prospective Norwegian Mother and Child Cohort Study, which followed children born between 2002 and 2008 to the end of March 2012. The team was predominantly interested in folic acid use from 4 weeks before to 8 weeks after conception, and relative risks of ASD were estimated through analyses that adjusted for maternal education level, year of birth and parity.

> "The idea that a nutritional supplement may reduce the risk of autistic disorder deserves future work..."

At the end of follow-up, 270 children had been diagnosed with ASD. Of these, 114 were diagnosed with autistic disorder, 56 with Asperger's syndrome and 100 with pervasive developmental disorder not otherwise specified. Of the cohort whose mothers had taken folic acid, 0.10% had autistic disorder compared with 0.21% of children who had not been exposed to folic acid. No such association with autistic disorder has been demonstrated with prenatal fish oil supplements.

The idea that a nutritional supplement may reduce the risk of autistic disorder deserves future research and should be confirmed in other populations.

Source: Surén P, Roth C, Bresnahan M *et al.* Association between maternal use of folic acid supplements and risk of autism spectrum disorders in children. *JAMA* 309(6), 570–577 (2013).

– All stories written by Sarah Freeston

About the News

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