Research Brief

A SUMMARY OF A PUBLISHED ARTICLE

Brain differences in fragile X are detectable by six months of age

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THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL and THE INFANT IMAGING STUDY NETWORK (IBIS)

UNC School of Medicine researchers used MRIs and computer models to show that babies who develop the neurodevelopmental condition fragile X syndrome have less white matter circuitry compared to other babies.

April 4, 2018. Mark Derewicz, University of North Carolina Healthcare

CHAPEL HILL, NC – For the first time, UNC School of Medicine researchers have used MRIs to show that babies with fragile X syndrome had less-developed white matter compared to infants that did not develop the condition. White matter is in the under layer of the brain, beneath gray matter, and it contains signal transmitters that connect regions of the brain. Brain regions need to communicate to carry out actions and behavior. The researchers imaged various sections of white matter from different angles to determine which pathways are affected in fragile X.

Early Detection

The study, published in *JAMA Psychiatry*, shows that there are brain differences related to fragile X syndrome established well before a diagnosis is typically made at age three or later.

"It's our hope that earlier diagnosis and intervention will help children with fragile X and their families," said co-first author Meghan Swanson, PhD, postdoctoral research fellow at the Carolina Institute for Developmental Disabilities at the UNC School of Medicine. "We also hope that this knowledge might inform drug development research."

So far, drug clinical trials have failed to demonstrate change in treatment targets in individuals with fragile X. One of the challenges has been identifying good treatment outcome measures or biomarkers that show response to intervention.

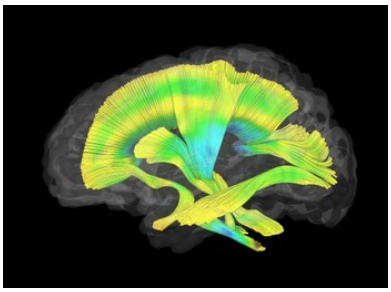
"One of the exciting things about our findings is that the white matter differences we observe could be used as an objective, quantifiable physiological marker to evaluate treatment effectiveness," said co-senior author Heather C. Hazlett, PhD, assistant professor of psychiatry at the UNC School of Medicine.

Participants and Methods

For this study, Swanson, Hazlett, and colleagues imaged the brains of 27 infants who went on to be diagnosed with fragile X and 73 who did not develop the condition. The researchers focused on 19 white matter fiber tracts in the brain. Fiber tracts are bundles of myelinated axons – the long parts of neurons that extend across the brain or throughout the nervous system. Think of bundles of cables laid across the brain. These bundles of axons connect various parts of the brain so that neurons can rapidly communicate with each other. This communication is essential, especially for proper neurodevelopment during childhood.

Results

Imaging and analytical analysis showed significant differences in the development of 12 of 19 fiber tracts in babies with fragile X from as early as six months of age. The babies who wound up being diagnosed with fragile X had significantly less-developed fiber tracts in various parts of the brain. This diminished connectivity impacts language, cognitive skills, memory and repetitive movements, among other things. White matter changes rapidly in infancy and continues to change into adulthood. This suggests that white matter could be a target for intervention throughout the lifespan.



This image shows all of the white matter fiber tracts investigated in this study. (courtesy of Meghan Swanson, PhD)

"These results substantiate what other researchers have shown in animal models – the essential role of fragile X gene expression on early development of white matter in babies," said co-first author Jason Wolff, PhD, former postdoctoral fellow at UNC-Chapel Hill and now assistant professor of educational psychology at the University of Minnesota. "Our work highlights that white matter circuitry is a potentially promising and measurable target for early intervention. However, achieving the goal of infant intervention for fragile X would likely require expanded newborn screening efforts."

Other Authors

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