CENTER ON HUMAN DEVELOPMENT & DISABILITY
UNIVERSITY of WASHINGTON

CHDD Outlook 2013 Issue #5
News from the Center on Human Development and Disability at the University of Washington Health Sciences Center

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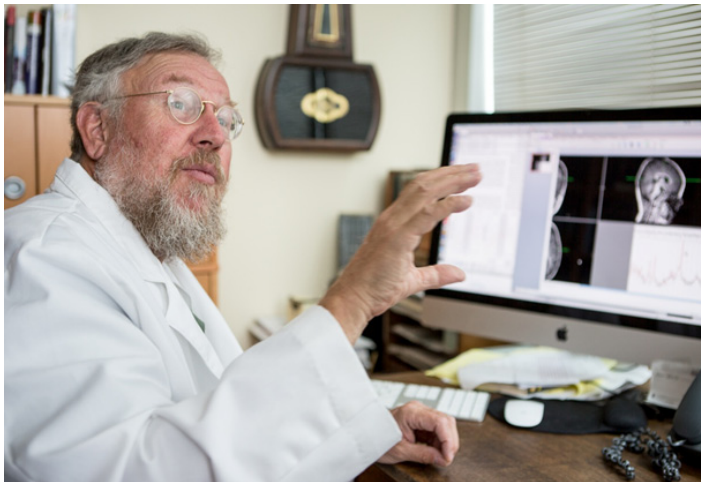
Brain Imaging and Autism

by Sally James



Stephen Dager's research includes the study of brain chemistry changes and the effects across important developmental periods in young children.

Using sophisticated magnetic resonance imaging techniques, researchers for the first time have been able to identify developmental patterns of chemical changes in the brains of children diagnosed with autism that differ from patterns observed in the brains of typically developing children and in children with developmental delays. "We found a very distinct longitudinal pattern of brain chemical alterations that changed over time, studying children with autism between 3 and 10 years of age," explained Stephen Dager, M.D. Dager is a professor of radiology and adjunct professor of bioengineering, and a research affiliate and associate director at the Center on Human Development and Disability (CHDD). Part of the excitement generated by these findings is that this exploration may help unravel mechanisms that underlie how autism unfolds in the developing brain and what differentiates it from developmental delays.

These research findings were published recently in JAMA Psychiatry. This published work is part of a long-term program of research known as the Neuroimaging of Autism project that Dager has led for 15 years, and which is funded by the National Institutes of Health. Collaborator Annette Estes, Ph.D., director of the Autism Center, also based at the CHDD, led the diagnostic team that assessed the original group of 45 children with autism. The team studied chemical patterns in the brains of those children at three ages: 3 to 4, 6 to 7, and 9 to 10 years. More than half the original group remained for the entire length of the study. The chemistry changes observed in the children between 3-10 years of age is thought to reflect downstream effects of a developmental alteration that occurs earlier in their lives.

Brain chemical measures provide insights into brain development, as well as brain metabolism and function. Some of the most important chemicals investigated were N-acetylaspartate, choline, creatine, myo-inositol and a combined measure of glutamine and glutamate. Several of these, in particular N-acetylaspartate, (NAA), measured at very low levels in the children with autism, as

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> *Dr. Stephen Dager*

well in as the children with developmental delays at 3-4 years of age. Progressive normalization of the altered chemistry occurred in the children with autism, but less so for children with developmental delays, reaching similar levels as measured in typically developing children by 9-10 year of age. NAA is believed to play multiple roles in brain development and homeostasis, in particular by promoting connections between neurons and myelinization. The myelin sheath plays an essential role in helping the conductivity of neurons. "We found a pattern [in autism] of early chemical alterations at the cellular level that over time resolved – a pattern similar to what others have observed in adults during recovery from a closed-head injury," Dager noted.

Following the same group of children over time is a researcher's dream, Dager said, because the team is able to witness changes in anatomy and in brain chemistry across important developmental periods. The imaging findings provided a unique window into how the disorder arises. "We are currently investigating whether much earlier chemical alterations occur that could influence the normal pattern of brain development in infants who go on to develop autism," Dager explained. In hopes of identifying even earlier changes, the team is now working with infants, starting at between 3 and 6 months of age, some at high risk of developing autism because of an older sibling with the disorder. In this study, Dager and Estes' team will be characterizing very early brain chemical changes as the infants develop. "We may have caught the tail end of a process that began earlier," Dager said. Could these chemical patterns lead to a biomarker that helps predict outcomes for children on the autism spectrum? Dager and Estes expressed hope for such a tool.

"If we can use these findings to help identify young children at particular risk and maximize their potential through earlier, targeted intervention, that would be a great gift," Dager said. Children diagnosed with autism can have extremely variable abilities and outcomes by the time they are adults. Some may be non-verbal whereas others may be highly verbal, sometimes having special skills or abilities, just to give one example. If patterns of brain chemical alterations could ultimately help to better define young children's potential, it would help families and clinicians to better focus available resources.

This study involved a wide range of interdisciplinary researchers including the UW Departments of Radiology, Speech and Hearing Sciences, Psychiatry and Behavioral Sciences, Anesthesiology, and Bioengineering.

CHDD is an interdisciplinary center dedicated to the prevention and amelioration of developmental disabilities through research, training, clinical service, and community outreach. CHDD includes the University Center of Excellence in Developmental Disabilities and the Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center.

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Center on Human Development and Disability, University of Washington, Box 357920, Seattle, Washington 98195-7920

For more information please contact us at chdd@uw.edu