New Insights into Developmental Abnormalities in Autism

Philadelphia, PA, October 23, 2007 – Autism research is a high priority in the medical community and three new studies being published in the upcoming November 1st issue of Biological Psychiatry add to the expanding insight into the developmental abnormalities associated with autism. Autism is the most severe condition in a group of developmental disorders known as the autism spectrum disorders (ASDs). It is characterized by impaired social interaction, problems with verbal and nonverbal communication, and unusual, repetitive, or severely limited activities and interests. Estimates provided by the National Institutes of Health indicate that three to six children out of every 1,000 will have an ASD and males are four times more likely to be diagnosed than females.

In the first study, Sacco and colleagues report that large head circumference in autistic patients is part of a generalized excessive body growth. “It has been known for quite some time that many autistic children display larger head sizes compared to same-age, same-sex unaffected individuals,” according to Dr. Antonio Persico, lead author on the project. He adds, “These results clearly indicate that autism is not simply ‘inside your head’, but instead affects the entire body.” The authors were also surprised to find that these results were significantly correlated with a history of allergies both in the patient and in his/her first-degree relatives. Dr. Persico explains that “allergies or immune disorders are much more frequent among autistic children with greater-than-normal body size (and even among their non-autistic parents and siblings), than in autistic children with normal or reduced body size.” This finding potentially links large head circumference in autism to an early immune system abnormality.
In the second article, Hobbs and colleagues compared standard measurements of head and body size in fetal ultrasound reports from children who were later diagnosed with autism with control ultrasounds (i.e., children who were not diagnosed with autism). Dr. Janet Lainhart, the senior author, reveals the impetus behind their study: “There is substantial evidence that the developmental neuropathology of autism begins before birth in at least some cases. Because autism is not diagnosed until after birth, fetal development in children who go on to develop autism has not [yet] been examined.” Their results suggest a subtle disturbance in the uniformity of fetal brain growth in autism, but fetal head circumference is not abnormal, indicating enlarged head circumference occurs later in the developmental cycle. Dr. Lainhart notes that “this report opens up an entirely new area of research applicable not only to autism but also to other neurodevelopmental psychiatric disorders.” Of this study, noted autism expert and Deputy Editor of Biological Psychiatry, Daniel Geschwind, M.D., Ph.D., comments that “this is the first study of any kind of prenatal development in children with autism and thus will likely serve as a landmark in the field.”

In the third investigation, Tsuchiya and colleagues state that “accumulating evidence suggests that the immune system plays a role in the pathophysiology of autism.” Thus, they investigated the serum levels of a particular molecule, called PECAM-1, in subjects with high-functioning autism as compared to those in normal subjects. These molecules play a key role in the immune response of the central nervous system, and they found that the serum levels were significantly lower in the autistic group. Dr. Kenji Hashimoto, the head author, also notes that they found “a negative correlation between serum levels of PECAM-1 and head circumference at birth in the autistic subjects.” In other words, the more “normal” (i.e., higher) the serum level of PECAM-1, the more “normal” (i.e., smaller) the head circumference at birth. Thus, alterations in immune function may be related to head size in autism.

John H. Krystal, M.D., Editor of Biological Psychiatry and affiliated with both Yale University School of Medicine and the VA Connecticut Healthcare System, comments, “We are accustomed to think of the development of the brain in isolation from the development of the body and yet many factors that regulate brain development also regulate the development of the body. Together, these studies point to a complex group of neural mechanisms that might be altering the development of brain and body in
autism." Dr. Geschwind summarizes: "These studies add to a growing body of knowledge documenting the biomedical aspects of autism spectrum disorders, areas that extend far beyond behavioral or even cognitive measures. We now need to extend these types of investigations to larger populations to understand their co-occurences with other features of this very heterogeneous disorder."

Notes to Editors:
The first article is “Clinical, Morphological, and Biochemical Correlates of Head Circumference in Autism” by Roberto Sacco, Roberto Militteri, Alessandro Froli, Carmela Bravaccio, Antonella Gritti, Maurizio Elia, Paolo Curatolo, Barbara Manzi, Simona Trillo, Carlo Lenti, Monica Saccani, Cindy Schneider, Raun Melmed, Karl-Ludvig Reichelt, Tiziana Pascucci, Stefano Puglisi-Allegra and Antonio M. Persico. Drs. Sacco and Persico are from the Laboratory of Molecular Psychiatry and Neurogenetics, University "Campus Bio-Medico" and I.R.C.C.S. “Fondazione Santa Lucia” in Rome, Italy. Drs. Militteri, Froli, and Gritti are affiliated with the Department of Child Neuropsychiatry, II University of Naples in Naples, Italy. Dr. Bravaccio is with the Department of Child Neuropsychiatry, University "Federico II" in Naples, Italy. Dr. Elia is from the Unit of Neurology and Clinical Neurophysiopathology, I.R.C.C.S. “Oasi Maria S.S.”, Troina, EN, Italy. Drs. Curatolo and Manzi are with the Department of Child Neuropsychiatry, University of “Tor Vergata” in Rome, Italy. Dr. Trillo is affiliated with ASL RM/B, Rome, Italy. Drs. Lenti and Saccani are with the Department of Child Neuropsychiatry at the University of Milan, Milan, Italy. Dr. Schneider is with the Center of Autism Research and Education, while Dr. Melmed is from the Southwest Autism Research and Resource Center, both in Phoenix, Arizona. Dr. Reichelt is with the Department of Pediatric Research, Rikshospitalet, University of Oslo, Norway. Drs. Pascucci and Puglisi-Allegra are affiliated with the Department of Psychology, University “La Sapienza” and I.R.C.C.S. “Fondazione Santa Lucia” in Rome, Italy. This work was supported by the National Alliance for Autism Research (Princeton, New Jersey), the Fondation Jerome Lejeune (Paris, France), the Cure Autism Now Foundation (Los Angeles, California), and Telethon-Italy (GGP02019), and is largely the product of the Italian Society for Autism
Research and Training (www.sirfa.org), a network of scientists and clinicians working together since 1997.

The second article is “A Retrospective Fetal Ultrasound Study of Brain Size in Autism” by Kyle Hobbs, Anne Kennedy, Molly DuBray, Erin D. Bigler, P. Brent Petersen, William McMahon and Janet E. Lainhart. Mr. Hobbs and Drs. McMahon and Lainhart are with the School of Medicine. Drs. Kennedy and Bigler are from the Department of Radiology. Drs. Bigler, McMahon and Lainhart are also affiliated with the Department of Psychiatry, and The Brain Institute. Ms. DuBray and also Dr. Lainhart are with the Interdepartmental Program in Neuroscience. All above-listed affiliations are at the University of Utah, Salt Lake City, Utah. Dr. Bigler is also with the Departments of Psychology and Neuroscience at Brigham Young University in Provo, Utah. Dr. Petersen is from the Carmen B. Pingree School for Children with Autism, Salt Lake City, Utah. This work was supported by the National Institutes of Child Health and Human Development (NICHD, Grant U19 HD35476), the NICHD Collaborative Programs of Excellence in Autism, the National Institutes of Health/Department of Health and Human Services Short-Term Training: Students in Health Professional Schools (Grant 5 T35 HL007744) (KH) and a Neuroscience Training Grant (MD). Additional financial aid in-kind support for this work was provided by Valley Mental Health and the Utah Autism Foundation.

The third article is “Decreased Serum Levels of Platelet-Endothelial Adhesion Molecule (PECAM-1) in Subjects with High-Functioning Autism: A Negative Correlation with Head Circumference at Birth” by Kenji J. Tsuchiya, Kenji Hashimoto, Yasuhide Iwata, Masatsugu Tsujii, Yoshimoto Sekine, Genichi Sugihara, Hideo Matsuazaki, Shiro Suda, Masayoshi Kawai, Kazuhiko Nakamura, Yoshio Minabe, Atsuko Yagi, Masaomi Iyo, Nori Takei and Norio Mori. Drs. Tsuchiya, Iwata, Sekine, Sugihara, Matsuazaki, Suda, Kawai, Nakamura, Minabe, Yagi, Takei, and Mori are affiliated with the Department of Psychiatry and Neurology, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan. Dr. Hashimoto is with the Division of Clinical Neuroscience, Chiba University Center for Forensic Mental Health, Chiba, Japan. Dr. Tsujii is from the Faculty of Sociology, Chukyo University, Toyota, Aichi, Japan. Dr. Iyo is with the Department of Psychiatry, Chiba University Graduate School of Medicine, Chiba, Japan. Dr. Takei is also with the Division of Psychological Medicine, Institute of Psychiatry, London, UK.

Full text of the article mentioned above is available upon request. Contact Jayne M. Dawkins at (215) 239-3674 or ja.dawkins@elsevier.com to obtain a copy or to schedule an interview.

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