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Carnegie Mellon and University of Pittsburgh Scientists Discover Biological Basis for Autism

PITTSBURGH—A team of brain scientists at Carnegie Mellon University and the University of Pittsburgh have made a groundbreaking discovery into the biological basis for autism, a mysterious brain disorder that impairs verbal and non-verbal communications and social interactions.

Using functional magnetic resonance imaging (fMRI) scans, the researchers have found numerous abnormalities in the activity of brains of people with normal IQs who have autism. The new findings indicate a deficiency in the coordination among brain areas. The results converge with previous findings of white matter abnormalities in autism. (White matter consists of the "cables" that connect the various parts of the brain to each other). The new findings led the researchers to propose a new theory of the basis of autism, called underconnectivity theory, which holds that autism is a system-wide brain disorder that limits the coordination and integration among brain areas. This theory helps explain a paradox of autism: Some people with autism have normal or even superior skills in some areas, while many other types of thinking are disordered. The team's study will be published in the August edition of the British journal *Brain* and is available online at www.brain.oupjournals.org.

In explaining the theory, Marcel Just, one of the study's lead authors and director of Carnegie Mellon's Center for Cognitive Brain Imaging, compared the brain of a normal person to a sports team in which the members cooperate and coordinate their efforts. In an autistic person, though some "players" may be highly skilled, they do not work effectively as a team, thus impairing an autistic's ability to complete broad intellectual tasks. Because this type of coordination is critical to complex thinking and social interaction, a wide range of behaviors are affected in autism.

The research team believes these are the first findings in autism of differences in the brain activation patterns in a cognitive (non-social) task. The study produced two important new findings that help make sense of previous mysteries: The autistic participants had an opposite distribution of activation (compared to the control group) in the brain's two main language areas, known as Broca's and

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Wernicke's areas. There was also less synchronization of activation among key brain areas in the autistic participants compared to the control group.

To obtain technically acceptable fMRI data from high-functioning autistic participants, the researchers flew in people with autism from all over the eastern United States. High-functioning participants with autism (with IQ scores in the normal range) are rare, accounting for about 10 percent of all people with autism. Using non-invasive fMRIs, the team looked at the brains of 17 people with autism and 17 control subjects as they read and indicated their comprehension of English sentences. In both the healthy brains and in the brains with autism, language functions were carried out by a similar network of brain areas, but in the autism brains the network was less synchronized, and an integrating center in the network, Broca's area, was much less active. However, another center, Wernicke's area, which does the processing of individual words, was more active in the autism brains.

The brain likely adapts to the diminished inter-area communication in autism by developing more independent, free-standing abilities in each brain center. That is, abnormalities in the brain's white matter communication cables could lead to adaptations in the gray matter computing centers. This sometimes translates into enhanced free-standing abilities or superior ability in a localized skill.

These findings provide a new way for scientists and medical researchers to think about the neurological basis of autism, treating it as a distributed system-wide disorder rather than trying to find a localized region or particular place in the brain where autism lives. The theory suggests new research to determine the causes of the underconnectivity and ways to treat it. If underconnectivity is the problem, then a cognitive behavioral therapy might be developed to stimulate the development of connections in these higher order systems, focusing on the emergence of conceptual connections, interpretive language and so on. Eventually, pharmacological or genetic interventions will be developed to stimulate the growth of this circuitry once the developmental neurobiology and genetics of these brain connections are clearly defined by research studies such as these.

The research team is jointly headed by Just, the D.O. Hebb Professor of Psychology at Carnegie Mellon, and Dr. Nancy Minshew, professor of psychiatry and neurology at the University of Pittsburgh School of Medicine and director of its Center for Autism Research. Individuals with High Functioning Autism and Asperger's Syndrome between 10 and 55 years of age who are interested in participating in similar studies can send email to autismrecruiter@upmc.edu or call Nikole Jones at 412-246-5481.