

**Written Testimony of
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House Government Reform Subcommittee on Human Rights & Wellness
September 8, 2004**

"Thank you for this opportunity to tell you about significant advances in understanding the neural basis of this enigmatic and tragic disorder called autism. I come before you with pride that an arm of my government is motivated by compassion to seek the advances of medical science in understanding this disorder. I am going to describe some of the new findings from my research center and others that together paint a different picture of autism than the one we had even 10 years ago. With the help of federal and private funding, significant new inroads have been made.

This statement is written in language that I hope every educated layman can understand. It includes a little bit of technical information, but no more than the information we have about how our cars or our computers work. We need to understand how the brain works, and what it is that is disordered in autism. Armed with this knowledge, we can see how to approach the problem of autism right now, in terms of new types of therapies, and we can see how to target the next iteration of research so that we can approach a cure.

I am going to tell you my punch line right now. Autism doesn't live in one particular part of the brain. Rather, it is a neural systems disorder. The disorder is the result of underdevelopment of the connectivity among different brain areas. In modern computer terms, the problem isn't with this microchip or that microchip, but with the network connectivity among processing centers or chips.

This oversimplified metaphor goes a long way to explain the basic enigma of autism. The metaphor explains how it is possible that intelligent people with autism can have some well-developed skills, but can still be very unlike unaffected people in terms of their thinking and interpersonal abilities, and still have considerable difficulty living an independent life.

Here is a picture of the problem in microcosm. One of the areas in which people with autism (at least those with IQ's in the normal range) do as well as and sometimes better than controls is in word reading. The perception of single words is enhanced. The capacity to pronounce them, spell them, define them is superior to other children of their age and IQ. You may find children with autism or Asperger's syndrome competing successfully in spelling bees. Yet at the same time, if you ask people with autism to follow some complicated instructions e.g. comprehend a complex sentence, they do worse than their control group. So the enigma is, how can people with autism be better than average in word reading, but worse than average at understanding complicated sentences?

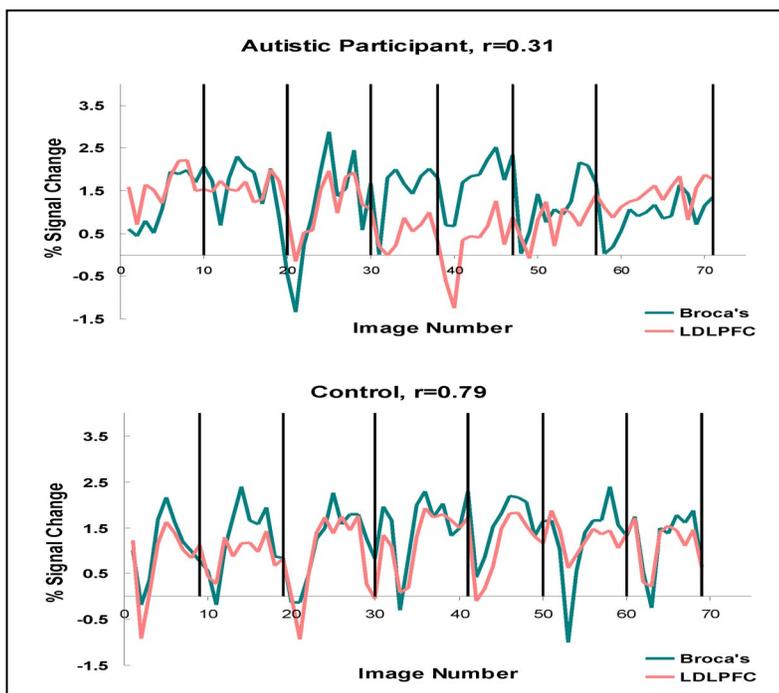
That last question was one that we were able to answer with a brain imaging study. My colleagues and I, particularly Dr. Nancy Minshew, tested a group of 17 adults with autism who had IQ's in the normal range, and compared their brain activity with a group

of matched control subjects. The task we asked them to perform was to read a sentence like "The farmer was followed by the parent" and then answer a question like "Who was doing the following, the farmer or the parent?" They did this while they were lying in an MRI scanner and reading the sentence on a projector screen in the scanner. We measured their brain activity (using functional MRI) literally measuring the oxygen concentration in every part of their brain every 3 seconds. By seeing where the oxygen was going, we can tell which parts of the brain are at work and how hard they are working.

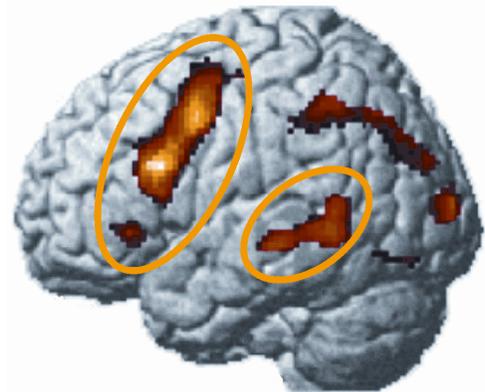
There were 4 absolutely fascinating and unexpected results, all converging on the same new theory.

First, the autism group had less activation in Broca's area (a sentence integration area, in the leftmost oval) than the control group and more in Wernicke's area (a word processing area, in the rightmost oval). The people with autism are doing less integrative thinking and are focusing more on the words in isolation (Just et al., 2004).

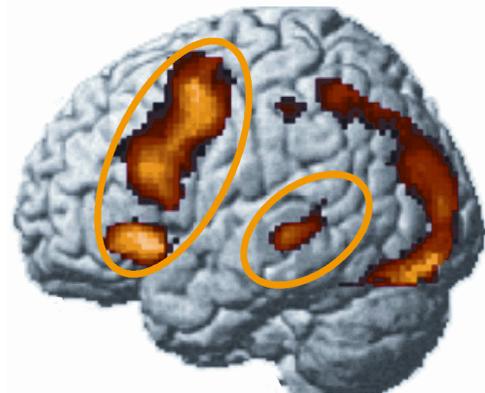
Second, the brain activity was less synchronized between various brain areas in the adults with autism. For the control subjects, the activity in one brain area went up and down at the same time as in another brain area. The areas were more synchronized, or better coordinated. The figure below shows that the red and green lines (activity levels in two brain areas) track each other considerably less well in the person with autism as indicated by the r value.



a. Autism Group



b. Control Group



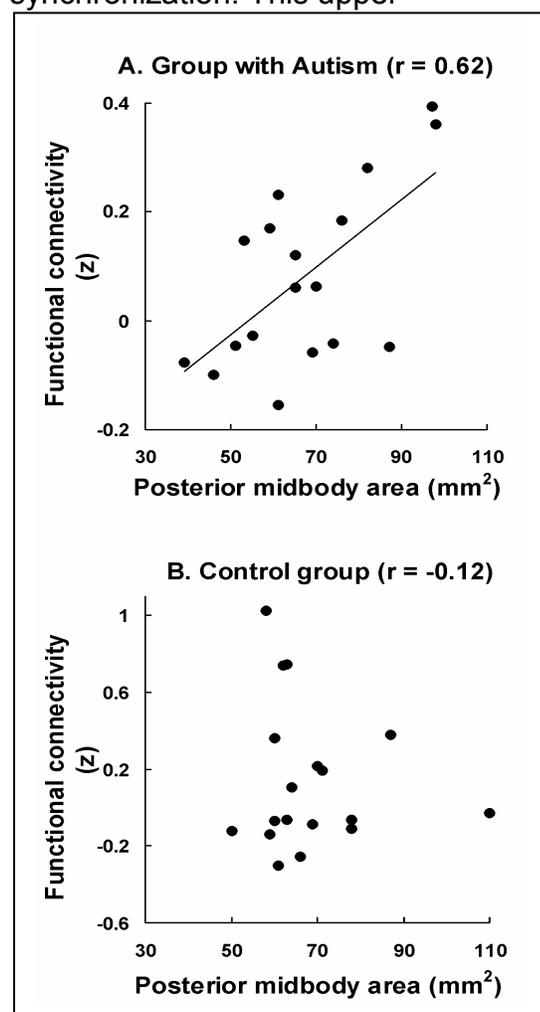
Third, one of the major fiber tracts in the brain connecting the left and right side of the brain was slightly smaller in the people with autism. This fiber tract is called the corpus callosum. It doesn't do any processing itself but it does connect the different brain areas of the brain that do the processing. Martha Herbert and her colleagues (2004) have reported similar abnormalities of the cabling (white matter) in autism. It is the white matter of the brain that is thought to cause the brain in autism to grow too large in early childhood at the time of onset of symptoms.

Fourth, the size of the corpus callosum was correlated with how synchronized the brain areas in the left and right hemisphere were. The diameter of this cable -the corpus callosum - was correlated with the amount of synchronization of the two brain areas that it connected. The smaller it was, the lower the degree of synchronization. This upper scatterplot shows the correlation, where functional connectivity is the measure of synchronization. The lower scatterplot shows that in the control group, which had a larger corpus callosum, there was no relation between the size of the cable portion and the amount of synchronization.

All four of the above findings point to the same conclusion: underconnectivity of brain areas in autism.

There is additional evidence which I have not shown you to support this underconnectivity conclusion. For example, the findings have been obtained not just in a language task, but also in a problem-solving task, and a social task, thus occurring in all three of the main symptom domains of autism. The theory also predicts that information transfer between brain regions will be reduced and a study requiring formation of a visual image from a verbal description has demonstrated this to prediction to be true. Also, the theory predicts particular difficulty in multitasking in autism, even in cases where each of the two tasks can be performed perfectly well by itself, but is much more poorly performed than by controls in a multitasking situation (Garcia-Villamizar et al., 2002). The reason that difficulties are greater in multitasking is that executing two concurrent tasks requires an especially large amount of inter-area coordination, and underconnectivity makes such a multi-tasking much more challenging.

The new findings aren't just scientific esoterica to be buried in a journal. They provide the basis for developing new therapies that attempt to minimize or overcome the problems of underconnectivity. The new results also help set the sights for the next round of research, to find out why brain connections aren't developing normally, and what genetic or pharmacological interventions might help remediate this problem.



I came here to show you the scientific ledgers from our laboratories, not the financial ledgers. But at the end of the day, both ledgers have to balance. The current level of federal funding has enabled us to come this far, and now is the time to accelerate, not to slow down. We are now more sure than ever that we are on the right road, and our target is clearer. Federally supported research centers like the NICHD Collaborative Programs of Excellence in Autism (CPEA's) as well as others are leading the charge. Your continued and increasing support is essential to make this vital journey reach its destination, to use the power of science and medicine in the service of innocent victims of autism and their families. We also wish to express our tremendous appreciation of the individuals who have participated in our studies. We wish to encourage others to do so as the pace of progress is only as fast as the numbers of individuals who volunteer. The importance of normal controls cannot be under-emphasized.

Thank you for your interest in this area of medical research science. With your help, we can continue to make critical new advances in the field of autism research that will change peoples' lives."

References

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