MRI study: Does the amygdala shrink in autistic individuals with severe social deficits?

The amygdala, a brain region involved in fear recognition, may shrink in severely-affected autistic individuals, according to a new study.

Richard Davidson and colleagues used magnetic resonance imaging (MRI) and eye-tracking technology to study 28 males with autism spectrum disorders (ASD), ranging in age from 8 to 25, and 26 controls. The researchers asked participants to identify happy, angry, or sad facial expressions in pictures of faces.

Autistic participants with small amygdala volumes took longer than other participants to identify the expressions in the pictures, and spent less time looking at the eyes of subjects in the pictures compared to other facial areas. Those with the smallest amygdala volumes, the researchers report, took 40% longer to perform the emotion-recognition task than those with the largest volumes. In addition, ASD participants with the largest amygdala sizes looked at the eyes in the pictures four times longer than those with the smallest. (Amygdala size was not linked to gaze fixation in non-disabled controls.) Group comparisons showed that amygdala size increased early in autistic subjects with normal eye fixation, but increased only a small amount in those with poor eye fixation. Smaller amygdala size also correlated with severe non-verbal social impairment in childhood for ASD subjects.

These findings build on earlier research by the same team, showing that the amygdala is over-active in autistic individuals during eye-gazing. In addition, the new findings may offer an explanation for differing findings reported by studies measuring amygdala size in autism.

These studies appear to be contradictory, with some reporting enlargement, others reporting abnormally small size, and still others showing no differences between non-disabled and autistic subjects. Davidson and colleagues suggest that in autistic individuals, the amygdala first attempts to compensate for chronic stress by becoming hyperactive, with the toxic effects of this chronic over-activation eventually causing cell death and atrophy. According to their theory, autistic children who are the least stressed by social interaction would experience slower amygdala shrinkage than those with higher stress levels.

Studying siblings of autistic individuals, the researchers found that non-autistic siblings show a similar pattern of smaller amygdala size and reduced eye fixation when looking at faces. However, while autistic participants exhibited less activation of the fusiform gyrus (a face-processing area) on both sides of the brain during this task, siblings showed reduced activation on only one side. Also, eye fixation time and amygdala activation were not linked in the siblings, indicating that looking at faces is not a negative experience for them. These findings, the researchers say, suggest an "intermediate pattern" in siblings of autistic children.

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"Amygdala volume and nonverbal social impairment in adolescent and adult males with autism," B. M. Nacewicz, K. M. Dalton, T. Johnstone, M. T. Long, E. M. McAuliff, T. R. Oakes, A. L. Alexander, and R. J. Davidson, *Archives of General Psychiatry*, Vol. 63, No. 12, December 2006, 1417-28. Address: rjdavids@wisc.edu.

Pycnogenol effective for ADHD, increases glutathione levels

Pycnogenol, an extract from the bark of the maritime pine tree, is frequently used to treat symptoms of attention deficit hyperactivity disorder (ADHD). A new study by German and Slovakian researchers indicates that the substance is effective, and a separate report from the same research group suggests one reason for pycnogenol's effects: it increases levels of glutathione, a potent antioxidant.

The second finding is highly relevant to autism because research increasingly implicates reduced levels of glutathione as a factor in autism spectrum disorders. Glutathione helps to protect against oxidative stress (damage caused to cells by rogue molecules called free radicals), a process strongly linked to autism.

In the first, study, a double-blind, placebo-controlled trial, J. Trebaticka and colleagues studied the effects of pycnogenol on 61 children (50 boys and 11 girls) with ADHD. They report, "Results show that one month [of] pycnogenol administration caused a significant reduction of hyperactivity, [and] improved attention and visual-motoric coordination and concentration of children with ADHD."

In a study published separately, the researchers measured levels of active and inactive glutathione in the treated children. The researchers found that after pycnogenol administration, levels of active glutathione increased markedly and the ratio of reduced (active) to oxidized (inactive) glutathione improved. Total antioxidant status was initially low in the ADHD group but normalized in those taking pycnogenol.

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"Treatment of ADHD with French maritime pine bark extract, Pycnogenol," J. Trebaticka, S. Kopasova, Z. Hradecna, K. Cinovsky,I. Skodacek, J. Suba, J. Muchova, I. Zitnanova, I. Waczulikova, P. Rohdewald, and Z. Durackova, *European Child and Adolescent Psychiatry*, Vol. 15, No. 6, September 2006, 329-35. Address: J. Trebaticka, Department of Child Psychiatry, Child University Hospital, Faculty of Medicine, Comenius University, Limbova 1833 40 Bratislava, Slovakia.

—and—

"The effect of polyphenolic extract from pine bark, Pycnogenol, on the level of glutathione in children suffering from attention deficit hyperactivity disorder (ADHD)," M. Dvorakova, M. Sivonova, J. Trebaticka, I. Skodacek, I. Waczulikova, J. Muchova, and Z. Durackova, *Redox Report*, Vol. 11, No. 4, 2006, 163-72. Address: M. Dvorakova, Department of Medical Chemistry, Biochemistry and Clinical Biochemistry, Faculty of Medicine, Comenius University, Bratislava, Slovakia.

Galantamine reduces autistic children's behavior problems

Galantamine, a substance extracted from a flowering plant called the snowdrop (and marketed both as a nutrient and as a drug under the name Reminyl), can significantly reduce symptoms of autism, according to a new study.

Rob Nicolson and colleagues administered galantamine for 12 weeks to 13 autistic children in an open-label trial. Parents rated the children monthly using two behavioral scales, and a physician rated them using two different scales.

The researchers report, "Patients showed a significant reduction in parent-rated irritability and social withdrawal on the Aberrant Behavior Checklist as well as significant improvements in emotional lability and inattention on the Conners' Parent Rating Scale-Revised. Similarly, clinician ratings showed reductions in the anger subscale of the Children's Psychiatric Rating Scale." Eight of the children were judged to be responders on the Clinical Global Impressions scale.

The researchers suggest that galantamine may be particularly beneficial for autistic children who exhibit aggression, out-of-control behavior, and inattention. They note that while galantamine's effects in this study were more modest than the effects of risperidone (one of the most common drug treatments for autism), galantamine—unlike risperidone— appears to have few significant side effects. In the current study, only two children experienced side effects (headaches in one case, and digestive upset in another).

The findings are consistent with those of an earlier study by Helmut Niederhofer et al. (see ARRI 16/4), which found that galantamine was at least moderately effective in reducing the behavior problems of autistic children who did not respond to other medications.

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"A prospective, open-label trial of galantamine in autistic disorder," R. Nicolson, B. Craven-Thuss, and J. Smith, *Journal of Child and Adolescent Psychopharmacology*, Vol. 16, No. 5, October 2006. Address: Rob Nicolson, 800 Commissioners Road East, E2-601, London, Ontario, Canada N6C-2V5, rnicolso@uwo.ca.