Mirror neurons again implicated in autism

New evidence implicating malfunctioning "mirror neurons" as a factor in autism was reported in December by Mirella Dapretto and colleagues.

Scientists first identified mirror neurons—sometimes called "monkey see, monkey do" neurons—in macaques. Research showed that these neurons are activated both when a monkey sees another monkey performing an act, and when the monkey performs the act itself. Since then, studies have revealed the existence of a similar system in humans. involving in particular the pars opercularis in the inferior frontal gyrus.

Recently (see ARRI 19/1), Lindsay Oberman and colleagues used EEGs to analyze mirror neuron activity in high-functioning autistic males and nondisabled controls. The researchers found evidence that mirror neurons in the autistic subjects fired only when they themselves performed an act, and not when they watched others doing the same action.

In the new study, Mirella Dapretto and colleagues used functional magnetic resonance imaging (fMRI) to measure the brain activity of 10 high-functioning autistic children and 10 nondisabled controls. When the researchers asked the children to imitate the emotions displayed in pictures, both groups of children could perform the tasks—but unlike the controls, Dapretto and colleagues say, "children with autism showed no mirror neuron activity in the inferior frontal gyrus (pars opercularis)." In agreement with the researchers' speculation that mirror neurons communicate with the limbic system (a region of the brain involved in emotional responses) via an area of the cerebral cortex known as the insula, autistic individuals also showed reduced activity in both the insula and the periamygdaloid region of the limbic system.

Noting that autistic individuals are impaired in understanding the emotions of others, the researchers theorized that deficits in the mirror neuron system should occur not just during imitation, but also during simple observation of others. As predicted, their control subjects showed stronger activation of the right pars opercularis when observing facial expressions than did the autistic group. The difference was not due to a failure of the autistic group to pay attention to the facial expressions, as the autistic children showed normal activation in brain regions associated with face processing.

Moreover, Dapretto and colleagues report that in autistic subjects, greater levels of activity in the pars opercularis correlated with higher levels of social ability. Greater activity in the insula and limbic structures

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Essential fatty acids: more strong evidence of benefits

British researchers recently reported that children with developmental coordination disorder improve remarkably when treated with essential fatty acids (EFAs) (see ARRI 19/1). Other new studies indicate that EFAs can strongly benefit children with autism or attention deficit hyperactivity disorder (ADHD), could be helpful in cases of intractable epilepsy, and can markedly improve cognition in people without disabilities. Among recent findings:

—Kalpana Joshi and colleagues administered supplements of flax oil to 30 children with ADHD. Flax oil is high in the fatty acid alpha linolenic acid (ALA), which is a precursor to the essential fatty acid docosahexaenoic acid (DHA). The children received flax oil supplementation corresponding to 200 mg ALA content, as well as 25 mg of vitamin C twice per day. (Vitamin C is an antioxidant that can inhibit harmful peroxidation of fatty acids.)

The researchers report that levels of red blood cell membrane fatty acids rose significantly in treated children, and that "there was significant improvement in the symptoms of ADHD reflected by reduction in total hyperactivity scores of ADHD children derived from ADHD rating scales." The children showed highly significant reductions in impulsivity, restlessness, inattention, self-control problems, and psychosomatic problems, as well as improvements in social functioning and learning. All children completed the study, and none experienced any side effects.

—Louise Patrick and Ronald Salik treated 18 children with autism or Asperger syndrome, ranging in age from 3 to 10, with essential fatty acids derived from fish oil and borage oil. Total daily dosage consisted of 247 mg of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and 40 mg of gamma-linolenic acid (GLA), as well as 27 I.U. of vitamin E. The researchers evaluated the subjects at baseline and after 45 and 90 days of treatment, using 49 items from the Assessment of Basic Language and Learning Skills (ABLLS) test. They report that all of the children displayed significant increases in language and learning skills, although two parents withdrew their children from the study due to increased activity.

—Alan Yuen and colleagues administered 1 gram of EPA and 0.7 gram of DHA for 12 weeks to 57 patients with epilepsy. The researchers report that the patients experienced fewer seizures during the first six weeks of therapy, but the effects did not last over the full course of the study. Yuen et al. say larger studies are needed to investigate the effects of different omega-3 fatty acid preparations, different doses, and longer treatment duration. *(Editor's note: Researchers in Israel, who asked patients with epilepsy to use a dietary spread containing high levels of omega-3 fatty acids, did see long-term reductions in seizure frequency and strength—see ARRI 16/3.)*

—A team of Italian researchers headed by Giuliano Fontani gave 33 healthy adults supplemental omega-3 fatty acids (4 grams of fish oil per day) for 35 days, while administering a placebo (olive oil) to 16 control subjects. The researchers report that omega-3 supplementation was "associated with an improvement of attentional and physiological functions, particularly those involving complex cortical processing." Subjects also showed a marked increase in vigor and decreased levels of anger, anxiety, fatigue, depression, and confusion. No subjects reported adverse effects.

> Patrick and Salik report that all children completing a trial of essentail fatty acid supplementation displayed significant increases in language and learning skills.

Their findings and those of other researchers, Fontani and colleagues say, "strengthen the hypothesis of a direct action of omega-3 fatty acids on the central nervous system." This effect, they say, most likely stems from these acids' protective effects on the structure and function of cell membranes, and consequent modulation of nerve cell signaling.

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"Supplementation with flax oil and vitamin C improves the outcome of attention deficit hyperactivity disorder (ADHD)," Kalpana Joshi, Sagar Lad, Mrudula Kale, Bhushan Patwardhan, Sahebrao P. Mahadik, Bindu Patni, Arti Chaudhary, Sheila Bhave, and Anand Pandit, *Prostaglandins, Leukotrienes and Essential Fatty Acids*, November 25, 2005 (epub ahead of print publication). Address: Kalpana Joshi, Interdisciplinary School of Health Sciences (ISHS), University of Pune, Ganeshkhind, Pune-411007, Maharashtra, India, kalpana@unipune.ernet.in.

—and—

"The effect of essential fatty acid supplementation on language development and learning skills in autism and Asperger's syndrome," Louise Patrick and Ronald Salik, *Autism/Asperger's Digest*, January/February 2005.

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"Omega-3 fatty acid supplementation in patients with chronic epilepsy: a randomized trial," A. W. Yuen, J. W. Sander, D. Fluegel, P. N. Patsalos, G. S. Bell, T. Johnson, and M. J. Koepp, *Epilepsy and Behavior*, Vol. 7, No 2, September 2005, 253-8. Address: A. W. Yuen, Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London WC1N 3BG, U.K.

—and—

"Cognitive and physiological effects of omega-3 polyunsaturated fatty acid supplementation in healthy subjects," G. Fontani, F. Corradeschi, A. Felici, F. Alfatti, S. Migliorini, and L. Lodi, *European Journal of Clinical Investigation*, Vol. 35, 2005, 691-9. Address: Giuliano Fontani, Dipartimento di Fisiologia, Sezione di Neuroscienze e Fisiologia Applicata, Universita di Siena, Via A. Moro 3, I-53100, Siena, Italy, fontanig@unisi.it.