Biomedical Update:

More research points to melatonin

The tiny cone-shaped pineal gland, located deep within the brain, secretes a substance called melatonin. This hormone, released in larger amounts during dark hours than light hours, is involved in regulating circadian rhythms—patterns of activity associated with day and night, such as sleeping—and may play a role in emotions and in the development of psychiatric disorders.

Several Japanese researchers have suggested that autistic children's odd sleep-wake cycles might be a symptom of melatonin abnormalities. More recently, U.S. researchers Ronald Chamberlain and Barbara Herman suggested that over-secretion of melatonin may cause autism, by starting a "cascade of biochemical effects" leading to abnormal levels of serotonin and opioids. (High levels of serotonin, one of the brain's messenger chemicals, are common in autistic children, and many researchers believe abnormal levels of opioids—natural opium-like chemicals in the body—also play a role in the disorder.)

Now, Edward Ritvo and colleagues offer more evidence linking melatonin abnormalities to autism. The researchers studied concentrations of melatonin in overnight and first-voiding urine samples of 10 autistic individuals, 25 relatives of people with autism, and 10 non-disabled controls with no family history of autism. The researchers say that while nocturnal melatonin production was similar for all groups, "melatonin production by people with autism, some of their parents and some of their unaffected sibs appeared to persist into the daylight hours." Extended daylight secretion of melatonin, they say, is "most unusual."

The researchers caution that nighttime light exposure and bedtime hours, both of which can affect melatonin production, were not controlled for in their study.

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"Elevated daytime melatonin concentrations in autism: a pilot study," Edward R. Ritvo, Riva Ritvo, Arthur Yuwiler, Ann Brothers, B.J. Freeman and Selma Plotkin; *European Child and Adolescent Psychiatry*, Vol. 2, Issue 2, April 1993, pp. 75-78. Address: Edward Ritvo, Dept. of Psychiatry, UC Los Angeles, 760 Westwood Plaza, Los Angeles, CA 90024.

Autism and tuberous sclerosis

When a family has more than one child with autism—or has a young autistic child with epilepsy—doctors should consider the possibility of tuberous sclerosis (TSC), a new report by Ann Hunt and Charles Shepherd recommends.

Hunt and Shepherd say that of 21 children ages 3-11 with tuberous sclerosis they located in a previous study, five (three boys and two girls) had autism and and four others had symptoms of pervasive developmental disorder (similar to autism, but less severe). All four of the children with symptoms of PDD were girls.

"Tuberous sclerosis could be a significant cause of autism and pervasive developmental disorders," the researchers say, "particularly in girls." Early diagnosis of TSC in affected autistic children is important, they say, since TSC is a dominant genetic disorder.

Tuberous sclerosis occurs when a defective protein disrupts cell differentiation and migration, causing abnormal tissue growths in the brain and other organs. Symptoms include epilepsy, mental retardation (in some but not all cases), socially impaired behavior and overactivity. Symptoms can range from severe to almost undetectable.

The researchers note that outward symptoms of TSC, which include a red facial rash, white skin patches, cafe au lait spots and other skin lesions, may not be readily apparent in young children. Seizures are not always present in autistic children with TSC either, they say; two of the girls with autism and TSC in this study had not had seizures for many years.

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"A prevalence study of autism in tuberous sclerosis," Ann Hunt and Charles Shepherd, *Journal of Autism and Developmental Disorders*, Vol. 23, No. 2, 1993, pp. 323-339. Address: Ann Hunt, Section of Child and Adolescent Psychiatry, University of Oxford, Park Hospital for Children, Old Road, Headington, Oxford OX3 7LQ, England.

Autism/allergy link supported by French study

A new report by French researchers adds support to studies showing that some cases of autism may be caused or exacerbated by sensitivities to foods or other allergens.

B. Bidet et al. used the Human Basophil Degranulation test, which is designed to detect immediate hypersensitivity at the cellular level, to test 10 autistic subjects and 10 control subjects (four non-disabled controls and six with depressive disorder). The five allergens tested for were mites, grass pollens, milk, egg, and wheat flour.

The researchers report that among the 10 patients with autism tested, seven exhibited at least one positive test toward mites or pollen, and five toward at least one food allergen. Only one control subject reacted to mites, and none reacted to food allergens. Their results, they say, "should lead to further studies on the relationship between allergy and autism," and to increased testing of the effects of allergen-free diets for autistic individuals.

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"Allergic sensitization in infantile autism" (letter), B. Bidet, M. Leboyer, B. Descours, M.P. Bouvard, and J. Benveniste, *Journal of Autism and Developmental Disorders*, Vol. 23, No. 2, June 1993, pp. 419-420.

Parietal defects reported

Eric Courchesne and colleagues, who first identified defects of the cerebellum in autistic individuals using magnetic resonance imaging (MRI), now report that MRI scans also reveal parietal lobe abnormalities in many individuals with autism.

The parietal lobe is one of four lobes into which each hemisphere of the cerebrum is divided. It is involved in sensing temperature, touch, pressure and pain, and in understanding speech and using words to express feelings and thoughts.

Courchesne et al. performed MRI scans on 21 individuals with autism, excluding subjects with severe mental retardation, cerebral palsy, epilepsy, other known neurologic disease, or Fragile X syndrome. The scans were randomly mixed with scans of three control groups (including normal subjects and those with other neurological disorders), and were reviewed by a neuroradiologist blind to the diagnosis of the subjects. The MRIs revealed that:

—the parietal lobes were abnormal in appearance in nine (43%) of autistic subjects.

—Seven subjects showed evidence of cortical volume loss in the parietal lobes, extending in some cases into the adjacent cerebral lobes. Three had white matter volume loss.

—Two autistic subjects showed thinning of the corpus callosum, a strip of nerve fibers that connects the two hemispheres of the brain.

No abnormalities were seen in the normal control subjects. The controls with neurologic abnormalities had various abnormalities consistent with their disorders but did not show any patterns similar to those seen in the autistic subjects.

The subjects whose MRIs showed parietal abnormalities performed poorly on the Posner test—a visual spatial attention test which is difficult for people with parietal lobe damage—while those with no evidence of defects performed normally.

Defects of the parietal lobes, the researchers say, could be a secondary effect of defects of the cerebellum. Researchers believe the cerebellum may play a critical role in the process whereby cells in the cerebral cortex develop and become specialized. Earlier MRI studies by Courchesne, as well as post mortem studies by Margaret Bauman and Thomas Kemper, revealed that the cerebellum is frequently abnormal in autism, and that, in particular, the number of certain cerebellar cells (Purkinje cells) is reduced. Abnormal output from these cells in the cerebellum, Courchesne et al. speculate, could lead to aberrant development of cells in the parietal lobes.

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"Parietal lobe abnormalities detected with MR in patients with infantile autism," Eric Courchesne, Gary A. Press, and Rachel Yeung-Courchesne; *AJR*, 1993, 160:387-393. Address: Eric Courchesne, Dept. of Neurosciences, School of Medicine, University of California, San Diego, La Jolla, CA 92093.