

# Fetal Testosterone Theory of Autism Gathering Steam

BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE INTERNATIONAL CONGRESS OF THE ROYAL COLLEGE OF PSYCHIATRISTS

EDINBURGH — Why should being male so markedly increase the likelihood of ending up with a diagnosis of an autism spectrum condition?

One explanation gaining increased traction as a result of multiple converging lines of evidence is the fetal testosterone theory of autism, Simon Baron-Cohen, Ph.D., said in the annual Blake Marsh Lecture at the meeting.

Dr. Baron-Cohen is the principal architect of the theory, which asserts that autism is linked to in utero exposure to very high levels of testosterone, with resultant extreme masculinization of the



**The number of autistic traits a child displayed was positively correlated with fetal testosterone level, independent of sex.**

DR. BARON-COHEN

brain and mind. In other words, autism can be thought of as a case of “extreme male brain.”

“I think that this hormone—testosterone—at the fetal stage of development, and the genes that regulate it, may be part of the story.

“I don’t suggest that it’s all of the story because autism is complex and multifactorial. But this may be one of the factors to look at more carefully,” said Dr. Baron-Cohen, professor of developmental psychopathology and director of the autism research center at the University of Cambridge (England).

The prevalence of autism spectrum conditions in the general population is about 1%. Classic autism has a male to female ratio of 4:1, whereas in Asperger’s syndrome it is 9:1.

Fetal testosterone levels are on average twice as high in males as in females. But levels vary up to 20-fold among male fetuses, he said.

Dr. Baron-Cohen and coworkers are conducting a landmark, ongoing, longitudinal study of 235 typically developing children whose fetal testosterone levels are known because their mothers underwent amniocentesis.

In a recent report, the investigators had parents rate their children for autistic traits at age 8 years using the Childhood Autism Spectrum Test and the Autism Quotient—Children’s Version.

They found that the number of autistic traits that a child displayed was positively correlated with fetal testosterone level, independent of sex (Br. J. Psychol. 2009; 100:1-22).

The hallmarks of autism spectrum conditions are social and communication difficulties, narrow interests, and extreme

need for routine. Those characteristics can be viewed as extreme manifestations of inherently male interests and behaviors. In studies of spontaneous toy choice that have been replicated hundreds of times throughout the world, psychologists have shown that, given a choice, young boys will more often choose to play with toy vehicles and constructional toys such as Legos, whereas girls tend to be drawn more to dolls and emotional stories about them, Dr. Baron-Cohen said.

“On average, males’ attention is more easily drawn to systems of one kind or another, and on average females’ attention is more easily drawn to people and their emotional lives,” he continued.

These two psychological processes—empathy and systematizing—show clear sex differences in the population.

In other studies of the 8-year-olds with known fetal testosterone values, those with higher fetal testosterone scored lower on several different tests of empathy and higher on tests of systematizing and attention to detail than did children with lower fetal testosterone.

Earlier studies of this cohort demonstrated that at age 12 months, those with higher in utero testosterone were less likely to make eye contact with their mothers, and at age 2 years their vocabulary and language development were more limited than in the kids with lower fetal testosterone.

In other studies, Dr. Baron-Cohen’s group, as well as other investigators, have shown that typically developing girls score higher than boys on tests of the cognitive aspects of empathy, and individuals with Asperger’s syndrome score lower than either of the other groups.

Exactly the opposite was seen on psychological tests of systematizing and attention to detail.

Could these gender differences in interests and behavior simply be the result of cultural influences, such as social pressure on boys to become firemen and engineers and on girls to become nurses and elementary school teachers?

Dr. Baron-Cohen doesn’t think so. He and his coworkers addressed this issue in a study of 24-hour-old babies. They placed two objects, one at a time, in the babies’ hospital rooms: an image of a human face and a mechanical mobile. Then they filmed how long the babies looked at each. The girls tended to look longer at the face, whereas the boys were drawn to the mobile.

Another line of evidence supporting the fetal testosterone theory of autism comes from genetic studies done by Dr. Baron-Cohen’s group.

They found that patients with Asperger’s syndrome showed differences from controls in a set of more than a dozen sex steroid genes known to regulate testosterone production or be involved in sex hormone transport.

Dr. Baron-Cohen’s studies are funded by the U.K. Medical Research Council. He declared no financial conflicts. ■

# Insomnia Diagnosed Almost 30% of Time by Child Psychs

BY ROBERT FINN

PUBLISHED ONLINE IN ADDICTIVE BEHAVIORS

Child psychiatrists report that nearly a third of the children they see in a typical month have insomnia as a major problem, according to a survey completed by 1,273 members of the American Academy of Child and Adolescent Psychiatry.

Virtually all (96.4%) of the respondents said that they prescribed at least one type of prescription drug for insomnia during a typical month, and 88.3% reported recommending at least one over-the-counter medication, wrote Dr. Judith A. Owens of Brown University in Providence, R.I., and her colleagues.

The study was published online (Sleep Med. 2010[doi:10.1016/j.sleep.2009.11.015]).

Psychiatrists estimated that they treated insomnia with medications for 29% of the 13- to 18-year-old patients, 25% of the 6- to 12-year-olds, 17% of the 3- to 5-year-olds, and 3.5% of those aged 2 years and younger.

The relationship between medication use for insomnia and the child’s age was statistically significant.

Among nonprescription medications, antihistamines were the most commonly recommended, followed by melatonin, herbals such as chamomile tea, and pain-reliever combinations such as Tylenol PM.

This order of preference was the same regardless of the patient’s diagnosis.

Among prescription medications, on the other hand, significant differences were found in medication preferences depending on the patient’s diagnosis. For children with attention-deficit/hyperactivity disorder (ADHD), 81% of psychiatrists prescribed an alpha-agonist such as clonidine, compared with 67% who prescribed an alpha-agonist for mental retardation/developmental delay (MR/DD) and autism spectrum disorders, 40% who prescribed a drug in this class for anxiety disorders, and 31% who prescribed it for mood disorders. The differences were statistically significant.

Child psychiatrists frequently used antidepressants—particularly sedating antidepressants—for insomnia, especially in patients with anxiety and mood disorders. Among the respondents, 85% said they used sedating antidepressants for insomnia in children with mood disorders, 82% used them

in anxiety disorders, 76% in MR/DD and autism, and 71% in ADHD.

Slightly more than half of child psychiatrists (51%-52%) used atypical antipsychotics for insomnia in children with mood disorders or with MR/DD and autism. In contrast, only 33%-34% used atypical antipsychotics in children with ADHD or anxiety disorders.

Short-acting hypnotics were the choice of 42% of child psychiatrists treating children with mood disorders and 41% of those treating children with anxiety disorders. Child psychiatrists were significantly less likely to use short-acting hypnotics for children with MR/DD and autism (21%) or ADHD (18%).

Investigators sent the eight-page survey to 6,091 listed members of the American Academy of Child and Adolescent Psychiatry in the fall of 2003, with a reminder 1 month later to nonrespondents. In all, 1,601 sur-

## VITALS

**Major Finding:** Child psychiatrists report that insomnia is a major problem for 28% of the patients they see in a typical month. In a typical month, 96% of respondents recommended a prescription medication, and 88% recommended an over-the-counter medication.

**Data Source:** Surveys completed by 1,273 child psychiatrists during a 6-month period beginning in the fall of 2003.

**Disclosures:** The study was supported by an unrestricted grant from Sanofi-Aventis. The investigators disclosed that none of them received a salary or other compensation for this work.

veys (26.3%) were returned, but only 1,273 (20.9%) were usable.

Psychiatrists with a greater number of years in practice were significantly less likely than their less experienced colleagues to prescribe medication for insomnia for patients in most categories.

Similarly, psychiatrists with an academic appointment at a medical school were significantly less likely to recommend medication than were psychiatrists in community settings.

The investigators noted that few well-designed, controlled studies have been published on the use of medications for insomnia in children.

This lack of information on efficacy, tolerability, dosing, and safety in children, “significantly hampers the rational clinical use of these medications in child psychiatry clinical practice,” they wrote.

“Clinical trials of these drugs are needed to establish effective dosing ranges, to address safety and tolerability issues, to assess withdrawal and discontinuation effects, and to determine the relative efficacy in terms of sleep induction and maintenance.” ■