For Conduct Disorder, It's Nature *and* Nurture

Any search for genetic risk factors in psychiatric illnesses must consider environmental exposures.

BY BRUCE JANCIN
Denver Bureau

ASPEN, COLO. — A large twin registry study has replicated the findings of an earlier landmark New Zealand study showing that polymorphisms of the monoamine oxidase A gene modify the risk of antisocial behavior in boys exposed to familial adversity, Robert Emde, M.D., said at a psychiatry conference sponsored by the University of Colorado.

"These are impressive studies. They indicate our genetic influences get reordered depending on the environmental circumstances we're exposed to," observed Dr. Emde, professor of psychiatry and director of the program for early developmental studies at the university in Denver.

The confirmatory work comes from the Virginia Twin Study of Adolescent Behavioral Development, in which Debra L. Foley, Ph.D., and her associates at Virginia Commonwealth University in Richmond reported on 514 male twins aged 8-17 years in the registry (Arch. Gen. Psychiatry 2004; 61:738-44).

All of the twins were genotyped as to their functional polymorphisms of the MAO-A gene and assessed for conduct disorder. The boys and their parents were interviewed regarding the presence or absence of familial adversity as defined by a history of known risk factors for conduct disorder: interparental violence, parental neglect, and inconsistent discipline.

The prevalence of conduct disorder among the boys was 11.5%. The prevalence of any of the low-activity MAO-A alleles previously linked to antisocial behavior was 29.4%. Inconsistent parental discipline was part of the upbringing of 17.3% of the boys, exposure to interparental violence occurred in 2.5%, and parental neglect in 12.6%.

As expected, each of the three familial adversities was independently associated with increased risk of conduct disorder in the boys. The key finding was that a low-activity MAO-A allele was also significantly associated with increased risk of developing conduct disorder, but only in the presence of an adverse childhood environment. A low-activity MAO-A genotype in the absence of familial adversity didn't confer significantly increased risk.

Dr. Emde noted that these findings agree with the Dunedin Multidisciplinary Health and Development Study, a prospective study of 1,037 children born in Dunedin, New Zealand, between April 1972 and March 1973. Only 12% of Dunedin males had both a low-activity MAO-A allele and a prospectively documented history of childhood maltreatment, but they accounted for 44% of court convictions for violent offenses through age 26 years among male study participants, he said at the conference, also sponsored by the Colorado Psychiatric Society and the Denver Institute for Psychoanalysis.

The Virginia and Dunedin studies 'indicate our genetic influences get reordered depending on the environmental circumstances we're exposed to.'

Low-activity MAO-A genotype Dunedin males with probable or severe childhood maltreatment were also 2.8-fold more likely than nonmaltreated males having the low-activity MAO-A polymorphism to be diagnosed with conduct disorder (Science 2002;297:851-4).

In Dunedin, as in the Virginia Twin Study, a low-activity MAO-A genotype in the absence of childhood adversity or maltreatment wasn't associated with significantly increased risk of being diagnosed with conduct disorder.

The Virginia investigators noted that one major implication of the consistent findings in their study and Dunedin is that the search for genetic risk factors for psychiatric disorders is likely to yield inconsistent results unless environmental exposures are also taken into account.

Frederick S. Wamboldt, M.D., said that the Dunedin and Virginia twin studies provide new insight into one of the great debates in psychiatry: the role of nature versus nurture in human development.

"It isn't really genes versus environment, it's genes and environment—but in a complex way. It's not a simple thing," said Dr. Wamboldt, head of the division of psychosocial medicine at National Jewish Medical and Research Center, Denver, and professor of medicine and of psychiatry at the University of Colorado. ■

Genetic Psychiatric Disorders Cited In Fetal Alcohol Effects Patients

BY LINDA LITTLE
Contributing Writer

GRAPEVINE, TEX. — The behavioral and cognitive defects in children with fetal alcohol effects may be partly attributable to genetic psychiatric disorders, researchers reported in a poster presentation at a meeting sponsored by the American College of Medical Genetics.

"Physicians need to ask about psychiatric and behavioral illnesses in families when diagnosing children with fetal alcohol effects [FAE]," said Helga V. Toriello, Ph.D., director of genetics services, Spectrum Health, Grand Rapids, Mich. "Acquiring a family history is important, because they suddenly may be dealing with genetic factors rather than alcohol."

While the diagnostic criteria for fetal alcohol syndrome are firm, the criteria for fetal alcohol effects are less clear and may overlap with other psychiatric and behavioral disorders, she said.

Researchers at Spectrum and DeVos Children's Hospital, also in Grand Rapids, found that 95% of children thought to have fetal alcohol effects also had psychiatric or behavioral disorders and that 89% had a first-degree relative with a psychiatric or behavioral disorder.

The study included 100 children aged 3-19 years who had been seen to determine whether they had fetal alcohol syndrome. None of the children fit the criteria for fetal alcohol syndrome and thus could be considered to have FAE.

But after conducting family histories, the researchers found a high rate of psychiatric and behavioral illnesses such as bipolar depression and attention-deficit disorder, not only in the children but in first-degree relatives.

'When we did a family history, there was a high frequency of one or both parents having a mental illness or behavioral disorder.'

"This raises the question of how much of the behavioral problems are due to psychiatric illness or alcohol exposure," she asked. "A genetic condition might be contributing to the child's behavior."

Psychiatric and behavioral problems such as depression, anxiety, bipolar disorder, and attention-deficit hyperactivity disorder are known to be highly heritable.

Additionally, there appears to be a comorbidity of alcoholism and mental illness. For example, at least 20% of those with mood or anxiety disorders also have substance abuse disorder. And at least 20% of those with substance abuse problems also have mood or anxiety disorders.

The researchers found that children with bipolar depression had split verbal and performance IQ, executive dysfunction, and attention problems—all common features also reported in children exposed to alcohol.

Also, some individuals with psychiatric and behavioral illnesses have similar characteristics as those exposed to alcohol prenatally. For example, in bipolar depression, there is sexually inappropriate behavior, anger, hyperactivity, and learning disabilities, features also found in alcohol exposure.

Dr. Toriello said the researchers are not saying that alcohol does not have an effect, but it may not be the only reason for the child's behavior. "When we did a family history, there was a high frequency of one or both parents having a mental illness or behavioral disorder. It might be that a genetic condition is contributing to the child's behavior rather than strictly alcohol exposure." ■

Trajectory of Adolescent Substance Abuse Can Begin As Early as Preschool

ASPEN, COLO. — Surveys consistently show that 90% of all youths have experimented with drugs and alcohol by the time they finish high school. Yet only a minority develop substance abuse problems, Paula D. Riggs, M.D., said at a psychiatry conference sponsored by the University of Colorado.

Convergent evidence from multiple genetic studies as well as longitudinal behavioral studies indicate that those who will go on to adolescent substance use disorder can often be identified as early as preschool, Dr. Riggs said.

The developmental trajectory that leads to adolescent substance use disorder begins in early childhood. Youngsters in substance abuse treatment programs are more likely than are their non–drug-abusing peers to have displayed a particular constellation of temperament traits as toddlers and preschoolers. This constellation consists of aggressiveness, impulsivity, poor attentiveness and persistence, and difficulty in regulating affect and behavior.

These aspects of temperament are quite heritable. In addition, the home life of affected children is often characterized by conflict and poor parental monitoring.

Without intervention, children with this pattern of difficult temperament often develop oppositional defiant disorder, learning disabilities, conduct disorder, and/or attention-deficit hyperactivity disorder by the time they enter school. They may be placed in special education classes where they associate with a deviant peer group. They become deficient in social skills and coping strategies. Eventually they turn to drugs and alcohol as their coping strategy.

If primary care physicians were to identify preschoolers who show the red-flag characteristic temperament constellation and refer them for a comprehensive psychologic assessment and evaluation, it could have a huge impact on the problem of teen substance abuse down the road. "We have early interventions that help reduce the risk of later problems," Dr. Riggs said at the conference, which was also sponsored by the Colorado Psychiatric Society and the Denver Institute for Psychoanalysis.

—Bruce Jancin