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Hormone Imbalance Linked to Behavior

By Natalie Angier

CASTING a slender ray of light on a mystifying behavioral syndrome, researchers linked an inherited defect in the body's thyroid hormone system to attention-deficit disorder, a common psychological problem in children. The work is the first to identify a specific gene associated with attention deficit difficulties, and it suggests that a fraction of children with the problem may in fact have an undiagnosed thyroid disorder.

Child psychiatrists and other experts on the behavioral problem, however, emphasized that the finding was preliminary and that it was likely to be of relevance to only a small number of the millions of children who have the attention-deficit disorder. Many researchers insisted that much work remained to be done before they would recommend that all children with an attention deficit diagnosis have their thyroid hormone levels checked. Possible Clue to Other Ills

Nevertheless, they said that any possible insight into the cause and physiology of the ailment was welcome and that an understanding of how thyroid

metabolism shapes brain development may yield clues to other neurological defects underlying other types of attention-deficit problems.

"Attention deficit is almost surely a heterogeneous disease, with a variety of causes," said Dr. Peter Hauser of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md., the main author on the new study. "But finding this gene could lead to a conceptual change in thinking about the disorder."

The report appears in the current issue of *The New England Journal of Medicine*.

About 4 percent of school-age children are thought to suffer from attention-deficit disorder, sometimes called attention deficit-hyperactivity disorder. Though symptoms vary, children with the disorder often are extremely restless, impulsive, unable to concentrate, disruptive in class and unpopular with their peers and may end up failing their schoolwork. For reasons that remain unclear, boys are eight times as likely to have the disorder as girls.

The usual treatment is a low

dose of Ritalin or similar amphetamine, sometimes combined with behavioral therapy. But amphetamines do not cure the disease, and many people continue to suffer all their lives.

In the new work, Dr. Hauser, his supervisor Dr. Bruce D. Weintraub and their co-workers discovered that children suffering from a rare familial disease, generalized resistance to thyroid hormone, also exhibit a very high rate of the attention-deficit disorder, suggesting an association.

Researchers believe that thyroid resistance is caused by an inherited defect in the gene that produces the thyroid hormone receptor, a protein studding the surface of many cells in the body. In its healthy version, the receptor responds to thyroid hormone, a molecule that helps control metabolism, heart rate and, in the growing fetus, brain development. But in those with generalized hormone resistance, the receptor seems to react sluggishly to its hormonal tweak, resulting in short stature in some cases.

In the new work, researchers now suggest that a defective receptor could cause behavioral

problems as well, perhaps by subtly interfering with normal brain development. Through structured psychiatric interviews, the scientists determined that 70 percent of the 27 children and half of the 22 adults known to have generalized hormone resistance also met the criteria for attention deficit disorder, shockingly high percentages.

But Dr. Hauser and his colleagues still have no idea how common thyroid hormone resistance is in the general population. They are now working with a newborn-screening program in New York to get a rough estimate. Generalized hormone resistance can be detected by comparing the rates of three hormones in the thyroid loop and seeing if the feedback signals between brain and endocrine system are working. Other so-called autosomal dominant diseases like general-

ized hormone resistance afflict about one in 10,000 births, but Dr. Hauser said he had no idea if the figure would apply to this disease. And without knowing the rate of hereditary hormone resistance, scientists cannot say how many cases of attention deficit-disorder may stem from thyroid problems. 'Neurologically Based'

"This is the \$1 million question now," said Dr. Alan J. Zametkin of the National Institute of Mental Health in Bethesda, another author of the new report. "If I had to guess I'd say the thyroid levels will turn out to be absolutely normal in the vast majority" of children with attention-deficit disorder.

Dr. Zametkin recently reported on another apparent defect in those with attention-deficit disorder, an abnormality in how certain regions of the brain use

glucose. The latest study, he said, "is the second bit of evidence that the disease is neurologically based, that it's not because the kids weren't brought up right, or because their teachers are not paying them enough attention."

But other researchers said that the association between hormone resistance and attention-deficit disorder may be only coincidental.

"It's an interesting hypothesis and it's something that should be followed up on," said Dr. James M. Swanson, director of the University of California Child Development Center at Irvine. "But I'm worried that parents whose kids have been diagnosed with the disorder are going to start demanding a thyroid test, and that we'll end up with a lot of false positive results that mean nothing at all."