

## Dopamine

### ADHD study ties brain proteins to symptoms

Zosia Bielski

From Friday's Globe and Mail Last updated on Friday, Sep. 11, 2009 10:31AM EDT

A brain-imaging study by U.S. researchers is providing the first definitive proof that patients with attention deficit hyperactivity disorder (ADHD) have lower-than-normal levels of the proteins that regulate our experiences of motivation and reward.

Deficits in the brain's dopamine-regulated reward system might help account for the clinical symptoms of ADHD, which include inattention and reduced motivation, as well as a susceptibility to drug abuse and obesity, said co-author Gene-Jack Wang, chair of the medical department at Upton, N.Y.'s Brookhaven National Laboratory.

The study, published in the current issue of the Journal of the American Medical Association, took nine years to complete: It took that long to find "drug-naive" participants, that is people who had not taken any medication to treat their ADHD, or abused drugs.

"There were several studies done before us that suggested the dopamine system may be involved. There were drug studies showing that yes, people with ADHD, once they received medication [such as] Ritalin, it helped them to relieve symptoms. But exactly which area and what happened we weren't quite clear on," Dr. Wang said.

ADHD is a childhood neurobiological disorder that often persists into adulthood. Three core symptoms are an inability to regulate attention and activity, as well as difficulty with inhibitory behaviour resulting in impulsivity, according to the Centre for ADHD/ADD Advocacy Canada.

The study involved 53 adult ADHD patients and 44 healthy control subjects.

The researchers used positron emission tomography (PET) to measure two parts of their dopamine system: receptors, which bind to the reward signals, and transporters, which take up and recycle excess dopamine after the signals go out. Lying in a PET scanner, each patient was injected with a small amount of a radiotracer compound, which bound itself to the receptors and transporters.

The findings revealed that, compared with healthy control subjects, ADHD patients had lower levels of dopamine receptors and transporters in the midbrain and accumbens, a pathway in the brain that manages reinforcement, motivation and learning associations between stimuli and reward.

The reason various subjects may be "not as interesting" for ADHD patients is that they cannot process the rewards, Dr. Wang said.

Although the research supports the continued use of stimulant medications that raise dopamine and increase attention - a common treatment for ADHD - they also suggest "interventions to enhance the saliency of school and work tasks to improve performance."

"There is room to develop," Dr. Wang said. "We cannot only rely on medication. It's overall treatment for the person, for example getting teachers to look at these people in different ways, and make lessons more interesting for them."

The findings may also help explain why ADHD patients are more likely to abuse drugs and become obese: Some of the Brookhaven studies suggested that patients may be unconsciously attempting to boost their dopamine levels. Finding ways to improve the function of the reward system could help mitigate these consequences, Dr. Wang said.

Umesh Jain, staff psychiatrist at the Centre for Addiction and Mental Health's division of child and family, said the research has broad implications beyond ADHD to "anything to do with impulse control."

"This study has lots to do with things that humans get themselves into trouble with: gambling, addictions, shopping, bulimia, mania," said Dr. Jain, who is also president of the Canadian Attention Deficit Hyperactivity Disorder Resource Alliance.

The study's lead author was Nora Volkow, director of the National Institute on Drug Abuse and a long-time collaborator on neuro-imaging research at Brookhaven.