Long-term ADHD drug use appears safe, brain development not affected

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Drugs used to treat Attention Deficit Hyperactivity Disorder (ADHD) do not appear to have long-term effects on the brain, according to new animal research from Wake Forest Baptist Medical Center.

As many as five to seven percent of elementary school children are diagnosed with ADHD, a behavioral disorder that causes problems with inattentiveness, over-activity, impulsivity, or a combination of these traits. Many of these children are treated with psychostimulant drugs, and while doctors and scientists know a lot about how these drugs work and their effectiveness, little is known about their long-term effects.

Linda Porrino, Ph.D., professor and chair of the Department of Physiology and Pharmacology, along with fellow professor Michael A. Nader, Ph.D., both of Wake Forest Baptist, and colleagues conducted an animal study to determine what the long-lasting effects may be. Their findings were surprising, said Porrino.

"We know that the drugs used to treat ADHD are very effective, but there have always been concerns about the long-lasting effects of these drugs," Porrino said. "We didn't know whether taking these drugs over a long period could harm brain development in some way or possibly lead to abuse of drugs later in adolescence."

Findings from the Wake Forest Baptist research are published online this month in the journal *Neuropsychopharmacology*.

The researchers studied 16 juvenile non-human primates, whose ages were equivalent to 6-to 10-year-old humans. Eight animals were in the control group that did not receive any drug treatment and the other eight were treated with a therapeutic-level dose of an extended-release form of Ritalin, or methylphenidate (MPH), for over a year, which is equivalent to about four years in children. Imaging of the animals' brains, both before and after the study, was conducted on both groups to measure brain chemistry and structure. The researchers also looked at developmental milestones to address concerns that ADHD drugs adversely affect physical growth.

Once the MPH treatment and imaging studies were concluded, the animals were given the opportunity to self administer cocaine over several months. Nader measured their propensity to acquire the drug and looked at how rapidly and in what amounts, to provide an index of vulnerability to substance abuse in adolescence. As reported in the research paper, they found no differences between groups – monkeys treated with Ritalin during adolescence were not more vulnerable to later drug use than the control animals.

"After one year of drug therapy, we found no long-lasting effects on the neurochemistry of the brain, no changes in the structure of the developing brain. There was also no increase in the susceptibility for drug abuse later in adolescence," Porrino said. "We were very careful to give the drugs in the same doses that would be given to children. That's one of the great advantages of our study is that it's directly translatable to children."

Porrino said non-human primates provide exceptional models for developmental research because they undergo relatively long childhood and adolescent periods marked by hormonal and physiological maturation much like humans.

"Our study showed that long-term therapeutic use of drugs to treat ADHD does not cause long-term negative effects on the developing brain, and importantly, it doesn't put children at risk for substance abuse later in adolescence," she said.

One of the exciting things about this research, Porrino said, is that a "sister" study was conducted simultaneously at John Hopkins with slightly older aged animals and different drugs and their findings were similar. "We feel very confident of the results because we have replicated each other's studies within the same time frame and gotten similar results," she said. "We think that's pretty powerful and reassuring."

Provided by Wake Forest University Baptist Medical Center