Science and Drugs for ADHD

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At least in theory, the use of medications for any disorder should be based on a scientific understanding of the drug's efficacy and its risks. It is also helpful if science has been able to determine, to at least some degree, the biological nature of the disorder, and the drug's mechanism of action. Together, this scientific information should provide doctors with a rationale for the use, or non-use, of the drugs. Thus, a review of the scientific literature should help answer questions about the wisdom of using Ritalin and other stimulants to treat children diagnosed with ADHD.

The biology of ADHD

While there have been claims made that ADHD is due to a chemical imbalance, there is no scientific evidence that shows that to be true. There is no biological test for ADHD; the diagnosis, of course, is based on an observation of a child's behavior. Thus, all science today can tell us is this: There is no *known* biological abnormality in children diagnosed with ADHD.

Ritalin's mechanism of action

It is now well understood that Ritalin, which is the trade name for methylphenidate, is similar to cocaine in its pharmacological properties. Both up dopamine levels in the brain, and both do so by blocking the transporter molecule involved in the reuptake of dopamine from the synaptic cleft. Researchers at the Brookhaven National Laboratory have found that Ritalin is as potent as cocaine in its

effect on the dopamine system.[1] Methylphenidate, however, is cleared more *slowly* from the brain than cocaine, which is why it isn't as addictive as cocaine.

Thus, Ritalin *perturbs* normal function in the brain. In response to this perturbation, the brain goes through a series of compensatory adaptations. Since Ritalin interferes with the normal reuptake of dopamine, and thus has the effect of at least temporarily upping the amount of this chemical messenger, the brain tones down its whole dopaminergic system. Neurons both release less dopamine and down-regulate (or decrease) their number of dopamine receptors. As part of this adaptation process, notes Steven Hyman, former director of the NIMH, there are also changes in intracellular signaling pathways and gene expression. After a few weeks, the patient's brain, Hyman wrote in 1995, is functioning in a manner that is "qualitatively as well as quantitatively different from the normal state."[2]

In other words, Ritalin and other ADHD drugs cause the brain to function in an *abnormal* manner. And given that understanding, we can now properly phrase the therapeutic question: Does this perturbation of normal function help or harm children?

Efficacy studies

In September 2005, a research group set up by 12 states, known as the Drug Effectiveness Review Project at Oregon State University, reported that they had conducted a meta-analysis of 2,287 studies of ADHD drugs. The group basically looked at all the studies of ADHD drugs that had been done anywhere in the world during the

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[1] Volkow, N. (1995). Is methylphenidate like cocaine? Studies on their pharmacokinetics and distribution in the human brain. *Arch Gen Psychiatry* 52: 456-463.

[2] In this paper, Hyman was providing a model for how *all* psychotropic drugs work. A drug perturbs a neurotransmitter system, and the brain then tries to compensate for this perturbation. Hyman S. (1996). Initiation and adaptation: A paradigm for understanding psychotropic drug action. *American Journal of Psychiatry* 153 (151-161.)

past 30 years. Based upon this exhaustive review, the group concluded that that there is no "good quality evidence on the use of drugs to affect outcomes relating to global academic performance, consequences of risky behaviors, social achievements, etc."[3] In other words, even though we have been using these drugs for more than 30 years, there is no good scientific evidence that they improve the very behavioral symptoms they are said to target. At least in the aggregate, there is no reason to believe that the drugs provide a long-term benefit to children so medicated.

Risks of Ritalin and other ADHD drugs

Given that Ritalin and other ADHD drugs perturb normal function, we should expect that they will cause a wide range of adverse effects. Physical side effects may include cardiovascular problems, nervousness, insomnia, weight loss, and facial tics. It is also now fairly well established that chronic administration of Ritalin and other ADHD drugs may cause cognitive impairment, a dulling of emotions, social isolation, obsessive-compulsive behaviors, psychosis and mania. Finally, there is reason to be concerned that these drugs may cause the brain to shrink over the long-term, and that they may damage the dopamine system permanently, such that children who have been so medicated will be more likely to be depressed as adults, or will not be able to feel as much "joy" as they would otherwise, since dopamine is the brain's reward system.[4] The Drug Effectiveness Review Project noted that, in fact, there is "no evidence of long-term safety of drugs used to treat ADHD in young children" or "adolescents."

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[3] The report can be accessed on the Internet at: www.ohsu.edu/drugeffectiveness/reports/final.cfm

[4] For a review of whether the drugs may cause brain shrinkage, see Leo, J. (2003), Broken brains of flawed studies? A critical review of ADHD neuroimaging research. *The Journal of Mind and Behavior*, 24:29-56. Research on rats is raising the concern that ADHD drugs may permanently damage the brain's reward system. See Carlezon, W. (2003). Enduring biological effects of early exposure to methylphenidate in rats. *Biol psychiatry* 54(12):1330-7.

Conclusion

Thus, from a scientific viewpoint, here's what we can say about ADHD and the drug we use to treat this disorder. There is no known biological abnormality in children so diagnosed. Ritalin and other ADHD drugs "perturb" normal neurotransmitter activity in the brain, and in response the brain undergoes a compensatory adaptation that leaves it functioning in an abnormal manner. There is no good evidence that the drugs provide a benefit, in terms of improving the child's behavior, over the long-term. The drugs may cause a host of physical and psychiatric problems, and there is reason to be concerned that the drugs, over the long-term, may cause permanent changes in the brain.

In short, this is a scientific record of a paradigm of care that is doing harm. There is no scientific rationale for the widespread use of these drugs, and thus we can only conclude that this is a paradigm of care that serves other interests. It certainly brings profits to drug companies, and perhaps parents and school teachers find the drugs beneficial because the children, with their behavior dampened by the drugs, become more manageable. But, given what science tells us about how the drugs affect the brain and how they affect children over time, we should not pretend it is for their benefit.