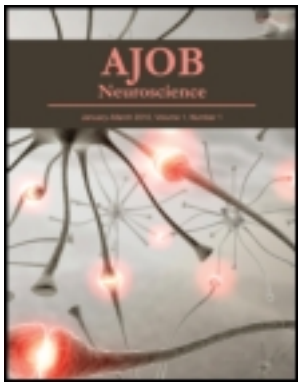

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Cognitive Enhancement with Amphetamine: History Repeats Itself

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Cognitive Enhancement with Amphetamine: History Repeats Itself

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Those who follow the cognitive enhancement literature will have noticed a shift of late. A decade ago, discussions of cognitive enhancement displayed the assumption that stimulants such as amphetamine and methylphenidate are effective enhancers, boosting the attention and executive function of healthy normal individuals (e.g., Chatterjee 2004; Farah et al. 2004; Fukuyama 2002; President's Council on Bioethics 2003).

Nowadays, the emerging view of stimulants for cognitive enhancement in normal individuals is much more cautious, if not outright skeptical. For example, Hall and Lucke (2010) refer to the "very weak evidence that putatively neuroenhancing pharmaceuticals in fact enhance cognitive function." Ilieva, Boland, and Farah (2013, 496) suggest that Adderall "has no more than small effects on cognition in healthy young adults." Advokat (2010, 1256) concludes that "the evidence does not support the conclusion that stimulants are cognitive 'enhancers'" (see also Chamberlain et al. 2010; Repantis et al. 2010; Smith and Farah 2011).

What is going on? If current views are correct, and stimulants have unreliable and generally small effects on cognition, why do so many people use them for cognitive enhancement? And what explains the findings published in the earlier literature? The first question is answered, at least in part, by Vrecko's (2013) fascinating study. He shows that users themselves describe stimulants' most prominent effects as improved mood, energy, goal-directed activity, and motivation—in short, as emotional rather than cognitive. Given the widespread effects of stimulant medications on the brain, encompassing both the mesocortical dopamine pathway involved in attention and executive function and the mesolimbic dopamine pathway involved in wanting and liking, it is not hard to understand why these effects would influence motivation. In our own research we have seen evidence that Adderall (a mixture of amphetamine salts) affects how normal healthy people feel about their work performance, quite apart from any real impact on that performance (Ilieva et al. 2013). We conducted a double-blind, placebo-controlled trial of Adderall on a variety of executive functions measures, along with tests of creativity and intelligence. At the conclusion of cognitive testing, participants rated the effect of the pill they had taken, from extremely detrimental to extremely beneficial for task

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performance. Although the drug did not improve any of the cognitive functions measured, participants (who were unaware of the identity of the pill) rated Adderall as more helpful than placebo. These ratings were uncorrelated with objective measures of cognitive enhancement, suggesting that the perception of drug effectiveness was unrealistic.

This still leaves the second question posed earlier: Why did the research literature shift from positive to negative over the past 10 years? This pattern, of initially robust findings gradually becoming harder to replicate, has been observed in many areas of science. The initial appearance of positive results that are false or inflated, and therefore eventually discounted, has been attributed to a number of factors including publication bias (Lehrer 2010). Particularly "at risk" are research areas, like cognitive enhancement, in which many different groups are flexibly testing for enhancement with a variety of tasks and measures, in small samples that limit study power (for more on the role of flexibility and study power see Ioannides 2005).

The shift from positive results to replication problems has happened before on the very topic of amphetamine and cognitive enhancement. We quote here from an unpublished Office of Naval Research Technical Report entitled "A Viewpoint on Drug Enhancement" by Paul M. Hurst (1966), available as a scanned image of a typewritten document at www.dtic.mil/dtic/tr/fulltext/u2/635948.pdf: "Shortly after the discovery of the 'stimulatory' properties of the amphetamines, some investigators [citations of studies from the 1930s] reported that these drugs increase test intelligence. These results were not confirmed, however, in subsequent studies [citations from the 1940s and 1950s]. Other investigators [citations from 1940s through 1960s] have tested the effects of amphetamines on a wide variety of higher mental functions . . . with results ranging in general from no observed effect to a modest facilitation." The author goes on to say: "Any real effect . . . could well be due to motivational rather than cognitive mechanisms . . . " (5–6). The students who spoke to Vrecko would seem to agree with this conclusion of a half century earlier. So would a growing number of contemporary neuroscientists, in a reversal of their initial assumptions. These lines of evidence, old and new, converge to suggest new avenues for enhancement research focusing on the relations between motivation and cognition, and the effects of stimulants on these systems.

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