

This study was a triple-blind randomised controlled crossover trial with 7-14 year olds with ADHD currently taking a psychostimulant (≥ 20 mg/day).

Children were tested twice on executive function (EF) measures, reading, and math two weeks apart.

EFs, which are associated with prefrontal cortex (PFC), include abilities like selective attention, self-control, reasoning, and problem-solving.

Half the children were tested first on their full dose of stimulants then half that. The other children were tested in the reverse order.

Hypothesis

Children with ADHD will show better cognitive performance when on half their normal stimulant dose.

(For the rationale, see third column.)

Effects of Low-Dose vs. Normal-Dose Psychostimulants on Executive Functions in Children with **Attention-Deficit / Hyperactivity Disorder**

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> Children with ADHD are being overmedicated

> > Flanker / Reverse Flanker Task: Accuracy on Incongruent Trials



Most children performed better on half their prescribed dose of stimulant. None performed worse.

In treating ADHD, the benchmark for determining treatment effectiveness should not focus on behavior alone.

Physicians should have cognitive testing done to help them determine the optimal treatment dose.

Spencer, R.C., et al. (2015). The cognition-enhancing effects of psychostimulants involve direct action in the PFC. *Biol Psychiatry,* 77, 940-950. Spencer, R.C., et al. (2012). Psychostimulants act within the PFC to improve cognitive function. *Biol Psychiatry*, 72, 221-227.

for optimal cognitive performance.

Session 1 Session 2

An unusual property of the dopamine (DA) system in prefrontal cortex (PFC) is a relative dearth of DA transporter (DAT).

DAT is abundant in the striatum and in most DA-rich brain regions but sparse in PFC. At moderate to high doses, stimulants act on DAT, inhibiting re-uptake of DA.

Thus moderate to high doses treat hyperactivity and impulsivity (Weiss et al. 2003), both of which are linked to the striatum (Carmona et al., 2009).

> But those doses have little effect on PFC because PFC has little DAT.

The mode of action of stimulants is different at low doses. At low doses they preferentially increase DA release in PFC and preferentially enhance signal processing in PFC

(Schmeichel & Berridge 2013; Spencer et al. 2012, 2015).

Thus, the best doses of stimulants for controlling behavioral problems are likely too high for aiding cognition.





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