

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.)

References Cited

Carmona, S., et al. (2009). Ventro-striatal reductions underpin symptoms of hyperactivity and impulsivity in ADHD. Biol Psychiatry, 66, 972-977. Schmeichel, B.E., & Berridge, C.W. (2013). Neurocircuitry underlying the preferential sensitivity of prefrontal catecholamines to low-dose psychostimulants. *Neuropsychopharmacol, 38*, 1078-1084.

Patients with ADHD are being Overmedicated (for Optimal Cognitive Performance) Daphne S. Ling, Kristina Balce, Margaret Weiss, Candice Murray, & Adele Diamond Department of Psychiatry, University of British Columbia, Vancouver, BC Canada daphne.ling@ubc.ca adele.diamond@ubc.ca ²University of Arkansas and Arkansas Children's Hospital, Little Rock, AR, USA 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. Congruent Trials Incongruent Trials **Incongruent minus Congruent (Mixed Block)** 250 At half his normal dose, this 200 child with ADHD had more 150 correct responses. Incongruent Accuracy (Low Dose): 83.33% He was also quicker to 50 Incongruent Accuracy (High Dose): 43.75% respond.

Increase in Flanker Effect when on the higher dose is not due to practice effects. The order in which the higher dose was given had no significant effect.

Full

Dose 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.



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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