Cognitive Effects of Stimulant, Guanfacine, and Combined Treatment in Child and Adolescent Attention-Deficit/Hyperactivity Disorder

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Abstract
Objective
Psychostimulants are partially effective in reducing cognitive dysfunction associated with attention-deficit/hyperactivity disorder (ADHD). Cognitive effects of guanfacine, an alternative treatment, are poorly understood. Given its distinct action on α2A receptors, guanfacine may have different or complementary effects relative to stimulants. This study tested stimulant and guanfacine monotherapies relative to combined treatment on cognitive functions important in ADHD.

Method
Children with ADHD (n = 182; age 7-14 years) completed an eight-week double blind randomized controlled trial with three arms: d-methylphenidate (DMPH), guanfacine (GUAN), or combination treatment with DMPH and GUAN (COMB). A non-clinical comparison group (n = 93) had baseline testing, and a subset was re-tested 8 weeks later (n = 38). Analyses examined treatment effects in four cognitive domains (working memory, response inhibition, reaction time, and reaction time variability) constructed from 20 variables.

Results
The ADHD group showed impaired working memory relative to the non-clinical comparison group (effect size = -0.53 SD units). The treatments differed in effects on working memory but not other cognitive domains. Combination treatment improved working memory more than GUAN, but was not significantly better than DMPH alone. Treatment did not fully normalize the initial deficit in ADHD relative to the comparison group.

Conclusion
Combined treatment with DMPH and GUAN yielded greater improvements in working memory than placebo or GUAN alone, but the combined treatment was not superior to DMPH alone, and did not extend to other cognitive domains. Although GUAN may be a useful add-on treatment to psychostimulants, additional strategies appear necessary to achieve normalization of cognitive function in ADHD.