Effects of d-Methylphenidate, Guanfacine, and Their Combination on Electroencephalogram Resting State Spectral Power in Attention-Deficit/Hyperactivity Disorder

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Abstract

Objective
Psychostimulant medications are the gold standard of treatment for attention-deficit/hyperactivity disorder (ADHD); however, a significant minority (~30%) of individuals with ADHD fail to respond favorably. Noradrenergic agents are increasingly used as ADHD monotherapies or adjuncts for suboptimal stimulant response, yet knowledge of their cortical effects is limited. This study is the first to examine comparative effects of guanfacine (an alpha adrenergic 2A agonist), psychostimulant, and their combination on resting state cortical activity in ADHD.

Method
The sample comprised 179 participants aged 7 to 14 years old with ADHD (113 boys, 55 girls). Participants were randomized to one of three blinded conditions: guanfacine (GUAN), d-methylphenidate (DMPH), or a combination (COMB). Electroencephalography (EEG) was performed pre-, mid-, and post-medication titration, with concomitant assessment of behavioral and cognitive functioning.

Results
Analyses of spectral power measures during resting EEG suggested that each medication condition displayed a distinct profile of effects on cortical activity. Significant time effects suggested that GUAN decreased global alpha-band (8-12 hertz [Hz]) power, DMPH and COMB increased centro-parietal beta-band (13-21 Hz) power, and COMB resulted in decreased theta-band (4-7 Hz) power. Relative to other medication groups, COMB was associated with significantly lower theta power and DMPH with higher beta-band power compared to the GUAN group. Medication-related changes in theta power were correlated with improvements in behavioral and cognitive functioning.

Conclusion
These data revealed distinct underlying medication-related effects on neural mechanisms. The COMB condition uniquely exhibited an EEG profile that was associated with improved behavioral and cognitive functioning.