Striatal Activation Predicts Differential Therapeutic Responses to Methylphenidate and Atomoxetine

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Abstract

Objective
Methylphenidate has prominent effects in the dopamine-rich striatum that are absent for the selective norepinephrine transporter inhibitor atomoxetine. This study tested whether baseline striatal activation predicts differential response to the two medications in youth with attention-deficit/hyperactivity disorder (ADHD).

Method
Thirty-six youth with ADHD performed a go/no-go test during functional magnetic resonance imaging at baseline and were treated with methylphenidate and atomoxetine using a randomized cross-over design. Whole-brain task-related activation was regressed on clinical response.

Results
Task-related activation in right caudate nucleus was predicted by an interaction of clinical responses to methylphenidate and atomoxetine (F1,30 = 17.00; p < .001). Elevated caudate activation was associated with robust improvement for methylphenidate and little improvement for atomoxetine. Rate of robust response was higher for methylphenidate than atomoxetine in youth with high (94.4% versus 38.8%; p = .003; number needed to treat = 2, 95% CI 1.31 – 3.73) but not low caudate activation (33.3% versus 50.0%; p = .375). Further, response to atomoxetine predicted motor cortex activation (F1,30 = 14.99; p < .001).

Conclusion
Enhanced caudate activation for response inhibition may be a candidate biomarker of superior response to methylphenidate over atomoxetine in youth with ADHD, purportedly reflecting the dopaminergic effects of methylphenidate but not atomoxetine in striatum, while motor cortex activation may predict response to atomoxetine. These data do not yet translate directly to the clinical setting, but the approach is potentially important for informing future research and illustrates that it may be possible to predict differential treatment response using a biomarker-driven approach.

Clinical trial registration information—Stimulant Versus Nonstimulant Medication for Attention Deficit Hyperactivity Disorder in Children; https://clinicaltrials.gov/; NCT00183391.