Executive Function in Adults With Attention-Deficit/Hyperactivity Disorder During Treatment With Atomoxetine in a Randomized, Placebo-Controlled, Withdrawal Study.


Abstract
We assessed the executive function in adults with attention-deficit/hyperactivity disorder (ADHD) during atomoxetine treatment in a randomized withdrawal trial. Responders (Conners' ADHD Rating Scale-Investigator Rated: Screening Version [adult prompts] ≥30% reduction from baseline and Clinical Global Impression Scale-ADHD Severity score ≤3) to open-label atomoxetine (40-100 mg/d, 12 weeks) entered a 37-week double-blind maintenance period. Patients who maintained response (double-blind atomoxetine for 12 weeks) were randomized 1:1 to atomoxetine (80-100 mg/d, n = 266) or placebo (n = 258) for 25 weeks (total duration, 1 year). Patients and investigators were blinded to response criteria and randomization timing. Change in executive function was assessed with the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) Self-Report and Informant T scores from the randomization to the last-observation-carried-forward postrandomization week 25 (after week 17). Of the enrolled patients (n = 2017; mean age, 33.2 years; male, 58.7%), 524 responders were randomized. During open-label atomoxetine, subscales and individual items on both BRIEF-A questionnaires showed significant improvement (P < 0.001). After randomization, the following T scores improved significantly (P ≤ 0.05) with patients in the atomoxetine group versus those in the placebo group: global executive composite, behavioral regulation, and metacognition indices; plan/organize, working memory, inhibit, task monitor and shift (both BRIEF-A questionnaires), emotional control and organization of materials (BRIEF-A Informant), and initiate (BRIEF-A Self-Report). Atomoxetine significantly improved the executive function compared with placebo, which was maintained for 25 weeks or more; the executive function of patients in the placebo group worsened but did not return to baseline levels after randomization.