Fasoracetam in adolescents with ADHD and glutamatergic gene network variants disrupting mGluR neurotransmitter signaling.

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Abstract

The glutamatergic neurotransmitter system may play an important role in attention-deficit hyperactivity disorder (ADHD). This 5-week, open-label, single-blind, placebo-controlled study reports the safety, pharmacokinetics and responsiveness of the metabotropic glutamate receptor (mGluR) activator fasoracetam (NFC-1), in 30 adolescents, age 12-17 years with ADHD, harboring mutations in mGluR network genes. Mutation status was double-blinded. A single-dose pharmacokinetic profiling from 50-800 mg was followed by a single-blind placebo at week 1 and subsequent symptom-driven dose advancement up to 400 mg BID for 4 weeks. NFC-1 treatment resulted in significant improvement. Mean Clinical Global Impressions-Improvement (CGI-I) and Severity (CGI-S) scores were, respectively, 3.79 at baseline vs. 2.33 at week 5 ($P < 0.001$) and 4.83 at baseline vs. 3.86 at week 5 ($P < 0.001$). Parental Vanderbilt scores showed significant improvement for subjects with mGluR Tier 1 variants ($P < 0.035$). There were no differences in the incidence of adverse events between placebo week and weeks on active drug.

The trial is registered at https://clinicaltrials.gov/ct2/show/study/NCT02286817 .