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NEW RESEARCH - ARTICLES

A Double-Blind Placebo-Controlled Trial of Fluoxetine for Repetitive Behaviors and Global Severity in Adult Autism Spectrum Disorders

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Objective: The effects of fluoxetine and placebo on repetitive behaviors and global severity were compared in adults with autism spectrum disorders (ASDs).

Method: Adults with ASDs were enrolled in a 12-week double-blind placebo-controlled fluoxetine trial. Thirty-seven were randomly assigned to fluoxetine (N=22) or placebo (N=15). Dosage followed a fixed schedule, starting at 10 mg/day and increasing as tolerated up to 80 mg/day. Repetitive behaviors were measured with the compulsion subscale of the Yale-Brown Obsessive Compulsive Scale; the Clinical Global Impression (CGI) improvement scale was used to rate improvement in obsessive-compulsive symptoms and overall severity.

Results: There was a significant treatment-by-time interaction indicating a significantly greater reduction in repetitive behaviors across time for fluoxetine than for placebo. With overall response defined as a CGI global improvement score of 2 or less, there were significantly more responders at week 12 in the fluoxetine group than in the placebo group. The risk ratio was 1.5 for CGI global improvement (responders: fluoxetine, 35%; placebo, 0%) and 1.8 for CGI-rated improvement in obsessive-compulsive symptoms (responders: fluoxetine, 50%; placebo, 8%). Only mild and moderate side effects were observed.

Conclusions: Fluoxetine treatment, compared to placebo, resulted in significantly greater improvement in repetitive behaviors, according to both the Yale-Brown compulsion subscale and CGI rating of obsessive-compulsive symptoms, as well as on the CGI overall improvement rating. Fluoxetine appeared to be well tolerated. These findings stand in contrast to findings in a trial of citalopram for childhood autism.

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Autism spectrum disorders (ASDs) are defined by three core symptom areas: impairments in social relatedness, deficits in social communication, and restricted, repetitive behaviors and interests. While advances have been made in ASD intervention research, the vast majority of studies have focused on pediatric populations. Of the children with ASDs, 75%–80% continue to meet ASD criteria in adolescence and adulthood (1–4), and ASDs in adulthood are characterized by persistent functional deficits in core and associated symptom domains (5). The growing needs of adults with ASDs are reflected in a 48% increase in prescriptions of psychopharmacological agents from 1993 to 2001 and increasing prescriptions for older individuals with autism (6). Selective serotonin reuptake inhibitors (SSRIs) were reported to be the fastest growing class of psychopharmacologic agents prescribed, growing by 3.5 times in that 8-year period (6).

The interest in SSRIs for the treatment of ASDs stems from a hypothesized role for serotonin (5-HT) in the pathophysiology of ASDs and the similarities between repetitive behaviors in ASDs and obsessive-compulsive disorder (OCD), a condition for which SSRIs are a first-line treatment. It has been hypothesized that dysfunction of 5-HT regulation in ASDs occurs during early developmental periods, results in cortical morphogenetic abnormalities and altered 5-HT neurotransmission, and influences symptom domains such as anxiety and rigidity (7, 8). The most consistent biological finding is elevated platelet 5-HT levels in approximately 30% of individuals with autism (9). Genetic findings suggest a role for the serotonin-transporter-linked polymorphic region (5-HTTLPR) promoter locus on