Subjects were randomly assigned to fluoxetine versus matching placebo for 8 weeks of treatment. The active intervention (10 mg of fluoxetine for the first 4 weeks of treatment) was considered to be a moderate antidepressant dose for children and adolescents (Cornelius et al., 2001). In this study, patients were treated for 16 weeks to allow for a more complete clinical response and for the occurrence of any late-onset side effects. The rationale for this treatment duration was supported by the findings of a recent placebo-controlled trial of fluoxetine for treatment-resistant depression in children and adolescents (Hollander et al., 2009). The study enrolled outpatient youths aged 12-17 with current major depressive disorder or dysthymic disorder according to K-SADS-PL and a CDRS-R total score of greater than 70. The majority of participants were male (64%) and most were White (46%). Participants had a variety of concomitant disorders, including anxiety disorders, Attention-Deficit/Hyperactivity Disorder (ADHD), and conduct disorder (CD). The study also excluded youth with a current history of suicidal ideation or the presence of frank suicidal ideation on the baseline Screen for Child Suicide Risk (SSR). The study protocol was approved by the institutional review board at the University of Cincinnati, and written informed consent was obtained from parents of all participants and assent was obtained from all participants. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and Good Clinical Practice guidelines. Participants were screened to rule out current major depressive disorder or dysthymic disorder according to K-SADS-PL and a CDRS-R total score of greater than 70. Participants were also excluded if they had a history of non-compliance or intolerance to fluoxetine or failed 4-weeks of treatment with a non-TCA, non MAOI antidepressant during the current depressive episode. The study also excluded participants with a history of substance abuse or dependence within the past year, current use of illicit substances, or family history of alcoholism or drug addiction. Additional inclusion criteria for subjects included a score of at least 50 on the K-SADS-PL Depressive Symptom Severity Scale and a score of at least 40 on the K-SADS-PL Anxiety Symptom Severity Scale. Subjects were also required to have a score of at least 60 on the CDRS-R Total Score and a score of at least 7 on the CGI-S Total Score. The study also excluded participants who had a history of psychiatric hospitalization or who were currently receiving psychotherapy. The study was designed as a double-blind, randomized, placebo-controlled trial with a 16-week treatment period. The primary outcome measure was the Children's Depression Rating Scale (CDRS-R), and the secondary outcome measure was the Clinical Global Impressions Scale-Severity (CGI-S). Outcome scores were compared between treatment groups across time using a mixed-effects model with repeated measures. The statistical analysis was performed using a linear mixed-effects model, which accounted for the within-subject correlation of repeated measures. The model included fixed effects for treatment group, time, and the interaction between treatment and time. The model also included random effects for intercept and slope to account for individual variability. The model was further adjusted for covariates such as age, gender, and baseline depression severity. The model was found to be adequate for the analysis, and the results were robust to the inclusion of additional covariates. The results showed a significant interaction between treatment and time, indicating that the treatment effect was not consistent across the entire treatment period. The effect sizes were calculated using Cohen's d and were found to be moderate in size. The analysis also showed that the active treatment group had a greater improvement in depressive symptoms compared to the placebo group. The results were significant at the p < 0.05 level. The primary outcome measure was the Children's Depression Rating Scale (CDRS-R), and the secondary outcome measure was the Clinical Global Impressions Scale-Severity (CGI-S). Outcome scores were compared between treatment groups across time using a mixed-effects model with repeated measures. The statistical analysis was performed using a linear mixed-effects model, which accounted for the within-subject correlation of repeated measures. The model included fixed effects for treatment group, time, and the interaction between treatment and time. 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