Exploring the Relationship Between Antidepressant Treatment, Neurochemicals in the Brain and Anxiety/Depression Symptoms in Youth

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Introduction. Pediatric mental health disorders are associated with significant morbidity and mortality. Investigating factors influencing symptoms and treatment response aids in optimizing therapies. Neurochemicals can serve as proxies for neurobiological processes altered in these disorders. The impact of antidepressant treatment on brain metabolism is limited in pediatrics; this study aims to evaluate relationships between neurochemicals and anxiety and depressive symptoms in fluoxetine-treated youth.

Methods. Adolescents aged 12-21yr, on steady-state fluoxetine, underwent 1H-MRS, measuring glutamate (Glu), glutamine (Gln), myoinositol (mI), choline (Cho), N-acetylaspartate (NAA) and creatine (Cr), reported as ratios to Cr. Depressive and anxiety symptoms were assessed using PHQ-9 and PROMIS Anxiety scales, respectively. Participants with PHQ-9 scores ≥11 or PROMIS Anxiety t-scores ≥60 were considered non-responders. Statistical analyses included Student's t-test and Spearman's rho, using JMP Pro v17.

Results. In 46 youth (mean age 16.1 ± 1.9 years), NAA levels did not correlate with anxiety symptom severity (Spearman's $\rho = -0.146$, $p = 0.333$). When stratified by fluoxetine response, NAA was significantly higher in responders compared to non-responders (NAA mean 1.67±0.09 vs 1.57±0.11, $p = 0.004$, Cohen's $d = 0.94$). Other neurochemicals did not differ between groups, nor correlate with anxiety or depression symptom severity.

Conclusions. In fluoxetine-treated youth, anxiety responders had increased NAA compared to non-responders. NAA, a marker of neuronal integrity, is often lower in psychiatric disorders relative to controls, with some evidence suggesting normalization following treatment in adults. Our findings support the need for further research into NAA as a potential biomarker for fluoxetine response.