The efficacy of N-acetylcysteine as an adjunctive treatment in bipolar depression: an open label trial.

Evidence is accumulating to support the presence of redox dysregulation in a number of psychiatric disorders, including bipolar disorder. This dysregulation may be amenable to therapeutic intervention. Glutathione is the predominant non-enzymatic intracellular free radical scavenger in the brain, and the most generic of all endogenous antioxidants in terms of action. N-acetylcysteine (NAC) is a glutathione precursor that effectively replenishes brain glutathione. Given the failure of almost all modern trials of antidepressants in bipolar disorder to demonstrate efficacy, and the limited efficacy of mood stabilisers in the depressive phase of the disorder, this is a major unmet need. This study reports data on the treatment of 149 individuals with moderate depression during the 2 month open label phase of a randomised placebo controlled clinical trial of the efficacy of 1g BID of NAC that examined the use of NAC as a maintenance treatment for bipolar disorder. In this trial, the estimated mean baseline Bipolar Depression Rating Scale (BDRS) score was 19.7 (SE=0.8), and the mean BDRS score at the end of the 8 week open label treatment phase was 11.1 (SE=0.8). This reduction was statistically significant (p<0.001). Improvements in functioning and quality of life were similarly evident. These open label data demonstrate a robust decrement in depression scores with NAC.
treatment. Large placebo controlled trials of acute bipolar depression are warranted.