The efficacy of adjunctive N-acetylcysteine in major depressive disorder: a double-blind, randomized, placebo-controlled trial.

Major depressive disorder (MDD) is one of the most common psychiatric disorders, conferring considerable individual, family, and community burden. To date, treatments for MDD have been derived from the monoamine hypothesis, and there is a paucity of emerging antidepressants, especially with novel mechanisms of action and treatment targets. N-acetylcysteine (NAC) is a redox-active glutathione precursor that decreases inflammatory cytokines, modulates glutamate, promotes neurogenesis, and decreases apoptosis, all of which contribute to the neurobiology of depression. Participants with a current episode of MDD diagnosed according to DSM-IV-TR criteria (N = 252) were treated with NAC or placebo in addition to treatment as usual for 12 weeks and were followed to 16 weeks. Data were collected between 2007 and 2011. The omnibus interaction between group and visit for the Montgomery-Asberg Depression Rating Scale (MADRS), the primary outcome measure, was not significant (F,???.? = 1.98, P = .067), and the groups did not separate at week 12 (t???.? = -1.12, P = .265). However, at week 12, the scores on the Longitudinal Interval Follow-Up...
Evaluation of Range of Impaired Functioning Tool (LIFE-RIFT) differed from placebo (P = .03). Among participants with a MADRS score ≥ 25, NAC separated from placebo at weeks 6, 8, 12, and 16 (P < .05). Additionally, the rate of change between baseline and week 16 was significant (t???.?? = -2.11, P = .036). NAC treatment was superior to placebo at week 16 for secondary readouts of function and clinical impression. Remission and response were greater in the NAC group at week 16, but not at week 12. The NAC group had a greater rate of gastrointestinal and musculoskeletal adverse events. Being negative at the week 12 end point, and with some positive secondary signals, the study provides only limited support for the role of NAC as a novel adjunctive therapy for MDD. These data implicate the pathways influenced by NAC in depression pathogenesis, principally oxidative and inflammatory stress and glutamate, although definitive confirmation remains necessary. www.anzctr.org.au Identifier: ACTRN12607000134426.