The Effect of N-Acetyl Cysteine on Brain Function in Early-Stage Schizophrenia

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Schizophrenia is a severe and debilitating mental illnesses that typically begins during late adolescence or early adulthood and persists for a lifetime. Existing treatments can subdue the psychotic symptoms but do not slow the progression of the disease, resulting in severe cognitive deficits. Thus, therapeutic treatments that could slow neurobiological changes seen in the progression of the disease, may dampen the degenerative nature of the disease. N-acetyl cysteine (NAC) is a known neuroprotective agent that acts via its antioxidant properties and promotion of glutamate release. We are examining whether NAC impacts brain functioning over the course of a year in the early stages of schizophrenia. Sixty patients with early-stage schizophrenia were randomized to receive NAC or placebo treatment for one year. At baseline, 6 months, and 12 months, subjects performed an n-back test during fMRI to measure brain activity during working memory processes and assess cognitive ability. We will examine whether NAC impacts brain activity during the n-back task in frontoparietal regions involved in working memory. We will also examine behavioral performance on the n-back task, including accuracy and reaction times. We hypothesize that subjects in the NAC group will have greater frontoparietal brain activity and superior performance on the n-back task, relative to the placebo group. We expect changes to increase with time and as cognitive load increases. The goal is to identify whether NAC may be a potential treatment that can alter the trajectory of schizophrenia during its the early stages to minimize lifelong impact.

Schizophrenia is a severe, debilitating mental illnesses that typically begins during early adulthood and persists for a lifetime. Existing treatments can treat psychotic symptoms but do not slow the progression of the disease, resulting in severe cognitive deficits. Therapeutic treatments that could slow the neurobiological changes seen in schizophrenia may dampen the degenerative nature of the disease. One potential treatment is N-acetyl cysteine (NAC), a known neuroprotective agent that acts via its antioxidant properties and promotion of glutamate release. We examined whether NAC impacts brain functioning over the course of a year in early stage schizophrenia. Sixty patients with early-stage schizophrenia were randomized to receive NAC or placebo treatment for one year. At baseline, 6 months, and 12 months, subjects performed an n-back test during fMRI to measure brain activity during working memory processes and assess cognitive ability. A matched group of healthy adults received a single baseline scan. At baseline, patients had decreased activation in the superior frontal gyrus and increased activation in the anterior cingulate cortex. Furthermore, patients had poorer performance on the n-back task. NAC did not have a significant effect on performance of the n-back task, but there was a small effect of NAC on activity in the anterior cingulate cortex. The cognitive deficits and decreased frontal lobe activity in patients supports previous research indicating cognitive and neurobiological abnormalities in schizophrenia. Differences in the anterior cingulate cortex has found mixed support in prior research and may indicate the importance of attentional control in cognitive deficits.