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Reviews

Improvement of cognitive function in schizophrenia with *N*-acetylcysteine: A theoretical review

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Andrea Phillipou, David J. Castle, Erica Neill, Matthew E. Hughes, Cherrie Galletly, ...show all

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Abstract

Objectives: Schizophrenia is a debilitating psychiatric illness associated with positive and negative symptoms as well as significant impairments in cognition. Current antipsychotic medications do not alleviate these cognitive deficits, and more effective therapeutic options are required. Increased oxidative stress and altered antioxidant levels, including glutathione (GSH) have been observed both in individuals with cognitive impairment and in people with schizophrenia. A GSH precursor, the antioxidant *N*-acetylcysteine (NAC) has been investigated as a novel treatment for the cognitive symptoms of schizophrenia, and recent research suggests that NAC may be a promising adjunctive treatment option. However, the current literature lacks integration as to why NAC may effectively improve cognition in schizophrenia. The present theoretical synthesis aimed to address this gap by examining the processes by which NAC may improve cognitive function in schizophrenia. **Methods:** The schizophrenia literature was reviewed in three key domains: cognitive impairment, the relationship between oxidative stress and cognition, and the efficacy of NAC as a novel treatment. This led to a theoretical analysis of the neurobiological processes by which NAC may improve cognition in schizophrenia. **Results:** This theoretical review concluded that improved cognition may result from a combination of factors, including decreased oxidative stress, neuroprotection of cognitive networks and an increase in glutamatergic modulation of the *N*-methyl-D-aspartate receptor system. Whilst a number of mechanisms by which NAC may improve cognition and symptoms in schizophrenia have been proposed, there is still limited understanding of the specific metabolic pathways involved and how they interrelate and modify specific symptomology. **Discussion:** Exploration of how NAC treatment may act to improve cognitive function could guide clinical trials by investigation of the specific neurotransmitter systems and processes involved, allowing for targeted neurological outcome measures. Future research would benefit from the investigation of both in vivo cortical GSH concentration and peripheral plasma GSH in a population of individuals with chronic schizophrenia.

Q Keywords: [Glutathione](#) [Oxidative stress](#) [N-acetylcysteine](#) [Schizophrenia](#) [Psychosis](#) [Cognitive dysfunction](#) [Neurocognition](#)

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