Antioxidant effect of N-Acetylcysteine Amide against Aβ1-42 peptide-induced histopathological changes in the rat brain

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Abstract

Oxidative stress (OS) is a key factor in initiation of many neurodegenerative disorders including Alzheimer's disease (AD). Hence, antioxidant therapy to combat the neurodegenerative diseases like AD is one of the most explored research topics in the past decade. Among the inbuilt antioxidant defense in the brain, the glutathione is one of the major antioxidants. N-Acetyl cysteine, a glutathione precursor, was found to provide neuroprotective effects in animal models of AD and currently tested in clinical trials. Now, the amide form of NAC, N-Acetylcysteine amide (NACA) is said to provide extended bioavailability compared to its parental form NAC. The present study evaluates the neuroprotective effects of NACA against Aβ1-42 peptide induced AD-like pathology in rats. The AD-like pathology was induced in rats by intraventricular administration of Aβ1-42 peptide through stereotaxic surgery. The experiment consists of control and sham groups also. NACA was administered seven consecutive days after inducing AD-like pathology or for fourteen days (a week before and a week after inducing AD-like pathology). The learning and memory activities are evaluated through Morris water maze and passive avoidance tests. The antioxidant effects are evaluated through estimation of lipid peroxidation, reduced glutathione and the total antioxidants in the hippocampal and prefrontal cortical region of the brain. The histopathological evaluation of the hippocampus and the prefrontal cortex were performed using a variety of studies which includes neuronal proliferation, neuronal degeneration, expression of neurofibrillary tangles, β amyloid expression, synaptophysin expression and gliosis. The study clearly demonstrated that the administration of NACA has minimized the cognitive deficits observed in the form of learning and memory by enhancing the antioxidant defense in the hippocampus and medial prefrontal cortex. In addition to this the NACA exerted its neuroprotective effects in all the other parameters studied. This study demonstrates the neuroprotective effects of NACA against β amyloid induced histopathological changes. The study suggests that the NACA can be considered for future clinical trials.

Recent Publications

1. Benterud et al., (2017) N-Acetylcysteine Amide Exerts Possible Neuroprotective Effects in Newborn Pigs after Perinatal Asphyxia. Neonatology, 111(1), 12–21.

2. Kawoos et al., (2017) Protective Effect of N-Acetylcysteine Amide on Blast-Induced Increase in Intracranial Pressure in Rats. Frontiers in neurology, 8, 219.

3. Kawoos et al., (2019) N-acetylcysteine Amide Ameliorates Blast-Induced Changes in Blood-Brain Barrier Integrity in Rats. Frontiers in neurology, 10, 650.

4. Zhou et al., (2018) N-acetylcysteine amide provides neuroprotection via Nrf2-ARE pathway in a mouse model of traumatic brain injury. Drug design, development and therapy, 12, 4117–4127.

5. Kim et al., (2022) Neuroprotective effects of N-acetylcysteine amide against oxidative injury in an aging model of organotypic hippocampal slice cultures. Neuroreport 2;33(4):173-179.

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Biography

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