9. RiboCeine and Alzheimer's Disease

Emokpae O, Ben-Azu B, Ajayi AM, Umukoro S. D-Ribose-L-Cysteine attenuates lipopolysaccharide-induced memory deficits through inhibition of oxidative stress, release of proinflammatory cytokines, and nuclear factor-kappa B expression in mice. Naunyn-Schmiedeberg's Archives of Pharmacology, 07 January 2020.

Overview: Oxidative stress-mediated cellular injury plays a crucial role in the pathophysiology of Alzheimer's disease (AD), a progressive neurodegenerative disorder characterized by gradual deterioration in cognition and other behavioral phenotypes. The increase in lipid peroxidation and reduced endogenous antioxidant levels that occur in AD suggests oxidative stress contributes to the pathology of the disease. Lipid peroxidative tissue damage caused by free radicals triggers a vicious cycle of neuroinflammation that leads to progressive degeneration of the neuronal pathways responsible for learning and memory. Glutathione (GSH) is the most important intracellular antioxidant defense molecule in mammalian tissues, especially in the brain. This study seeks to evaluate the effects of D-Ribose-L Cysteine (DRLC) on memory deficits and the biochemical and histomorphological changes induced by lipopolysaccharide (LPS) in mice. Systemic administration of LPS causes a cluster of behavior derangements including memory decline through the induction of oxidative stress and neuroinflammation. The LPS-induced memory deficits closely reflects the pathologic changes seen in patients with AD and therefore this animal model can be used to detect compounds with cognitive-enhancing activities.

Methods: The study protocol included 60 male mice and had 6 study groups with 10 animals per group. Group 1 was the Control Group – Placebo; Group 2 was the negative control – AD; Group 3 received DRLC at 25mg/Kg; Group 4 received DRLC at 50mg/Kg; Group 5 received DRLC at 100mg/Kg and Group 6 received donepezil* (DPZ) at 1mg/Kg. Groups 2-6 received LPS to induce memory deficits (AD). * FDA approved drug to treat dementia, aka Aricept®. 26

Results: DRLC reversed LPS-induced memory impairment and improved social recognition memory and interaction deficits. DRLC improved brain GSH, catalase and decreased malondialdehyde (marker for oxidative stress), and the inflammatory markers, tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6). There was also a decrease expression of nuclear transcription factor kappa-B (NF-kB). The involvement of NF-kB in neurodegenerative diseases such as AD, is well reported in the literature.

Conclusion: The results of this study suggest that DRLC has memory enhancing effects in mice treated with LPS, which induces memory deficits, through mechanisms related to the inhibition of oxidative stress, release of proinflammatory cytokines and expression of nuclear transcription factor kappa-B.

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