

Nicotinamide Riboside Supports Brain Health: Assessing the Evidence

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Objectives: Alterations in neurobiology are linked to mild cognitive decline and various diseases including Alzheimer's Disease (AD), ALS, and Autism Spectrum Disorder (ASD). Declines in brain health are associated with neuroinflammation, nicotinamide adenine dinucleotide (NAD⁺) deficits, and are often accompanied by changes in memory and social behaviors. The NAD⁺ precursor, nicotinamide riboside (NR) is a clinically proven, safe dietary supplement in humans. The objective of this review is to evaluate the effectiveness of NR on improving brain function and neurobiology in preclinical models, to support translation into future clinical studies.

Methods: Peer-reviewed, published preclinical studies evaluating NR on various parameters of brain health and neurodegeneration were reviewed. Complimentary endpoints associated with multiple studies were identified to conclude potential mechanisms of action across multiple disease models and justify translation into human studies.

Results: A total of 20 preclinical studies have been published evaluating NR on various aspects of brain health in cell culture and rodent models. NR was evaluated in preclinical models of AD, ALS, Gulf War Illness, ASD, obesity-induced cognitive decline, alcohol-induced depression, and maternal supplementation, amongst others. Though various doses of NR were tested, 400 mg/kg/day (estimated at 1300 mg/day for an adult human) was most frequently utilized dose. NR increased NAD⁺ levels in the brain of mice following oral supplementation in seven separate studies. Multiple studies demonstrated NR-induced improvements in cognitive performance, behavior, and slowing of disease progression. The mechanisms of NR-induced augmentations were repeatedly associated with decreased neuroinflammation, potentially through a decrease in the cGAS-STING pathway, attenuation of neuronal degradation, reduction in amyloid- β , increase in brain-derived neurotrophic factor, and an increase in sirtuins.

Conclusions: As the safety of NR has been demonstrated in multiple clinical studies, and oral NR supplementation has been shown to be successful in multiple preclinical models of neurodegeneration and brain function, there is ample evidence to support clinical evaluation of NR as a support for brain health.

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