Updates in Neurology: Nicotinamide Riboside and Mitochondrial Support

Liz Sutherland, ND

Restorative Medicine Digest

September 2, 2022

Mitochondrial dysfunction is associated with both aging and a wide array of neurodegenerative disorders such as Alzheimer's disease,[1] Parkinson's disease,[2] and amyotrophic lateral sclerosis (ALS).[3]Mitochondrial dysfunction increases with age, leading to high levels of reactive oxygen species and prolonged oxidative stress. Therapeutic approaches that help regulate mitochondrial biogenenesis and mitophagy (a specialized form of autophagy that removes impaired mitochondria) could potentially have positive effects on the early stages and severity of neurodegenerative conditions,[4] as well as supporting healthy aging in general.[5]

Studies suggest that raising intracellular concentrations of NAD+ (nicotinamide adenine dinucleotide) may be crucial in this regard.[6,7] NAD+ is an essential coenzyme and substrate in multiple biological processes including the modulation of cellular metabolism, cell signaling, transcription, and DNA repair.[8] Of particular interest, is the relationship between NAD^+ and a family of proteins known as sirtuins. Sirtuins are a group of protein deacetylases/deacylases that act as evolutionarily conserved epigenetic mediators between energy metabolism and aging in a wide array of organisms.[9] The beneficial effects on lifespan observed with caloric restriction are attributed to sirtuins.[10] Sirtuins require NAD+, and while humans can biosynthesize NAD+ via endogenous pathways and from dietary precursors in foods that contain vitamin B3, our ability to do so wanes with age.[11] Systemic levels of NAD+ have been shown to decline by over 50% after the age of 40, and low levels are associated with mitochondrial dysfunction.[12] Supplementation with key NAD+ intermediates, therefore, may be beneficial for long-term optimal mitochondrial function and neurological health.[13]

Nicotinamide riboside (NR) is a highly bioavailable form of vitamin B3. In a mouse model of Alzheimer's disease, NR increased brain NAD+ levels by 70%. It also increased levels of PGC-1?, a protein that protects against mitochondrial dysfunction, by 50%. Mice showed significant improvement in memory-based tasks by the end of this study.[14] An in vitro study using stem cells from a patient with Parkinson's disease found that NR raised NAD+ levels and led to significant improvements in measures of mitochondrial function.[15] Another in vitro study found that NR was able to increase the concentration of NAD+ in mammalian cells by up to 270%.[16] A pilot study found that an oral dose of NR increased blood concentration of NAD+ up to 2.7-fold in a single human subject. This same study also found that single doses of NR at 100, 300, and 1000 mg resulted in dose-dependent increases in blood levels of NAD+.[17] In a double-blind placebo-controlled trial of overweight but otherwise healthy human subjects, NR doses of 100, 300, and 1000 mg resulted in approximate increases in blood levels of NAD+ of 22%, 51%, and 142% respectively, within two weeks of supplementation, with results being maintained throughout the rest of the 8-week study period.[18]

Clinical Implications

Mitochondrial dysfunction has been identified in the early stages of many neurodegenerative disorders. NR

supplementation appears able to restore intracellular concentrations of NAD+, with potentially innumerable beneficial metabolic consequences, including biosynthesis of NAD+-dependent sirtuin proteins, some of which are located exclusively in the mitochondria.[19]

Supporting mitochondrial health in your patients with neurodegenerative disorders may prove to be an invaluable part of their therapeutic protocol.

References

1. https://pubmed.ncbi.nlm.nih.gov/20624441/
2. https://pubmed.ncbi.nlm.nih.gov/27546335/
3. https://www.sciencedirect.com/science/article/pii/S030439401730544X
4. https://onlinelibrary.wiley.com/doi/full/10.1111/cns.13116
5. https://www.tandfonline.com/doi/full/10.1080/15384101.2016.1181876
6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7352172/
7. https://www.sciencedirect.com/science/article/pii/S1550413118301220
8. https://www.sciencedirect.com/science/article/abs/pii/S0014299920302508
9. https://pubmed.ncbi.nlm.nih.gov/27164052/
10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5979282/
11. https://pubmed.ncbi.nlm.nih.gov/22848760/
12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5795269/
13. https://pubmed.ncbi.nlm.nih.gov/28721271/
14. https://pubmed.ncbi.nlm.nih.gov/23312803/
15. https://pubmed.ncbi.nlm.nih.gov/29874584/
16. https://pubmed.ncbi.nlm.nih.gov/18052316/
17. https://pubmed.ncbi.nlm.nih.gov/27721479/
18. https://pubmed.ncbi.nlm.nih.gov/31278280/
19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3616313/

DOI: https://doi.org/10.14200/rmd.2022.0001

Categories: Restorative Medicine Digest

AARM™

27 State Street, Suite 5 | Montpelier, VT 05602 | 866-962-2276