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Caffeine and coffee as therapeutics against Alzheimer's disease.

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Abstract

Epidemiologic studies have increasingly suggested that caffeine/coffee could be an effective therapeutic against Alzheimer's disease (AD). We have utilized a transgenic mouse model for AD in well-controlled studies to determine if caffeine and/or coffee have beneficial actions to protect against or reverse AD-like cognitive impairment and AD pathology. AD mice given caffeine in their drinking water from young adulthood into older age showed protection against memory impairment and lower brain levels of the abnormal protein (amyloid-beta; Abeta) thought to be central to AD pathogenesis. Moreover, "aged" cognitively-impaired AD mice exhibited memory restoration and lower brain Abeta levels following only 1-2 months of caffeine treatment. We believe that the cognitive benefits of chronic caffeine administration in AD mice are due to caffeine itself, and not metabolites of caffeine; this, because our long-term administration of theophylline to AD mice provided no cognitive benefits. In acute studies involving AD mice, one oral caffeine treatment quickly reduced both brain and plasma Abeta levels - similarly rapid alterations in plasma Abeta levels were seen in humans following acute caffeine administration. "Caffeinated" coffee provided to AD mice also quickly decreased plasma Abeta levels, but not "decaffeinated" coffee, suggesting that caffeine is critical to decreasing blood Abeta levels. Caffeine appears to provide its disease-modifying effects through multiple mechanisms, including a direct reduction of Abeta production through suppression of both beta- and gamma-secretase levels. These results indicate a surprising ability of moderate caffeine intake (the human equivalent of 500 mg caffeine or 5 cups of coffee per day) to protect against or treat AD in a mouse model for the disease and a therapeutic potential for caffeine against AD in humans.

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