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The Role of Coffee in Alzheimer Disease

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Abstract

Alzheimer disease (AD) is the most frequent cause of dementia in elderly. It leads to progressive cognitive decline due to accumulation of two proteins (β -amyloid peptide (A β) and Tau) in the forms of senile plaques and neurofibrillary tangles in the brain. A lot of studies suggest that regular moderate coffee consumption over a lifetime reduces the risk of developing AD, particularly in the elderly. Caffeine has well-known short-term stimulating effects on central nervous system, but the long-term impacts on cognition have been less clear. Thus, the putative protective effect of caffeine against AD is of great interest. In this report, we discuss the neuroprotective effect of caffeine in AD. The findings of the previous studies indicate the ability of moderate caffeine intake to protect against AD via prevention of (A β) buildup. This finding might open possibilities for prevention or postponing the onset of AD. In conclusion, coffee drinking may be associated with a decreased risk of AD.

Introduction

Alzheimer disease (AD) is a neurodegenerative disorder; the most common cause of dementia in older adults, with an increasing incidence as a function of age [1, 2]. The disease usually manifests with memory impairment, altered mood and behavior, and loss of learned motor skills and language. Over time, disorientation and aphasia often develop; patients in the final phases of AD often become mute and immobile [1]. The fundamental abnormality in AD is the accumulation of two proteins amyloid-beta peptide (A β) and naturally present Tau protein in the forms of plaques and tangles, respectively; in specific brain regions, and the definitive diagnosis of AD is based on the observation of characteristic brain lesions: senile plaques and neurofibrillary tangles. These changes result in secondary effects including neuronal dysfunction, neuronal death, and inflammatory reactions. A β peptides derive from the cleavage of amyloid precursor protein (APP) by the enzymes β - and γ -secretases. After generation of A β , it is highly prone to aggregation; it first forms small oligomers, and these eventually propagate into large aggregates and fibrils. These aggregates deposit in the brain and are visible as plaques. Tau is a microtubule-associated protein present in the neural axons. The physiologic and pathologic functions of Tau are also regulated by phosphorylation. Changes in Tau phosphorylation may affect multiple Tau functions and facilitate Tau aggregation. With the development of tangles in AD, tau protein,

becomes hyperphosphorylated, and loses the ability to bind to microtubules. Finally, neuroinflammatory processes are considered to have a role in AD [1]. Coffee is one of the most popular drinks in the world. It contains many different components, mostly caffeine, polyphenol, trigonelline, and others. Caffeine is a psychoactive and neurostimulating substance and has multiple effects on the brain, it helps concentration, and affects sleep also improves mood and memory [2]. Caffeine (1,3,7-trimethylxanthine) is a purine-like alkaloid with diverse biological actions; it acts as a non-selective adenosine receptor antagonist. Adenosine receptors (A_1R , $A_{2A}R$, $A_{2B}R$ and A_3R) are G-protein-coupled receptors found in a variety of different cells through the body; A_1R is abundant in the cerebellum and the cerebral cortex, while $A_{2A}R$ is found predominantly in the striatum, basal ganglia, olfactory cortex, glia and the hippocampus. At 300 mg of consumption, caffeine affects all adenosine receptors, but it has the highest interaction with A_1R and $A_{2A}R$ [3]. It is believed that caffeine exhibits neuroprotective effects by blocking adenosine receptors. This results in higher concentrations of serotonin and acetylcholine – neurotransmitters in the central nervous system. Caffeine increases neural activity, leading to downstream stimulatory effects on the neurons. Also it stabilizes blood-brain barrier (BBB) integrity, which contributes to brain homeostasis. However, the detailed molecular mechanism of caffeine's action on BBB remains poorly understood [2]. In addition to its potential as an antioxidant compound, it is able to protect against oxidative stress in AD. Another positive effect of caffeine, it reduces amyloid production and increases amyloid clearance through its interaction with β - and γ -secretase [3]. In Humans, cognitive benefits of caffeine have been reported [1]. Most human epidemiological studies suggest that a lifetime of regular coffee/caffeine consumption reduces the risk of developing Alzheimer's disease, particularly in the elderly [4].

Aim of the study

The main aim of this study was to provide a review about the effect of coffee on Alzheimer disease, to shed the light on the possibility for stopping AD.

Materials and Methods

The first study was performed over 21-year follow-up (875 women and 534 men,

50 years of age at the beginning of the study) comparing between two groups of people (moderate coffee consumer and low coffee consumers) [3]. The second study was performed by examining 10 men and 263 women over the age of 65 years [3]. The third study was performed on 54 AD patients with an average daily caffeine intake of 74 ± 98 mg throughout the 20 years that preceded their diagnosis, while the age-matched controls had an average daily intake of 199 ± 136 mg during the corresponding 20 years of their life [3]. The fourth study was performed over 10 years; on animal model treated with caffeine at 1.5 mg/d in mice reduced A deposition in the hippocampus (40%) and the entorhinal cortex (46%) [3].

Results

The first study showed that drinking (3-5 cups) of coffee was associated with decrease the risk of AD (62%-64%) and dementia (65%-70%) later in life, compared to low coffee consumers (0-2 cups) [3]. The second study revealed that coffee consumption was associated with a 31% lower risk of AD (OR=0.69, CI=0.5-0.96) in the Canadian population [3]. The third study displayed that exposure to caffeine was found to be significantly associated with a 60% reduced risk of AD (OR=0.40, CI=0.25-0.67) [3]. The fourth study confirmed that with caffeine, A 1-40 and A 1-42 levels were reduced in the cortex (25% and 51%, respectively) and hippocampus (37% and 59%, respectively) [3].

Discussion

The accumulation of two proteins (A) and Tau protein in the forms of plaques and tangles in the brain in AD is the principle theory in the pathogenesis of AD. While the accumulation of amyloid-beta peptide remains highly characteristic of AD. This accumulation of amyloid-beta peptide (A) leading to memory loss due to the loss of synapses in the limbic cortex, primarily in the hippocampus. This synapse was seen to be the main target of the toxic A oligomers. AD's signature characteristics include tau deposits made up of proteins and A plaques that have been found to be significantly reduced with caffeine by scientists. Caffeine also prevents the loss of memory during aging and the progression in AD. Interestingly anti-amyloid-

beta peptide (A β) drugs are thought to reduce brain amyloid levels and enhance memory problems. The data obtained from these human studies indicate the protective effect of caffeine lowering the risk of AD. However, it support that caffeine is beneficial also in animal models, which reduce A β plaques of AD by inhibition of β - and γ -secretase via caffeine. This indicates the target therapeutic effect of caffeine against AD. In addition to the effect of caffeine as adenosine receptor antagonist in AD. Evidence has shown that consumption of caffeine can protect against AD and can also contribute to symptom remission for those already affected. Mice studies on caffeine's potential role in AD appear consistent. Coffee was used in these experiments to slow down or prevent A β plaques from growing. Intriguing findings are obtained, with positive evidence from animal models suggesting ways to stop amyloid plaque formation or allow the brain to clear the deposits as they develop [3]. This new evidence points to the promise of new and safer treatment in humans. As well as the positive effect of caffeine on humans that have been shown in the three above mentioned studies also confirm the relation between caffeine and AD in which the caffeine is related to reduce the risk for developing AD. The previous data suggest the protective effect of caffeine/coffee in AD. All the previous studies showed that coffee/caffeine lowers the risk of AD.

Conclusion

This report concludes that the caffeine consumption may protect against AD. The data obtained from these studies indicating there are ways to stop the formation of A β plaques production by the reduction of β - and γ -secretase activities. This revealed the therapeutic benefits of coffee. Inhibition of these secretases represents an obvious logical strategy to inhibit the generation of A β . This finding might open possibilities for stopping or prevention of AD.

Future work

Further research is needed to investigate the effects of caffeine in AD patients. Further research must evaluate the potential benefits of caffeine in AD patients, and the side effects associated with its chronic use in this patient population.

References

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