



Contents lists available at BioMedSciDirect Publications

## International Journal of Biological & Medical Research

Journal homepage: [www.biomedscidirect.com](http://www.biomedscidirect.com)



### Review Article

## Caffeine and Alzheimer's disease

Prenya Rajendran<sup>a</sup>, Achal Bhatt<sup>b</sup>, Sachin Manthuruthil<sup>c</sup>, Sandeep Pericherla<sup>d</sup>.

<sup>a</sup>American University of Antigua, New York City, NY, USA.

<sup>b</sup>Windsor University School of Medicine, Brightons Estates, Cayon, St Kitts, West Indies -

<sup>c</sup>Sri Ramachandra Medical College, Chennai, India.

#### ARTICLE INFO

##### Keywords:

Iron deficiency anemia

Oxidants

Antioxidants

Pregnancy

#### ABSTRACT

Caffeine is a commonly used, unregulated psychoactive substance in use by up to 90% of adults in North America on a daily basis. Caffeine acts by competitively inhibiting the inhibitory effects of adenosine, thus enhancing the action of other neurotransmitters i.e. epinephrine, norepinephrine, acetylcholine, dopamine and serotonin. A1 and A2a Adenosine receptors in the basal ganglia are inhibited specifically, and competitively by caffeine. In both animal and human studies, 300-500 mg per day of caffeine consumption has been shown to both acutely and chronically reduce blood plasma, and brain levels of amyloid-beta protein, a central player in the development of Alzheimer's Disease. Cognitive decline, dementia and Parkinson's Disease are also positively affected by long term caffeine consumption. Evidence also exists demonstrating improvement of already lost memory and cognitive function of Alzheimer's Patients. The various individually active metabolites of Caffeine (paraxanthine, theophylline and theobromine) have physiological activity yet their administration alone does not produce similar cognitive benefits, nor alter blood and brain levels of amyloid-beta, indicating the key importance of caffeine itself.

© Copyright 2010 BioMedSciDirect Publications IJBMR -ISSN: 0976:6685. All rights reserved.

### 1. Introduction

Caffeine is the most commonly used unregulated psychoactive substance used in the world. Up to 90% of North Americans report to use caffeine on a daily basis [1]. Common natural sources include the Coffee plant, Tea plants, Yerba Mate and Kola Nut. It is a white crystalline xanthine alkaloid which generally acts as a stimulant in human physiology. Caffeine is classified as "GRAS" by the US FDA (Generally Recognized as Safe) [2] although there is considerable recent controversy regarding the safety of caffeine addition to alcoholic beverages [3].

#### Mechanism of Action and Metabolism:

There are multiple mechanisms of action of caffeine in the body and brain, the most notable of which affects A1 and A2a Adenosine receptors in the basal ganglia. Caffeine binds to these receptors due to similarity in chemical structure and thus acts as a competitive inhibitor to the inhibitory effects of adenosine on other neurotransmitters at neuronal junctions, namely acetylcholine, epinephrine, norepinephrine, dopamine, serotonin, and also

endorphins [4]. Specifically, the excitatory effects of caffeine are mediated through action of methyl-xanthine on serotonin. The cognitive enhancement, and memory recall associations follow thus, and are likely explained by the arousal of this mechanism [5]. Absorption of Caffeine in the body is through mucosal membranes. Intestinal and rectal absorption peaks between 45 to 60 minutes [6]. The metabolism of caffeine is done primarily through hepatic CYP450 enzyme, specifically CYP1A2. The metabolism yields other active compounds, of note being paraxanthine, theobromine and theophylline all of which are excreted through the urine [7].

#### Neuroprotective Effects and Effects on Alzheimer's disease:

Alzheimer's Disease (AD) and dementia are growing health concerns particularly in the elderly and there is no definitive curative treatment. Multiple studies have shown statistically significant improvement in cognitive functioning and favorable effects in cognitive decline, Alzheimer's Disease and Dementia in moderate coffee drinkers [8]. Similar studies were carried out with Tea consumption and though some positive associations were found, it was not as favorable as with coffee consumption. The relative doses of caffeine may play a role in these findings as one 8oz cup of coffee contains up to 200 mg of caffeine whereas an 8oz cup of green tea contains up to 40 mg caffeine. Studies in mice have demonstrated significant reduction of the abnormal protein amyloid-beta in the brain of subjects with moderate caffeine intake

\* Corresponding Author : Prenya Rajendran,

Medical student, American University of Antigua, New York City, NY, USA.  
email: Doctorid1001@gmail.com

since young adulthood. Amyloid-beta protein is currently thought to play a central role in the pathogenesis of Alzheimer's Disease. Further, "aged" subjects with existing cognitive impairment showed memory improvement and reduced levels of amyloid-beta protein with as little as one to two months of regular caffeine consumption [9]. The beneficial effect is thought to be directly from caffeine, and not its metabolites (paraxanthine, theobromine, theophylline), as similar trials carried out with metabolites and various other substances (primarily theophylline) did not produce similar results. Very rapid alterations in plasma, and brain amyloid-beta levels are observed with acute caffeine administration [9]. A similar experiment done using decaffeinated coffee did not produce equivalent results, suggesting the underlying involvement of caffeine itself in the mechanism. Coffee and Teas provide antioxidants and other nutritive substances and chemicals thought to be beneficial to human health however they do not appear to play a direct role in affecting brain and plasma amyloid-beta levels and preventing/reversing cognitive decline of Alzheimer's Disease. The proposed mechanism by which caffeine influences amyloid-beta levels is through beta and gamma secretase level modulation [10]. The effective dose varies by study but is between 300-500 mg per day which translates into 3-5 cups of brewed coffee or ten or more cups of green tea per day.

#### Conclusion:

Though caffeine is in common use throughout the world, only recently are its potential therapeutic values being investigated seriously in cases of Alzheimer's Disease, Parkinson's Disease, Dementia and other type of cognitive decline conditions. Animal studies and human studies both demonstrate significant positive effects from 300-500 mg per day of caffeine consumption with specifically caffeine dose dependent statistical improvement. Similar improvement is not noted with single metabolite or antioxidant administration alone. Existing studies and data are strongly suggestive of therapeutic and preventive potential.

#### References:

- [1] Lovett R (2005-09-24). Coffee: The demon drink? New Scientist (2518).
- [2] Database of Select Committee on GRAS Substances (SCOGS) Reviews: Caffeine. U.S. Food and Drug Administration Website. 10/31/2006. <http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=scogsListing&id=42>
- [3] Serious Concerns Over Alcoholic Beverages with Added Caffeine. U.S. Food and Drug Administration Website. November 17, 2010 <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm233987.htm> accessed on 5/5/2013.
- [4] Fisone G, Borgkvist A, Usiello A. Caffeine as a psychomotor stimulant: mechanism of action. *Cell. Mol. Life Sci.* 2004; 61 (7-8): 857-72. doi:10.1007/s00018-003-3269-3. PMID 15095008
- [5] Nehlig A, Daval JL, Debry G. Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. *Brain Res Brain Res Rev.* 1992 May-Aug;17(2):139-70.
- [6] Liguori A, Hughes JR, Grass JA (1997). Absorption and subjective effects of caffeine from coffee, cola and capsules. *Pharmacol. Biochem. Behav.* 58 (3): 721-6. doi:10.1016/S0091-3057(97)00003-8. PMID 9329065
- [7] "Caffeine". The Pharmacogenetics and Pharmacogenomics Knowledge Base. Accessed on 2013/5/5.
- [8] Eskelinen MH, Kivipelto M. Caffeine as a protective factor in dementia and Alzheimer's disease. *J Alzheimers Dis.* 2010;20 Suppl 1:S167-74. doi: 10.3233/JAD-2010-1404.
- [9] Arendash GW, Cao C. Caffeine and coffee as therapeutics against Alzheimer's disease. *J Alzheimers Dis.* 2010;20 Suppl 1:S117-26. doi: 10.3233/JAD-2010-091249.