

Abstract

Caffeine is the most widely used psychostimulant in Western countries, with antioxidant, anti-inflammatory and anti-apoptotic properties. In Parkinson's disease, caffeine was found to be beneficial in men; however, the effect of caffeine in female PD patients is controversial due to caffeine's competition with estrogen for the estrogen metabolizing enzyme, CYP1A2. In Alzheimer's disease (AD), caffeine is beneficial in both men and women, in humans and animals. Caffeine is protective in PD and AD at dosages equivalent to 3-5 mg/kg. Caffeine's most salient mechanisms of action relevant to neurodegenerative diseases need to be further explored.

Introduction

- ❖ Caffeine (1,3,7-trimethylxanthine) is the most widely used psychostimulant in Western countries [1].
- ❖ The average Canadian consumes 210-238 mg/d of caffeine [1].
- ❖ Caffeine is quickly absorbed through the gastrointestinal tract and crosses the blood-brain barrier [1].
- ❖ Chronic caffeine intake ameliorates oxidative stress and improves mitochondrial function [1].

Rationale

This review investigates the effects of caffeine on neurodegenerative disorders, including Alzheimer's disease (AD) and Parkinson's disease (PD).

Methods

Pubmed and Google Scholar were searched through to October 7, 2016 for terms "caffeine AND Alzheimer's disease" or "caffeine AND Parkinson's disease".

Caffeine, adenosine and adenosine receptors

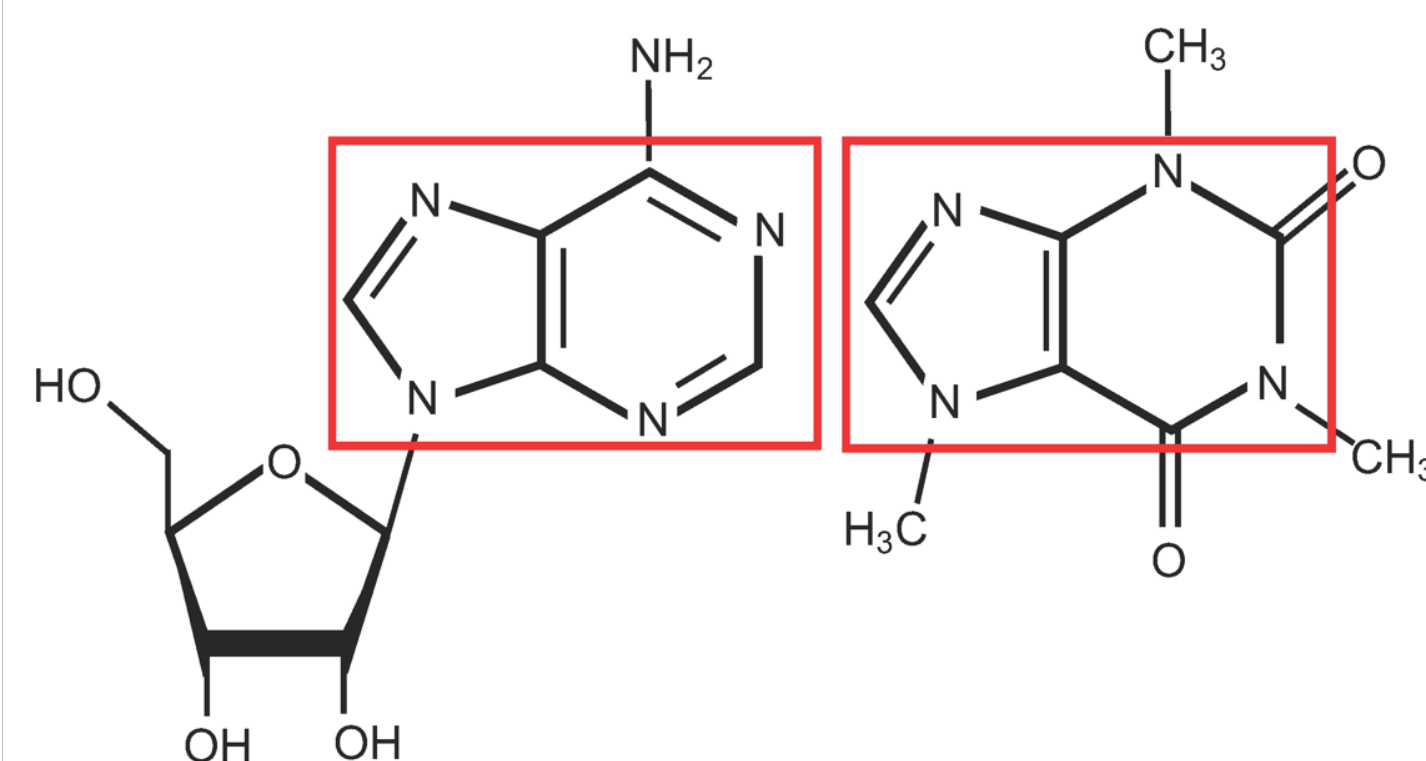


Figure 1. The chemical structure of adenosine (left), an endogenous adenosine receptor agonist, and caffeine (right), an exogenous adenosine receptor antagonist [1].

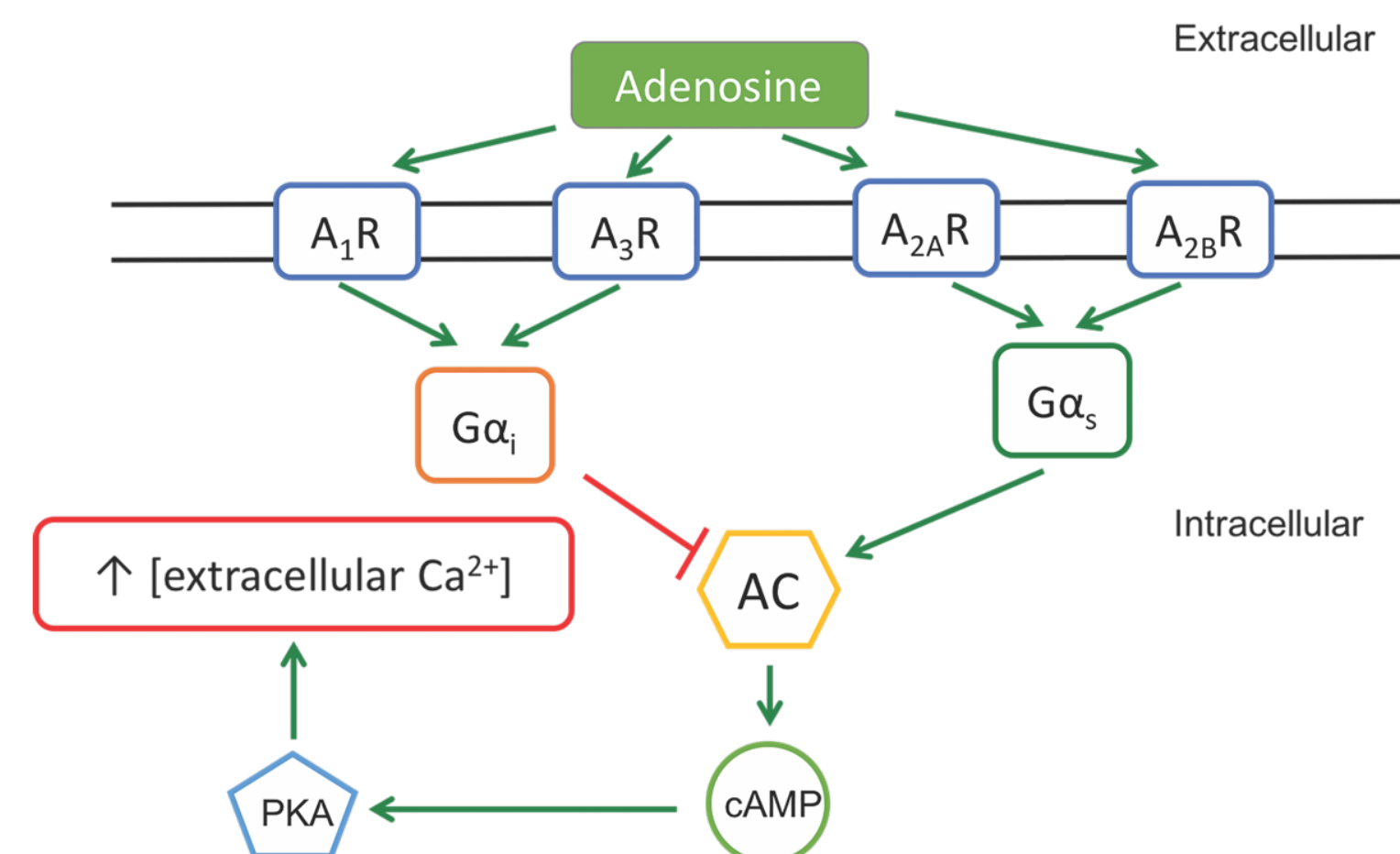


Figure 2. When adenosine binds to A1R and A3R, it lowers AC activity, cAMP production, PKA activation and calcium entry into the cell. When adenosine binds to A2AR and A2BR, G_s is activated, increasing AC activity, cAMP production, PKA activation and calcium entry into the cell [2].

Caffeine and Parkinson's disease - Men

- ❖ Coffee consumption:
 - ❖ ↓ risk of PD
 - ❖ ↓ striatal neuron damage
 - ❖ ↑ motor function [3,4]

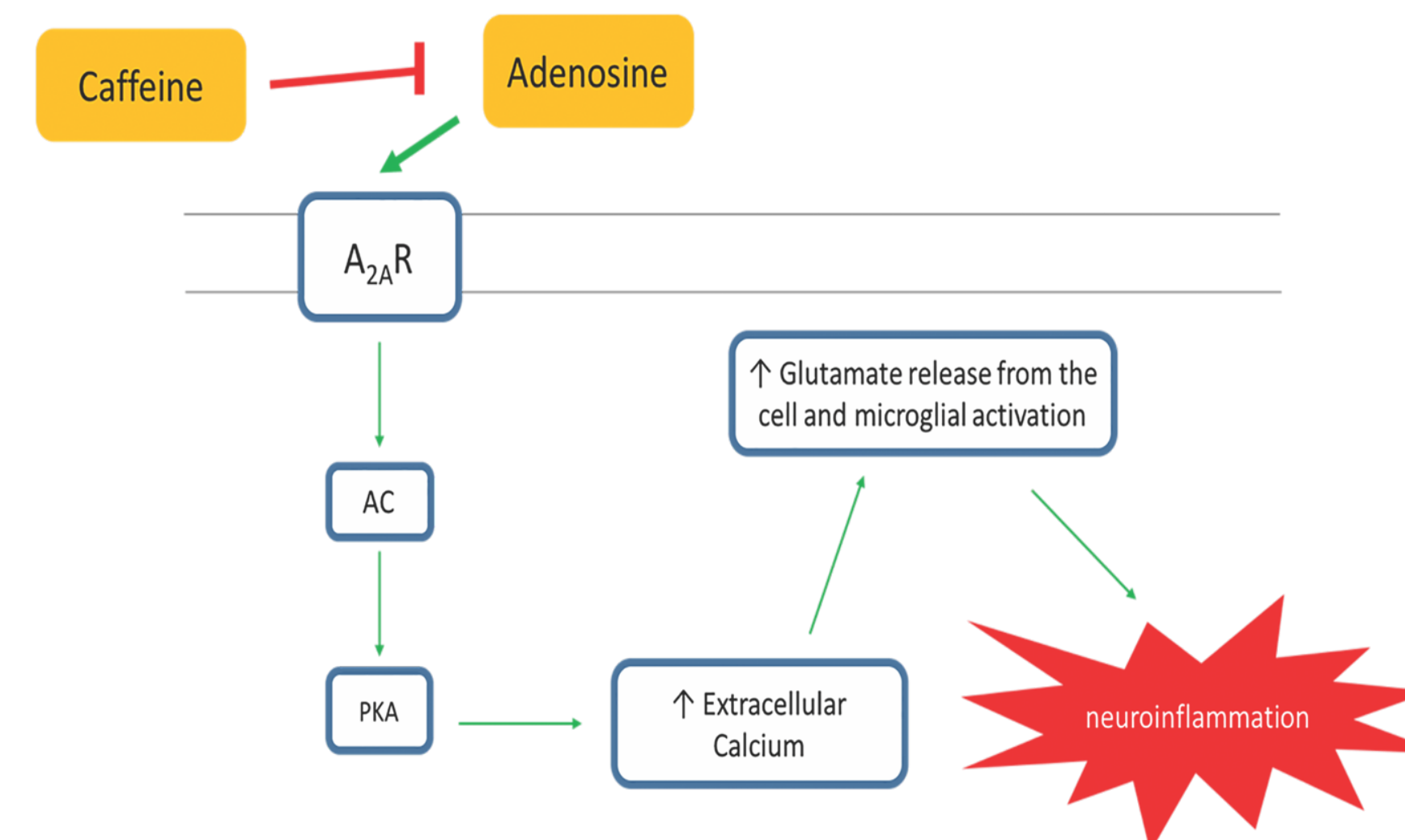


Figure 3. Through activation of the A2AR, adenosine increases extracellular calcium inside the cell, resulting in an increase in glutamate, leading to neuroinflammation. By inhibiting the binding of adenosine to its receptor, caffeine decreases glutamate release, thus reducing neuroinflammation [3].

Caffeine and Parkinson's disease - Women

- ❖ Coffee consumption:
 - ❖ Low caffeine (68mg/d) + postmenopausal hormone = ↓ risk of PD [5].
 - ❖ High caffeine (668 mg/d) + postmenopausal hormone = ↑ risk of PD [5].
 - ❖ Estrogen may prevent the neuroprotective effects of caffeine

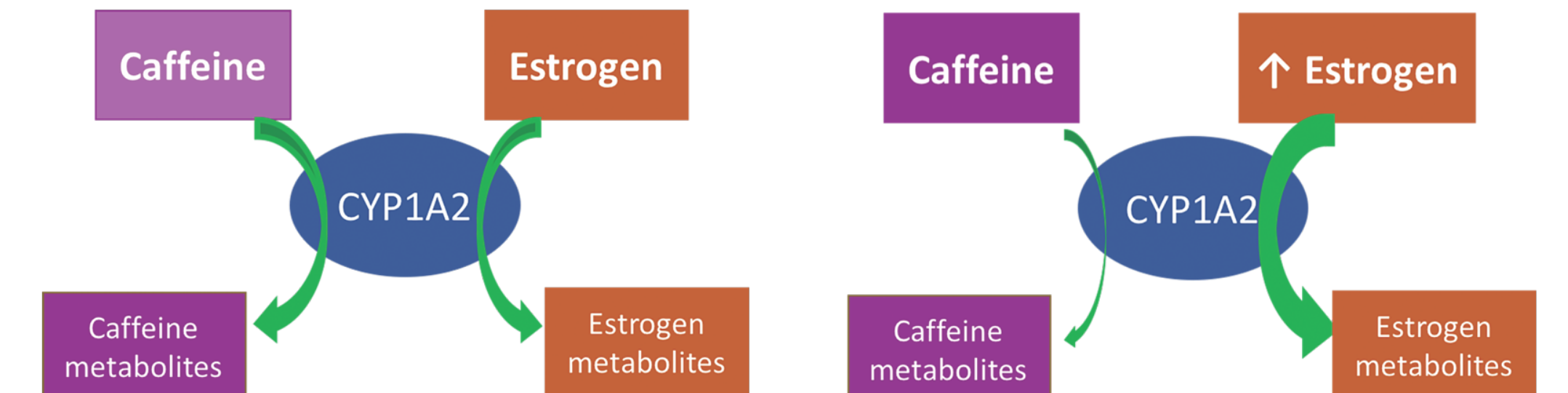


Figure 4. Metabolism of estrogen inhibits metabolism of caffeine [6].

Caffeine and Alzheimer's disease

- ❖ Coffee consumption:
 - ❖ ↓ 65-70% risk of AD
 - ❖ ↓ 54% in cognitive decline
 - ❖ Enhances memory [7]
 - ❖ ↓ Aβ burden
 - ❖ Protect against cell death

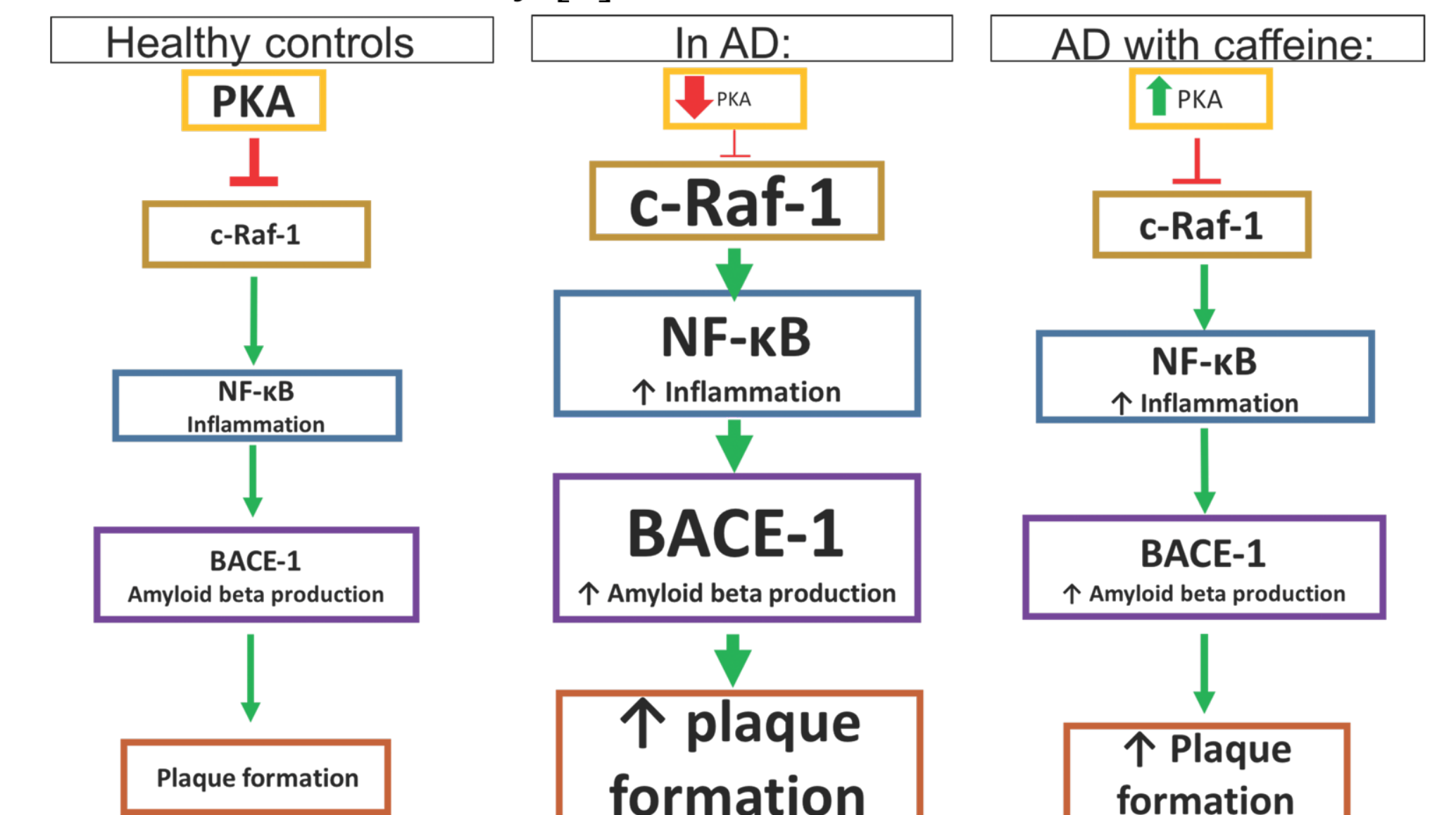


Figure 5. Caffeine normalizes the otherwise reduced PKA levels in APPsw mice, therefore inhibiting c-Raf-1 activation, NF-κB pathway activation and BACE-1 production, leading to lower levels of plaque formation [8].

Conclusion

- ❖ At average levels of caffeine consumption, caffeine's main mechanism of action is antagonism of adenosine receptors.
- ❖ Caffeine consumption, at dosages 3-5 mg/kg, is associated with a lower risk of PD and AD.
- ❖ Further research in women regarding the effects of caffeine in neurodegenerative diseases is warranted.

References

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