The Effect of Caffeine on Amyloid-Beta in Late-Onset Alzheimer's Disease

Eleanor Liu

Introduction

Alzheimer's

- Neurodegenerative
- Caused by plaques and tangles in brain
- Typically late-onset

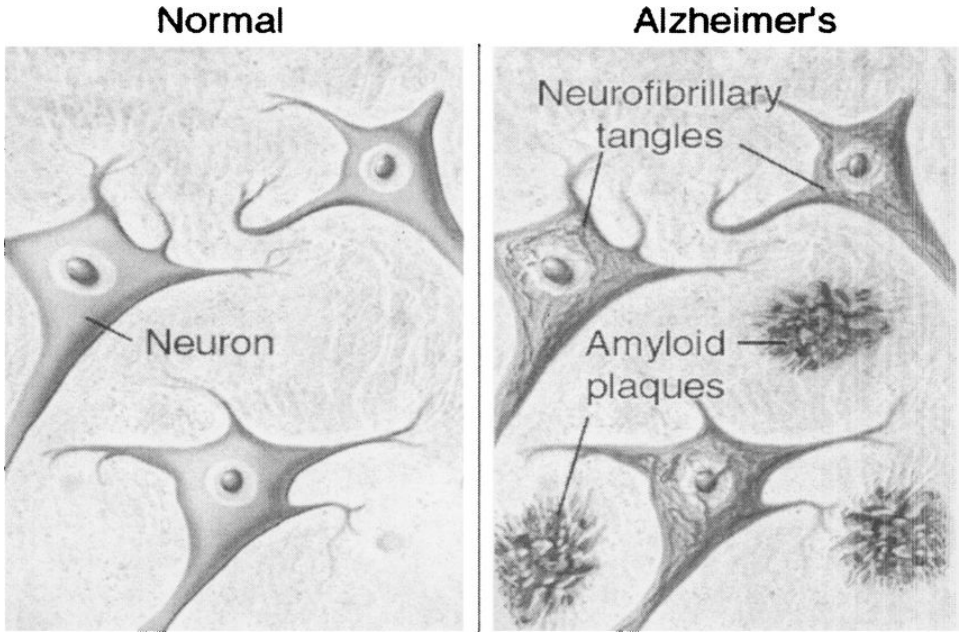


Fig. 1: Comparison between normal neurons and neurons found in Alzheimer's disease

65

number of seconds between each new case of Alzheimer's

145%

increase in deaths due to Alzheimer's from 2000

Health

- Cognitive function loss
  - Bodily function
- Psychological problems
- 1 in 3 mortality rate

Societal

- Caregiving
  - $234 billion
  - 18.5 billion hours
- Federal costs
  - $290 billion
  - $1.1 trillion by 2050

Amyloid-Beta Proteins

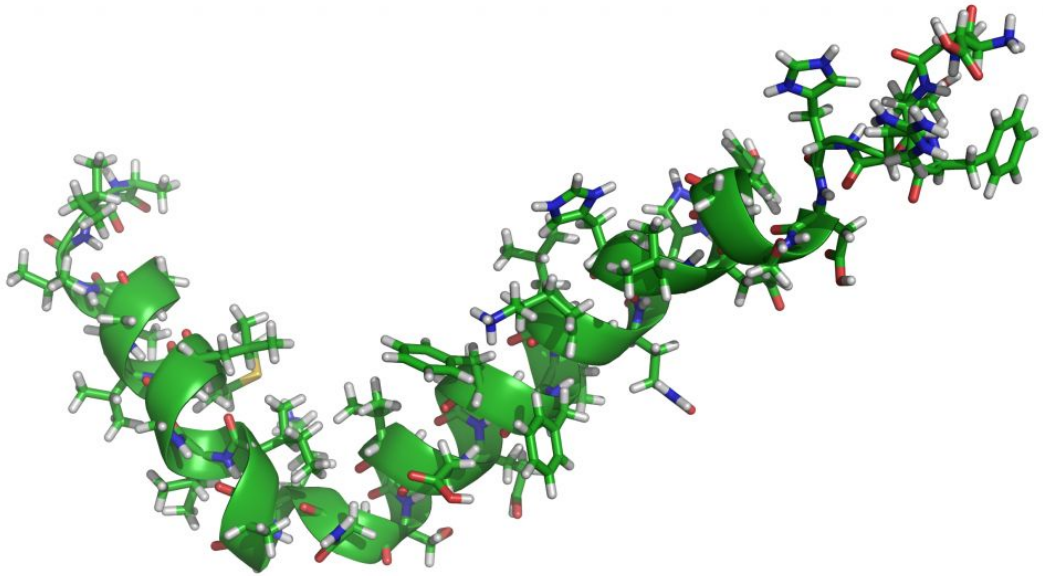


Fig. 2: Three-dimensional structure of an amyloid-beta protein

Amyloid-Beta Plaque Formation

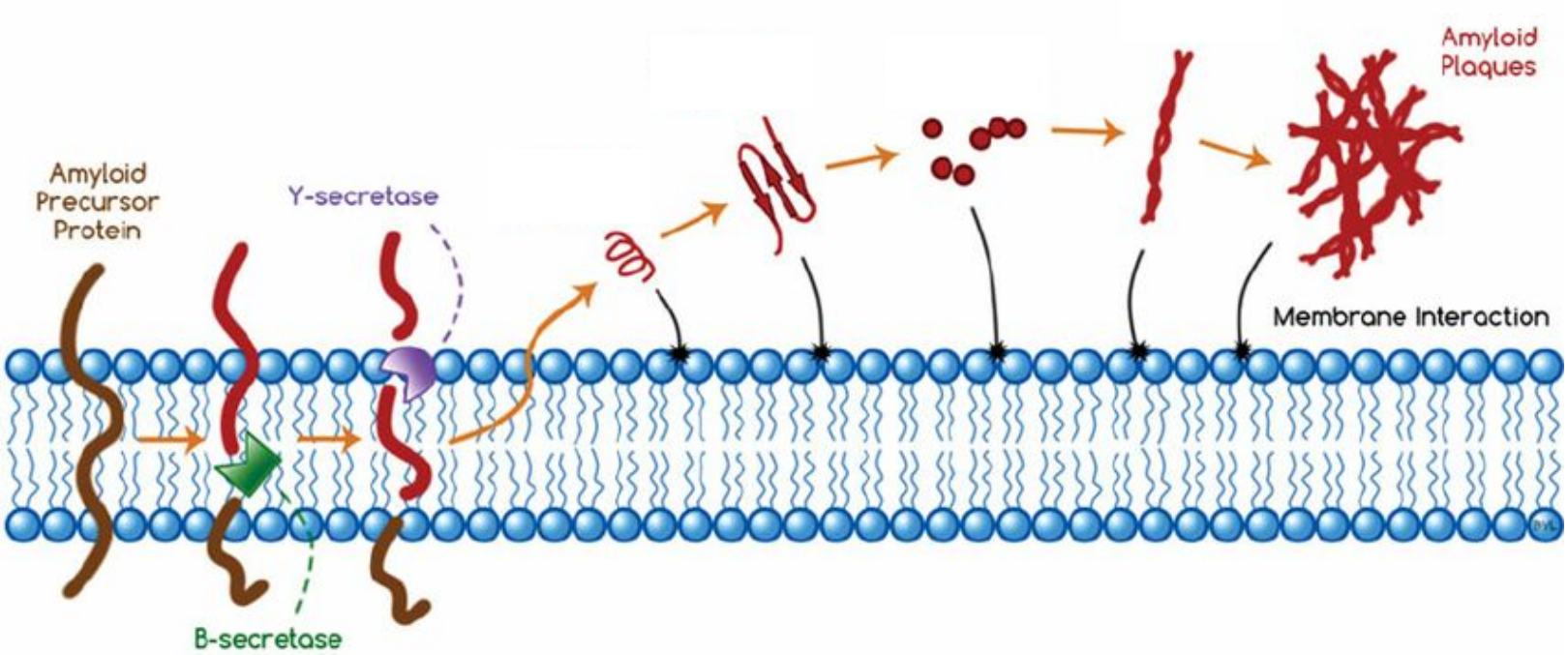
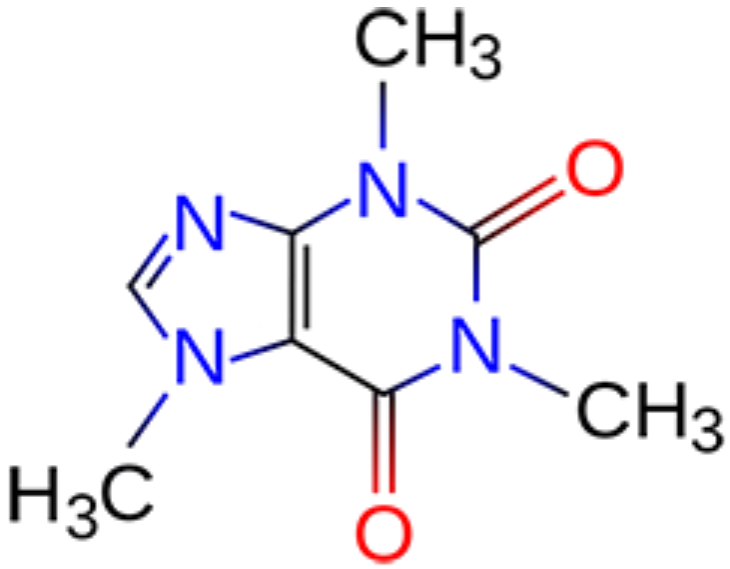


Fig. 3: Formation of amyloid-beta clusters from parent protein, amyloid precursor protein.

Caffeine

- Stimulant affecting nervous system
- Effects are due to its function as molecular antagonist
    - Adenosine



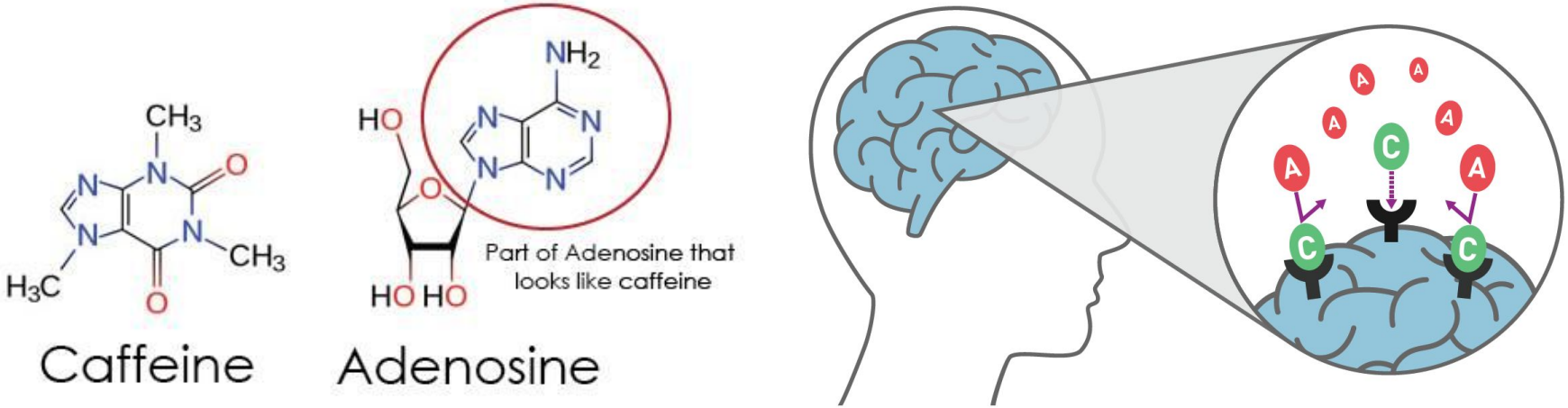


Fig. 4: Caffeine binds to the adenosine receptors in the cell membrane of neurons through antagonism.

Caffeine

Anti-oxidation

- Prevents cell damage from harmful particles

Anti-inflammation

- Prevents self-detrimental immune response

Neuroprotection

- Prevents unhealthy neuron death from toxic proteins

Purpose:

to investigate a correlation between **caffeine concentration** in the brain and the presence of **amyloid-beta** proteins that cause **Alzheimer's disease**

Research Question

Is there a relationship between **caffeine concentration** in the brain and **amyloid-beta protein levels** significant to **late-onset Alzheimer's disease** development?

Null Hypothesis

no correlation between caffeine concentration and neural amyloid-beta protein levels exists

Alternative Hypothesis

a statistically significant relationship between caffeine concentration and neural amyloid-beta protein levels exists, specifically a negative correlation

Methods

Literature Search

- Peer-reviewed articles
- Online databases
- Scientific journals

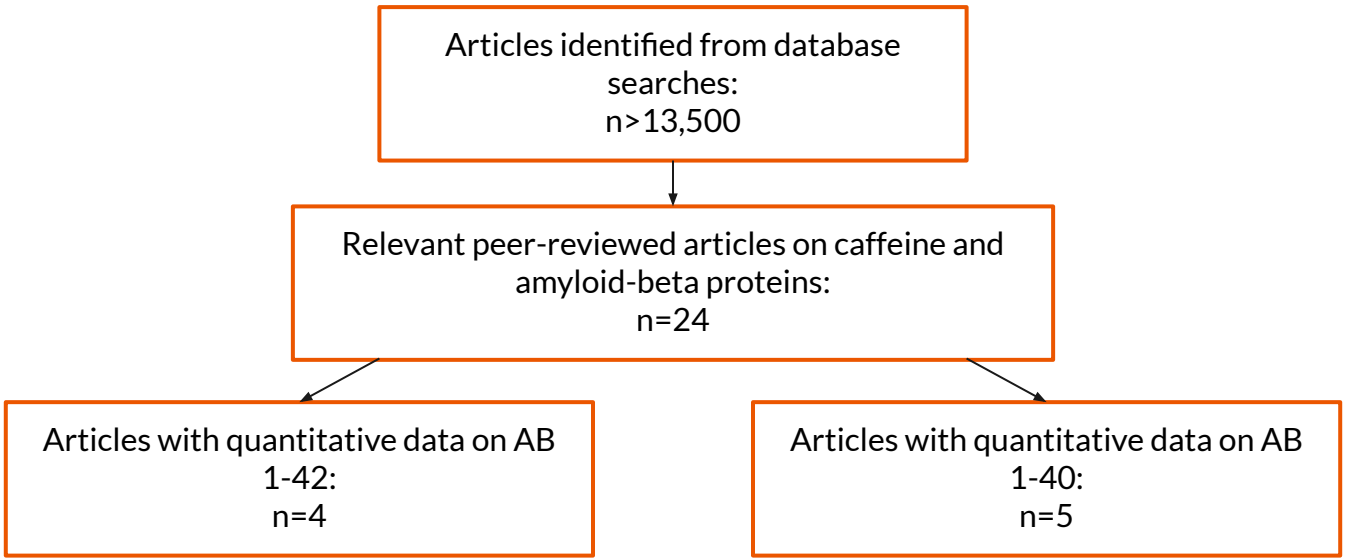
Literature Collection

- Reference pages
- Filter through articles for relevant information and data
  - Amyloid-beta 1-40, 1-42
  - Transgenic mice

Data Collection

- Compile quantitative data
- Synthesize and analyze data

Literature Collection Process



Data Analysis

- Statistical analysis
- Linear regression model
  - R^2 = 1.00, 100% model fit
- One-tailed t-test
  - $p < 0.05$, statistically significant

Results & Discussion

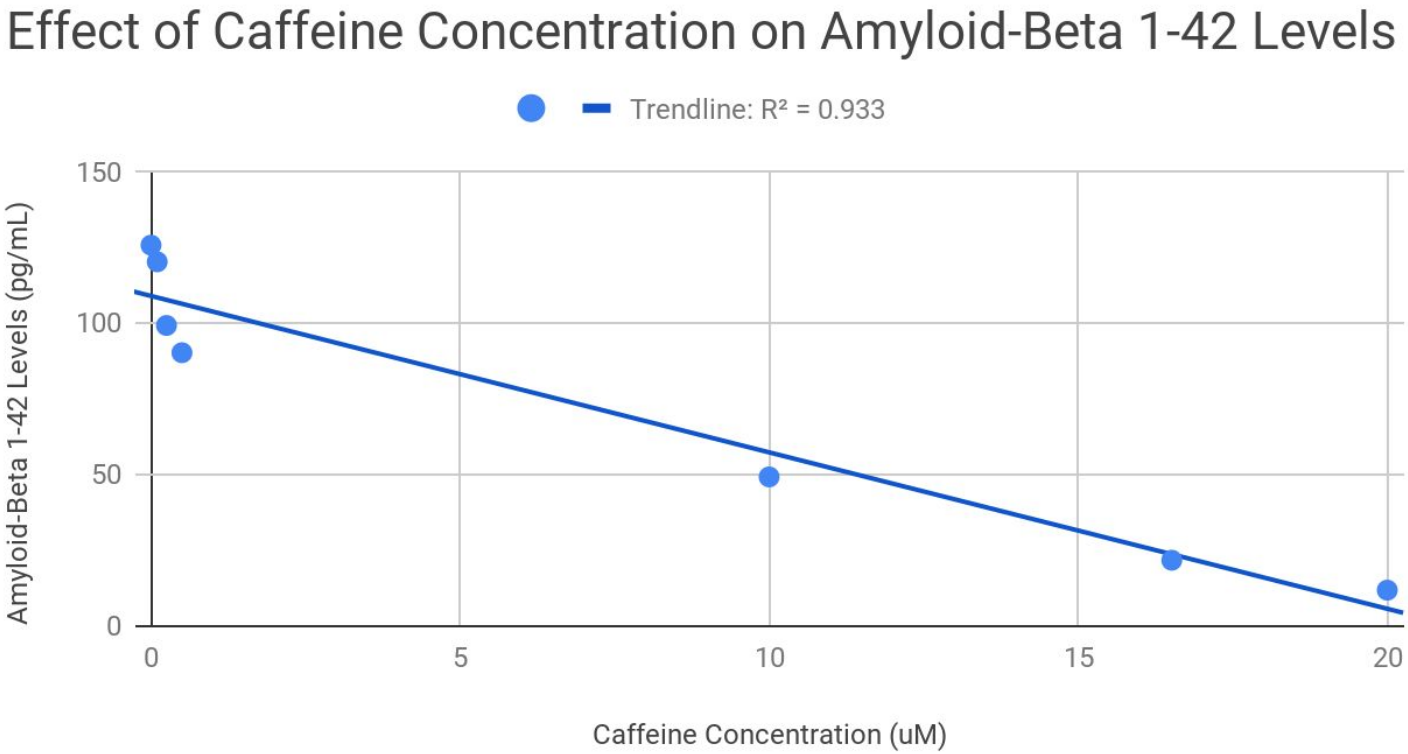


Fig. 5: Scatter plot with trendline showing the correlation of caffeine concentration and amyloid-beta 1-42 levels in late-onset Alzheimer's affected mice brain cells.

$R^2 = 0.933$

93.3% fit with linear regression model

$p = 0.0042$

$p < 0.05$ is statistically significant

supports alternative hypothesis

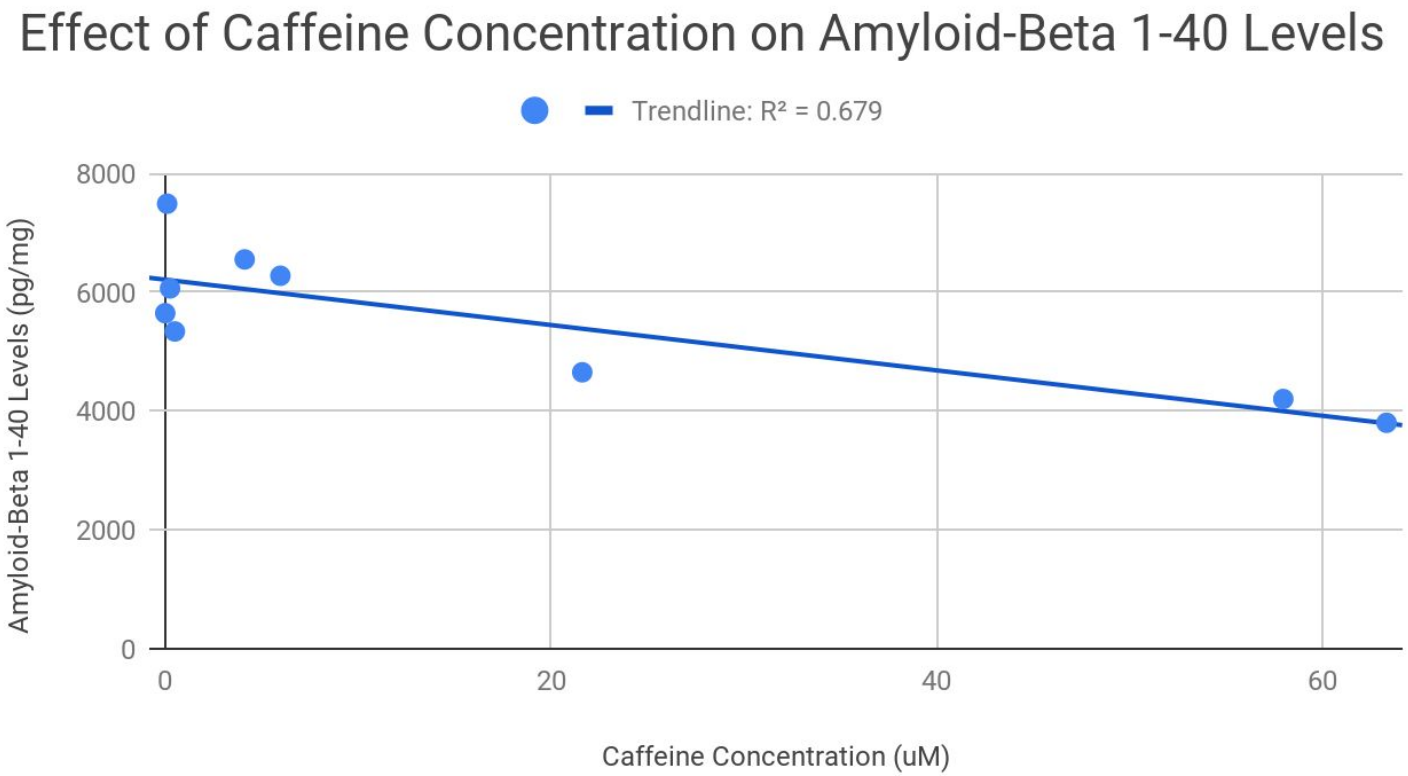


Fig. 6: Scatter plot with trendline showing the correlation of caffeine concentration and amyloid-beta 1-40 levels in late-onset Alzheimer's affected mice brain cells.

$R^2 = 0.679$

67.9% fit with linear regression model

$p = 0.00000033$

$p < 0.05$ is statistically significant

supports alternative hypothesis

Discussion

- Both amyloid-beta 1-40 and 1-42 tests had $p < 0.05$
- Statistically significant relationship

accept alternative hypothesis, reject null hypothesis

Conclusion:

caffeine **does** have a statistically significant effect on the levels of amyloid-beta protein in the brain

Limitations

- Systematic literature review
  - Conflict of interest
- Data approximation
- Extraneous variables in caffeine samples

Further Work

- Further clinical research
- Treatment options
- Application to other neurodegenerative diseases

Acknowledgments

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References

Alzheimer's Association. (2019). [Infographic of facts and figures pertaining to Alzheimer's disease]. *Alzheimer's Disease Facts and Figures*. Retrieved from https://www.alz.org/alzheimers-dementia/facts-figures

Amyloid beta precursor protein. (2019). Retrieved from https://ghr.nlm.nih.gov/gene/APP

Arendash, G. W., Schleif, W., Rezai-Zadeh, K., Jackson, E. K., Zacharia, L. C., Cracchiolo, J. R.,...Tan, J. (2006). Caffeine protects Alzheimer's mice against cognitive impairment and reduces brain β-amyloid production. *Neuroscience*, *142*, 941-952. doi:10.1016/j.neuroscience.2006.07.021

Arendash, G. W. & Cao, C. (2010). Caffeine and coffee as therapeutics against Alzheimer's disease. *Journal of Alzheimer's Disease*, *20*, 117-126. DOI 10.3233/JAD-2010-091249

Cao, C., Cirrito, J. R., Lin, X., Wang, L., Verges, D. K., Dickson, A.,...Potter, H. (2009). Caffeine suppresses amyloid-β levels in plasma and brain of Alzheimer's disease transgenic mice. *Journal of Alzheimer's Disease*, *17*, 681-697. DOI 10.3233/JAD-2009-1071

Chu, Y., Chang, W., Black, R. M., Liu, J., Sompol, P., Chen, Y.,...Cheng, I. H. (2012). Crude caffeine reduces memory impairment and amyloid $\beta_{1\text{-}42}$ levels in an Alzheimer's mouse model. *Food Chemistry*, *135*, 2095-2102. http://dx.doi.org/10.1016/j.foodchem.2012.04.148

Drolle, E., Hane, F. T., Lee, B., & Leonenko, Z. (2014). Atomic force microscopy to study molecular mechanisms of amyloid fibril formation and toxicity in Alzheimer's disease. *Drug Metabolism Reviews*, *46*(2). DOI: 10.3109/03602532.2014.882354

Li, S., Geiger, N. H., Soliman, M. L., Hui, L., Geiger, J. D., & Chen, X. (2015). Caffeine, through adenosine A_3 receptor-mediated actions, suppresses amyloid-β protein precursor internalization and amyloid-β generation. *Journal of Alzheimer's Disease*, *47*(1), 73-83. doi:10.3233/jad-142223

Rivera-Oliver, M. & Díaz-Ríos, M. (2014). Using caffeine and other adenosine receptor antagonists and agonists as therapeutic tools against neurodegenerative diseases: A review. *Life Sciences*, *101*(0), 1-9. doi: 10.1016/j.lfs.2014.01.083

Zhang, L., Zhou, Z., Wang, Z., Du, Y., He, Z., Cao, C., & Zhou, S. (2014). Coffee and caffeine potentiate the antiamyloidogenic activity of melatonin via inhibition of Aβ oligomerization and modulation of the Tau-mediated pathway in N2a/APP cells. *Drug Design, Development, and Therapy*, *9*, 241-272. http://dx.doi.org/10.2147/DDDT.S71106

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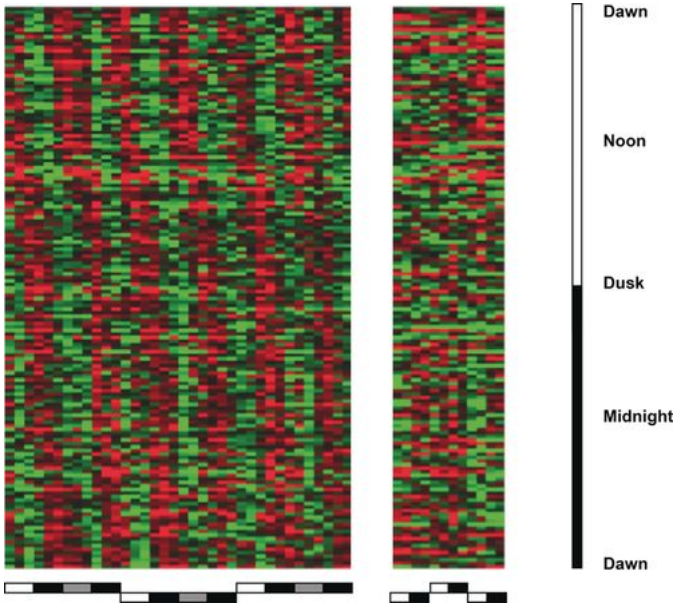
Adenosine Antagonists

- Antagonists: molecules blocking adenosine receptors
- Shown to have neuroprotective effects

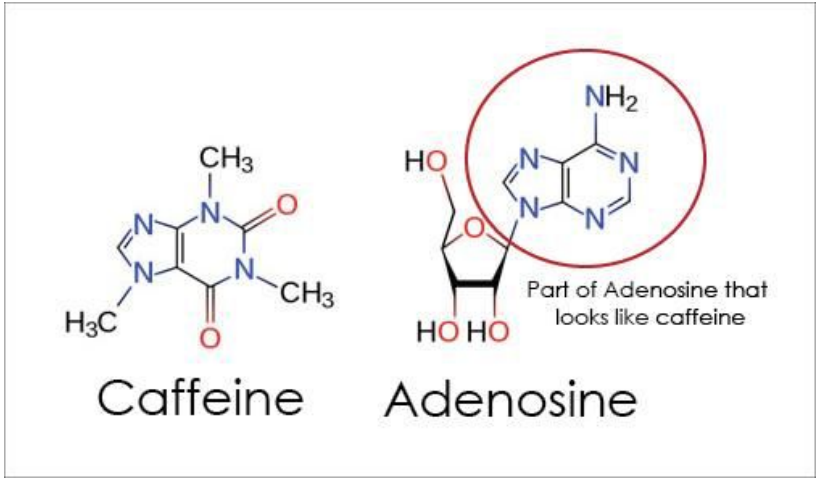
Circadian Rhythm

- Circadian rhythm
- clock, per, timeless genes



Caffeine/Adenosine Relationship

- Caffeine
- Adenosine antagonism



Articles identified from search:
n>13,500

Relevant peer-reviewed articles on caffeine and amyloid-beta proteins:
n=24

Articles with quantitative data on AB 1-40:
n=5

Articles with quantitative data on AB 1-40:
n=4