

How does Caffeine Affect the Neurotransmitters and the Normal Functioning of the Enzymes in our Body

Isha Joshi

How to cite this article:

Isha Joshi. How does Caffeine Affect the Neurotransmitters and the Normal Functioning of the Enzymes in our Body. Indian J Biol 2020; 7(2):99-102.

Abstract

Background: In USA, an adult has a daily intake of caffeine which is 2.4 mg kg⁻¹ body weight. Caffeine is taken in mostly as coffee and most of the people think that it has a direct or an indirect relationship with their health (Madeira, Boia, Ambrósio, & Santiago, 2017). This is a clear indication that people think that caffeine is affecting their health but they are not sure how. Previous studies have shown that caffeine behaves as a stimulant drug which makes a person very active through a very prominent increase in a person's productivity, (Yamato et al., 2002). This information will be drawn in from this source to determine the reason for the increment of productivity. It has also been listed that caffeine basically affects the parts of the brain which are responsible for a person's emotional response (The hippocampus) and these have always been the target organs for researchers (Yamato et al., 2002). This information links neurotransmitters directly to caffeine as hippocampus area is largely governed by the action of neurotransmitters (Tao & Auerbach, 2000).

Keywords: Caffeine; Enzymes; Neurotransmitters; Acetylcholine; Heart rate; Troponin; Adrenaline; Phenylethanolamine N-methyltransferase; Blood pressure.

Introduction

A heavy heart rate variability has been noticed in people who intake caffeine and caffeine also takes a toll on the functionality of their nervous system and muscles (Rauh, Burkert, Siepmann, & Mueck-Weymann, 2006). Heart rate is administered through blood by "enzymes" (Bhagat, Narang, Sharma, Dash, & Chauhan, 2009). Caffeine also impairs a person's basic decision-making ability but the more research is still required on how the complex decision making ability is affected and which elements of the human body are involved. (Häusser, Schlemmer, Kaiser, Kalis, & Mojzisch, 2014). This is a clear indication by the authors that research which should be done on neurotransmitters because they are responsible for complex decision making (Fecteau, Fregni, Boggio, Camprodon, & Pascual-Leone, 2010). This research

Author's Affiliation: Senior Student, Department of Biology, George Mason University, Fairfax, VA 22030, United States.

Corresponding Author: Isha Joshi, Senior Student, Department of Biology, George Mason University, Fairfax, VA 22030, United States.

E-mail: ishajoshi.va@gmail.com

should be conducted because neurotransmitters influence the way enzymes work in a human body (Owolabi, Olatunji, & Olanrewaju, 2017). Enzymes represent the entire meshwork of the human body and the body cannot function if the functioning of enzymes is altered in any way ("BPS Publications," n.d.). Studies have indicated that any drug that enters the body alters the way human enzymes work (Abdullah & Ismail, 2018). But no research is available on caffeine's ability to affect the normal function of enzymes indirectly, by directly affecting the neurotransmitter balance in

our body. The question arises how caffeine affects the neurotransmitters, and can it be a reason for the impairment of normal enzymes functioning in the human body? The purpose of this literature review will be to determine the effects of caffeine on neurotransmitters and to show that if the normal functioning of the enzymes is altered or not.

Decoding the neurotransmitter-enzyme dynamic relationship

How does caffeine affect the neurotransmitter balance?

The main ways that caffeine affects the neurotransmitters is by altering the adenosine receptors and vasoconstriction in the brain which indicates that it attacks our system at a neural level (Diukova et al., 2012). It increases the levels of the neurotransmitter which is known as glutamate (Owolabi, Olatunji, & Olanrewaju, 2017). Glutamate is known to make a person hyper active (primary effect noted after the ingestion of caffeine) (Vyleta & Smith, 2008). It has been proved that the administration of caffeine increases the rate of release of "acetylcholine" neurotransmitter from the hippocampus (Souza et al., 2015). All the sources that have been mentioned above agree that caffeine is responsible for the neurotransmitter imbalance. Glutamate, adenosine and acetylcholine are known to be some of the major neurotransmitters present in the human body and are also known to interact with one another on a constant basis ("Fine-tuning neuromodulation by adenosine - ScienceDirect," n.d.).

How does this imbalance indirectly affect the enzyme functioning?

Previous studies have indicated that caffeine increases the heart rate (Rauh, Burkert, Siepmann, & Mueck-Weymann, 2006). Heart rate alterations (caused by muscle movement) are a major reason for a heart attack (Christoffels, 2011). Studies have shown that an increase in the levels of the enzyme "troponin" leads to a heart attack (Skeik & Patel, 2007). As stated earlier, caffeine is proven to increase the amount of neurotransmitter "glutamate" in the body (Owolabi, Olatunji, & Olanrewaju, 2017). Studies have indicated that glutamate makes the muscles more permeable (easy entry) to Calcium which is needed to trigger troponin's action on the muscles (Kajioka et al., 2012). The patients who have been victims of heart attacks are mostly required to limit their caffeine intake (Srivastava, Fazzari, George, & Marzo, 2017). This literature review can justify the reason for this requirement

as caffeine can be seen to promote heart attacks through altering the neurotransmitter balance and indirectly altering the functioning of the enzyme troponin. Here, caffeine can increase the levels of glutamate which in turn can result in increased levels of calcium. Which can trigger an increase in the levels of the enzyme troponin and finally result in a hyperactive muscle (heart attack by muscle spasms or tachycardia).

How is the decision-making ability impaired?

Complex decision-making ability is altered because of the neurotransmitter imbalance and studies have shown that it is mainly impacted by hypervigilance or we can say "panic" (Phillips & Ogeil, 2015). It has been determined that in this case a neurotransmitter named "adrenaline" is the reason for the panic and stress (Battram, Graham, & Dela, 2007). The amount of "phenylethanolamine N-methyltransferase" in mice with high levels of adrenaline and caffeine (mammals like humans) was found to be higher than the normal levels (Henry & Stephens, 1980). This enzyme is known to be responsible for the formation of "adrenaline" (Kaneda et al., 1988). This information clearly indicates that due to the high levels of adrenaline, the levels of the enzyme responsible for its formation also increased. In this case too, the increase in the levels of phenylethanolamine N-methyltransferase can lead to cardiovascular uncomfot (Hou, Wang, Gao, Liu, & Liu, 2012).

Conclusion:

It was seen that caffeine altered the levels of the neurotransmitter acetylcholine which can increase the permeability of muscle cells to calcium (hyperactive muscles after excessive consumption of caffeine) and caffeine also altered the levels of phenylethanolamine N-methyltransferase which can lead to the accumulation of stress due to neurotransmitter (adrenaline imbalance) and indirect hyperactivity of the enzyme. The information presented clearly indicates that excessive consumption of caffeine can be a very good reason for the indirect alteration of the normal functioning of enzymes. Here, the audience will be able to see the newly established relationship between the functioning of an enzyme with a neurotransmitter which is in the complete control of a drug (like a cascade reaction which involves so many steps before it could produce a final product). It can also be seen this way that a foreign substance is controlling the most important elements of our

body. This review also relates calcium levels to caffeine intake (increased calcium levels can also be a reason for heart attacks).

This review did not offer any practical tests that could be conducted to test the disturbed enzyme function and elevated neurotransmitter levels. Further research can be conducted to determine how these levels can be tested in laboratories so that “caffeine dependent” neurotransmitter imbalances and enzyme impairment (leading to consequences like heart attacks) can be prevented on a premature clinical level (before the person is a victim, as stated above). Researchers can also further investigate the relationship between calcium levels and occurrences of heart attacks by doing statistical analysis on a population level. The levels of adrenaline can be tested by measuring the blood pressure as adrenaline increases the blood pressure (Struthers, Reid, Whitesmith, & Rodger, 1983).

These tests can be done on a group of patients who already suffer from neurotransmitter imbalance (through diseases like dementia). This will help the researchers in reducing the extra work (very difficult to identify caffeine addicts from a vast population) and they will be sure that the patients have neural imbalance. They can then detect the levels of calcium (which will also help in determining if calcium is only associated in the case of caffeine dependent imbalance or in every neural imbalance. Techniques like DNA sequencing can be used in case the physical presence of the patients becomes an ethical issue (emotional values of families associated with dementia patients).

Caffeine consumption is increasing day by day among and is widespread among all the age groups. Under these circumstances, it is very important that every person should have the knowledge of how many dangerous consequences (like heart attacks and increased anxiety levels due to stress) lie ahead of them. This is an issue which is ignored and never taken seriously because caffeine has made a certain place in everyone’s life. Everyone should care about this topic because not just heart attacks or stress, impairment of enzymes in the body can also be fatal. Every reaction that is carried in our body is due to thousands of enzymes working together. Even if the functioning of a single enzyme is altered, severe mutations can also arise.

References

1. Abdullah, N. H., & Ismail, S. (2018). Inhibition of UGT2B7 Enzyme Activity in Human and

Rat Liver Microsomes by Herbal Constituents. *Molecules* (Basel, Switzerland), 23(10). <https://doi.org/10.3390/molecules23102696>

2. Battram, D. S., Graham, T. E., & Dela, F. (2007). Caffeine’s impairment of insulin-mediated glucose disposal cannot be solely attributed to adrenaline in humans. *The Journal of Physiology*, 583(3), 1069-1077. <https://doi.org/10.1113/jphysiol.2007.130526>
3. Bhagat, H., Narang, R., Sharma, D., Dash, H. H., & Chauhan, H. (2009). ST elevation—an indication of reversible neurogenic myocardial dysfunction in patients with head injury. *Annals Of Cardiac Anaesthesia*, 12(2), 149-151. <https://doi.org/10.4103/0971-9784.53446>
4. BPS Publications. (n.d.). Retrieved May 6, 2019, from <https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1046/j.1365-2125.1998.00721.x>
5. Christoffels, V. (2011). Regenerative medicine: Muscle for a damaged heart. *Nature*, 474(7353), 585-586. <https://doi.org/10.1038/474585a>
6. Costabel, J. P., Burgos, L. M., & Trivi, M. (2017). The Significance Of Troponin Elevation In Atrial Fibrillation. *Journal of Atrial Fibrillation*, 9(6). <https://doi.org/10.4022/jafib.1530>
7. Diukova, A., Ware, J., Smith, J. E., Evans, C. J., Murphy, K., Rogers, P. J., & Wise, R. G. (2012). Separating neural and vascular effects of caffeine using simultaneous EEG-FMRI: Differential effects of caffeine on cognitive and sensorimotor brain responses. *NeuroImage*, 62(1), 239-249. <https://doi.org/10.1016/j.neuroimage.2012.04.041>
8. Fecteau, S., Fregni, F., Boggio, P. S., Camprodon, J. A., & Pascual-Leone, A. (2010). Neuromodulation of decision-making in the addictive brain. *Substance Use & Misuse*, 45(11), 1766-1786. <https://doi.org/10.3109/10826084.2010.482434>
9. Fine-tuning neuromodulation by adenosine - ScienceDirect. (n.d.). Retrieved May 7, 2019, from <https://www.sciencedirect.com/mutex.gmu.edu/science/article/pii/S0165614700015170>
10. Henry, J. P., & Stephens, P. M. (1980). Caffeine as an intensifier of stress-induced hormonal and pathophysiologic changes in mice. *Pharmacology Biochemistry and Behavior*, 13(5), 719-727. [https://doi.org/10.1016/0091-3057\(80\)90017-9](https://doi.org/10.1016/0091-3057(80)90017-9)
11. Hou, Q. Q., Wang, J. H., Gao, J., Liu, Y. J., & Liu, C. B. (2012). QM/MM studies on the catalytic mechanism of Phenylethanolamine N-methyltransferase. *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics*, 1824(4), 533-541. <https://doi.org/10.1016/j.bbapap.2012.01.017>

12. Jezová, D., Juránková, E., & Vidas, M. (1995). [Glutamate neurotransmission, stress and hormone secretion]. *Bratislavske Lekarske Listy*, 96(11), 588–596.
13. Kajioka, S., Takahashi-Yanaga, F., Shahab, N., Onimaru, M., Matsuda, M., Takahashi, R., ... Naito, S. (2012). Endogenous Cardiac Troponin T Modulates Ca²⁺-Mediated Smooth Muscle Contraction. *Scientific Reports*, 2, 979. <https://doi.org/10.1038/srep00979>
14. Kaneda, N., Ichinose, H., Kobayashi, K., Oka, K., Kishi, F., Nakazawa, A., Nagatsu, T. (1988). Molecular cloning of cDNA and chromosomal assignment of the gene for human phenylethanolamine N-methyltransferase, the enzyme for epinephrine biosynthesis. *Journal of Biological Chemistry*, 263(16), 7672–7677.
15. Madeira, M. H., Boia, R., Ambrósio, A. F., & Santiago, A. R. (2017). Having a Coffee Break: The Impact of Caffeine Consumption on Microglia-Mediated Inflammation in Neurodegenerative Diseases. *Mediators of Inflammation*, 1–12. <https://doi.org/10.1155/2017/4761081>
16. Owolabi, J. O., Olatunji, S. Y., & Olanrewaju, A. J. (2017). Caffeine and Cannabis Effects on Vital Neurotransmitters and Enzymes in the Brain Tissue of Juvenile Experimental Rats. *Annals of Neurosciences*, 24(2), 65–73. <https://doi.org/10.1159/000475895>
17. Owolabi, J. O., Olatunji, S. Y., & Olanrewaju, A. J. (2017). Caffeine and Cannabis Effects on Vital Neurotransmitters and Enzymes in the Brain Tissue of Juvenile Experimental Rats. *Annals Of Neurosciences*, 24(2), 65–73. <https://doi.org/10.1159/000475895>
18. Phillips, J. G., & Ogeil, R. P. (2015). Decision-making style, nicotine and caffeine use and dependence. *Human Psychopharmacology: Clinical and Experimental*, 30(6), 442–450. <https://doi.org/10.1002/hup.2496>
19. Rauh, R., Burkert, M., Siepmann, M., & Mueck-Weymann, M. (2006). Acute effects of caffeine on heart rate variability in habitual caffeine consumers. *Clinical Physiology and Functional Imaging*, 26(3), 163–166. <https://doi.org/10.1111/j.1475-097X.2006.00663.x>
20. Skeik, N., & Patel, D. C. (2007). A review of troponins in ischemic heart disease and other conditions. *The International Journal of Angiology : Official Publication of the International College of Angiology, Inc*, 16(2), 53–58.
21. Souza, A. C., Souza, A., Medeiros, L. F., De Oliveira, C., Scarabelot, V. L., Da Silva, R. S., ... Torres, I. L. S. (2015). Maternal caffeine exposure alters neuromotor development and hippocampus acetylcholinesterase activity in rat offspring. *Brain Research*, 1595, 10–18. <https://doi.org/10.1016/j.brainres.2014.10.039>
22. Srivastava, A., Fazzari, M., George, B., & Marzo, K. (2017). PATIENT PERCEPTIONS ON THE IMPACT OF CAFFEINE CONSUMPTION AFTER A MYOCARDIAL INFARCTION OR PERCUTANEOUS CORONARY INTERVENTION. *Journal of the American College of Cardiology*, 69(11), 2542. [https://doi.org/10.1016/S0735-1097\(17\)35931-4](https://doi.org/10.1016/S0735-1097(17)35931-4)
23. Struthers, A. D., Reid, J. L., Whitesmith, R., & Rodger, J. C. (1983). Effect of intravenous adrenaline on electrocardiogram, blood pressure, and serum potassium. *Heart*, 49(1), 90–93. <https://doi.org/10.1136/hrt.49.1.90>
24. Tao, R., & Auerbach, S. B. (2000). Regulation of serotonin release by GABA and excitatory amino acids. *Journal of Psychopharmacology*, 14(2), 100–113. <https://doi.org/10.1177/026988110001400201>
25. Vyleta, N. P., & Smith, S. M. (2008). Fast Inhibition of Glutamate-Activated Currents by Caffeine. *PLOS ONE*, 3(9), e3155. <https://doi.org/10.1371/journal.pone.0003155>
26. Yamato, T., Yamasaki, S., Misumi, Y., Kino, M., Obata, T., & Aomine, M. (2002). Modulation of the stress response by coffee: an in vivo microdialysis study of hippocampal serotonin and dopamine levels in rat. *Neuroscience Letters*, 332(2), 87–90. [https://doi.org/10.1016/S0304-3940\(02\)00828-5](https://doi.org/10.1016/S0304-3940(02)00828-5)