

# [Genes and environment on drug addiction and the reward circuit](https://assignbuster.com/genes-and-environment-on-drug-addiction-and-the-reward-circuit/)

Genetic Influence of Stress Related Genes in Prolonged Drug addiction and its impact on the Decline of Reward Sensitivity in the Brain

Abstract:

This paper is written with the intent of critiquing and synthesizing two journal articles on prolonged drug addiction with it broken down into two main components. The possible genetic causes of prolonged drug addiction and its long-term impact on the reward circuitry in the brain. The first journal focuses on the genetic factors that can have on addiction bringing into light how some people may be more susceptible to drug addiction than others. The second journal articlefocuses its research on how prolonged usage of drugs can result in reduced judgment levels. The article will emphasize the importance of connecting two main components of drug addiction: genetic influence and the long-term impact, two ideas that should be studied in tandem.

Genetic Influence of Stress Related Genes in Prolonged Drug addiction and its Impact on the Decline of Reward Sensitivity in the Brain

In Thompson, Gerson, Stolyarova, Bugarin, Hart, Jentsch, and Izquierdo’s (2016) study, and Levaran, Rosa, Randesi, Rotrosen, Adelson, and Kreek’s study (2018) both had a focus toward addiction and the impact on the brain’s reward circuit, but the two journals had different focuses towards how they studied the subject. The 2016 study had a focus towards the direct impact prolonged usage of drugs can have towards a brain’s reward circuitry using rats as an observational model in how the reward circuitry can be impacted. Whereas, the 2018 study focused on the way certain gene expression, especially in genes related towards stress, seemed to be linked towards having a higher rate of becoming addicted to methamphetamines. Such research was conducted by using blood samples taken from a select population with classification into ethnicity taken into account and then comparing the genetic structures of each towards a set of people known to have drug addiction. Running statistical analysis found some people had a higher chance of developing drug addiction based on their genetic expression.

While both of these studies provide great insight into how addiction can impact the body and mind as well as how some people may be more likely to develop, they both lacked in certain components that would further their research and insight into addiction. The 2016 study had an emphasis on observational studies with certain scenarios given to rats, but failed to assess whether or not genetic expression had a play into impacting a rat’s reward circuitry after long term exposure to methamphetamines. The 2018 study while providing great insight into how people may be statistically more likely to develop drug addiction lacks in considering how also the behavior of those with drug addiction may change. This critique focuses on synthesizing these two articles together with the hope to have a much larger understanding of how drug addiction can have a much larger impact on certain parts of our population as well as to how drug addiction can impact a person’s behavior, especially when it comes to the brain’s reward circuitry. This critique will continue by further assessing the articles strengths and weaknesses and provide an analysis on the result and also a further explanation in how the information presented in the two journals can be synthesized together.

Literature Review

In Thompson, Gerson, Stolyarova, Bugarin, Hart, Jentsch, and Izquierdo’s (2016) study, they used two groups of male Long-Evans rats all weighing between 250 and 300 grams. They placed them in 12 hour day and night cycle condition with standard food and water and applied operant conditioning on them separating them into groups of rats exposed to methamphetamine, and those who were not in order to create a control group and an independent variable for an observational study. According to Thompson (2016) in the first experiment the rats were then placed into a cage that contained two water bottles attached to either end of the cage. One water bottle had pure water whereas the other would contain a solution with varying levels of sucrose concentration that increased as each day went by from 1% to 2%, and doubling each time. To prevent side preference for the rats, they rotated the side in which a normal water bottle was placed and the tampered bottle was placed. The results of such experiment were the notice that all rats preferred the intake of sucrose water over regular water regardless of addiction toward methamphetamines. The other experimentation conducted was through the usage of food restriction with habituation of pressing a lever for food with each consecutive lever press giving varying amounts of food over food present in the cage without needing to do further work, but being less appealing to the rats. The results of such experiment was that rats treated with methamphetamines had less of a desire to work for more rewarding and appealing food than rats conditioned with saline as a control group.

It can be noted that though the initial experiment of sucrose treat water bottles and normal water bottles, and the secondary experiment of having food presently available though less desirable over food that was more desirable but required additional work tested for two components of the brain’s reward circuitry. In the first experimentation by having an equal amount of work required for the rats to either get sucrose or normal water, tested for the question of whether or not addiction impacted a person’s overall motivation to pursue anything with a higher amount of reward over a normal living. Through this first experiment it can be seen how even though the rats were pretreated with the usage of methamphetamines, if the amount of work needed to pursue something more desirable is the same as placing the exact same amount of work to gain something mediocre the work will be place towards stimulating a response in the brain’s reward circuit. During the second experimentation however, when placed with the scenario of getting a more rewarding item of food over an item that was easier to gain, yet being less rewarding, indicates the fact that if further work is required to gain a more rewarding item over something that can be gain easily, rats treated with methamphetamines will be less “ motivated” to go toward a higher reward for further work.

The second article focuses on the genetic component that can be found in humans that suffer from drug addictions.  (Levaran, Rosa, Randesi, Rotrosen, Adelson, and Kreek 2018) This study was conducted by having two focuses samples that were part of a group of multi-ancestry data base containing subjects with heroin addictions and a control group, 1001 people to be precise. The study was conducted focusing on predominantly European populations as well as African ancestry in the USA. Doing so created a select population group that could be studied, yet had enough of a diverse genetic and ethnic group so that variation in genetic code could be noted. In addition having a diverse population to analyze this helped also eliminating factors such as socioeconomic level and environment that could influence and skew the results of the study. According to Rosa (2016) preforming such research helped expand previous studies on the topic by focusing on a select gene and a single nucleotide polymorphism within genes that correlated to stress and stress management. The results of such study was the discovery that a specific gene known as the CRHR2 gene and its lincRNAs where associated with being more prevalent in patients with addictions. This result is interesting as with prior knowledge that the lincRNA plays a role in adaptive behavior and neurological diseases, has prompted further question into to what extent and how this gene is expressed into a person’s overall observable behavior.

Article Critique:

Both journals provided insight into the ways the brain’s reward circuitry can be affected or be more susceptible to drug addiction with enough background to continue into their research. In the rats study, their results were statistically significant with analysis indicating that the “ motivation” towards stimulating the reward circuit in the brain can be altered significantly over the prolonged usage of drugs and addiction to them.  As for the gene expression study on a human population, through their statistical analysis, it was determined that a specific set of genes and their lincRNAs have a huge role in affecting the impact of behavior adaptation and the probability of developing an addition towards drugs such as heroin as seen in their statistical study of blood samples given by patients suffering from drug addiction.

While both studies provide a huge insight into how development of drug addiction can affect the brain’s reward circuitry as well as how some specific portions of the population can be more susceptible than others to the development of addiction, there are limitation that can be seen in both of the studies. During the rat’s studies, with it being a behavior observation that specifically studied rats treating as if the results can directly apply to humans would be a stretched and would be rash to do so. Rather it sets the precedent for further studies in how addiction can alter the pursuit of stimulating the reward circuit in the brain. Further modeling needs to be conducted further before results can be truly being applied to humans and specifically those suffering from a form of addiction.

In addition, the rat study was only conducted on male rats where as further studies should take into account females rats to see whether or not the impact of estrogen seen to be in higher levels in females will impact the desire and pursuit to stimulate a response in the reward circuit for further work as well as an equal amount of work. Only then such testing can take the next step in seeing addiction being observed and analyzed in larger specimens such as monkeys, which may provide a more clear picture as to how addiction could impact the reward circuit in humans without crossing ethical boundaries.

According to Pinel and Barnes (2018) prolonged usage of drug addiction can follow a paradigm known as incentive-sensitization theory, where it can explain that how some drug users can become addiction to drugs while others not as much. This idea in particular deals with the fact that those addicted to the drug will actively seek it out and make it a priority to get it where they “ want” the drug where as those not addicted to the drug simply  “ like” the hedonistic feeling of the medication. This sort of paradigm needs to be also considered during the rat study and their behavior towards stimulating the brain’s reward circuit as it did not consider the fact that there would be a distinction between rats that “ want” the drug and in turn stimulate the reward circuit, and those who simply just “ like” the drug and not pursue it further if it took further amounts of work to gain it. This sort of distinction is important as it possible that it may have skewed results in where there was an increased positive result for those not pursuing the drug as seen in their second experiment with food easily and readily available over further work needed to be done to gain access to stimulating the reward circuit of the brain. (Thompson, Gerson, Stolyarova, Bugarin, Hart, Jentsch, and Izquierdo’s 2016)

In the journal article that focused on the human population and their study of genetic information of those with addiction, too also lacked in some aspects. Taking the blood samples of those suffering from addiction and synthesizing their genetic code as well as only taking blood samples of those who lived in the USA, discounted the fact of how long their population has lived there for with their research not stating or taking into account this. This is of a huge importance as some genes may have been expressed more prevalently if their environment was quite different than that of the USA than those who have lived in the USA their entire lives. As such this may have impacted the result seen with having less people having the expressed genes related to stress to be more prevalent and also vice versa.  (Levaran, Rosa, Randesi, Rotrosen, Adelson, and Kreek 2018)

Another factor that should also be taken into account was the fact that the behavior and “ levels” of drug addiction was not noted during their statistical analysis of genetic information. According to Barnes and Pinel (2018) , addiction does have a major genetic component towards it , but gene regulation can either downplay or up play the gene expressions in DNA based on the behavior and environment around the individual. As such without taking into account such factors it too could have skewed the result of their gene study with perhaps those with higher levels of certain gene expression being higher due to their environment and behavior towards certain subjects. (Levaran, Rosa, Randesi, Rotrosen, Adelson, and Kreek 2018)

Conclusion

In order to fully understand and assess the way drug addiction can impact the human body and mind it both aspects on this condition need to be viewed in tandem of one another. In addition the development of experiments and studies to further understand how drug addiction can impact a person’s brain reward circuit should take into account both the behavior of the individual and the genetic code and expression the individual may have physiologically. Without studying them together an incomplete picture can be formed about drug addiction and worse yet an improper conclusion could form on subject of drug addiction its affects on reward circuitry. Overall both journal articles provided adequate research and helped tackle the question of how drug addiction can impact behavior on stimulating the reward circuit and the influence genetic structure can have overall whether or not addiction develops within an individual.

## References:

* Alvandi, M. S., Bourmpoula, M., Homberg, J. R., & Fathollahi, Y. (2017). Association of contextual cues with morphine reward increases neural and synaptic plasticity in the ventral hippocampus of rats. Addiction Biology, 22(6), 1883–1894. https://doi. org/10. 1111/adb. 12547
* Ja-Hyun eBaik. (2013). Dopamine Signaling in reward-related behaviors. Frontiers in Neural Circuits, Vol 7 (2013). https://doi. org/10. 3389/fncir. 2013. 00152/full
* Thompson, A., Gerson, J., Stolyarova, A., Bugarin, A., Hart, E., Jentsch, J., & Izquierdo, A. (2017). Steep effort discounting of a preferred reward over a freely-available option in prolonged methamphetamine withdrawal in male rats. Psychopharmacology, 234(18), 2697–2705. https://doi. org/10. 1007/s00213-017-4656-z
* Levran, O., Correa da Rosa, J., Randesi, M., Rotrosen, J., Adelson, M., & Kreek, M. J. (2018). A non-coding CRHR2 SNP rs255105, a cis-eQTL for a downstream lincRNA AC005154. 6, is associated with heroin addiction. Plos One, 13(6), e0199951. https://doi. org/10. 1371/journal. pone. 0199951
* Levran, O., Peles, E., Randesi, M., Correa da Rosa, J., Ott, J., Rotrosen, J., … Kreek, M. J. (2015). Synaptic Plasticity and Signal Transduction Gene Polymorphisms and Vulnerability to Drug Addictions in Populations of European or African Ancestry. CNS Neuroscience & Therapeutics, 21(11), 898–904. https://doi. org/10. 1111/cns. 12450
* Pinel, J. P., & Barnes, S. J. (2018). Biopsychology (10th ed.). Pearson Education.
* Stephens, D. N., King, S. L., Lambert, J. J., Belelli, D., & Duka, T. (2017). GA Radke, A. K., Jury, N. J., Kocharian, A., Marcinkiewcz, C. A., Lowery, G. E. G., Pleil, K. E., … Lowery-Gionta, E. G. (2017). Chronic EtOH effects on putative measures of compulsive behavior in mice. Addiction Biology, 22(2), 423–434. https://doi. org/10. 1111/adb. 12342
* BAA receptor subtype involvement in addictive behaviour. Genes, Brain & Behavior, 16(1), 149–184. https://doi. org/10. 1111/gbb. 12321
* Zastrozhin MS, Grishina EA, Denisenko NP, Skryabin VY, Markov DD, Savchenko LM, … Sychev DA. (2018). Effects of CYP2D6 genetic polymorphisms on the efficacy and safety of fluvoxamine in patients with depressive disorder and comorbid alcohol use disorder. Pharmacogenomics and Personalized Medicine, Vol Volume 11, Pp 113-119 (2018), 113. Retrieved from http://0-search. ebscohost. com. library. 4cd. edu/login. aspx? direct= true&db= edsdoj&AN= edsdoj. f6ce8b66cb0b4d5c84ca10cade531917&site= eds-live