

Parental THC Usage Leads to Drug Seeking Behavior in Subsequent Generations



Kate Adams, Kathryn Atherton, Jared Boyden, Margaret Christy, Chrishan Fernando, Mekenzie Gear, Madison Smith

Purdue University, Purdue Honors College



Background

- Classical genetics is marked by genetic determinism – the idea that each generation's genetic expression is unaffected by the experiences of prior generations.
- Epigenetics is the study of changes in gene expression that do not involve alterations to the DNA sequence but are still passed down to subsequent generations.
- Chemical tags (methyl and acetyl groups) can be attached to or removed from segments of DNA. These tags cause DNA to be expressed at lower or higher levels, respectively. Methyl groups cause DNA to coil and prevent it from being read. On the other hand, acetyl groups cause DNA to unwind and make it easier to read. These chemical tags together make up what is known as the epigenome (Fried, 2003).
- Various studies have examined the long-term impact of drug use on an individual; however, this study researched the effects on subsequent generations and found drug exposure in adult rats negatively affected their offspring.

Main Question

Does cannabis use during adolescence cause epigenetic changes that lead to drug-seeking behaviors in subsequent generations?

Results

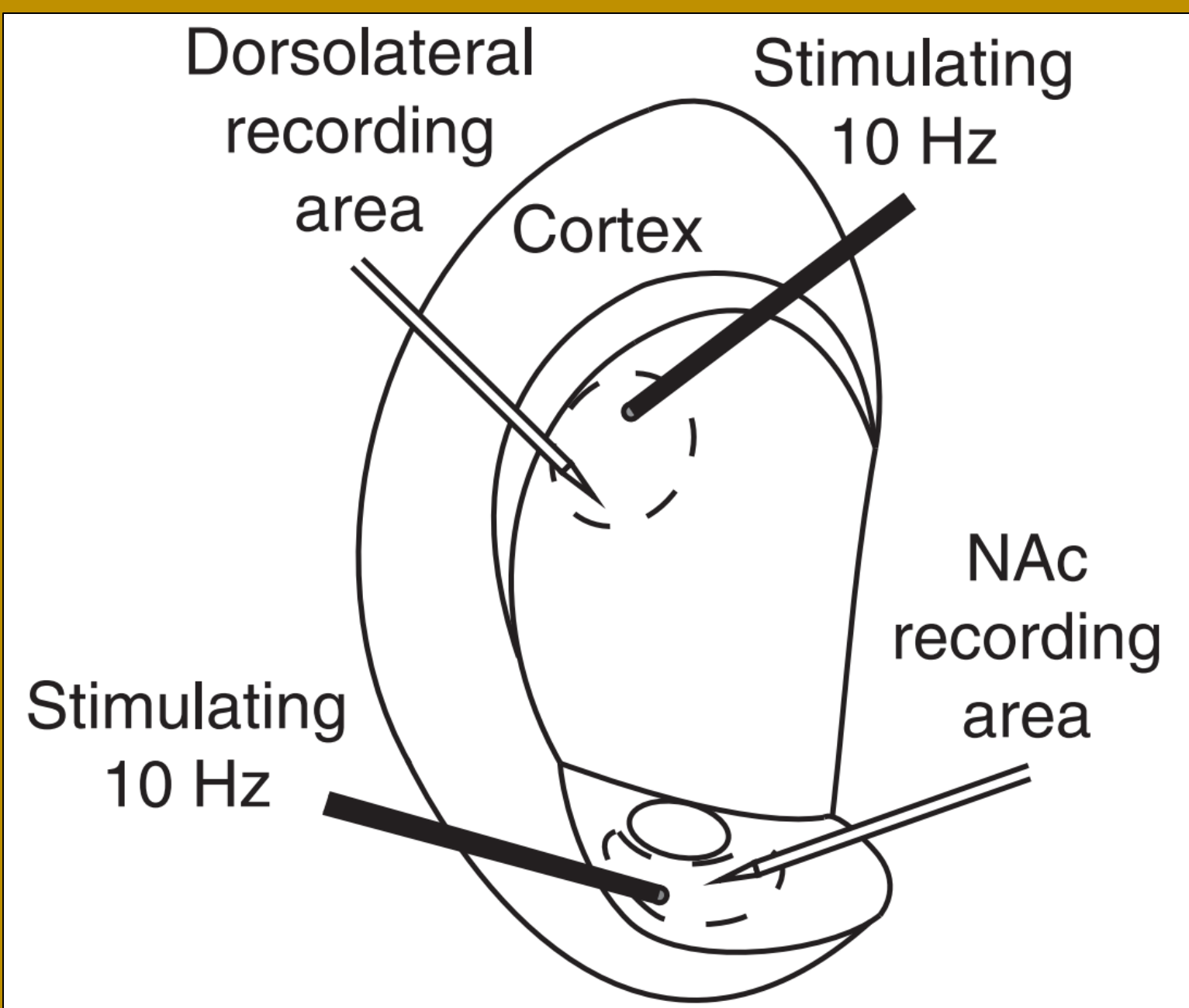


Figure 1: Schematic of Coronal Striatal Slice

This figure shows the coronal striatal section of the brain. The LTD in the dorsal section of the brain was larger than in the main striatum. In addition, “LTD in dorsal striatum was significantly larger with a main effect of parental treatment in offspring of THC-exposed parents... These findings demonstrate that that parental THC exposure leads to a significant cross-generational effect on dorsal striatal LTD in adult offspring” (Szutorisz; 2014).

Results

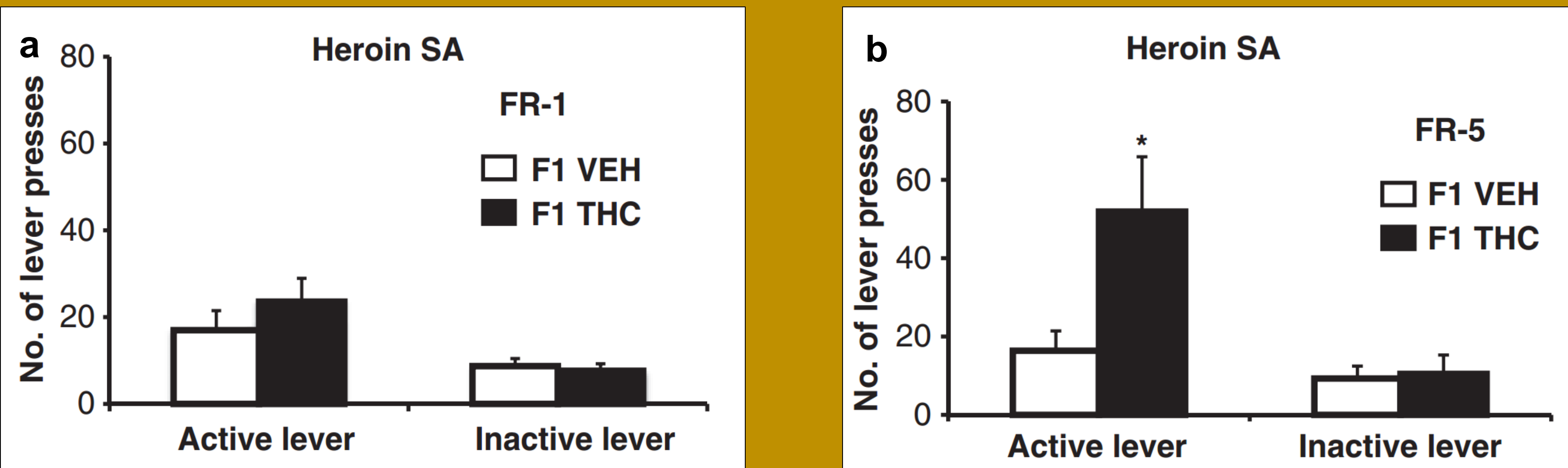


Figure 2: Work Effort for Self-Administration (SA) of Heroin

These two figures show how much effort F1 THC mice were willing to put forth to self administer the heroin versus the effort put forth by the F1 VEH mice. The active lever administered heroin, while the inactive lever administered saline solution as the control. Figure (2a) shows the number of lever presses with a fixed ratio of 1 lever press. Figure (2b) shows the number of lever presses with a fixed ratio of 5 lever presses.

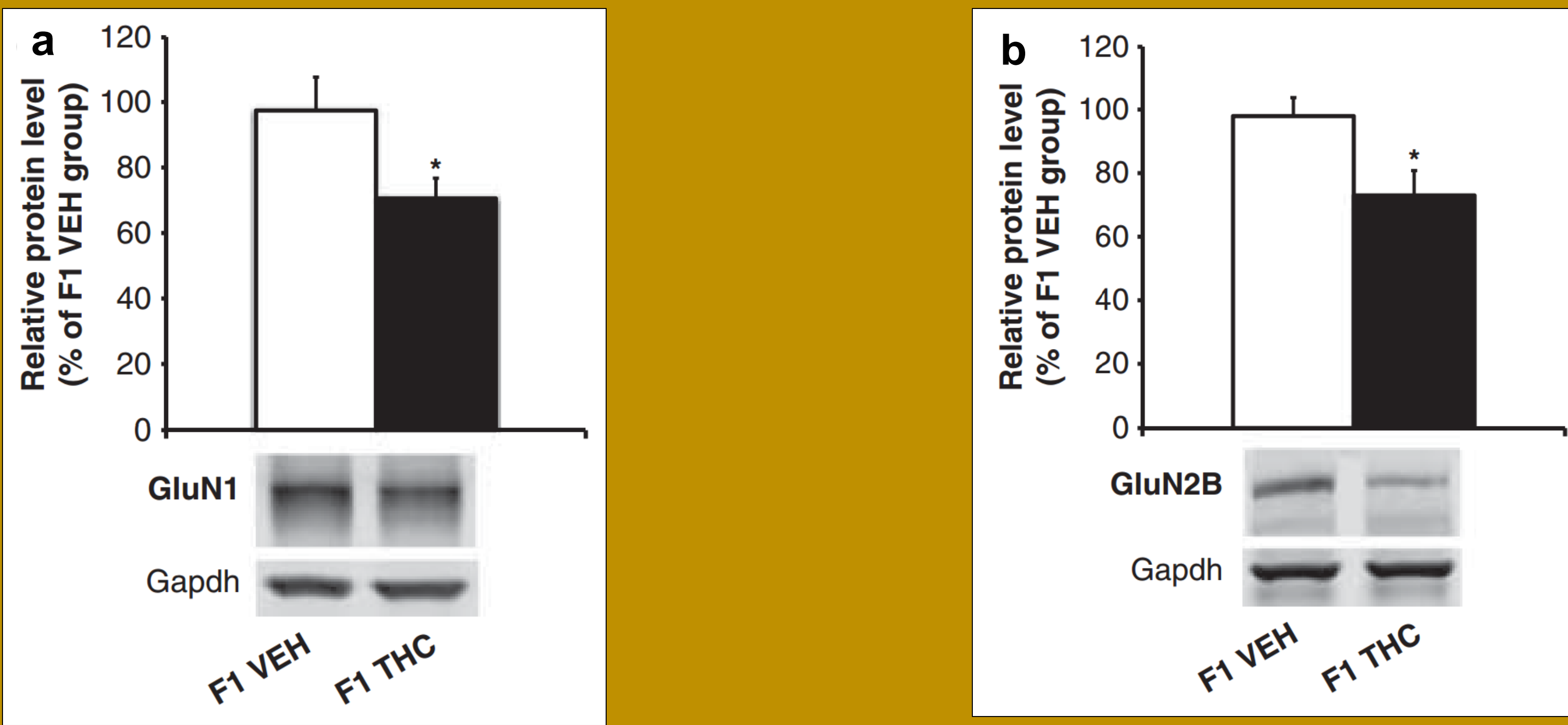


Figure 3: Abnormal NMDA Receptor Subunit Levels

These two figures demonstrate the protein level of F1 THC mice relative to F1 VEH at 100%. Both figures show levels detected by western blotting. Figure (3a) shows GluN1 levels, figure (3b) shows GluN2B levels, and Gapdh serves as the control. The F1 THC mice show a decreased expression of each receptor subunit protein.

Significance to Humans

While it is unethical to perform experiments such as these on humans, there have been longitudinal studies that may corroborate the findings of the THC study in the rat model. For example, longitudinal studies such as the Ottawa Prenatal Prospective Study (Fried, Watkinson, & Gray, 2003) and the Maternal Health Practices and Child Development Project (Goldschmidt, Richardson, Willford, & Day, 2008) have shown that maternal usage of cannabis during pregnancy demonstrates a positive correlation with increased drug usage in offspring. Similarly, research has been done on the effects of THC on male fertility, and was found to decrease sperm motility and functionality (Whan, West, McClure, & Lewis, 2006).

The rat model study is a traditional study that shows a much clearer link between THC usage in parents and drug-seeking behavior in offspring. Although the experiment was performed on rats, the results are still applicable to humans. If the use of drugs such as marijuana and cocaine hold effects on offspring, the social and medical results alone are extreme (Vassoler, White, Schmidt, Sadri-Vakili, & Pierce, 2013). Perhaps younger generations could sue their parents for their past mistakes. Furthermore, the manipulation and study of epigenetics could become more prevalent in the medical field as a means to promote healthier progeny. However, the implications could create more problems than the world is ready to face.

Conclusion

While the F1 THC and F1 VEH groups responded roughly the same for the FR-1 level tests, the F1 THC group pressed the level much more than the F1 VEH group on the FR-5 schedule. These results demonstrate that the offspring of the F0 THC rats were more willing to work for heroin which suggests that adolescent THC usage in the F0 THC rats likely contributed to drug-seeking behavior in their offspring.

While the study did not examine methylation and acetylation patterns directly, the authors looked at protein levels to examine the potential for epigenetic effects as a cause for the increased drug-seeking behavior in offspring. The study found lower levels of the glutamate receptor subunits GluN1, GluN2B, and Gapdh in the F1 THC group than the F1 VEH group (Szutorisz, 2014). Glutamate receptors are implicated in drug addiction. Furthermore, decreased levels of these proteins suggest that the genes that code for them are being inhibited. This means that the F0 THC rats may have passed drug-seeking behavior to the F1 rats via epigenetic effects.

References

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