ASHES, Vol. 7(10) – Nicotine… a gateway drug?

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Many people refer to marijuana as a gateway drug to other illicit drug use. However, some researchers have questioned whether this presumption has distracted researchers from considering the possibility that other more easily attainable substances might act as gateway drugs – for example, nicotine (Volkow, 2011). The week's ASHES reviews an animal model study that explores whether nicotine exposure is associated with later cocaine use behavior (Levine et al., 2011).

Methods

- Researchers separated mice into three groups: control group (exposed to saline); cocaine only group (exposed to cocaine for 7 days); and nicotine and cocaine group (exposed to nicotine for 7 days followed by cocaine for 4 days).
- The researchers monitored cocaine-related behavior and physiological changes/differences among experimental groups following substance exposure.
    - Conditioned place preference (CPP) measured a study subject's preference (i.e., time spent in an area) for the area where they received a reward (e.g., a drug), compared to a control area (Levine, et al., 2011).
    - Brain ΔFosB levels – ΔFosB is a protein in the brain that increases in response to cocaine use. Researchers administered nicotine and/or cocaine and tested for the extent of ΔFosB among the experimental groups.
    - Long Term Potentiation (LTP) – Long-term cocaine administration decreases LTP (Levine, et al., 2011). Researchers observed group-based differences for neuronal LTP responses.

Results

- As Figure 1 shows, the cocaine only group displayed significantly greater CPP than the control group (76.5s versus 247.1s, $p < 0.05$, 223.2%

difference). Similarly, the mice pretreated with nicotine showed significantly greater CPP than the cocaine only group (247.1s versus 441.2s, $p < 0.05$, 78.6% difference).

- The nicotine and cocaine group had 74.9% greater ΔFosB levels compared with the cocaine only group (from cocaine only at 3.5 ± 0.69 to nicotine and cocaine at 6.12 ± 0.8, $P < 0.05$).
- Neurons in brain slices from the nicotine and cocaine group differed, evidencing a 46.6% LTP decrease compared with the control group and by a 27.3% decrease compared with the cocaine only group (control: 129 ± 6%, cocaine only: 112 ± 5%, nicotine and cocaine: 88 ± 6%).

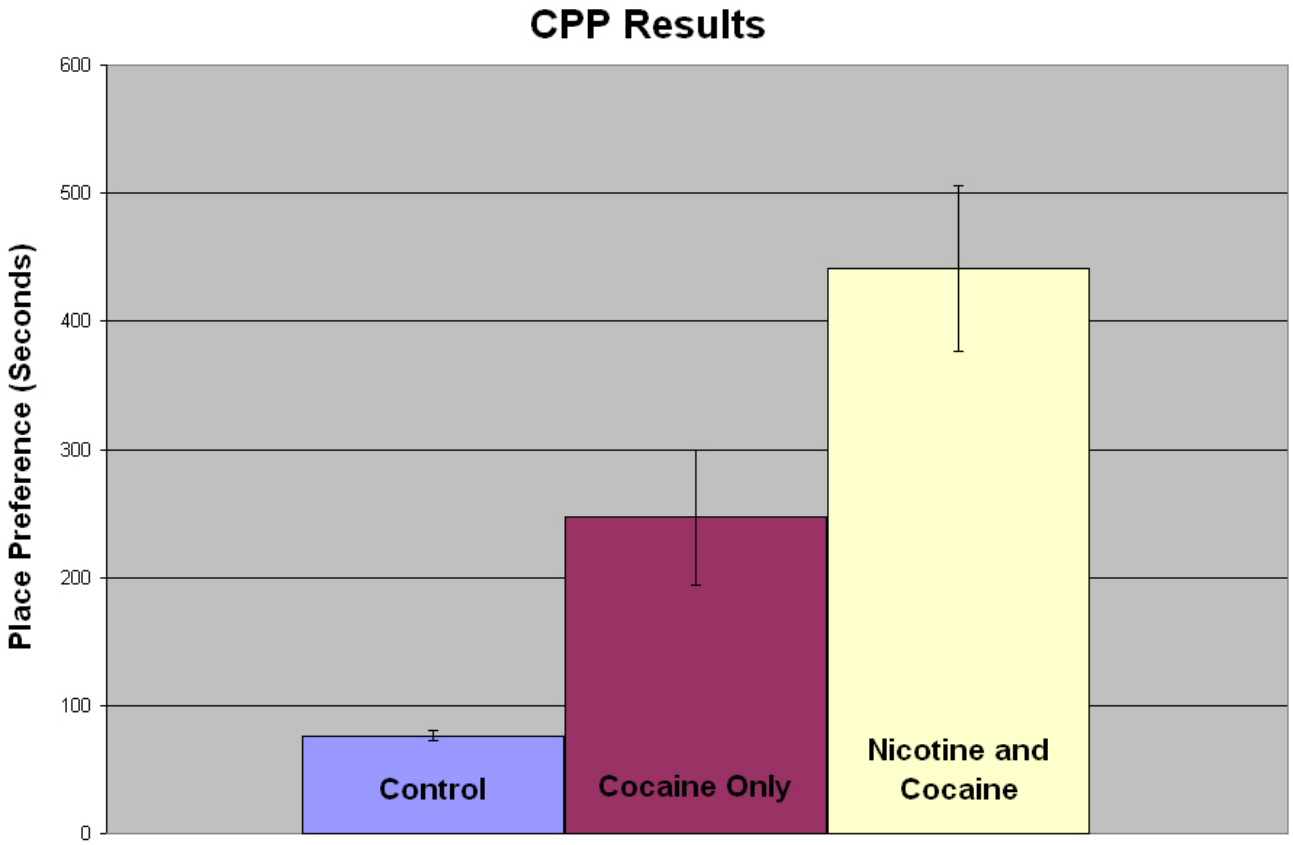

Figure. Conditioned Place Preference (CPP) Results among Groups. Click image to enlarge.

Limitations

- This research was conducted with mice. There is preliminary evidence to suggest that nicotine could have the same priming effects for enhancing cocaine's effects among humans (Grant, Kaplan, Shepard, & Moore, 2003; Kandel, Yamaguchi, & Chen, 1992), but more research is needed to determine if this is accurate.
- The researchers did not control for the priming effects of other

substances prior to cocaine.

Discussion

Nicotine exposure altered the brain's response to cocaine for the above behavioral and physiological/molecular measures. This suggests that nicotine primes the brain to enhance cocaine-associated rewards. The research design could be stronger if the researchers added an additional group, such as saline followed by cocaine, to control for the experiential effects of consuming a substance prior to cocaine. Without additional information it is difficult to attribute the priming to nicotine only. Nevertheless, this preliminary research could facilitate research for the development of new medication for cocaine addiction based on an understanding of the brain's response to cocaine following nicotine exposure. It is also possible to speculate that smoking cessation could have an effect for cocaine addiction among those who are comorbid (Volkow, 2011).

–Tasha Chandler and Daniel Tao

References

Grant, B. F., Kaplan, K. D., Shepard, J., & Moore, T. (2003). Source and Accuracy Statement for Wave I of the 2001-2002 National Epidemiologic Survey on Alcoohl and Related Conditions. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism.

Kandel, D. B., Yamaguchi, K., & Chen, K. (1992). Stages of progression in drug involvement from adolescence to adulthood: Further evidence for the gateway theory. Journal of Studies on Alcohol, 53, 447-457.

Levine, A., Huang, Y., Brisaldi, B., Griffin, E. A., Jr., Pollak, D. D., Xu, S., . . . Kandel, E. R. (2011). Molecular mechinisms for a gateway drug: Epigenetic changes initiated by nicotine prime gene expression by cocaine. Science Translational Medicine, 3(107), 107ra109. doi: 10.1126/scitranslmed.3003062

Volkow, N. D. (2011). Epigenetics of nicotine: Another nail in the coughing. Science Translational Medicine, 3(107), 107ps143. doi: 10.1126/scitranslmed.3003278

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