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Trans-generational resilience to addiction: role of cortical BDNF

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Cocaine self-administration induces epigenetic hyperacetylation of the *bdnf* promoter and increases expression of BDNF protein in the reward pathway from the ventral tegmental area (VTA) to the nucleus accumbens (NAc) and the medial prefrontal cortex (mPFC) of rats[1]. Now Vassoler et al[2] have shown that 60 days of cocaine self-administration in male rats not only induces hyperacetylation of the *bdnf* promoter in their sperm, but also in the mPFC of their drug-naïve male (but not female) progeny. Similar to previous studies[3], increased BDNF in the mPFC of the sons suppressed their responses to cocaine and cocaine cues, and this suppressive trans-generational effect was prevented by systemic injections of an antagonist of TrkB, the BDNF receptor. These findings from a rat model of drug addiction lead to the unexpected (paradoxical) conclusion that a father's cocaine addiction epigenetically protects his son from addiction.

This study has potential implications for human addiction because the concentrations of BDNF are increased in the serum of cocaine addicts and predict how quickly they relapse to drug use during abstinence[4]. Thus, it will be interesting to determine in future studies whether male cocaine addicts also pass a similar cocaine epigenetic suppression effect onto their sons. Additionally, serum BDNF concentrations are lower in people with depression, eating disorders, and other cognitive disorders[5]. If decreased acetylation of the *bdnf* promoter is similarly decreased in these patients and passed to their sons, then the findings from Vassoler et al.[2] may be part of a larger story of *bdnf* epigenetic alterations that are passed from generation to generation. Finally, an important question for future research is whether the trans-generational effect of increased *bdnf* acetylation in the mPFC is also observed in other brain reward areas like the VTA and nucleus accumbens in which increased concentrations of BDNF are linked to an increased vulnerability to relapse after prolonged abstinence from an addictive drug[1].

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References

1. Ghitza UE, et al. Role of BDNF and GDNF in drug reward and relapse: a review. Neurosci Biobehav Rev 35, 157–171 (2010). [PubMed: 19914287]

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2. Vassoler FM, White SL, Schmidt HD, Sadri-Vakili G & Pierce RC Epigenetic inheritance of a cocaine-resistance phenotype. Nat Neurosci 16, 42–47 (2013). [PubMed: 23242310]
3. Berglind WJ, et al. A BDNF infusion into the medial prefrontal cortex suppresses cocaine seeking in rats. Eur J Neurosci 26, 757–766 (2007). [PubMed: 17651427]
4. D'Sa C, Fox HC, Hong AK, Dileone RJ & Sinha R Increased serum brain-derived neurotrophic factor is predictive of cocaine relapse outcomes: a prospective study. Biol Psychiatry 70, 706–711 (2011). [PubMed: 21741029]
5. Nagahara AH & Tuszynski MH Potential therapeutic uses of BDNF in neurological and psychiatric disorders. Nat Rev Drug Discov 10, 209–219 (2011). [PubMed: 21358740]