

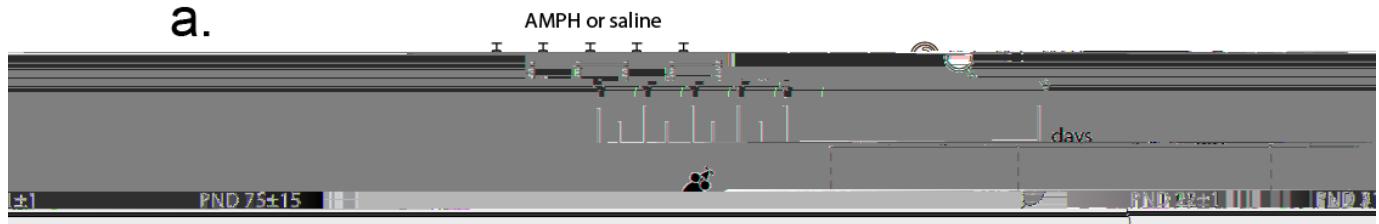
Sex differences in cognitive development following adolescent amphetamine exposure

Sonia Israel (Supervisor: Dr. Cecilia Flores)

Teenagers are vulnerable. Illicit drug use during adolescence significantly increases the risk of developing and struggling with addiction throughout life.^{1,2,3} Addiction is a chronic, relapsing brain disease associated with deficits in cognitive functions mediated by y y vulli]TJETtaupy . sy e6(P7(cF3(a)C1 0l)4(/P </>MCID 15>BDC BT1 0 0692 Tf1 0 0 1 4

In adulthood, we administered a Go/No-Go Task adapted to mice in operant conditioning chambers.

a.



b



Figure 1. **(a)** Experimental timeline of pre-treatment and behavioural assessments in female and male mice (AMPH: amphetamine). **(b) (Left panel)** Female mice treated with amphetamine showed robust drug-induced locomotor activity (two-way ANOVA; main effect of treatment, $F_{1,68} = 77.97$, $p < 0.0001$; main effect of time, $F_{4,68} = 17.62$, $p < 0.0001$; interaction effect, $F_{4,68} = 14.41$, $p < 0.0001$). **(Right panel)** Male mice treated with amphetamine showed robust drug-induced locomotor activity (two-way ANOVA; main effect of treatment, $F_{1,72} = 80.73$, $p < 0.0001$; main effect of time, $F_{4,72} = 21.28$, $p < 0.0001$; interaction effect, $F_{4,72} = 18.18$, $p < 0.0001$). **(c)** Behavioral inhibition is not

References

1. Anthony, J. C., & Petronis, K. R. (1995). Early-onset drug use and risk of later drug problems. *Drug and Alcohol Dependence*, 40(1), 9–15. doi:10.1016/0376-8716(95)01194-3
2. Jordan, C. J., & Andersen, S. L. (2017). Sensitive periods of substance abuse: Early risk for the transition to dependence. *Developmental Cognitive Neuroscience*, 25, 29-44. <http://dx.doi.org/10.1016/j.dcn.2016.10.004>
3. McCabe, S. E., West, B. T., Morales, M., Cranford, J. A., & Boyd, C. J. (2007). Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction*, 102(12), 1920–1930. doi:10.1111/j.1360-0443.2007.02015.x
4. Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. *Nature Publishing Group*, 12(11), 652–669. doi:10.1038/nrn3119
5. Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., et al. (2004). Dynamic mapping of h(V)5(o)-ETBT11n. c58 Tmh

Neuroscience : the Official Journal of the Society for Neuroscience, 21(22), 8819–8829.

7. Schulz, K. M., & Sisk, C. L. (2016). The organizing actions of adolescent gonadal steroid hormones on brain and behavioral development. *Neuroscience & Biobehavioral Reviews*, 70, 148–158. doi:10.1016/j.neubiorev.2016.07.036
8. Sisk, C. L. (2017). Development: Pubertal Hormones Meet the Adolescent Brain. *Current Biology*, 27(14), R706–R708. doi:10.1016/j.cub.2017.05.092
9. Sisk, C. L., & Zehr, J. L. (2005). Pubertal hormones organize the adolescent brain and behavior. *Frontiers in Neuroendocrinology*, 26(3-4), 163–174. doi:10.1016/j.yfrne.2005.10.003
10. Van Swearingen, A. E. D., Walker, Q. D., & Kuhn, C. M. (2012). Sex differences in novelty- and psychostimulant-induced behaviors of C57BL/6 mice. *Psychopharmacology*, 225(3), 707–718. doi:10.1007/s00213-012-2860-4
11. Piekarski, D. J., Boivin, J. R., & Wilbrecht, L. (2017). Ovarian Hormones Organize the Maturation of Inhibitory Neurotransmission in the Frontal Cortex at Puberty Onset in Female Mice. *Current Biology*, 27(12), 1735–1745.e3. doi:10.1016/j.cub.2017.05.027
12. Drzewiecki, C. M., Willing, J., & Juraska, J. M. (2016). Synaptic number changes in the medial prefrontal cortex across adolescence in male and female rats: A role for pubertal onset. *Synapse*, 70(9), 361–368. doi:10.1002/syn.21909
13. Willing, J., & Juraska, J. M. (2015). The timing of neuronal loss across adolescence in the medial prefrontal cortex of male and female rats. *Neuroscience*, 301, 268–275. doi:10.1016/j.neuroscience.2015.05.073

14. Giedd, J. N., Raznahan, A., Mills, K. L., & Lenroot, R. K. (2012). Review:
magnetic resonance imaging of male/female differences in human adolescent
brain anat

20. Gourley, S. L., Zimmermann, K. S., Allen, A. G., & Taylor, J. R. (2016). The Medial Orbitofrontal Cortex Regulates Sensitivity to Outcome Value. *The Journal of Neuroscience*, 36(16), 4600–4613. doi:10.1523/JNEUROSCI.4253-15.2016
21. Fillmore, M. T., Rush, C. R., & Marczinski, C. A. (2003). Effects of d-amphetamine on behavioral control in stimulant abusers: the role of prepotent response tendencies. *Drug and Alcohol Dependence*, 71(2), 143–152.
22. Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., et al. (2012). Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nature Reviews Drug Discovery*, 11(2), 141–168. doi:10.1038/nrd3628
23. Greenfield, S. F., Back, S. E., Lawson, K., & Brady, K. T. (2010). Substance Abuse in Women. *The Psychiatric Clinics of North America*, 33(2), 339–355. doi:10.1016/j.psc.2010.01.004
24. Kuhn, C. (2015). Emergence of sex differences in the development of substance use and abuse during adolescence. NCBI. *Pharmacology & Therapeutics*, 153, 55–78. doi:10.1016/j.pharmthera.2015.06.003
25. Shulman, E. P., Harden, K. P., Chein, J. M., & Steinberg, L. (2014). Sex differences in the developmental trajectories of impulse control and sensation-seeking from early adolescence to early adulthood. *Journal of Youth and Adolescence*, 44(1), 1–17. doi:10.1007/s10964-014-0116-9