




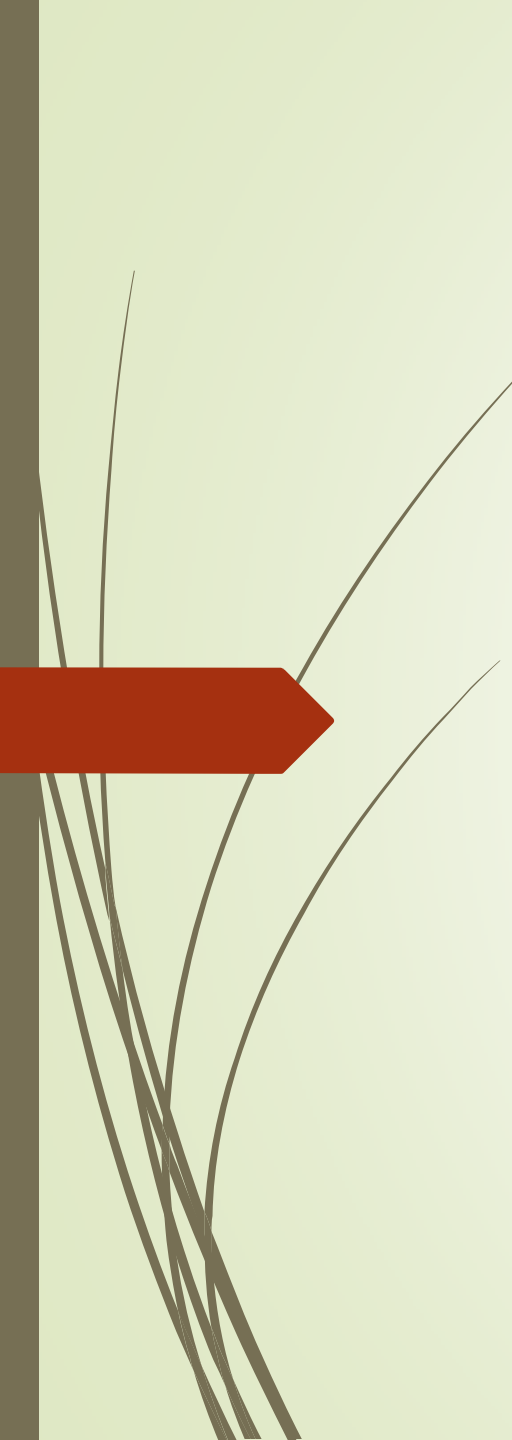
Hacking the stress system: the stress response as an adaptive trait that can work for or against you

III - On the genetics and epigenetics of stress resilience / sensitivity (L)



Notable issues and caveats:

- Convergence
 - Divergence
 - Gene environment interactions
 - Individual variation
- 



Genetics are an incredibly bad predictor of behaviour. Genes express themselves in interaction with the environment and behaviour is exceptionally susceptible to this interaction. Moreover, most biological processes that give rise to behaviour do so without reference to value judgements.

The curious case of testosterone

- ▶ Its competition within a social context, not aggression!
 - ▶ In a context that values aggression, testosterone stimulates aggression but in a context which does not, it doesn't.
 - ▶ Suppression in low-ranking males
 - ▶ No linear relation between testosterone and behaviour



Edwards, D. A. (2006). Competition and testosterone. *Hormones and Behavior*, 50(5), 681–683. <https://doi.org/10.1016/j.yhbeh.2006.09.005>
Delisi, L. E. (2009). Handbook of Neurochemistry and Molecular Neurobiology. *Handbook of Neurochemistry and Molecular Neurobiology*
Schizophrenia, 27, 107–241. <https://doi.org/10.1016/j.jns.2009.03.019>
Sapolsky, R., & Balt, S. (1996). Reductionism and variability in data: a meta-analysis. *Perspectives in Biology and Medicine*, 39(2).

Intra-group competition against a backdrop

- ▶ Inter-group competition can, and often does, involve efforts to outdo one another in the extent to which victories are gained against otherwise anonymous members of targeted outgroups, rather than each other.



The even more curious case of aggression

- ▶ Aggression can derive from a wide range of brain states
 - ▶ Testosterone (competition – threads to one's position in the social context)
 - ▶ Oxytocin (protection of the in-group)
 - ▶ B-endorphin (to ensure in-group belonging)
 - ▶ Norepinephrine (stress – fight or flight)



Sapolsky, R. M. (2017). Behave! The biology of humans at our best and worst. In *Penguin Press* (1st ed.).

<https://doi.org/10.1111/1467-8357.00356>

Machin, A. A. J., & Dunbar, R. I. M. (2011). The brain opioid theory of social attachment : a review of the evidence. *Behaviour*, 148(9), 985–1025.

Genetic disruption of the stress system

- ▶ Although there seem to be heritable components to stress sensitivity and there are specific genetic disorders in which the stress system is dysregulated, in general there is remarkably little evidence for genetic 'determinism'. Potential exceptions:
 - ▶ A polymorphism on the OPRM
 - ▶ DAT Polymorphisms in major depression
- ▶ Rather many genes which code for components of the stress system express dysfunctional if, and only if, certain conditions are met.

Opmeer, E. M., Kortekaas, R., & Aleman, A. (2010). Depression and the role of genes involved in dopamine metabolism and signalling. *Progress in Neurobiology*, 92(2), 112–133. <https://doi.org/10.1016/j.pneurobio.2010.06.003>

Gelernter, J., & Polimanti, R. (2021). Genetics of substance use disorders in the era of big data. *Nature Reviews Genetics*, 22(11), 712–729. <https://doi.org/10.1038/s41576-021-00377-1>

Nugent, N. R., Lally, M. A., Brown, L., Knopik, V. S., & McGeary, J. E. (2012). OPRM1 and diagnosis-related posttraumatic stress disorder in binge-drinking patients living with HIV. *AIDS and Behavior*, 16(8), 2171–2180. <https://doi.org/10.1007/s10461-011-0095-8>



Generational trauma; echoes from the womb

- ▶ Trauma, and the accompanied increased stress response can be transmitted from parents to children.
 - ▶ Rats
 - ▶ Holocaust survivors / Winter war children
 - ▶ Dutch hunger winter syndrome

Matthews, S. G., & Phillips, D. I. W. (2010). Minireview: Transgenerational inheritance of the stress response: A new frontier in stress research. *Endocrinology*, 151(1), 7–13. <https://doi.org/10.1210/en.2009-0916>

Schulz, L. C. (2010). The Dutch hunger winter and the developmental origins of health and disease. *Proceedings of the National Academy of Sciences of the United States of America*, 107(39), 16757–16758. <https://doi.org/10.1073/pnas.1012911107>



Experiences and gene expression

- Post-traumatic stress disorder
 - Only after trauma
 - OPRM1 polymorphism
- Cheating
 - Vasopressin
 - Context

Zietsch, B. P., Westberg, L., Santtila, P., & Jern, P. (2015). Evolution and Human Behavior Genetic analysis of human extrapair mating : heritability , between-sex correlation , and receptor genes for vasopressin and oxytocin. *Evolution and Human Behavior*, 36(2), 130–136. <https://doi.org/10.1016/j.evolhumbehav.2014.10.001>

Nugent, N. R., Lally, M. A., Brown, L., Knopik, V. S., & McGeary, J. E. (2012). OPRM1 and diagnosis-related posttraumatic stress disorder in binge-drinking patients living with HIV. *AIDS and Behavior*, 16(8), 2171–2180. <https://doi.org/10.1007/s10461-011-0095-8>



Downstream effects

- ▶ The altered function of one gene can have unforeseen effects further down the line
 - ▶ Complex integrated network
 - ▶ Nonlinearity
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