




# Disclaimer

**I am not a psychiatrist! I am a scientist!  
Especially if you are experiencing  
mental health issues, do NOT try  
anything we discuss today without first  
consulting your specialist. None of the  
information discussed today reflects  
individual differences and your  
personal physician can judge much  
better than I ever can, how this  
information may affect you.**



Through the study of stress related disorders, we can gain knowledge of the stress system in healthy populations, that we would otherwise not be privy to.

# One example

- ▶ Attention deficit / hyperactive disorder (ADHD)
  - ▶ Diminished dopamine signalling in the frontal cortex
  - ▶ Short bursts of hyper focus
  - ▶ Methylphenidate (Ritalin), a common neurotropic treatment for ADHD, also mitigates symptoms in PTSD
  - ▶ If we can figure out how to hyper focus works in ADHD and can be reproduced, we can potentially increase cognitive and physical output out put in non ADHD individuals



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Antshel, K. M., Biederman, J., Spencer, T. J., & Faraone, S. V. (2016). The Neuropsychological Profile of Comorbid Post-Traumatic Stress Disorder in Adult ADHD. *Journal of Attention Disorders*, 20(12), 1047–1055. <https://doi.org/10.1177/1087054714522512>

Aga-Mizrachi, S., Cymerblit-Sabba, A., Gurman, O., Balan, A., Shwam, G., Deshe, R., ... Avital, A. (2014). Methylphenidate and desipramine combined treatment improves PTSD symptomatology in a rat model. *Translational Psychiatry*, 4(9). <https://doi.org/10.1038/tp.2014.82>

# The role of stress in mental disorders

- ▶ Stress plays a role in most mental disorders. Even in disorders where it does not play a causal role, it usually makes things much worse
- ▶ Three levels of analysis (which are completely artificial)
  - ▶ Genetics
  - ▶ Epigenetics
  - ▶ Context

# 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 OPRM1 (protects against PTSD but increases sensitivity to addiction)
  - ▶ 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 (i.e. epigenetics).

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>

# Heritability

- ▶ Many mental disorders come with a certain level of heritability. However this may not necessarily derive from genetic predispositions alone.
  - ▶ Prenatal influences (see lecture 3)
  - ▶ Parental behaviour
  - ▶ Societal interactions

# Contextual influences on mental disorders

- ▶ Sometimes, mental disorders are mostly the result of circumstances. Of course, however, a certain susceptibility is required, so genetics and epigenetics do play a role.
  - ▶ Post-traumatic stress disorder
    - ▶ Triggered by trauma
  - ▶ Multiple personality disorder (nowadays dissociative Identity disorder) and the satanic panic

Mulhern, S. (2008). *Satanism , Ritual Abuse , and Multiple Personality Disorder : A Sociohistorical Perspective* SATANISM , RITUAL ABUSE , AND MULTIPLE PERSONALITY DISORDER : 7144. <https://doi.org/10.1080/00207149408409359>

Spanos, N. P. (1994). *Multiple Identity Enactments and Multiple Personality Disorder : A Sociocognitive Perspective. II*(1), 143–165.

Mac Gillavry, D. W., & Ullrich, D. (2020). A novel theory on the predictive value of variation in the  $\beta$ -endorphin system on the risk and severity of PTSD. *Military Psychology*, 1–14. <https://doi.org/10.1080/08995605.2020.1730111>



# Stress in mental disorders I: It does not cause it, but does make everything much worse.

- ▶ Schizotypal episodes
  - ▶ Schizophrenia
    - ▶ Delusions (usually auditory hallucinations) (dopaminergic component)
    - ▶ Disordered thought
    - ▶ Highly disturbing and stressful
  - ▶ Schizotypal experiences
    - ▶ Religious visions
    - ▶ Random, usually non-stressful, experiences

Smith, L., Riley, S., & Peters, E. R. (2009). Schizotypy, delusional ideation and well-being in an American new religious movement population. *Clinical Psychology and Psychotherapy*, 16(6), 479–484. <https://doi.org/10.1002/cpp.645>

Howes, O., McCutcheon, R., & Stone, J. (2015). Glutamate and dopamine in schizophrenia: An update for the 21st century. *Journal of Psychopharmacology*, 29(2), 97–115. <https://doi.org/10.1177/0269881114563634>

# Stress in mental disorders II: the trigger and accelerator

- ▶ Major depression
  - ▶ Strong evidence for a genetic predisposition
  - ▶ Stress triggers the disorder (3-4 episodes of severe prolonged stress)
  - ▶ After the first episode it becomes much easier to trigger the next one

# Symptoms and importance to stress research

- ▶ The inability to get back on your feet after a period of grieving
  - ▶ Symptom clusters
    - ▶ Psychomotor retardation (noradrenergic disruption)
    - ▶ Anhedonia (dopaminergic disruption)
    - ▶ The inability to find comfort (serotonergic disruption)

Moret, C., & Briley, M. (2011). The importance of norepinephrine in depression. *Neuropsychiatric Disease and Treatment*, 7(SUPPL.), 9–13. <https://doi.org/10.2147/NDT.S19619>

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Kilpatrick, D. G., Ph, D., Koenen, K. C., Ph, D., Ruggiero, K. J., Ph, D., ... Gelernter, J. (2007). The Serotonin Transporter Genotype and Social Support and Moderation of Posttraumatic Stress Disorder and Depression in Hurricane-Exposed Adults. *American Journal of Psychiatry*, 164(November), 1693–1699.

# Stress induced mental disorders III: disorders in which stress is the defining feature

- ▶ Post-traumatic stress disorder
  - ▶ Reaction to extreme stressor
    - ▶ Acute or repeated exposure
  - ▶ Hypervigilance
  - ▶ Flashbacks and intrusive thoughts
  - ▶ Nightmares

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th. In *American Journal of Psychiatry*. <https://doi.org/10.1176/appi.books.9780890425596.744053>

World Health Organization. (1993). *The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research* (pp. 155–157). pp. 155–157. [https://doi.org/10.1002/1520-6505\(2000\)9:5<201::AID-EVAN2>3.3.CO;2-P](https://doi.org/10.1002/1520-6505(2000)9:5<201::AID-EVAN2>3.3.CO;2-P)

# Neuromodulators involved in PTSD

- ▶ Noradrenaline & the locus coeruleus
- ▶ Dopamine
- ▶  $\beta$ -endorphin
  - ▶ Morphine
  - ▶ Post-combat delayed onset
- ▶ Oxytocin

van Zuiden, M., Frijling, J. L., Nawijn, L., Koch, S. B. J., Goslings, J. C., Luitse, J. S., ... Olff, M. (2017). Intranasal Oxytocin to Prevent Posttraumatic Stress Disorder Symptoms: A Randomized Controlled Trial in Emergency Department Patients. *Biological Psychiatry*, 81(12), 1030–1040.

<https://doi.org/10.1016/j.biopsych.2016.11.012>

Ullrich, D., & Mac Gillavry, D. W. (2021). Mini-review : A possible role for galanin in post-traumatic stress disorder. *Neuroscience Letters*, 756(May), 135980.

<https://doi.org/10.1016/j.neulet.2021.135980>

Lee, J. C., Wang, L. P., & Tsien, J. Z. (2016). Dopamine rebound-excitation theory: Putting brakes on PTSD. *Frontiers in Psychiatry*, 7(SEP).

<https://doi.org/10.3389/fpsy.2016.00163>

Pan, X., Kaminga, A. C., Wen, S. W., & Liu, A. (2018). Catecholamines in post-traumatic stress disorder: A systematic review and meta-analysis. *Frontiers in Molecular Neuroscience*, 11(December). <https://doi.org/10.3389/fnmol.2018.00450>

# Relevance to peak performance

- ▶ Most mental disorders, except perhaps under certain specific circumstances PTSD, are detrimental to peak performance.
  - ▶ Dopamine and noradrenaline disruption can massively affect physical and mental output.
  - ▶ Conversely, practices that raise reactivity or sensitivity of these neuromodulators can thus protect or even boost output
    - ▶ Cold exposure (see lecture 6)
    - ▶ Nutritional solutions (see lecture 9)
    - ▶ Behavioural practices
      - ▶ Physical exercise
      - ▶ Communal synchronisation
      - ▶ Meditation

