DGCN05 – Practical Training & Thesis

Project proposal

Project title:	Getting Trauma Under Control: Learning to Self-Regulate PTSD Brain Networks Through Prospective Neurofeedback Training
On-site supervisor[1]:	Dr. Florian Krause
Principal Investigator:	Prof. Dr. Erno J. Hermans
Donders Theme(s):	Development and lifelong plasticity (Theme 3)
Research centre:	DCCN, DCMN

Project description:

Posttraumatic Stress Disorder (PTSD) is a highly prevalent mental health condition that can develop after traumatic experiences. The World Health Organisation has observed that over 70% of all people world-wide experience lifetime traumas, of which 5.6% develop PTSD, resulting in an estimated lifetime prevalence of 3.9%[2]. These numbers are expected to further increase as a result of the ongoing COVID-19 pandemic[3]. Current gold-standard therapies for PTSD include Prolonged Exposure (PE) Therapy, Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing (EMDR), and Narrative Exposure Therapy[4]. Notably, these first-line treatments are all past-focused and aim to help patients "work through" individual traumas by changing their subjective experience and impact. However, the mechanism that underlies these approaches – extinction learning – is known to be strongly context-dependent, and learning within the context of the therapy only is inevitably subject to relapse[5]. Failing to prevent so-called "renewal" of fear[6] and a lack of generalization beyond the specifics of the trauma memory might explain the currently low treatment success rates (lower than 50% in some cases)[1,7].

Recent findings from cognitive psychology and neuroscience research, however, now shift the focus away from the trauma memory itself, and rather attributes the underlying core-deficit in PTSD to its maladaptive control[8]. In particular, it has been shown that the brain of patients with PTSD responds differently to intrusive thoughts – one of PTSD's main symptoms[9]. Compared to healthy controls, patients fail to actively suppress the memory associated with the intrusion via frontal executive control brain regions. Findings from neuroimaging research suggest the underlying neural mechanism to be an imbalance in large-scale brain networks: a weakly connected and hypoactive executive control network (ECN) and default mode network (DMN) are destabilized by an overactive and hyperconnected salience network (SN)[10].

[1] If more on-site supervisors are involved, please add their names as well.

We believe that directly training this capability to self-regulate large-scale brain network balance presents a novel, potentially very effective, treatment opportunity. Current advances in real-time functional Magnetic Resonance Imaging (rtfMRI) now also allow for the extraction of accurate moment-to-moment information from the individual nodes of the involved networks, and make learning to voluntarily control them via Neurofeedback training a feasible possibility[11,12]. We have already developed a novel network-based real-time fMRI Neurofeedback paradigm for training control over the relative balance between SN and ECN in particular, and have demonstrated that using this procedure, healthy individuals can learn to voluntarily shift neural resources between the two networks[13], and we also have some first evidence of the feasibility of applying this in daily life and its effects on self-reported stress measures[14]. In this project, we will now test the feasibility of applying this paradigm in the context of PTSD. We will evaluate Neurofeedback self-regulation performance and its effects on "suppression-induced forgetting" (a behavioural measure of memory control, which has been shown to be impaired in PTSD), real-life intrusions, as well as neural mechanisms of memory control.

Relevant literature:

1. Cusack, K. *et al.* Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. *Clinical Psychology Review* **43**, 128–141 (2016).
2. Koenen, K. C. *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med* **47**, 2260–2274 (2017).
3. Dutheil, F., Mondillon, L. & Navel, V. PTSD as the second tsunami of the SARS-Cov-2 pandemic. *Psychological Medicine* 1–2 (2020) doi:10.1017/S0033291720001336.
4. Najavits, L. M. The problem of dropout from "gold standard" PTSD therapies. *F1000Prime Rep* **7**, (2015).
5. Bouton, M. E. Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biol Psychiatry* **52**, 976–986 (2002).
6. Bouton, M. E., Winterbauer, N. E. & Todd, T. P. Relapse processes after the extinction of instrumental learning: Renewal, resurgence, and reacquisition. *Behav Processes* **90**, 130–141 (2012).
7. Schottenbauer, M. A., Glass, C. R., Arnkoff, D. B., Tendick, V. & Gray, S. H. Nonresponse and Dropout Rates in Outcome Studies on PTSD: Review and Methodological Considerations. *Psychiatry* **71**, 134–168 (2008).
8. Catarino, A., Küpper, C. S., Werner-Seidler, A., Dalgleish, T. & Anderson, M. C. Failing to Forget. *Psychol Sci* **26**, 604–616 (2015).
9. Mary, A. *et al.* Resilience after trauma: The role of memory suppression. *Science* **367**, (2020).
10. Akiki, T. J., Averill, C. L. & Abdallah, C. G. A Network-Based Neurobiological Model of PTSD: Evidence From Structural and Functional Neuroimaging Studies. *Curr Psychiatry Rep* **19**, 81 (2017). 11. Kim, H.-C. *et al.* Mediation analysis of triple networks revealed functional feature of mindfulness from real-time fMRI neurofeedback. *Neuroimage* **195**, 409–432 (2019).
12. Pamplona, G. S. P. *et al.* Network-based fMRI-neurofeedback training of sustained attention. *NeuroImage* **221**, 117194 (2020).
13. Krause, F., Kogias, N., Krentz, M., Lührs, M., Goebel, R., & Hermans, E. J. (2021). Self-regulation of stress-related large-scale brain network balance using real-time fMRI neurofeedback. *NeuroImage, 243, 118527*.
14. Krause, F., Schepers, M., Kogias, N., Yoldas, R., Vassena, E., Tutunji, R., Lührs, M., Goebel, R., & Hermans, E. J. (in preparation). Effects of large-scale brain network neurofeedback training on stress in real life.

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