AUGMENTATIVE TRANSCRANIAL MAGNETIC STIMULATION FOR VIRTUAL REALITY EXPOSURE THERAPY IN ACROPHOBIA

Cybinski, L. a, Gall, D. b, Gromer, D. b, Raij, T. c,d, Gundelach, F. a, Unterecker, S. a, Erhardt-Lehmann, A. a,e, Mühlberger, A. f, Deckert, J. a, Polak, T. a, Pauli, P. b, Herrmann, M. a

^a Center of Mental Health, Dept. of Psychiatry, Psychosomatics, and Psychotherapy, University Hospital of Wuerzburg, Germany, Department of Psychology, Clinical Psychology, and Psychotherapy), University of Wuerzburg, Wuerzburg, Germany, Germany, Department of Psychology, Clinical Psychology, and Psychotherapy), University of Wuerzburg, Wuerzburg, Germany, Department of Psychology, Clinical Psychology, ^c Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, USA, ^e Department of Translational Research in Psychiatry, Max Planck Institute of Psychiatry, Munich, Germany, ^f Department of Clinical Psychology and Psychotherapy, Institute of Psychology, University of Regensburg, Regensburg, Germany

INTRODUCTION

- Anxiety disorders (and especially specific phobias) are among the most prevalent mental health disorders worldwide (Dattani et al., 2021)
- The gold standard treatment for specific phobias is in-vivo or virtual reality (VR) exposure therapy (Bandelow et al., 2021), but not all patients benefit from these treatment approaches (e.g., van Dis et al., 2018)
- Recent laboratory study showed promising results of transcranial magnetic stimulation (TMS) enhancing extinction learning processes (Raij et al., 2018), which are underlying learning processes in exposure therapy (Craske et al., 2014)

RESULTS

- No group differences regarding age, gender, and other baseline measurements
- **Primary Outcome**: Significant time main effect (anxiety: F(1,76) =85.8, p < .001; avoidance: F(1,75) = 118.1, p < .001), but no significant group main effect or time x group interaction (ps > .050)

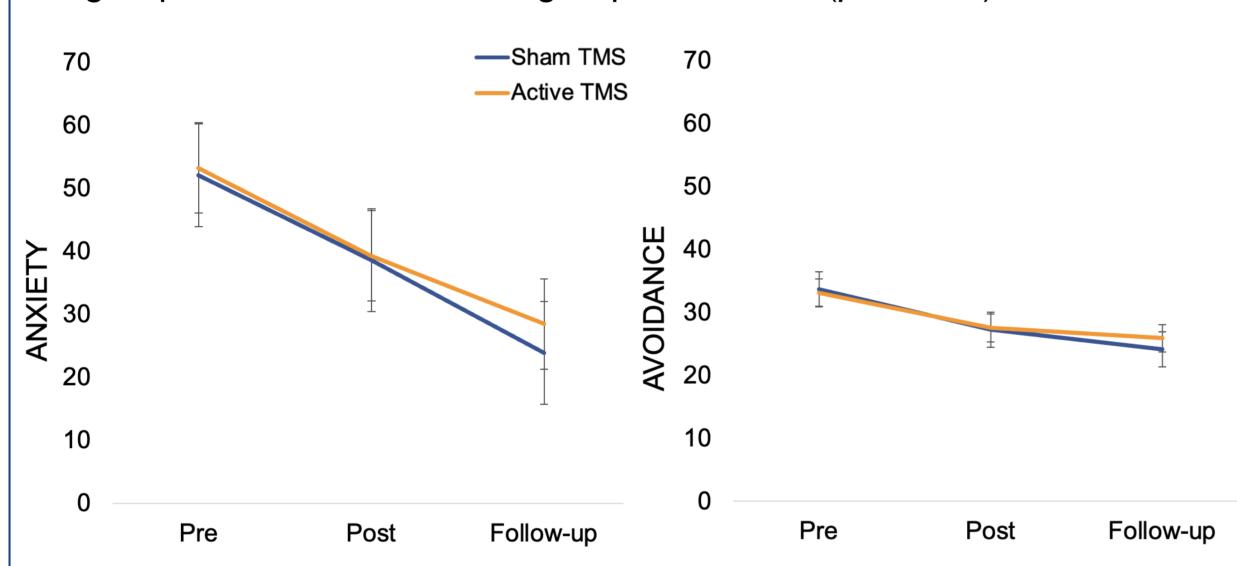


Fig 3. Trajectories of mean anxiety and avoidance scores (Acrophobia Questionnaire) pre, post-treatment, and at 6-month follow-up. Error bars represent +/- 1 standard error.

Secondary Outcomes: Significant time main effect for all secondary outcomes (ps > .001), but no significant group main effect or time x group interaction (ps > .050), except for response rates:

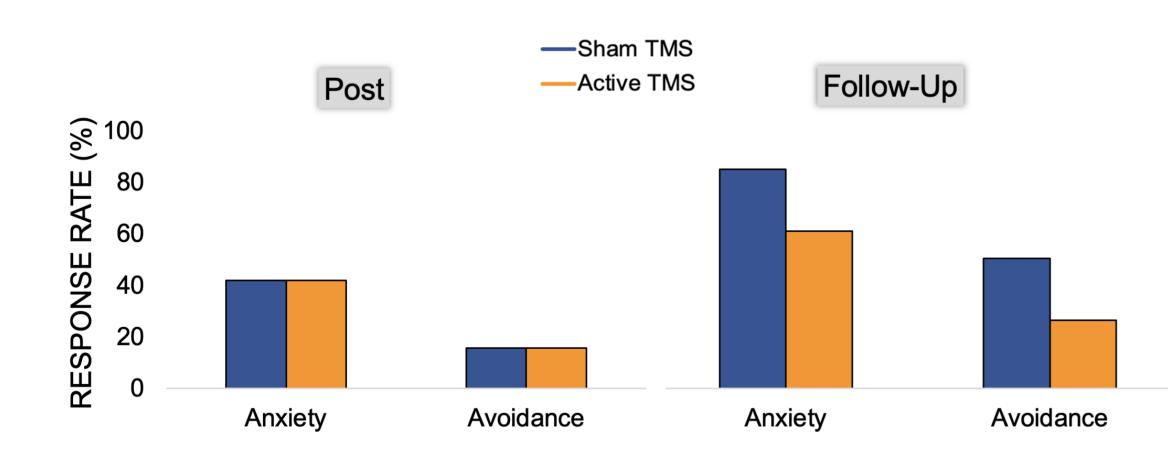


Fig 4. Responder rates for anxiety and avoidance in percent. Response is defined as a 30% score reduction from pre- to post-treatment, or follow-up.

- No significant group effect for post-treatment (ps > .050), but for follow-up (anxiety: F(1,72) = 5.2, p = .025; avoidance: F(1,71) = 4.0, p = .049
- No significant group effect for exposure session variables (e.g., maximal anxiety, maximal height, etc.), TMS side effects, estimation of group affiliation, frequency of exercises during the 6 months, etc.

OBJECTIVE

Transfer laboratory results (Raij et al., 2018) into a clinical trial and examine whether TMS enhances therapeutic effects

METHODS

- N = 76 participants with acrophobia (according to DSM-5), randomized, double-blind in active or placebo conditions
- Study design:

Screening

Pre-Treatment: Diagnostic/MRI session



- Behavioral Approach Tasks (BAT) in-vivo and VR (HMD)
- Structural MRI



Fig 1. BAT in VR (Picture: VT Plus GmbH)

Treatment

- 2 therapist-guided height-specific exposure exercises in a 5-sided 3D multisensory PsyCAVE (4x3x2.95m)
- Active or placebo repetitive TMS over the left frontal prefrontal cortex (PFC; functionally connected to the ventromedial PFC), before each exposure exercise

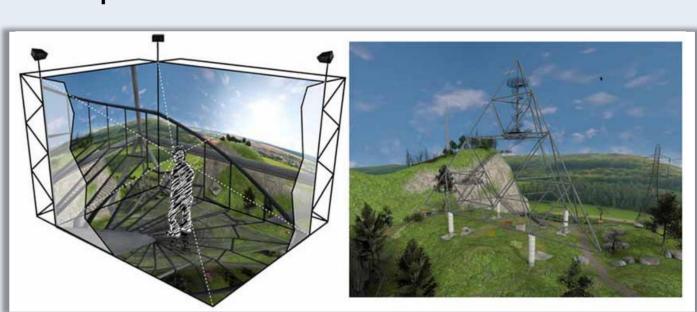


Fig 2. VR exposure therapy environment (Picture: Gromer et al., 2018)

Post-Treatment: Diagnostic session

- Questionnaires
- BAT in-vivo and VR

Follow-Up: Diagnostic session after 6 months

- Questionnaires
- BAT in-vivo and VR
- Statistical analyses: Linear mixed models for continuous primary (AQ) and secondary outcomes (e.g., maximal anxiety in BATs), and mixed logistic regression models for binary outcomes, with time, group, time x group interaction as fixed factors, and subject as a random factor

CONCLUSION

- As expected, both groups showed significant symptom reduction after two VR exposure sessions at post-treatment and follow-up
- No additional rTMS effect was found (in contrast to Herrmann et al., 2017, a study of TMS over the medial PFC)
- Optimal rTMS localization and stimulation parameters are still not fully understood and require further research

LITERATURE

- Bandelow, B., Aden, I., Alpers, G. W., Benecke, A., Benecke, C., Deckert, J., . . . Beutel, M. E. (2021). Deutsche S3-Leitlinie Behandlung von Angststoerungen, Version 2. Retrieved from: www.awmf.org/leitlinien/detail/ll/051-028.html [04.04.2023] Craske, M. G., Treanor, M., Conway, C., Zbozinek, T., & Vervliet, B. (2014). Maximizing Exposure Therapy: An Inhibitory Learning Approach. Behaviour Research and Therapy, 53, 10–23. doi: 10.1016/j.brat.2014.04.006.
 - Dattani, S., Ritchie, H., & Roser, M. (2021). Mental Health. Retrieved from: https://ourworldindata.org/mental-health [04.04.2023]
 - Herrmann, M. J., Katzorke, A., Busch, Y., Gromer, D., Polak, T., Pauli, P., & Deckert, J. (2017). Medial prefrontal cortex stimulation accelerates therapy response of exposure therapy in acrophobia. Brain stimulation, 10(2), 291–297. https://doi.org/10.1016/j.brs.2016.11.007 Raij, T., Nummenmaa, A., Marin, M.-F., Porter, D., Furtak, S., Setsompop, K., & Milad, M. R. (2018). Prefrontal Cortex Stimulation Enhances Fear Extinction Memory in Humans. Biological Psychiatry, 84(2), 129–137. doi: 10.1016/j.biopsych.2017.10.022. Epub 2017 Nov 6. https://doi.org/10.1016/j.biopsych.2017.10.022 van Dis, E. A. M., van Veen, S. C., Hagenaars, M. A., Batelaan, N. M., Bockting, C. L. H., van den Heuvel, R. M., Cuijpers, P., & Engelhard, I. M. (2020). Long-term Outcomes of Cognitive Behavioral Therapy for Anxiety-Related Disorders: A Systematic Review and Meta-analysis. JAMA psychiatry, 77(3), 265–273. https://doi.org/10.1001/jamapsychiatry.2019.3986