Towards precision psychotherapy for non-respondent patients: design and methods of a naturalistic observational CBT-trial for single-case prediction with machine learning

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Background

Cognitive behavioral therapy (CBT) works - but not equally well for all patients. Less than 50% of patients with internalizing disorders achieve clinically meaningful improvement, with negative consequences for patients and healthcare systems (1). The Research Unit RU 5187 seeks to improve this situation by an in-depth investigation of the phenomenon and single-case prediction of treatment non-response (TNR) to naturalistic CBT (2).

What is the bio-behavioral signature of TNR towards CBT? **Can we predict TNR on the single patient level?**

We train AI to predict CBT outcomes!

Methods

The RU comprises nine specialized sub-projects coordinated by a central project that oversees administration, promotes young researchers, advances gender equality, manages network funds, and enhances scientific communication. It includes three core science projects (SP1, SP2, SP3) and six specific projects focused on EEG/HRV assessment, psychological measures, Ambulatory Assessment, and neuroimaging.

Figure 1: Sub-projects of the RU 5187

- ▶ SP1: Single-case prediction of TNR to CBT in the outpatient sector: a prospective-longitudinal observational study
- ▶ SP2: Methods toolbox and infrastructure for predictive analytics
- ▶ SP3: Neuroimaging backbone and large-scale data harmonization
- ▶ SP4: Brain-electrical and cardiovascular indicators of emotion regulation as predictors of TNR to CBT
- ▶ SP5: Transdiagnostic psychological factors as predictors of TNR and cost-effectiveness measures related to predictive analytics
- ▶ SP6: Digital Phenotyping of emotion (dys-)regulation as transdiagnostic process and proxy for markers of TNR
- ▶ SP7: ACC-based biomarkers for predicting treatment (non)response to cognitive behavioral therapy in internalizing disorders
- ▶ SP8: Dynamic causal modelling of emotion regulation as predictors of treatment (non-) response to CBT in internalizing disorders
- ▶ SP9: Generalizing predictive patterns of TNR: from specific phobia and obsessive-compulsive disorder to the anxiety spectrum

Recruitment setting/plan:

585 Patients from four academic outpatient clinics in Berlin.

Primary and secondary outcomes:

BSI-Global severity index and clinical structured interviews for the specific disorder.

Emotion regulation:

We will investigate emotion regulation (ER) strategies, targeted by CBT (figure 1) as a core predictor, from implicit to explicit and automatic to controlled.

CBT intervention:

CBT manuals plus ecological and personalized approaches. The numbers of vary, averaging 24-42 sessions.

Figure 2: Neurodynamics of ER in Internalizing Disorders, Targeted by CBT Techniques

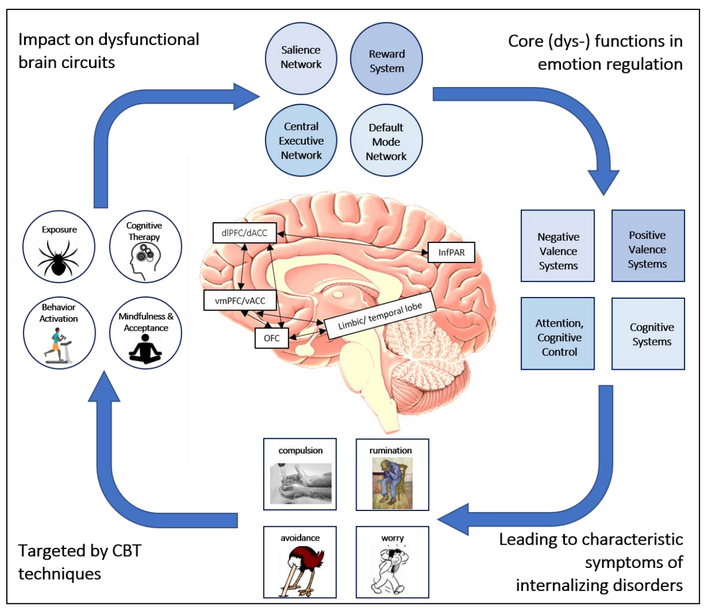
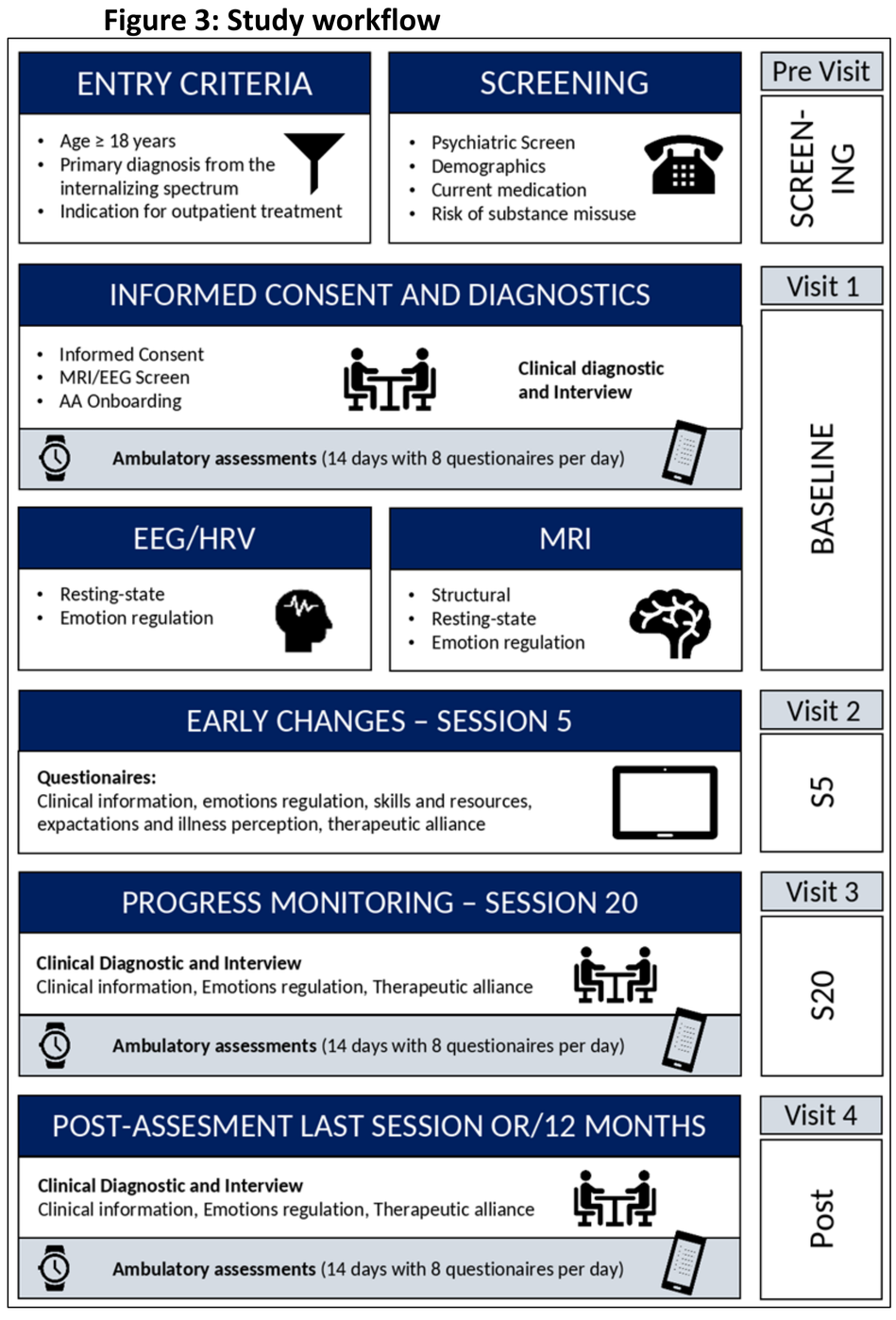


Figure 3: Study workflow



Discussion

This research unit aims to advance precision psychotherapy by:

1. Investigating bio-behavioral signatures of TNR focused on emotion regulation.
2. Developing a multilevel and multi-method assessment battery to identify optimal predictors, combinations, and cost-efficient proxies.
3. Utilizing a comprehensive, ecologically valid sample to enhance clinical practice translation for diverse patient characteristics.

Our goal is to deepen the understanding of TNR to better meet the needs of this vulnerable and resource-intensive patient group.

References

[1] Cuijpers, P., Miguel, C., Ciharova, M., Harrer, M., … Karyotaki, E. (2024). Absolute and relative outcomes of psychotherapies for eight mental disorders: A systematic review and meta-analysis. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, *23*(2), 267–275.
[2] Hahn, T., Nierenberg, A. A., & Whitfield-Gabrieli, S. (2017). Predictive analytics in mental health: Applications, guidelines, challenges and perspectives. *Molecular Psychiatry*, *22*(1), Article 1.

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