Towards Precision Psychotherapy for Non-Respondent Patients: Recruitment Status and Descriptive Analysis of a Naturalistic Observational CBT Trial for Single-Case Prediction with Machine Learning

Chantal Unterfeld[1,*], Till Langhammer[1], Felix Blankenburg[2,3], Susanne Erk[4], Lydia Fehm[1], John-Dylan Haynes[4], Stephan Heinzel[5], Kevin Hilbert[6], Frank Jacobi[7], Norbert Kathmann[1], Christine Knaevelsrud[8], Babette Renneberg[9], Kerstin Ritter[4], Nikola Stenzel[7], Henrik Walter[4], Ulrike Lueken[1,10]

1 Department of Psychology, Humboldt-Universität zu Berlin, Berlin, 2 Neurocomputation and Neuroimaging Unit, Freie Universität Berlin, Berlin, 3 Berlin School of Mind and Brain, Berlin, 4 Charité - Universitätsmedizin Berlin, Berlin, 5 Department of Educational Sciences and Psychology, TU Dortmund University, Dortmund, 6 Department of Psychology, Health and Medical University Erfurt, Erfurt, 7 Psychologische Hochschule Berlin, Berlin, 8 Department for Clinical Psychological Intervention, Freie Universität Berlin, Berlin, 9 Department of Clinical Psychology and Psychotherapy, Freie Universität Berlin, Berlin, 10 German Center for Mental Health (DZPG), partner site Berlin/Potsdam

Background

Cognitive Behavioral Therapy (CBT) is effective but doesn't help all patients equally; less than 50% with internalizing disorders achieve meaningful improvement[1]. The Research Unit RU 5187 investigates treatment non-response (TNR) in naturalistic CBT[2]. We aim to identify bio-behavioral signatures of TNR and predict it at the individual level using machine learning. This poster presents the recruitment status and descriptive analysis of our ongoing trial toward precision psychotherapy for non-respondent patients.

Recruitment Status and Descriptive Analysis

Recruitment Status

We aim to recruit 585 patients from four academic outpatient clinics in Berlin to ensure our sample reflects typical outpatient populations. Minimal exclusion criteria will be applied to maximize ecological validity. Eligible participants will be adults diagnosed with internalizing disorders—including anxiety disorders, Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder (PTSD), and unipolar depression—who are scheduled to receive cognitive behavioral therapy (CBT) at the participating clinics.
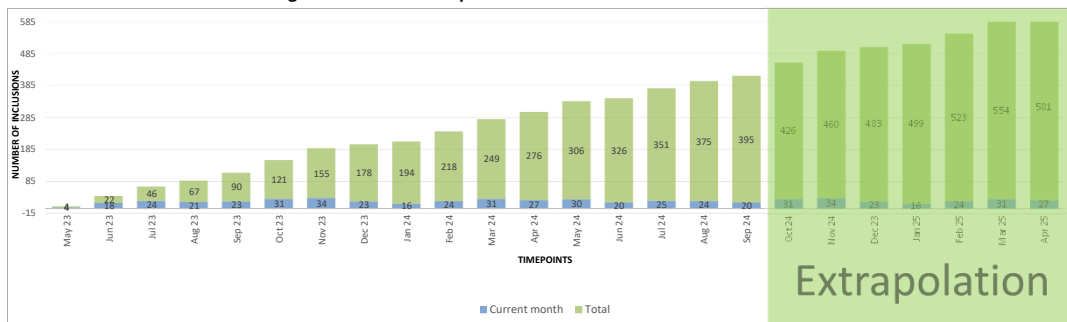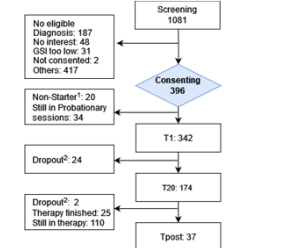

Figure 1: Recruitment process

Figure 2: Recruitment flowchart

[1]Non-Starter: Termination during probationary sessions
[2]Dropout reasons (multiple answers possible): Patient is dissatisfied with treatment outcomes [3], unwilling or unable to engage in exposure therapy [1], unreachable [3], lacks motivation for therapy or change [1], or faces practical constraints (e.g., relocation, time availability) [1]. Therapist canceled therapy due to unspecified reasons [1]. Other/unknown reasons [2]. Patient no longer wishes to participate [5], did not attend 12 sessions [7], has bipolar disorder [1], or had a (partial) inpatient stay [8].

Descriptives

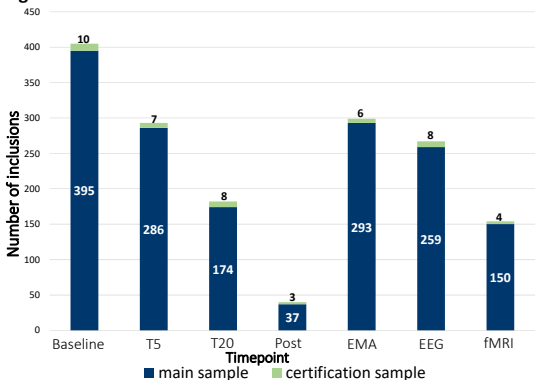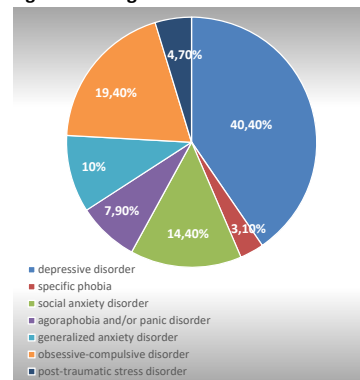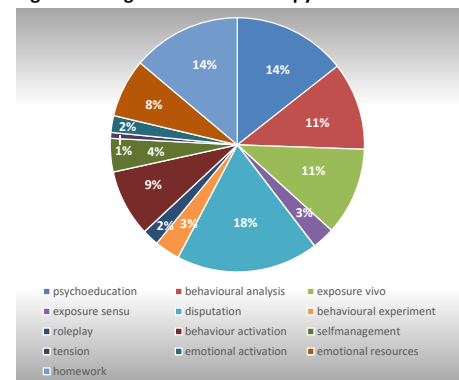Figure 4a: Current recruitment numbers

Figure 4b: Diagnosis distribution

Diagnosis distribution:
- depressive disorder — 40,40%
- specific phobia — 3,10%
- social anxiety disorder — 14,40%
- agoraphobia and/or panic disorder — 7,90%
- generalized anxiety disorder — 10%
- obsessive-compulsive disorder — 19,40%
- post-traumatic stress disorder — 4,70%

Table 1: Descriptive data

Sample characteristics		All patients (n = 396)		HSA-HU (n = 119)		ZPHU (n = 57)		HSA-FU (n = 70)		HSA-PHB (n = 150)		χ^2/F	p
Demographic	Female gender, n (%)	232	(58.58)	66	(55.46)	36	(61.40)	49	(70.00)	82	(54.67)	4.11	0.250
	Age	34.12	(12.11)	37.43	(13.6)	35.02	(10.72)	31.44	(10.79)	32.34	(11.35)	5.39	<.01[1]
	School (years)	16.92	(4.21)	17.05	(3.82)	15.78	(3.07)	18.1	(4.09)	16.71	(4.85)	3.43	0.02[2]
	Psychotropic drugs, n (%)	125	(31.57)	40	(33.61)	21	(36.84)	26	(37.14)	38	(25.33)	3.55	0.314
Clinical	CGI	4.67	(0.89)	4.92	(0.8)	4.62	(0.71)	4.8	(1.01)	4.4	(0.89)	6.81	<.001[3]
	BSI – GS	68.62	(30.19)	63.74	(32.04)	62.77	(26.40)	75.19	(31.08)	72.72	(28.99)	3.29	<.05[4]
	BDI-II	22.95	(9.48)	22.74	(10.22)	22.95	(9.39)	22.71	(9.25)	23.20	(9.07)	0.06	0.981
	HAM-A	20.72	(7.73)	18.82	(8.04)	18.55	(7.39)	24.83	(6.46)	20.35	(7.52)	5.08	0.002[5]
	MADRS	21.19	(7.47)	26.45	(6.41)	19.73	(8.23)	25.03	(8.23)	19.72	(7.12)	6.73	<.001[6]
	Y-BOCS	26.52	(5.32)	28.00	(4.31)	20.10	(5.76)	/	/	22.16	(3.92)	16.38	<.001[7]
	CAPS-5	31.67	(8.26)	37.00	(8.49)	25.00	/	32.25	(8.88)	28.00	(6.08)	0.67	0.584

Note: Means, standard deviations (SD), group comparision was conducted with ANOVA + Post-Hoc-Tests (Tukey HSD) or Chi²-Test; CGI (Clinical Global Impressions), BSI -GS (Brief Symptom Inventory – Global Score), BDI-II (Beck Depression Inventory), HAM-A (Hamilton Anxiety Rating Scale), MADRS (Montgomery-Åsberg Depression Rating Scale), Y-BOCS (Yale-Brown Obsessive Compulsive Scale), CAPS-5 (Clinician-Administered PTSD Scale for DSM-5)
[1]FU/PHB<HU; [2]ZPHU<FU; [3]PHB<ZPHU/HU/FU; [4]n.s on group-level; [5]HU/ZPHU/PHB < FU; [6]ZPHU/PHB < HU/FU; [7]ZPHU/PHB < HU

Therapy content

Figure 5: Usage of different therapy methods

Therapy methods:
- psychoeducation — 14%
- behavioural analysis — 14%
- exposure vivo — 11%
- exposure sensu — 11%
- disputation — 3%
- behavioural experiment — 18%
- roleplay — 9%
- behaviour activation — 4%
- selfmanagement — 2%
- tension — 1%
- emotional activation — 2%
- emotional resources — 8%
- homework — 3%

Therapy Completion Overview:
On average, patients who have completed therapy so far have had 27.6 sessions over 311 days.
(Note: Some therapies continue beyond the post-assessment, as our observation period is limited to only one year.)

Manual Adherence:
Manual adherence is generally rated as moderate to high.

Manual Usage:
Approximately two-thirds of therapists use manuals during therapy.

Manual Orientation:
58.6% of therapy sessions are guided by the manual.

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.

Presented at „Symposium PRECISION PSYCHOTHERAPY SIGNATURES, PREDICTIONS, & CLINICAL UTILITY", october 10, 2024 Berlin (Germany)
Contact: chantal.unterfeld@hu-berlin.de
-no conflict of interests-

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

FOR 5187 PREACT · Psychologische Hochschule Berlin · CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN · Freie Universität Berlin · HUMBOLDT-UNIVERSITÄT ZU BERLIN · DFG

Till Langhammer[1,*], Chantal Unterfeld[1], Felix Blankenburg[2,3], Susanne Erk[4], Lydia Fehm[1], John-Dylan Haynes[4], Stephan Heinzel[5], Kevin Hilbert[6], Frank Jacobi[7], Norbert Kathmann[1], Christine Knaevelsrud[8], Babette Renneberg[9], Kerstin Ritter[4], Nikola Stenzel[7], Henrik Walter[4], Ulrike Lueken[1,10]

1 Department of Psychology, Humboldt-Universität zu Berlin, Berlin, 2 Neurocomputation and Neuroimaging Unit, Freie Universität Berlin, Berlin, 3 Berlin School of Mind and Brain, Berlin, 4 Charité - Universitätsmedizin Berlin, Berlin, 5 Department of Educational Sciences and Psychology, TU Dortmund University, Dortmund, 6 Department of Psychology, Health and Medical University Erfurt, Erfurt, 7 Psychologische Hochschule Berlin, Berlin, 8 Department of Clinical Psychological Intervention, Freie Universität Berlin, Berlin, 9 Department of Clinical Psychology and Psychotherapy, Freie Universität Berlin, Berlin, 10 German Center for Mental Health (DZPG), partner site Berlin/Potsdam

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
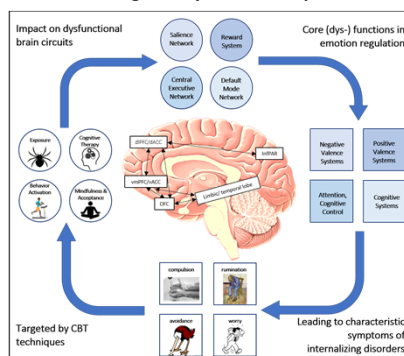

Figure 3: Study workflow

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.

Presented at „Symposium PRECISION PSYCHOTHERAPY SIGNATURES, PREDICTIONS, & CLINICAL UTILITY", october 10, 2024 Berlin (Germany)
Contact: till.langhammer@hu-berlin.de
-no conflict of interests-