Metta-based Cognitive Behavioral Therapy for Anhedonia in patients with depression: Study protocol summary

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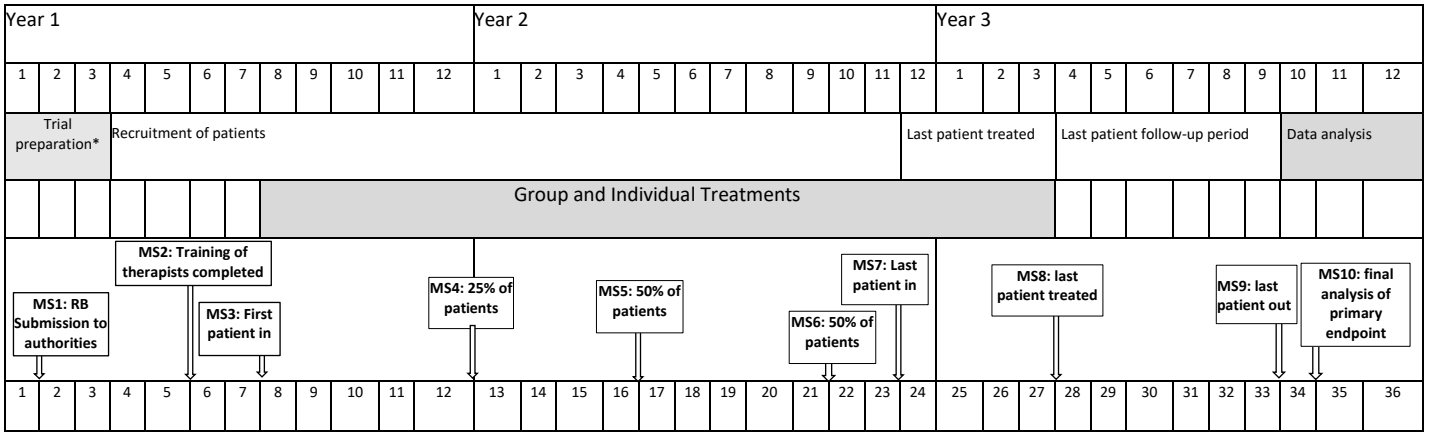
Objectives:	To compare MeCBT as a cost-effective combination of group and individual intervention against an active control (nondirective supportive Psychotherapy, nsPT) in patients with increased anhedonia in a randomized, controlled observer blind trial with three time points: (T0) before intervention; (T1) after intervention; (T2) at 6-month follow-up. Primary outcome: Change on anhedonia (clinician rating), assessed with changes in clinician-rated Anhedonia (CAINS) as primary outcome. We expect a significant decline of anhedonia symptoms and a significantly larger effect for MeCBT compared to nsPT. Secondary outcome measures include self-rated social and physical anhedonia, quality of life, symptoms of depression, emotional and cognitive-behavioral avoidance, social functioning, prosocial interactions and benevolence. We expect significant superiority by MeCBT at T1 and T2 in all these secondary variables.
Interventions:	Experimental intervention: MeCBT consisting of 8 sessions group treatment and 8 sessions individual treatment focusing on metta mediation and behavioral activation. Control intervention: NsPT consisting of group and individual treatment of the same timeframe as the experimental intervention and including psychoeducation and supportive interventions. Both treatment arms receive treatment-as-usual (TAU) by their physician. Antidepressive medication will be controlled for its impact on outcome. Duration of intervention per patient: 13 weeks¸ 6-month follow-up.
Key inclusion and exclusion criteria	Key inclusion criteria: 1) primary DSM-5 diagnoses of depressive disorder, confirmed by the SCID depression section 2) increased anhedonia (SHAPS > 2), 3) on/off medication stable for at least 4 weeks before inclusion, 4) age between 18 and 65 years; 5) informed consent. Key exclusion criteria: current substance use disorders, acute/past manic or psychotic symptoms, PTSD, OCD, eating disorders, odd/dramatic personality disorders, acute suicidality, severe medical conditions; concurrent psychotherapy
Outcomes:	Primary efficacy endpoint: change of Anhedonia-Asociality subscale score (CAINS) at T1 Key secondary endpoint(s): Key secondary endpoint(s): depressive symptomatology (QIDS-C; BDI-II), quality of life (WHOQoL), social functioning (SASS), emotional and cognitive-behavioral avoidance (BADS), physical and social anhedonia (PSAS), prosocial interactions (SRQ) and benevolence (FWW) at T1. Two intermediate measurements of CAINS and SRQ are taken after group sessions and after half of individual sessions for mediation analysis. Assessment of safety: Risk of suicidality will be carefully monitored.
Trial type:	Randomized, active control, observer-blind, parallel-group

Statistical analysis:	Efficacy: Multilevel models will be used to test between-group differences (Me-CBT/ nsPT) in changes of outcome measures as dependent variables over assessments. Description of the primary efficacy analysis and population: Modified Intention-to-treat analysis (mITT) for patients who have undergone at least one group session. Multiple imputation will be used in mITT analyses to estimate missing endpoint data. Safety: Safety has been confirmed in pilot studies; participants will be closely examined for worsening of intervention-related symptoms. Secondary endpoints: secondary outcome will be tested using multilevel analysis as for the primary outcome.
Sample size	To be assessed for eligibility: *N*=300 (exclusion ratio of 3:1) To be allocated to trial: *n*=100 To be analyzed: *n*=100
Trial duration	First patient in to last patient out (months): 26 Duration of the entire trial (months): 36 Recruitment period (months): 19
Trial center	Center for Psychotherapy, Goethe University Frankfurt

Milestones:



MS= Milestone *training of therapists and clinical raters, submission of applications to ethics

Trial flow