Borderline Personality Disorder and Emotion Regulation

Effects of emotion-focused vs. cognitive schema therapy interventions on emotion regulation deficits in borderline personality disorder - associations between clinical efficacy, brain network function and local glutamate/GABA metabolism

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Statistical Analysis Plan

Data evaluation and analysis

The SPSS software package (IBM Corp. released 2013, IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA) will be used to perform the following statistical tests to address verification (or falsification) of the previously formulated hypotheses.

Cross-sectional analysis of baseline (T0) MRI-data

Separate for rs-fMRI and ^{1}H-MRS data: A seed-based correlation analysis will be used to explore the whole-brain RSFC pattern of the regions being central to this study, i.e., the aMCC and DLPFC. Analysis of variance (ANOVA) will be applied to test for RSFC differences between patient groups and controls, as well as for group differences of the local Glx and GABA concentrations and the Glx/GABA balance in the aMCC and DLPFC between patients and controls.

Associations between rs-fMRI and ^{1}H-MRS data: A linear mixed model analysis will be performed to investigate differences of associations between RSFC in SN and ECN networks and Glx or GABA concentrations at the aMCC and DLPFC between patients and controls.

Follow-up (T0-T1, T1-T2, T0-T2) analysis of treatment effects on primary and secondary outcome criteria

Evaluation of changes of core symptoms and their clinical significance: In each therapeutic condition the improvement of each patient in measures of the primary and secondary outcome criteria will be estimated by the Reliable Change Index (RCI) (Wise, 2004)(Jacobson and Truax, 1991), which summarizes changes at the level of an individual in the context of observed changes for the whole sample. The RCI provides information about the functioning of an individual before/after therapy on an outcome measure, including the normative information about this measure (Atkins *et al.*, 2005) by dividing the difference between pre- and post-treatment scores by the standard error (that includes also the reliability coefficient, not only the standard deviation of the measure) (Hurst and Bolton, 2004). The change will be considered as being unlikely the product of measurement error (i.e., considered reliable), if the RCI is greater than 1.96. When the individual has a change score greater than 1.96 it can be assumed that the individual has improved.

Follow-up (T0-T1, T1-T2, T0-T2) analysis of treatment effects on MRI target parameters (RSFC, Glx, GABA) and of potential associations between these neurobiological changes and clinical improvement according to outcome criteria

Separate for rs-fMRI and ^{1}H-MRS data: Analysis of variance (ANOVA) for repeated measures will be applied to test for effects of group belonging (ST-EF, ST-AC, and healthy subjects; ST-EF *vs*. ST-AC) on changes of RSFC, Glx and GABA over time, as well as for within-subject changes between T1 and T2 scans.

Associations between RSFC and the local Glx and GABA concentrations: A linear mixed model analysis will be performed to investigate changes after 9 weeks (and 6 month respectively) of either therapeutic condition (ST-EF, ST-AC) compared to unspecific changes over time in healthy controls as well as between treatment groups. In a first step, this analysis will be performed separately in both treatment groups and healthy controls and for both neurotransmitters (Glx, GABA) and both spectroscopic and functional connectivity target regions (aMCC, DLPFC). In the second step, potential treatment condition driven differences in the correlations between metabolic and RSFC parameters will be investigated by applying the same model including the factor treatment group.

Interrelation between clinical outcome parameters and neurobiological findings: A linear mixed model analysis will be used that includes those MRI-data (RSFC, Glx, GABA) that have been significantly affected by therapy (***T0-T1, T1-T2, T0-T2***) and those clinical scores that reached the highest RCI. The detected significant interactions will be compared between the ST-EF and ST-AC treatment condition.

Data handling

Prior to starting recruitment of the participants, a project specific database will be created, which considers all GCP requirements in terms of user authentication, anonymization of participants, audit log and query management. This database will contain all project related data (demographic data, RSFC, ^{1}H-MRS and psychopathology data). All clinical ratings will be determined according to the corresponding manuals and will be separately stored for the time points T0, T1 and T2.

MRI data (anatomic and rs-fMRI data) will be acquired in the DICOM-Standard format, ^{1}H-MRS data are collected in a vendor specific format (.rda and .dat Siemens files). All raw and processed data are stored on a RAID computer system, which is serviced by the MPJ and equipped for standardized data access and management. All data will be available to longitudinal research and joint research with cooperation partners in this field.