Transcranial alternating current stimulation for cognitive deficit in schizophrenia: effects and electrophysiological changes

Statistical analysis plan

Statistical analyses: Efficacy and safety analysis will be applied for the intention-the-treat (ITT) dataset, as the comparison between active tACS and sham tACS in behavioural (clinical and cognitive) data pre-intervention, post-intervention, and in follow-up. The primary endpoint will be RBANS Delayed memory score change. The primary and secondary endpoints involving behavioural data (PANSS, RBANS all domains and overall score, TMT, WCST) will be calculated using mixed model for repeated measures without imputation of missing data and, as a sensitivity analysis, by analysis of covariance with last observation carried forward approach. The effect size (between-group difference) will be calculated as Cohen's d. For neurophysiological measurements, the dataset will consist of participants with baseline measurement and at least one post-baseline measurement. For EEG analyses, raw EEG data will be pre-processed using common pre-processing techniques (e.g. filters, independent component analysis - ICA, visual inspection). After that, pre-processed EEG data sets will be merged for statistical analysis. In resting-state EEG, power spectral density (PSD), and selected connectivity parameters in pre- vs. post- vs. follow-up will be analysed. In task-related EEG, ERP parameters will be assessed. Furthermore, for TMS measurements the ANOVA model will be used, and will include the within-subject factor “inter-stimulus interval” (given number of milliseconds). In case of deviation from normality, data will be transformed.

Power analysis: The total sample size of 60 subjects will allow to detect effect size of 0.7 or larger for two groups in two-tailed t-test (or effect size f of 0.4 in case of ANCOVA), with alpha of 0.05 and power (1-beta) of 0.8 (calculated via G* Power). Therefore, our sample should be sensitive enough to allow for moderate-to-large between-group effect in primary (and secondary) behavioural endpoints, and also for analysis of neurophysiological markers in “completers”, if 15% dropout rate is included. This sample size is in line with other NIBS interventional studies.