Official title: *Arbitration Between Habitual and Goal-directed Behavior in Obsessive-compulsive Disorder: Circuit Dynamics and Effects of Noninvasive Neurostimulation*

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Scientific background

Accumulating evidence suggests an imbalance between habitual and goal-directed behavior in favor of habitual control in parallel with an exaggerated tendency toward compulsive/harm avoidance behavior in OCD. However, the underlying neural mechanism of habitual/goal-directed imbalance in OCD has yet to be investigated.

Objective

The objective of this project was to explore the neurobehavioral characteristics of an arbitration mechanism, which has been demonstrated to regulate contributions of goal-directed and habitual strategies of action selection in non-clinical populations, in OCD.

Design

We recruited 30 male and female adults (age 18-65) with OCD and 30 age-, sex-, and education-matched healthy (medically, neurologically and psychiatrically) controls for this project. Each participant came for three sessions. There were 3-8 days interval between sessions:

Session 1 that included initial clinical assessment and obtaining T1 structural image.

Session 2 and 3 that included performing two separate decision-making and symptom provocation-avoidance tasks (see below for more information) by participants with OCD and healthy controls under two conditions: while scanned inside the MRI scanner (no tDCS) or while receiving tDCS neurostimulation outside the scanner (no fMRI imaging). As participants performed each task twice, there might be an order effect on task performance. For minimizing the impact of such a potential order effect on imaging and tDCS results, participants were randomly assigned to undergo scanning in the session 2 and then receive tDCS in the session 3

or in the opposite order (tDCS in session 2 and then imaging in session 3) but in each session only one of imaging or tDCS experiments (for both tasks) could be conducted for each participant.

OCD-relevant and aversive picture rating (explained below) could be done always in the session 3 as the last experiment.

Methods:

We examined the activity and connectivity patterns of the arbitration regions that have been previously determined to comprise the right and left inferior lateral prefrontal cortex (ilPFC) and right frontopolar cortex (FPC) in individuals with OCD. We acquired functional magnetic resonance imaging (fMRI) data while participants performed a decision-making (DM) task in which goal-directed and habitual action selection strategies compete to govern behavior control. Furthermore, we tested activity and network connectivity of the arbitration regions during the performance of a more clinically relevant symptom provocation-avoidance (SP-A) task. To additionally probe this mechanism, we used the non-invasive brain stimulation method of transcranial Direct Current Stimulation (tDCS). Excitatory and inhibitory currents applied by tDCS over a targeted arbitration region, the left ilPFC, while participants performed the DM and SP-A tasks to further corroborate whether the target arbitrator has causal effects on task performance and habitual/goal-directed action selection balance.

Statistical analysis plan:

For this study we assumed a data loss of about 10% leading to a final usable data sample size of n=30 OCD participants and 30 age-, sex, and education matched healthy controls for a final sample size of n=60. This sample size could provide sufficient power (>.8) to detect group differences of d=.73, and associations between continuous variables as small as r=.35. For regression analyses within the OCD sample, we are able to detect associations as small as r=.48 reliably (power>.8)**.** In Gillan et al, 2015 study (fMRI imaging of avoidance decision-making in OCD), the differences in the BOLD signal in the medial orbitofrontal cortex during acquisition of avoidance between OCD and controls showed effect sizes of d=1.23, and during overtraining of avoidance effect sizes of 1.19. Association between behavioral measures (urge to respond) and activity in the caudate showed an effect size of r=.63. The proposed study provides a power of >.99 for effects of this size, and based on this we consider this study to be sufficiently powered for the fMRI aims. Effect sizes in Gillan et al., 2011 study, for the association between a behavioral measure comparable to the paradigm proposed here and OCD symptom severity is r=.56, an effect size that can be reliably (power=.91) detected in the OCD sample in this study (n=30). In a comparable tDCS/decision making study (Weissengruber et al. 2020), showed the behavioral effects of cathodal stimulation with effect sizes of d=.77 for model-free action selection, and d=.65 for reduction of switching. The proposed sample size provides power of .97 and .92 respectively to detect effects of this size. Based on these studies with comparable experimental design, we consider the proposed project to be sufficiently powered to detect the OCD related group differences in both behavioral and imaging data, association between behavioral and imaging data, and effects of tDCS on behavioral performance in an instrumental decision-making experimental paradigm.

Behavioral data analysis for neurostimulation experiments:

The effect of anodal (excitatory), cathodal (inhibitory) or sham tDCS stimulation on the prevalence of model-based (MB) and model-free (MF) action selection (number of trials in which MB or MF strategy could be used for action selection) and their ratio could be tested during the decision-making task performance. ANOVA and linear mixed-effects model could be applied, respectively, to compare the effect of different stimulation conditions (anodal, cathodal and sham) on behavioral performance and to compare the effect of two active stimulations (anodal, cathodal) as separate condition factors against sham, while controlling for the time factor between baseline (imaging with no tDCS) and tDCS sessions and treating participants as random effects. For symptom provocation-avoidance task, the effect of anodal, cathodal or sham tDCS stimulation could be evaluated on the timing of avoidance behavior (the duration of time that participants tolerate the OCD-relevant or aversive pictures before pushing the stop button).

Imaging (fMRI) data analysis:

In the 1st level (within subject) analysis, we could contrast BOLD signal during decision-making, OCD- and aversive- relevant stimuli presentation compared to a (cross-hair) baseline. The General Linear Model (GLM) method with permutation testing for group-level comparisons could be applied to measure the level of activity ***in the regions of interest*** derived from Lee et al. study for the arbitration (the right and left ilPFC and right PFC), habitual (posterior putamen and supplementary motor area) and goal-directed regions (the vmPFC and caudate) during the decision-making task. For the symptom provocation-avoidance task, the total duration of photo presentation, defined as *avoidance timing*, could be divided into two intervals: 1) starting time of photo presentation until 1-second before pushing the stop button (exposure period), and 2) the 1-second period just before pushing the button. The second interval that

models the avoidance decision period in an approach similar to the Banca et al. study could be focused to test our hypotheses. For all regions mentioned above, activity level could be measured during the avoidance decision period (1 s) by employing GLM with permutation testing for group-level comparisons.