Representational dynamics of concurrent visuospatial working memories in Schizophrenia

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Abstract

Schizophrenia (SCZ) is a neuropsychiatric disorder whose core symptomatology includes impairments in working memory (WM) and higher executive functions. A wide range of WM function alterations in SCZ have been described, such as increased distractibility, decreased capacity and precision, differential biases, and more. In this ongoing study, we use a novel visual dual-task paradigm to examine the potential crosstalk between concurrent WM representations in SCZ versus healthy controls. Preliminary behavioral results indicate a possible attraction between concurrent WM items as well as an effect on response variance. Using simultaneous EEG and eye-tracking and representational similarity analysis, we explore the possible neural mechanisms underlying these effects, as well as the dynamics of maintained orientation representations. Finally, we examine previously observed oscillatory WM phenomena in SCZ, such as aberrant frontal gamma oscillations, and their relation to task performance.

Keywords: Schizophrenia; working memory; distraction; dual-task; representational similarity analysis; EEG; eye-tracking

Background

Schizophrenia (SCZ) is a major psychiatric condition characterized by positive symptoms (e.g., hallucinations, delusions, disorganized speech and thoughts), negative symptoms (e.g., flattened affect) and general cognitive impairments (American Psychiatric Association, 2013; Rahman & Lauriello, 2016). These impairments span multiple domains including learning, planning, abstract thinking, and language, and are believed to not only precede the onset of psychosis (the prodromal phase) but to be present throughout the course of the disorder (Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005; Zhou, Li, Zhao, Ou, & Zhao, 2022). Virtually all of these cognitive abilities rely crucially on working memory (WM), i.e., the goal-directed maintenance and manipulation of information in the service of upcoming tasks (D'Esposito, 2007).

In recent years, substantial progress has been made in characterizing the neural representation of WM information in the (healthy) human brain, using e.g., multivariate neuroimaging analyses of human fMRI and EEG/MEG. An emerging view (Christophel, Klink, Spitzer, Roelfsema, & Haynes, 2017) is that WM representations are not static, but highly dynamic both temporally and spatially across brain regions. Whether and how these representational dynamics of WM are altered in SCZ remains to be investigated.

Previous research into WM deficits in SCZ has typically focused on reductions in storage capacity and precision, as well as on impairments in executive control functions more generally (Gold et al., 2010; Lee & Park, 2005). The relation of these deficits to local and long range cortical dysfunction in SCZ has been studied in the context of neural oscillations (Hirano & Uhlhaas, 2021). Abnormal prefrontal gamma oscillations (Missonnier et al., 2020; Senkowski & Gallinat, 2015), abnormal low frequency (theta/delta) to gamma coupling (Barr et al., 2017; Lynn & Sponheim, 2016; Missonnier et al., 2020), as well as abnormal frontal activity in the theta, alpha and beta ranges (Adams et al., 2020; Erickson, Albrecht, Robinson, Luck, & Gold, 2017; Haenschel et al., 2009; Schmiedt, Brand, Hildebrandt, & Basar-Eroglu, 2005) associated with impairments in executive function recruitment, have all been observed in SCZ. These phenomena show promise in helping to explain deficits across more complex working memory tasks.

Experimentally, a domain particularly interesting for SCZ is how and whether WM is protected from distraction by task-irrelevant sensory input. SCZ has been associated with high distractibility in comparison to healthy controls, as well as a deficit in discerning the salience and relevance of sensory inputs (Becske et al., 2022; Demeter, Guthrie, Taylor, Sarter, & Lustig, 2013). While there is ample literature on inferential and encoding impairments in SCZ (Averbeck, Evans, Chouhan, Bristow, & Shergill, 2011; Sterzer et al., 2018) the role of attention control particularly in WM maintenance and retrieval remains poorly understood. Additionally, recent WM studies in SCZ have predominantly targeted spatial WM (Cano-Colino & Compte, 2012; Glahn et al., 2003).

This study draws inspiration from the distraction and dual task literature and expands on the question of how (and whether) dynamic switching of endogenous attention between simultaneously attended tasks is affected in SCZ. In particular, if working memory representations are less stable and less precise in SCZ, is awareness of ”where” in the task one is also an effected representation? How is top down selection of task relevant WM content bound to this ”task context” representation? We explore these questions through a mixed analysis of time frequency features in EEG as well as representational similarity analysis (RSA) of both EEG and eye-tracking data.

Methods

During simultaneous EEG and eye-tracking, we ask participants to remember two object orientations by performing a short delayed comparison task nested in the maintenance period of a longer delay task. In each trial, a sample object is presented whose orientation needs to be maintained by the participant. This is followed by a long delay. During recall at the end of the trial, participants continuously adjust a probe such that its orientation matches that of the sample object presented at the start of the trial. In two thirds of trials, the main delay period described above is interrupted by a short task, mimicking the structure of the main task. During the main delay of these trials, participants are additionally presented with another sample object whose orientation needs to be maintained. After a short delay, participants are tested on this additional sample. Here, participants make a binary judgement about whether the sample was presented clockwise or counterclockwise with respect to the probe. The third of trials without this inner task serve as a baseline for the outer task. These two trial types are depicted in Fig. 1.

In order to further manipulate potential interference between the tasks, in half of the trials with an inner delay task the two nested tasks involve the same object identity, while in the remaining half the two nested tasks have unique objects. This results in three task conditions : no inner task (condition 1), inner task with shared object identity (condition 2), inner task with unique objects (condition 3). We hypothesize that allowing the nested tasks to share a feature value (object identity) would increase the potential WM crosstalk, seen in a greater attraction of the outer recalled orientation to the inner WM sample, and that conditions 2 and 3 would show greater response variance than condition 1. We further hypothesize that these effects would be amplified in the patient group.

This study is currently underway with N=8 control and N=6 patient participants recorded. Data are being collected with a 128-channel passive EEG system with custom electrode placement and a Tobii4C eye-tracker.

Preliminary Results

Behaviour Inspired by work on distractor induced bias (Bansal et al., 2020; Murray et al., 2014), we examine the bias produced by the inner WM orientation on the outer WM orientation by calculating the response error in the direction of the inner sample for each combination of inner/outer sample orientation distances. Although we do not currently observe a significant difference in bias between groups, this is likely due to our current sample size. On the single-subject level we see that while some participants show the expected attraction curve, many show neither attraction bias nor a drop in performance in trials with the inner task present. These high performing subjects are present in both groups. There is additionally some preliminary evidence that on trials with an inner task the response variance in the patient group is increased.

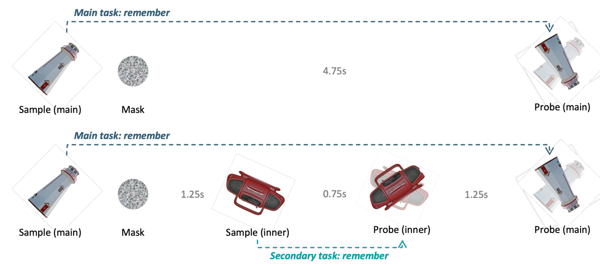

Figure 1: Illustration of task structure. (Above) Trials with no nested task. (Below) Trials with a nested task in the main delay period.

EEG Preliminary results show a possible increase in frontal and posterior gamma power in the patient group, consistent with some literature findings (Senkowski & Gallinat, 2015, see review by). They also indicate a possible decrease in power in the lower frequencies ($\leq$20Hz) in the patient group. This ”high-noise” regime is expected in SCZ and is evident in the shape of stimulus ERPs. Preliminary RSA results show the effect of this noise regime, with no decodability yet of sample orientations from the posterior ERP in SCZ. We will present full RSA results of orientation geometries at each time-point and across brain regions (frontal, central-medial, and posterior). We expect to present further analyses of time-locked time-frequency features, including potential top-down and bottom-up communication between frontal and posterior channels. Lastly, we will examine the correlation of these features with behavioral measures, as well as clinical symptoms in the patient group.

Eye-tracking We examine dynamic attentional shifts between the tasks using time-resolved RSA of eye-tracking data. Recently, Linde-Domingo and Spitzer (2023) used this technique to show high decodability of orientation WM geometries from micro patterns in gaze position (excluding saccades) with high temporal precision. We will apply this same analysis to infer which item is currently held in working memory by comparing the correlation of gaze patterns at each time point to the model geometries assumed for either the outer or inner sample orientations.

Discussion

Due to the involvement of WM in most observed SCZ cognitive deficits, understanding its alterations could further our understanding of the cognitive states underlying the presentation of schizophrenic symptoms. Time frequency signatures such as aberrant gamma oscillations have already provided phenomenological targets for neuronal (and synaptic) models of working memory, on which pharmacological hypotheses have been tested. Finally, examining possible alterations of endogenous control signals in complex WM tasks could lead to developments in global circuit modelling of attention control and manipulation and their role in maintaining representational stability during distraction/ dual-tasking.

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