Exogenous Cues Aid Salient Distractor Suppression and Enhance Attentional Prioritization during Visual Working Memory Encoding in Schizophrenia

Running Title: Attentional Prioritization in Schizophrenia

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ABSTRACT

Background

People with schizophrenia (PSZ) are impaired in attentional prioritization of non-salient but relevant stimuli over salient distractors during visual working memory (VWM) encoding. Conversely, guidance of top-down attention by exogenous predictive cues is intact. Yet, it is unknown whether this preserved ability can help PSZ overcome impaired attentional prioritization in the presence of salient distractors.

Methods

We employed a visuospatial change-detection task using four Gabor Patches with differing orientations in 66 PSZ and 74 healthy controls (HCS). Two patches flickered which were either the targets or non-targets and either a predictive or a non-predictive cue was displayed to manipulate top-down attention, resulting in four conditions.

Results

Across all conditions, PSZ stored significantly less information in VWM than HCS (all $p < 0.001$). PSZ stored significantly more flickering and non-flickering information in the predictive cue conditions compared to the non-predictive cue conditions ($p = 0.049$, $d = 0.5$; $p < 0.001$, $d = 1.0$). Additionally, PSZ stored significantly more flickering than non-flickering information in the non-predictive cue conditions ($p < 0.001$, $d = 0.9$). These effects were not observed in HCS.

Conclusions

Our findings indicate that attentional prioritization is disrupted in schizophrenia, but the top-down utilization of cues is intact. We conclude that additional top-down information significantly improves the amount of information encoded in PSZ. We report a specific deficit in attentional control, which is possibly mediated by

GABAergic inhibition in early visual areas. This finding proposes a mechanism that enhances attentional prioritization and could be utilized in future therapies.

INTRODUCTION

Visuospatial working memory (VWM) and attention are two intricately and bi-directionally related cognitive domains (Cowan, 2001; Gazzaley & Nobre, 2012; J. S. Mayer et al., 2007) essential for elucidating the basis of perturbed information processing in schizophrenia (Carter & Barch, 2007). The role of top-down attention for the encoding of VWM representations is particularly important due to clear behavioral (B. Hahn et al., 2010; Hartman, Steketee, Silva, Lanning, & McCann, 2003; Jutta S Mayer & Park, 2012) and neurophysiological (Bittner et al., 2015; Haenschel et al., 2007) evidence for a primary impairment of this VWM component process in people with schizophrenia (PSZ).

Specifically, top-down attention is crucial for selecting goal-relevant information to be stored in VWM and the efficiency of this mechanism has a considerable influence on VWM capacity (Cowan & Morey, 2006; Vogel, McCollough, & Machizawa, 2005). During VWM encoding, top-down attention, which is driven by stimulus relevance, competes with bottom-up attention, which is driven by stimulus salience (Liesefeld, Liesefeld, Sauseng, Jacob, & Müller, 2020; Lorenc, Mallett, & Lewis-Peacock, 2021). Both salience and relevance of an object influence its processing in VWM (Constant & Liesefeld, 2021). If multiple items compete for limited attentional resources, selection of relevant and inhibition of irrelevant information depends on the successful execution of two top-down control processes (Desimone & Duncan, 1995). First, the control of selection aids the identification of relevant information, which should be selected (S. J. Luck & Gold, 2008). Second, the implementation of selection enables the differential processing of relevant and irrelevant information (S. J. Luck & Gold, 2008). Neural computations during attentional competition assign a distinct priority to each stimulus, which is the combined representation of its salience and behavioral

relevance (Fecteau & Munoz, 2006). To this end, the control of attentional selection is guided by an attentional set, which induces a top-down attentional bias toward task-relevant information based on current goals (Bichot, Rossi, & Desimone, 2005; Corbetta & Shulman, 2002; Nicholas Gaspelin & Steven J Luck, 2018; Wolfe, 1994). According to the signal suppression hypothesis, this mechanism also facilitates the active suppression of automatic attentional capture by visually salient distractors through inhibitory mechanisms (N. Gaspelin & S. J. Luck, 2018; Sawaki & Luck, 2010). Thus, generating a priority map involves the parallelized up- and down-weighting of stimuli, both of which are essential elements of the implementation of selection (Nicholas Gaspelin & Steven J Luck, 2018).

Behavioral VWM experiments using flickering stimuli as part of an encoding array clearly indicate a strong attentional bias in PSZ toward highly salient stimuli, even if they are behaviorally irrelevant (B. Hahn et al., 2010). This bottom-up attentional bias surpasses the top-down bias induced by the attentional set. This results in a failure to correctly prioritize non-salient but relevant stimuli over salient but irrelevant distractors. Consequently, these distractors are encoded into WM with inadequately high priority. The correlation between the magnitude of the bottom-up attentional bias and reduced VWM capacity (B. Hahn et al., 2010) underscores its importance for VWM dysfunction. These findings indicate a specific impairment of the implementation of attentional selection in PSZ, when top-down control is required to overcome salient distractors. Importantly, control of attentional selection relying solely on an internally generated attentional set is also disturbed in PSZ (Fuller et al., 2006).

Conversely, patients' ability to utilize external spatial cues to guide top-down attention during VWM encoding and to prioritize information correctly without the presence of salient distractors is intact (James M Gold et al., 2006). This is

indicative of an 'island of preserved cognitive function' (J. M. Gold, Hahn, Strauss, & Waltz, 2009), which can provide important clues about the cognitive and neurophysiological mechanisms underlying attentional and VWM encoding dysfunction. However, it remains unknown whether top-down attentional control of PSZ aided by external cues can prevail when directly challenged by highly salient distractors. Elucidating this issue is crucial for models of impaired attentional control and stimulus prioritization during VWM encoding. In this context, impaired inhibition due to disturbances in the GABAergic system – a central pathophysiological mechanism in schizophrenia (Howes & Shatalina, 2022; Lewis, Hashimoto, & Volk, 2005) – is highly pertinent.

There is converging evidence that the suppression of attentional capture by salient stimuli relies on top-down inhibitory mechanisms inducing local inhibition of such stimuli in early visual areas (Nicholas Gaspelin & Steven J Luck, 2018). This process is primarily mediated by inhibitory GABAergic interneurons (Buschman & Kastner, 2015; Zhang et al., 2014). Notably, post-mortem studies have consistently demonstrated widespread abnormalities in cortical inhibitory GABAergic interneurons in PSZ resulting in reduced inhibition (Lewis, 2014). Neuroimaging, behavioral and computational data also support a central role of reduced GABAergic inhibition for cognitive dysfunction (Shaw et al., 2020). Therefore, impaired GABAergic inhibition in early visual areas might be a crucial mechanism underlying the insufficient suppression of attentional capture by salient stimuli in PSZ.

Yet, the successful use of spatial cues by PSZ to overcome this deficit would indicate that enhancing inhibitory control of attentional selection exerted by frontal-parietal areas could sufficiently strengthen local inhibition within early visual areas. Moreover, it would imply that impaired control of selection is the central attentional

deficit. The goal of the current study was to test these hypotheses in a behavioral VWM experiment directly contrasting top-down and bottom-up attentional processes during VWM encoding. To this end, we employed a VWM paradigm containing an equal number of salient (flickering) and non-salient (non-flickering) Gabor patches with different orientations. These were preceded by either a predictive cue indicating the location of task-relevant stimuli, or a non-predictive cue providing no such information.

METHODS AND MATERIALS

Participants

We recruited 66 PSZ from psychiatric outpatient facilities in and around Frankfurt am Main, Germany. We established diagnoses of all patients according to DSM-5 criteria based on a clinical interview and careful chart review at a consensus conference. We used the Positive and Negative Syndrome Scale (PANSS) to assess current psychopathology. All patients were on stable antipsychotic medication for at least one month at the time of the study.

74 healthy control subjects (HCS) were recruited by online and printed advertisements. They were screened using the German version of the Structural Clinical Interview SCID-I from the Diagnostic and Statistical Manual, Version IV (Saß, Wittchen, Zaudig, & Houben, 2003). They reported no history of any psychiatric illness and no family history of psychiatric illness in first-degree relatives. All participants reported no history of neurological illness and no drug use (excluding nicotine) within the past six months.

We matched groups for age, sex, premorbid IQ, years of education, and parental years of education (Table 1). Premorbid verbal intelligence was assessed by the German Mehrfachwahl-Wortschatz-Intelligenz Test (Lehrl, Merz, Burkhard, &

Fischer, 2005). The ethics committee of the University Hospital Frankfurt approved all study procedures. Subjects provided written informed consent after receiving a complete description of the study.

Working Memory Task

A visuospatial change detection task using Gabor patches (Figure 1) was implemented on a personal computer using Presentation software version 14.9 (www.neurobs.com). Stimuli were presented on a grey background (RGB values: 191, 191, 191) in a dimly lit room with a viewing distance of approximately 60 cm. Gabor patches had a visual angle of 0.96° each and were placed on an imaginary circle with a visual angle of the diameter of 3.82°. Throughout the experiment a black fixation cross (visual angle: 0.48°) was presented at the center of the screen. Subsequently, either a predictive cue or a non-predictive cue was presented by briefly turning the fixation cross white for 300 ms. For predictive cues, the white arms of the fixation cross indicated the future locations of task relevant Gabor patches. For non-predictive cues, the entire fixation cross turned white, providing no location information. After a 300 ms preparation interval, the encoding array consisting of four Gabor patches shown at four fixed locations equally spaced on an imaginary circle around the fixation cross was displayed for 400 ms. Two of the four patches flickered at a frequency of 7.5 Hz. Before each block, participants were informed about the currently task-relevant Gabor patches (flickering or non-flickering) and of the high likelihood that they would be probed during retrieval. Predictive cues always correctly indicated the future locations of the task-relevant Gabor patches. In the predictive cue conditions, participants therefore were provided with two sources of information about the targets: the instruction before the block and the additional cue at the start of each trial. The delay phase lasted for

2000 ms on average, with a jitter of +/- 250 ms. During retrieval, one Gabor patch was shown within a white box at one of the four fixed locations for 3000 ms. These locations were randomized but counterbalanced. 'Change' trials featured a minimum Gabor patch rotation of 45°. The other three Gabor patches were blurred out. Participants had to indicate by button press if the orientation of the highlighted Gabor patch was identical to or differed from the Gabor patch shown at the same location in the encoding array (for further details, see supplementary materials). This resulted in four conditions: flickering / predictive cue, flickering / non-predictive cue, non-flickering / predictive cue, non-flickering / non-predictive cue.

In 80% of trials, we probed a task-relevant Gabor patch (target trials). In 20% of trials, we probed a task-irrelevant Gabor patch (catch trials). Catch trials were introduced to assess each participants' efficiency of attentional prioritization, which was operationalized as the difference between the amount of task-relevant and task-irrelevant information stored in VWM. A total of 400 trials were presented, 100 for each condition, divided into eight blocks, counterbalanced in order across participants and groups. Each block began with a short practice of four trials to ensure understanding of the current instructions.

Additionally, to gain an independent estimate of VWM capacity, we employed a 60-trial canonical visual change detection task (Barnes-Scheufler et al., 2021) (see supplementary materials for further details).

Analysis of Behavioral Data

The amount of information stored in VWM was quantified using Cowan's K, where K = (hit rate + correct rejection rate − 1) × memory set size (Cowan, 2001; Rouder, Morey, Morey, & Cowan, 2011). We used a set size of two items, as only two targets were instructed to be encoded, thus there was a theoretical maximum of

K = 2 (Feldmann-Wustefeld & Vogel, 2018). Statistical analyses were conducted using SPSS (IBM) Version 22, and R (www.r-project.org). Using a binomial expansion on the 400 trials, we determined that an accuracy of 56% had a cumulative probability of P(X > x) 0.009, i.e., the probability of getting 224 correct responses or more by chance was less than 1%. Accordingly, we excluded the participants with an accuracy below 56% (n = 3, all PSZ).

The main analysis consisted of a linear mixed-model with a random intercept. We based this analysis solely on target trials, to study the differential processing of task-relevant information. Significant between group main effects and interactions were further analyzed post-hoc using the Kenward-Roger degrees-of-freedom method with pairwise t-tests adjusted with the Tukey method. Significant within group effects and interactions were further analyzed post-hoc using the Kenward-Roger degrees-of-freedom method with pairwise t-tests adjusted with the Tukey method. Cohen's d was calculated to estimate effect sizes.

Independent 2-tailed t-tests were conducted between groups in each condition to investigate possible differences in attentional prioritization (Cowan's K for target trials minus Cowan's K for catch trials).

To assess the relationship between the ability to prioritize task-relevant information and WM capacity, we correlated the efficiency of attentional prioritization (Cowan's K for target trials minus Cowan's K for catch trials) in each participant across all four conditions with an independent estimate of VWM capacity (Pashler's K, (Pashler, 1988)) derived from a canonical visual change detection task (Barnes-Scheufler et al., 2021). Additionally, we calculated separate Spearman correlations between Cowan's K with Pashler's K for each target condition.

RESULTS

Averaged across all target conditions, HCS encoded 1.27 items, which corresponded to an accuracy of 82% (Figure 2). PSZ encoded 0.95 items, corresponding to an accuracy of 74%. HCS encoded more information into VWM in all four target conditions: flickering / predictive cue (mean = 1.32, SD = 0.39), flickering / non-predictive cue (mean = 1.29, SD = 0.41), non-flickering / predictive cue (mean = 1.28, SD = 0.39), non-flickering / non-predictive cue (mean = 1.20, SD = 0.43) than PSZ : flickering / predictive cue (mean = 1.07, SD = 0.36), flickering / non-predictive cue (mean = 0.97, SD = 0.46), non-flickering / predictive cue (mean = 0.99, SD = 0.43), non-flickering / non-predictive cue (mean = 0.77, SD = 0.44).

The factor of cue had a significant effect across both groups (FE = -0.80, p = 0.023; Table 2). We also observed a significant effect of group with less information encoded in PSZ (FE = -0.293, $p < 0.001$), as well as a significant effect of cue in PSZ (FE = -0.141, p = 0.006). Furthermore, there was no interaction between salience and cue (FE = 0.055, p = 0.262). The R squared marginal, only when considering fixed effects was much lower (R^2 =0.1655) than the R^2 with the random effect for intercept (R^2 = 0.7752), providing a measurement of the goodness of fit (Barton & Barton, 2015). We observed a significant reduction of the amount of information stored in VWM in target trials in PSZ compared to HCS in each condition ($p < 0.001$ for all, Table 3). There were no significant differences between conditions in HCS, however there was a trend level improvement in the amount of stored information in the flickering / non-predictive cue condition compared to the non-flickering / non-predictive cue condition (p = 0.050, d = 0.4).

PSZ stored significantly more information in the flickering / predictive cue condition compared to the flickering / non-predictive cue condition (p = 0.049, d = 0.5). There was no significant interaction of salience and cue in HCS, and this null

effect was further supported with a Bayes Factor of 1/3, indicating that the null hypothesis was three times more likely than the alternative hypothesis (see Supplementary Materials for more information). Additionally, PSZ stored significantly more information in the non-flickering / predictive cue condition compared to the non-flickering / non-predictive cue condition ($p < 0.001$, $d = 1.0$), an effect again not observed in HCS. Finally, PSZ stored significantly more information in the flickering / non-predictive cue condition compared to the non-flickering / non-predictive cue condition ($p < 0.001$, $d = 0.9$). Further results can be found in Tables 4 and 5.

Our independent estimate of WM capacity did not correlate with the efficiency of attentional prioritization across all conditions in HCS (Mean = 3.31, SD = 0.58, $r_s = 0.16$, $p = 0.167$), or in PSZ (Mean = 2.97, SD = 0.67, $r_s = 0.18$, $p = 0.150$). However, in HCS we observed a significant correlation between Cowan's K and working memory capacity (Pashler's K) in target trials of all four conditions (Table S4). In PSZ, Cowan's K correlated significantly with working memory capacity (Pashler's K) only in the two non-predictive cue conditions (Table S4).

DISCUSSION

We studied the competition between bottom-up and top-down attentional processes during VWM encoding in PSZ and HCS in order to elucidate how disturbed attentional control contributes to VWM dysfunction in schizophrenia. Overall, we observed a significant effect of group with a decreased amount of information stored in VWM in PSZ across all conditions. We also observed an overall significant effect of cue, which was also significant in the PSZ group. This effect was also evident in the post-hoc tests, which indicates that compared to non-predictive cues in PSZ predictive cues increased the amount of information stored in VWM for both salient

and non-salient targets. Importantly, we did not observe an effect of cue in HCS. This demonstrates that predictive cues helped to overcome a deficit in attentional control specific to the PSZ group. Notably, this improvement was not sufficient to increase the amount of stored information up to the level of HCS.

Overall, there was no significant effect of salience. For salient targets, the use of predictive cues did not significantly increase the amount of stored information in either group. However, with non-predictive cues, PSZ stored significantly more information for salient compared to non-salient targets. HCS showed a trend in the same direction. Thus, in the absence of predictive cues, stimulus salience did affect attentional control, indicating the presence of a bottom-up bias.

We could replicate a previous report by Hahn and colleagues of a bottom-up attentional bias toward salient distractors during VWM encoding in PSZ (B. Hahn et al., 2010). The central question of our study was concerned with the effect of a predictive cue on the processing of salient distractors in PSZ. For the non-flickering conditions, where patients had to suppress highly salient stimuli, the addition of a predictive cue significantly increased the amount of stored information only in PSZ. This indicates that patients were able to utilize exogenous cues to enhance attentional prioritization of task-relevant information. It remains an open question whether the use of feature-based instead of spatial-based cues can lead to a similar beneficial effect.

Importantly, we did not observe any difference between groups in the amount of stored information for catch trials (see Supplementary Materials). This would be compatible with the notion, that down-weighting is not disturbed in schizophrenia, but rather up-weighting seems to be impaired.

Furthermore, the presentation of a predictive cue enhanced the suppression of irrelevant salient information in PSZ, which indicates a strengthening of inhibitory

mechanisms. This suggests that disturbed inhibition in PSZ thought to underlie impaired control of attentional selection is not an irreversible phenomenon, but that it can be partially counteracted by aiding the internally generated attentional set with exogenous spatial cues. Additionally, our results are compatible with the interpretation that enhanced inhibitory control during attentional selection might increase local inhibition within early visual areas. Increased inhibition could result in a relative enhancement of the cued locations in the attentional priority map by suppressing task-irrelevant locations. This interpretation would also be in line with the signal suppression hypothesis.

We observed a significant reduction in the amount of stored information for the non-flickering / non-predictive cue condition in PSZ compared to HCS. This indicates that PSZ are considerably more susceptible to failures of implementing selection in the presence of salient distractors without the aid of an exogenous cue than HCS. This results in greater interference with the prioritization of information during VWM encoding in PSZ. Notably, another study investigating distractor processing during VWM encoding in PSZ did not report evidence for a bottom-up attentional bias (Erickson et al., 2015). Here, stationary rotating motion was used to generate salient distractor stimuli. However, this manipulation of stimulus properties might not have been sufficiently salient to trigger automatic attentional capture, especially in light of the extensive evidence for motion processing impairments in PSZ (Chen, 2011). By contrast, flickering of visual stimuli has been shown to be particularly salient (Merigan & Maunsell, 1993).

Importantly, there is converging evidence of attentional hyperfocusing during visual information processing in PSZ (Britta Hahn et al., 2022; Steven J Luck, Leonard, Hahn, & Gold, 2019). Increased vulnerability to attentional capture by salient distractors in PSZ could also be interpreted as a manifestation of attentional

hyperfocusing, i.e. hyperfocusing on irrelevant information. This could imply a shared mechanism involving abnormal GABA-mediated inhibition for both phenomena. However, the exact relationship between the failure to implement attentional selection in the presence of salient visual distractors and the degree of attentional hyperfocusing in PSZ remains to be investigated. As attentional hyperfocusing appears to constrain the amount of information PSZ can encode into VWM (Steven J Luck, Hahn, Leonard, & Gold, 2019), it is conceivable that it contributed to the general VWM impairment we observed in PSZ across all task conditions. However, we were not able to make any inferences regarding this interpretation based on our current paradigm.

Our results are well in line with a differential impairment of the two attentional constructs of proposed by Luck & Gold. The control of selection appears to be largely intact in PSZ as the amount of stored information increased significantly when predictive cues were used to guide top-down attention. Conversely, the implementation of control appears to be impaired in PSZ as less information was encoded across all conditions. Post-hoc within group analyses also revealed that our independent estimate of VWM capacity correlated significantly with the amount of stored information in target trials of each condition in HCS, but only in the non-predictive cue conditions in PSZ (Table S4). This could indicate that VWM capacity in PSZ is generally constrained by their degree of impaired attentional control, which is fully evident only when unaided by predictive exogenous cues. By contrast, WM capacity did not correlate with the efficiency of attentional prioritization in either HCS or PSZ. This further supports the notion, that attentional prioritization and the encoding of information into WM are two separate constructs. Interestingly, there was one significant difference between groups in the attentional prioritization of the non-flickering / non-predictive cue condition, with more information being encoded

in HCS (Table S7). The difference between the amount of stored information in target and catch trials was smallest in PSZ in this condition, most likely due to hyperfocusing on salient, irrelevant information in the absence of an additional top-down predictive cue. Interestingly, we observed a significant correlation of age and the cue effect only in HCS (r_s = 0.240, p = 0.040; Table S3), indicating that with increasing age, the difference in amount of information encoded between predictive and non-predictive cue conditions increases. This could provide more information to what specific cognitive processes deteriorate in the aging brain. Additionally, in PSZ we observed a significant negative correlation between flickering and non-flickering conditions and premorbid IQ (r_s = -0.254, p = 0.039; Table S3). This implies with increasing IQ, the difference in amount of information encoded between flickering and non-flickering conditions decreases. It appears therefore, that patients with higher IQ were better able to guide attention to the task-relevant target items whether they were more or less salient. This is relevant considering that premorbid IQ has been reported to predict functional outcome in PSZ (Leeson, Barnes, Hutton, Ron, & Joyce, 2009).

To summarize, the current paradigm allowed us to study two central attentional processes, the control of attention and the implementation of selection and their contribution to VWM encoding deficits in PSZ. We were able to delineate the extent of intact and impaired aspects of these processes and to provide novel constraints for models of attentional dysfunction in the context of VWM. The neurophysiological underpinnings of our findings should be illuminated using functional neuroimaging. The relevance of such a study is underscored by the inclusion of both attention and working memory as constructs in the cognition domain of the Research Domain Criteria initiative (Insel et al., 2010). Given the presence of deficits in attention and working memory in other neuropsychiatric

disorders such as bipolar disorder, our paradigm might therefore be useful for studying the pathophysiology of impaired information across diagnostic categories.

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ETHICAL STANDARDS:

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1. Participant characteristics of both groups including information regarding demographics, psychopathology and current medication.

	HCS (n = 74)	PSZ (n = 66)	Statistic	df	p
Demographics					
Age, Years	36.70 (13.02); range 19-61	37.59 (10.45); range 20-57	t = 0.48	138	0.656
Sex, Male/Female	45 / 29	44 / 22	X^2 = 0.517	1	0.294
Participant Education, Years	16.26 (2.12)	15.76 (2.77)	t = -1.19	138	0.238
Parental Education, Years	14.93 (3.02)	14.82 (3.31)	t = -0.21	138	0.831
Premorbid IQ	113.93 (11.16)	109.89 (13.40)	t = -1.95	138	0.054
Schizophrenia		44			
Schizoaffective disorder		22			
Psychopathology					
PANSS Positive		10.13 (3.53)			
PANSS Negative		11.72 (3.83)			
PANSS General		22.78 (4.85)			
PANSS Total		44.47 (9.81)			
Medication					
FGA	0	1			
SGA	0	58			
FGA + SGA	0	5			
Lithium	0	3			
Valproate	0	2			
Antidepressants	0	15			

Table 2. Results of the linear mixed model investigating the effects of cue (predictive cue / non-predictive cue) and salience (flickering / non-flickering) in target trials in both PSZ and HCS.

	FE	SE	t	df	p
Cue	-0.080	0.035	-2.286	420	0.023*
Salience	0.035	0.035	1.008	420	0.314
Salience x Cue	0.055	0.049	1.123	420	0.262
PSZ	-0.293	0.069	-4.233	215	< 0.001***
Salience PSZ	0.041	0.051	0.800	420	0.424
Cue PSZ	-0.141	0.051	-2.771	420	0.006**
Salience X Cue PSZ	0.069	0.072	0.958	420	0.338

Table 3. Results of post-hoc between group comparisons across all four task conditions in target trials.

	t	df	p
Flickering / predictive cue	3.62	218	< 0.001***
Flickering / non-predictive cue	4.65	218	< 0.001***
Non-flickering / predictive cue	4.20	218	< 0.001***
Non-flickering / non-predictive cue	6.22	218	< 0.001***

Table 4. Results of post-hoc within group comparisons in HCS across all four task conditions in target trials.

	t	df	p	ES
Flickering / predictive cue vs Flickering / non-predictive cue	0.69	426	0.900	0.1
Flickering / predictive cue vs Non-flickering / predictive cue	-1.00	426	0.750	0.2
Non-flickering / predictive cue vs Non-flickering / non-predictive cue	2.27	426	0.107	0.4
Non-flickering / non-predictive cue vs. Flickering / non-predictive cue	-2.58	426	0.050	0.4

Table 5. Results of post-hoc within group comparisons in PSZ across all four task conditions in target trials.

	t	df	p	ES
Flickering / predictive cue vs Flickering / non-predictive cue	2.59	426	0.049*	0.5
Flickering / predictive cue vs Non-flickering / predictive cue	-2.04	426	0.176	0.4
Non-flickering / predictive cue vs Non-flickering / non-predictive cue	5.93	426	< 0.001***	1.0
Non-flickering / non-predictive cue vs. Flickering / non-predictive cue	-5.34	426	< 0.001***	0.9

TABLE LEGENDS:

Table 1. Values are mean (SD), or n. All statistics reported are 2-tailed. Asteriks indicate significance $p < 0.001$ = ***, $p < 0.01$ = ** $p < 0.05$ = *. Abbreviations: HCS = healthy control subjects, PSZ = people with schizophrenia, PANSS = Positive and Negative Syndrome Scale, FGA = first-generation antipsychotics, SGA = second-generation antipsychotics, df = degrees of freedom.

Table 2. Asteriks indicate significance $p < 0.001$ = ***, $p < 0.01$ = ** $p < 0.05$ = *. Abbreviations: PSZ = people with schizophrenia, FE = fixed effect estimates, SE = standard error, df = degrees of freedom.

Table 3. Asteriks indicate significance $p < 0.001$ = ***, $p < 0.01$ = ** $p < 0.05$ = *. Abbreviations: df = degrees of freedom.

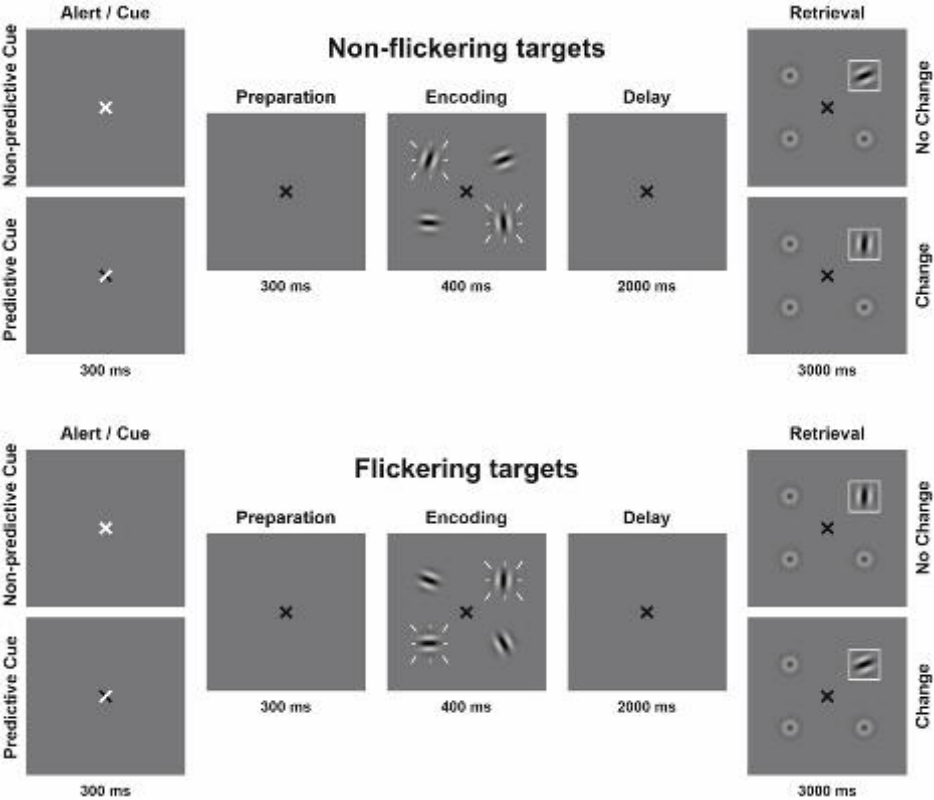
Table 4. Abbreviations: df = degrees of freedom, ES = effect size.

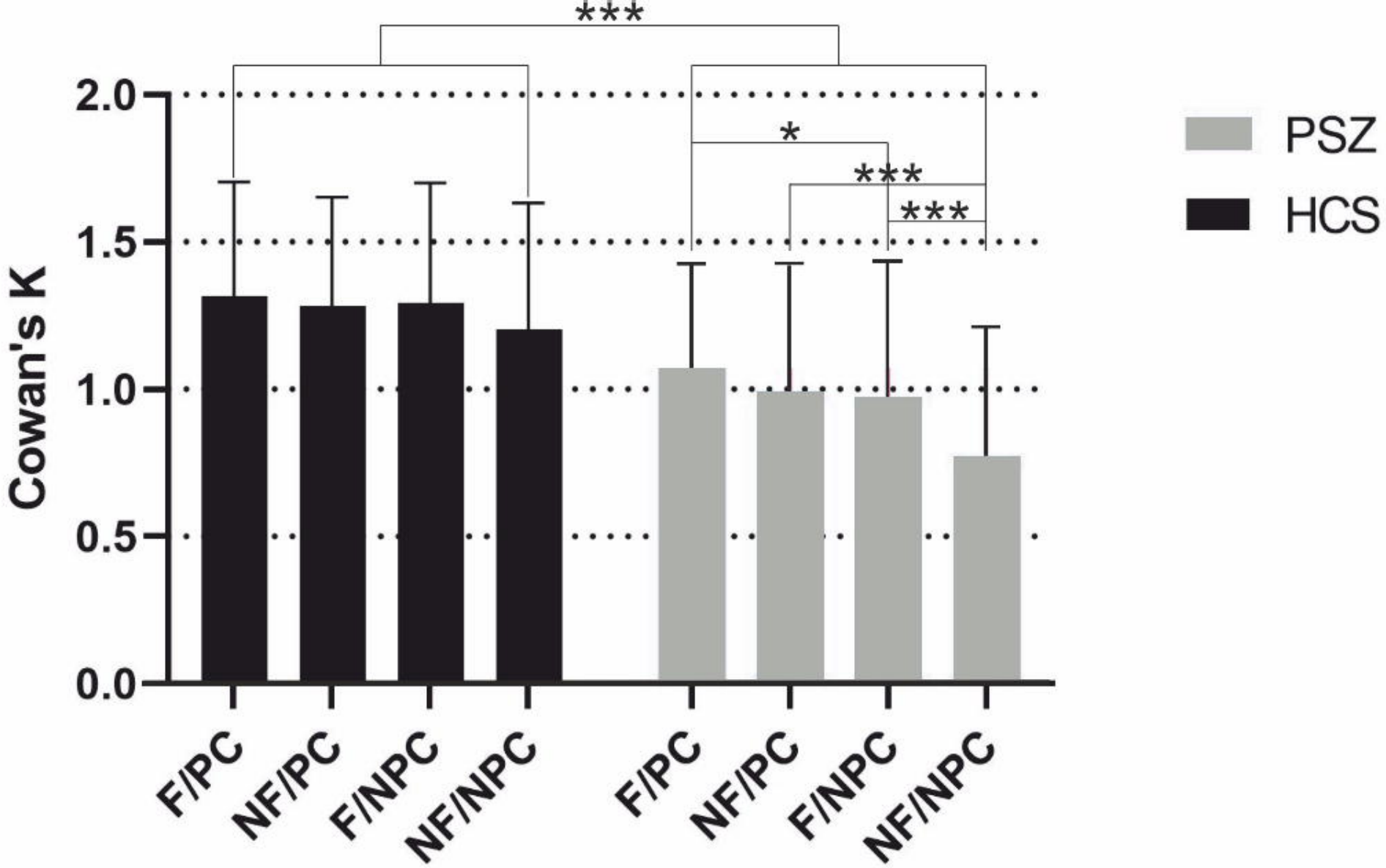
Table 5. Asteriks indicate significance $p < 0.001$ = ***, $p < 0.01$ = ** $p < 0.05$ = *. Abbreviations: df = degrees of freedom, ES = effect size.

FIGURE LEGENDS:

Figure 1. Visual change detection task with four conditions; flickering / predictive cue, flickering / non-predictive cue, non-flickering / predictive cue, non-flickering / non-predictive cue. Flickering is indicated by white dashes around stimuli. The set size of four items was kept constant.

Figure 2. Amount of information stored in VWM in target trials, estimated with Cowan's K in healthy control subjects = HCS and people with schizophrenia = PSZ. F/PC = flickering / predictive cue, NF/PC = non-flickering / predictive cue, F/NPC = flickering / non-predictive cue, NF/NPC = non-flickering / non-predictive cue. Within and between group contrasts are displayed. * Indicates $p < 0.05$, *** indicates $p < 0.001$ Error bars indicate standard deviation.


Non-flickering targets
Alert / Cue
Non-predictive Cue
Predictive Cue
300 ms
Preparation
300 ms
Encoding
400 ms
Delay
2000 ms
Retrieval
No Change
Change
3000 ms
Flickering targets
Alert / Cue
Non-predictive Cue
Predictive Cue
300 ms
Preparation
300 ms
Encoding
400 ms
Delay
2000 ms
Retrieval
No Change
Change
3000 ms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2.0
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Cowan's K
PSZ
HCS
F/PC
NF/PC
F/NPC
NF/NPC
F/PC
NF/PC
F/NPC
NF/NPC