Divergent roles of early visual cortex and inferior frontal junction in visual working memory

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A B S T R A C T

Background: Recent studies indicate that both prefrontal and visual regions play critical roles in visual working memory (VWM), with prefrontal regions mainly associated with executive functions, and visual cortices linked to representations of memory contents. VWM involves the selective filtering of irrelevant information, yet the specific contributions of the prefrontal regions and visual cortex in this process remain unclear.
Objective: To understand the dynamic causal roles of prefrontal and visual regions in VWM.
Methods: The differentiation of VWM components was achieved using a computational model that incorporated a swap rate for non-target stimuli. Single-pulse magnetic transcranial stimulation (spTMS) was delivered to the early visual cortex (EVC) and the inferior frontal junction (IFJ) across different phases of an orientation recall task that with or without distractors.
Results: Our results indicate that spTMS over the EVC and IFJ influences VWM particularly when distractors are present. VWM precision can be impacted by spTMS applied to either region during the early retention, while spTMS effect is especially prominent when EVC is stimulated during the late retention phase and when directed at the ipsilateral EVC. Conversely, the probability of accurately recalling the target exhibited comparable patterns when spTMS was administered to either the EVC or IFJ.
Conclusions: We highlight the "sensory recruitment" of VWM characterized by critical involvement of EVC particularly in the information-filtering process within VWM. The maintenance of memory content representations necessitates ongoing communication between the EVC and IFJ throughout the entirety of the VWM process in a dynamic pattern.

1. Introduction

Visual working memory (VWM) is a high-level cognitive function characterized by a limited capacity [1]. Prefrontal regions are central to this process, specifically in representing varying numbers of items [2–5]. However, recent studies propose a novel theoretical framework emphasizing that "precision" in VWM is critical for accurately modeling and understanding this cognitive system [6]. Evidence suggests visual areas are responsible for the precise processing and maintenance of visual contents, whereas prefrontal regions predominantly act as "high-level" mediators [7–9]. This "sensory recruitment" hypothesis is supported by findings from multiple functional magnetic resonance imaging (fMRI) studies that have successfully decoded neural patterns corresponding to VWM attributes, such as orientation, color, spatial location, and motion direction, with signals originating from the visual cortex [10–15]. Importantly, these studies reveal that the decoding accuracy is correlated with individual VWM precision [12].

Non-invasive neurostimulation research utilizing transcranial magnetic stimulation (TMS) has substantiated the critical role of both prefrontal and visual regions in VWM [16]. For example, single-pulse TMS (spTMS) applied over the early visual cortex (EVC) during the early retention can compromise accuracy [17,18] and precision [19]. Additionally, high-frequency repetitive TMS (rTMS) targeting the MT + area has demonstrated potential in enhancing VWM precision in tasks involving motion directions [20]. However, limitations exist in prior studies, some of which applied traditional accuracy measures without

dissociating distinct components of VWM (e.g., precision and capacity representations) [17,18], or confined their investigation to the early retention, omitting the later phases [19]. Moreover, while the majority of studies adhere to retinotopic organization of the visual cortex, emphasizing the processing of contralateral visual stimuli in VWM, some studies also underscore the relevance of ipsilateral or global sensory involvement [21–24]. Although the function of the EVC in VWM retention may resemble its role during visual encoding, the necessity for additional regulatory dynamics both within and between the EVC and higher cognitive control areas, actively sustain relevant visual representations over temporal delays, is apparent [25].

In everyday scenarios, distractions commonly interfere with the VWM process. Studies have indicated that individuals with reduced working memory capacity may experience difficulties attributable to their impaired capability to exclude irrelevant information in VWM [26]. This ability to engage in goal-directed selective attention is closely related to neural processes within the prefrontal and intraparietal cortices [27–29]. Meanwhile, recent fMRI studies employing multivariate approaches have proposed that visual areas might also play a role in the discrimination of task-relevant stimuli, and that attentional mechanisms can modulate visual representations within the visual cortex [30, 31]. However, the correlational nature of fMRI data poses limitations on conclusively affirming the criticality of visual cortex activities in the presence of distractors.

Research by Zanto and colleagues demonstrates that low-frequency rTMS over the inferior frontal junction (IFJ) can impair top-down control from prefrontal to visual regions, resulting in diminished performance in VWM tasks that involve distractions [32]. Notably, the modulation of visual processing by the IFJ can occur as early as 100 ms after the stimulus onset, consistent with color-based attention influencing feedforward information flow [33–35], and is linked to working memory performance [36]. Visual areas processing task-relevant information exhibited functional connectivity to the prefrontal areas including IFJ, while visual areas processing task-irrelevant information are more likely connected to the default mode network [37]. Our previous findings further suggest both the IFJ and EVC are crucial loci for achieving precision in VWM [38]. However, prior studies have not delineated the critical temporal windows for IFJ activity, nor its interaction with EVC in modulating selective attention across different VWM components. Elucidating this time course would provide insight into the dynamics supporting goal-directed VWM.

In the present experiment, we aim to examine the causal role of the EVC and IFJ at various stages throughout the VWM process, utilizing color-based selective attention as a guiding mechanism. Participants were instructed to memorize the orientations of bars of a specific color while disregarding the orientations of bars in other colors during a delay-recall working memory task. Concurrently, spTMS was applied over the EVC or IFJ during the stimulus presentation, early retention, and late retention phases, based on the hypothesis that VWM is a highly dynamic process [39]. Prior to the main experimental procedures, T1-weighted imaging was conducted to guide the localization of TMS. A mixture model was used to dissociate precision and capacity components of VWM [35,36]. The primary aim of this study was to discern whether different components of VWM are processed at specific temporal windows in the EVC and IFJ. Additionally, in an exploratory manner, we assessed whether the effects of spTMS exhibited lateralization in relation to the retinotopic organization of the visual cortex.

2. Materials and methods

2.1. Participants

Twenty-six right-handed, healthy participants (15 females; average age: 22.92 ± 3.33 years), all possessing normal or corrected-to-normal vision, were recruited for the study. Participants reported no history of neurological, psychiatric, or related disorders. Ethical approval for the study was granted by the University Committee on Human Research Protection at East China Normal University. All participants provided informed consent prior to participation and received compensation for their involvement.

2.2. Experimental procedure and stimuli

All stimuli were generated using MATLAB R2016b (MathWorks, MA, USA) and Psychtoolbox-3 (www.psychtoolbox.org), and were presented on a 24-inch LCD monitor set to a resolution of 1280 × 1024 pixels and a refresh rate of 60 Hz. Participants were positioned 60 cm away from the monitor, seated in a comfortable chair, and were instructed to remain still throughout the execution of the tasks.

At the onset of the experiment, participants were provided with comprehensive instructions, which included information regarding the color of the target bars. The target bars were either blue (R = 22, G = 80, B = 196) or yellow (R = 169, G = 67, B = 10), presented against a brown background (R = 41, G = 30, B = 34). Each bar was positioned at 10 degrees of visual angle from the fovea and measured 3.7° in length of visual angle. The initial target color was randomly assigned and maintained consistently for the first half of the blocks, with a change implemented for the second half.

A complete trial was structured as depicted in Fig. 1. Each trial began with a fixation cross presented for 200–300 ms, followed by exposure of the sample array for 200 ms. Subsequently, a delay period of 900 ms ensued, during which participants were required to memorize the orientations of the target color bars while disregarding the others. After the delay, a single target color bar was reintroduced in its original orientation, with one end oriented towards the fixation cross. Participants then adjusted the orientation of the bar using a mouse to align it with their memory representation, and confirmed their response by clicking within a 10-s window. Precision was emphasized, and the distance between the recorded orientation and the actual orientation of the target bar was quantified as the response error.

The experiment employed a 2 × 2 × 3 within-subjects factorial design. The independent variables included: TMS site (EVC vs IFJ), distraction state (2 targets [t2] vs 2 targets + 2 distractors [t2d2]), and stimulation time (50 ms, 400 ms, 800 ms after stimulus onset). The distribution of targets and distractors was balanced across the left and right visual fields; specifically, in the t2 condition, one target was presented in each visual field, while in the t2d2 condition, each visual field contained one target and one distractor. The orientation of the two targets was either vertical or diagonal, and this arrangement was counterbalanced across tasks. TMS sites (EVC or IFJ) were stimulated in separate randomized blocks, whereas the other variables were intermixed within each block. The sequence of all stimulation times and distraction states was counterbalanced within each block to control for order effects.

Participants engaged in a total of 28 blocks, of which 24 included TMS and 4 were conducted without TMS. Excluding an initial practice block, each experimental block comprised 48 trials. In the TMS blocks, each distraction state and time point combination was represented by 8 trials. Conversely, in the no-TMS blocks, each distraction state was tested across 24 trials. The TMS blocks were divided into 8 sessions. Within each session, participants completed 3 blocks receiving TMS over the same brain site. The order of the sessions followed the ABBA experimental design, with half of the participants receiving stimulation over the EVC site in the first session (A) and stimulation over the IFJ site in the second session (B), while the other half followed the reverse order. The position of the baseline no-TMS blocks was fixed, with one occurring at the beginning of the experiment, another after the fourth TMS session, and the final one at the end.

2.3. Transcranial magnetic stimulation

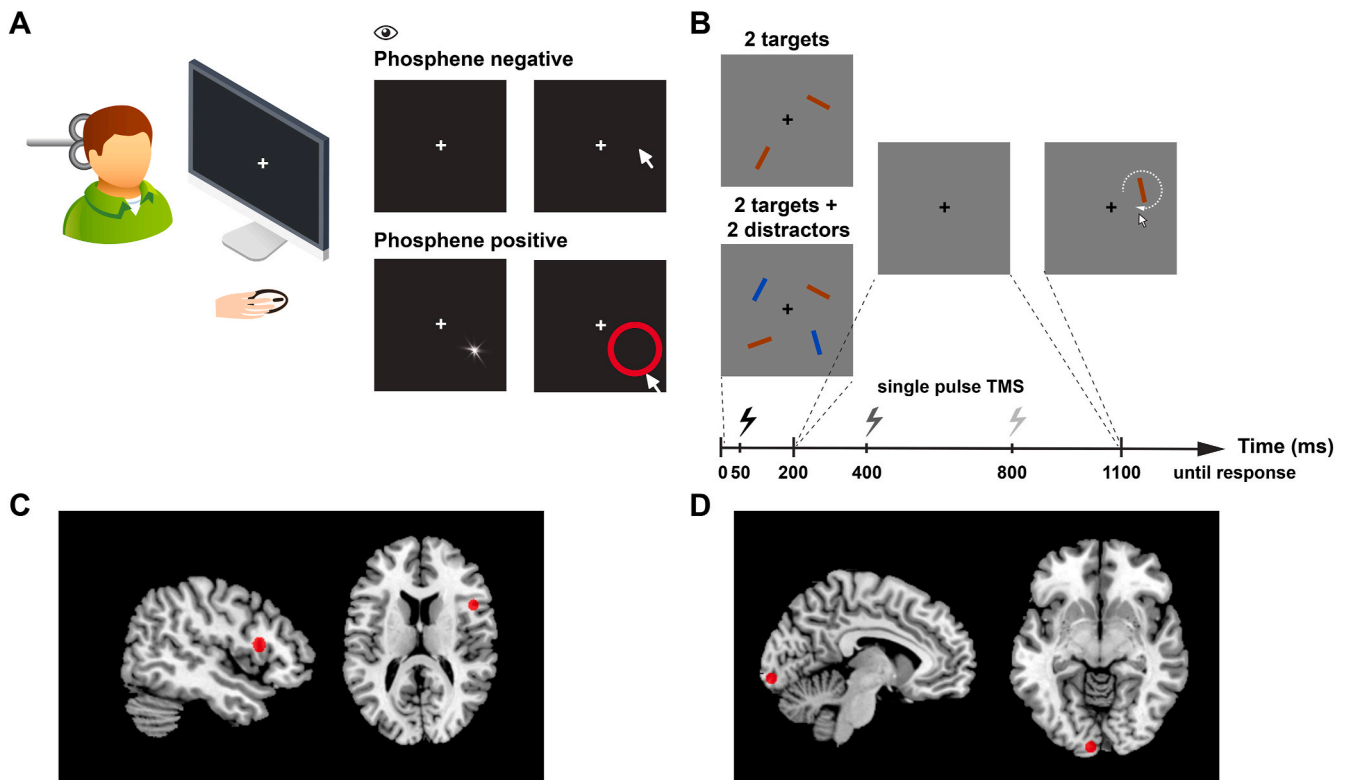TMS was administered using a Magstim Rapid2 stimulator equipped

Fig. 1. Experiment setup. A. Illustration of phosphene threshold measurement. Participants were required to draw the range of phosphenes they perceived on a black screen while single-pulse TMS (spTMS) was delivered to the EVC. B. Experiment procedure. Displays consisted of either two target items or two targets alongside two distractors on a grey screen. Participants were instructed to memorize the targets, identified by color, and subsequently report the orientation of the probed item following a brief delay. Single-pulse TMS (spTMS) was delivered at 50 ms, 400 ms or 800 ms after stimuli onset. C. Location of IFJ stimulation. D. Average location of EVC stimulation. This was individualized based on the phosphene localization reported during the experiment. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

with a 70-mm figure-eight-shaped coil (The Magstim Company, Whitland, UK). The timing of pulses was controlled using Matlab R2016b. For precise stereotaxic registration of the TMS coil to the targeted brain regions, the anatomical images were transformed and imported into the BrainSight™ neuronavigation software (BrainSight 2.0, Rogue Research, Montreal, Canada). The IFJ target was based on predefined coordinates (MNI coordinates: x = 48, y = 14, z = 14, Fig. 1C) [38], close to the IFJ location most relevant to working memory and cognitive control shown in a meta-analysis [40]. The left EVC was initially identified anatomically using the Calcarine sulcus and subsequently validated using phosphene mapping. Mean EVC stimulation coordinates were x = −7 (range: −23 to −1), y = −97 (range: −119 to −89), z = −7 (range: −21 to 7) (Fig. 1D). TMS intensity was set to 90 % of each individual's phosphene threshold. Details of TMS settings are reported in the Supplementary Methods.

2.4. Data analysis

Primary VWM performance was assessed using circular standard deviation (CSD) of the response error between reported and actual target orientation. CSD was calculated for each distraction state/time combination for EVC and IFJ stimulation. Percent CSD change (normalized to baseline) indicated the spTMS effect.

To obtain indices of different VWM components-particular memory precision and capacity-we employed a widely used mixture model proposed by Bays and colleagues (https://www.paulbays. com/toolbox/index.php#mixture_methods) (see Supplementary Methods for details) [41,42]. The model incorporates three free parameters: 1) Concentration parameter (kappa) of the von-Mises distributions, convertible to model SD; 2) Probability of random guessing, Pu;

3) Probability of erroneously reporting a non-probed target item, Pn. From these parameters, the probability of accurately remembering the target item (Pt) was calculated as: Pt = 1 – Pu – Pn. The maximum likelihood estimation was used to model the dataset. The "model SD" parameter was utilized as an index representing the precision of memory processing, where a lower SD indicates greater precision/quality in recalling item details. The P_t can be transformed linearly to estimate memory capacity [43].

The statistical analyses mainly employed frequentist methods using IBM SPSS statistics 26. The normality of data was assessed by values of skewness and kurtosis (Table S1) [44,45]. Comparisons between conditions were conducted using repeated-measures ANOVAs. Mauchly's Test of Sphericity was used to test the assumption of sphericity. If sphericity was not assumed, Pillai's Trace correction was used with Multivariate Tests. Frequentist post-hoc analyses were adjusted using the Least Significant Difference (LSD) correction for multiple comparisons.

We also conducted one-sample t-tests for each dependent variable as a sanity check to examine the TMS effects across different brain regions and distraction state relative to a zero effect (i.e., no TMS). We reported Bayes factors (BF_{10}) calculated using JASP [46] as supplement, given its advantage in providing evidence for supporting not only alternative (H_1) but also null (H_0) hypotheses. For Bayesian one-sample t-tests, the default prior 0.707 was utilized, and the hypothesis tested was $\mu \neq 0$.

3. Results

3.1. General effects of spTMS

We firstly performed a three-way repeated-measures ANOVA of CSD

for two TMS sites, two distraction states, and three time points and found a significant main effect of distraction state (F(1,25) = 6.699, p = 0.016, η_p^2 = 0.211, Fig. 2, Table S2), confirming a significantly greater impact of spTMS in the t2d2 condition (post-hoc: p = 0.016, LSD corrected). The interaction of distraction state x time was also significant (F (2,50) = 7.439, p = 0.001, η_p^2 = 0.229). Post-hoc analyses revealed a significantly greater impact of stimulation 800 ms compared to 50 ms within the t2 condition (p = 0.036, LSD corrected). Furthermore, a larger effect was observed at 400 ms relative to 50 ms at t2d2 (p = 0.005, LSD corrected). Significant differences were also found between t2 and t2d2 conditions at 400 ms (p = 0.006, LSD corrected) and at 800 ms (p = 0.004, LSD corrected). No significant effect of stimulation site was revealed (F(1,25) = 0.169, P = 0.684, η_p^2 = 0.007).

To confirm whether spTMS had impacts on EVC and IFJ under various experimental conditions, we then conducted one-sample t-tests of CSDs for each dependent variable (Fig. 2). Significant spTMS effects were found only for the t2d2 condition (Table S3). Specifically EVC stimulation at 400 ms (t(25) = 2.540, p = 0.018, Cohen's d = 0.4981; BF_{10} = 2.933) and 800 ms (t(25) = 3.170, p = 0.004, Cohen's d = 0.6216; BF_{10} = 10.292) significantly increased the CSD, reflecting a decrease in VWM performance. Similarly, TMS over IFJ at 400 ms (t(25) = 3.293, p = 0.003, Cohen's d = 0.6458; BF_{10} = 13.359) and 800 ms (t (25) = 2.126, p = 0.044, Cohen's d = 0.4170; BF_{10} = 1.410) in the t2d2 condition also impacted general performance. Moreover, Bayesian inference provided moderate evidence supporting the null hypothesis (BF_{10}s: 1/3-1/10) that spTMS had no effect in the t2 condition for EVC at all three time points and for IFJ at 50 ms and 400 ms (see Table S3 for details).

3.2. Performance changes characterized by model fitting

The above preliminary analyses supported spTMS impact on VWM performance only when distractors were presented. To gain a deeper understanding of the changes in VWM characteristics, a model fitting analysis was conducted to differentiate various components of VWM. Due to the absence of significant effects of spTMS in the t2 condition, data from this condition were excluded from further statistical analyses. For the remaining data, a 2 (site) x 3 (timepoints) repeated-measures ANOVA was conducted for each parameter of the model separately.

A significant interaction was found for model SD (F(2,50) = 5.390, p = 0.008, η_p^2 = 0.177, Fig. 3A, Table S4). Post-hoc tests showed larger spTMS effects due to EVC stimulation compared to IFJ stimulation at 800 ms (p = 0.005, LSD corrected). Model SD changes were also smaller

after EVC stimulation at 50 ms compared to 400 ms (p = 0.021, LSD corrected) and 800 ms (p = 0.001, LSD corrected), and smaller SD change after IFJ stimulation at 50 ms compared to 400 ms (p = 0.042, LSD corrected). A main effect of time was also significant (F(1,25) = 5.057, p = 0.010, η_p^2 = 0.168), with differences observed between 50 ms and 400 ms (p = 0.002, LSD corrected), and 50 ms and 800 ms (p = 0.014, LSD corrected). Sanity checks conducted with one-sample t-tests corroborated a spTMS effect solely over EVC at 800 ms (t(25) = 2.990, p = 0.006, Cohen's d = 0.5864; BF_{10} = 7.093). Bayesian inference supported the absence of effects in other conditions (BF_{10} < 0.333), with the exception of IFJ at 400 ms (BF_{10} = 0.533), as detailed in Table S5.

For the remaining three model parameters, no interactions or main effects were detected (Fig. 3B–D). Sanity checks using Bayesian one-sample t-tests (Table S5) revealed moderate evidence of spTMS effects over EVC at 800 ms (BF_{10} = 6.058), and over the IFJ at 50 ms (BF_{10} = 4.094) and 800 ms (BF_{10} = 5.122) for Pt. These findings suggest that spTMS may influence the probability of accurately remembering the target, regardless of the stimulation site.

3.3. Ipsilateral EVC versus contralateral EVC

In an exploratory manner, trial data were categorized based on the ipsilateral and contralateral orientation relative to the target location. Given that spTMS was consistently delivered to the left EVC, trials with targets appearing on the left side of the screen were classified as ipsilateral, whereas those with targets on the right side of the screen were designated as contralateral.

The three-way repeated-measures ANOVA of CSD indicated a significant interaction between distraction state and time (Fig. S1, Table S6). Modelling results identified a marginal interaction effect for model SD indicated by specific spTMS at the late retention (Fig. S2, Table S8). Detailed results are shown in Supplementary Results.

4. Discussion

This study was conducted to elucidate the contributions of the early visual cortex (EVC) and the inferior frontal junction (IFJ) to various phases of Visual Working Memory (VWM) in the presence of distractors, employing an orientation delay-recall task. Our findings indicate that single-pulse transcranial magnetic stimulation (spTMS) applied to both the EVC and IFJ influenced VWM performance; however, these effects were particularly pronounced when distractors were introduced when memory load was below the VWM capacity limit. Notably, a behavioral
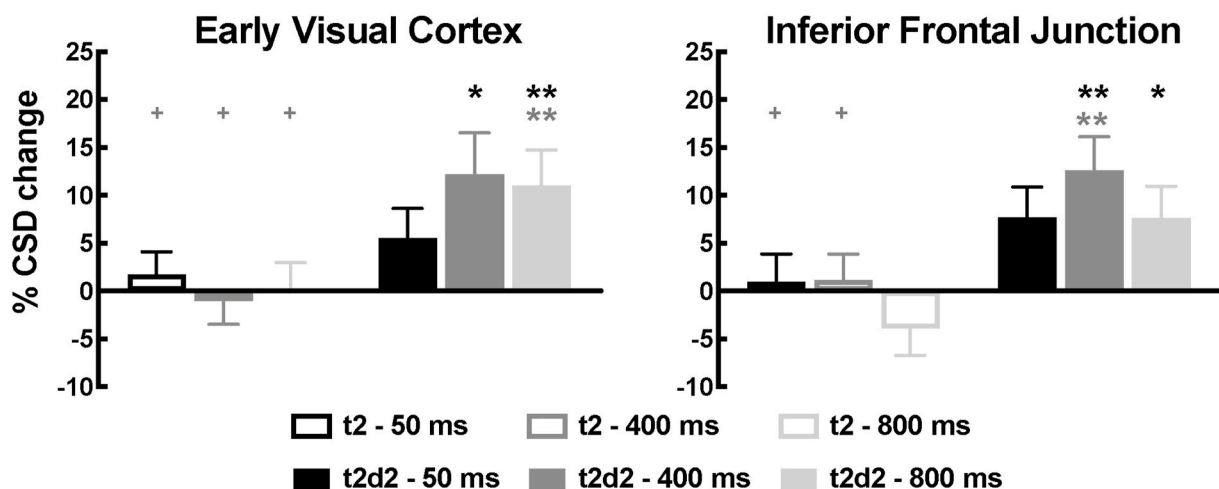

Fig. 2. Circular standard deviation (CSD) results for EVC and IFJ. Outcomes were calculated as the percentage of CSD change against the baseline (no-TMS condition). t2: 2 targets; t2d2: 2 target +2 distractors. Asterisks and crosses indicate the one-sample t-test results. Black asterisks indicate frequentist significance: *p < 0.05, **p < 0.01; Grey asterisks indicate Bayesian inference evidence supporting H1: * moderate evidence (3<BF_{10} < 10), ** strong evidence (10<BF_{10} < 30); Grey crosses indicate Bayesian inference evidence supporting H0: 1/10<BF_{10} < 1/3.
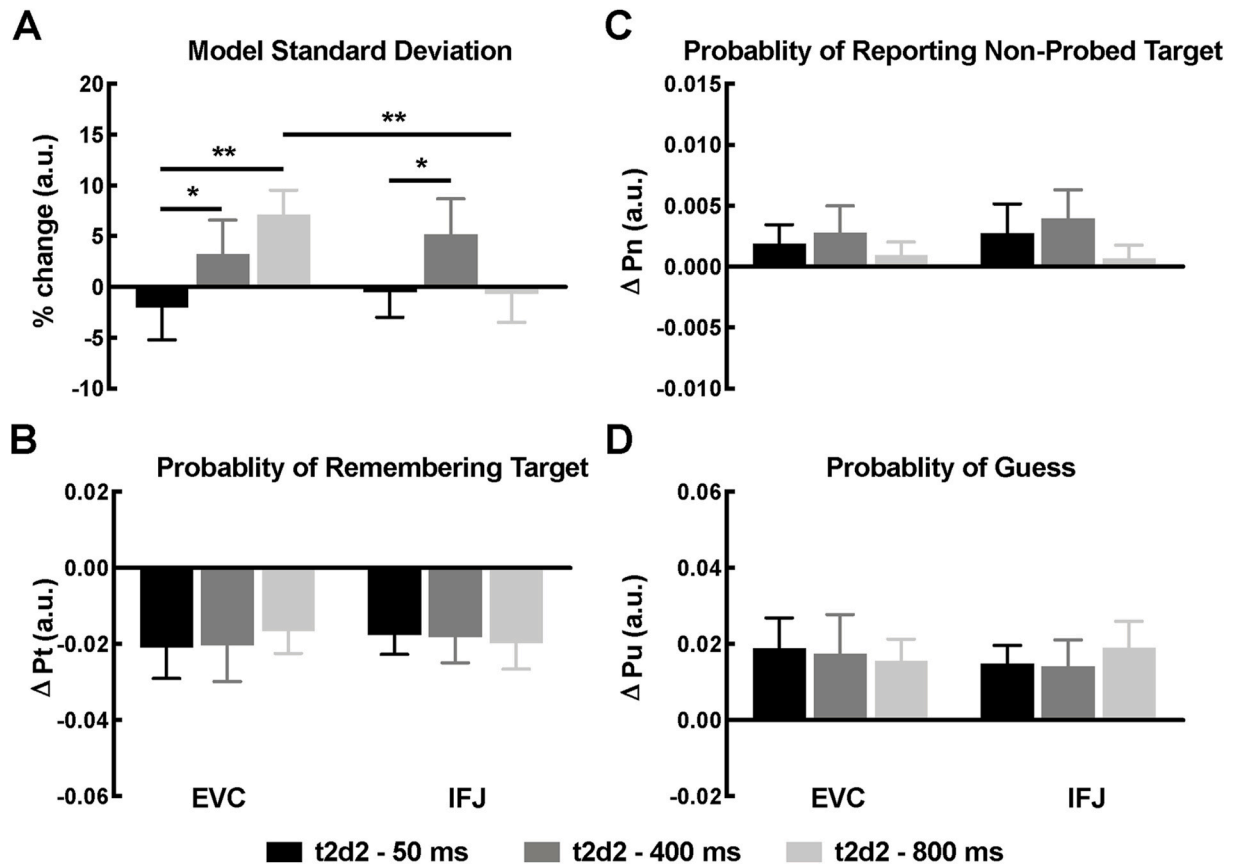
Fig. 3. Mixture model fitting results for EVC and IFJ. A. Percentage changes in model fitted standard deviation (SD) relative to baseline (no-TMS condition). B. Changes in the probabilities of accurately recalling the target item (Pt) against baseline. C. Changes in the probabilities of erroneously reporting the non-probed target item (Pn) against baseline. D. Changes in the probabilities of guessing (Pu) against baseline. Asterisks indicate the significance of repeated-measure ANOVA results: *p < 0.05, **p < 0.01.

model used to deconstruct the components of VWM revealed that the EVC exhibited more significant effects than the IFJ during the late retention phase in terms of precision. Additionally, spTMS applied to both regions appeared to affect VWM capacity. Exploratory analyses of ipsilateral versus contralateral hemisphere stimulation indicated a trend toward a greater impact of spTMS particularly on memory precision component in the ipsilateral EVC compared to the contralateral EVC during late retention. Overall, these results provide critical insights into the dynamic roles of these cortical areas in VWM processing under varied conditions.

Our findings highlight the involvement of both EVC and IFJ in VWM, particularly when distractors are present. Distractor processing requires the ability to selectively attend to relevant visual information while inhibiting the processing of irrelevant stimuli. Studies have indicated that VWM is more susceptible facing high cognitive load, such as scenarios with high memory load and high executive control demands [18, 19], in line with the concept of VWM emphasizing the manipulation of memory information. Early work demonstrated that distractors may also be stored into VWM for some individuals, resembling target representations [47]. Therefore, a key function of VWM is to optimally allocate the limited cognitive resources for improving task performance. It has been widely acknowledged that distraction filtering is govern by the prefrontal regions, while some studies indicate that attention can enhance the discriminability and fidelity of population coding in the visual cortex [31]. Our findings that spTMS effects occurred specifically when distractors are present highlight the role of EVC and IFJ in VWM manipulation rather than pure storage.

The ventrolateral prefrontal regions, including the IFJ, have been implicated in regulating working memory and attention-related

functions [33,48–52]. There is substantial evidence of structural connectivity between the IFJ and ventral visual pathway, which appears to play a pivotal role in non-spatial visual processing, including components of working memory [53,54]. Moreover, the IFJ has been specifically implicated as a critical prefrontal node involved in the top-down modulation of working memory, applicable not only in the visual domain [33,38,55], but also to auditory processing [56,57]. In this study, we provide causal evidence that neuromodulation of IFJ and EVC can impact VWM, emphasizing the integrative role of IFJ and EVC in VWM under conditions of selective attention.

Our results correspond with prior research emphasizing the involvement of the EVC in representing high-fidelity visual information, thereby supporting the "sensory recruitment" hypothesis [58]. While there is substantial support for the sensory account of VWM storage in the literature, there have been contrasting viewpoints suggesting otherwise [for reviews, see [59,60]]. For instance, a well-designed fMRI study demonstrated that during memory retention with visual interference, memory contents could not be decoded from the visual cortex but were decodable from higher-level regions. These findings indicate that sensory recruitment might be dispensable, with greater necessity for top-down modulation from the frontal/parietal storage sites [61]. However, this perspective has been contested by theories proposing that VWM storage can flexibly shift between different memory stores based on task demands [62]. Here, we provide causal evidence that the involvement of the EVC is not only essential but distinctly critical for VWM precision, particularly evidenced by the impact of spTMS on EVC for distractor filtering and its exclusive role in the late retention phase.

Accordingly, we emphasize the importance of timing in VWM processing. Initial visual information may be processed in a feedforward

manner from 40 ms to 70 ms after stimulus onset [63], while the engagement of selective attention may occur between 100 and 200 ms [64]. Considering the acute effect of spTMS (i.e., 5–40 ms) [65], our lack of significant stimulation effects at 50 ms during visual processing corroborates the flexibility of initial VWM storage mechanisms.

Additionally, the specific impact on EVC rather than IFJ during the late retention phase underscores the necessity of sensory recruitment beyond pure top-down modulation in this highly dynamic VWM process. It has been well-established that early and late delay periods in VWM may play distinctive roles, as distractors introduced to these two phases show different influence to VWM performance [59,66]. Evidence suggests that the early delay in VWM may function more to encode and actively maintain the memory information, while the late retention involves more abstract and categorical representations that serve the later retrieval stage [67]. One study has shown that category selectivity cannot be decoded from prefrontal areas during the late delay, whereas posterior regions such as visual areas contain this information [68]. Interestingly, a recent study using a neural generative model has shown that the involvement of visual regions during the late delay period is critical for VWM content representation. This cannot be attributed to sensory processing, indicated by a larger decoding error distribution observed in a passive viewing task compared to a VWM task during the same delay period [69]. In line with previous findings, we speculate that the specific role of EVC on VWM precision during late retention may indicate its function in higher-level content representation relating to retrieval, while both IFJ and EVC are implicated in early VWM maintenance.

In an exploratory manner, we observed a trend where the spTMS effect on memory precision appeared more pronounced in the ipsilateral EVC during late retention. The literature on the lateralization of VWM representations within the EVC presents mixed findings. Some neuro-imaging studies suggest exclusive contralateral representation [70], while others indicate involvement of both hemispheres [23,24,71]. A critical determinant in these discrepancies may be the temporal dynamics. For instance, one study found that early retention is represented bilaterally, whereas late retention predominantly involves the ipsilateral V1 [22]. This is consistent with our finding of a potentially enhanced spTMS effect on ipsilateral V1 during late retention.

Contrasting results from TMS studies also contribute to this debate. A previous study noted that only contralateral spTMS diminished VWM accuracy, however, only valid under relatively high memory load [18]. Recent research has also indicated differential impacts of spTMS on ipsilateral versus contralateral EVC [72], although a study reported no significant effects after controlling for baseline [73]. Given these considerations, the issue of EVC lateralization in VWM remains contentious, emphasizing the need for future research using varied memory loads and refined designs to disentangle lateralization effects across different VWM components.

Worth mentioning, Schurgin et al. introduced a novel computational model that effectively captures most aspects of recall task data with only one free parameter (memory strength d'), which emphasizes the relationship between stimuli and their psychological similarity [74]. Based on this model, small and large response errors arise from a single process, thus do not represent multiple psychological components. Consequently, the significance of delving into aspects such as the guessing rate with TMS might be less substantial. And we indeed observe unrobust TMS effects in terms of the guessing rate. This state-of-art psychophysical model posits significant potential in providing a unifying theory regarding VWM as a continuous processing system, rather than categorizing memory into discrete items. Further investigation of this innovative approach is necessary, incorporating diverse participant populations to validate and extend its applicability.

This study provides valuable insights but is subject to several limitations. A major limitation is the reliance on a "no-TMS" condition instead of employing "sham stimulation". An attempt was made to use a 90° tilted coil for sham during the piloting phase, but participants consistently identified these trials as sham. Alternative approaches such as using vertex stimulation or active control were considered but dismissed, as no brain region is entirely isolated from the interconnected brain network [75,76]. As a compensatory measure in our study, TMS conditions were normalized to the "no-TMS" condition for comparative analyses. Additional potential confounders include blinks, muscle twitching, and trigeminal nerve stimulation, which occurred following IFJ-TMS but not EVC-TMS. As a result of the complex design, the study overlooked several control conditions, notably those involving higher memory loads and stimulation of the right EVC to mitigate lateralization bias. Additionally, increasing the number of trials per condition would strengthen model fitting results.

5. Conclusion

In summary, our study investigated spTMS impact of EVC and IFJ across different phases of VWM, including visual encoding, early retention, and late retention. The findings reveal that spTMS over EVC and IFJ selectively influenced VWM performance with distractor presence. Computational modeling further elucidated the role of EVC in precision representation during the late retention phase. This research supports the "sensory recruitment" theory and provides novel insights into the dynamic interplay between visual and prefrontal cortical areas in the processing of VWM.

Data availability

Data and experimental materials used in this study are available upon request.

CRediT authorship contribution statement

Yi-Jie Zhao: Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Xinying Zhang:** Writing – original draft, Investigation, Formal analysis, Data curation. **Yixuan Ku:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2024.06.001.

References

[1] Cowan N. The magical number 4 in short-term memory: a reconsideration of mental storage capacity. Behav Brain Sci 2001;24:87–114.

[2] Fuster JM, Alexander GE. Neuron activity related to short-term memory. Science (80-) 1971;173:652–4.

[3] Funahashi S, Bruce CJ. Mnemonic coding of visual space in the monkey ' s dorsolateral prefrontal cortex. J Neurophysiol 1989;61:331–49.

[4] Miller EK, Erickson CA, Desimone R. Neural mechanisms of visual working memory in prefrontal cortex of the macaque. J Neurosci 1996;16:5154–67.

[5] D'Esposito M, Postle BR. The cognitive neuroscience of working memory. Annu Rev Psychol 2015;66:115–42.

[6] Ma WJ, Husain M, Bays PM. Changing concepts of working memory. Nat Neurosci 2014;17:347–56.

[7] Postle BR. Working memory as an emergent property of the mind and brain. Neuroscience 2006;139:23–38.

[8] Postle BR. How does the brain keep information "in mind". Curr Dir Psychol Sci 2016;25:151–6.

[9] Ku Y, Bodner M, Zhou Y-D. Prefrontal cortex and sensory cortices during working memory: quantity and quality. Neurosci Bull 2015;31:175–82.

[10] Harrison SA, Tong F. Decoding reveals the contents of visual working memory in early visual areas. Nature 2009;458:632–5.

[11] Serences JT, Ester EF, Vogel EK, Awh E. Stimulus-specific delay activity in human primary visual cortex. Psychol Sci 2009;20:207–14.

[12] Emrich SM, Riggall AC, LaRocque JJ, Postle BR. Distributed patterns of activity in sensory cortex reflect the precision of multiple items maintained in visual short-term memory. J Neurosci 2013;33:6516–23.

[13] Xing Y, Ledgeway T, McGraw PV, Schluppeck D. Decoding working memory of stimulus contrast in early visual cortex. J Neurosci 2013;33:10301–11.

[14] Ester EF, Sprague TC, Serences JT. Parietal and frontal cortex encode stimulus-specific mnemonic representations during visual working memory. Neuron 2015; 87:893–905.

[15] Christophel TB, Klink PC, Spitzer B, Roelfsema PR, Haynes J-D. The distributed nature of working memory. Trends Cognit Sci 2017;21:111–24.

[16] Phylactou P, Traikapi A, Papadatou-Pastou M, Konstantinou N. Sensory recruitment in visual short-term memory. A systematic review and meta-analysis of sensory visual cortex interference using transcranial magnetic stimulation, 29. Springer US; 2022.

[17] Silvanto J, Soto D. Causal evidence for subliminal percept-to-memory interference in early visual cortex. Neuroimage 2012;59:840–5.

[18] van de Ven V, Jacobs C, Sack AT. Topographic contribution of early visual cortex to short-term memory consolidation: a transcranial magnetic stimulation study. J Neurosci 2012;32:4–11.

[19] van Lamsweerde AE, Johnson JS. Assessing the effect of early visual cortex transcranial magnetic stimulation on working memory consolidation. J Cognit Neurosci 2017;29:1226–38.

[20] Zokaei N, Manohar S, Husain M, Feredoes E. Causal evidence for a privileged working memory state in early visual cortex. J Neurosci 2014;34:158–62.

[21] Ester EF, Serences JT, Awh E. Spatially global representations in human primary visual cortex during working memory maintenance. J Neurosci 2009;29:15258–65.

[22] Zhao Y, Kay KN, Tian Y, Ku Y. Sensory recruitment revisited: ipsilateral V1 involved in visual working memory. Cereb Cortex 2022;32:1470–9.

[23] Lorenc ES, Sreenivasan KK, Nee DE, Vandenbroucke ARE, D'Esposito M. Flexible coding of visual working memory representations during distraction. J Neurosci 2018;38:5267–76.

[24] Jia K, Li Y, Gong M, Huang H, Wang Y, Li S. Perceptual learning beyond perception: mnemonic representation in early visual cortex and intraparietal sulcus. J Neurosci 2021;41:4476–86.

[25] Gazzaley A, Nobre AC. Top-down modulation: bridging selective attention and working memory. Trends Cognit Sci 2012;16:129–35.

[26] Vogel EK, Machizawa MG. Neural activity predicts individual differences in visual working memory capacity. Nature 2004;428:748–51.

[27] Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 2002;3:215–29.

[28] Chun MM, Johnson MK. Memory: enduring traces of perceptual and reflective attention. Neuron 2011;72:520–35.

[29] Liesefeld AM, Liesefeld HR, Zimmer HD. Intercommunication between prefrontal and posterior brain regions for protecting visual working memory from distractor interference. Psychol Sci 2014;25:325–33.

[30] Sprague TC, Serences JT. Attention modulates spatial priority maps in the human occipital, parietal and frontal cortices. Nat Neurosci 2013;16:1879–87.

[31] Vo VA, Sprague TC, Serences JT. Spatial tuning shifts increase the discriminability and fidelity of population codes in visual cortex. J Neurosci 2017;37:3386–401.

[32] Zanto TP, Rubens MT, Thangavel A, Gazzaley A. Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. Nat Neurosci 2011;14:656–61.

[33] Zanto TP, Rubens MT, Bollinger J, Gazzaley A. Top-down modulation of visual feature processing: the role of the inferior frontal junction. Neuroimage 2010;53: 736–45.

[34] Zhang W, Luck SJ. Sudden death and gradual decay in visual working memory: research report. Psychol Sci 2009;20:423–8.

[35] Zanto TP, Toy B, Gazzaley A. Delays in neural processing during working memory encoding in normal aging. Neuropsychologia 2010;48:13–25.

[36] Zanto TP, Gazzaley A. Neural suppression of irrelevant information underlies optimal working memory performance. J Neurosci 2009;29:3059–66.

[37] Chadick JZ, Gazzaley A. Differential coupling of visual cortex with default or frontal-parietal network based on goals. Nat Neurosci 2011;14:830–2.

[38] Zhao Y, Kuai S, Zanto TP, Ku Y. Neural correlates underlying the precision of visual working memory. Neuroscience 2020;425:301–11.

[39] Liu J, Zhang H, Yu T, Ni D, Ren L, Yang Q, et al. Stable maintenance of multiple representational formats in human visual short-term memory. Proc Natl Acad Sci U S A 2020;117:32329–39.

[40] Bedini M, Olivetti E, Avesani P, Baldauf D. Accurate localization and coactivation profiles of the frontal eye field and inferior frontal junction: an ALE and MACM fMRI meta-analysis. Brain Struct Funct 2023;228:997–1017.

[41] Bays PM, Catalao RFG, Husain M. The precision of visual working memory is set by allocation of a shared resource. J Vis 2009;9(7):1–11.

[42] Schneegans S, Bays PM. No fixed item limit in visuospatial working memory. Cortex 2016;83:181–93.

[43] Gold JM, Hahn B, Zhang W, Robinson BM, Kappenman ES, Beck VM, et al. Reduced capacity but spared precision and maintenance of working memory representations in schizophrenia. Arch Gen Psychiatr 2010;67:570–7.

[44] George D, Mallery P. IBM SPSS statistics 26 step by step. 16th editi. New York: Routledge; 2019.

[45] Gravetter FJ, Wallnau LB, Forzano L-AB, Witnauer JE. Essentials of statistics for the behavioral sciences (MindTap course list) - softcover. Belmont: Cengage Learning; 2020.

[46] JASP Team. Jasp. Comput Software 2023., Version 0.17.

[47] Vogel EK, McCollough AW, Machizawa MG. Neural measures reveal individual differences in controlling access to working memory. Nature 2005;438:500–3.

[48] Roth JK, Serences JT, Courtney SM. Neural system for controlling the contents of object working memory in humans. Cerebr Cortex 2006;16:1595–603.

[49] Nee DE, Jonides J. Common and distinct neural correlates of perceptual and memorial selection. Neuroimage 2009;45:963–75.

[50] Zhao J, Mo L, Bi R, He Z, Chen Y, Xu F, et al. The VLPFC versus the DLPFC in downregulating social pain using reappraisal and distraction strategies. J Neurosci 2021;41:1331–9.

[51] Soyuhos O, Baldauf D. Functional connectivity fingerprints of the frontal eye field and inferior frontal junction suggest spatial versus nonspatial processing in the prefrontal cortex. Eur J Neurosci 2023;57:1114–40.

[52] Baldauf D, Desimone R. Neural mechanisms of object-based attention. Science (80-) 2014;344:424–7.

[53] Bedini M, Baldauf D. Structure, function and connectivity fingerprints of the frontal eye field versus the inferior frontal junction: a comprehensive comparison. Eur J Neurosci 2021;54:5462–506.

[54] Bedini M, Olivetti E, Avesani P, Baldauf D. The anatomical pathways underlying spatial versus non-spatial attention. Cognit Process 2021;22:35–6.

[55] Higo T, Mars RB, Boorman ED, Buch ER, Rushworth MFS. Distributed and causal influence of frontal operculum in task control. Proc Natl Acad Sci U S A 2011;108: 4230–5.

[56] Vries IEJ De, Marinato G, Baldauf D. Decoding object-based auditory attention from source- reconstructed MEG. Alpha Oscillations 2021;41:8603–17.

[57] Deutsch P, Czoschke S, Fischer C, Kaiser J, Bledowski C. Decoding of working memory contents in auditory cortex is not distractor-resistant. J Neurosci 2023;43: 3284–93.

[58] Scimeca JM, Kiyonaga A, D'Esposito M, D'Esposito M, D'Esposito M. Reaffirming the sensory recruitment account of working memory. Trends Cognit Sci 2018;22: 190–2.

[59] Xu Y. Reevaluating the sensory account of visual working memory storage. Trends Cognit Sci 2017;21:794–815.

[60] Xu Y. Sensory cortex is nonessential in working memory storage. Trends Cognit Sci 2018;22:192–3.

[61] Bettencourt KC, Xu Y. Decoding the content of visual short-term memory under distraction in occipital and parietal areas. Nat Neurosci 2015;19:150–7.

[62] Gayet S, Paffen CLE, Van der Stigchel S. Visual working memory storage recruits sensory processing areas. Trends Cognit Sci 2018;22:189–90.

[63] Lamme VAF, Roelfsema PR. The distinct modes of vision offered by feedforward and recurrent processing. Trends Neurosci 2000;23:571–9.

[64] Gazzaley A. Influence of early attentional modulation on working memory. Neuropsychologia 2011;49:1410–24.

[65] Sliwinska MW, Vitello S, Devlin JT. Transcranial magnetic stimulation for investigating causal brain-behavioral relationships and their time course. J Vis Exp 2014:1–9.

[66] Marini F, Scott J, Aron AR, Ester EF. Task-irrelevant distractors in the delay period interfere selectively with visual short-term memory for spatial locations. Atten Percept Psychophys 2017;79:1384–92.

[67] Treisman AM, Zhang W. Location and binding in visual working memory. Mem Cognit 2006;34:1704–19.

[68] Linden DEJ, Oosterhof NN, Klein C, Downing PE. Mapping brain activation and information during category-specific visual working memory. J Neurophysiol 2012;107:628–39.

[69] Li HH, Sprague TC, Yoo AH, Ma WJ, Curtis CE. Joint representation of working memory and uncertainty in human cortex. Neuron 2021;109:3699–3712.e6.

[70] Pratte MS, Tong F. Spatial specificity of working memory representations in the early visual cortex. J Vis 2014;14:1–12.

[71] Ester EF, Sutterer DW, Serences JT, Awh E. Feature-selective attentional modulations in human frontoparietal cortex. J Neurosci 2016;36:8188–99.

[72] Phylactou P, Shimi A, Konstantinou N. Causal evidence for the role of the sensory visual cortex in visual short-term memory maintenance, 10; 2023.

[73] Grassi PR, Bannert MM, Bartels A. The causal involvement of the visual cortex in visual working memory remains unclear : a comment on Phylactou et al. PsyArXiv Prepr 2023. https://doi.org/10.31234/osf.io/t3z7u.

[74] Schurgin MW, Wixted JT, Brady TF. Psychophysical scaling reveals a unified theory of visual memory strength. Nat Human Behav 2020;4:1156–72.

[75] Dowdle LT, Brown TR, George MS, Hanlon CA. Single pulse TMS to the DLPFC, compared to a matched sham control, induces a direct, causal increase in caudate, cingulate, and thalamic BOLD signal. Brain Stimul 2018;11:789–96.

[76] Jung J, Bungert A, Bowtell R, Jackson SR. Vertex stimulation as a control site for transcranial magnetic stimulation: a concurrent TMS/fMRI study. Brain Stimul 2016;9:58–64.