

Practice-Related Improvement in Working Memory is Modulated by Changes in Processing External Interference

Anne S. Berry,¹ Theodore P. Zanto,¹ Aaron M. Rutman,¹ Wesley C. Clapp,¹ and Adam Gazzaley¹

¹*Departments of Neurology and Physiology, W. M. Keck Foundation Center for Integrative Neuroscience, University of California, San Francisco, California*

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Berry AS, Zanto TP, Rutman AM, Clapp WC, Gazzaley A. Practice-related improvement in working memory is modulated by changes in processing external interference. *J Neurophysiol* 102: 1779–1789, 2009. First published July 8, 2009; doi:10.1152/jn.00179.2009. Working memory (WM) performance is impaired by the presence of external interference. Accordingly, more efficient processing of intervening stimuli with practice may lead to enhanced WM performance. To explore the role of practice on the impact that interference has on WM performance, we studied young adults with electroencephalographic (EEG) recordings as they performed three motion-direction, delayed-recognition tasks. One task was presented without interference, whereas two tasks introduced different types of interference during the interval of memory maintenance: distractors and interruptors. Distractors were to be ignored, whereas interruptors demanded attention based on task instructions for a perceptual discrimination. We show that WM performance was disrupted by both types of interference, but interference-induced disruption abated across a single experimental session through rapid learning. WM accuracy and response time improved in a manner that was correlated with changes in early neural measures of interference processing in visual cortex (i.e., P1 suppression and N1 enhancement). These results suggest practice-related changes in processing interference exert a positive influence on WM performance, highlighting the importance of filtering irrelevant information and the dynamic interactions that exist between neural processes of perception, attention, and WM during learning.

INTRODUCTION

Optimal cognitive performance requires effective top-down control mechanisms to allocate resources toward relevant information but also to direct attention away from intervening information not directly related to one's primary goals. This ability maximizes performance by preventing external interference from overloading a system with limited capacity (Vogel et al. 2005). Such goal-directed processes are believed to be mediated via the prefrontal cortex exerting modulatory influences on neural activity in sensory cortices, selectively enhancing and suppressing activity associated with relevant and irrelevant information, respectively (Desimone and Duncan 1995; Knight et al. 1999). The negative influence of external interference on behavior is clear from findings that working memory (WM) performance is disrupted when intervening stimuli are introduced during the memory maintenance period of a task (Chao and Knight 1998; Clapp et al. 2009; Jha et al. 2004; Postle et al. 2005; Sakai et al. 2002a). Studies have further revealed that successful suppression of interference confers a behavioral benefit on WM performance in young (Clapp et al. 2009; Sreenivasan and Jha 2007; Zanto and Gazzaley 2009)

and older adults (Gazzaley et al. 2005). Indeed, optimal WM performance relies on successful suppression of irrelevant stimuli within 200 ms of stimulus onset as revealed using P1 and N1 event-related potential (ERP) markers of attentional modulation (Clapp et al. 2009; Gazzaley et al. 2008; Zanto and Gazzaley 2009). It has also been shown that training can induce plasticity in visual cortex based on immediate behavioral requirements (Crist et al. 2001). We hypothesize that sensory processing of external interference is plastic in young adults, such that it is modifiable with practice. Thus we expect that the impact of interfering information on WM performance will scale with practice-related changes in neural activity associated with processing interference.

While it is established that WM performance can improve with practice, most studies attribute improvements to enhanced processing of relevant information, such as encoded cue and tested probe stimuli (Landau et al. 2004; McEvoy et al. 1998). In terms of mechanism, practice-related improvement in WM has been associated with increased neural efficiency as reflected by reduced activity in task-relevant areas (Garavan et al. 2000; Gevins et al. 1997; Jansma et al. 2001; Landau et al. 2004; McEvoy et al. 1998). However, our understanding of the neural basis of changes in interference processing with practice and its influence on behavioral performance is limited. Functional MRI results have revealed that practice on the Stroop task leads to diminished activation in visual cortical regions associated with the representation of task irrelevant information (Milham et al. 2003). Behavioral studies report an influence on perception of more efficient suppression of interfering visual stimuli with practice as measured via diminution of the motion aftereffect (Vidnyanzky and Sohn 2005) and decreased dominance of interfering information in a binocular rivalry paradigm (Paffen et al. 2008). Yet it has not been established if and how practice-induced changes in processing external interference influence WM.

The current study explored two distinct forms of interference, i.e., *distraction* (stimuli to-be-ignored) and *interruption* (stimuli requiring attention). Distraction involves encountered stimuli that are irrelevant and should be ignored (e.g., radio playing while attempting to rehearse a phone number). This filtering of irrelevant sensory input is thought to be dependent on top-down suppression (Duncan et al. 1997). Interruption by external interference involves intervening stimuli that are purposefully attended to as an aspect of a secondary task (e.g., answering phone call while holding something in mind). An interruption requires a reallocation of cognitive resources, as well as processes involved in reactivating the disrupted representation afterward. (Sakai et al. 2002b).

Address for reprint requests and other correspondence: A. Gazzaley, University of California, San Francisco, 600 16th St., Genentech Hall, MC2240 Rm. N472J, San Francisco, CA 94158 (Email: adam.gazzaley@ucsf.edu).

The goal of the study was to assess the relationship between practice-mediated changes in WM performance and changes in neural activity associated with relevant information to be maintained in WM and with interruptors and distractors that interfere with WM. We evaluated practice effects in three WM tasks by comparing across two blocks (i.e., blocks 1 and 2) within a single experimental session while neural activity was recorded with 64-channel electroencephalography (EEG). The WM tasks involved a delayed-recognition paradigm in which participants were instructed to maintain in mind the direction of motion of a field of dots across a delay interval (Fig. 1). One of the tasks involved no interference (NI), whereas the other two tasks included motion interference that consisted of a field of rotating dots presented in the middle of the delay period. These intervening stimuli were either to-be-ignored distractors (distracting stimulus: DS) or interruptors that required a simple perceptual discrimination (interrupting stimulus: IS). A passive viewing task using the same temporal design served as a baseline (B) from which to measure enhancement of neural processing of encoded and interruptor stimuli and the suppression of distractors. Neural measures from posterior electrodes were evaluated to examine practice-related changes in early visual cortical activity (i.e., P1 and N1 amplitudes).

METHODS

Participants

Twenty participants [24.2 ± 0.49 (SE) yr; 9 females] gave consent to participate in the study. All volunteers had normal or corrected-to-normal vision, and none used any medication known to affect cognition. Participants were paid for their participation and gave informed consent in accordance with the guidelines set by the Committee on Human Research at the University of California, San Francisco.

Stimuli

The stimuli consisted of a circular aperture containing 290 dots ($0.08 \times 0.08^\circ$ each) that subtended 8° of visual angle at a 75-cm viewing distance and were centered at the fovea. This field of 290 spatially random gray scale dots moved with 100% coherence at an oblique angle at $10^\circ/s$. Stimuli were presented with a gray fixation cross in the center of the circular aperture with a black background of luminance level 0.32 cd/m^2 . All four sectors of the aperture were used (i.e., northeast, northwest, southeast, southwest) except the cardinal directions (up, down, left, right) (Appelle 1972). The experimental stimuli consisted of 12 different directions of motion (3 per sector). Stimuli were presented through E-Prime software (Psychology Software Tools) run on a Dell Optiplex GX620 and a ViewSonic G220fb CRT monitor.

Thresholding

Participants completed a motion thresholding test prior to the onset of the main experiment to minimize the effects of individual differences in discriminability. A staircase procedure (2° increments) required participants to determine whether two motion stimuli were moving in the same direction. The two 100% coherent motion stimuli were presented for 800 ms each and separated by 2,000 ms. An angle of discrimination (the difference between 2 directions of motion) was selected for each participant as the largest angle at which discrimination performance was $<100\%$. During the experiment, one sector for motion direction was randomly selected per trial. Trials in which the probe did not match the cue utilized two directions of motion within that sector, separated by the participant's angle of discrimination. For

example, if the angle of discrimination were 20° , two possible directions of motion in that sector might be: 30° and 50° .

Experimental procedure

To optimize learning during EEG recordings, participants received minimal practice prior to the onset of the experiment and were given performance feedback on each trial (Herzog and Fahle 1997; Shiu and Pashler 1992). Participants were presented with four different tasks randomized across eight blocks, with two blocks per task (Fig. 1). There were three WM tasks: IS, DS, and NI. A fourth baseline (B) task instructed participants to passively view the stimuli. For the NI task, a 100% coherent motion cue was presented (800 ms), followed by a delay period (7 s) in which participants were instructed to mentally rehearse the encoded motion cue, and the trial concluded with the presentation of a probe motion stimulus (800 ms). Participants were instructed to make a match/nonmatch button press response as quickly and accurately as possible. For the two interference tasks, DS and IS, a counter-clockwise circular motion stimulus was inserted in the middle (400-ms jitter) of the delay period. In the DS task, participants were instructed to ignore the distracting motion stimulus. In the IS task, participants were asked to attend to the interruptor and judge whether the swirl was fast or slow. A button press response was required if the interrupting motion was fast, but no response was required if the interrupting motion was slow. For the IS task, there were 10% imperative trials where the interfering motion stimulus was fast; these trials were eliminated from analysis. In the B task, participants were instructed not to remember either stimulus but to merely view them. At the probe, participants saw an arrow and made a button press indicating the direction (left or right). Responses were recorded $\leq 4,000$ ms after stimulus onset. For all WM tasks, 50% of the probe stimuli matched the previously presented cue stimulus, whereas the other 50% did not. A recent study using this paradigm with complex stimuli (faces and scenes) as opposed to motion stimuli was performed while EEG and fMRI was recorded (Clapp et al. 2009).

Participants were instructed to respond as quickly as possible without sacrificing accuracy during all tasks. Each task was performed two times, blocks 1 and 2, with 40 trials in each block (44 in the IS task). Prior to the start of the experiment, participants were shown 20 examples of fast and slow interruptor swirls used in the IS task. The experiment took 1 h 15 min to complete with ~ 40 min separating blocks of the same task.

Data acquisition

Participants sat in an armchair in a dark, sound-attenuated room and were monitored by camera during all tasks. Data were recorded during eight blocks lasting ~ 8 min each and a total of 80 trials per task. Electrophysiological signals were recorded with an ActiveTwo BioSemi 64-channel Ag-AgCl active electrode EEG acquisition system in conjunction with ActiView software (BioSemi). Signals were amplified and digitized at 1,024 Hz with a 24-bit resolution. All electrode offsets were between ± 20 mV. Anti-aliasing filters were used during data acquisition, and the data were referenced to the average off-line. Precise markers of stimulus presentation were acquired using a photodiode.

Data analysis

EEG preprocessing: Eye movement artifacts were removed using Brain Vision Analyzer (Brain Products GmbH) through an independent component analysis (ICA). Only ICA components consistent with topographies for eye blinks and horizontal eye movement were removed. Additionally, individual trials containing artifacts with a voltage threshold of $\pm 50 \mu\text{V}$ were removed. Using this artifact rejection protocol, fewer than eight trials were rejected per block. Data were band-pass filtered between 1 and 30 Hz. Recordings from

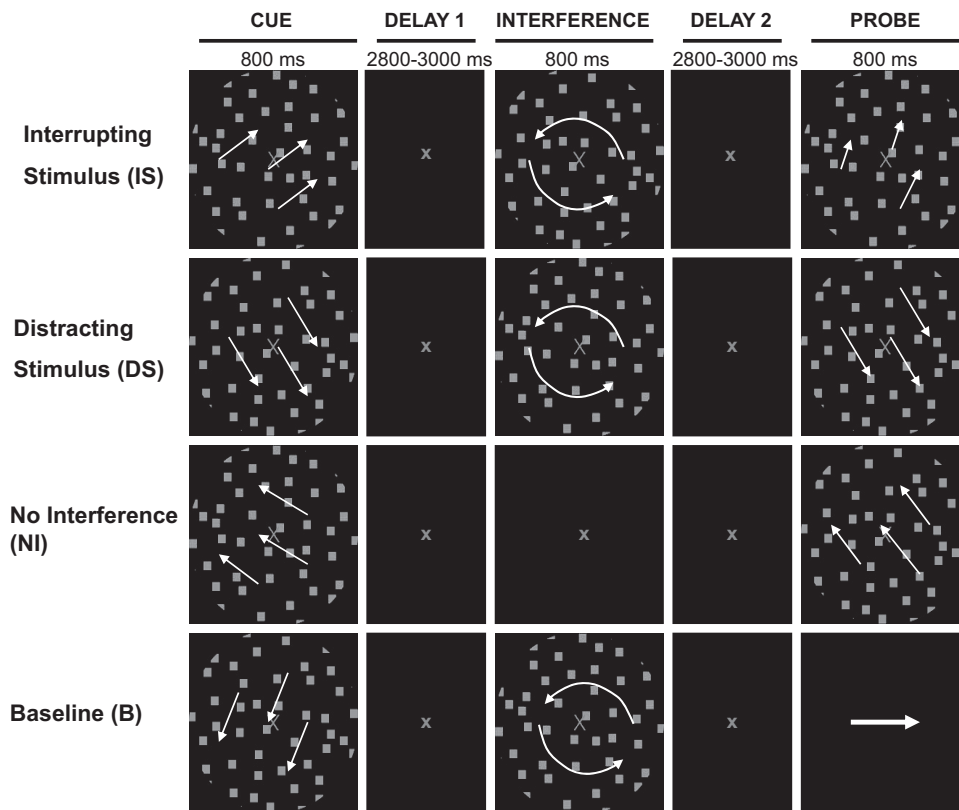


FIG. 1. Experimental paradigm. Four tasks were presented in a delayed-recognition design using coherent motion stimuli. There were 3 working memory (WM) tasks for motion direction: interrupting stimulus (IS), distracting stimulus (DS) and no interference (NI). A 4th task to establish baseline measures instructed participants to passively view the stimuli (B). For all WM tasks, a cue was presented (800 ms), which participants were instructed to encode and rehearse until the presentation of the probe motion stimulus (800 ms). At the probe, participants made a match/nonmatch button press response as quickly and accurately as possible. In the 2 interference tasks, counter-clockwise circular motion was inserted in the middle of the delay period. In the IS task, participants made a speed discrimination judgment of the interruptor. A button-press response was required if the interruptor motion was fast, but no response was required if the interruptor motion was slow. In the DS task, participants were instructed to ignore the distracting motion stimulus. For the baseline task, participants responded to the direction of an arrow, left or right. Responses were required for probe stimuli and for 10% of IS intervening stimuli. Thin arrows indicate motion and were not present in the experiment.

eye electrodes were assessed to ensure participants did not avert their gaze during the interference period. Electrodes placed at the outer canthi of both eyes (REOG, LEOG), inferior and superior to the right eye (IEOG, Fp2) were referenced to the left mastoid and averaged without undergoing artifact rejection.

EEG analysis

A 200-ms prestimulus baseline was subtracted from each trial prior to calculating the evoked-response potential (ERP). Trials were averaged into task and block-specific grand average ERPs for each participant. ERP peaks were obtained from posterior scalp sites over preselected latency ranges (P1 range: 60–140 ms; N1 range: 120–220 ms). ERP statistical analysis used an electrode of interest (EOI) method (Bach and Hoffmann 2000; Gazzaley et al. 2008; Heinrich et al. 2004, 2005; Hoffmann et al. 1999, 2001; Maurer and Bach 2003; Mercier et al. 2009; Rutman et al. 2009). A unique electrode was selected for each participant for use in group-level statistical analysis. EOIs were defined for each participant as the posterior electrode whose grand average of all tasks averaged together (IS, DS, NI, and B) had the largest ERP peak amplitude. This method is designed to identify the electrode most sensitive to the neural responses associated with the task stimuli. EOIs for interfering stimuli were selected independently from cue and probe EOIs. Separate EOIs were selected for P1 and N1 peaks. EOIs were selected from the following posterior electrodes: P9, P7, P5, P6, P8, P10, PO7, PO3, POz, PO4, PO8, O1, Oz, O2, Iz.

To measure relative attentional enhancement and suppression of cue, interfering, and probe stimuli due to the WM tasks, P1 and N1 waveforms for passively viewed stimuli (B) were used as baselines. Peak amplitudes greater than B were defined as enhancement, whereas peak amplitudes smaller than B were defined as suppression. ERP statistical analysis was performed using 4×2 ANOVA (4 task \times 2 block) for the cue period and 3×2 ANOVA (3 task \times 2 block) for the interference and probe periods, and the Greenhouse-Geisser cor-

rection was applied when sphericity was violated. Post hoc paired *t*-tests were performed to probe main effects and interactions and corrected for multiple comparisons through the false discovery rate (FDR) (Benjamini 1995).

Behavioral analysis

Behavioral data were analyzed using 3×2 ANOVA (3 task \times 2 block) and the Greenhouse-Geisser correction was applied when sphericity was violated. χ^2 test was used to confirm parametric distribution. Post hoc paired *t*-tests were used to probe significant main effects of task, practice, and task by practice interactions and were FDR corrected. Response time (RT) outliers (± 2 SD from the group mean) were removed from analysis.

Neural-behavioral correlations

Neural-behavioral correlations were used to evaluate the impact of cue, interfering, and probe stimuli processing on WM performance. Additionally, neural-behavioral correlations were used to probe the impact of practice-related changes in cue, probe and interference processing with WM performance. Correlations were two-tailed Pearson's or Spearman's (accuracy data) correlations and corrected for multiple comparisons through FDR. Correlation analyses relied on neural indices of enhancement and suppression indexed to passive baseline values to minimize individual differences in overall signal magnitude. Similarly, RTs from the passive baseline task were subtracted from RTs from the WM tasks to account for individual differences in motor speed. These motoric speed-corrected RTs are referred to as the "RT index."

RESULTS

Behavioral data

Angles of discrimination ranged from 9 to 29° across participants (mean $20.25 \pm 1.43^\circ$). WM accuracy and RT data

were subjected to separate two-way ANOVA with factors of task (IS vs. DS vs. NI) and practice (block 1 vs. block 2). Accuracy analyses revealed a main effect of task [$F(2,38) = 7.36$; $P < 0.01$], a main effect of practice [$F(1,38) = 9.62$; $P < 0.01$], and a significant interaction between task and practice [$F(2,38) = 3.51$; $P < 0.05$]. Post hoc paired *t*-test analyses revealed subtle, but significant, differences in accuracy between all tasks ($P < 0.05$ for all comparisons), such that participants were most accurate when no interference was present (NI = 89.3 ± 1.89%), exhibited disrupted WM accuracy with the introduction of a distractor (DS = 87.5 ± 1.75%), and further disruption during interruption which required discrimination (IS = 85.2 ± 1.90%). Interestingly, these significant differences between tasks were driven by performance on the first block (NI > IS, $P < 0.001$; NI > DS, $P < 0.01$; DS > IS, $P < 0.05$), as performance between tasks for block 2 were not significantly different (NI > IS, $P = 0.39$; NI > DS, $P = 0.89$; DS > IS, $P = 0.44$). Collapsed across tasks, accuracy was higher on the second block compared with the first block, revealing a significant practice effect; further post hoc analyses revealed this effect was generated only by tasks in which interference was present (block 1 vs. 2: IS, $P < 0.01$; DS, $P < 0.05$; NI, $P = 0.91$, FDR corrected). Mean improvement for IS was greater than that for DS, but was not significant (Fig. 2A; $P = 0.24$).

RT analysis using the same ANOVA revealed a main effect of task [$F(2,38) = 3.55$; $P < 0.05$], a main effect of practice [$F(1,38) = 30.62$; $P < 0.001$] and no task by practice interaction [$F(2,38) = 1.28$; $P = 0.289$]. Post hoc paired *t*-test analyses revealed RT was faster for DS relative to IS ($P < 0.05$, FDR corrected), and significantly faster in block 2 versus block 1 for both IS ($P < 0.01$, FDR corrected) and DS ($P < 0.01$, FDR corrected) but not NI ($P > 0.05$, FDR corrected). This result is consistent with practice-related improvement in accuracy during tasks with interference (Fig. 2B).

Posterior electrode EEG data

P1 and N1 amplitude are modulated by attention (Hillyard and Anllo-Vento 1998) and are localized to visual areas in lateral extrastriate cortex (Di Russo et al. 2002; Gomez Gonzalez et al. 1994). These neural markers were selected to evaluate activity modulation in the different tasks, the relationship between activity and performance and changes with practice. Analyses focused on waveforms time-locked to cue, interfering, and probe stimuli.

CUE STIMULI. P1 and N1 peak amplitude measures from posterior EOIs time-locked to the onset of the cue stimuli were submitted to separate repeated-measures ANOVA with factors of task (IS vs. DS vs. NI vs. B) and practice (block 1 vs. block 2). Analysis for P1 amplitude revealed a main effect of task [$F(3,57) = 3.96$; $P < 0.05$], no effect of practice [$F(1,57) = 0.00$; $P = 0.975$], and no task by practice interaction [$F(3,57) = 0.23$; $P = 0.874$]. Mean amplitudes and SE for block 1 tasks were IS: 6.48 ± 0.89 μV, DS: 6.25 ± 0.96 μV, NI: 6.63 ± 0.91 μV, B: 5.70 ± 0.97 μV and block 2 tasks were IS: 6.43 ± 0.75 μV, DS: 6.49 ± 0.92 μV, NI: 6.75 ± 0.83 μV, B: 5.37 ± 0.91 μV. Post hoc paired *t*-test revealed P1 amplitudes from IS, DS, and NI cue stimuli were significantly greater than baseline cue stimuli ($P < 0.05$, FDR corrected) but were not significantly different from each other. Analyses for N1 amplitude revealed no effect of task [$F(3,57) = 2.46$; $P = 0.072$] or practice [$F(1,57) = 0.700$; $P = 0.407$] and no task by practice interaction [$F(3,57) = 0.95$; $P = 0.423$]. Mean amplitudes and SE for block 1 tasks were IS: -8.88 ± 0.76 μV, DS: -7.80 ± 0.71 μV, NI: -8.39 ± 0.78 μV, B: -8.27 ± 0.70 μV and block 2 tasks were IS: -8.50 ± 0.73 μV, DS: -8.18 ± 0.71 μV, NI: -8.25 ± 0.90 μV, B: -7.68 ± 0.83 μV. Although there was not a main effect of task, paired *t*-test revealed N1 amplitudes from IS and NI cue stimuli were significantly greater than baseline cue stimuli ($P < 0.05$).

Regression analysis was performed to evaluate if individual differences in P1 and N1 measures for cue stimuli were associated with WM performance. There were no significant correlations between P1 or N1 enhancement of the cue stimuli (indexed to baseline stimuli: IS-B; DS-B; NI-B) and WM performance measures of accuracy or RT index (IS-B; DS-B; NI-B; all P1 correlations *r* range: 0.06–0.28, *P* range: 0.31–0.83; all N1 correlations *r* range: 0.04–0.24, *P* range: 0.38–0.88). Additionally, there were no practice-related correlations, such that changes in enhancement from block 1 to block 2 did not correlate with changes in WM performance (all P1 correlations *r* range: 0.02–0.26, *P* range: 0.35–0.94; all N1 correlations *r* range: 0.01–0.29, *P* range: 0.29–0.96).

INTERFERING STIMULI. P1 amplitude data from posterior EOIs were submitted to an ANOVA for the interfering stimuli to reveal a significant effect of task [$F(2,38) = 4.26$; $P < 0.05$], no main effect of practice [$F(1,38) = 0.33$; $P = 0.570$] and no task by practice interaction [$F(2,38) = 2.00$; $P = 0.151$]. Mean amplitudes and SE for block 1 tasks were IS: 7.53 ± 0.88 μV, DS: 7.11 ± 0.91 μV, B: 7.58 ± 1.09 μV and for block 2 tasks

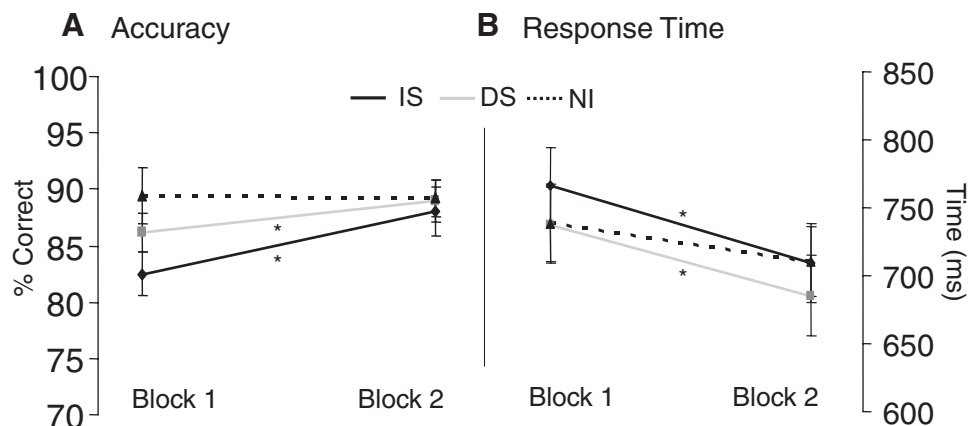


FIG. 2. Behavioral results. A: WM accuracy with practice. Accuracy performance increased for both IS and DS interference tasks from block 1 to block 2 but did not change in the NI task. B: WM response time with practice. Response times (RTs) decreased for both interference tasks (IS and DS) from block 1 to block 2 but did not change in the NI task. Error bars represent SE. *, significant differences associated with practice [$P < 0.05$, false discovery rate (FDR) corrected].

were IS: $7.81 \pm 0.94 \mu\text{V}$, DS: $6.30 \pm 0.93 \mu\text{V}$, B: $7.68 \pm 0.85 \mu\text{V}$. Post hoc evaluation of task effects revealed a significant difference in P1 amplitude to interfering stimuli between IS and DS (IS > DS; $P < 0.01$, FDR corrected), significant suppression of P1 amplitude for DS distractors below passive viewing baseline (suppression index = B-DS; B > DS; $P < 0.05$, FDR corrected), and no significant enhancement for IS interruptors above baseline (enhancement index = IS-B; Fig. 3; IS vs. B; $P > 0.05$, FDR corrected).

Significant suppression of P1 amplitude was identified for ignored distractors in agreement with previous reports of selective P1 amplitude suppression for irrelevant information relative to baseline (Luck and Hillyard 1995; Luck et al. 1994). Therefore regression analysis was performed to evaluate if individual differences in distractor P1 suppression were associated with differences in WM measures of accuracy and RT. Suppression indices were significantly and negatively correlated with the RT index (Fig. 4A; $r = -0.478$, $P < 0.05$, FDR corrected) but not with accuracy ($r = 0.277$, $P > 0.05$, FDR corrected). Namely, participants who demonstrated the greatest neural suppression of the P1 amplitude exhibited the fastest WM response times.

Given the correlation between the suppression and RT indices, an additional regression analysis was performed to determine if changes in suppression across blocks correlated with practice-related improvements in RT. Figure 4B shows that improved distractor suppression with practice correlated with a decrease in RT between blocks 1 and 2 ($r = -0.544$, $P < 0.05$). Thus those participants who exhibited the greatest increases in suppression of distractors in the DS task with practice showed the greatest behavioral gains.

Repeated-measures ANOVA for N1 amplitude showed a significant effect of task [$F(2,38) = 6.42$; $P < 0.01$], no

main effect of practice [$F(1,38) = 3.36$; $P = 0.075$] and no interaction [$F(2,38) = 0.34$; $P = 0.7113$]. Mean amplitudes and SE for block 1 tasks were IS: $-9.83 \pm 0.71 \mu\text{V}$, DS: $-9.07 \pm 0.67 \mu\text{V}$, B: $-9.11 \pm 0.77 \mu\text{V}$ and block 2 tasks were IS: $-9.58 \pm 0.57 \mu\text{V}$, DS: $-8.76 \pm 0.68 \mu\text{V}$, B: $-8.43 \pm 0.64 \mu\text{V}$. Post hoc t -test showed there was a significant difference between DS and IS (IS > DS*; $P < 0.01$, FDR corrected), significant enhancement relative to baseline (IS > B*; $P < 0.05$, FDR corrected), but no significant suppression (B vs. DS; $P > 0.05$; Fig. 5). [*Note: greater is more negative for the N1.]

Significant enhancement of N1 amplitude was identified for interruptors in which a perceptual discrimination was required (IS) similar to previous studies reporting selective N1 amplitude enhancement for relevant stimuli relative to baseline (Luck and Hillyard 1995; Luck et al. 1994). Therefore further analysis evaluated if individual differences in interruptor enhancement were associated with differences in WM performance. Individual enhancement indices of N1 amplitude (enhancement index = IS-B) significantly correlated with WM accuracy (Fig. 6A; $r = 0.625$, $P < 0.005$, FDR corrected) but not RT ($r = 0.336$, $P > 0.05$, FDR corrected), such that those participants who showed the greatest enhancement for the interruptor (i.e., more negative enhancement index of N1 amplitude – negative x axis) were the least accurate in WM recognition after the delay period. These results suggest that the more processing of the interrupting stimulus during the discrimination task, the lower the WM performance.

Given the correlation between the enhancement index and accuracy, an additional regression analysis was performed to determine if changes in enhancement across blocks correlated with improvements in accuracy across blocks. Anal-

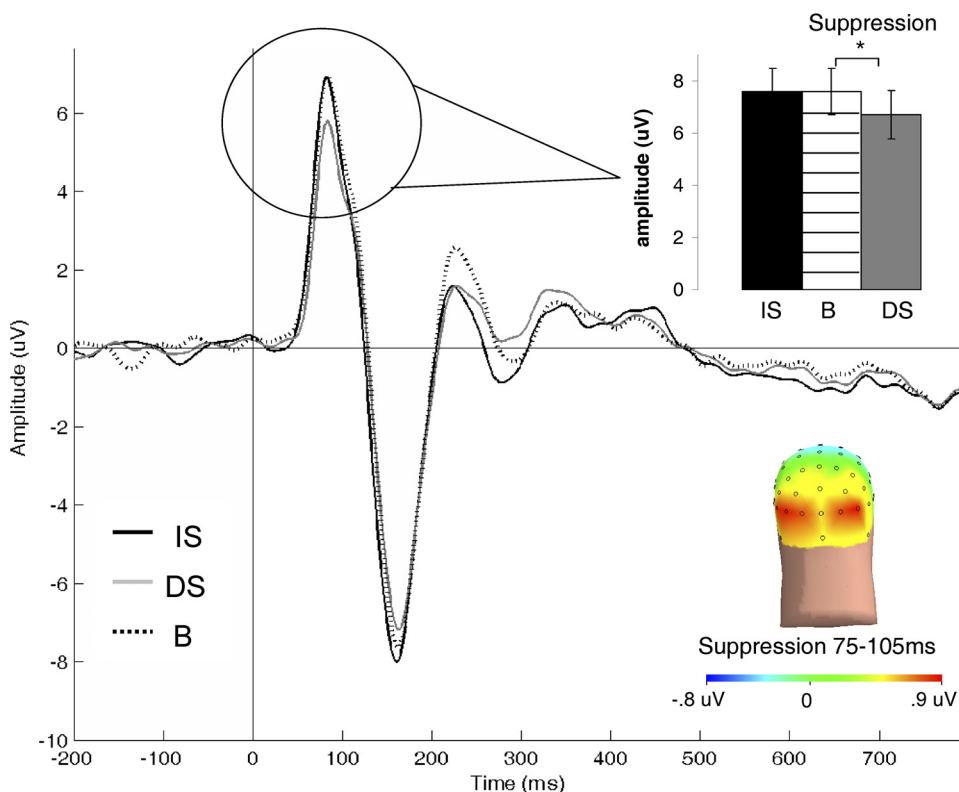


FIG. 3. Modulation of the P1 component during the interference period. Grand average waveforms (block 1 and block 2 combined) of P1 posterior electrode of interest (EOIs, $n = 20$) during the interference period showed significant differences across tasks. P1 peak amplitudes for IS interruptors were greater than peak amplitudes for DS distractors, but not baseline stimuli. DS peak amplitudes were significantly smaller than baseline peak amplitudes [B > DS: P1 suppression]. The topographic ERP difference map shows suppression (B-DS) during the P1 time frame of 75–105 ms (peak latency mean for DS and B ± 1 SD) based on the grand average across all participants and electrodes. Of the posterior electrodes, the following electrodes were identified as participants' P1 intervening stimuli EOIs: Iz, O1, O2, P8, P9, P10, PO3, PO4, PO7, PO8. This grand average was created using the unique EOIs for each participant. Positive amplitudes are plotted as up going. Error bars represent SE. *, significant differences ($P < 0.05$, FDR corrected).

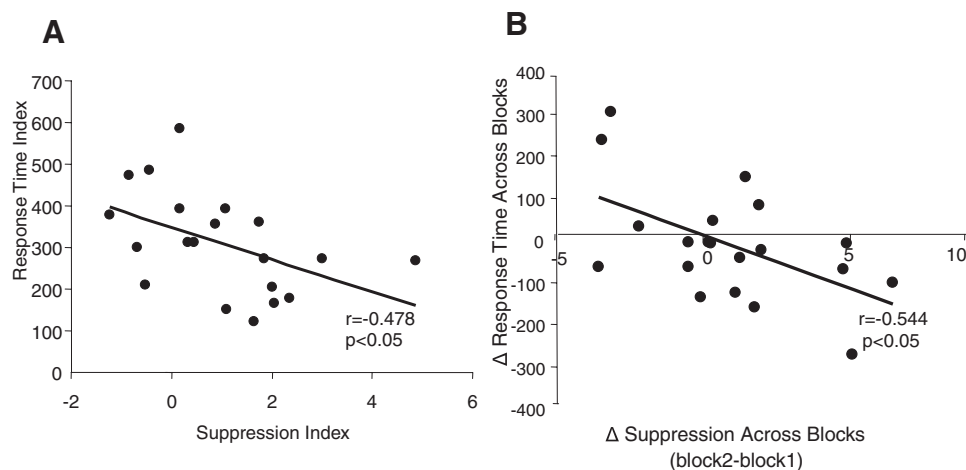


FIG. 4. Neural-behavioral correlation for the DS task: P1 suppression index vs. RT index. *A*: suppression index predicted WM response time. The index of P1 peak amplitude suppression (B-DS) correlated with baseline-corrected WM RT measures for the distractor stimulus task (RT index: DS-B; $r = -0.478$, $P < 0.05$, FDR corrected). Participants showing greatest suppression of the distractor had fastest WM RT. This correlation reflects overall performance combined for block 1 and block 2. *B*: improved suppression of the distractor predicted improved WM response time with practice. Individual changes in P1 peak amplitude suppression (B-DS) for block 2 - block1, correlated with individual DS RT improvement for block 2 - block 1 ($r = -0.544$; $P < 0.05$). Participants who improved in their ability to suppress the distractor showed the most improved WM RT.

ysis revealed decreased enhancement correlated with improved IS accuracy from block 1 to block 2 ($r = 0.544$, $P < 0.05$, FDR corrected) such that those participants who most diminished their processing allocation to the interruptor in the IS task with practice (i.e., a more positive difference in enhancement across blocks), showed the greatest WM accuracy improvement (Fig. 6*B*).

P1 and N1 ERP data for the interference period were reanalyzed using a cluster approach: data from each EOI were averaged with the three to four electrodes surrounding it.

Analysis revealed comparable results to the single EOI method. Specifically, P1 peak amplitude analysis resulted in a significant main effect of task, no effect of practice, and no task by practice interaction (same as for the single EOI). Post hoc assessment of the main effect of task was also consistent with the single EOI method. Similarly, N1 amplitude results demonstrated a main effect of task, no effect of practice, and no task by practice interaction, which were consistent with the single EOI method as were post hoc assessments of the main effect of task. All statistical linear-

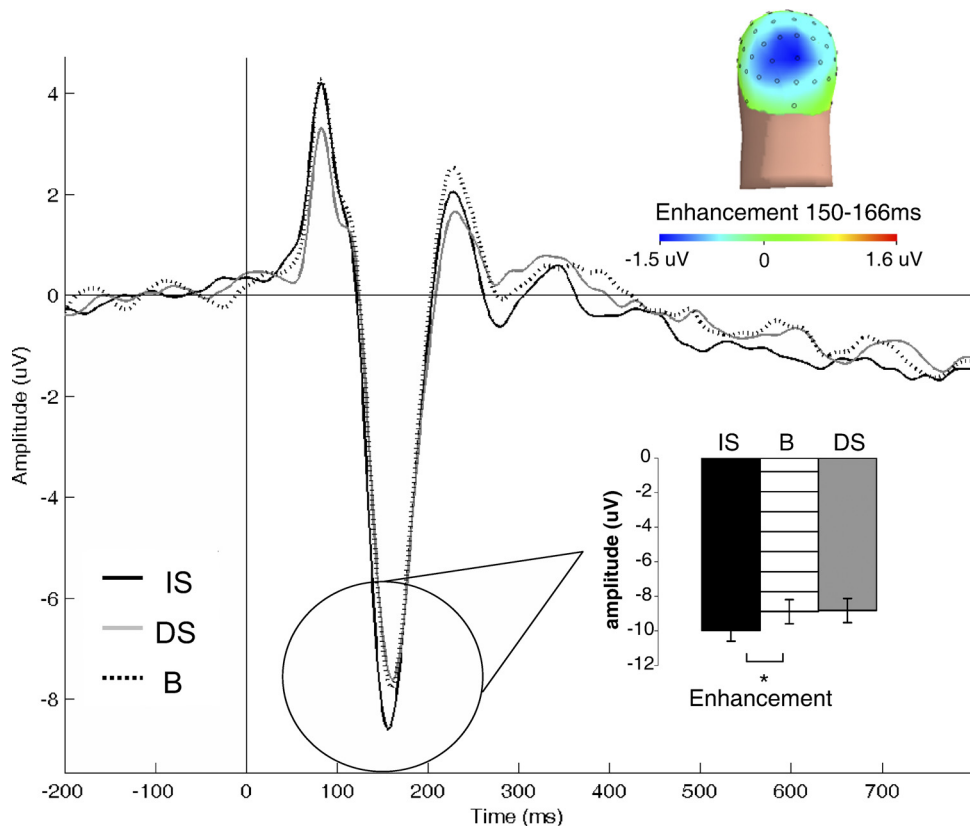


FIG. 5. Modulation of the N1 component during the interference period. Grand average waveforms (blocks 1 and 2 combined) of N1 posterior EOIs ($n = 20$) during the interference period showed significant differences across tasks. N1 peak amplitudes for IS interruptors were greater (more negative) than peak amplitudes for DS distractors and baseline stimuli (IS > B: N1 enhancement). DS peak amplitudes were not significantly different from baseline amplitudes. The topographic ERP difference map shows enhancement (IS-B) during the N1 time frame of 150–166 ms (peak latency mean for IS and B ± 1 SD) based on the grand average across all participants and electrodes. Of the posterior electrodes, the following electrodes were identified as participants' N1 interference period EOIs: O2, P7, P8, P10, PO7, PO8. This grand average was created using the unique EOI for each participant. Positive amplitudes are plotted as up going. Error bars represent SE. *, significant differences ($P < 0.05$, FDR corrected).

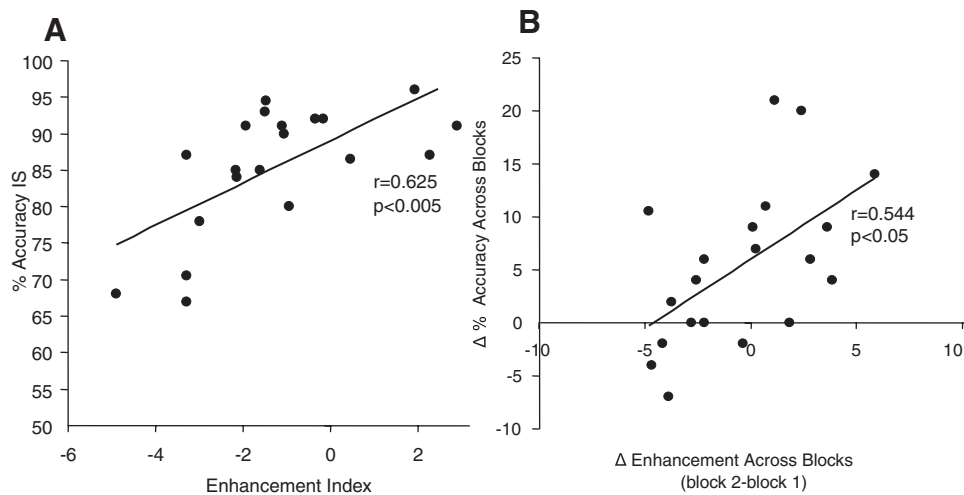


FIG. 6. Neural-behavioral correlation for the IS task: N1 enhancement index vs. IS accuracy. *A*: enhancement index predicted WM accuracy. The index of N1 peak amplitude enhancement (IS-B) correlated with WM accuracy for the IS task ($r = 0.625$; $P < 0.005$, FDR corrected). Participants who did not enhance or only modestly enhanced processing (positive enhancement indices, positive x axis) of the interruptor showed the greatest WM accuracy. This correlation reflects overall performance combined for blocks 1 and 2. *B*: decreased enhancement predicts improved WM accuracy with practice. Decreases in N1 peak amplitude enhancement (IS-B), block 2- block 1, correlated with IS accuracy improvement (block 2- block 1; $r = 0.544$; $P < 0.05$). Participants who decreased their enhancement of the interruptor (positive difference values, positive x axis) showed the most improvement in WM accuracy.

regression analyses results remain with this approach, although some as one-tailed comparisons. For additional details, see supplemental data.¹

PROBE STIMULI. P1 amplitude data from posterior EOIs were submitted to an ANOVA for the probe stimuli to reveal no significant effect of task [$F(2,38) = 0.400$; $P = 0.673$], no main effect of practice [$F(1,38) = 0.204$; $P = 0.657$], and no task by practice interaction [$F(2,38) = 1.62$; $P = 0.851$]. Mean amplitudes and SE for block 1 tasks were IS: $6.98 \pm 0.84 \mu\text{V}$, DS: $7.13 \pm 0.82 \mu\text{V}$, NI: $6.79 \pm 0.84 \mu\text{V}$ and for block 2 tasks were IS: $6.97 \pm 0.73 \mu\text{V}$, DS: $7.12 \pm 0.90 \mu\text{V}$, NI: $7.06 \pm 0.80 \mu\text{V}$.

N1 amplitude data from posterior EOIs were submitted to an ANOVA for probe stimuli to reveal a significant effect of task [$F(2,38) = 4.30$; $P = 0.021$], no effect of practice [$F(1,38) = 2.534$; $P = 0.128$], and no task by practice interaction [$F(2,38) = 0.772$; $P = 0.469$]. Mean amplitudes and SE for block 1 tasks were IS: $-8.99 \pm 0.82 \mu\text{V}$, DS: $-9.02 \pm 0.87 \mu\text{V}$, NI: $-10.1 \pm 1.02 \mu\text{V}$ and for block 2 tasks were IS: $-8.63 \pm 0.83 \mu\text{V}$, DS: $-8.83 \pm 0.85 \mu\text{V}$, NI: $-9.37 \pm 1.05 \mu\text{V}$. Post hoc evaluation of task effects revealed a significant difference in N1 amplitude to probes between NI and IS (NI > IS*; $P \leq 0.05$, FDR corrected) and between NI and DS (NI > D*; $P \leq 0.05$, FDR corrected), and no difference between IS and DS ($P = 0.58$, FDR corrected) [*Note: greater is more negative for the N1].

Regression analysis was performed to evaluate if individual differences in P1 and N1 measures for probe stimuli were associated with WM performance. There were no significant correlations between P1 or N1 amplitude for probe stimuli and WM performance measures of accuracy or RT index (IS-B; DS-B; NI-B; all P1 correlations r range: 0.07–0.19, P range: 0.50–0.80; all N1 correlations r range: 0.04–0.127, P range: 0.65–0.88). Additionally, there were no practice related correlations, such that changes in amplitude from block 1 to block

2 did not correlate with changes in WM performance (all P1 correlations r range: 0.06–0.34, P range: 0.22–0.83; all N1 correlations r range: 0.07–0.27, P range: 0.33–0.80).

PEAK LATENCY. P1 and N1 latency data for the cue stimuli showed no effect of task, no effect of practice, and no task by practice interaction. For interfering stimuli, both P1 and N1 latencies show a main effect of task such that IS interruptors peaked earlier than DS distractors. These markers of attentional modulation are consistent with the results from the peak amplitude analysis. P1 and N1 latencies also show an effect of practice such that P1 latencies are later in block 2 for IS and DS tasks, and later in block 2 in all tasks for the N1 component. For the probe stimuli, P1 latencies showed no effect of task, practice, and no interaction. The N1 latencies showed a main effect of task, no effect of practice, and no task by practice interaction. N1 latencies for IS and DS were significantly earlier than NI, but not different from each other. For additional information, see supplemental data.

EYE MOVEMENT. To ensure that all observed practice effects were not due to eye movement, electrooculographic data were analyzed. Vertical (VEOG = FP2-IEOG) and horizontal (HEOG = REOG-LEOG) difference waves were calculated from the raw data and baseline corrected to the mean prestimulus activity. The magnitude of eye movement was computed as follows: $(\text{VEOG}^2 + \text{HEOG}^2)^{1/2}$. The variance in the magnitude of eye movement was computed across trials at each time point between 60 and 220 ms poststimulus onset, which encompasses the ERP peaks of interest (P1 and N1). The variance was compared between blocks 1 and 2 for each condition via two-tailed paired t -test. Uncorrected for multiple comparisons, no practice effects were observed at any time point tested regardless of condition ($P > 0.05$). This indicates that the practice effects observed in the ERP are not due to learned eye movements.

¹ The online version of this article contains supplemental data.

DISCUSSION

The current study supports previous reports that interference introduced during a period of WM maintenance impairs recognition performance. Different types of interference, interruptors and distractors, elicited differential P1 and N1 neural modulation, suggesting that independent attentional mechanisms underlie processing these distinct forms of interfering stimuli. Furthermore the degree of interference processing as reflected by P1 and N1 modulation indices predicted subsequent WM performance, while the same measures for cue and probe stimuli did not correlate with performance. In terms of practice effects, WM measures of recognition accuracy and RT improved significantly over the course of a single experimental session for tasks that included interfering stimuli (IS and DS) but not for the same task without interference (NI). Moreover, changes in neural indices of interference processing in posterior cortices that correlated with overall performance (i.e., increased suppression in DS, and decreased enhancement in IS) predicted improvement in WM performance with practice. This was not true for neural indices associated with the cue and probe stimuli of any task. Overall, these findings converge to reveal that the degree to which interference is processed exerts an influence on WM performance and supports our hypothesis that susceptibility to interference effects can change with practice over the course of hours.

Processing of interference and WM

We replicate previous behavioral findings that interference introduced during the delay period of a WM task interferes with memory performance (Chao and Knight 1998; Clapp et al. 2009; Jha et al. 2004; Postle et al. 2005; Sakai et al. 2002a). Additionally, the more attention to intervening information required by task demands, the greater the deviation in performance from a task without interference (i.e., accuracy: NI > DS > IS). The same results were found in a recent study that used the same paradigm, but complex visual stimuli (i.e., faces and scenes) (Clapp et al. 2009). An explanation for this finding is that the processing of interfering stimuli disrupts WM performance through the engagement of capacity-limited cortical networks that are common to both WM maintenance and attention (Desimone 1998; Kastner and Ungerleider 2000; Ungerleider et al. 1998). Another possibility is that generating a representation of additional information in visual cortices (i.e., interfering stimuli) leads to disruption in maintaining a representation of information relevant for the WM task. The impact of a failure to filter interference on WM performance was revealed by recent studies that demonstrated a selective deficit in the suppression of interfering information is associated with impairments in WM performance of older adults (Gazzaley et al. 2005, 2008).

To evaluate neural signatures of processing interference, both interruptions and distractions, we examined established ERP markers of top-down modulation. Previous spatial attention and visual search studies report enhancement of relevant (or validly cued) stimuli and suppression of irrelevant (or invalidly cued) stimuli by implementing "neutral," baseline tasks (Luck and Hillyard 1995; Luck et al. 1994). These studies demonstrate unique modulatory roles of the P1 and N1 amplitudes in selective attention. Specifically, P1 amplitude reveals suppression of processing at ignored locations, possibly reduc-

ing sensory gain of interfering information, and N1 amplitude exhibits enhancement of processing at attended locations, presumably reflecting the application of a limited-capacity discriminative process to relevant information (Luck and Hillyard 1995). Here we replicate these ERP findings but for low-level, feature-based tasks. Distractors in the DS task displayed selective P1 amplitude suppression (i.e., this task elicited significantly smaller P1 amplitudes than stimuli in the baseline task), and interruptors in the IS task that required a discrimination evaluation displayed significant N1 amplitude enhancement (i.e., N1 amplitudes were more negative than those for passively viewed stimuli). While it has been observed that ignored, or invalidly cued, stimuli evoke smaller P1 amplitudes than attended or validly cued stimuli for spatial (Heinze et al. 1994; Hopfinger and Mangun 1998; Mangun and Hillyard 1990; Mangun et al. 1993), object (Gazzaley et al. 2008), and feature attention (Zanto and Gazzaley 2009; Zhang and Luck 2009), a finding often interpreted as neural suppression, a recent, provocative study suggests P1 amplitude increases mediated by stimulus evoked alpha oscillations reflect attentional suppression (Freunberger et al. 2008). Reconciliation of these seemingly discrepant findings are still pending explanation.

Indices of interruptor enhancement and distractor suppression were used as markers to evaluate the impact of resource allocation to different interference types on WM performance. Using these indices, we determined that WM performance on both IS and DS tasks correlated with the degree of interference processing. Thus independent of the nature of the task, greater processing of interruption and distraction was directly associated with reduced WM performance. This same finding was recently shown using the same paradigm but with complex visual stimuli (faces and scenes) using both fMRI and EEG recordings (Clapp et al. 2009). In contrast, enhancement of cue or probe stimuli did not predict WM performance measures, suggesting that differences in recognition performance between individuals was most dependent on the efficiency of processing interference. WM RT measures correlated with P1 attentional modulation of distractors, whereas accuracy measures correlated with N1 attentional modulation of interruptors. It is unclear why these neural-behavioral relationships dissociated across these behavioral measures. P1 and N1 waveforms are considered independent components (Luck and Hillyard 1995; Luck et al. 1990, 1994), a view that may support their differential association with distinct behavioral measures. Previous studies report relationships between modulation of the P1 and RT for the features color (Zhang and Luck 2009) and motion (Zanto and Gazzaley 2009) and modulation of the N1 and RT for color (Zanto and Gazzaley 2009). However, to our knowledge, there are no studies demonstrating a relationship between attentional modulation of N1 for motion and behavioral measures of RT or accuracy.

Influence of practice on interference processing and WM

WM performance as evaluated by recognition accuracy and RT measures improved from block 1 to block 2, revealing an influence of practice on performance across a single experimental session. Previous studies have reported similar WM practice effects across a session (Koch et al. 2006; Landau et al. 2004, 2007) as well as longer-term learning with training

across multiple sessions (Garavan et al. 2000; Jansma et al. 2001; Klingberg et al. 2002; Olesen et al. 2004). Importantly, our analyses revealed that WM significantly improved only for the delayed-recognition tasks in which interference was present (IS and DS) and not on the NI task, which lends further support to the conclusion that interference processing was the critical factor for WM performance. We feel it is unlikely that changes in NI were masked by a ceiling effect, as accuracy was $\sim 90\%$ and RT was ~ 700 ms, thus exhibiting room for improvement.

Behavioral improvements in both IS and DS tasks were associated with decreases in neural modulation measures to the interfering stimuli (i.e., more distractor suppression and less interruptor enhancement). However, there was not a significant task \times practice interaction for P1 or N1 amplitudes for interfering stimuli, although a priori *t*-test revealed a significant increase in P1 suppression for distractors ($P = 0.02$). Individual variability in physiological changes associated with practice may have precluded a statistical interaction at the group level. Importantly, regression analysis revealed variability in modulation indices across individuals was correlated with performance variability and thus suggests that the learning effect is related to physiological changes. The current findings linking practice-related WM improvement with decreased interference processing are in line with reports of decreases in visual cortical activity with learning in previous ERP (Pourtois et al. 2008), fMRI (Milham et al. 2003; Mukai et al. 2007), and PET (Schiltz et al. 1999) studies.

Interestingly, behavioral improvements with practice were not associated with changes in visual cortical activity during the cue or probe periods. Evidence of an absence of change in cue and probe period visual cortical activity with practice (block 1, block 2) and a nonsignificant correlation with WM improvement contributes to the argument that gains in WM performance were not modulated by a nonspecific change of state across the blocks but were specific to changes in processing interfering stimuli. It is possible that the presentation of interfering motion stimuli impacts probe motion discrimination through adaptation effects (Van Wezel and Britten 2002). Larger (more negative) N1 amplitudes for NI probes relative to IS and DS probes that follow interfering stimuli may contribute to WM performance differences across tasks. However, the lack of correlation between probe N1 amplitude and WM performance and lack of correlation between changes in probe N1 amplitude and improved WM performance across blocks argues against this possibility. Furthermore, while adaptation has been reported for motion stimuli (Raymond and Isaak 1998), to our knowledge, the effect of motion adaptation on discrimination has not been reported for stimuli moving in different directions (i.e., the cue and probe stimuli are linear motion, while the interruptors are circular motion).

The apparent dissociation of practice-related changes in interference processing from cue processing is interesting to consider in light of the WM load theory of selective attention (Lavie et al. 2004). According to this theory, WM processing and interference filtering share common resources such that high WM load conditions lead to impaired interference filtering through depletion of limited cognitive control resources (de Fockert et al. 2001; Rissman et al. 2009). In the current study, decreased effective WM load with practice might have occurred through facilitation of processing cue stimuli, thus leading to improved filtering of interfering stimuli. However,

neural measures during the cue period do not correlate with behavior and did not change with practice, suggesting that changes in interference processing can be independent of processing of encoded stimuli. It seems that learning effects specific to interfering stimuli can mediate WM performance enhancements independent of effective WM load changes.

Perceptual and attentional learning are two examples of practice-related effects on processing in the visual system. It is well established that with practice, stimulus/feature discrimination and detection become faster and more accurate, a process known as perceptual learning. For example, improved discrimination has been demonstrated with practice observing stimulus motion (Ball and Sekuler 1982, 1987; Fahle 2002), orientation (Fiorentini and Berardi 1980; Ramachandran and Braddick 1973), and spatial frequency (Fiorentini and Berardi 1980). Such improvement may be mediated via sharpening or tuning of neurons in visual cortical regions for relevant information (Fine and Jacobs 2002) and reflected as decreases in visual cortical activity (Mukai et al. 2007; Pourtois et al. 2008; Schiltz et al. 1999). Another practice-related effect, attentional learning, results in more efficient suppression of task-irrelevant visual stimuli. For example, attentional learning has been measured behaviorally via diminution of the motion aftereffect, reflecting improved suppression of distracting motion stimuli (Vidnyanszky and Sohn 2005) and decreased dominance of distracting information in a binocular rivalry paradigm (Paffen et al. 2008).

Although the differential impact of interference in the IS and DS tasks on WM performance seems to be associated with the degree of stimulus processing demanded by the tasks, the nature of the processing may provide a clue as to the changes that contribute to WM practice effects. During the DS task, participants attempted to ignore the distractors, whereas during the IS task, they performed a speed of rotation discrimination on the interruptor. Thus the learning that takes place in DS may be largely attentional, consistent with studies that have revealed increases in attentional suppression of task-irrelevant stimuli with practice (Vidnyanszky and Sohn 2005), whereas the learning in IS may be largely perceptual, displaying comparable neural changes to those observed with practice on low-level discrimination tasks (Mukai et al. 2007; Pourtois et al. 2008; Schiltz et al. 1999). However, it is reasonable that there is also a contribution of attentional learning in the processing of the interruptors in the IS task as participants may learn how to direct less attention to the interruptors with practice. We propose that rapid perceptual and attentional learning directed at the processing of interference is a mechanism of improved WM performance with practice.

Conclusions

The current study offers new perspectives on the neural changes that underlie cognitive performance improvements with practice. Here we show that changes with practice in the neural processing of interfering stimuli, and not WM task-relevant cue or probe stimuli, are correlated with performance enhancement. Moreover, the data reveal that comparable degrees of improvement occur for different types of WM interference. These results highlight the importance of restricting the contents of WM maintenance to relevant information to achieve optimal WM performance and the integrative, dynamic

relationship between neural processes of attention, perception, and WM.

Evidence of WM improvement with practice and the relationship between changes in interference processing and performance enhancement is particularly alluring because it suggests that distractibility is plastic and may be manipulated in a manner that beneficially impacts cognitive performance. These results are particularly relevant for the study of attention deficit hyperactivity disorder in which distractibility is increased (Gumenyuk et al. 2005) and normal aging in which there is a selective-suppression deficit (Gazzaley et al. 2005, 2008). Further investigation will focus on the impact of extensive long-term training designed to selectively improve suppression abilities and WM performance in young and older adults.

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