Stimulation along the anterior-posterior axis of lateral frontal cortex reduces visual serial dependence

Daniel P. Bliss Citizen Science Program, Bard College, Annandale-on-Hudson, NY, USA

Dobromir Rahnev School of Psychology, Georgia Institute of Technology, Atlanta, GA, USA

Wayne E. Mackey Department of Psychology, New York University, New York, NY, USA

Clayton E. Curtis Department of Psychology, New York University, New York, NY, USA
Center for Neural Science, New York University, New York, NY, USA

Mark D'Esposito Helen Wills Neuroscience Institute and Department of Psychology, University of California, Berkeley, Berkeley, CA, USA

Serial dependence is an attractive pull that recent perceptual history exerts on current judgments. Theory suggests that this bias is due to a form of short-term plasticity prevalent specifically in the frontal lobe. We sought to test the importance of the frontal lobe to serial dependence by disrupting neural activity along its lateral surface during two tasks with distinct perceptual and motor demands. In our first experiment, stimulation of the lateral prefrontal cortex (LPFC) during an oculomotor delayed response task decreased serial dependence only in the first saccade to the target, whereas stimulation posterior to the LPFC decreased serial dependence only in adjustments to eye position after the first saccade. In our second experiment, which used an orientation discrimination task, stimulation anterior to, in, and posterior to the LPFC all caused equivalent decreases in serial dependence. In this experiment, serial dependence occurred only between stimuli at the same location; an alternation bias was observed across hemifields. Frontal stimulation had no effect on the alternation bias. Transcranial magnetic stimulation to parietal cortex had no effect on serial dependence in either experiment. In summary, our experiments provide evidence for both functional differentiation (Experiment 1) and redundancy (Experiment 2) in frontal cortex with respect to serial dependence.

Introduction

In the study of perceptual decision-making, serial dependence refers to an attractive pull that recent perceptual history exerts on current judgments. When observers are shown a stimulus and prompted shortly afterward to report one of its features, they instead report a blend of the last few trials, weighted by recency (Fischer & Whitney, 2014). What is odd about this tendency is that it is both beneficial and in violation of what the observer is consciously trying to do. It is beneficial in that, when perceptual uncertainty is relatively high, serial dependence reduces the total error of the perceptual report (Cicchini, Mikellidou, & Burr, 2018). It is in violation of the observer's conscious intentions in that, in the experiments where serial dependence has been found to occur, the observer is trying to treat each stimulus as if it has nothing to do with those that came before it. Indeed, in these experiments, the stimuli on successive trials are statistically independent of each other. What all of this implies is that serial dependence is informationally encapsulated, in the sense of Fodor (1983). It is a processing step that operates on the time series of

Citation: Bliss, D. P., Rahnev, D., Mackey, W. E., Curtis, C. E., & D'Esposito, M. (2023). Stimulation along the anterior-posterior axis of lateral frontal cortex reduces visual serial dependence. *Journal of Vision*, *23*(7):1, 1–16, https://doi.org/10.1167/jov.23.7.1.

https://doi.org/10.1167/jov.23.7.1 Received December 7, 2022; published July 3, 2023 ISSN 1534-7362

perceptual estimates, but that does not incorporate (at least some of) the observer's interpretation of or intentions regarding these estimates. This implies something about the neural substrate that implements serial dependence. This substrate is not reconfigured moment to moment to support the observer's goals. Instead, the feature of neural circuitry responsible for serial dependence must be fixed.

One physiological mechanism that could introduce serial dependence during decision-making is synaptic augmentation (Bliss & D'Esposito, 2017), a form of short-term plasticity prevalent specifically in the frontal lobe (Hempel, Hartman, Wang, Turrigiano, & Nelson, 2000; Wang et al., 2006). Areas of the prefrontal and motor cortex in the frontal lobe play an indispensable role in decision-making. Neurons in these areas track perceptual evidence, compute decision variables, and convert decision variables into action plans (Heekeren, Marrett, & Ungerleider, 2008). Unlike synapses in the occipital lobe, which rarely augment, frontal synapses exhibit robust augmentation that does not require long-range input or neuromodulation to be triggered (Hempel et al., 2000). Above, we argued that the neural mechanism of serial dependence must be fixed. Is short-term plasticity not the opposite of fixed? What we are claiming is fixed here is the capacity for short-term plasticity. When frontal cortex circuitry is activated, synapses invariably augment. The capacity for synaptic augmentation likely depends on the expression of specific, genetically encoded cellular machinery (Zucker & Regehr, 2002; Jackman & Regehr, 2017).

Synaptic augmentation is a critical component of models of "activity-silent" working memory (Stokes, 2015; Mongillo, Barak., & Tsodyks, 2008), yet canonical neural models of decision-making in the frontal cortex (Compte, Brunel, Goldman-Rakic, & Wang, 2000; Wang, 2002; Wong & Wang, 2006; Engel & Wang, 2011) typically ignore synaptic augmentation. Bliss and D'Esposito (2017) took the most recent iteration of these models (Engel & Wang, 2011) and endowed its synapses with dynamics set to match results from patch-clamp recordings in the prefrontal cortex (Wang et al., 2006). When neurons in the model were injected with current meant to represent stimulus-driven input from visual cortex, the decision they produced shifted gradually within each trial toward the feature value processed on the preceding trial. In the terminology of dynamical systems, synaptic augmentation deepened the attractor basin for the previous trial's decision. Strikingly, even though the model parameters were set based on data from the prefrontal cortex of nonhuman mammals, the rate of the increase in serial dependence across the delay period of each simulated trial was a close match to human psychophysical performance (Bliss, Sun, & D'Esposito, 2017).

If synaptic augmentation in the frontal cortex is responsible for serial dependence, then manipulation of neural activity in the frontal cortex should modulate serial dependence. One technique that has been used to stimulate frontal cortex in the study of serial dependence is transcranial magnetic stimulation (TMS). A single pulse of TMS to the cortex induces a brief burst of action potentials limited to neurons within two millimeters of the stimulation site (Romero, Davare, Armendariz, & Janssen, 2019). The application of hundreds of pulses of TMS over a short time span can induce long-lasting changes in neural excitability, depending on the pattern of stimulation. One such pattern, termed continuous theta-burst stimulation (cTBS)— a 50-Hz burst of three pulses repeated every 200 ms for 40 seconds— has been shown, when applied to motor cortex, to suppress motor evoked potentials for an hour (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). Hence, whereas individual pulses of TMS directly excite neurons under the coil, cTBS depresses their responsiveness to stimuli for an extended period of time.

In an effort to study effects on serial dependence, Barbosa et al. (2020) applied a single pulse of TMS to the lateral prefrontal cortex (LPFC) of human subjects during every intertrial interval (ITI) of an oculomotor delayed response task. Based on earlier theory (Mongillo et al., 2008), the authors reasoned that driving LPFC neurons to fire during the ITI would boost synaptic augmentation from the previous trial and thereby increase serial dependence in behavior. Consistent with this interpretation, serial dependence was stronger after mild prefrontal stimulation (70% of resting motor threshold). This effect disappeared when stimulation intensity was increased to 130% of motor threshold. Barbosa et al. used a model circuit with synaptic augmentation to explain the disappearance of serial dependence after especially strong stimulation during the ITI. A large burst of noise injected into the model neurons caused synapses to saturate, removing the imprint left by the previous trial. Reduction of serial dependence has also been induced with especially strong stimulation of premotor cortex during the ITI of a visual motion task (de Azevedo Neto & Bartels, 2021). In the same visual motion task, equally strong stimulation of visual area hV5/MT+ in the occipital lobe left baseline levels of serial dependence unchanged (de Azevedo Neto & Bartels, 2021).

This collection of results raises questions about the neural architecture that supports serial dependence. Are the LPFC and premotor cortex the only frontal regions involved? Is their involvement general or limited to a certain stimulus type or action format? The LPFC seems to play a general role. Stimulation of the LPFC affects serial dependence in both eye movements that report stimulus location (Barbosa et al., 2020) and manual button presses that classify visual motion as to the left or right (Bonaiuto, de Berker, & Bestmann, 2016). The nature of the roles that other

frontal areas play is yet to be determined. Many areas distributed widely across cortex are important for the maintenance of perceptual evidence, decision variables, and action plans during decision-making (Christophel, Klink, Spitzer, Roelfsema, & Haynes, 2017). It could be that multiple frontal areas have internal dynamics susceptible to serial dependence during the formation of each decision and that the final decision (executed as motor output) incorporates input from several (or all) of these areas.

The aim of the current study was to clarify the organization of serial dependence throughout the lateral frontal cortex. We conducted two experiments that used distinct decision-making tasks with distinct task-relevant visual features and response formats. In our first experiment, TMS was applied to two regions of lateral frontal cortex: the LPFC and the precentral sulcus (PCS), which is posterior to the LPFC. TMS was also directed to an area outside frontal cortex, namely, the posterior parietal cortex (PPC). In this first experiment, participants completed an oculomotor delayed response task similar to the one used by Barbosa et al. (2020). In our version of the task, two stages of the motor response could be distinguished: an initial memory-guided saccade followed by adjustments to achieve final eye position. A brief burst of TMS was delivered during the delay period of each trial. A previously published analysis of this dataset (Mackey & Curtis, 2017) found that stimulation of the LPFC had no effect on the general accuracy of eye movements, whereas stimulation of PCS decreased accuracy for the memory-guided saccade, with no effect on the final eye position. This analysis did not address possible effects on serial dependence.

Our second experiment used an orientation discrimination task. TMS was applied to three regions of the lateral frontal cortex: the PCS, LPFC, and a region in the anterior prefrontal cortex (aPFC) near the frontal pole. In a control session, the primary somatosensory cortex (S1) was stimulated. TMS was applied before behavioral testing using the cTBS protocol to decrease neural excitability for the duration of the task. A previously published analysis of this dataset (Rahnev, Nee, Riddle, Larson, & D'Esposito, 2016) found no effects on the accuracy of decision-making after cTBS to any of the frontal regions. Possible effects on the serial dependence of the perceptual decision were not addressed.

As stated, the TMS protocols used in our experiments have distinct effects on neural circuitry. But for reasons we will now explain, we expect them to have similar effects on serial dependence. Brief bursts of stimulation (Experiment 1) induce a transient increase in firing. When stimulation is delivered during task performance (as in Experiment 1), the TMS-evoked response does not summate with task-related firing (Romero et al., 2019). That is, neurons already active in the task are affected less by TMS than inactive neurons. For this reason, we interpret TMS in Experiment 1 as likely to be disruptive to the normal functionality of the targeted circuits, decreasing the contrast between the firing rates of the normally active and normally inactive neurons. cTBS (Experiment 2) chronically suppresses firing. This would also decrease the contrast between the firing rates of normally active and normally inactive neurons, because normally active neurons are susceptible to suppression and normally inactive neurons are not. Lower contrast in the firing rates would translate to lower contrast in the pattern of augmented synaptic strengths, and less of an imprint of the previous trial in the synapses. Hence, we expect TMS in both experiments to decrease serial dependence.

Methods

Experiment 1

Analysis of this dataset unrelated to serial dependence is reported in Mackey and Curtis (2017).

Subjects

Subjects were nine neurologically healthy adults (two female) with normal or corrected-to-normal vision. All gave written informed consent before the experiment and received monetary compensation afterwards. All experimental procedures were approved by the Institutional Review Board at New York University.

TMS

TMS was administered with a Magstim Rapid 2 Magnetic Stimulator with a figure-eight coil (70-mm diameter double circle). The PCS and PPC stimulation sites were chosen based on results from a separate functional magnetic resonance imaging (fMRI) study of the same subjects (Mackey & Curtis, 2017). In this separate study, visual fields were mapped in the frontal and parietal cortex in each individual subject. The maps in the left superior PCS and in the left third intraparietal sulcus area of the PPC were chosen for stimulation in the current experiment. The PCS stimulation site corresponds approximately with the frontal eye fields. LPFC stimulation was directed to the posterior third of the right intermediate frontal sulcus. Stimulation intensity was set to 53% of the maximum stimulator output. Stimulation was applied as a train of three pulses at 50 Hz in the middle of the delay period of every trial of the task.

Experimental procedure

Monocular eye movement data were collected at 1,000 Hz using an SR Research EyeLink 1000 eye tracker. Subjects sat in a darkened room, and a chin rest was used to prevent head movement. Nine-point calibrations were performed at the beginning of each session and between runs as necessary. Experimental stimuli were programmed with the MATLAB MGL Toolbox and displayed against a gray background.

At the start of each trial, subjects fixated a black cross over white dots at the center of the screen. A yellow cue (0.5° in diameter) then appeared for 200 ms. The cue was always presented away from the cardinal axes, but otherwise its polar angle around fixation was random from trial to trial. Subjects were instructed to remember the cue's location for a delay period that varied randomly among the values 3.0, 3.5, 4.0, 4.5, and 5.0 seconds. At the end of the delay period, a sound coupled with the disappearance of the fixation point signaled that subjects should shift their gaze to the location in memory. Participants were given 800 ms to make an initial saccade followed by corrective adjustments to their eye position as needed. At the end of the response period, a green dot appeared at the correct location for 700 ms. Participants were trained to fixate this dot. A 1.5-second ITI followed, during which subjects maintained fixation on a central blue square. Each run consisted of 30 trials. Subjects completed 10 runs per session and were encouraged to take breaks between runs as desired.

Analysis

Eye movement data were transformed to degrees of visual angle using a third-order polynomial algorithm that fits eye positions to locations in the visual field. The data were then scored offline with the iEye toolbox (https://github.com/wemackey/iEye). Instances of eye velocity of more than 30°/s were marked as saccades and confirmed by visual inspection. Reaction time was measured from the onset of the response cue to the onset of the first saccade. Trials with reaction times less than 100 ms or more than 900 ms were excluded from analysis. Trials were also excluded when subjects broke fixation early or made an initial memory-guided saccade of less than 5° eccentricity.

The MATLAB function loess was used to apply a low-pass filter to the responses as a function of stimulus location, yielding an estimate of the response bias for each location. This bias was then subtracted from each individual response. The residual error after subtraction was used to measure serial dependence as follows.

We fit a function developed by Clifford, Wenderoth, and Spehar (2000) to the group dataset of residual errors, separately for the initial memory-guided saccade, post-saccade eye position adjustments, and the final eye position (the saccade plus the adjustments). What follows is a derivation of this function, first in words and then with equations. We note that the function was developed originally to capture repulsive aftereffects, which follow a pattern exactly opposite that of serial dependence. We highlight the parameters of the model that allow it to fit serial dependence as well as repulsive aftereffects. Clifford et al. (2000) theorized that repulsive aftereffects are consequences of self-calibration and decorrelation within visual neural circuitry. We make no effort to relate this normative theory to serial dependence in the current article, but it may be a fruitful angle for future work to explore.

The Clifford et al. function represents stimuli as unit-length vectors pointing out from the origin of a Cartesian coordinate system (where the origin, in the case of our Experiment 1, corresponds with the fixation point). Vectors are rotated about the origin to express them relative to the location of the previous stimulus. After rotation, a 0° vector points in the direction of the previous stimulus, and all nonzero angles represent nonzero distances from the previous stimulus. Vectors with this interpretation are the input to the Clifford et al. function. The function scales and shifts each input vector along the horizontal axis (the axis parallel to the previous stimulus). The updated angle of the vector after scaling and shifting can be solved for using the Pythagorean identity. The updated angle represents the angle of the observer's response (again expressed relative to the previous stimulus location). We will call the angle of the input vector θ_S (the current stimulus relative to the previous stimulus) and the updated angle θ_R (the current response relative to the previous stimulus). The relevant trigonometric equations follow.

For unit-length input vector θ_S, the vertical distance from the origin is $\sin(\theta_S)$ and the horizontal distance from the origin is $\cos(\theta_S)$. Per the Pythagorean theorem, the length of the vector itself is $\sqrt{\cos^2(\theta_S) + \sin^2(\theta_S)}$. The Clifford et al. function scales and shifts only the horizontal component of this vector, such that the updated vector length is

$$\sqrt{(s\cos(\theta_S) - c)^2 + \sin^2(\theta_S)},$$

where s does the scaling and c does the shifting. When $s > 1$, the aftereffect is attractive for small interstimulus differences and repulsive for large interstimulus differences (serial dependence); when $s < 1$, the aftereffect is repulsive for small interstimulus differences and attractive for large interstimulus differences. Having $c < 0$ contributes an aftereffect that is attractive across the full range of relative stimulus angles; for $c > 0$, the contribution to the aftereffect is repulsive across the full range. During model fitting, s and c are the only parameters that are free. The angle of the scaled and shifted vector is computed using the definition of the

sine function:

$$\sin(\theta_R) = \frac{\sin(\theta_S)}{\sqrt{(s\cos(\theta_S) - c)^2 + \sin^2(\theta_S)}}.$$

It is helpful to rewrite this equation so that the function explicitly solves for the error of the subject's response (E) across all relative stimulus angles:

$$E = \arcsin\left(\frac{\sin(\theta_S)}{\sqrt{(s\cos(\theta_S) - c)^2 + \sin^2(\theta_S)}}\right) - \theta_S.$$

Note that here E and θ_S are the variables plotted on the y axis and x axis, respectively, of Figure 1b. The scipy function least_squares was used to find the values of s and c that minimized the difference between E and the observed errors. We measured the amplitude of serial dependence as the peak-to-peak (maximum minus minimum) of E across all relative stimulus angles. The peak-to-peak depends on both s and c.

Statistical significance was determined using permutation tests. To determine whether the amplitude of serial dependence was greater than chance, we first shuffled the vector of values for θ_S relative to the vector of residual errors. The number of shuffles conducted varied between 1,000 and 10,000, depending on available computing resources. We fit the equation for E to each shuffled dataset. As p values we report the proportion of shuffled datasets with an amplitude of serial dependence greater than the amplitude for the unshuffled dataset.

To determine whether the amplitude of serial dependence was greater in one condition than in another, we first combined the data from the two conditions and shuffled the condition labels. We then separated the conditions using the shuffled labels and fit the equation for E to each. This process was repeated 1,000 times. One-tailed p values are reported for predicted differences between conditions; otherwise two-tailed p values are reported. One-tailed p values were computed as the proportion of the shuffled datasets with an amplitude difference between conditions greater than the amplitude difference for the unshuffled dataset. Two-tailed p values were computed as the proportion of shuffled datasets with an absolute amplitude difference between conditions greater than the absolute amplitude difference for the unshuffled dataset.

Data availability

The data are available from Clayton E. Curtis upon request.

Experiment 2

Analysis of this dataset unrelated to serial dependence is reported in Rahnev et al. (2016).

Subjects

Subjects were 17 adults (11 female) with normal or corrected-to-normal vision. All gave written informed consent before the experiment. The procedures were approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley.

cTBS

cTBS was administered with a Magstim Super Rapid Stimulator with a figure-eight coil (70-mm diameter double circle) connected to two booster modules. The LPFC and PCS stimulation sites were chosen based on results from a control condition without TMS, which was completed while participants underwent fMRI. The details of the imaging procedure are in Rahnev et al. (2016); we report no imaging results in the current manuscript. Individual activations for the contrast task > background were used to identify a region of interest within the right LPFC and within the right PCS in each individual subject. Coordinates for the right aPFC stimulation ([27, 53, 25] in Montreal Neurological Institute space) were taken from a previous study (Fleming, Huijgen, & Dolan, 2012). For S1, stimulation was directed to the right postcentral gyrus.

Stimulation intensity for cTBS was set to 80% of the individual motor threshold (35.5% of maximum stimulator output, on average). The motor threshold was determined immediately before each delivery of cTBS, as follows. First, the site of stimulation in the motor cortex that induced maximal hand twitch was identified. Then, starting at 30% of the maximum stimulator output, the stimulation intensity was adjusted to find the lowest intensity for which a single pulse of TMS induced a motor-evoked potential larger than 50 μV peak-to-peak on 5 of 10 consecutive trials. This intensity was chosen as that session's motor threshold. No twitches of muscles other than those in the hand were elicited by stimulation at this intensity and location.

After identification of the motor threshold, cTBS was delivered as five bursts of three 50-Hz pulses every second for 40 seconds. Behavioral testing commenced after the completion of cTBS.

Experimental procedure

Participants completed the task without TMS while undergoing fMRI with the room lights turned off. For the sessions with TMS, they sat at a computer

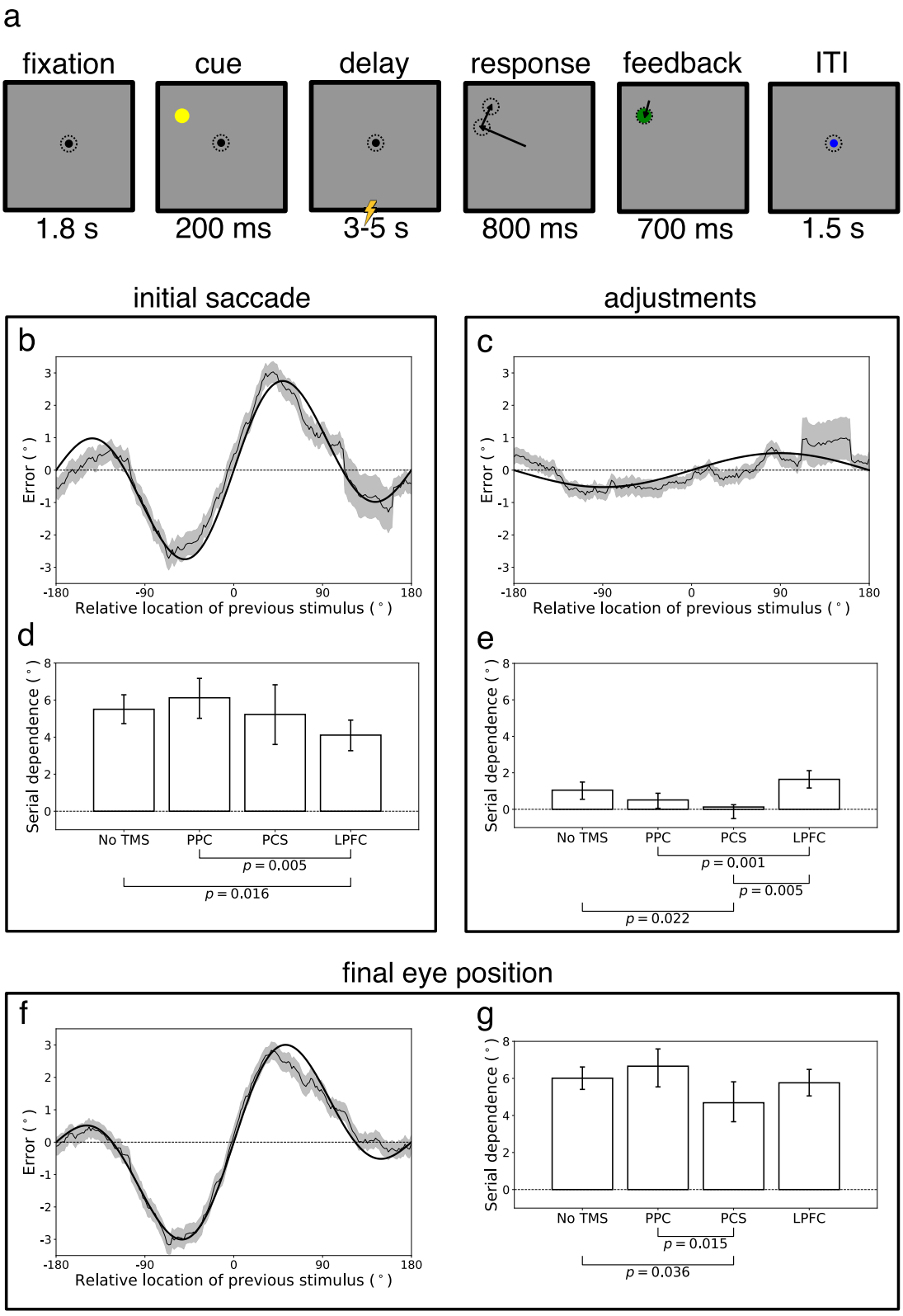

Figure 1. (a) Oculomotor delayed response task. For each trial, participants viewed a yellow cue peripheral to fixation and then made a memory-guided saccade to its location. Participants were allowed to adjust their gaze subsequently, such that the final eye position at the end of the response period could differ from the memory-guided saccade. The cue was shown again at the end of the trial as feedback. Arrows and dotted circles in this figure were not stimuli in the experiment; they indicate where participants would have been directing their gaze. The lightning bolt indicates that transcranial magnetic stimulation (TMS) was applied in the middle of the delay period. (b) Errors in the initial saccade for the baseline condition without TMS, combining data from all subjects. Positive values

→

←
on the *x* axis indicate that the previous trial was more clockwise than the present trial, and positive errors indicate that the reported location was more clockwise than the true target location. Thick black line shows the fit of the Clifford et al. (2000) model to the data. The peak-to-peak (maximum minus minimum) of the fit gives the amplitude of serial dependence. (c) Errors in post-saccade eye position adjustments for the no TMS condition, combining data from all subjects. (d) Serial dependence in the initial saccade for each TMS condition. Bar heights are group fits; error bars depict bootstrapped 90% confidence intervals. (e) Serial dependence in post-saccade adjustments for each TMS condition. (f) Errors in final eye position (sum of the initial saccade and post-saccade adjustments) for the no TMS condition, combining data from all subjects. (g) Serial dependence in final eye position for each TMS condition.

in a darkened room. Experimental stimuli were programmed with the MATLAB Psychophysics Toolbox and displayed against a gray background.

Subjects maintained fixation on a central square for the entirety of the task. At the start of each trial, an attentional pre-cue and speed or accuracy instruction were displayed for 1 second. The attentional pre-cue was an arrow of length 3° and height 1° that pointed left or right. The speed or accuracy instruction was the word "FAST" in green or "ACCURATE" in red, in Arial font. The color of the pre-cue always matched that of the speed or accuracy instruction. The pre-cue and speed or accuracy instruction remained on the screen when the orientation stimuli were presented. The stimuli were grayscale gratings with diameter 3° displayed 9° to the left and right of fixation. The gratings had spatial frequency 0.5 cycles per degree and were embedded in a background of uniformly distributed intensity values at approximately 8% contrast (contrast was adjusted for individual participants during training on the task). After 200 ms, the gratings were replaced with a post-cue in the form of an empty white circle with diameter 4° positioned where one of the gratings had been. Participants then pressed one of two buttons to indicate whether that grating had been tilted 45° clockwise or counterclockwise of vertical. The subjects were told that the pre-cue would be to the same side as the post-cue on two-thirds of trials. Owing to a programming error, the non–post-cued grating was always tilted counter-clockwise. (Random tilt from trial to trial was intended.) Experimenters were unaware of this error when the results from this dataset were published previously (Rahnev et al., 2016). The tilt of the other (post-cued) grating was random, as were the direction and validity of the cue. All of our analyses pertain to the post-cued grating and ignore the non–post-cued grating. After indicating their clockwise or counter-clockwise decision, participants made a second button press to rate their perceptual confidence on a scale from 1 to 4. Button presses were made on an fMRI-compatible button box in the no-TMS session and on a standard computer keyboard in the cTBS sessions. Each run consisted of four blocks of 30 trials. Subjects completed four runs per session. They took 15-second breaks between blocks and unlimited breaks between runs.

Analysis

Using detection theory, we computed the decision criterion c as

$$c = -\frac{Z(H) + Z(F)}{2},$$

where $Z(H)$ is the z-score of the hit rate and $Z(F)$ is the z-score of the false alarm rate. The hit rate was defined as the proportion of counter-clockwise stimuli to which the participant responded counter-clockwise. The false alarm rate was defined as the proportion of clockwise stimuli to which the participant responded counter-clockwise. Serial dependence was calculated as a shift in criterion dependent on the choice made on the preceding trial:

$$c_{sd} = c_{cw} - c_{ccw}.$$

Here, c_{cw} is the criterion calculated using only trials preceded by a clockwise choice, and c_{ccw} is the criterion calculated using only trials preceded by a counter-clockwise choice. Serial dependence was computed separately for each subject, and significance was determined using t tests. One-tailed p values are reported for predicted differences; otherwise two-tailed p values are reported.

Data availability

The data are available at https://github.com/DobyRahnev/TBS-to-PFC.

Results

Experiment 1

Nine participants completed the oculomotor delayed response task depicted in Figure 1a. For each trial, participants viewed a yellow cue peripheral to fixation and then made a memory-guided saccade to its location. The cue appeared at a random location along the circumference of an invisible circle centered on

the fixation dot, with radius approximately 10° (visual angle). Participants were allowed to make corrective adjustments to their gaze throughout an 800-ms response window, such that final eye position could differ from the initial saccade. Errors were recorded in degrees of polar angle around the invisible circle. The cue reappeared on the screen at the end of the trial as feedback. Each participant completed 300 trials per experimental session.

For each session, TMS was applied to a single location on the cortex—PCS, LPFC, or PPC—or not applied at all. Each participant was recruited to receive TMS to all three locations (one session for each) and to complete one control session without TMS. Seven participants completed all four sessions, one completed only the no-TMS and PCS sessions, and one completed only the no-TMS, LPFC, and PPC sessions. TMS was applied as a train of three pulses at 50 Hz in the middle of the delay period of every trial of the task.

Serial dependence is observed when participant responses are drawn away from the target stimulus and toward a stimulus presented on an earlier trial. We tested for one-back serial dependence separately in the initial saccade and subsequent adjustments. In the control session without TMS, both of these response metrics exhibited serial dependence (initial saccade, $p < 10^{-5}$; adjustments, $p = 0.002$). Attraction toward the preceding trial's cue increased with increasing polar distance from the current trial's cue up to about 45° for the initial saccade (Figure 1b). At greater distances, the bias diminished, such that it was absent or slightly repulsive when successive stimuli were on opposite sides of the screen. This variation of the bias over interstimulus distances is well fit by the geometric model of visual aftereffects of Clifford et al. (2000). The Clifford et al. function represents the stimuli as vectors in two-dimensional space. To estimate the observer's response, the function scales and shifts the stimulus vector along the axis parallel to the vector for the previous stimulus. A detailed description of the model is given in the Methods. Unlike other functions that have been used to estimate serial dependence, such as the derivative of Gaussian, the Clifford et al. function is able to fit the repulsive effect at large interstimulus distances (Figure 1b). We took the peak-to-peak (maximum minus minimum) of the Clifford et al. model fit as the amplitude of serial dependence—the dependent variable in our analyses. The amplitude of serial dependence was significantly greater (two-tailed $p < 10^{-4}$) in the initial saccade (group peak-to-peak = 5.50°) than in the subsequent adjustments to eye position (Figure 1c; group peak-to-peak = 1.05°).

As a control analysis, we looked for one-forward serial dependence—a deviation of responses in the direction of the stimulus one trial into the future. No such spurious response bias was detected for either the initial saccade ($p = 0.384$) or subsequent adjustments to eye position ($p = 0.720$). This result suggests that the one-back serial dependence we observed was due to a genuine bias in how participants processed the stimuli, rather than a chance correlation between the particular sequence of errors participants happened to make and the particular randomized sequence of stimuli they were shown.

Next, we examined the effects of TMS on serial dependence (Figures 1d, e). TMS to PPC nonsignificantly increased serial dependence in the initial saccade (PPC vs. no TMS, two-tailed $p = 0.435$) and nonsignificantly decreased serial dependence in subsequent adjustments to eye position (two-tailed $p = 0.135$). The pattern induced by LPFC stimulation was opposite of this: LPFC TMS decreased serial dependence in the initial saccade (one-tailed $p = 0.016$) and nonsignificantly increased serial dependence in subsequent adjustments (two-tailed $p = 0.106$). This effect was such that the PPC and LPFC conditions were significantly different from each other for both response stages, in opposite directions. That is, LPFC stimulation decreased serial dependence in the initial saccade (one-tailed $p = 0.005$) and increased serial dependence in the adjustments (two-tailed $p = 0.001$) relative to PPC stimulation.

Stimulation of the PCS also induced changes in serial dependence, but limited to the post-saccade adjustments. For the initial saccade, all statistical comparisons with the PCS condition were nonsignificant (PCS vs. no TMS, one-tailed $p = 0.395$; PCS vs. PPC, one-tailed $p = 0.196$; LPFC vs. PCS, two-tailed $p = 0.313$). TMS to PCS suppressed serial dependence in adjustments after the initial saccade—compared to both the no-TMS (one-tailed $p = 0.022$) and LPFC (two-tailed $p = 0.005$) conditions (PCS vs. PPC: one-tailed $p = 0.180$). In summary, it was only stimulation of the frontal regions (LPFC and PCS) that altered serial dependence relative to the no-TMS condition. We observed a double dissociation between LPFC and PCS. With respect to the initial memory-guided saccade, stimulation of LPFC but not PCS decreased serial dependence. With respect to eye-position adjustments following the initial saccade, stimulation of PCS but not LPFC decreased serial dependence.

We separately assessed the impact of TMS on the final eye position (Figures 1f, g), the sum, on each trial, of the initial saccade and subsequent adjustments. Only stimulation of PCS affected serial dependence in the final eye position, reducing it compared with both the no-TMS (one-tailed $p = 0.036$) and PPC (one-tailed $p = 0.015$) conditions (LPFC vs. PCS: two-tailed $p = 0.164$). No other statistical comparisons were significant (PPC vs. no TMS: two-tailed $p = 0.396$; LPFC vs. no TMS: one-tailed $p = 0.321$; LPFC vs. PPC: one-tailed $p = 0.126$). The null results here for PPC and LPFC indicate that the effects in opposite directions for the initial saccade and subsequent adjustments canceled out in their sum, the final eye position.

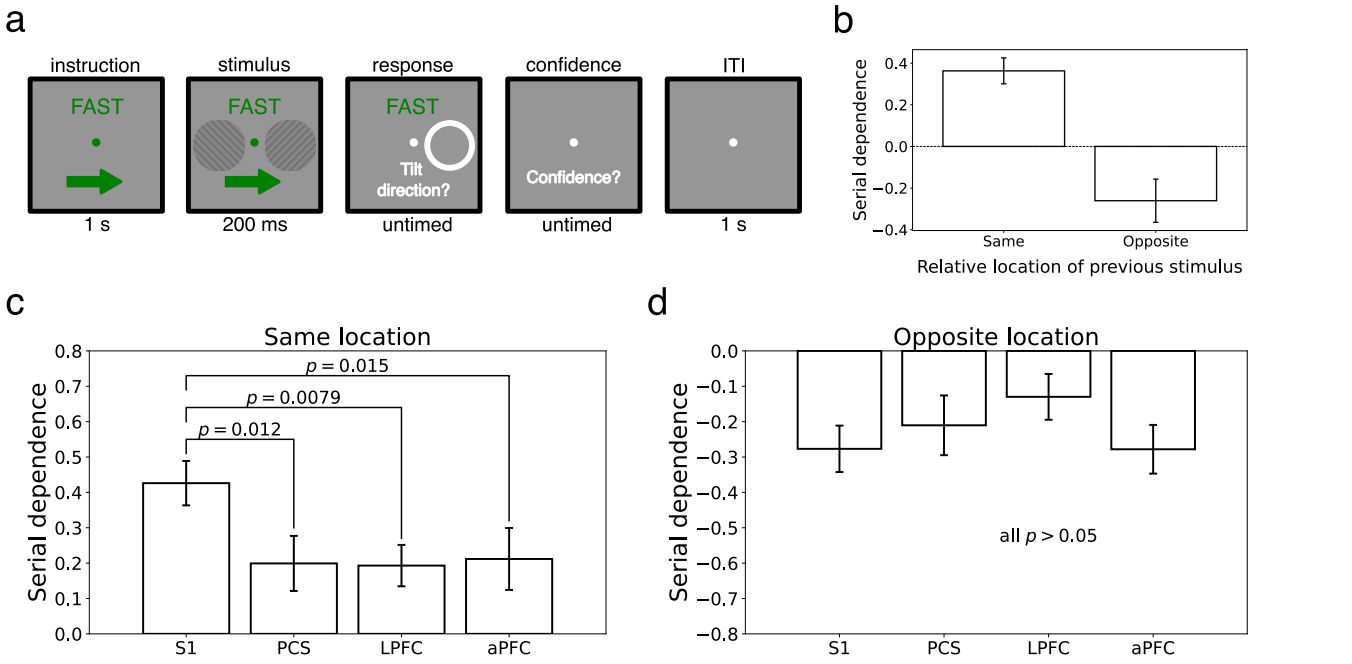

Figure 2. (a) Orientation discrimination task. For each trial, participants viewed two gratings on either side of fixation and reported the tilt direction of one with a button press. Participants rated their confidence at the end of each trial. No feedback was provided. Participants were pre-cued to one side and asked to emphasize speed or accuracy. Both of these instructions were random from trial to trial. (b) Serial dependence (measured as a shift in decision criterion that favors repetition of the one-back response) for the baseline condition without transcranial magnetic stimulation (TMS). (c) Serial dependence for consecutive post-cued stimuli at the same location, split by continuous theta-burst stimulation (cTBS) condition. Error bars depict the standard error of the mean. (d) Serial dependence for consecutive post-cued stimuli at opposite locations, split by cTBS condition.

Experiment 2

Seventeen participants completed the orientation discrimination task depicted in Figure 2a. Each trial began with a pre-cue to attend left or right and an instruction to emphasize speed or accuracy. Two noisy gratings then appeared on either side of fixation. A post-cue to one of the gratings prompted participants to report its orientation as clockwise or counterclockwise of vertical (±45°). The post-cue was to the same side as the pre-cue on two thirds of trials. Participants rated their perceptual confidence at the end of each trial. No feedback was provided. There were 480 trials per session.

At each session, cTBS was applied to one cortical location—PCS, LPFC, aPFC, or S1—or not applied at all. Each participant received cTBS to all four locations (one session for each) and completed an initial testing session without TMS. cTBS was delivered prior to the start of the task.

In discrimination tasks, serial dependence manifests as a shift in decision criterion that favors repetition of an earlier trial's response. We tested for one-back serial dependence in the control condition without TMS and found that participants shifted their decision criterion toward the preceding response when they were post-cued to the same location on both trials ($t_{16} = 5.65$, one-tailed $p = 1.8 \times 10^{-5}$). That is, participants favored the same orientation judgment for consecutive stimuli at the same position relative to fixation, even though the actual tilt of the stimulus was updated randomly from trial to trial. In contrast, when the post-cues on consecutive trials were to opposite sides of fixation, participants were biased to report opposite tilts for the gratings ($t_{16} = -2.44$, one-tailed $p = 0.013$). These results replicate St. John-Saaltink et al. (2016) and imply that serial dependence was sensitive to spatial distance, positive at the same location and negative across locations (Figure 2b). We emphasize that cued location and orientation were independently random from trial to trial. In the trial sequences generated for participants, the frequency with which they were cued to the same orientation on back-to-back trials was not significantly different from 50% (same location: $t_{16} = -0.29$, two-tailed $p = 0.78$; opposite location: $t_{16} = 0.11$, two-tailed $p = 0.91$). Hence, the spatial pattern of participants' choice biases could not have been inherited from the statistics of what they were shown.

An effect unrelated to trial history that could have induced artifactual serial dependence in participants' responses is the Simon effect. In the context of our

analysis, a Simon effect would have manifested as a tendency to press the left response button when the cued stimulus was on the left (and right button when cued right)—contra the task instructions. This would keep responses the same from trial to trial for the same cue location, and opposite for opposite cue locations. We found no evidence of such a Simon effect in our data. The proportion of left button presses (counter-clockwise orientation judgments) was equivalent for post-cues to the left and right ($t_{16} = -1.26$, two-tailed $p = 0.23$).

Next, we examined the effects of cTBS. cTBS to S1 had no effect on serial dependence (S1 vs. no TMS, same location: $t_{16} = 0.88$, two-tailed $p = 0.39$; opposite location: $t_{16} = -0.14$, two-tailed $p = 0.89$). This provides our analysis with two statistically equivalent control conditions against which to compare frontal stimulation. We note that the S1 condition is the better control condition, because it is matched to the frontal conditions in all respects except for the site of stimulation in the cortex. Any generic effects on behavior that result from undergoing the cTBS procedure are not controlled for by the no-TMS condition. We compared the frontal conditions to both control conditions and report results for the comparisons to S1 first.

For consecutive orientation judgments at the same location, cTBS to all three frontal regions reduced serial dependence (PCS vs. S1: $t_{16} = -2.51$, one-tailed $p = 0.012$; LPFC vs. S1: $t_{16} = -2.70$, one-tailed $p = 0.0079$; aPFC vs. S1: $t_{16} = -2.37$, one-tailed $p = 0.015$). Frontal stimulation caused an equivalent reduction regardless of which region was targeted (LPFC vs. PCS: $t_{16} = -0.075$, two-tailed $p = 0.94$; aPFC vs. PCS: $t_{16} = 0.11$, two-tailed $p = 0.91$; aPFC vs. LPFC: $t_{16} = 0.17$, two-tailed $p = 0.87$). In contrast, cTBS to frontal cortex had no effect on the bias to alternate responses when the opposite location was cued relative to the preceding trial (PCS vs. S1: $t_{16} = 1.055$, two-tailed $p = 0.31$; LPFC vs. S1: $t_{16} = 1.53$, two-tailed $p = 0.15$; aPFC vs. S1: $t_{16} = -0.021$, two-tailed $p = 0.98$). The three frontal conditions did not differ from each other with respect to the negative serial dependence for opposite locations (LPFC vs. PCS: $t_{16} = 0.90$, two-tailed $p = 0.38$; aPFC vs. PCS: $t_{16} = -0.93$, two-tailed $p = 0.37$; aPFC vs. LPFC: $t_{16} = -1.70$, two-tailed $p = 0.11$). These results suggest that the positive and negative serial biases, distinguished by the visual distance across which they operate, rely on different cortical areas. Only the positive bias for stimuli at the same location was found to depend on intact functionality across a large portion of lateral frontal cortex, from the PCS to the frontal pole (Figures 2c, d).

We now report the results for the comparisons to the no-TMS condition: For consecutive orientation judgments at the same location, TMS to PCS and LPFC reduced serial dependence (PCS vs. no TMS: $t_{16} = -1.98$, one-tailed $p = 0.032$; LPFC vs. no TMS: $t_{16} = -2.03$, one-tailed $p = 0.030$). Although serial dependence was numerically reduced after TMS to aPFC, the effect failed to cross the threshold for statistical significance ($t_{16} = -1.57$, one-tailed $p = 0.068$). TMS to frontal cortex had no effect on the bias to alternate responses when the opposite location was cued relative to the preceding trial (PCS vs. no TMS: $t_{16} = 0.47$, two-tailed $p = 0.64$; LPFC vs. no TMS: $t_{16} = 1.24$, two-tailed $p = 0.23$; aPFC vs. no TMS: $t_{16} = -0.18$, two-tailed $p = 0.86$).

As a final analysis, we investigated whether the speed/accuracy instruction or the validity of the pre-cue had any effect on the positive serial dependence participants exhibited for orientations at the same location. We examined the effects of cue validity and speed/accuracy from both the one-back and zero-back (current) trial on the current trial's response. Neither cue validity (one-back: $t_{16} = 1.50$, two-tailed $p = 0.15$; zero-back: $t_{16} = 1.31$, two-tailed $p = 0.21$) nor the speed/accuracy instruction (one-back: $t_{16} = 0.42$, two-tailed $p = 0.68$; zero-back: $t_{16} = 0.79$, two-tailed $p = 0.44$) had any effect on same-location serial dependence in the control condition without TMS. We note that these statistical tests were underpowered compared with our other analyses. Further study of the role of these factors in serial dependence may be warranted.

Discussion

Theory and experiments have converged on the thesis that decision-making circuitry in the frontal lobe is responsible for serial dependence, but it has been unclear which regions of frontal cortex are involved. Our experiments provide evidence for both functional differentiation (Experiment 1) and redundancy (Experiment 2) along lateral frontal cortex with respect to serial dependence.

Our first experiment required subjects to shift their gaze to a location that had been cued visually several seconds earlier. We distinguished two stages of the motor response: the first saccade and subsequent eye position adjustments, which were allowed to continue until the end of the 800-ms response period. The initial saccade can be interpreted in only one way. The subject makes a decision about where the cue was shown and directs his eyes to that location. In contrast, before our analysis, the post-saccade adjustments would have been ambiguous. Does the subject make these adjustments to correct random motor errors—to get his gaze closer to the location he originally intended? Or does the subject change his intention? The latter interpretation implies that the subject's memory of the cue changes over time. Each response—each saccade and adjustment—would

represent a new decision based on the current state of the memory. The results of our first experiment support the interpretation that post-saccade adjustments reflect, at least in part, updates to the perceptual decision, not just corrections of random motor errors. We draw this conclusion because both response stages exhibited serial dependence in our control condition without TMS. If post-saccade adjustments were merely corrections for motor noise, they would bear no consistent relationship with the location of the preceding trial's cue. What seems most likely to us is that the reason there is serial dependence in the adjustments is that the adjustments are based on further scrutiny of the memory of the cue, and this memory is subject to serial dependence that increases over time. Serial dependence has been found in other experiments to accumulate in memory over time (Papadimitriou, Ferdoash, & Snyder, 2015; Fritsche, Mostert, & de Lange, 2017; Bliss et al., 2017), and it also accumulates (at the same rate) in the model neural circuit with synaptic augmentation of Bliss and D'Esposito (2017).

TMS to LPFC in Experiment 1 decreased serial dependence in the initial saccade, but increased (nonsignificantly) serial dependence in the adjustments, such that there was no net effect on the eye position at the end of the trial. Stimulation of PCS had the opposite effect, decreasing serial dependence in the final eye position without affecting the initial saccade. How should we interpret this double dissociation? We have found it helpful to compare our results with those of Mackey and Curtis (2017). We mentioned in the Introduction that they found that TMS to PCS decreased the accuracy of the saccade. Somehow, the subject corrected this during the adjustment period, because the accuracy of the final eye position was unchanged relative to the no TMS baseline. We believe these effects can be related in a straightforward way to the effects on serial dependence that we observed. Our proposal is that TMS to PCS caused random motor errors. (PCS corresponds approximately with the frontal eye fields.) The subject identified these random errors as a departure from his intended movement after the completion of the saccade and corrected them. He moved his gaze closer to the location he originally intended. Per our reasoning in the preceding paragraph, when post-saccade adjustments are merely corrections for random motor errors, they bear no relationship to the preceding trial—no serial dependence. And that is exactly what we found—no serial dependence in the adjustments after TMS to PCS.

What about LPFC? Mackey and Curtis (2017) found that TMS to LPFC had no effect on accuracy. We interpret the effect of TMS to LPFC as a direct effect on serial dependence. The reasoning we laid out in the Introduction applies here. We interpret TMS as having decreased the contrast between the most and least active neurons in the targeted population. This, we argue, would have decreased the contrast in the pattern of augmented synapses, leaving less of an imprint of the decision to bias activity on the next trial. This explains why we observed a decrease in serial dependence in the initial saccade after TMS to LPFC. Our results show that this effect was only temporary. During the adjustment period, without any TMS-evoked random errors to correct, subjects would have updated their perceptual decision based on their evolving memory of the cue. The memory that subjects consulted must have had all of the serial dependence missing from their initial saccade, because post-saccade adjustments brought the final eye position to a location equivalent to that of the no TMS baseline. We conclude that serial dependence in the initial saccade is determined (at least in part) by a population vector in the LPFC. Subsequent adjustments seem to draw from the decision vectors in other areas—perhaps other parts of frontal cortex—which would have been unaffected by TMS to LPFC.

In our second experiment, cTBS to all three frontal sites decreased serial dependence. One interpretation of this result is that the mechanism responsible for serial dependence—which we propose is synaptic augmentation—is present throughout the lateral frontal cortex. Many neural populations generate decision vectors simultaneously. Synaptic dynamics in each circuit introduce a shift toward the previous trial's decision, and decision-making samples from these. In this interpretation, the decision vectors across cortical regions are largely redundant, at least with respect to serial dependence. Of course, neurons in the lateral frontal cortex are devoted to many things unrelated to serial dependence, and detailed reviews have been written on the evidence for functional differentiation (unrelated to serial dependence) along the anterior–posterior axis (e.g., Badre & D'Esposito, 2009; Badre & Nee, 2018).

Another interpretation is that the apparent redundancy of areas across the frontal cortex for serial dependence is an artifact of our use of cTBS. The concern would be that the 40 seconds of continuous stimulation caused not just long-lasting but also spatially widespread decreases in neural excitability, disrupting—possibly indirectly, via network interactions—mostly the same large swath of frontal cortex in every condition. The most direct evidence we have that three distinct regions were targeted in our study comes from the previously published analysis of this dataset (Rahnev et al., 2016). This analysis revealed a triple dissociation among the aPFC, LPFC, and PCS: stimulation of the aPFC increased subjects' metacognitive ratings (the correspondence between reported confidence and decision accuracy), stimulation of the LPFC decreased the effect of the speed or accuracy instruction on reaction times, and stimulation of the PCS decreased the effect of the pre-cue on

reaction times. That said, repetitive stimulation of even a single cortical neuron can have widespread consequences. For example, in a study by Li, Poo, and Dan (2009), a few minutes of pulsed current injections to just one neuron in rat cortex induced a long-lasting switch in the global state of the brain, from slow-wave sleep to rapid eye movement sleep (and vice versa). Although the brief burst of action potentials induced by a single pulse of TMS is restricted to neurons within 2 mm of the stimulation site (Romero et al., 2019), it is possible that repetitive stimulation would cause network interactions sufficient to trigger some sort of global change in cortical functionality that decreased serial dependence. Repeating our second experiment with a more transient manipulation—such as single pulse TMS—might reveal areal differences that cTBS has obscured.

We have characterized the immediate effect of TMS as a decrease in contrast between the most and least active neurons in the targeted circuit. Does this decrease in contrast have anything to do with the perceived contrast of the stimulus? When visual stimuli are presented at low contrast, serial dependence increases (Manassi, Liberman, Kosovicheva, Zhang, & Whitney, 2018). Other manipulations that decrease perceptual certainty increase serial dependence—such as when stimuli are oriented away from cardinal axes (Cicchini, Mikellidou, & Burr, 2017; Cicchini et al., 2018), embedded in noise (Gallagher & Benton, 2022), or presented at low spatial frequency (Cicchini et al., 2018; Ceylan, Herzog, & Pascucci, 2021). We see no reason to infer that TMS to frontal cortex has the effect of decreasing perceptual certainty. We interpret the decision vectors in frontal cortex as post-perceptual. Noise injected into the frontal cortex causes random motor errors (PCS, Experiment 1) and/or local failures to fully implement serial dependence (LPFC, Experiment 1; all three frontal regions, Experiment 2), not perceptual uncertainty.

The notion that serial dependence operates on post-perceptual decision variables fits with recent research on the oculomotor tracking of visual motion. Goettker and Stewart (2022) had subjects first track a cartoon car moving at either 5°/s or 15°/s, and then track a probe stimulus moving at 10°/s. The probe stimulus was either a cartoon car or a Gaussian blob. The velocity at which subjects tracked the probe was biased toward the velocity for the prior cartoon, regardless of whether the probe stimulus was itself another cartoon car. First, this finding reflects the point we made in the Introduction about serial dependence being informationally encapsulated (Fodor, 1983). Even when observers know that they are now viewing a blob that has nothing to do with the previous cartoon car, serial dependence occurs. We believe this finding fits with a post-perceptual origin for serial dependence, because the commonality between the car and blob in this experiment is at the decision level—a decision about how to track has to be made for both. Aside from motion, they share no visual features. The car and blob may evoke similar activity in motion-sensitive area hV5/MT+ in the occipital cortex, but presumably evoke quite different patterns of activity in the other early visual cortical areas. We noted in the Introduction that TMS to hV5/MT+ during a visual motion task had no effect on serial dependence (de Azevedo Neto & Bartels, 2021). Serial dependence in this task (as in ours) may originate in the decision circuitry of frontal cortex, where the neurons activated by task-relevant car and blob stimuli would likely be largely overlapping.

In a second experiment, Goettker and Stewart (2022) adjusted the cartoon so observers would interpret the car as being farther away. This adjustment induced an altered sense of velocity, because far-away objects are generally interpreted as moving faster in reality than their visual appearance indicates. Unsurprisingly, observers were still able to track the cartoon at the literal velocity of the pixels on the screen, and serial effects were toward the literal velocity of the prior stimulus, not toward the interpretation given to it. This result shows that serial dependence is implemented in the brain so as to allow for sensible interaction with the environment. It would be strange indeed if watching NASCAR on TV induced eye movements 100 mph faster than watching an Olympic track event. The authors claim that this result can be taken as evidence for an early perceptual origin of serial dependence. The argument seems to be that, if serial dependence happened at the level of the post-perceptual decision, it would have to incorporate the interpretation given to the stimulus and ignore the literal velocity. We see no reason to accept this argument. The distinction between the literal image velocity and the interpretation is available to post-perceptual decision-making (which is what makes appropriate action planning in response to the video possible).

Stronger evidence that serial dependence is integrated early into perceptual processing comes from a recent study by Cicchini, Benedetto, and Burr (2021). In their design, the response observers made for a stimulus was susceptible to influence from both contemporaneous flanking stimuli and the preceding stimulus at the same location. The pattern of errors was such that observers' perceptual estimates must first have been shifted toward the preceding stimulus and only afterward shifted away from the flankers. Yet the shift away from flankers results in an obvious perceptual illusion, termed the tilt illusion (see Figure 1 in Clifford, 2014 to verify the illusion for yourself). We believe that this result implies that serial dependence should also produce an illusion. To date, a clear perceptual illusion for serial dependence has not been demonstrated. Various articles (e.g., Manassi & Whitney, 2022) refer to the serial dependence bias as an illusion, but alternative explanations for their

results are plausible. Genuine illusions can be verified by each observer subjectively. The observer knows, for example, that a particular grating is vertical, and yet cannot help that it looks tilted. A paradigm capable of producing this sort of experience for serial dependence has not yet entered the literature. Adaptation, a bias in the direction exactly opposite serial dependence, does produce an illusion. We believe that a carefully designed stimulus sequence should be able to reveal a subjectively verifiable illusion corresponding with serial dependence if it is indeed perceptual in nature. This would be an important direction for future research.

Does the Cicchini et al. (2021) result imply that serial dependence originates in early visual cortex? Visual surround effects—of which the flanker effect of Cicchini et al. (2021) is one—are present in the evoked responses of neurons as low in the visual cortical hierarchy as V1 (Schwartz, Hsu, & Dayan, 2007). That said, surround effects are slow to develop after stimulus onset and depend on feedback from higher areas (Keller, Roth, & Scanziani, 2020). Bidirectional interactions between the frontal and occipital cortex may be required to integrate the surround effect into a representation that already includes serial dependence. Although counter-intuitive, it is possible that, in the course of these interactions, some contributions from the frontal cortex precede contributions from the occipital cortex. Thus, the finding that serial dependence precedes the flanker effect need not imply any particular anatomical arrangement—such as that serial dependence must be driven by neurons as low in the cortical hierarchy as V1, where flanker effects have been observed.

In our first experiment, we found no evidence that PPC contributes to serial dependence. Other studies have indicated that PPC does play a role in serial dependence. Inactivation of mouse PPC suppressed serial dependence in an auditory decision-making task (Akrami, Kopec, Diamond, & Brody,2018). In a study that measured human cortical activity using magnetoencephalography during a visual motion discrimination task, gamma-band power in the intraparietal sulcus tracked the previous trial's decision specifically in subjects who were biased to repeat choices (Urai & Donner, 2022). Our results suggest that this neural signature of the previous trial in human PPC either does not contribute causally to serial dependence or does not generalize from motion discrimination to spatial delayed response tasks. Another possibility is that the delivery of TMS in our experiment was mistimed to detect the influence of PPC. In the Akrami et al. (2018) study, mice could not prepare their response until two sounds separated in time had been presented, and inactivation specifically during the delay period between these two stimuli removed serial dependence. Our experiment allowed subjects to prepare their response immediately upon perception of a single stimulus. Our application of TMS at the midpoint of the delay period may have been too late to alter the PPC's contribution to serial dependence. We note, however, that TMS to PPC in our experiment did decrease accuracy (Mackey & Curtis, 2017); the null result was specific to serial dependence. Further research is needed to clarify whether and when the PPC affects visual serial dependence in humans.

When consecutive stimuli were on opposite sides of fixation in our second experiment, subjects were biased to alternate their motor response. We considered that subjects might have been susceptible to a Simon effect—biased to press the left response button to a leftward cue (and right button to a rightward cue). Such an effect would have resulted in a trial-to-trial bias to repeat choices for the same location and alternate them for opposite locations. However, we found no evidence of a Simon effect in participants' baseline responses without TMS. The bias to alternate responses was not affected by cTBS to any of the sites we targeted in frontal cortex. That cTBS had different effects on 1) positive serial dependence for the same location and 2) the alternation bias for opposite locations suggests that these are two distinct biases with distinct neural mechanisms. This interpretation was not obvious a priori. The repetition and alternation biases could, in principle, have shared the same neural implementation as two branches of a unitary decision policy for managing uncertainty (if same location, respond same; if different location, respond different).

Urai and Donner (2022) found that response alternation during visual motion discrimination was predicted by beta-band power in primary motor and premotor cortex. This suggests a division of labor along the anterior–posterior axis in frontal cortex, with more anterior areas (aPFC, LPFC, and PCS) contributing to response repetition and more posterior areas (premotor and motor cortex) to response alternation. Interpretation of the alternation bias in our experiment as originating from motor rather than visual circuitry seems reasonable in that the bias does not depend on retinotopic overlap between consecutive stimuli. It may be that the motor system briefly adapts to every motor response and that positive serial dependence overrides the negative motor bias when there is retinotopic continuity with the preceding trial. The premotor cortex, which has been linked to both repetition (de Azevedo Neto & Bartels, 2021) and alternation (Urai & Donner, 2022), may be a hub at which these competing biases are resolved.

Our suggestion that the motor system is susceptible to adaptation that serial dependence must override raises an alternative interpretation of the first result we mentioned in this Discussion. We argued that, because post-saccade adjustments in Experiment 1 exhibited serial dependence, they cannot have been corrections of random motor errors exclusively. But what if post-saccade adjustments were corrections for

motor adaptation? What if, relative to the subject's intention, the initial saccade was biased away from the saccade direction of the preceding trial? If the subject could detect this error, his attempts to correct it would seem in our analysis to be movements attracted to the preceding trial's cue location. A similar argument could be made that TMS to LPFC in this experiment increased motor adaptation in the initial saccade, and that we misinterpreted this as decreased serial dependence. We believe that, considered en masse, the evidence from both experiments supports our original conclusions. However, much remains to be learned about the neural implementations of both serial dependence and adaptation. The experiments reported in this article provide a starting point for understanding the role of lateral frontal cortex in history-dependent perceptual decision-making.

Keywords: serial dependence, frontal cortex, decision making, transcranial magnetic stimulation, parietal cortex

Acknowledgments

D. P. Bliss thanks Jennifer M. Bliss for discussions that helped with the framing of the Introduction.

Supported by the National Eye Institute (R01 EY-016407, R01 EY-027925, and R01 EY-033925 to C. E. Curtis) and NIH Grants MH63901 and NS79698.

Commercial relationships: none.
Corresponding author: Daniel P. Bliss.
Email: daniel.p.bliss@gmail.com.
Address: Citizen Science Program, Bard College, Annandale-On-Hudson, NY 12504, USA.

References

Akrami, A., Kopec, C. D., Diamond, M. E., & Brody, C. D. (2018). Posterior parietal cortex represents sensory history and mediates its effects on behavior. *Nature, 554*, 368–372, doi:10.1038/nature25510.

Badre, D., & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nature Reviews Neuroscience, 10*(9), 659–669, doi:10.1038/nrn2667.

Badre, D., & Nee, D. E. (2018). Frontal cortex and the hierarchical control of behavior. *Trends in Cognitive Sciences, 22*(2), 170–188, doi:10.1016/j.tics.2017.11.005.

Barbosa, J., Stein, H., Martinez, R. L., Galan-Gadea, A., Li, S., Dalmau, J., … Compte, A. (2020). Interplay between persistent activity and activity-silent dynamics in the prefrontal cortex underlies serial biases in working memory. *Nature Neuroscience, 23*(8), 1016–1024, doi:10.1038/s41593-020-0644-4.

Bliss, D. P., & D'Esposito, M. (2017). Synaptic augmentation in a cortical circuit model reproduces serial dependence in visual working memory. *PLoS One, 12*(12), e0188927, doi:10.1371/journal.pone.0188927.

Bliss, D. P., Sun, J. J., & D'Esposito, M. (2017). Serial dependence is absent at the time of perception but increases in visual working memory. *Scientific Reports, 7*(1), 14739, doi:10.1038/s41598-017-15199-7.

Bonaiuto, J. J., de Berker, A., & Bestmann, S. (2016). Response repetition biases in human perceptual decisions are explained by activity decay in competitive attractor models. *eLife, 5*, e20047, doi:10.7554/eLife.20047.001.

Ceylan, G., Herzog, M. H., & Pascucci, D. (2021). Serial dependence does not originate from low-level visual processing. *Cognition, 212*, 104709, doi:10.1016/j.cognition.2021.104709.

Christophel, T. B., Klink, P. C., Spitzer, B., Roelfsema, P. R., & Haynes, J.-D. (2017). The distributed nature of working memory. *Trends in Cognitive Sciences, 21*(2), 111–124, doi:10.1016/j.tics.2016.12.007.

Cicchini, G. M., Benedetto, A., & Burr, D. C. (2021). Perceptual history propagates down to early levels of sensory analysis. *Current Biology, 31*(6), 1245–1250, doi:10.1016/j.cub.2020.12.004.

Cicchini, G. M., Mikellidou, K., & Burr, D. C. (2017). Serial dependencies act directly on perception. *Journal of Vision, 17*(14), 1–9, doi:10.1167/17.14.6.

Cicchini, G. M., Mikellidou, K., & Burr, D. C. (2018). The functional role of serial dependence. *Proceedings of the Royal Society of London: Biological Sciences, 285*, 20181722, doi:10.1098/rspb.2018.1722.

Clifford, C. W. G. (2014). The tilt illusion: Phenomenology and functional implications. *Vision Research, 104*, 3–11, doi:10.1016/j.visres.2014.06.009.

Clifford, C. W. G., Wenderoth, P., & Spehar, B. (2000). A functional angle on some after-effects in cortical vision. *Proceedings of the Royal Society of London: Biological Sciences, 267*, 1705–1710, doi:10.1098/rspb.2000.1198.

Compte, A., Brunel, N., Goldman-Rakic, P. S., & Wang, X. J. (2000). Synaptic mechanisms and network dynamics underlying spatial working memory in a cortical network model. *Cerebral Cortex, 10*(9), 910–923, doi:10.1093/cercor/10.9.910.

de Azevedo Neto, R. M., & Bartels, A. (2021). Disrupting short-term memory maintenance in premotor cortex affects serial dependence in visuomotor integration. *Journal of Neuroscience, 41*(45), 9392–9402, doi:10.1523/JNEUROSCI.0380-21.2021.

Engel, T. A., & Wang, X.-J. (2011). Same or different? A neural circuit mechanism of similarity-based pattern match decision making. *Journal of Neuroscience, 31*(19), 6982–6996, doi:10.1523/JNEUROSCI.6150-10.2011.

Fischer, J., & Whitney, D. (2014). Serial dependence in visual perception. *Nature Neuroscience, 17*(5), 738–743, doi:10.1038/nn.3689.

Fleming, S. M., Huijgen, J., & Dolan, R. J. (2012). Prefrontal contributions to metacognition in perceptual decision making. *Journal of Neuroscience, 32*(18), 6117–6125, doi:10.1523/JNEUROSCI.6489-11.2012.

Fodor, J. A. (1983). *Modularity of mind*. Cambridge, MA: MIT Press.

Fritsche, M., Mostert, P., & de Lange, F. P. (2017). Opposite effects of recent history on perception and decision. *Current Biology, 27*(4), 590–595, doi:10.1016/j.cub.2017.01.006.

Gallagher, G. K., & Benton, C. P. (2022). Stimulus uncertainty predicts serial dependence in orientation judgements. *Journal of Vision, 22*(1), 1–14, doi:10.1167/jov.22.1.6.

Goettker, A., & Stewart, E. E. M. (2022). Serial dependence for oculomotor control depends on early sensory signals. *Current Biology, 32*(13), 2956–2961, doi:10.1016/j.cub.2022.05.011.

Heekeren, H. R., Marrett, S., & Ungerleider, L. G. (2008). The neural systems that mediate human perceptual decision making. *Nature Reviews Neuroscience, 9*(6), 467–479, doi:10.1038/nrn2374.

Hempel, C. M., Hartman, K. H., Wang, X.-J., Turrigiano, G. G., & Nelson, S. B. (2000). Multiple forms of short-term plasticity at excitatory synapses in rat medial prefrontal cortex. *Journal of Neurophysiology, 83*(5), 3031–3041, doi:10.1152/jn.2000.83.5.3031.

Huang, Y.-Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex. *Neuron, 45*(2), 201–206, doi:10.1016/j.neuron.2004.12.033.

Jackman, S. L., & Regehr, W. G. (2017). The mechanisms and functions of synaptic facilitation. *Neuron, 94*(3), 447–464, doi:10.1016/j.neuron.2017.02.047.

Keller, A. J., Roth, M. M., & Scanziani, M. (2020). Feedback generates a second receptive field in neurons of the visual cortex. *Nature, 582*, 545–549, doi:10.1038/s41586-020-2319-4.

Li, C.-Y. T., Poo, M.-M., & Dan, Y. (2009). Burst spiking of a single cortical neuron modifies global brain state. *Science, 324*(5927), 643–646, doi:10.1126/science.1169957.

Mackey, W. E., & Curtis, C. E. (2017). Distinct contributions by frontal and parietal cortices support working memory. *Scientific Reports, 7*(1), 6188, doi:10.1038/s41598-017-06293-x.

Manassi, M., Liberman, A., Kosovicheva, A., Zhang, K., & Whitney, D. (2018). Serial dependence in position occurs at the time of perception. *Psychonomic Bulletin & Review, 25*, 2245–2253, doi:10.3758/s13423-018-1454-5.

Manassi, M., & Whitney, D. (2022). Illusion of visual stability through active perceptual serial dependence. *Science Advances, 8*, eabk2480, doi:10.1126/sciadv.abk2480.

Mongillo, G., Barak., O., & Tsodyks, M. (2008). Synaptic theory of working memory. *Science, 319*(5869), 1543–1546, doi:10.1126/science.1150769.

Papadimitriou, C., Ferdoash, A., & Snyder, L. H. (2015). Ghosts in the machine: Memory interference from the previous trial. *Journal of Neurophysiology, 113*(2), 567–577, doi:10.1152/jn.00402.2014.

Rahnev, D., Nee, D. E., Riddle, J., Larson, A. S., & D'Esposito, M. (2016). Causal evidence for frontal cortex organization for perceptual decision making. *Proceedings of the National Academy of Sciences of the United States of America, 113*(21), 6059–6064, doi:10.1073/pnas.1522551113.

Romero, M. C., Davare, M., Armendariz, M., & Janssen, P. (2019). Neural effects of transcranial magnetic stimulation at the single-cell level. *Nature Communications, 10*(1), 2642, doi:10.1038/s41467-019-10638-7.

Schwartz, O., Hsu, A., & Dayan, P. (2007). Space and time in visual context. *Nature Reviews Neuroscience, 8*, 522–535, doi:10.1038/nrn2155.

St. John-Saaltink, E. S., Kok, P., Lau, H. C., & de Lange, F. P. (2016). Serial dependence in perceptual decisions is reflected in activity patterns in primary visual cortex. *Journal of Neuroscience, 36*(23), 6186–6192, doi:10.1523/JNEUROSCI.4390-15.2016.

Stokes, M. G. (2015). "Activity-silent" working memory in prefrontal cortex: A dynamic coding framework. *Trends in Cognitive Sciences, 19*(7), 394–405, doi:10.1016/j.tics.2015.05.004.

Urai, A. E., & Donner, T. H. (2022). Persistent activity in human parietal cortex mediates perceptual choice repetition bias. *Nature Communications, 13*, 6015, doi:10.1038/s41467-022-33237-5.

Wang, X.-J. (2002). Probabilistic decision making by slow reverberation in cortical circuits. *Neuron, 36*(5), 955–968, doi:10.1016/S0896-6273(02)01092-9.

Wang, Y., Markram, H., Goodman, P. H., Berger, T. K., Ma, J., & Goldman-Rakic, P. S. (2006). Heterogeneity in the pyramidal network of the medial prefrontal cortex. *Nature Neuroscience, 9*(4), 534–542, doi:10.1038/nn1670.

Wong, K.-F., & Wang, X.-J. (2006). A recurrent network mechanism of time integration in perceptual decisions. *Journal of Neuroscience, 26*(4), 1314–1328, doi:10.1523/JNEUROSCI.3733-05.2006.

Zucker, R. S., & Regehr, W. G. (2002). Short-term synaptic plasticity. *Annual Review of Physiology, 64*, 355–405, doi:10.1146/annurev.physiol.64.092501.114547.