Review

Cortical mechanisms for trans-saccadic memory and integration of multiple object features

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Constructing an internal representation of the world from successive visual fixations, i.e. separated by saccadic eye movements, is known as trans-saccadic perception. Research on trans-saccadic perception (TSP) has been traditionally aimed at resolving the problems of memory capacity and visual integration across saccades. In this paper, we review this literature on TSP with a focus on research showing that egocentric measures of the saccadic eye movement can be used to integrate simple object features across saccades, and that the memory capacity for items retained across saccades, like visual working memory, is restricted to about three to four items. We also review recent transcranial magnetic stimulation experiments which suggest that the right parietal eye field and frontal eye fields play a key functional role in spatial updating of objects in TSP. We conclude by speculating on possible cortical mechanisms for governing egocentric spatial updating of multiple objects in TSP.

Keywords: trans-saccadic perception; saccades; spatial updating; parietal eye fields; frontal eye fields; transcranial magnetic stimulation

1. INTRODUCTION

One of the longstanding problems in cognitive neuroscience, and vision science in particular, is how we perceive the visual world as richly detailed and unified despite the discontinuous and sparsely detailed manner in which it is visually processed. To elaborate, one typically makes three to five rapid eye movements, called saccades, per second [1]. Since visual processing is partially suppressed every time a saccade is made [2], useful vision is limited to discrete eye fixations when the eyes are relatively stationary. The perceptual experience of a continuous and unified visual world from disparate fixations separated by saccades is known as trans-saccadic perception (TSP) [3]. It is generally thought that TSP involves building an internal representation of an object or scene through the accumulation of visual information across saccades as the eyes are directed to the object's or scene's different regions. This version of TSP implies an interaction of two central processes: (i) the storage of visual information across a saccade in memory, and (ii) the spatial updating of stored information by taking into account the eye's rotation during the saccade.

This view raises a number of questions. Specifically, how is stored visual information from pre- and post-saccadic stimuli spatiotopically integrated across saccades? How many objects can be stored across saccades in so-called trans-saccadic memory? How does this compare with simple visual working memory

without eye movements? And what are the underlying cortical mechanisms that govern egocentric spatial updating of multiple objects in TSP? In this paper, we review the literature relating to these issues with a focus on our recent behavioural and transcranial magnetic stimulation (TMS) studies, finally speculating on the possible mechanisms.

2. SOLVING THE SPACE CONSTANCY PROBLEM

First, we will cover the necessary background of the cognitive literature related to TSP before proceeding to the topic of the neurophysiology of TSP. One central aspect of TSP is related to the classic problem of space constancy [4]. When the eyes move, the image of the visual world moves across the retina. However, our perceptual experience does not match this raw retinal data of the world moving. We still perceive a stable and unmoving visual world when we make eye movements. This visual stability during eye movements (and also head movements) is known as space constancy.

The brain could use two sources of visual information to maintain spatial constancy across saccades: allocentric cues and egocentric cues. Allocentric cues are used to derive an object's location by its relative position to other objects in the world, independent of the observer. Space constancy across saccades could be maintained by matching pre- and post-saccadic allocentric information from the visual scene while the attributes of the saccade itself are disregarded [5–8]. However, one problem with allocentric mechanisms is that they require a certain amount of visual processing time after the saccade [9], whereas optimal TSP

would be instantaneous, or even predictive. Another potential problem is that the retinal overlap between pre- and post-saccadic perspectives might sometimes be insufficient to use allocentric cues.

An alternative mechanism that deals with both of these problems is to use egocentric information, somehow combining the original retinal location of the visual stimulus with oculomotor information to re-compute its location during the saccade (e.g. [10]). This requires that the visual system has access to oculomotor information related to either eye position and/or the metrics of the saccade [11–14].

3. EXPERIMENTAL DEMONSTRATIONS OF EGOCENTRIC MECHANISMS FOR TSP

Normally both allocentric and egocentric cues for TSP are available, and an optimal visual system should make use of both, depending on which is most reliable for a particular task [15]. One advantage of using allocentric cues in the maintenance of spatial constancy across saccades is that the relative positions of objects do not tend to change when the eyes move. Indeed, several studies have shown that when allocentric cues are available, trans-saccadic memory of a target object's position is encoded according to its relative spatial relationship to other stimuli in the environment [7,16,17]. This allocentric coding of a target's location in trans-saccadic memory has been shown to be superior to remembering a target's location when it is presented in isolation [18]. However, a recent experiment showed that even when allocentric cues are present across eye movements, subjects relied more heavily on their egocentric sense of target location, especially when the allocentric cue was not stable [19]. But what about the contribution of egocentric mechanisms to TSP? It is difficult to study allocentric mechanisms in the absence of egocentric mechanisms in healthy subjects, but egocentric mechanisms are easily studied in the laboratory by removing allocentric cues. Surprisingly, few psychophysical studies have directly tested the role of egocentric measures of saccade metrics in the spatiotopic integration of perceptual features across saccades. Two such studies [20,21] indicate that pre- and post-saccadic stimuli can be spatially updated and integrated as a more complex representation by relying solely on the egocentric measures of the saccade that presumably arise from internal oculomotor signals. The experimental paradigm and main results from our study [21] are shown in figure 1. Again, one expects that in normal daylight conditions both mechanisms—egocentric and allocentric—are used, the first being faster and the second being more precise [9].

4. VISUAL MEMORY CAPACITY IN TSP

Despite the intuitive and appealing assumption that highly detailed visual information is accumulated and spatially fused across saccades in a point-to-point manner, several studies show that this is not the case [22–28]. These sets of findings have sometimes led to a viewpoint of the opposite extreme: that there is no need to construct and maintain an internal model of the visual world in memory across saccades because

information of the visual world is constantly available 'out there'; and, in a sense, the world itself acts as a kind of 'external memory store' [26,29,30].

Currently, most investigators take a view which is intermediate between the spatiotopic fusion hypothesis and the external memory hypothesis, i.e. it is generally believed that simple visual working memory without eye movements has a fixed capacity of about three to four salient items [31–36]. However, this fixed-capacity model of visual working memory has recently been challenged. Other models postulate that the capacity of visual working memory is either contingent on the complexity of the stored items [37] or a limited resource distributed between a non-fixed number of items in the visual scene [38]. However, these alternative views of visual working memory remain controversial ([39–41]; but also see [42]).

Visual working memory appears to activate separate cortical systems for object identity and object location (i.e. spatial information). Functional brain imaging studies of human prefrontal cortex activity during visual working memory tasks have shown that object memory is associated with ventro-lateral prefrontal cortex activity, whereas spatial memory is associated with dorso-lateral prefrontal cortex activity [43–45]; but for a different interpretation of the role this dissociation of prefrontal activity might play in working memory, see [46]. This dissociation of object and spatial working memory has also been found between the ventral and dorsal visual processing streams in the human brain. Object working memory is governed by occipital and inferotemporal cortical areas of the ventral stream, whereas spatial working memory is governed by dorsal streams areas, particularly of the right posterior parietal cortex and premotor cortex (specifically an area called the frontal eye fields, FEFs) [47–50]. In particular, enhancement of memory-related activity of the human intraparietal sulcus has been shown to be strongly correlated with the number of objects held in visual working memory, up to the capacity limit of about four items [51]. However, results from another functional brain imaging study show that in addition to the memory-related activity in the inferior intraparietal sulcus that is fixed to the number of stored items (up to four), memory-related activity in the superior intraparietal sulcus and lateral occipital areas are mediated by the complexity of these representations [52]. These findings are suggestive of a model of visual working memory that is a hybrid of the fixed-capacity and variable-capacity views.

It also turns out that the capacity of visual working memory is not reduced when observers are required to remember the details and locations of multiple objects across a saccade, apparently regardless of the type of stimuli used [53–58]. Furthermore, visual working memory and memory in TSP (so-called trans-saccadic memory) has also been shown to have similar storage durations and both are resistant to masking effects [59]. It has thus been argued that, since they show similar properties, visual working memory and TSP share essentially the same storage mechanisms [59,60].

However, TSP is more complicated than memorizing objects within a single fixation. Remembering what and where objects are in a scene across a saccade
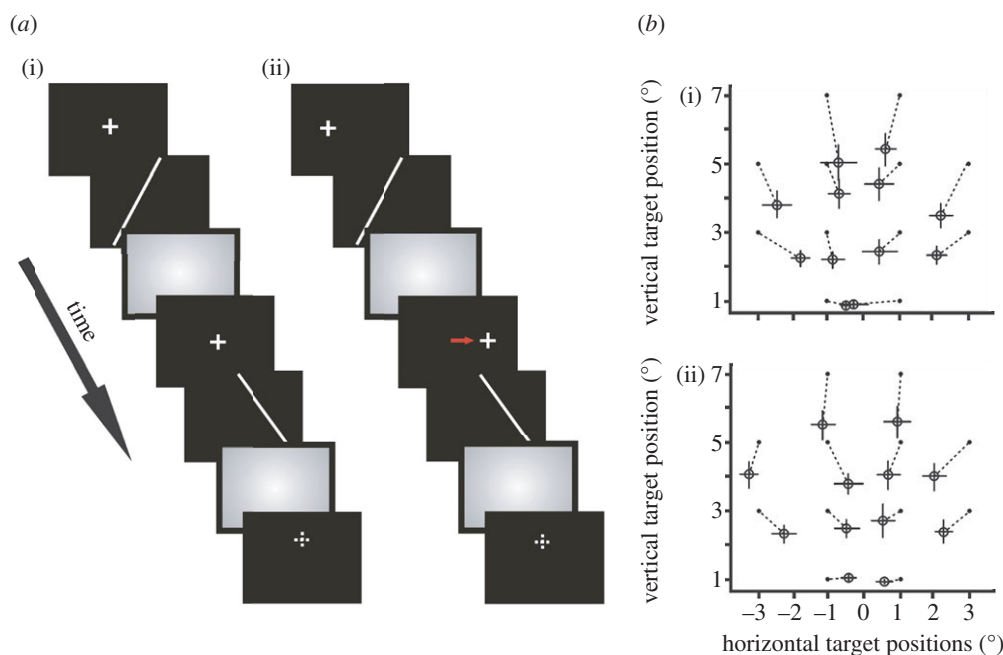
Figure 1. Trans-saccadic integration task and sample data (modified from [21]). (*a*) The experimental paradigm consisted of (i) a fixation task and (ii) a saccade task. In both tasks, subjects were presented with two orienting bars shown as the white bars (40 ms), each followed by a visual mask (300 ms). Subjects viewed both bars either while maintaining eye fixation on the fixation-cross (shown as white cross) at head-centre (fixation task) or by fixating each bar in turn by making a saccade depicted by the red arrow (saccade task). Subjects used a computer-mouse to move a cursor (depicted by the dotted cross) to where they estimated the bars would have intersected had they been presented simultaneously. (*b*) Mean pointing positions (open circles) for each possible intersection position (specified by a dashed line to closed circle) across all subjects ($n = 7$) in (i) the fixation task and (ii) the saccade task. The horizontal and vertical standard deviations of pointing performance for a particular intersection are indicated by the length of the bars within each open circle. Pointing was statistically the same between the fixation task and saccade task. Integrating the two bars in the fixation task is a matter of remembering their orientations and positions in retinal coordinates. In the saccade task, both pre-saccadic and post-saccadic bars are encoded in the same retinal coordinates, i.e. the fovea. To perform the saccade task accurately, subjects must be able to integrate the bars according to their spatial coordinates (not tied to their retinal coordinates) by taking into account the change in eye position.

suggests that TSP involves additional computational demands that the visual system must solve to spatially update stored object representations held in memory. As the findings by Hayhoe *et al.* [20] and Prime *et al.* [21] suggest, one way the visual system might spatially update stored object representations across the saccade in trans-saccadic memory is to use the egocentric measures of the saccade to take the change of eye position into account.

This possibility was recently tested in our laboratory [58]. We estimated the storage capacity of simple feature objects in both a visual working memory task (comparing stimuli presented within a single fixation) and a trans-saccadic memory task (comparing stimuli presented in different fixations separated by a saccade). The details of these tasks are shown in figure 2. Briefly, in the main task testing trans-saccadic memory, subjects were required to compare the feature details of pre- and post-saccadic memory probes presented at the same spatial location. As in our previous study, we eliminated allocentric cues so that subjects were forced to rely on their egocentric measures of the saccade to match the pre- and post-saccadic memory probes.

Our data revealed no significant differences in the accuracy of comparing luminance or orientation within a single fixation (the *fixation task*) and in different fixations (the *saccade task*) (figure 3a). To estimate

the memory capacity we used a simple statistical model that generated a set of predictive curves for different hypothetical storage capacities (shown in figure 3b), and calculated the mean square residual errors between these predictive curves and the data curves to determine which curve predicting a specific memory capacity best fitted our data. Overall, we found the estimated numerical memory capacity in both the *fixation* and *saccade* tasks was three to four items (figure 3c). This finding is consistent with the results from previous trans-saccadic memory studies [53–57], and shows that an intervening saccade during the memory interval between target display and memory probe does not significantly reduce the number of objects subjects can remember.

Perhaps more importantly, we showed that subjects can use the egocentric sense of eye movement size and magnitude to solve the saccade task. We proposed that an efference copy of the oculomotor command was used to spatially update stored representations in a gaze-centred reference frame across the saccade, linked to more complex feature maps shared with the working memory system [21,58]. Thus, TSP may reflect a two-stage process where stored representations in visual working memory are synthesized with spatial updating processes that 'remap' these memory representations during the saccade (a similar hypothesis was put forth by Melcher & Colby [3]).
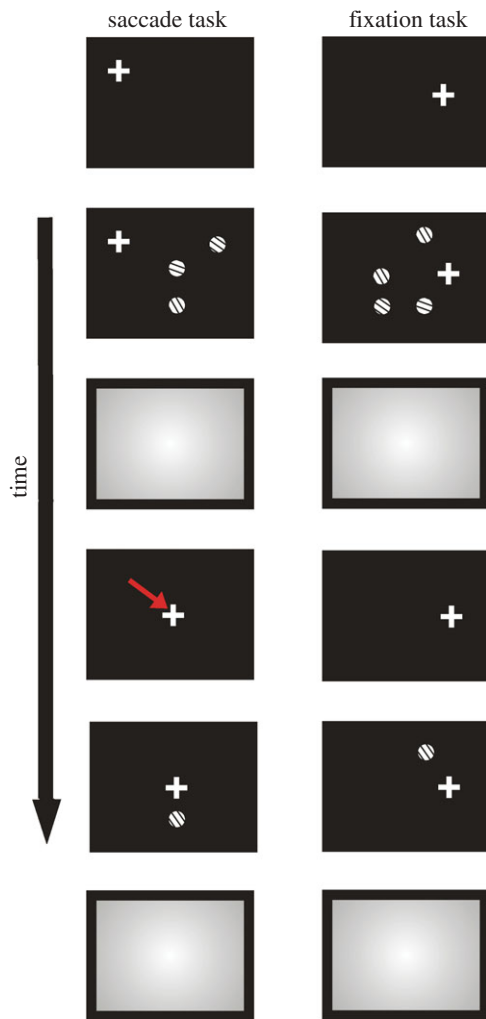
Figure 2. Experimental paradigm of trans-saccadic memory experiment (modified from [58]). Experimental paradigm testing trans-saccadic memory in saccade task and simple visual working memory without saccades in fixation task. Each trial in the saccade task began with a fixation-cross which was followed by a target display (100 ms) consisting of 1–15 feature objects, either grey circles of varying luminances or gabor patches of varying orientations. This target display was followed immediately by a mask (150 ms) and another fixation-cross in a different location. Subjects were instructed to saccade to the new fixation-cross as soon as it appeared, depicted by the red arrow. After the saccade a probe was presented (100 ms) at the same location as one of the feature objects in the target display. Subjects were required to perform a two-alternative force choice to indicate how the probe's features differed relative to the features of the target. The fixation task was identical to the saccade task except subjects maintained eye fixation through target display and probe presentations, as the fixation point remains fixed in the same position throughout the trial.

5. TMS STUDIES OF CORTICAL MECHANISMS GOVERNING TSP

Presently, little is known about the cortical mechanisms that govern TSP. Neurophysiological evidence of spatial updating during saccades, a key aspect of TSP, have been found in several areas of the monkey brain involved in different aspects of visual processing and saccade programming, such as the superior colliculus [62], extrastriate visual areas (e.g. [63–67]),
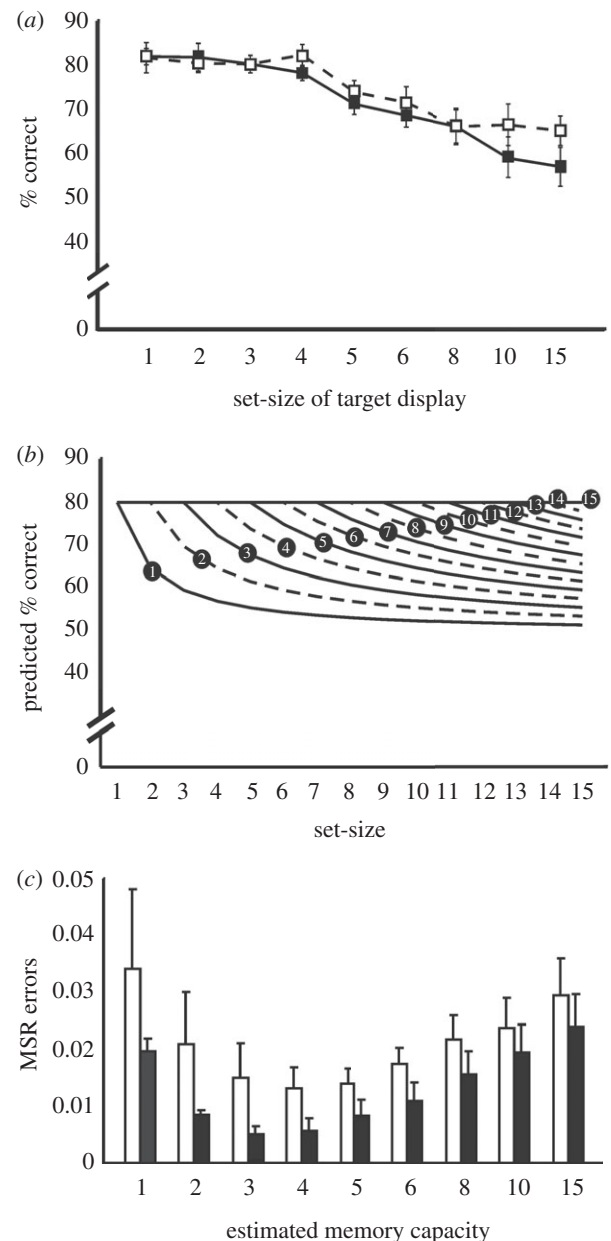

Figure 3. Main results of luminance comparisons in both the saccade and fixation tasks (modified from [58]). (*a*) Mean percentage correct across all subjects is plotted against set-size of target display for each task (saccade task, filled squares; fixation task, open squares). Error bars represent standard error. A goodness-of-fit test yielded no significant difference between the two tasks. (*b*) Simple predictive model. Each curve predicts percentage of correct responses as a function of set-size for each possible capacity of trans-saccadic memory. Theoretical capacities are indicated by the numbers above each curve. The curves are alternate solid and dashed only to make reading the figure easier. The predictive curves were generated from a computational model that took into account the maximum percentage correct at discriminating the feature objects with only one item as determined in a previous study [61] and remembering a random subset of multiple items in the target display (for more details about the computational model, see [58]). (*c*) To estimate our subjects' memory capacity in each task we calculated the mean square residual (MSR) errors to determine the best fit between the data curves and each predictive curve in this model. The least MSR errors indicated that subjects were able to remember about three to four items in both the saccade task (filled bars) and fixation task (open bars). A statistical comparison of the MSR errors between the saccade task and fixation task yielded no significant difference ($p = 0.69$).

the lateral intraparietal area [10,68], and the FEFs [69–71]. These studies show that the location of a remembered pre-saccadic stimulus encoded on the retinotopic map in these brain areas is spatially 'remapped' to reflect the stimulus's post-retinal location immediately before the saccade is executed. More recent functional magnetic resonance imaging (fMRI) studies have revealed similar remapping activity in the human brain. In their fMRI study, Merriam *et al.* [72] found remapping activity in the human parietal eye fields (PEFs), analogous to the monkey's lateral intraparietal suclus [73]. In their study, subjects were briefly presented with a visual stimulus in one visual hemifield, which elicited activity in their contralateral PEF, and then they had to make a saccade to bring the location of the now extinguished stimulus to the other hemifield, which resulted in activity shifting to the PEF in the opposite hemisphere (i.e. originally ipsilateral to the stimulus). In a follow-up study they also found remapping across hemispheres in the human visual cortex [74].

In another fMRI study, Medendorp *et al.* [75] also found remapping activity across hemispheres in different regions of the human posterior parietal cortex that correspond to the PEF and parietal reach region (for review of the different functional regions of the posterior parietal cortex see [76]). In their task, subjects were required to make either a delayed saccade or delayed pointing movement to a remembered target location after making an intervening saccade between target presentation and response. The novel results from this study show that remapping plays a role in updating spatial goals across saccades for goal-directed actions in a gaze-centred frame of reference. Further evidence of remapping activity for goal-directed actions was provided by a magnetoencephalography study that recorded parietal oscillatory activity from subjects performing a delayed anti-saccade task where a saccade is made to the opposite hemifield of a previously presented visual target [77]. Initial parietal gamma-band (40–100 Hz) activity that revealed enhanced activations contralateral to target location, reflecting maintenance of the memory representation of the target during the delay interval, was followed by sustained ipsilateral gamma activity, reflecting a remapping from stimulus-to-goal selectivity of the saccade.

This spatial remapping mechanism has been thought to play a role in maintaining perceptual stability of the visual world across saccades by anticipating the post-saccadic spatial image of the world [78]. Alternatively, and perhaps in line with the results from the cited studies by Medendorp *et al.* ([75] and Van Der Werf *et al.* [77]), Bays & Husain [79] have argued that the primary role of spatial remapping may be to aid sensorimotor control. They cite saccadic suppression of displacement studies (e.g. [80]) that show despite subjects' failure to perceive a visual target's intrasaccadic location shift, their online pointing movements showed corrections that accounted for the target's displacement. Bays & Husain [79] argue that these results are evidence that spatial remapping mechanisms are more involved in updating motor actions rather

than perception. Because spatial remapping seems to be the underlying neural mechanism for a trans-saccadic internal representation of object locations for motor control, we and others [3,21,58] have hypothesized that spatial remapping may also be used by the perceptual system to retain and update visual features across saccades. This hypothesis predicts that cortical areas involved in saccade-related remapping, such as the PEF and FEF, should also be involved in TSP.

To test this hypothesis, in two separate studies we applied TMS to the PEF and the FEF as subjects performed a trans-saccadic memory task [81,82]. TMS is a safe and non-invasive method of mapping cortical functions by using magnetic fields that pass through a subject's skull to stimulate a cortical area and measuring any perceptual or behavioural changes to the subject's performance in an experimental task [83]. TMS is usually associated with excitatory effects of the stimulated neural tissue, inducing a kind of 'neural noise', but low-frequency repetitive TMS has been shown to have an inhibitory effect, i.e. decreasing the cortical excitability [84]. Any ensuing change to task performance is taken as evidence that the stimulated brain region plays a functional role in the putative cognitive processes that are involved in performing the task [85,86].

In our first TMS study [81], we wanted to determine whether the PEF plays a functional role in TSP. We tested subjects' memory performance using the same basic experimental paradigm from our previous trans-saccadic memory experiment cited above shown in figure 2 [58]. Subjects were required to remember the orientation and locations of one to eight gabor patches and compare the orientation of one of the gabor patches with a similar looking memory probe presented in the same location. The memorized targets and the memory probe were presented either within the same fixation (the fixation task) or in separate fixations separated by a saccade (the saccade task). Note again that in the saccade task, subjects had to somehow account for eye movement in order to solve the spatial aspect of the task. Subjects performed both tasks while TMS was applied over either their left or right PEFs. TMS was delivered at one of three timings, 100, 200 or 300 ms after the presentation of the second fixation-cross. The second fixation-cross in the saccade task is the saccade-go signal, which means that these TMS timings occurred around the time of the subjects' saccade. All these TMS conditions were compared with a 'no TMS' baseline condition.

We found that in both the saccade and fixation tasks, subjects made significantly more errors when TMS was delivered over the right PEF, but not the left PEF, compared with the baseline No-TMS condition (figure 4*a*). In the saccade task, right PEF stimulation yielded TMS-induced errors in all three timing conditions (i.e. 100, 200 and 300 ms). However, we found the largest TMS effect in the saccade task at the 200 ms condition, the timing that most closely coincided with the time of the saccade. These errors in the saccade task were not due to changes to the saccade metrics (i.e. saccade

accuracy or latency). In the fixation task, right PEF stimulation yielded a similar disruption to the visual working memory task without a saccade, albeit to a lesser extent. This lateralized TMS effect to the right hemisphere is consistent with previous findings that suggest that the right hemisphere has a privileged role in a variety of visuospatial tasks [87–89], and is consistent with previous TMS studies that show stimulation applied only to the right posterior parietal cortex disrupts spatial remapping [90,91] and spatial working memory [92].

As in our earlier cited trans-saccadic memory study, we used our predictive model (shown in figure 3b) to estimate our subjects' memory capacity in both the no TMS condition and the right PEF TMS condition where we found TMS effects at the 200 ms timing. Recall that our model shows what performance we can expect from the subjects for a variety of different potential memory capacities. Figure 4b shows the mean square residual (MSR) errors calculated between the 200 ms data curves of each task from figure 4a and each predictive curve from our model. The least MSR errors indicate which predictive curve of a specific memory capacity best fits our data, which in this case is a memory capacity of three items in the no TMS condition for both tasks, replicating our previous findings. However, this memory capacity was reduced to one item at the 200 ms TMS condition, corresponding with the largest TMS-induced errors. This is consistent with a complete loss of spatial memory, in which case our task could still be solvable for one feature.

Our second TMS study was a duplicate of our PEF TMS study, but this time we applied TMS over the right and left FEF [82]. The main results showing TMS effects in this study are shown in figure 5. We found that magnetically stimulating either the left or right FEF elicited greater errors in the saccade task compared with a baseline no TMS condition (figure 5a). Like our PEF TMS results, these TMS-induced errors were greatest when the TMS pulse was delivered at 200 ms timing coinciding with the time of the saccade and not due to changes in the saccade metrics. In contrast, no TMS effect was found in the fixation task. And like our previous PEF TMS study, the observed TMS effects yielded a general reduction in the estimated memory capacity (figure 5b), down to one feature when the TMS pulse coincided with a saccade.

One difference between the PEF and FEF results was the TMS effects' region-specific cortical asymmetry. While trans-saccadic memory was disrupted only during right PEF TMS, disruption to trans-saccadic memory was found during TMS to both left and right FEF. We have suggested that this difference may be consistent with the view that the FEF and PEF subserve different functions in visuospatial processing and oculomotor control. The PEF has been likened to a salience map of object locations that integrates sensory and motor information for a variety of visuospatial tasks [99–101]. As mentioned earlier, the right hemisphere appears to have a privileged role in spatial processing (e.g. [87]). In contrast, the bilateral FEF TMS effect may reflect the FEFs role

in later stages of oculomotor processing downstream from the PEF, where there are less asymmetry effects on the saccade efference signals used for updating [102] necessary for solving the saccade task.

Another difference between the PEF and FEF results was the TMS effect for just one feature during PEF, but not FEF, stimulation. This is consistent with the posterior parietal cortex having a role in specifying some rudimentary features [103–105] or general attention [106]. Though the FEFs also have neurons involved in visual discrimination [107,108], we suggest that the FEF effect we observed may have been a more pure spatial effect due also in part to its task-dependence, occurring only in the saccade task. Our FEF TMS results are more consistent with another FEF TMS study that found TMS-induced disruption to spatial memory, but not object memory [109]. But note that TMS of both structures resulted in degraded memory for *multiple* objects.

These are not the first experiments to show that FEF and PEF are involved in short-term memory [47,51,110], but they were the first to demonstrate that they play a specific role in the trans-saccadic memory of multiple objects. These results link TSP and gaze-centred remapping in two ways. First circumstantially because both the PEF and FEF have been shown to participate in gaze-centred remapping [10,70]. More specifically, in both experiments, we found the strongest TMS effect when magnetic stimulation was applied around the time of the saccade. This is unlikely to have occurred if trans-saccadic integration were the product of placing object representations into a stable frame of reference (e.g. head, body or allocentric coordinates) before the occurrence of the saccade. Instead, we propose that the TMS-induced errors were due to TMS injecting 'neural noise' into the spatial remapping mechanisms that arise in the PEF [10,68,75] and FEF [69–71] around the time of a saccade, and that these signals are used for updating perceptual memory.

6. POSSIBLE CORTICAL MECHANISMS OF TSP

If the spatial remapping mechanisms found in the PEF and FEF are involved in TSP, as our data suggest, this leads to another question: how is spatial remapping used to update feature information across saccades? Visual processing in the cortex is segregated into two broadly separate pathways: one pathway, called the ventral stream, projects information from the visual cortex to the temporal cortex for object perception, and the other pathway, called the dorsal stream, projects visual information to the posterior parietal cortex for spatial perception and visuomotor action [111,112]. Thus, the question of how object feature information is spatially updated in trans-saccadic memory is synonymous with how these two visual streams that make up the visual system interact.

In our PEF TMS study [81], we addressed this issue by considering four different possibilities (figure 6). Note that our TMS results do not offer any definitive conclusions about which of these possibilities are the most probable—our intention is to
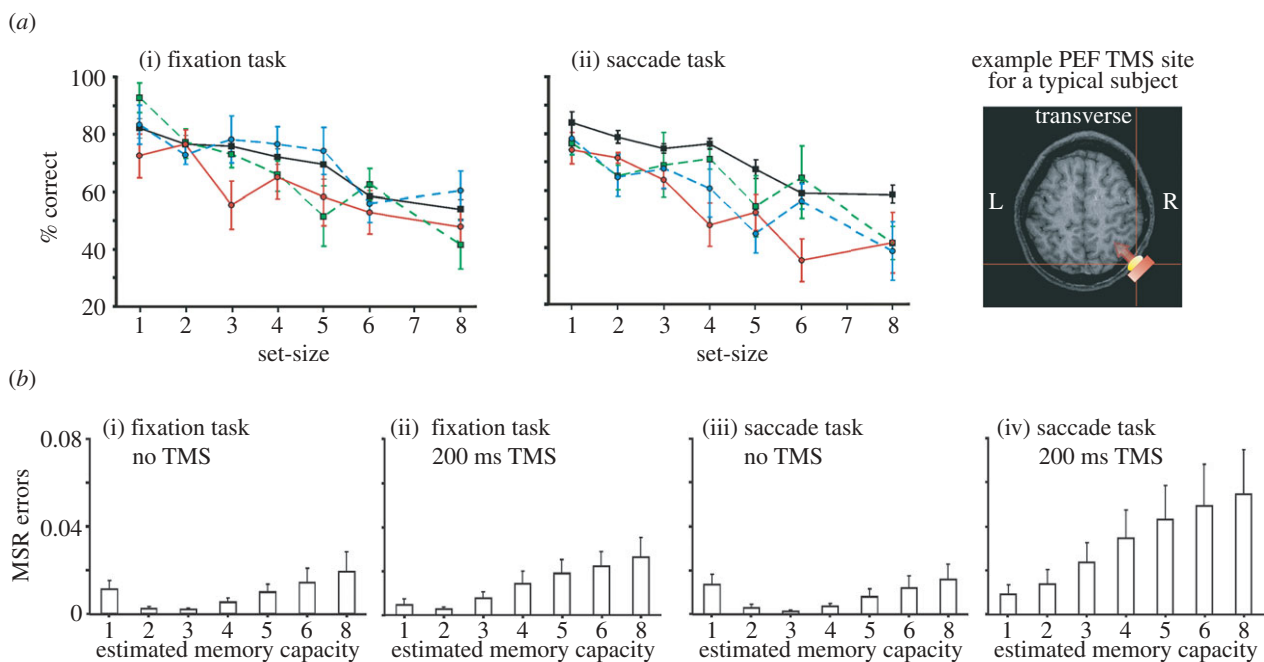
Figure 4. Main results of right PEF TMS (modified from [81]). The experimental design in this study was similar to our earlier trans-saccadic memory study shown in figure 2 with the addition of applying a TMS pulse over the left or right PEF at 100, 200 or 300 ms after the onset of the second fixation-cross. (*a*) Main results showing TMS effects only found during right PEF stimulation. Mean percentage correct response is plotted against set-size of target display (set-size ranged from 1 to 6 or 8 targets, randomly determined) in both the fixation task (i) and the saccade task (ii). The baseline no TMS condition is shown by the solid black curve. Coloured data curves represent the three TMS conditions of different stimulation times relative to the onset of the second fixation-cross: green curve for 100 ms stimulation time, red curve for 200 ms stimulation time and blue curve for 300 ms stimulation time. The only TMS effect in the fixation task was found when stimulation was delivered to the right PEF stimulation at 200 ms (the duration after the onset of the second fixation-cross). All three stimulation times yielded TMS-induced errors in the saccade task with the largest disruption at 200 ms, the stimulation time coinciding closest to the time of the saccade. (*b*) Mean square residual (MSR) errors estimating our subjects'memory capacity are shown for the no TMS baseline condition (black data curves) and the 200 ms stimulation time (red data curves), where we found the largest TMS effects. We calculated the MSR errors using a modified version of our predictive model from figure 3*b* that took into account the baseline shift of the data curves at one item (i.e. the theoretical ceil limit was set to the actual mean percentage correct obtained at one item set-size). MSR errors in the no TMS baseline condition replicated our previous findings indicating an estimated memory capacity of three items in both the fixation and saccade tasks (*b* (i) and (iii), respectively). MSR errors in the right PEF TMS condition at 200 ms stimulation time showed a general reduction in the estimated memory capacities in both tasks, down to two items in the fixation task and one item in the saccade task (*b* (ii) and (iv), respectively). The novel findings from this study show that the right PEF plays a functional role in trans-saccadic memory. We hypothesized that the strongest TMS effect occurring around the time of the saccade was due to TMS disrupting the PEFs spatial remapping mechanisms that updates object locations during saccades, an operation that is crucial for accurate performance in our trans-saccadic memory task. The stimulation site for the right PEF is shown with the position of high-intensity signal markers placed on the subject's skull (P4). Red bars indicate the position of the TMS coil. To localize left and right PEFs, we placed the TMS coil over P3 and P4, respectively, according to the 10–20 electroencephalogram (EEG) coordinate system [93,94], using commercially available 10–20 EEG stretch caps for 20 channels. TMS sites (P3 and P4) overlay left and right dorsal PPC, respectively, and include the intraparietal sulcus corresponding to the putative human parietal eye fields [95]. The PEF sites were confirmed with anatomical magnetic resonance imaging brain scans.

simply offer different speculative explanations of our results. We first considered the possibility, illustrated in figure 6*a*, that the ventral and dorsal streams may operate independently in TSP. This 'non-interaction' possibility is consistent with evidence that dorsal stream operations might also include object feature processing in both the monkey [104,105,113] and human [114,115] brains. One may suggest that our TMS results can be explained by disruption to these rudimentary dorsal object feature processes. However, this 'non-interaction' possibility seems unlikely as it has been challenged by recent behavioural [116–118] and functional brain-imaging studies [103,119–121], and is inconsistent with the TMS experiments described above. These experiments suggest that TSP

requires integrating information from the dorsal and ventral visual streams.

One way to integrate information from both streams would be through feed-forward pathways towards common target areas of the frontal cortex (figure 6*b*), for example in the dorso- or ventro-lateral prefrontal cortex [122,123]. Alternatively, the dorsal and ventral visual streams may interact by engaging in 'cross talk' through parallel connections, shown in figure 6*c* [124,125]. However, these two possibilities pose a new problem, i.e. information from the two visual streams does not share a common spatial code for direct integration in TSP. To explain, the two visual streams encode visual information in different frames of reference. Many parietal areas within the dorsal stream,
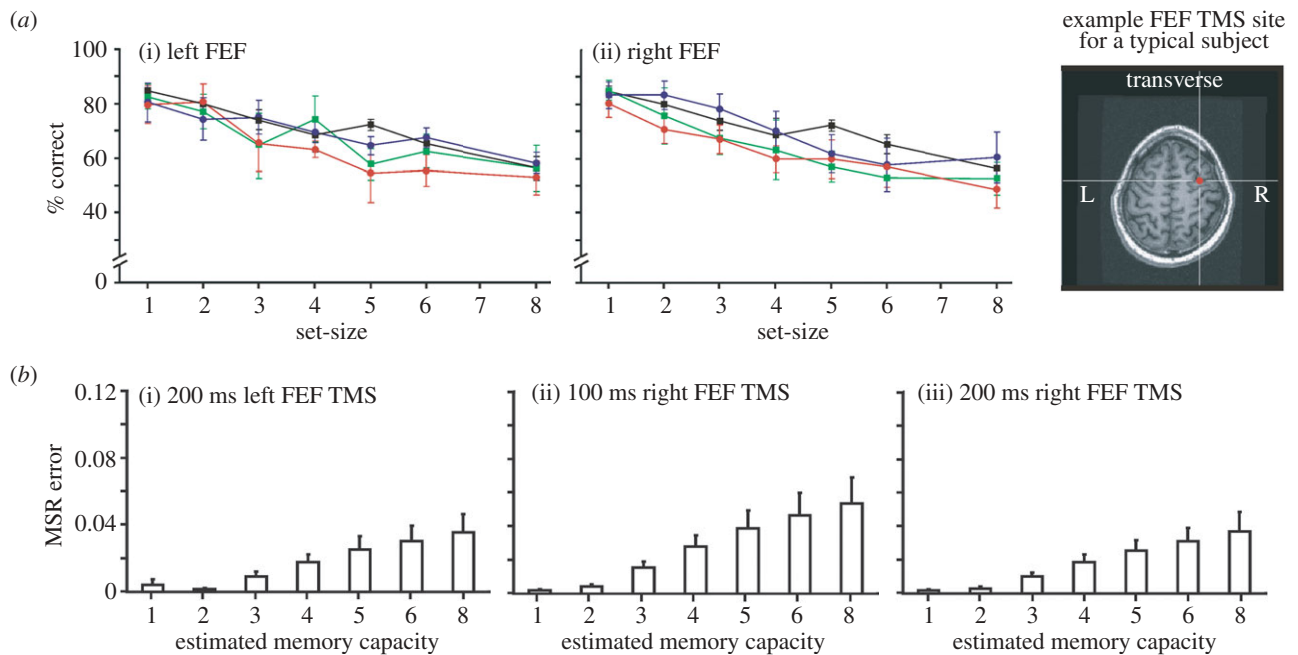
Figure 5. Main results in FEF TMS study (modified from [82]). (*a*) Mean percentage correct plotted against set-size in the saccade task for no TMS condition (black data curve) and FEF TMS conditions of different stimulation times: 100 ms (green data curve), 200 ms (red data curve) and 300 ms (blue data curve). (i) and (ii) show the results during left and right FEF stimulation, respectively. No significant differences between no TMS and TMS conditions were found in the fixation task and are not included here. In both left and right TMS conditions, the largest TMS effects were found when stimulation was delivered at the time of the saccade, around the 200 ms stimulation time. A TMS effect was also found during right FEF TMS at the 100 ms stimulation time. (*b*) Mean square residual (MSR) errors estimating our subjects' memory capacity are shown for the three TMS conditions that yielded significant effects compared with the no TMS baseline condition. We calculated the MSR errors using a modified version of our predictive model from figure 3b that took into account the baseline shift of the data curves at one item (i.e. the theoretical ceil limit was set to the actual mean percentage correct obtained at one item set-size). The MSR errors indicated a general reduction in the estimated memory capacities in the (i) 200 ms left TMS, (ii) 100 ms right TMS, and (iii) 200 ms right TMS. These results show evidence that the FEFs play a functional role in trans-saccadic memory. We proposed that the largest TMS effects found when stimulation was delivered closest to the timing of the saccade was due to TMS disrupting the spatial remapping signals occurring in the FEF during saccades. Left and right FEF stimulation sites were determined individually in each subject using frameless stereotaxy. Before testing, a T1-weighted MR brain scan was obtained from each subject. To localize FEF, we selected stereotaxic coordinates (left FEF: $x = -32$; $y = -2$; $z = 46$; right FEF: $x = 32$; $y = -2$; $z = 47$) based on a previous review of several brain imaging studies identifying activation foci for FEF [96]. These anatomical coordinates corresponding to left and right FEF were then converted from standardized stereotaxic space [97] into each subject's native coordinate space [98]. TMS coil placement was guided by online TMS–MRI coregistration. To coregister the TMS coil placement and scalp topography in real 3-D space with cortical regions identified in the MRI of the subject's head, we used an ultrasound-based TMS–MRI coregistration system and Brain Voyager QX software (Brain Voyager TMS Neuronavigator; Brain Innovation, Maastricht, The Netherlands). Once the local spatial coordinate system is defined for the subject's head and the TMS coil in real 3-D space, these coordinate systems are coregistered with the coordinate system of the MR space.

including the PEF, encode visual information in eye-centred coordinates [126]. In contrast, the ventral stream is composed of hierarchical operations of increasingly more complex object feature analysis and spatial invariance [127,128], encoding visual information in a kind of object-based reference frame that represents an object as a three-dimensional spatial arrangement of its parts centred on the object itself [129].

The fourth possibility, depicted in figure 6*d*, proposes that visual feature analysis from the ventral stream and spatial remapping signals from the PEF in the dorsal stream and the FEF are combined in early visual areas through re-entrant feedback connections that send information back down to the visual cortex. Similar feedback projections have been proposed to also explain conscious perception of visual information [130–134] and visual attention

[135,136]. These models are consistent with what is known about the visual system's anatomical connections in the primate brain: the dorsal and ventral streams project signals in a feed-forward manner through parallel pathways converging in prefrontal regions [124,137,138]; the dorsal and ventral streams are also linked by lateral connections between the temporal and parietal cortices [139,140]; and, descending pathways from the inferior temporal and parietal cortices also project backward to early visual areas [141].

This last hypothesis of re-entrant interacting pathways provides a convenient explanation of the early aspects of TSP, by allowing the gaze-centred remapping signals and features signals to interact at a level which is well known to possess multiple retinotopic maps of visual space. This is consistent with evidence that show saccade-related activity possibly related to
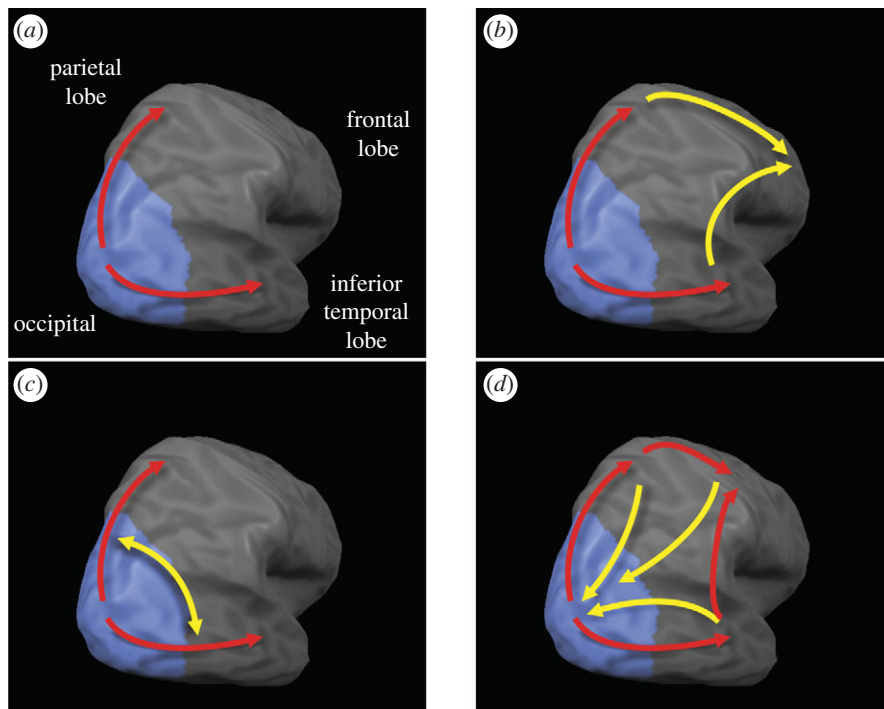
Figure 6. Different possible explanations of how visual streams may be involved in trans-saccadic memory (modified from [81]). (*a*) The 'no-interaction' hypothesis suggests that trans-saccadic memory does not rely on binding of visual information between the dorsal and ventral streams. (*b*) Alternatively, integration of visual information for trans-saccadic memory may occur by feed-forward connections to frontal cortical regions. (*c*) Another possibility is that visual information is integrated for trans-saccadic memory through parallel connections between dorsal and ventral streams. (*d*) Lastly, trans-saccadic memory may result from interactions between the visual streams, including signals from frontal eye fields, through re-entrant pathways to earlier visual areas.

spatial remapping occurs in early visual areas such as V1 [142–144], V2 and V3 [65,66,145,146], V4 [64,67,147], V5 [63,148] and V6 [149], possibly due to feedback signals originating from the FEF [64,150,151] and the PEF [131,152]. This re-entrant feedback hypothesis is supported by other TMS studies. Experiments combining TMS and fMRI have shown that magnetically stimulating either the FEF [153] or PEF [154] modulates visual cortex BOLD (blood-oxygen-level-dependent) activity in the human brain. Other studies have shown that TMS applied to the FEF modulates event-related potentials (ERP) recorded from posterior electrodes over the visual cortex [155,156]. Also, Silvanto *et al.* [157] showed that magnetically stimulating the FEFs decreases the intensity of TMS-induced phosphenes during V5 stimulation when FEF stimulation was applied 20–40 ms prior to V5 stimulation. Moreover, micro-stimulation of FEF neurons in the monkey brain has been shown to modulate neural activity in V4 [158].

The re-entrant interaction hypothesis is currently speculative, and difficult to test, but there are some recent studies that might give us some insight into how this might be done. As mentioned earlier, evidence that the FEF and PEF exert control over early visual processing through re-entrant pathways has been found using concurrent TMS–fMRI [153,154]. Using concurrent TMS–fMRI could be one way to test whether information is integrated through re-entrant interactions during our trans-

saccadic memory task. In which case, one can investigate whether TMS-induced disruptions to trans-saccadic memory when magnetic stimulation is applied to either the FEF or PEF is correlated with event-related changes in early visual BOLD activity. Alternatively, in a study similar to the previously mentioned TMS–ERP study [155], it may be possible to take advantage of ERP temporal resolution and chart the possible chronometry of the information transfer between higher to lower visual areas; and then follow this up with TMS to the FEF, PEF and visual cortical areas at different points along this time-course. Finding a TMS effect when magnetically stimulating an area of the visual cortex some point after the timing of the TMS effect during FEF and PEF stimulation might provide support for the direction of the information transfer. Another way to test the re-entrant pathway hypothesis is to use our trans-saccadic memory experiment in an event-related fMRI study to reveal the topography of cortical BOLD activity, and apply the event-related BOLD data to a Granger causality analysis [159]. Granger causality analysis is a statistical measure of prediction that is capable of predicting the causal interplay between different cortical areas. Granger analysis can be used to predict the BOLD activity in the visual cortex based on the BOLD activity in either the FEF or PEF as subjects perform our task. Such an analysis has been used in a recent fMRI study testing the influence of the FEF and intraparietal sulcus on visual occipital activity during a visuospatial attention task [160]. Of course,

all of these are only ideas of how one might test the re-entrant hypothesis.

It is not our conjecture that the re-entrant pathway / spatial remapping mechanism is the only mechanism used by this network for perceptual updating. Our previously cited TMS studies do not offer definitive answers regarding the other possibilities shown in figure 6—they only implicate these structures and saccade-related updating as part of the mechanism. All of the above mechanisms, and various frames of reference, could be involved, depending on the details of the task.

7. CONCLUSION

In this review paper, we have discussed the recent evidence that memory of visual information across a saccade, so-called trans-saccadic memory, is limited to about three to four items (e.g. [53,54,58]), the same memory capacity as simple visual working memory without saccades (e.g. [33]). But as we argue here, TSP is a more complex process than visual working memory in the absence of saccades because it involves additional computations the visual system must solve. That is, TSP integrates pre- and post-saccadic stimuli by relying on spatial updating mechanisms that take into account the egocentric measures of the saccade [20,21]. In two recent TMS studies, we showed evidence that suggests the spatial updating processes for motor targets found in the PEFs [81] and the FEFs [82] also plays a functional role in updating feature objects in TSP. We have proposed that TSP reflects a process whereby feature information from the ventral stream and spatial updating signals from the dorsal stream, including the FEF, are synthesized in part through re-entrant pathways that feed back to earlier visual areas.

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