The Planning and Guiding of Reading Saccades: a Repetitive Transcranial Magnetic Stimulation Study

A previous positron emission tomography study that investigated the cortical areas involved in directing eye movements during text reading showed two areas of extra-occipital asymmetry: left > right posterior parietal cortex (PPC), and right > left frontal eye-field (FEF). We used the temporal resolution of repetitive TMS (rTMS) to isolate the contributions of the left and right PPC and FEF to the planning and execution of rightward reading saccades. We present eye-movement data collected during text reading, which involves the initiation and maintenance of a series of saccades (scanpath). rTMS over the left but not right PPC slowed reading speeds for the whole array of words, indicating that this area is involved throughout the scanpath. rTMS over the right but not the left FEF slowed the time to make the first saccade, but only when triggered before the stimuli appeared, demonstrating that the role of this region is in the preparation of the scanpath. Our results are compatible with the hypotheses that the left PPC maintains reading saccades along a line of text while the right FEF is involved in the preparation of the motor plan for the scanpath at the start of each new line of text.

Introduction

Text reading differs from single word reading in two important respects. Firstly, the reader’s eye move in a series of saccades across the word arrays, placing high acuity foveal vision on each word in turn to allow word-form recognition (Rayner and Bertera, 1979). Secondly, in left-to-right readers, attention is skewed towards new words to the right of fixation and away from words to the left. Subjects skip over some words, especially short function words (e.g. and, the), when sentient meaning limits the possibilities for ensuing words, and perception of their shape and length in right parafoveal vision, extending 5° to the right of fixation, may be sufficient to confirm their identity (Rayner and McConkie, 1976). However, the major role of right parafoveal vision during reading is in the planning of the next saccade, so that foveal vision is moved to the optimal viewing position for whole word recognition (Nazir et al., 1992). The role of right parafoveal vision in sensorimotor integration during text reading has been shown both in normal subjects and in patients (McConkie and Rayner, 1976; Zihl, 1995).

The posterior parietal cortex (PPC) and frontal eye fields (FEF) are involved in directing visuo-spatial attention and guiding eye movements. The level of co-dependence between these regions and the occipital cortex caused Ferrier to mistakenly identify lateral parietal cortex as primary visual cortex, after it was observed that monkeys with bilateral lesions appeared unable to see (Glickstein, 1985). It is not yet clear whether these extra-occipital areas mediate the attentional components of visuo-spatial tasks or if they plan and execute saccadic eye movements (Nobre et al., 1997): they may do both (Corbetta, 1998).

The greater activity in the left PPC relative to the right during the execution of reading saccades, reported in a previous positron emission tomography (PET) study (Leff et al., 2000), is in accord with current views on saccades to contralateral hemispace in normal subjects (Pierrot-Deseilligny et al., 1995) and patients (Pierrot-Deseilligny et al., 1987). Our finding of greater activity in the right FEF relative to the left during reading is, however, open to other interpretations. PET measurements of regional cerebral blood flow (rCBF) sum metabolic activity associated with neural transients over 30 s. During this period, subjects were mainly making rightward saccades across the word arrays, but they also made a leftward saccade as each new array was presented, a potential confounding factor when interpreting the activations in FEF.

Transcranial magnetic stimulation (TMS) (Walsh and Cowey, 1998) has been used to very briefly disrupt different types of saccades: voluntary (Elkington et al., 1992), memory-guided (Muri et al., 1994), reflex and anti-saccades (Muri et al., 1991). TMS inhibits saccadic activity but does not produce saccades (Wessel and Kompf, 1991), unlike direct electrical stimulation of appropriate cortical regions in animals (Schall, 1991) and humans (Rasmussen and Penfeld, 1948). The superior temporal resolution of TMS allowed us to time our interference to coincide only with rightward-reading saccades.

Materials and Methods

Experimental Design

Subjects were seated 65 cm from the centre of an Apple Mac Powerbook 540c, set at eye level. The stimuli consisted of five unassociated words in a horizontal array. The absence of sentential meaning prevented the subjects using ‘top-down’ processing to guess the next word, ensuring a saccade followed by a fixation for each word in the array (McConkie and Rayner, 1975). A cross hair on the left of the screen appeared between word arrays, and the subjects were instructed to fixate on this while awaiting the next array. The stimuli were present for 1800 ± 200 ms, depending on the speed of the reader, with an interstimulus interval of 4 s. Subjects were instructed to read aloud all the words in the array, their responses being recorded onto audiotape; there was no evidence that TMS affected the motor output of words. All stimuli used were single-syllable English words (nouns and verbs) obtained from the MRC Psycholinguistics database. Words were four or five characters long, mean imageability 511 (range 353–647, with a total possible range of 100–700) (Coltheart, 1981), and mean log frequency 1.5 (range 10–99 words per million) on the Kucera and Francis scale (Kucera and Francis, 1967). The stimuli were selected randomly by PsyScope software (Cohen et al., 1993). Trials were blocked with trains of rTMS triggered either at the same time as the stimuli appeared on the screen, or at 100 or 500 ms prior to their appearance. There were 40 trials for each site, with rTMS delivered pseudorandomly on 50% of the trials. No subject had >7 runs of 40 stimuli on the same day.

Subjects

A total of 14 subjects were studied (mean age 32.1 years; SD 8.3), between eight and three of them in any one study. They were English speaking, right-handed volunteers with no history of neurological disease. Data from two subjects had to be excluded from the analyses; one subject’s...
eye-recording trace was marred by interference from the rTMS trials, and the second subject had too few trials due to coil failure. Each subject gave informed consent to participate in the study. The National Institute of Neurology Local Ethics Committee approved the project.

**Repetitive Transcranial Magnetic Stimulation**

rTMS was delivered by a Magstim Rapid stimulator (Magstim Co., Whitland, UK) and a 7 cm mean diameter figure of eight coil with a maximum output of 2 T. Stimulation intensity was set to be 10% above motor threshold for producing a visible twitch of the contralateral hand or fingers. The threshold for producing a visible twitch of activated muscle is slightly less (usually up to 5% of maximum stimulator output) than the threshold for producing an EMG response in relaxed muscle. Stimuli were applied either over the FEF or PPC. For the FEF the coil was held in an anterior–posterior orientation, and then moved anterior to the hand area of the motor cortex until a point was reached where all motor responses disappeared (usually 3 cm), a functional definition supported by a recent review (Paus, 1996). For the PPC the coil was held with a lateral-medial orientation at a position defined on the basis of the previous functional imaging study (Leff et al., 2000), 7 cm posterior and 5 cm lateral to the vertex. For all sites, stimulation consisted of a train of 15 pulses of TMS at 10 Hz (i.e. 1500 ms of stimulation).

**Eye Movement Recording and Data Analysis**

Eye movements were recorded with a Microglide head mounted binocular infrared eye tracker (Microglide, Chicago, IL). The output was calibrated between each block of trials by asking subjects to saccade between the edges of the computer monitor, and data were collected for a period of 3500 ms starting 500 ms before the word stimuli appeared, using a CED 1401 A/D converter (Cambridge Electronic Devices, Cambridge, UK) and commercial data collection software (SIGAVG). Measurements were made offline using in-house software and an interactive cursor to identify saccadic onsets. Two measurements were recorded from each eye movement trace:

A. Time to first word (i.e. the time from the stimuli appearing to the end of the first rightwardsaccade onto the first word in the array).

B. Time across array (i.e. time taken to get from the first word to the last), which was expressed as time per word (Fig. 1).

Trials with blink artefact occurring before the first saccade were discarded, as were those with poor trace quality (~10% of all trials). Like others using TMS to study eye movement control, we excluded measurements where the time to make the first saccade was <100 ms from the appearance of the stimulus (Ro et al., 1997), as this short reaction time suggests an anticipatory saccade. Although we took each measurement from the end of a saccade, we ensured that a change in the reaction time in response to rTMS was due to saccade initiation and not to slowing of the actual saccade. The data were analysed statistically using the general linear model, with a univariate analysis of variance (ANOVA) (using SPSS software for the Apple Macintosh). Reading times were entered as the dependant variable; site (left, right or vertex) and rTMS (rTMS or no rTMS) were entered as fixed factors; individual subjects were entered as a random factor covariate of no interest.

**Results**

**Experiment 1: Effects of Late rTMS on Posterior Parietal Cortex — Time across Arrays**

Three subjects participated. Three sites were stimulated: the left PPC, the right PPC and the vertex. Subjects had trials both with and without rTMS. The onset of rTMS began as soon as a new array of words appeared, with the subjects’ eyes fixated on the interstimulus cross-hair to the left of the screen. Stimulation persisted for 1500 ms, therefore continuing for ~75% of the time taken to complete reading across all five words. We measured the time to saccade across the word array, that is, the time taken from the end of the first saccade to the first word, to the end of the last saccade to the last word, and expressed this as time per word (Fig. 1, measurement ‘B’). An ANOVA demonstrated that there was no main effect of rTMS \[F(1,2.0) = 3.62; P = 0.2\], but there was a main effect of site \[F(2,4.2) = 7.38; P < 0.05\]. The interaction between rTMS and site was highly significant \[F(2,4.4) = 25.29; P < 0.01\]. The mean times for each individual are shown in Figure 2, and demonstrate that stimulation over the left PPC was responsible for slowing text reading. The group mean reading time across the word arrays (in milliseconds per word), without and with rTMS applied to the left PPC, were 305 ± 7.8 (SEM) (95% confidence intervals 290–320) and 349 ± 8.4 (95% confidence intervals 332–365).

**Experiment 2: Effects of Late rTMS on Frontal Eye Field — Time to First Word**

Having confirmed the importance of the left PPC in executing reading saccades, we focused on the FEF. We used the same study design in terms of when the rTMS was triggered, except that stimulation over a control site was omitted, as the hypothesis was that rTMS over the right FEF would be relatively more disruptive to the execution of reading saccades than rTMS over the left FEF. However, pilot data from four subjects showed no difference in the time taken to complete reading saccades across the word arrays between stimulation of the left and right FEF (see experiment 4 for more details). We then tested an alternative hypothesis, that right FEF stimulation only affected the time taken from a stimulus appearing to the completion of
the saccade to the first word (Fig. 1, measurement ‘A’). This RT was delayed by 30 ms with rTMS over the right FEF in one subject only (Fig. 2), and there was no significant group effect of site by rTMS interaction \(F(1,3.0 = 2.33; P = 0.22)\).

Experiment 3: Effects of Early rTMS on Frontal Eye Field—Time to First Word

The data from experiment 2 prompted us to test a further hypothesis, that rTMS over the right FEF would disrupt preparation for the initiation of the reading scanpath (Fig. 1, measurement ‘A’). As we were uncertain about the optimum timing of the interval between the onset of rTMS and the appearance of the stimulus to observe this effect, the interval was set at either 100 or 500 ms between subjects. In practice, both intervals had an equal effect. rTMS was commenced before the word arrays appeared. Eight new subjects participated in this study. Two sites were stimulated, left and right FEF, and the time taken to initiate the saccade to first word was measured. Figure 2 shows the individual subjects’ mean data for left and right rTMS trials only; the no rTMS trial data has been excluded for clarity (although these data are included in Table 1). Seven of the eight subjects were slower initiating the first saccade when stimulation of the right FEF was contrasted with stimulation of the left FEF. There was a significant main effect of site \(F(1,7.1) = 9.51; P < 0.05\), but, more importantly, there was a site by rTMS interaction \(F(1,7.1) = 8.50; P < 0.05\).

Experiment 4: Effects of rTMS on Frontal Eye Field—Time across Arrays

Data from seven of the eight subjects in experiment 3 who been slower initiating the saccade to the first word when rTMS was applied to the right FEF were analysed: the measurement was the time taken across the arrays of words, expressed in milliseconds per word (see Fig. 1, measurement ‘B’). The purpose was to confirm the observation made in experiment 2, i.e. that there was no effect of rTMS over the FEF on time across the word arrays. The individual means are shown in Figure 2. There was no site effect when rTMS trials were compared \(F(1,7.0) = 2.17; P = 0.2\).

Summary

rTMS over the left PPC, but not over the right PPC and a control region over the vertex, slowed the scanpath across the arrays of five words: i.e. following fixation on each word of an array, the time to initiate the next saccade was delayed by a mean of 45 ms. rTMS over the right FEF, relative to the left, slowed the initiation of the first saccade by a mean of 18 ms, but only when it came on 100–500 ms before the appearance of the stimulus. Thus, the effect of rTMS over the right FEF was in interrupting the preparation for the initiation of the first reading saccades; once underway, reading saccades proceeded at normal speed, despite rTMS continuing for a further 1000–1400 ms after the initial saccade.

Discussion

By using rTMS rather than single shot TMS, it was demonstrated that interruption of left PPC function over 1500 ms resulted in continuous interference with the maintenance of a reading scanpath along an array of five words. The effect was robust.
delaying each new reading saccade by ∼50 ms irrespective of the position of a word in the array; and it was unambiguous, as the delay was evident when comparing both stimulation over the left PPC with no stimulation and stimulation over the left PPC with stimulation over the right PPC and the control region over the vertex. This result is in accordance with the an experiment reported by Elkingston (Elkingston et al., 1992), and complementary to our previous PET result: the latter established dominance of the left PPC over the right in text reading and this study has demonstrated that left PPC function is required for the efficient execution of each saccade in a scanpath across an array of words. Two other studies found increased reaction times when TMS was applied over the right PPC. One study used a visual search paradigm (Ashbridge et al., 1997), the other a visuo-spatial memory task (Oyachi and Ohtsuka, 1995). Both studies required the subjects to make bidirectional eye movements, and neither concluded that eye movements themselves had been influenced, ascribing the effects of TMS to disruption of attentional and memory components of the tasks respectively.

In contrast, the results from stimulation of left and right FEF were more complex. It became evident from the first study of FEF stimulation (Experiment 2) that the effect was fundamentally different from that observed with stimulation of PPC. When rTMS was triggered with the appearance of a stimulus, reading of the word arrays was completed in the same time as was recorded when no rTMS was delivered. This was the case for both the left and right FEF stimulation trials. This raised the obvious possibility that rTMS through the intact skull was unable to influence the activity of neural tissue in the FEF responsible for generating each reading saccade. For safety reasons it was not possible to test this hypothesis with rTMS at much greater strength to see if an effect could be observed. The other possibility is that FEF activity is minimal for the continued generation of reading saccades along a line of text once reading has been initiated, i.e. once a saccade has been made to the first word of the array. Scanning text is a heavily overlearned motor task, and although reading saccades are classified as voluntary, i.e. not reflexive, they are unique in that they explore a visual environment that is regularly ordered in a manner that is rarely encountered in a visual scene of non-verbal objects. It has been well established for sequences of finger movements that the associated premotor cortical signal on functional images declines as the sequences become overlearned (Jenkins et al., 1994). The FEF are located in dorsal premotor cortex (Brodmann’s area 6) (Paus, 1996). By extrapolation, the absence of a significant left FEF signal in response to rightwards-directed reading saccades in our previous PET study is not surprising: the null result does not mean that the left FEF was not involved, but that it was involved at a level that was below the ability of the methodology to detect. We also speculate that the volume of neural tissue in the left FEF that maintains overlearned reading saccades is small and not readily disrupted by rTMS at the strength we employed. However, preparation for the initial saccade in response to the appearance of a new array of words is, we argue, responsible for the signal in the right FEF that we observed in our previous PET study when the subjects read across words arrays.

Long TMS trains of the type used in these experiments can potentially produce activity in areas of brain distant from, but connected to, the point of stimulation (Paus et al., 1997). It is therefore possible that the disruptive effect of stimulation was due to activation of areas other than the FEF itself. Although this cannot be excluded entirely by the present data, we think it unlikely to be an important contributing factor; for example, stimulation of the FEF, which has substantial connections to the PPC, yielded different effects on eye movements than stimulation of the PPC during the same task. This suggests that much of the behavioural effects we observed were caused by interference with activity in structures stimulated under the coil.

Unfortunately, a potential source of converging evidence, namely studies on patients with lesions, does not exist. Patients with focal brain damage involving the frontal lobe may have a wide range of eye movement impairments (Sharpe, 1986; Pierrot-Desailligny et al., 1987; Pierrot-Desailligny, 1994; Rivaud et al., 1994; Lekwuwa and Barnes, 1996; Zihl and Hebel, 1997), although overall these studies emphasize the relative impairment of saccadic eye movements to visual targets in contralesional space. This was particularly evident when patients had larger lesions involving white matter connections to and from the FEF, suggesting that prominent saccadic eye movement abnormalities require widespread damage to the distributed network controlling eye movements, and not solely the loss of FEF function. However, none of these studies have investigated the effects of the lesions on reading. An EEG experiment on six normal subjects investigated the presence, if any, of a Bereitschaft potential associated with voluntary or reflexive saccades. The voluntary saccades were preceded by a slow negative shift over the FEF (not lateralized because of the spatial resolution of the technique) beginning ∼650 ms before the saccade, a potential that was not observed during the reflexive saccades (Kurtzburgh and Vaughn, 1982). However, the eye movements were made between two non-verbal targets, and their relevance to the eye movements associated with reading is unclear.

Other than our own study (Leff et al., 2000), functional neuroimaging studies in humans have not studied reading saccades. Those that have investigated non-reading saccades have not come to a clear consensus about either FEF or PPC function. Activity has been mapped to the intraparietal sulcus (Muri et al., 1996a; Nobre et al., 1997) or the superior parietal lobule (Corbetta et al., 1993, 1995) during either voluntary or reflexive saccadic tasks; in general, the signal has been greater in PPC contralateral to the saccade. Some studies have attempted to dissociate the cortical signal associated with visual attention per se from that associated with the production of eye-movements, but with little success (Corbetta, 1998). For the FEF, some imaging studies have shown increases in signal with attentional shifts or saccades to contralateral space (Corbetta et al., 1993), while others demonstrated bilateral signal for similar tasks (Nobre et al., 1997; Luna et al., 1998). A PET study that contrasted voluntary purposive saccades with visual fixation demonstrated superiority of the right FEF (Sweeney et al., 1996), irrespective of the direction of the saccade.

In terms of TMS, and with regard to the FEF, it has been demonstrated that saccades to an auditory stimulus were delayed if TMS was applied over the FEF 50 ms before the saccade was generated, i.e. after perception of the cue and during the planning of the saccade (Thickbroom et al., 1996). Disruption

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<tr>
<th>Presence of rTMS</th>
<th>Mean (ms)</th>
<th>SEM</th>
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<td>Right N</td>
<td>282</td>
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<td>Left Y</td>
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<tr>
<td>Left N</td>
<td>285</td>
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Table 1

Group mean RT of time to first word from Experiment 3, along with SEM and 95% confidence intervals for each of the four conditions.
of the planning of a saccade may also be evident in studies of antisaccades: although experimental effects have been attributed to saccadic suppression, antisaccades also require the preparation and planning of the antisaccade away from the target (Gaymard et al., 1999). Viewing the processes involved in the generation of antisaccades in this light, it is of interest that one of the earliest TMS studies found that antisaccades into right visual space were delayed when the TMS was applied to the right FEF, 50–90 ms after the appearance of the stimulus but prior to the execution of the antisaccade (Muri et al., 1991). Two studies applying TMS to right dorsolateral prefrontal cortex (DLPPC) found: a delay in memory guided saccades to the left (Muri et al., 1996b); and an increase in the number of express saccades (with latencies in the order of 100 ms) to the left (Muri et al., 1999). However, the DLPPC is both anatomically distinct from the FEF and has a separate role in the control of eye-movements (Pierrot-Deseilligny et al., 1995).

In conclusion, our results are compatible with two hypotheses: that the left PPC controls the ‘on-line’ maintenance and modification of a sensorimotor plan to read along individual lines of text; and that the right FEF is responsible for the preparation of this motor plan, which, during ordinary reading, occurs each time the reader starts a new line of text. To our knowledge, the temporal relationships between cortical regions involved in generating reading saccades has not previously been reported. Although the contribution of the left PPC in maintaining the scanpath along a line of text is not controversial, the role of the right FEF in preparing the scanpath at the beginning of each new line of text is unexpected. The role of the right FEF in reading would have been difficult to determine in patients because of the size and distribution of most right posterior frontal vascular lesions.

**References**


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