SPECIAL SECTION

OCULOMOTOR FUNCTIONS OF THE PARIETAL LOBE: EFFECTS OF CHRONIC LESIONS IN HUMANS

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ABSTRACT

This review summarises research in patients with chronic lesions of parietal oculomotor cortex and compares their oculomotor performance to patients with lesions of the frontal eye field (FEF). The observations identify the oculomotor functions for which these regions are indispensable, and explore dynamic interactions within cortical and subcortical networks for oculomotor control. The experiments examined endogenously generated saccades, saccades to visual targets, antisaccades, saccade choice and saccade remapping for inhibitory spatial tagging. The findings suggest that the key function of parietal oculomotor cortex is the computation of sensorimotor transformations, rather than the initiation of either voluntary or reflexive saccades. They also reveal the re-organisation of cortico-subcortical networks after brain injury, and provide insight into their dynamic interactions: FEF lesions result in disinhibition of reflexive saccades toward the contralesional field and an impairment of reflexive saccades toward the ipsilesional field; whereas parietal lesion result in the opposite pattern.

Key words: eye movements, frontal eye field, attention, Sprague effect, saccade

This special section of *Cortex* commemorates the 50th anniversary of the publication of *The Parietal Lobes* by Macdonald Critchley. The occasion was celebrated by a symposium at the meeting of the British Neuropsychological Society in March 2003. The theme of the symposium was to overview progress over the last half century: "What can we tell Critchley today?". While Critchley's book offers an otherwise comprehensive monograph on the topic, with insights that continue to stimulate clinicians and neuroscientists, it did not have a chapter on eye movements. Here I'll highlight contemporary concepts of parietal lobe function that have emerged from oculomotor research in neurological patients with chronic lesions of oculomotor cortex:

1) parietal lobe functions need to be understood in the context of a network of cortical and subcortical areas that work together in controlling visual orienting and other visually guided behaviour;

2) this network coordinates reflexive and voluntary eye movements to provide a continuity of experience and coherent behaviour;

3) the oculomotor function of the parietal lobe is best understood, not in terms of the generating reflexive or voluntary eye movements, but rather in computing the sensorimotor transformations needed for programming voluntary eye movements in response to visual stimuli.

THE VISUAL GRASP REFLEX AND THE SPRAGUE EFFECT

With the evolution of more complex behaviour, brain mechanisms for selective attention have emerged that provide the organism with greater flexibility: to respond to environmental events in one way under one set of circumstances, a different way under another, to not respond at all, or to delay a response pending further information. It is through such mechanisms that past learning, motivation, and emotion influence behaviour.

This selectivity of adaptive behaviour is achieved through an orchestration of subcortical reflex circuits by cortical processes which can activate or inhibit them (Easton, 1973). Our neural machinery for visual orienting is the product of its evolutionary history (Ingle, 1973), and offers an attractive model system for examining this integration of cortical and subcortical systems. All vertebrates have midbrain circuits for reflexively orienting the eyes toward salient events occurring in the visual periphery – the visual grasp reflex (VGR). In foveate mammals, including humans, these archetypal pathways function to align high acuity regions of the retina to the location of a sudden change in the visual periphery.

In submammalian vertebrates, the key midbrain structure involved in reflexive orienting is the optic tectum. Its homologue in mammals, the superior

colliculus, is integrated (via the basal ganglia and pulvinar) with oculomotor cortex of the frontal and parietal lobes. In everyday life there are constantly competing demands on systems for visual orienting by the outside world as well as from internally generated goals. Thus, while the VGR plays a critical defensive role in ensuring survival, reflexive eye movements must also be integrated with cortical mechanisms involved in strategic search under voluntary control.

Frontal and parietal cortex both have regions involved in oculomotor control. They are connected to one another and both are connected to the superior colliculus. The frontal eye fields (FEFs) are located just anterior to the motor hand area of each hemisphere, at the junction of the superior frontal sulcus and the precentral sulcus. It projects to the superior colliculus both directly and via the basal ganglia through the caudate nucleus and the substantia nigra *pars reticulata*. The substantia nigra has inhibitory, GABAergic projections to the colliculus on the same side, and crossed projections to the contralateral colliculus. The parietal eye fields are located in the intraparietal sulcus (IPS). They receive input from the colliculus through the pulvinar nucleus of the thalamus; and they project to the colliculus, both directly and through interactions with pulvinar and primary visual cortex.

We owe our contemporary appreciation of visual orienting – a dynamic interaction between the cerebral cortex and the brain stem – to the pioneering work of Sprague (1966) in cats. He was intrigued by the syndrome of hemispatial neglect, and discovered, perhaps, the most important thing we have learned since Critchley – how to fix it! In a classic experiment cats were rendered blind in one visual field by unilateral extirpation of occipital and parietal cortex. It was then shown that orienting toward the contralesional field was restored if the *opposite* superior colliculus was removed. A similar result was obtained if the inhibitory connections were severed between the contralesional substantia nigra *pars reticulata* and the ipsilesional colliculus (Wallace et al., 1989, 1990). Converging evidence for midbrain mediation of the Sprague effect was also demonstrated by Sherman (1974) who sectioned the interhemispheric commisure in monocular viewing cats, and showed that the Sprague effect was restricted to the temporal hemifield.

The Sprague effect is thought to work in the following way. Parieto-occipital projections to the ipsilateral superior colliculus normally exert a tonic facilitation on it. After parietal lesions the colliculus looses this tonic activation (Hovda and Villablanca, 1990). At the same time the opposite (contralesional) colliculus becomes hyperactive. This imbalance is sustained and aggravated by the mutually inhibitory connections between the two colliculi themselves. The more active contralesional superior colliculus is released from inhibition and produces disinhibited reflexive orienting to signals in the field ipsilateral to the cortical lesion. If the contralesional superior colliculus is then removed (or the fibres of passage from the substantia nigra *pars reticulata* to the opposite colliculus), the ipsilesional hyper-orienting is eliminated and contralesional orienting is restored.

The lesson here is that lesion-induced deficits may not be understood simply in terms of the absence of a putative function that is normally mediated by the lesioned tissue. Rather, the pathological behavior reflects the normal dynamic interactions of the region with other interconnected structures (Payne and Rushmore, 2004).

Investigating Oculomotor Cortex Function in Patients with Chronic Lesions

The novel contribution of my laboratory has been to attack the problem of understanding dynamic interactions between brain regions by focusing on oculomotor performance in patients with *chronic* lesions of oculomotor cortex. Why study chronic lesions? It may been argued that any interpretation of the effects of brain lesions is prejudiced by the "confounding influence of compensatory responses to brain injury" (Ungerleider and Haxby, 1994). It is certainly the case that, during the acute phase, diaschesis renders dysfunctional remote structures interconnected with the lesioned area. For example, acute lesions in the FEF can cause transient hemispatial neglect that quickly recovers. Since acute lesions of the FEF cause diaschesis, that can be measured experimentally as hypometabolism in remote structures including the superior colliculus (Deuel and Collins, 1984), transient neglect seen after FEF lesions may result, in part, because the ipsilesional superior colliculus is transiently dysfunctional. On the other hand, performance in patients with chronic lesions can be argued to reflect the function of a re-organised brain – not the normal function of the lesioned area. Can experimental observations in these patients tell us anything about the "normal" function of the damaged structure?

There are three reasons motivating our study of patients with chronic lesions. First, the presence of a persisting dysfunction in the chronic state may be the best evidence that the damaged structure is not only somehow involved in a given function – but *indispensable* for its normal operation. Not only does it normally contribute to a function but, because that function never fully recovers even after re-organisation and compensation, we can infer a primacy of the structure for a particular function within the network. Secondly, the "re-organisation" that takes place during recovery is *not random*. The "normal" state does reflect dynamic interactions between brain structures, and

the systematic way in which these dynamics alter after injury provides a special opportunity to understand these interactions. Finally and, for me as a clinician, the most important reason to study chronic lesions: people *do* get better after brain injury; and the motivation to understand the re-organisation of dynamic circuitry underlying this recovery is compelling.

An example of our approach, and the opportunities it offers, is illustrated by a study in which we examined the reorganization of dynamic interactions between the FEF and the midbrain by measuring the effects of chronic unilateral lesions of the human FEF on the latencies of saccadic eye movements. One experiment by Henik et al. (1994) compared saccades to peripheral visual targets and voluntary saccades. The patients in this study were part of a group of individuals who had suffered brain injuries, mostly from strokes, and who had been gracious in helping us to investigate the consequences of these injuries. Each was selected for having a single, unilateral lesion restricted to the frontal cortex. All had recovered from the acute phase of the illness and effects of diaschesis. None had visual field defects, hemispatial neglect, visual extinction or any obvious impairment of eye movements that could be observed on clinical examination. Most were studied several years after the ictus. All were competent and independent individuals, and had been active participants in neurobehavioral research over a number of years.

In order for us to make inferences about FEF function, we used the following approach. We compared the 9 patients in this frontal lesion group in whom the lesion included the FEF with 7 neurological control patients who had frontal lesions that spared the FEF. The FEF was identified on computer tomography (CT) or magnetic resonance imaging (MRI) scans as the most posterior part of the middle frontal gyrus where it joins the precentral sulcus. This region has been identified as the human FEF based on functional neuroimaging (see Paus, 1996, for a review).

The patients were tested in two saccade tasks: visually guided saccades to targets that appeared 10 degrees to left or right; and voluntary saccades from a symbolic arrow cue at the center of the display that pointed to a marker target, 10 degrees to the left or right. For the neurological control patients whose frontal lesions spared the FEF, the latencies of voluntary saccades were, as for normal individuals, longer than for visually summoned saccades. Moreover, the frontal lesions did not produce an asymmetry of eye movements. Saccade latencies were not different for contralesional and ipsilesional fields for either kind of eye movement.

In patients with FEF lesions (Figure 1) voluntary saccades latencies were longer to the contralesional field. The persistent impairment in initiating voluntary contralesional saccades, even

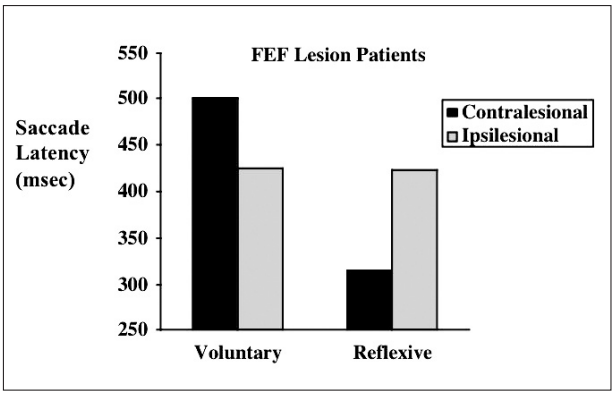

Fig. 1 – *Saccade latency for voluntary and visually summoned saccades toward the ipsilesional and contralesional fields for 9 patients with lesions of the FEF.*

years after the injury, is strong evidence that the FEF is critical in generating voluntary saccades. In contrast, visually guided saccades latencies were longer to targets in the *ipsilesional* field. A subsequent study replicated this effect and confirmed that, compared with controls, saccade latencies to ipsilesional visual targets were longer than those of normal controls, but those toward the contralesional field were not (Machado and Rafal, 2004b). Note that, in Figure 1, the latencies for saccades latencies toward ipsilesional visual targets were, quite abnormally, no faster than for voluntary saccades to that field.

These results indicate that FEF lesions have two separate effects on eye movements: 1) the FEF are involved in generating endogenous saccades to the contralateral field, and lesions in this region irrevocably increase their latency; 2) FEF lesions also appear to influence the *opposite* superior colliculus. It seems not to generate a VGR, and saccades made toward signals in the field ipsilesional to it must be made voluntarily without the usual advantage of this midbrain reflex.

We postulated that the loss of reflexive ipsilesional saccades was related to a re-organisation of fronto-collicular circuitry after brain injury that causes hyporeactivity of the contralesional superior colliculus. In order to confirm that this effect was due to re-organisation, rather than an immediate effect of FEF dysfunction, we conducted the same experiments in normal volunteers using single pulse transcranial magnetic stimulation (TMS) to transiently inactivate the FEF. Like chronic lesions in patients, TMS of the FEF does increase the latency for voluntary contralesional saccades (Ro et al., 1997, 1999). It does not, however, produce an asymmetry in the latencies for saccades to peripheral targets (Ro et al., 1997).

Thus, unilateral lesions of the FEF, in the chronic state, produce a kind of reverse Sprague effect that appears to reflect re-organisation of cortico-subcortical circuits. One explanation of this apparent reversed Sprague effect is that FEF

lesions disinhibit the ipsilesional substantia nigra *pars reticulata*, resulting in inhibition of the superior colliculus *opposite* to the FEF lesion.

Do the Parietal Eye Fields Command the Execution of Voluntary or Reflexive Saccades?

Neurophysiological observations, showing that parietal neurons discharge prior to the onset of saccades to peripheral visual targets, have been interpreted to implicate a "command function" for parietal cortex in the execution of eye movements (Mountcastle, 1976). Neuropsychological observations that patients with focal parietal lesions have increased latencies for saccades toward peripheral visual targets (Pierrot-Deseillgny et al., 1991) are consistent with the hypothesis that this region is involved in the execution of visually triggered saccades.

Before embracing this conclusion, however, alternative possibilities need to be excluded. In patients with acute lesions, especially, diaschesis affecting the superior colliculus could result, as suggested by Sprague's (1966) work, in defective visual orienting to visual targets. That is, the effect of parietal lesions on reflexive saccades could reflect remote effects on collicular function, rather indicating a direct role of parietal cortex in generating reflexive eye movements. Thus, it would be important to demonstrate that chronic parietal lesions cause a persistent deficit in initiating saccades to peripheral visual targets, in the same way that chronic lesions of the FEF produce a persistent deficit in initiating voluntary contralesional saccades.

In addition, it would be crucial to confirm that the deficit is specific to eye movements. An impairment in attending to contralesional stimuli can slow its processing (Rorden et al., 1997). In this case *any* response to it could be slowed. If patients are just as impaired, for example, in making manual key press responses to contralesional stimuli, then caution is needed in inferring a specific oculomotor function for reflexive saccades. Yamashita and I (unpublished observations) tested 12 patients with chronic lesions of parietal cortex in an experiment, similar to that described for frontal lesioned patients that measured latencies to initiate voluntary saccades and saccades to peripheral visual targets. These patients were also tested in an experiment in which they maintained fixation and were asked to make a key press response on detecting a peripheral target (using the same display as that used to study saccades to peripheral targets). Five patients had lesions in the right hemisphere and 7 in the left. In 4 patients the lesion involved oculomotor cortex in the region of the superior parietal lobule or the IPS, and in 5 the lesion involved the temporo-parietal junction (TPJ).

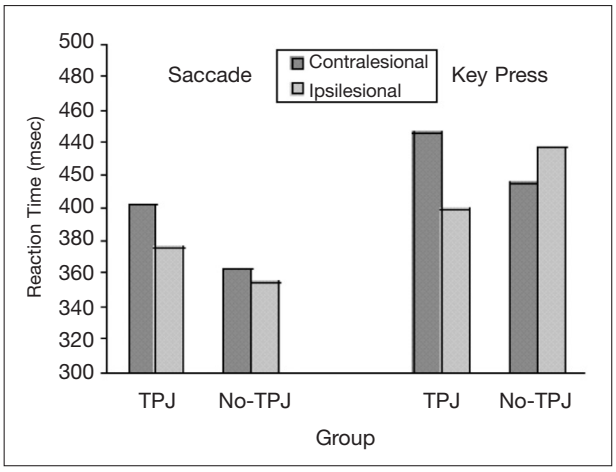

Fig. 2 – *Reaction time for saccade and key press responses to targets appearing in the contralesional and ipsilesional fields are shown for patients with lesions of the TPJ and for patients whose lesion involved more superior parts of the parietal lobe but spared the TPJ.*

Latencies for voluntary saccades toward the contralesional field (397 msec) were not slower than for those toward the ipsilesional field (404 msec). Thus, in contrast to patients with FEF lesions, we found no evidence that chronic parietal lesions affect the latency of voluntary contralesional saccades. Latencies for visually summoned saccades were longer toward contralesional targets (379 msec) than toward ipsilesional targets (364 msec), [$t(11) = 3.3$, $p < .01$] and there was a significant interaction between Task and Saccade Direction [$F(1, 11) = 9.36$, $p = .01$].

These results are consistent with previous reports that parietal lobe lesions result in increased latencies for saccades toward visual targets (Pierrot-Deseillgny et al., 1991). However, the deficit in responding to contralesional targets was not specific to saccades. The same deficit was observed for key press responses. Thus, the increase latencies for saccades to contralesional targets may have been due to a deficit in attention rather than a deficit in oculomotor initiation. If this were the case, we might expect the critical lesion to involve the TPJ, rather than the IPS region of oculomotor cortex. In this same group of patients, we had found that a deficit of attention was linked to TPJ, rather than superior parietal, involvement (Friedrich et al., 1998). To examine this issue, a mixed $2 \times 2 \times 2$ analysis of variance (ANOVA) was conducted on the median reaction time (RT) for each patient in both the key press and saccade tasks. Group (TPJ *vs.* No-TPJ) was a between group factor; within subject factors included Task (saccade *vs.* key press) and Direction (contralesional *vs.* ipsilesional). Five patients had lesions involving the TPJ, 7 had lesion involving parietal lobe, but sparing the TPJ (see Friedrich et al., 1998, for radiographic criteria for classification of the two groups). In four of the patients in the

No-TPJ Group, the lesion involved the superior parietal lobe and/or adjacent IPS. As shown in Figure 2, a Group × Direction interaction [F (1, 10) = 14.58, p < .003] reflects increased response times for contralesional targets only in the TPJ group [F (1, 10) = 28.9, p < .006]; and this was true for both saccade and key press tasks. By contrast an analysis of contralesional and ipsilesional response latencies, comparing patients with and without involvement of the superior parietal lobule or IPS, showed no difference between the two subgroups [F (1, 10) < 1.0]. In a more recent study (Machado and Rafal, 2004b), saccade latency toward peripheral targets was measured in 8 patients with lesions of intraparietal cortex. Saccade latencies were not longer for contralesional than for ipsilesional saccades.

These studies of patients with chronic lesions of parietal lobe show that damage to parietal oculomotor cortex does not produce persisting abnormalities of saccade latency for either voluntary or visually summoned saccades. When increased latencies for contralesional saccades are observed in patients with parietal lesions, they may reflect a deficit in attention rather than oculomotor programming, and may not necessarily implicate parietal oculomotor cortex in generating reflexive saccades.

Effects of Frontal Eye Field and Intraparietal Lesions on Antisaccades

Is the function of parietal "oculomotor" cortex to direct attention, rather than to generate motor commands for eye movement? Gottlieb and Goldberg (1999) explored this dichotomy by recording, in monkeys, from intraparietal neurons in prosaccade and antisaccade tasks. The reasoning was straightforward. If the function of intraparietal neurons is to promulgate motor commands, then they should be most active when the monkey executes a saccade toward the contralateral visual field – regardless of whether the saccade is executed toward a contralateral target (prosaccade) or away (antisaccade) from an ipsilateral target. They observed that intraparietal neurons were activated by the presentation of a contralateral target signal, even when it instructed the execution of a saccade toward the ipsilateral visual field. They interpreted the findings as being consistent with an attentional rather than motor account. Interestingly, they also observed that intraparietal neuron responses to contralateral targets were greater in the antisaccade then in the prosaccade task.

Recently, Machado and I (Machado and Rafal, 2004a, 2004b) compared patients with chronic unilateral intraparietal lesions and FEF lesions in prosaccade and antisaccade tasks.We measured both saccade latencies and, in the antisaccade task, errors; i.e., the frequency with which reflexive

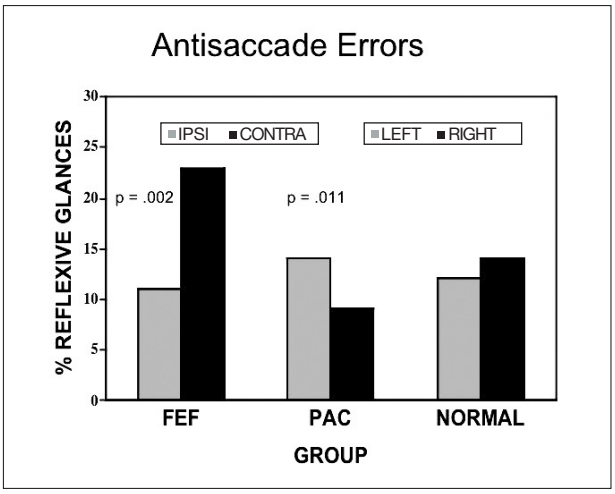

Fig. 3 – *Percent errors (reflexive glances) toward targets in the antisaccade task.*

glances were made toward, rather than away from, the target. Figure 3 shows the percent of errors, i.e., reflexive glances toward ipsilesional and contralesional signals in both groups of patients as well as normal controls. It shows that FEF lesions result in a disinhibited VGR toward contralesional signals, whereas the opposite is the case for parietal lesions. All 12 patients with FEF lesions made more reflexive glances toward contralesional than toward ipsilesional targets. Some of the patients with FEF lesions also had involvement of the middle frontal gyrus including the dorsolateral prefrontal cortex (DLPFC). Because DLPFC also has oculomotor activity, a separate analysis was conducted comparing those patients who did and did not have DLPFC involvement. This analysis revealed that the effect on reflexive saccades was due to FEF involvement by the lesion, and not to concomitant DLPFC damage.

By contrast, patients with lesions of intraparietal cortex made no more reflexive glances toward ipsilesional targets than did normal subjects; and made fewer reflexive glances toward contralesional than toward ipsilesional targets. These findings demonstrate a reduced VGR toward contralesional targets, consistent with Sprague's (1966) view that parietal lesions cause hyporeactivity in the ipsilesional superior colliculus. By contrast FEF lesions result in a disinhibited contralesional VGR.

In the patients with FEF lesions, latencies were longer for antisaccades away from contralesional signals – consistent with their difficulty in inhibiting a VGR toward them. Compared to normal controls they also had longer latencies for antisaccade away from ipsilesional targets, consistent with the findings of Henik et al. (1994) that FEF lesions increase the latency of voluntary contralesional saccades. The finding of particular interest in this study (Figure 4) was that, in contrast to the normal latencies for contralesional prosaccades in these same patients saccade

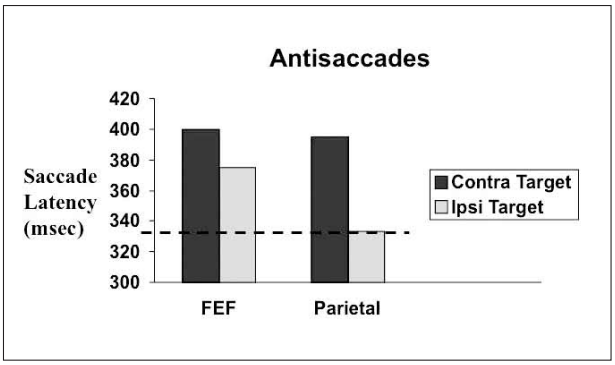

Fig. 4 – *Mean antisaccade latencies of patients with lesions of the frontal eye field and intraparietal cortex, for saccades directed away from contralesional and ipsilesional targets. Mean antisaccade latency for control subject is indicated by the dashed line.*

latencies for antisaccades away from contralesional visual targets were increased in comparison to antisaccades directed away from ipsilesional visual targets (Machado and Rafal, 2004b).

The effect of parietal lesions on latencies for prosaccades and antisaccades, therefore, converge nicely with the neurophysiological observations of Gottlieb and Goldberg (1999): intraparietal neuron activity in response to contralateral visual signals is greater than for prosaccades; and the response latencies to contralesional visual targets in patients with parietal are more affected for antisaccades than for prosaccades. It cannot be the case that the increase in latencies for antisaccades away from contralesional signals was due to a difficulty in inhibiting a VGR toward them (as was the case in patients with FEF lesion): they made *fewer* reflexive glances toward contralesional than toward ipsilesional signals. Nor can it be the case that they are impaired in shifting attention away from contralesional signals (Friedrich et al., 1985).

It seems, then, that neither the "motor" nor the "attentional" account is very satisfying. How, then, should we understand the fact that single unit activity in intraparietal cortex is greater for antisaccades than for prosaccades; and that, in patients, the latency of antisaccades away from contralesional signals is increased, whereas those for prosaccades toward them are not? Antisaccades require a process that transforms a sensory signal into a command to execute a voluntary saccade toward another location. Neurophysiological studies (Zhang and Barash, 2000, 2004) demonstrate that neurons in lateral intraparietal (LIP) code this transformation. Our observations in patients with chronic lesions of this region also demonstrate a role of parietal oculomotor cortex in mediating sensorimotor transformations necessary for voluntary saccades to be made in response to visual information – that is, in translating the visual environment into a code that can be utilised to guide goal directed behaviour.

Effects of Parietal Lesions on Selecting Targets for a Voluntary Saccade

We studied some of the same patients with parietal lesions in another experiment that requires a voluntary saccade to be generated toward a peripheral visual target (Ro et al., 2001). It employed a temporal order judgement paradigm. On each trial a visual signal was presented in both the ipsilesional and the contralesional fields, and the time interval between their onsets was manipulated. On some trials the contralesional target preceded the ipsilesional, on some the ipsilesional preceded the contralesional, and on some they onset simultaneously. The patients were tested in two tasks. One was a conventional temporal order judgement task in which they kept their eyes fixed, and reported which target, left or right, appeared first. In the other task, they were asked to make a saccade to one of the two targets. Unlike patients with hemispatial neglect, who had previously been tested in the identical experiment (Rorden et al., 1997), the patients with chronic parietal lesions (none of whom had neglect), showed no ipsilesional bias in the perceptual task in which they had simply to report which target onset first. By contrast, in the saccade task, the patients showed a bias to choose the ipsilesional target for their saccade. So not only do parietal lesions cause patients to be slow to make a saccade away from a contralesional signals, as in the antisaccade task, they also cause patients to be biased against making a saccade toward a contralesional signal under conditions where the saccade must be generated on the basis of a voluntary choice. As in the antisaccade task, the saccade choice task requires a sensorimotor transformation in which a voluntary saccade must be programmed in response to a visual signal.

Parietal Lobe Lesions Disrupt Saccadic Remapping of Inhibitory Location Tagging

As we search a visual scene for a target object toward which action is required, we are aided by an inhibitory process that tags recently attended locations (Posner and Cohen, 1984; Klein and MacInnes, 1999). This inhibitory tagging facilitates efficient search by favouring new objects over those that have already been sampled. Maintaining a coherent percept of the visual scene, that can be used to regulate visually guided behaviour while eye position continuously changes, requires that saccades be accompanied by remapping of the visual environment. That is, the inhibitory tag must be maintained in a scene based coordinate reference frame that must be updated after each eye movement. Since each eye movement is made to an object projected onto the retina, it must be accompanied by a visuomotor transformation that maps current retinal locations onto the scene based

reference frame. If the scene based reference frame is not updated after each eye movement, the inhibitory tag of the location just previously sampled will move with the eye – and the record of its position in the scene will not be durable or useful in guiding subsequent search.

Neurophysiological and neuropsychological studies have both implicated the parietal lobe in the remapping of the visual field following eye movements. Just before a saccade has occurred, neurons in LIP cortex shift their visual receptive field such that they respond to visual signals that are not currently in their receptive field, but which will be after the impending saccade is executed (Colby et al., 1995; Duhamel et al., 1992). The neuropsychological studies employed a double step saccade paradigm (Duhamel et al., 1992; Heide et al., 1995). Two flashes of light are presented in rapid sequence, and the patient is asked to make a saccade to both in the order they appeared. Both signals have disappeared before the saccades are made. Thus, the first saccade can be made to the retinal location of the first target. To make an accurate saccade to the place in the visual scene that the second target appeared, however, requires an "extraretinal" signal; that is, a "corollary discharge" record of the amplitude and direction of the saccade to the first target must be used in programming the second saccade. In this double-step saccade task, babies are able to make accurate saccades to the second target by about 6 months of age. Younger infants make the second saccade in retinotopic rather than scene based coordinates (Gilmore and Johnson, 1997). Duhamel et al. (1992) first used this double step saccade paradigm in a patient with hemispatial neglect with a large right fronto-parietal lesion. The striking and paradoxical finding was that, when the second saccade had to be made toward the contralesional field, the saccades were accurate; by contrast when the second saccade had to be made toward the ipsilesional (i.e., the 'good' field); the patient was not able to do so. In this condition, the first saccade had been made toward the contralesional field. The results demonstrate that, although, the patient was able to make visually guided saccades toward contralesional targets, these saccades are not accompanied by saccadic remapping; so the patient did not seem to be able to "remember" where the second target (in the 'good' ipsilesional field) had been flashed. Heide et al. (1995) subsequently confirmed this result in a group of patients with chronic lesions restricted to the parietal lobe.

In a recent study, we showed that intraparietal cortex is also involved in re-mapping an inhibitory tag that enables efficient visual search (Sapir et al., 2004). The display (Figure 5) consisted of 4 marker boxes, 8 degrees from fixation, forming an imaginary square. In separate blocks, each trial began with the eyes fixating a + located midway

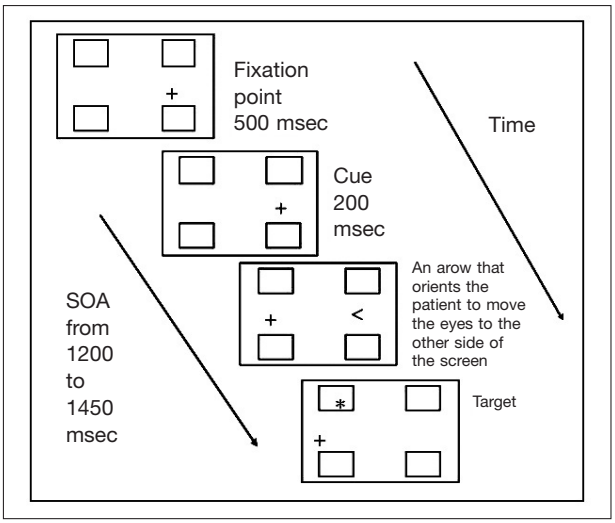

Fig. 5 – *Visual display used by Sapir et al. (2004) to examine saccadic remapping of inhibitory spatial tags (see text).*

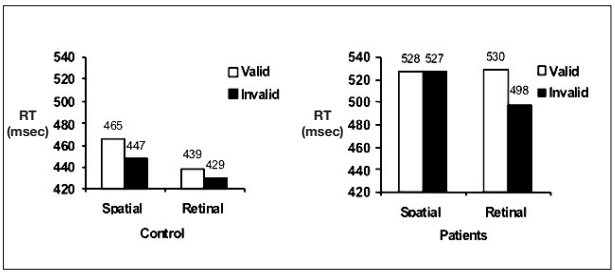

Fig. 6 – *Reaction Time (RT) to detect targets appearing at the spatial or retinal location of the cue, compared to uncued locations, for normal controls and for patients with lesions of intraparietal cortex.*

between the boxes in either the right or left field. A precue (the flashing of one of the boxes located above or below fixation that was not informative about the location of the forthcoming target) was presented to generate an inhibitory tag. Then, before the target appeared, the + sign was replaced by an arrowhead pointing toward a + sign located between the boxes in the opposite visual field and an eye movement was made to that location. After the eyes had fixated the new location, a target appeared, with equal probability, in one of the four boxes, and key press RT is measured. The target could, thus, occur at the environmental location of the precue (the same box that was flashed), at the retinotopic location of the precue (i.e., projected to the same point on the retina that was stimulated by the precue) or at one of the two corresponding uncued locations.

In normal individuals (see Figure 6), we confirmed Posner and Cohen's (1984) finding that inhibition of return (IOR) is remapped in "environmental" rather than retinotopic coordinates. In a group of 5 patients with lesions of superior intraparietal cortex we showed, as predicted, that IOR is mapped in retinotopic, rather than "environmental" coordinates.

Saccadic Remapping, Visual Working Memory and Hemispatial Neglect

We have seen that a failure of saccadic remapping prevents inhibitory spatial tagging that can be used to facilitate efficient visual search. This deficit may aggravate visual neglect by depriving patients of a useful memory trace of already sampled locations during visual search. Wojciulik et al. (2001) showed, in a single case study of a patient with hemispatial neglect, that an impairment in being able to mark already searched items does aggravate neglect. They tested their patient in two versions of a cancellation task. One was a conventional procedure in which the marks placed on each cancelled item were visible to the patient; in this situation there is no need for the patient to "remember" which items have already been cancelled. In a novel version of the task, the marks made by the patient were invisible. Neglect of contralesional items was greater in this condition. A subsequent study (Husain et al., 2001), in which eye movements were recorded in a series of patients, confirmed that, during visual search, patients with hemispatial neglect are prone to resample already inspected locations. They interpreted their findings as indicating that there is a deficit in spatial working memory in patients with this syndrome. As we have seen, however, a failure of saccadic remapping will prevent the establishment of a durable representation of searched locations. So the difficulty may lie in a failure to encode accurate location information in a scene based reference frame, rather than a failure in retrieving those locations from memory.

Sensorimotor Transformations, Selection for Action and Selection for Awareness

From the studies of patients with chronic lesions of parietal oculomotor cortex reviewed here, we can conclude that this region is not primarily involved in commanding the initiation of either voluntary or reflexive eye movements. Rather, its function is to mediate visuomotor transformation that processes visual information into a representation that can be used to guide voluntary actions. While this review focused on saccadic eye movements, the same framework could be applied to visually guided limb movements, mediated by other parts of intraparietal cortex.

More generally, this framework is consistent with the view that the function of the parietal lobe is selection for action. That is, its role is to select sensory information for action and to transform it into a representation of use to motor systems. This view is consistent with other observations in my laboratory showing that the exclusion from awareness that characterises hemispatial neglect is not due to a gating of sensory processing but, rather, gating at the level of response selection.

If attention gated access to consciousness entirely by attenuating the processing of unattended stimuli early in the visual pathway, then visual extinction in patients with hemispatial neglect could not be influenced by the semantic meaning of the competing stimuli or by the task used to test for it. Extinction is, however, determined both by what the competing stimuli are, and by task demands. Whether or not a contralesional object is extinguished is dependent upon: 1) whether the competing item is the same, or different, on the dimension to be reported (Baylis et al., 1993); 2) whether the competing objects are grouped on the basis of Gestalt principles (Mattingley et al., 1997; Ward et al., 1994); 3) the task used to probe for extinction – counting, identification or localization (Vuilleumier and Rafal, 2000); and 4) potential relevance – that is, real objects suffer less extinction than meaningless stimuli (Ward and Goodrich, 1996); and there is less extinction of socially or emotionally valenced stimuli (Vuilleumier, 2000; Vuilleumier and Schwartz, 2001a, 2001b).

Studies of patients with visual extinction in my laboratory have shown, consistent with a selection for action role of parietal lobe, that unawareness of contralesional items results from a competition, not for perceptual processing, but for response selection. The experiments were based on a simple bedside observation: that visual extinction is less when competing items, that have to be individually identified and reported, are different than when they are the same (Rafal, 1998). Moreover, the degree of extinction was determined specifically by whether the competing items were the same on the dimension (colour or shape) required for response selection (Baylis et al., 1993). Critically, subsequent work shows that the degree of extinction is determined by whether the competing items required the same response, regardless of whether they shared or differed in their visual features or semantics (Rafal et al., 2002, 2006). Not only was there more extinction between (ONE + ONE) than (ONE + TWO): there was just as much extinction between (ONE + 1) or (ONE + WON) as there was between (ONE + ONE).

Conclusions

This review has summarised what we have learned, from the study of patients with chronic lesions of frontal and parietal oculomotor cortex, about the role of these regions in controlling voluntary and reflexive saccadic eye movements. FEF lesions permanently impair the initiation of voluntary saccades toward the contralesional field, demonstrating that this region is critical for this function. By contrast, parietal lesions do not

permanently impair the initiation of either voluntary or reflexive saccades. It seems likely that, in the normal state, reflexive saccades are generated by a parieto-collicular circuit. Although the ability to initiate reflexive saccades does not depend on parietal cortex, there is evidence that projections from parietal cortex to the colliculus (via the posterior limb of the internal capsule) do contribute to the accuracy of reflexive saccades (Gaymard et al., 2003). The findings that chronic parietal lesions result in persistent deficits in antisaccade latencies, saccadic remapping, and in an oculomotor bias against generating voluntary saccades toward contralesional visual signals, suggest that the primary function of parietal oculomotor cortex is in mediating visuomotor transformations needed for transducing visual signals into an action based reference frame for voluntary saccades.

Persisting oculomotor deficits resulting from damage to oculomotor cortex afford solid evidence for their core functions – those functions for which they are indispensable: frontal cortex for generating voluntary saccades and parietal cortex for providing the necessary sensorimotor transformations. The effect of lesions in these regions on reflexive saccades also provides valuable insights into the dynamics of cortico-subcortical circuits in the integration of voluntary saccades with reflexive eye movements generated by the superior colliculus.

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