Cognitive Critique

A SHORT HISTORY OF THE STUDY OF THE INTERACTION BETWEEN OCULOMOTOR CONTROL AND SHIFTS OF VISUAL ATTENTION

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ABSTRACT

The study of the neural mechanisms underlying visual attention has been bound up with the study of oculomotor control for almost as long as both have been investigated scientifically. Before the 1970s, most knowledge about the neural mechanisms of visual attention and oculomotor control was derived from lesion studies in animals and from clinical case reports. The phenomenon of contralateral inattention following posterior parietal lobe injury in humans was well documented, but it did not seem possible to approach the study of the neural substrates of visual attention directly, given the technological limitations of the time. However, in the early 1970s, several laboratories began the study of the activity of single neurons in monkeys that were alert and performing learned behavioral tasks, including tasks involving voluntary eye movements and involving shifts of visual attention. A group at Johns Hopkins proposed that

some neurons in posterior parietal cortex participated in the initiation and control of visually-guided saccadic eye movements and visual pursuit movements, while another group argued that all neural activity in the posterior parietal lobe was related to visual attention rather than oculomotor control, and that only the frontal eye field, located in prefrontal association cortex, participated in active oculomotor control. From this difference of interpretation grew more than thirty years of active investigation and discussion that has involved many different laboratories as they worked toward further understanding of the neural circuitry underlying visual attention and oculomotor control. Neurophysiological, neuroanatomical, and functional imaging studies have led to the present concept of cortico-cortical networks which incorporate nodes that play a role in both oculomotor and visual attention functions. In fact, recent research results suggest that the functions of visual attention and oculomotor control may be inextricably linked with one another - perhaps two sides of the same coin. The present paper is intended to be a brief historical overview of the development of some of the current concepts of the interaction between the neural mechanisms of attention and those of oculomotor control.

INTRODUCTION

Selective attention is that property of the mind/brain that reduces the incoming sensory information with which we are constantly being bombarded to manageable proportions, allowing us to be enlightened rather than overwhelmed by our surroundings. This property of being able to choose from among the myriad sensory messages that are present at any given moment has fascinated thoughtful people for centuries. One of the most eloquent descriptions of selective attention was given by the eminent psychologist and philosopher, William James, over one hundred twenty years ago:

> Millions of items of the outward order are present to my senses which never properly enter into my experience. Why? Because they have no interest for me. My experience is what I agree to attend to. Only those items which I notice shape my mind — without selective interest, experience is utter chaos. Interest alone gives accent and emphasis, light and shade, background and foreground — intelligible perspective, in a word. It var-

> ies in every creature, but without it, the consciousness of every creature would be a gray chaotic indiscriminativeness, impossible for us to even conceive. (James 1890, p. 402-403)
>
> Every one knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others... (James 1890, p. 403-404)

Visual attention can be described in several ways (e.g. Moore 2006; Awh et al. 2006). A novel object might enter the visual field and capture an individual's attention, or the individual himself/herself might voluntarily shift attention from one object to another in an unchanging visual environment. These two types of attention are called "bottom-up" and "top-down" attention, respectively, or "stimulus-driven" and "goal-directed". When an individual attends to one particular object, he may direct his gaze and look directly at it (the usual situation, "overt" attention), or he may keep his gaze steady yet heighten his awareness of an object or location that is peripheral to his center of gaze ("covert" attention). A third way that visual attention can be characterized is by whether attention is directed toward a certain place, regardless of what object occupies that place ("spatial" attention) or is directed toward a particular object that is different in some way from an array of similar objects within the visual field ("feature-based" attention). Most of the investigations that will be discussed here address the underlying mechanisms of overt attention (including associated eye movements) and covert attention.

As important as the property of selective attention is in the study of cognition, attempts to study it scientifically were, for many years, limited to psychophysical studies, studies of patients with brain damage produced by strokes or traumatic injury, and electrical stimulation studies. The direct study of activity in the neural circuits that underlie selective attention and the neural connections that were involved in those circuits was not possible until comparatively recently, because such studies could only be carried out in anesthetized animals which, of course, do not display behavior related to attention. This situation led to certain biases of interpretation that

persisted even after evidence to the contrary was manifest, specifically, that neural activity in the frontal lobe is specifically motor in nature whereas neural activity in the parietal lobe is concerned only with sensation and attention. The present paper is a short history of the evolution of the current ideas about the cortical control of eye movements and attention. The story has two threads: (1) hypotheses of motor control gradually transitioned from a model in which eye movements were controlled by separate, serially connected centers in the cerebral cortex to the current model in which distributed neural networks control attention and associated eye movements; and (2) the former idea that a given geographical region of cerebral cortex served only a single behavioral or cognitive function has gradually given way to the idea that several functions can share a given region of cortex. This second idea seems to culminate in recent evidence that some critical aspects of spatial attention may be controlled by precisely the same neural circuitry in the prefrontal association cortex that controls voluntary eye movements. Sometimes these two threads have proceeded separately, and sometimes they have been intertwined.

SPATIAL ATTENTION AND OCULOMOTOR CONTROL IN 1970

In 1970, the predominant model of the neural control of voluntary eye movement was simple, logical, and straightforward: visual information from the retina arrived at primary visual cortex, was relayed to extrastriate cortex where additional processing synthesized a meaningful visual perception from the raw sensory information, was further relayed to parietal association cortex where the perceptual scene was analyzed and objects of interest were attended to; from there, signals were sent to the frontal eye fields where sensory and attention information were transformed into motor signals that were then sent to the brainstem oculomotor circuits to bring the image of an object of interest onto the fovea for high-acuity investigation (Figure 1) (see, for example, Truex and Carpenter 1964; Ruch and Patton 1965).

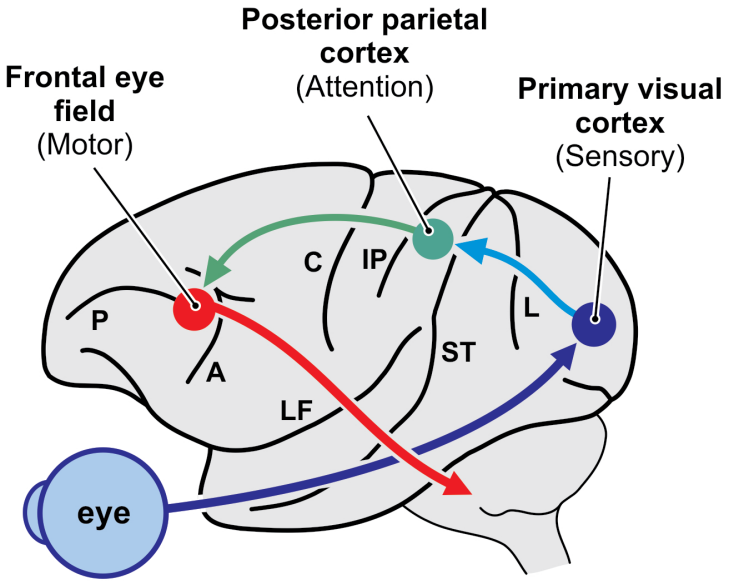

Figure 1. Serial model of visual sensorimotor processing, circa 1970. In this model, visual sensory information went from the retina to the primary visual cortex. From there, it went, via several processing centers in visual association cortex, to posterior parietal cortex. The posterior parietal cortex was thought to superimpose visual attention upon the basic visual sensory information and send resulting signals to the frontal eye field, the "final common pathway" for the oculomotor system. In the frontal eye field, motor signals were generated which were sent to the brainstem oculomotor circuits, resulting in appropriate movements of the eyes. A, arcuate sulcus; C, central sulcus; IP, intraparietal sulcus; L, lunate sulcus; LF, lateral fissure; P, principal sulcus; ST, superior temporal sulcus.

Two separate lines of reasoning had contributed to this model. *First*, electrical stimulation experiments, beginning with David Ferrier's work in the 1870s, had established the frontal lobe as the most important site in the cerebral cortex for motor activity in primates. *Second*, decades of reports on humans with brain damage had established the posterior parietal lobe as the most important region that played a role in visual attention. These lines of evidence will be reviewed individually, and then discussed in terms of their intersection in the development of our present day understanding of the neural circuits that subserve attention and oculomotor control.

Oculomotor Control and the Frontal Lobe

In 1875, Ferrier reported a series of experiments in which he used rudimentary electrical stimulation techniques to explore the excitability of large areas of the cerebral cortex of anesthetized monkeys (Ferrier 1875). He reported electrically-evoked eye movements in the frontal, parietal, and temporal lobes, and he reported electrically-evoked limb and face movements in both the frontal and parietal lobes (see Lynch and Tian 2006). However, as Ferrier's stimulation experiments were repeated and refined by other investigators over the next 100 years, the cortex of the frontal lobe became more and more identified with "motor" function. An important monograph, *The precentral motor cortex* (Bucy 1944), did much to reinforce the idea that "motor" cortex was, by definition, anterior to the central sulcus, and that all cortex posterior to the central sulcus was "sensory" in nature. The chapter in the Bucy monograph by Wilbur Smith, *The fontal eye fields* (Smith 1944), was instrumental in establishing the frontal eye field as the putative final common pathway from the cortex to the brainstem oculomotor system. In his chapter, Smith did discuss some of the complications surrounding any simple description of the function of the frontal eye field, but the mainly-motor hypothesis of frontal eye field function was well established. The idea of a single cortical center that collected the results of neural processing in the visual system and then sent a resultant signal to execute an appropriate eye movement was attractive and persisted for many years (e.g. Leichnetz and Goldberg 1988; Goldberg and Segraves 1989; Schall et al. 1995).

Spatial Attention and the Parietal Lobe

During the first half of the twentieth century, concepts of the brain mechanisms involved in spatial attention were dominated by the clinical observation that damage in the posterior parietal lobe of the minor hemisphere (usually the right hemisphere) often produced a profound disorder in an individual's ability *to attend* to sensory stimuli in his/her immediate environment, a condition termed *contralateral neglect*. This collection of symptoms was described very early by John Hughlings Jackson in 1876 (Friedland and Weinstein 1977). Similar reports were published by Pineas in 1931 and by Scheller and Seidemann in 1932 and by others (Critchley 1953). The first in-depth discussion of the neural basis of spatial attention seems to be a report by Sir Russell Brain in 1941 in which he reviews

previous case reports and then describes six patients who suffered disorders of attention following damage in the parietal lobe (Brain 1941). Patients with full-blown contralateral neglect, or with a less serious but similar disorder termed *contralateral inattention*, may be unaware of visual stimuli in the field of vision contralateral to the brain damage; may not hear sounds originating in contralateral space; may read words only on one side of a page; may draw details on only one side of a sketch; and may not recognize their own limbs on the side of their body contralateral to their brain damage. Although damage in prefrontal cortex of humans also occasionally produced disorders of spatial attention (Heilman and Valenstein 1972), contralateral inattention was much more common after parietal damage. For example, Ettlinger and colleagues reported a study of 80 patients who had unilateral cerebral lesions verified by CT scans and 34 control subjects. Performance testing disclosed that 30 of the patients with brain damage had contralateral neglect. Of these 30 patients, the brain damage was located in the parietal lobe or parieto-temporal junction of 20, the frontal lobe of 3, and the temporal lobe of 2 (Halsband et al. 1985). The function of spatial attention became closely associated with the right parietal lobe as a result of many such clinical reports.

THE NEURAL MECHANISMS OF SPATIAL ATTENTION AND OCULOMOTOR CONTROL BEGIN TO CONVERGE

In the 1950s and 1960s, much progress was made in understanding the neural circuitry that was responsible for the processing of sensory signals. However, it was not until the late 1960s and early 1970s that technological advances made it possible to directly address questions pertaining to the neural circuitry that underlies cognitive processes such as memory and attention. It was during this time that recording the neural activity of single brain cells in awake, trained animals - particularly monkeys - became possible on a practical scale. Improved recording equipment played a role in this development, but the critical factor was the availability of small, in-laboratory digital computers that could control complex behavioral paradigms and simultaneously record the vast amount of neural and behavioral data that was generated (November 2004). Among the laboratories that first turned this newfound technological capability to the study of somatomotor and oculomotor control

and visual attention were those of Vernon Mountcastle at Johns Hopkins, David A. Robinson at Johns Hopkins, Edward Evarts at the NIH, and Robert Wurtz at the NIH. It was at this point in time that the separate histories of oculomotor control and visual attention began to converge.

The first step away from the serial processing model of oculomotor control described above was made when Mountcastle and his colleagues recorded single-neuron activity from alert, behaving monkeys that had been trained to perform a variety of oculomotor and somatomotor tasks (Mountcastle et al. 1975; Lynch et al. 1977). The experimental paradigm will be explained in some detail, as most of the other animal research discussed below will involve variations on this same basic theme. Monkeys were trained to foveate and watch intently a small (1-2 mm diameter) spot of light and to signal the moment that the light dimmed slightly by moving a small lever. A given "trial" consisted of the fixation target light being turned on by the computer, the initiation of a randomly selected delay time (usually between 500 ms and 2 s) during which the monkey maintained fixation of the target light while waiting for it to dim, the dimming of the light, and a second delay time (usually 400-500 ms) during which the monkey had to move the lever to signal that he had noticed the dimming of the light. If successful, the monkey received a small fruit juice reward. The dimming of the light was so slight that the monkey had to be looking right at the light in order to detect the dimming. Eye position was monitored electronically during the task to ensure that the monkey was looking at the light throughout the trial period. If the monkey looked away, the trial was aborted and a new trial commenced. A small laboratory computer (at first, one of the original LINC machines; later, an early DEC PDP-11; see November 2004) controlled the behavioral paradigm, recorded electronic signals related to the monkey's correct or incorrect performance during a given trial, including reaction time from the dimming of the light to the monkey's response (pull of the lever), recorded the monkey's eye position throughout the trial at 5 ms intervals, and, finally, recorded the time of occurrence (with an accuracy of a few microseconds) of each action potential discharged by the neuron being studied during the course of the trial. A complete series of trials (a data collection "run"), perhaps comprising six or eight different sets of parameters, might consist of 100-150 individual trials. The amount of data collected in a single trial of this paradigm makes it obvious that only with the advent of

the small, dedicated laboratory computer could neurophysiological research of this complexity be carried on.

In these early experiments, the Mountcastle laboratory isolated and studied more than 2300 neurons in the posterior parietal association cortex (PPC) of 17 monkeys. They were able to identify and classify the response properties of over 1400 of these neurons and did computer-controlled data collection runs on 651 neurons. As might be expected, many of the neurons in the PPC responded to sensory stimuli, and their activity had attention-related components. For example, many neurons were active when the monkey looked at a raisin *when he was hungry*, yet the same stimulus would not evoke activity in that neuron if the monkey was no longer hungry and therefore not interested in the raisin. Similarly, a neuron might be very active when the monkey looked at the small target light in the behavioral paradigm when he was thirsty, but after the monkey had finished several data collection sets and was no longer thirsty, looking at the target light no longer evoked action potentials in the neuron.

The big surprise in these studies was that a large percentage of the PPC neurons did not respond to any sensory stimulus that could be delivered (visual, somatosensory, or auditory), yet were furiously active when the monkey made a goal-directed movement such as reaching for a raisin when hungry, or, in some cases, simply *looking at* the raisin when hungry, or executing a saccadic eye movement in order to watch for the dimming of a target light when thirsty. Careful study of the patterns of activity of these neurons disclosed that many of the neurons began to fire *before* the relevant movement began.

On the basis of the results described above, Mountcastle proposed that some neurons in the PPC were concerned with the initiation of goal-directed movements rather than the processing of strictly sensory information. The proposal of a movement-related component of the activity of the neurons in the posterior parietal cortex was not entirely novel. In Ferrier's early maps of electrical stimulation of the cortex, there were many stimulation points within posterior parietal cortex where eye movements were evoked. And later, in a largely neglected study, Elizabeth Crosby and colleagues demonstrated that electrical stimulation in the posterior parietal lobe (Brodmann's areas 5 and 7) produced movements of the limbs and eyes even after the cortex of the precentral and postcentral gyri had been removed (Fleming and Crosby 1955). Nevertheless, the de-

fenders of the serial model of sensorimotor processing were quick to respond to Mountcastle's suggestion. A group at the Armed Forces Radiobiology Research Institute recorded from 289 neurons in Area 7 of monkeys that had been trained in behavioral paradigms similar to those of Mountcastle and claimed that all of the neural activity observed by the Mountcastle group could be explained by sensory input to the neurons in question (Robinson et al. 1978). The Mountcastle group, of course, disagreed with these claims.

Lynch wrote a theoretical review in *The Behavioral and Brain Sciences* to examine, in detail, the issues involved (Lynch 1980). In this review, Lynch proposed that a given cortical region, such as the posterior parietal association cortex, could contain overlapping neural circuitry that played roles in several different functions, e.g. eye movement initiation, somatosensory processing, hand movement initiation, and the modulation of spatial attention. He argued that it was inconsistent with available data to consider one region as *only* "motor", another region as *only* "sensory", and another region as *only* concerned with some higher-order function such as attention. Further, Lynch cited the seminal studies of Schiller and his colleagues in which destruction of the frontal eye fields alone or the superior colliculus alone caused only minor disruptions of saccadic eye movements, whereas the destruction of both structures together caused profound eye movement deficits (Schiller et al. 1979, 1980). These studies seemed to provide overwhelming evidence that some neural functions are served by distributed, parallel systems rather than strictly serial systems. The review was published together with twenty-four commentaries by prominent neuroscientists. Thus the stage was set for 20 years of intense investigation, discussion, and argument, among many laboratories, concerning the interaction of the neural substrates of visual attention and oculomotor control.

Early efforts in several laboratories focused on working to establish that the neural activity observed in the PPC preceding saccadic eye movements was independent of any sensory input. Andersen devised a paradigm in which the time of appearance of the saccade target stimulus was separated in time from the time of the saccade itself (Andersen et al. 1987). Monkeys were trained to visually fixate a small centrally-located spot of light in total darkness; while the monkeys looked at the fixation target, a saccade target was blinked briefly (200 ms) at some location on the screen, and the monkey was required to remember the location of the saccade target for 500-1500 ms. At that time, the fixation target light was

turned off as a signal for the monkey to make a saccadic eye movement to the remembered target location. The neural activity associated with the initiation of the saccade was therefore well separated in time from even the brief appearance of a visual stimulus, yet 46 of the 78 parietal neurons tested in this paradigm showed clear presaccadic activity (Andersen et al. 1987). A number of similar studies reported neural activity in the PPC that preceded saccadic eye movements to briefly-appearing visual targets in otherwise total darkness (Gnadt and Andersen 1988; Barash et al. 1991a, 1991b) and saccadic eye movements made in total darkness to auditory signals (Mazzoni et al. 1996).

During this time, other groups focused their research on elucidating the attention-related functions of the posterior parietal cortex. Goldberg and colleagues developed a behavioral paradigm which made it possible to measure shifts in visual attention that were dissociated from shifts in the direction of gaze (Bushnell et al. 1981) and found that many parietal neurons were active when a monkey attended to the state of a light target in its peripheral visual field, while maintaining its gaze on a central fixation target. Colby and colleagues observed that the visual receptive fields of some parietal neurons shifted, just prior to an intended saccadic eye movement, to the position in space that it *would* occupy after the eye movement was completed (Duhamel et al. 1992). These studies, and others that followed, emphasized the role of the PPC in modulating visual attention while minimizing its possible role in controlling voluntary eye movements (e.g. Goldberg and Bruce 1985; Colby 1991; Colby and Goldberg 1999).

These behavioral neurophysiology studies supported earlier concepts of the role of the PPC in the faculty of selective visual attention that had been based on clinical reports in humans. However, the results of parietal lesion studies in monkeys were not as clear-cut as in humans. Whereas humans suffered profound contralateral neglect following parietal lesions, the effect was much milder in monkeys and generally consisted of "extinction" to the contralateral of two equal and simultaneous stimuli rather than full-blown neglect of single stimuli (Eidelberg and Schwartz 1971; Lynch and McLaren 1989).

During this period of time, the new advances in behavioral neurophysiology technology were also being brought to bear on the neural circuitry of the frontal eye field. Surprisingly, the first attempts to record in the frontal eye field in behaving monkeys found

neurons with visual receptive fields, neurons with activity related to the direction of gaze, neurons that were active during the fast phase of nystagmus, neurons with activity that began *after* the initiation of visually-evoked saccadic eye movement, but no neurons with activity that began *before* saccadic eye movements (Bizzi and Schiller 1970; Mohler et al. 1973). It was not until 1985 that Bruce and colleagues reported neurons in the frontal eye field of macaques, in the anterior bank of the arcuate sulcus, that were active prior to the initiation of saccades to visual targets (Bruce et al. 1985). This finding supported the idea that the frontal eye field contained neural circuitry that was involved in the initiation and control of saccades. However, there was a tendency to focus more on those neurons with presaccadic activity and not so much on the other neurons in the frontal eye field, including those with visual receptive fields and neurons with combined visual-presaccadic activity (Bruce et al. 1985). In addition to the categories of activity listed above, neurons with memory-related activity were later found in the frontal eye field (Sommer and Wurtz 2001).

NETWORK HYPOTHESIS OF CORTICAL CONTROL OF EYE MOVEMENTS

Evidence from lesion studies in monkeys was particularly unfavorable for the serial processing hypothesis of the cortical control of eye movements. If the neural circuit diagramed in Figure 1 is correct, and the frontal eye field is the sole region in the cerebral cortex that collects sensory information, calculates desired behavioral action, and sends the resulting motor signals to the brainstem oculomotor centers, then the destruction of the frontal eye field should produce a complete loss of visually-guided eye movements. This does not happen. Instead, complete destruction of the frontal eye field produces only transient, mild deficits of saccade accuracy and latency that resolve within a period of a few days to one or two weeks (Figure 2) (Schiller et al. 1979, 1980; Deng et al. 1986; Lynch 1992; Lynch and Tian 2006). Temporary chemical inactivation of the frontal eye fields, using bicuculline or muscimol, while monkeys are performing saccade tasks, does produced marked impairment of saccades (Dias et al. 1995; Dias and Segraves 1999), but the long-term duration of such impairments has not been measured and it is unlikely that such impairments would last longer than than the effects of surgical destruction of the frontal eye fields.

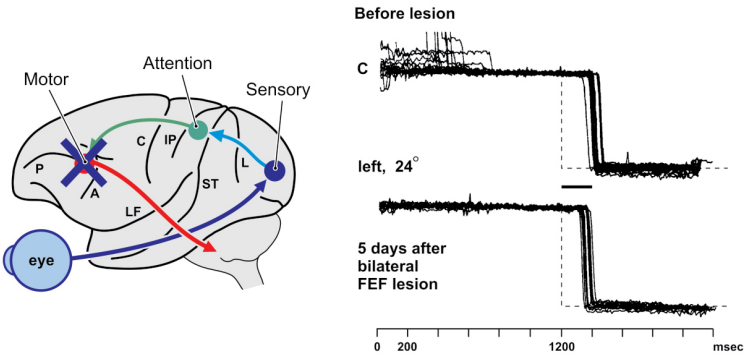

Figure 2. Rapid recovery of saccadic eye movements after bilateral destruction of the frontal eye fields. Both accuracy and latency of saccades returned to the normal range within five days following the lesion. The dashed line indicates the time at which the fixation target jumped from the center of the monkey's visual field to a position 24 degrees to the left of center. Fourteen eye position traces are superimposed in each grouping. (adapted, with permission, from Lynch JC, Tian JR (2006) Cortico-cortical networks and cortico-subcortical loops for the higher control of eye movements. Prog Brain Res 151:461-501)

These results, taken together, eliminated the possibility that the frontal eye field was the only cortical region that sent oculomotor signals to the brainstem and provided strong support for the idea that some motor functions were localized in more than one cortical region, that is, in a distributed cortical network.

During the late 1970s and the 1980s, the concept of distributed networks of neural circuits had been steadily gaining ground. One of the first explicit statements of the hypothesis that more than one cortical center might be involved in motor control was in a chapter by Mountcastle in 1978, titled "*An organizing principle for cerebral function: the unit module and the distributed system*" (Mountcastle 1978). In his conclusion, Mountcastle stated:

> An important feature of such distributed systems, particularly those central to primary sensory and motor systems, is that the complex function controlled or executed by the system is not localized in any one of its parts. The function is a property of the dynamic activity within the system: it resides in the *system* [ital-

> ics added] as such. Part functions, or simple aspects of system function, may be executed by local operations in restricted parts of such a system. This may explain why local lesions of a distributed system scarcely ever destroy system function completely, but degrade it to an extent determined by lesion size and the critical role of the locus destroyed for system function. The remarkable capacity for improvement of function after partial brain lesions is viewed as evidence for the adaptive capacity of such distributed systems to achieve a behavioral goal, albeit slowly and with error, with the remaining neural apparatus (pp. 40-41).

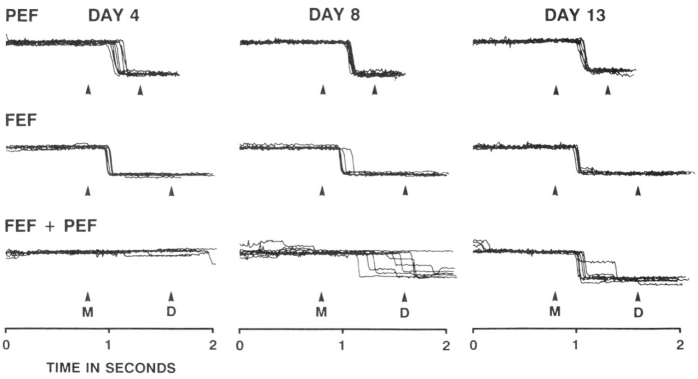

Figure 3. Eye position traces during horizontal 24 degree (top row) or 20 degree (middle and bottom rows) saccadic eye movements in macaque monkeys after bilateral destruction of only the frontal eye field (FEF); only the parietal eye field (PEF); or both eye fields together (FEF + PEF). Six to ten eye position traces are superimposed in each condition; performance is illustrated 4 days, 8 days, and 13 days after the surgical lesions. M, time of target movement from center of visual field to left part of visual field; D, time of target dimming. (Reproduced, with permission, from Lynch JC (1992) Saccade initiation and latency deficits after combined lesions of the frontal and posterior eye fields in monkeys. J Neurophysiol 68:1913-1916.)

Other investigators added to the evidence for distributed neural networks instead of simple serial processing models of oculomotor control (Rizzolatti et al. 1983; for reviews, see Lynch and Tian 2006; Lynch 2009). In 1992, Lynch published a direct test of Mountcastle's proposal, in which monkeys were trained to perform saccade tasks and performance was tested after lesions of frontal

eye fields alone, parietal eye fields alone, or both regions together (Lynch 1992). As illustrated in Figure 3, destruction of the frontal eye fields alone had a minimal effect on saccade accuracy or latency and saccades were essentially normal four days after surgery; destruction of the parietal eye fields alone had similar minimal effects on saccade performance. However, when a parietal lesion was added to a frontal eye field lesion, the effect on saccadic eye movement was devastating and recovery was prolonged. These results strongly supported the distributed network hypothesis.

The network hypothesis was also supported by numerous neuroanatomical studies (see Lynch and Tian 2006; Lynch 2009 for reviews). Barbas and Mesulam (1981) demonstrated that the neural connections *that originated in* the frontal eye field *and projected to* the parietal eye field were comparable in density to the neural connections that originated in the parietal eye field and projected to the frontal eye field, indicating that important neural information was traveling in *both* directions between these two centers, not simply traveling from posterior areas toward anterior areas. In addition, although about 25% of the input to the frontal eye field originated in the parietal eye field, about 50% of the input to the frontal eye field originated in visual association areas, suggesting that a considerable amount of higher-order visual processing was occurring within the frontal eye field. Huerta et al. (1987) confirmed these findings. Then, Lynch and Graybiel (Lynch et al. 1985) demonstrated that a major projection to the motor layers of the superior colliculus (an important oculomotor center in the brainstem) originated in the parietal eye field. These results gave additional support to the proposal that parietal association cortex could participate directly in the control of eye movements.

During the 1980s and 1990s, several neurophysiological studies implicated a number of cortical regions in the control of eye movements in addition to the frontal eye field (FEF) and parietal eye field (PEF). These included the supplementary eye field (SEF), prefrontal eye field (PFEF), middle superior temporal area (MT/MST), and the precuneus region (see Lynch and Tian 2006 for review). Each of these regions contained neurons which became active before or during eye movements; each of these regions was connected to each of the others; and each had an independent neural projection to the brainstem oculomotor circuitry (see figure 4). Tian and Lynch (1996) provided anatomical evidence that there were, in fact, two parallel corticocortical networks encompassing the FEF, PEF, SEF,

PFEF, MT/MST, and the precuneus region that subserved, respectively, purposeful saccadic and visual pursuit eye movements.

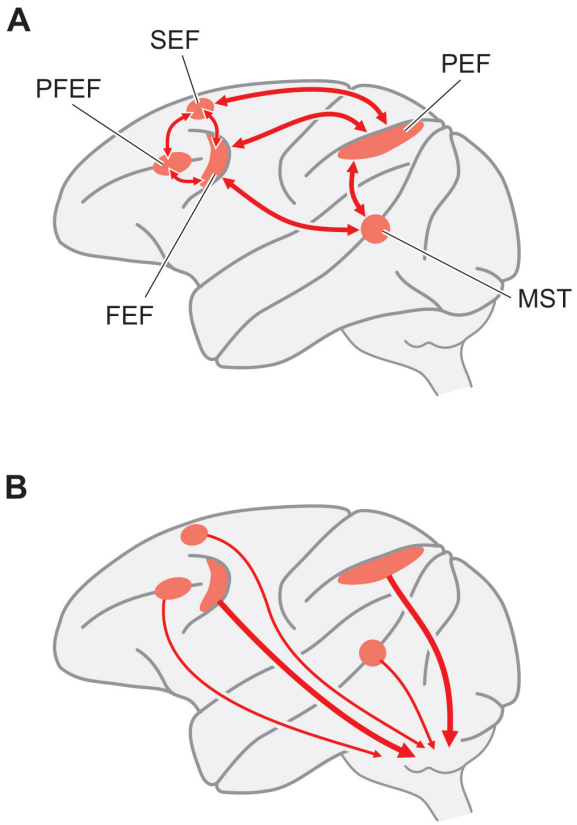

Figure 4. Five representative cortical eye fields depicted on a drawing of a macaque monkey brain: frontal eye field (FEF), parietal eye field (PEF), supplementary eye field (SEF), prefrontal eye field (PFEF), and medial superior temporal region (MST). A sixth eye field, the precuneus region (designated area 7m in monkeys) on the medial wall of the parietal lobe, is not illustrated. The upper drawing illustrates the bi-directional neural interconnections that each eye field has with most or all of the other eye fields. The lower drawing summarizes the results of a number of studies that have demonstrated that each eye field has its own independent neural projection to one or more brainstem nuclei involved in the control of eye movements, including the superior colliculus, pontine nuclei and cerebellum, mesencephalic and pontine reticular formations, and others. (For additional information, see (Lynch and Tian 2006; Lynch 2009)).

Finally, functional magnetic resonance imaging (fMRI) studies provided clear evidence that multiple cortical areas were active in conjunction with voluntary eye movements. Petit and colleagues (Petit et al. 1997; Petit and Haxby 1999) used fMRI to localize the cortical regions that were activated in humans during horizontal saccadic eye movements and during horizontal pursuit eye movements. They reported increased activity during oculomotor tasks in most of the same regions that were reported by Tian and Lynch as being interconnected with each other: PEF, FEF, SEF, MT/MST, and the precuneus region. Luna, Sweeney, and colleagues reported similar results in an independent series of experiments (Luna et al. 1998).

THE FRONTAL EYE FIELD AND ATTENTION

Although the role of the frontal eye field in oculomotor control was well established from the time of Ferrier, its possible role in other cognitive functions, and the control of selective attention in particular, was slower to be generally accepted. As early as 1895, Bianchi had reported that frontal lobe lesions in monkeys produced a collection of symptoms that included deviation of the eyes and head toward the side of the lesion, repetitive circling toward the side of the lesion, loss of finely controlled movements of the contralateral arm, and failure to respond to stimuli in the contralateral field of vision (Bianchi 1895). However, only qualitative descriptions of the behavioral deficits were offered and the extent of the cortical lesions in this study extended well beyond the electrophysiologically defined borders of the frontal eye field. Later studies, still only qualitative but with lesions more nearly restricted to the frontal eye field, found a similar collection of symptoms, including transient inattention to visual, auditory, and tactile stimuli contralateral to the lesioned hemisphere (Kennard 1939; Welch and Stuteville 1958). It was not until the 1970s that the first quantitative studies of the effect of lesions of the frontal eye field were possible. Latto and Cowey (1971) trained monkeys to maintain their gaze on a fixation target in the center of their visual field and detect the appearance of 50 ms flashes of individual small light bulbs in a square array of 120 bulbs arranged at 5 degree intervals. After unilateral frontal eye field lesions, monkeys made many more errors of detection of flashes in the visual field contralateral to the lesion than in the field

ipsilateral to the lesion. This deficit was attributed to inattention rather than to a visual sensory defect, and recovered in about two weeks. In somewhat different experiments, Crowne and colleagues trained monkeys to look at the center of a circular array of push-panels and to reach out and touch a panel when a light in the panel blinked briefly. Again, unilateral frontal eye field lesions produced neglect of visual stimuli in the visual hemifield contralateral to the lesion (Crowne et al. 1981). More recently, Schall and colleagues have demonstrated that single neurons in the FEF can be activated by covert shifts of attention in which no eye movements occur (Schall et al. 2004).

NETWORK HYPOTHESIS OF CORTICAL CONTROL OF ATTENTION

The concept of a distributed cortical network controlling visual attention was accepted more quickly than the idea that distributed cortical networks might be responsible for the control of voluntary eye movements. In 1981, Mesulam published an extensive review of evidence supporting the proposal that directed attention was controlled by a distributed network incorporating posterior parietal cortex, frontal cortex, and cingulate cortex, and included some subcortical structures (Mesulam 1981). A second major statement of the distributed network hypothesis of higher order cortical functions was published by Goldman-Rakic in 1988 in which she discussed the relative merits of distributed network models vs hierarchical models of cortical organization in the control of higher-order cognitive functions (Goldman-Rakic 1988). During the 1980s, rapid development of technologies permitted the imaging of events in the brain (changes in blood flow or blood oxygenation levels) that paralleled changes in neural activity, and it became practical to study cognitive functions in awake, behaving humans. With the advent of functional imaging studies of visual attention, the concept of a distributed cortical network that included frontal and parietal cortical regions, as well as other regions, became generally accepted (Corbetta et al. 1993; Corbetta 1998; Kastner and Ungerleider 2000; Astafiev et al. 2003; Peers et al. 2005; Buschman and Miller 2007; Bressler et al. 2008; Szczepanski et al. 2010).

VISUAL ATTENTION MEETS OCULOMOTOR CONTROL

After separate but sometimes overlapping lines of evidence pointed to both the cortical control of attention and the cortical control of oculomotor behavior being managed by parallel distributed networks rather than by serial, hierarchical mechanisms, the major three-part question became: (1) Did the same set of interconnected cortical areas control both attention and eye movements; or (2) was there partial but not complete overlap of the neural circuits that controlled attention and eye movements; or, at the extreme, (3) was the network that controlled visual selective attention completely separate from and independent of the network that controlled the execution of purposeful eye movements?

As the details of the cortical networks devoted to the control of attention were elucidated, the overlap between the cortical areas concerned with oculomotor control and those concerned with the control of attention was striking, and hypotheses that the two functions were closely related became numerous. Even before imaging studies became common, psychophysical studies were addressing the relationship between saccadic eye movements and the modulation of visual attention. Shepherd demonstrated that the reaction time to detect a brief visual stimulus in the peripheral visual field was shortened when the subject had knowledge that there was a high probability that the stimulus would appear in a certain region of the visual field (Shepherd et al. 1986). The stimulus detection reaction time was also shortened when the stimulus appeared just prior to the execution of a saccadic eye movement in the location to which the subject had been instructed to make the saccade. The change in attention level produced by the impending saccade was stronger than the effect of probability of appearance of the visual stimulus, suggesting that the neural circuitry responsible for controlling the eye movement also was involved in the modulation of visual attention level.

With the advent of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), the question could be addressed directly. Corbetta et al. (1993) and Nobre et al. (1997) were among the first to use PET to localize cortical regions that were activated during tasks involving shifts of visual attention. The two studies found that similar but not identical regions in the frontal and parietal lobes were the most highly activated during attention tasks. Corbetta and colleagues (Corbetta 1998) published

a meta-analysis of six PET studies of cortical regions involved in selective spatial attention and found similar results in all six studies, with largely overlapping regons in posterior parietal and prefrontal cortex showing the greatest increase in activity during a variety of visual attention tasks. The authors did a second meta-analysis of eight studies in which regions of cortical activity during saccadic eye movement tasks were localized, and then superimposed a flattened cortex map of the attention-related regions of activity upon a flattened cortex map of the saccade-related regions of activity and demonstrated a considerable, but not complete, overlap of the two sets of activity.Corbetta also published the results of an fMRI study of a single subject during both attention and eye movement tasks and demonstrated almost exact correspondence of the two patterns of activity, including increased activity in the frontal eye fields, parietal eye fields, supplementary eye fields, and posterior parietal association cortex as shown in Figure 5 (from Fig. 6, Corbetta 1998).

In 2000, Kastner and Ungerleider published an extensive review of studies of cortical mechanisms of visual attention and included a number of fMRI studies, which had inherently superior spatial resolution compared to the earlier PET studies (Kastner and Ungerleider 2000). Figure 6 from Kastner and Ungerleider shows that the areas of correspondence between eye-movement-activated regions and attention-activated regions is striking, and includes the FEF, SEF, and both superior and inferior parietal lobules. Numerous recent papers have confirmed the close relation between both the frontal eye field and posterior parietal cortex with the behavioral correlates of shifting visual attention and oculomotor control (Astafiev et al. 2003; Peers et al. 2005; Buschman and Miller 2007; Bressler et al. 2008; de Haan et al. 2008; Szczepanski et al. 2010). Results from these studies have generally been taken to support the premotor theory of attention (Rizzolatti et al. 1987), which proposes that a shift in visual spatial attention is the result of an intended but unexecuted saccadic eye movement and that shifts in visual attention and the execution of eye movements utilize the same neural circuitry. However, these functional imaging studies have been primarily concerned with the localization of regions of activity on a scale of a few millimeters and have not been able to address the question of whether the oculomotor and attention networks employ identical elements, or just happen to be located in close proximity to each other. Recent behavioral neurophysiology experiments have investigated this question directly.

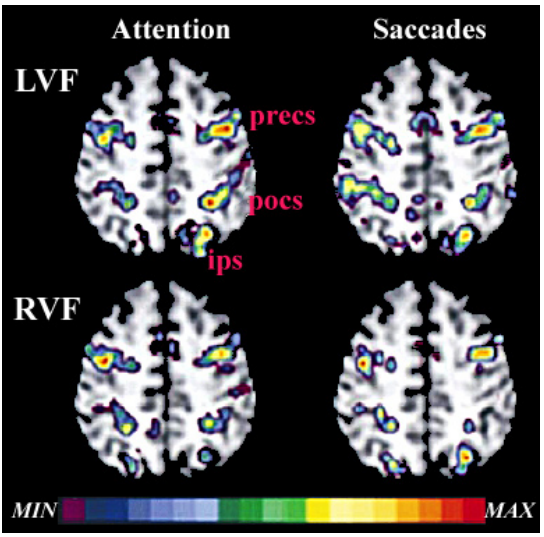

Figure 5. Functional MRI activity superimposed on anatomical MRIs from a single subject who was shifting attention into the left visual field (LVF) or right visual field (RVF) ("Attention") or who was making saccadic eye movements ("Saccades") into the left or right visual fields. Increased activity is seen in the regions of the frontal eye fields (precs), a postcentral cortical region - perhaps the superior parietal lobule (pocs), and the parietal eye field in the region of the intraparietal sulcus (ips) in both the attention and the saccade conditions. Right hemispheres are depicted on the right in this illustration. A color version of this figure is available in the online edition of Cognitive Critique. (Reproduced, with permission, from Fig. 6, Corbetta M (1998) Frontoparietal cortical networks for directing attention and the eye to visual locations: identical, independent, or overlapping neural systems? Proc Natl Acad Sci U S A 95:831-838.)

POSSIBLE CORRESPONDENCE OF ATTENTION AND OCULOMOTOR CIRCUITRY AT THE CELLULAR LEVEL

Hypotheses concerning the identity of the neural circuitry that serves higher-order cognitive functions such as visual attention are not easy hypotheses to test. The primary thrust of single-neuron neurophysiological studies over the past 60 years has been to determine the response properties of a neuron in a certain region of

the nervous system to learn if it carries a certain signal, or is activated by a certain sensory stimulus or behavior. For example, the investigator identifies a neuron in primary visual cortex that is activated when an image of a line of a certain width and orientation is projected on a certain region of the retina, or identifies a neuron in primary motor cortex that is active when a monkey reaches to touch a push-panel, or identifies a neuron in prefrontal cortex that is active while a monkey remembers a location to which he will make a saccadic eye movement after a certain time delay. These data provide the assurance that a given neural signal at least *exists* in a given brain region, but it is only after the accumulation of many such recording episodes, and combining the data from hundreds or thousands of individual neurons, that one begins to assemble a picture of all the various signals that may coexist in a given region of the brain such as the frontal eye field. Even then, however, one may not know how the various neural signals interact with each other to produce a given sensation or behavioral event.

The attempt to define the elements of a neural circuit that controls purposeful eye movements is fraught with many difficulties at our present stage of technological development, and to attempt to determine whether the elements of the cortical oculomotor circuit are also elements in a neural circuit for directing visual attention increases those difficulties many-fold. One must keep in mind that we are investigating *circuits,* comprising hundreds or thousands or millions of individual neurons. Just as it is not logical to expect every transistor in a computer or television receiver to be performing the same function, it is not necessary to find an individual neuron in the cortex that carries both oculomotor and attention signals in order to support the hypothesis that the two functions are controlled by the same neural circuits.

Numerous recent studies have addressed the question of how the neural circuitry for oculomotor control is related to the neural circuitry for shifting visual attention, and indeed whether the same circuitry might subserve both functions. In an attempt to get at the answer to this question, Moore and Fallah trained monkeys to fixate a central visual target, but to covertly direct their attention to a second visual stimulus projected somewhere on the 30 degree by 40 degree video monitor that the monkey was facing (Moore and Fallah 2001; Moore et al. 2003; Moore and Fallah 2004). The monkey's task was to maintain fixation on the central target but to move a lever within a short time period whenever the monkey detected a

slight dimming (40 ms duration) of the peripheral attention target. The monkey's task was made more difficult by flashing a distractor stimulus, identical to the attention target, at random locations around the screen. While the monkey performed this task, electrical microstimulation was administered through a microelectrode passing through the frontal eye field. When the current level was, on average, above 50 μA, saccadic eye movements were elicited. When the current level was below 50% of that level, saccadic eye movements were never elicited, but the monkey's performance on the attention task was enhanced. The conclusion was that while the low, subthreshold, level of microstimulation was insufficient to generate an eye movement by itself, it was nevertheless sufficient to alter the excitability of nearby neurons which were presumably involved in the attention task and thereby improve performance on the attention task. Given that the microstimulation current would have its effect within a sphere of less than about 200 μm, the neural elements that were influenced by the microstimulation had to be very close to each other and very possibly were components of the same general neural circuitry. The results of this study were therefore not definitive, but were highly suggestive.

In other experiments, Moore and Armstrong (Moore and Armstrong 2003; Armstrong and Moore 2007) observed that microstimulation in the frontal eye field which produced a saccade to a certain location in the visual field would, at stimulus strengths too low to actually elicit an eye movement, nevertheless alter the response of a visual neuron in visual association cortex (V4) to a stimulus when the saccade end-point coincided with the visual field of the V4 neuron, but does not affect the neuron's responsiveness if the saccade end-point is not in its receptive field. Most recently, Moore and Chang (2009) have reported that similar enhancement of V4 responses occurred just prior to voluntary saccadic eye movements if the end-point of the saccade lay within the V4 neuron's receptive field. In addition, Cavanaugh et al. (2006) have demonstrated that microstimulation within the oculomotor layers of the superior colliculus produces shifts of attention similar to those produced by microstimulation in the frontal eye field.

In a recent study, Thompson and colleagues have taken an important step toward identifying individual elements in the saccade/attention circuitry in the frontal eye field (Thompson et al. 2005). They trained monkeys to perform a saccade task and two attention tasks, including a pop-out visual search task in which eye move-

ments were prohibited. Activity was analyzed from 101 neurons that were classified as "visual", "visuomovement", or "movement" in nature. Neurons with visual activity had no activity associated with saccadic eye movements; neurons with movement activity had no activity associated with visual stimuli; and neurons with visuomovement activity fell somewhere in the middle. Statistical analysis disclosed that the majority of visually responsive neurons had activity that was modulated in the attention task even in the absence of evidence for saccade preparation, and the activity of pure movement neurons was not modulated in the attention task. Although these results represent the finest-grain analysis of the attention and saccade circuitry yet available, they do not unequivocally support or refute the premotor theory of attention. Thompson et al. (2005) conclude "Our results demonstrate that spatial attention corresponds to the visual selection stage of saccade production; it is a precursor to the motor activity that leads directly to saccade generation and therefore can affect eye movements." (p.9486)

The key question that centers on the premotor theory of attention seems to concern the definition of a "circuit". The premotor theory proposes that the same "neural circuitry" that controls visual attention also controls attention-related eye movements. If the Webster's definition of "circuit" ("an assemblage of electrical components") is accepted, then it would not seem surprising to find that some of the elements in a given circuit are performing a different function from other elements. It is the performance of the circuit as a whole that defines it, not the performance of an individual transistor or capacitor or neuron. Further research should perhaps focus on understanding the flow of neural information within the cortex without concentrating on arbitrary classifications such as "sensory" and "motor". Such an approach was suggested by Patricia Goldman-Rakic over twenty years ago:

> If subdivisions of limbic, motor, sensory, and associative cortex exist in developmentally linked and functionally unified networks, as the anatomical, physiological, and behavioral evidence reviewed here suggests, it may in the future be more useful to study the cortex in terms of information processing functions rather than traditional but artificially segregated sensory , motor, or limbic components and individual components within only one of those components (Goldman-Rakic 1988, p. 153).

CONCLUSION

In summary, ideas about the neural control of voluntary eye movements and of visual attention have evolved considerably over the past century. This paper has outlined some of the highlights of that evolution, while recognizing that the evolution of understanding is the foundation of scientific progress and that our understanding will continue to evolve in the future just as it has in the past. Our current understanding of the neural circuitry responsible for oculomotor control and for shifts of visual attention include several features which, together with their supporting lines of evidence, have been described in the present paper: (1) Voluntary, purposive eye movements are generated and controlled by a distributed, cortico-cortical network that includes the frontal eye field, parietal eye field, supplementary eye field, prefrontal eye field, medial superior temporal area, and the precuneus region. Each of these regions contains neurons that become active prior to saccades; each region shows increase of activity during functional imaging experiments (PET and fMRI) during oculomotor tasks; and each region has strong anatomical connections to the other regions. (2) When the frontal eye field is completely destroyed, monkeys recover the ability to make accurate saccades to visual targets within a few days. However, saccades to remembered target locations are seriously disrupted. (3) When two nodes of the cortical oculomotor system (e.g., the FEF and the PEF) are damaged together, or the FEF and the superior colliculus are damaged together, the impairment of voluntary eye movements is much greater than that which follows the destruction of any single node. (4) Covert visual attention shifts are controlled by a cortico-cortical network that includes the frontal eye field, parietal eye field, and probably additional posterior parietal, temporal, and cingulate cortical regions. (5) Functional imaging studies show that there is a high degree of overlap between some cortical areas (network nodes) involved in oculomotor control and cortical areas involved in visual attention. (6) Behavioral neurophysiology experiments have demonstrated that within areas of cortical overlap of oculomotor and attention networks, the neural elements of the two functions may be located within two or three hundred microns of each other, giving strong support to the hypothesis that the two circuitry controlling eye movements and visual attention overlap at the single neuron level. (7) Finally, although much of the recent behavioral neurophysiology research has been devoted to the study

of the mechanisms of attention and oculomotor control within the frontal eye field, it should be borne in mind that the functions of both visual attention and of oculomotor control recover very quickly and to a remarkable degree following the complete destruction of either the frontal eye field, the parietal eye field, or the superior colliculus. Further research should also concentrate on the flow of information within the remaining network following the loss one of its nodes.

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