Parietofrontal circuits in goal-oriented behaviour

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Abstract
Parietal and frontal cortical areas play important roles in the control of goal-oriented behaviour. This review examines how signal processing in the parietal and frontal eye fields is involved in coding and storing space, directing attention and processing the sensorimotor transformation for saccades. After a survey of the functional specialization of these areas in monkeys, we discuss homologous regions in the human brain in terms of topographic organization, storage capacity, target selection, spatial remapping, reference frame transformations and effector specificity. The overall picture suggests that bottom-up sensory, top-down cognitive signals and efferent motor signals are integrated in dynamic sensorimotor maps as part of a functionally flexible parietofrontal network. Neuronal synchronization in these maps may be instrumental in amplifying behaviourally relevant representations and setting up a functional pathway to route information in this parietofrontal circuit.

Introduction
A major goal in cognitive neuroscience is to understand how the brain represents space and how this representation is used to generate behaviour. To construct a spatial representation, the brain depends on inputs from our senses, including vision, touch and audition. In healthy subjects, the sense of vision, closely linked with eye movements, is most dominant. At the perceptual level, the pointing direction of the eyes in space (gaze) limits what we can see. We explore the visual environment by a series of active gaze fixations to identify objects of interest. These active fixations are achieved by saccades, which are rapid eye movements with speeds up to 500 deg/s. During these rapid gaze shifts, the visual world remains stable, even though the image of the world shifts on our retinas, an observation that relates back to Von Helmholtz (1867). At the motor level, saccades to visual targets require a transformation of the spatial information in the retinotopic reference frame to a temporally coded muscle-based command to generate the eye movement. Thus, visual space representation and eye movement control are tightly linked. Both processes involve spatial computations, attention, decision-making, remapping and reference frame conversions. Insights into how the brain performs these computations are therefore crucial to understand the neural basis of perception, cognition and sensorimotor integration.

It is generally accepted that interactions between parietal and frontal cortices play a central role in these computations. Monkey neurophysiology has implicated cortical areas, such as the dorsolateral prefrontal cortex, lateral intraparietal area (LIP) within the intraparietal sulcus (IPS), frontal eye fields (FEF) and supplementary eye field (SEF) in the programming of saccades. These areas project to subcortical structures such as the superior colliculus, and pontine and cerebellar nuclei (see Leigh & Kennard, 2004; Munoz & Everling, 2004; Johnston & Everling, 2008; for reviews). Based on functional neuroimaging, a similar cortical network (Fig. 1A) has been identified in the human brain (Sweeney et al., 1996; Cornelissen et al., 2002; Astafiev et al., 2003; Curtis & D’Esposito, 2003; DeSouza et al., 2003; Brown et al., 2004; Curtis & Connolly, 2008; Van Pelt et al., 2010).

Within the cortical oculomotor network, LIP (also called the parietal eye fields, PEF) and FEF are critical nodes for analysing the spatial aspects of orienting behaviour and setting up saccade plans. These two regions are strongly interconnected (Andersen et al., 1985; Blatt et al., 1990; Stanton et al., 1995; Bullier et al., 1996). Electrical stimulation of these areas elicits eye movements, though more easily in FEF than PEF (Robinson & Fuchs, 1969; Thier & Andersen, 1998). Conversely, reversible inactivation or lesions of these regions disrupt saccade execution (Sommer & Tehovnik, 1997; Li et al., 1999; Liu et al., 2010). In the present review, our main (but not exclusive) focus is on the functional specialization in this parietofrontal circuit. For simplicity, we use the terms PEF and FEF, respectively, in the general discussion of both monkey and humans findings. For the monkey, we consider PEF the same as LIP, and these terms can be used interchangeably; for the human, PEF collectively refers to all saccade-related areas in the IPS.

Over the past decade, important observations have been made that scratch beneath the surface of the interactions between PEF and FEF, by demonstrating how the brain implements functional connectivity between these regions in generating behaviour. Using functional magnetic resonance imaging (fMRI) and novel analysis tools has allowed new insights in decoding the human PEF and FEF, by revealing dynamic cortical maps with millimeter spatial resolution. More recently, newer techniques like transcranial magnetic stimulation (TMS) and magnetoencephalography (MEG) have advanced our
understanding in the temporal domain of the dynamic aspects of communication in this parietofrontal circuit. In this review we will summarize some of these new research findings, starting with an update of a fundamental organizing principle in the cerebral cortex – topographic organization.

**Topography**

Both PEF and FEF receive inputs from extrastriate areas in the occipital cortex (Andersen et al., 1990). Hence, perhaps not surprising, single-unit studies have shown that monkey areas PEF and FEF are organized in a topographic fashion, like many of the visual areas in the occipital cortex (PEF – Blatt et al., 1990; Ben Hamed et al., 2001; FEF – Robinson & Fuchs, 1969; Bruce & Goldberg, 1985; Schall, 1991). Most studies suggest that response fields of the neurons are anchored to the direction of gaze, coding predominately for contralateral space (Bruce et al., 1985; Ben Hamed et al., 2001). Recent monkey fMRI studies have confirmed these observations (Koyama et al., 2004; Kagan et al., 2010; Patel et al., 2010). There are, however, also some studies that report head-centred and hybrid (i.e. eye + head) reference frames in the IPS (Avillac et al., 2005; Mullette-Gillman et al., 2009).

Using phase-based mapping procedures in fMRI, the spatial organization of PEF and FEF has also been studied in humans. A landmark study was performed by Sereno et al. (2001), who asked subjects to make saccades to memorized targets that were stepped in a clockwise or counterclockwise direction on the screen. A region in the superior parietal cortex, considered to be the human analogue of monkey area PEF, showed robust topographic mapping of the remembered target angle. These topographical findings triggered many mapping studies on parietal and frontal cortex, which confirmed and extended Sereno et al.’s findings. To date, interestingly, as much as up to six separate topographic regions have been identified along the IPS, labelled from IPS₃ to IPS₆, with IPS₃ also sometimes referred to as V7 (for a review, see Silver & Kastner, 2009). Furthermore, a seventh topographic area is found in the superior parietal lobule. Functionally, the IPS maps may be homologues of the different subdivisions of the macaque’s IPS, but this is under current investigation. The most posterior map (area IPS₆/V7) shows a slight preference for saccade goals, while the more anterior- medial maps (IPS₂ and IPS₃) show a small preference for reach goals (Levy et al., 2007; Tosoni et al., 2008), consistent with observations reporting a caudo-rostral visual-to-somatic gradient in Posterior Parietal Cortex (Beurze et al., 2007, 2009; Levy et al., 2007; Stark & Zohary, 2008; Caminiti et al., 2010). However, none of these areas was found to respond exclusively to one of either effector types. Furthermore, most parietal maps can also be demonstrated when the focus of attention systematically traverses the visual field, without making eye movements, indicating that attentional networks overlap with networks for action planning in the parietal cortex (Silver et al., 2005; Swisher et al., 2007; Silver & Kastner, 2009; Szczepanski et al., 2010). Thus, brain activity in frontal and parietal cortex is essentially identical during covert and overt shifts of attention (lkai & Curtis, 2008).

Topographic representations for memory-guided saccades have also been demonstrated for the human FEF in the frontal cortex (Hagler et al., 2007) – one map was identified in the superior branch of the precentral sulcus and a second one in its inferior branch (Kastner et al., 2007). Only future research can resolve some of the mystery of what all the parietofrontal maps might be doing, how they are coordinated, and which are true homologues of monkey PEF and FEF. One way to investigate such homology is by testing how the various maps respond to the defining features of monkey PEF and FEF (cf. Schluppeck et al., 2006).

To program saccades in the frontoparallel plane the brain must code both direction and amplitude. Thus far, however, most human parietofrontal maps that have been reported for saccade planning only mapped target direction and ignored target eccentricity (but see Swisher et al., 2007). Future work should examine the coding of saccade amplitude in the human brain. Preliminary evidence suggests that both saccade amplitude and direction can be derived from blood oxygen level-dependent (BOLD) signals in human PEF and FEF (Leone et al., 2010).

Furthermore, the topographic maps for human saccade planning are often interpreted as retinotopic maps. Although this interpretation follows the monkey physiology, most available measurements only characterize the topographic relationship between cortical activation and target location on the retina with a fixed eye position (the eyes typically look straight forward). But without varying eye position, it cannot be established whether a topographic map reflects in fact a retinotopic organization. The maps could also code target location relative to the head, body or any other gaze-independent reference

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**Fig. 1.** fMRI of the human parietofrontal network for saccades. (A) The locations of parietal eye field (PEF), frontal eye field (FEF) and supplementary eye field (SEF) in two anatomical views in neurological convention and on an inflated representation of the left hemisphere. Gyri are represented by lighter areas, and sulci, by darker areas. (B) Left-right topography and repetition suppression in gaze-centred and gaze-independent reference frames during saccade preparation. A contralateral bias exists in the PEF and FEF (P < 0.001), but not in the SEF (P = 0.78). Repetition suppression unveils the use of a gaze-centred reference frame in all three regions. Data (in a.u.) combined across hemispheres. ***P < 0.001. Modified from Van Pelt et al. (2010).
frame. Testing how topographic maps change as a function of eye position can distinguish between gaze-centred (retinotopic) and gaze-independent (head/body) reference frames (Medendorp et al., 2003; Merriam et al., 2003; Sereno & Huang, 2006; Gardner et al., 2008). In this fashion, Medendorp et al. (2003) recently demonstrated that the human PEF employs a gaze-centred (retinotopic) reference frame.

While topography appears to be a defining characteristic of PEF and FEF, the region of the human SEP lacks a topographic organization (Kastner et al., 2007). If a region lacks a topographic organization, can we still unveil its reference frame? Recently, Van Pelt et al. (2010) applied a novel approach – repetition suppression – to investigate the reference frames in the parietofrontal cortex (Fig. 1B). Participants executed memory-guided saccades to peripherally presented targets. By varying the fixation position for the next trial, the authors made the next target identical in either gaze-centred coordinates, or in gaze-independent (read – head-centred) coordinates. A clear reduction of the BOLD signal was found in all, PEF, FEF and SEF, when the target location was repeated in gaze-centred coordinates, but not, or much less, during a repetition in a gaze-independent (i.e. head/body-centred) frame. Gaze-centred suppression was stronger during saccade planning than during execution (not shown), reflecting the important role of these regions in preparing the saccade. Van Pelt et al.’s results suggest that these centres, of which only the PEF and FEF have topographic distribution of spatially tuned neurons (Fig. 1B), employ a gaze-centred organization. Having identified the spatial organization of PEF and FEF, we next will dwell on the type of computation that is actually performed in these maps.

Attention vs. intention

In monkey delayed-saccade tasks, both PEF and FEF typically demonstrate visual responses besides the motor-related activity (PEF – Andersen et al., 1987; FEF – Bruce & Goldberg, 1985). Yet, pure movement neurons without visual responses are common in monkey FEF but rare in PEF. Also, during the memory interval in a delayed-saccade task, PEF and FEF neurons retain increased activity (see Munoz & Everling, 2004; for review). This delay activity has been associated with various cognitive functions, including spatial functions like spatially directed attention, spatial memory, oculomotor intention and state estimation (see Goldberg et al., 2006; Andersen & Cui, 2009; for reviews), as well as non-spatial functions, such as reward processing and decision-making (see Glömpcher, 2003; Gold & Shadlen, 2007, for reviews).

The premotor theory of attention (Rizzolatti et al., 1987) suggests that the spatial functions – spatial attention and saccadic eye movements – cannot even be separated. According to this theory, preparing a saccade involves the same process as orienting selective attention (covertly or overtly), regardless of whether the saccade is subsequently executed or not (but see Khan et al., 2009). This is consistent with the multiple topographic maps in the human cortex that respond equally during saccade planning and covert spatial attention (see previous section).

In the monkey, the FEF has traditionally been viewed as an oculomotor structure (Everling & Munoz, 2000), but recent evidence suggests an additional role in the guidance of spatial attention (Thompson et al., 1996; Wardak et al., 2006; Buschman & Miller, 2007). Recent experiments by Moore and his colleagues have convincingly shown that electrical stimulation of the FEF enhances a monkey’s sensitivity for a target. More specifically, with stimulating currents too low to evoke a saccade, they still found attentional facilitation at the location where a suprathreshold saccade would be driven to (see Moore, 2006; for a review). Analogous observations have recently also been made in humans (Ruff et al., 2006, 2008; Van Ettinger-Veenstra et al., 2009).

For the PEF, there has been intense debate about whether its role relates more closely to spatial attention (Goldberg et al., 2006; Gottlieb et al., 2009b) or to the intention to make a saccade (Andersen & Cui, 2009). A recent study by Lipata et al. (2009) reported that neuronal responses to a pop-out stimulus are smaller if it is overtly ignored, consistent with a role in attentional processing. Also, Gottlieb and co-workers have argued, based on a series of studies, that during covert visual search, PEF neurons reflect the top-down significance of the search target (Gottlieb et al., 2009a; for review). On the other hand, experiments testing effector-specificity in monkeys (saccade vs. reach) during effector choice tasks have shown a bias to saccade planning in both PEF and FEF (Cui & Andersen, 2007; Andersen & Cui, 2009; Lawrence & Snyder, 2009). Mirpour et al. (2010) showed that, during search, microstimulation biases saccade goal selection to the object represented at the stimulated location in PEF.

It has also been claimed that PEF and FEF contain specialized subpopulations of neurons specifically related to either saccade planning or attention (Murthy et al., 2001; Juan et al., 2004; Liu et al., 2010), yet others have argued that these populations may not operate fully independently of one another (Moore & Armstrong, 2003).

Using fMRI, Curtis et al. (2004) tested the functional specialization in the human frontoparietal circuit for attention and intention. To measure motor intention, they used an oculomotor delayed matching-to-sample task (match), in which the direction of the forthcoming saccade was known throughout the delay. To measure maintained spatial attention they used a non-matching-to-sample task (non-match), in which the saccade was unpredictable. When it was impossible to prepare a saccade until after the delay, activity in PEF was higher than in FEF, while activity in FEF was generally higher than in PEF when the forthcoming saccade vector was known throughout. These findings support the notion that FEF is more ‘motor’ than PEF (Curtis & D’Esposito, 2006). Recently, Connolly et al. (2007) made the same claim using the gap-paradigm. In their studies, a temporal gap was introduced between the extinction of a central fixation target and the illumination of an eccentric target for the saccade. They reported that, in the complete absence of spatial target information, the frontal cortex was more active than the parietal cortex, providing a neural correlate of preparatory set.

Priority

At an intermediate stage between spatial attention and saccade planning lies the proposition that PEF and FEF encode gaze-centred priority maps of behaviourally relevant stimuli in the surroundings that are used by the oculomotor system to generate saccades and by the visual system to guide spatial attention (see Fecteau & Munoz, 2006; for reviews; Serences & Yantis, 2006; Gottlieb et al., 2009b; Bisley & Goldberg, 2010). The concept of the priority map implies that stimuli with more behavioural relevance, either for action or outcome, are assigned more priority. Although it is obvious that task-specific motor, cognitive and motivational variables must shape these maps, it is not fully understood how these modulations come about. In terms of a priority map, areas PEF and FEF should be viewed neither strictly sensory nor strictly motor, but rather sensorimotor (Snyder et al., 2000), controlling attention and sensorimotor integration specific to the task. Patient and lesion studies provide causal evidence for this

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interpretation, showing that damage to these maps does not only impair attention and visual search (Husain & Nachev, 2007; Balan & Gottlieb, 2009), but also overt shifts of gaze (Pisella et al., 2009; Bays et al., 2010).

Storage

The concept of a priority map implies that the respective cortical areas have the capacity to represent and store multiple targets (or potential movement plans), with targets of high behavioural priority represented by greater activity than those with low priority (Bisley & Goldberg, 2010; Cisek & Kalaska, 2010). Tian et al. (2000) found many groups of neurons (cf. quasi-visual cells) simultaneously activated in FEF when several targets might be selected for action at a later stage. Likewise, FEF has been reported to be involved in control of sequences of saccades during a self-guided visual search task (Phillips & Segraves, 2010). In PEF, it has been shown that when an animal is presented with two potential targets, two populations of neurons become active. After identifying one of these targets as a saccadic goal, the associated neural population responds more strongly than the other group of neurons (Mazzoni et al., 1996; Platt & Glimcher, 1997; Powell & Goldberg, 2000). Supporting observations are also made in the human PEF by Medendorp et al. (2006) using double-saccades. After the first target was cued, the fMRI signal was related to the side of the visual field in which it had been presented. When the second target was added, the cortical activity depended on the respective locations of both targets, but was still significantly selective for the target of the first saccade.

Taken together, the human and monkey findings suggest that the sensorimotor maps in PEF and FEF act as storage centres by retaining target locations for subsequent saccades, but also prioritize the target for the first intended saccade. In this sense, target selection and movement preparation form an integrated process, played out across the parietofrontal network in a task-dependent manner (Cisek & Kalaska, 2010).

Remapping

A recurrent factor in the gaze-centred coding of a sensorimotor map is the occurrence of eye movements. Every time the eyes move the spatial registry of the map with the external world of targets and movement goals is changed. Maintaining the validity of a gaze-centred map with the external world requires that the representations on the map are actively remapped to compensate for each eye movement. Indeed the cortical maps in monkey PEF and FEF have been shown to compensate for intervening saccades, not only during double-saccade tasks (Gnadt & Andersen, 1988; Goldberg & Bruce, 1990; Mazzoni et al., 1996; Sommer & Wurtz, 2008), but also for stimuli that do not directly serve a movement goal (Duhamel et al., 1992; Nakamura & Colby, 2002; Heiser & Colby, 2006). The updating, or spatial remapping, typically starts prior to the saccade, suggesting that these dynamic sensorimotor maps are updated proactively, instantiating a spatially stable prediction map for goal-directed eye movements and spatial attention (Crapse & Sommer, 2008).

Gaze-centred remapping observations during saccades have also been made in humans. Using the coarse time resolution of fMRI, remapping was shown by the dynamic exchange of activity between the two cortical hemispheres when an eye movement brings the representation of a stimulus into the opposite hemifield (Medendorp et al., 2003; Merriam et al., 2003, 2007). Remapping has also been shown using the millisecond temporal resolution of electroencephalography (Bellebaum et al., 2005b) and TMS experiments (Rushworth & Taylor, 2006; Chang & Ro, 2007; Morris et al., 2007; Prime et al., 2008, 2010).

In computational terms, the anticipatory updating of the maps in PEF and FEF requires an effference copy of the eye movement command, which is transformed into gaze-centred coordinates by routing it through an internal representation of the dynamics of the eyes, called a forward internal model (Kawato, 1999; Vaziri et al., 2006; Munuera et al., 2009). Based on these results, it can be predicted that active head and body movements would also cause the updating of representations on these maps, but this has not been investigated at the physiological level. Recent work suggests that effference copies of saccades are relayed from subcortical structures and transmitted to these regions via the thalamus (Berman & Wurtz, 2008; Sommer & Wurtz, 2008; Prevosto et al., 2009). This explains why patients with thalamic lesions demonstrate clear impairments in relation to spatial updating (Bellebaum et al., 2005a; Ostendorf et al., 2010). Given that both PEF and FEF also receive sensory inputs, they are in a good position to infer a belief about the state of the world by combining this information with the anticipated representation based on motor outputs. For clarity, it should be noted that gaze-centred remapping does not contradict the idea that the same regions might also be involved in processing spatial attention (Golomb et al., 2008, 2010). But if the PEF and FEF also contain a forward internal model for updating sensorimotor representations in gaze-centred coordinates, this suggests a greater role than just establishing a priority map (Fig. 2).

Top-down remapping

If the PEF and FEF code dynamic gaze-centred sensorimotor maps, which compensate for intervening saccades, one may ask whether other task demands may also cause activity to shift on their maps. One such case is anti-saccades, where participants are instructed to look away from a stimulus, to a location into the opposite hemifield (Hallett, 1978; Munoz & Everling, 2004). Compared with a saccade toward the stimulus (a pro-saccade), correct performance of an anti-saccade requires the subject to first suppress the automatic response to look toward the flashed visual stimulus and then invert the stimulus location to the location of the goal of the saccade (called vector inversion). The suppression process is accomplished by biasing the activity levels of PEF and FEF, so that the process initiated by the incoming visual signal does not reach the saccade threshold before the vector inversion is completed (Munoz & Everling, 2004; Brown et al., 2007).

As to the second process (vector inversion), if PEF and FEF code and prioritize the location of the saccade goal, it requires them to remap, or invert, the representation of the sensory stimulus into a representation of the saccade goal. In PEF, Gottlieb & Goldberg (1999) showed that most neurons represent the visual cue, not the direction of the saccade (or the target for action). However, in a memory-delayed version of the anti-saccade task, population activity in PEF turns from the visual direction to the motor direction during the memory period (Zhang & Barash, 2000, 2004). This switching is accomplished very rapidly, within 50 ms from the arrival of the visual signals in LIP, and might represent a remapped visual response. Vector inversion signals are also seen in the FEF (Sato & Schall, 2003), in both its movement and visuomotor neurons. While the FEF movement neurons represent the actual saccade during anti-saccades, FEF’s visuomotor neurons were initially responsive to the stimulus cue, but then switched their activity and responded more to the virtual target.
placed on the opposite side, outside their receptive field, but toward the direction of the upcoming anti-saccade.

A number of studies have demonstrated vector inversion in the human brain (Everling et al., 1998; Medendorp et al., 2005b; Moon et al., 2007). Using a delayed anti-saccade paradigm in fMRI, Medendorp et al. (2005b) showed that the human PEF first responds preferentially to the target location presented in the contralateral visual field. However, when an anti-cue specified a saccadic response into the opposite visual field, this elicited a dynamic shift in cortical activity from one hemisphere to the other.

Taken together, the updating and anti-saccade paradigms indicate again that areas PEF and FEF should be regarded as neither explicitly sensory nor motor by nature. They instantiate a dynamic sensorimotor map by integrating bottom-up sensory, top-down cognitive signals and efference motor signals to guide overt and covert control in perception and action (Fig. 2).

Transformations

The ability to transform the dynamic, gaze-centred information into other reference frames is necessary for both action and perception. For eye movement execution, gaze-centred representations must be further transformed, as a function of eye position, by downstream mechanisms into head-centred muscle-based commands for the ocular muscles (Crawford et al., 2011). Spatial vision, object recognition and navigation also require gaze-centred information to be transformed in higher-level reference frames, like body- or world-centred coordinates. The PEF and FEF may be involved in these transformations – the representations in their sensorimotor maps are not only embodied in gaze-coordinates, but also show modulation by initial eye (and head) position (PEF – Andersen et al., 1987; FEF – Cassanello & Ferrera, 2007). These modulations, in the form of a so-called gain field (Andersen & Mountcastle, 1983), have a weighting effect, controlling the influence of individual neurons on the population output (Blohm & Crawford, 2009). Gain fields are probably based on efference copies rather than on muscle proprioception (Wang et al., 2007), and may support the transformation of gaze-centred representations into other gaze-independent (e.g. head- or body-centred) reference frames (Zipser & Andersen, 1988; Chang et al., 2009). Gain modulations may also allow other areas to read out signals from PEF and FEF in different coordinate frames. Using fMRI, gain field modulations (DeSouza et al., 2000) and/or gaze-dependent changes in baseline responses (Williams & Smith, 2010) have also been reported in the human parietofrontal network. So, even though PEF and FEF neurons primarily encode targets relative to the direction of gaze, modulations in this firing rate implicitly contain information on eye-, head- and body-posture, providing a mechanism to switch between the different reference frames and bias output to connected areas (Fig. 2).

Sounds and touch

If PEF and FEF code sensorimotor maps for cognitive processing and saccade generation in gaze-centred coordinates, then these maps may also be activated in response to signals from sensory modalities other than vision. Indeed, persistent responses in areas LIP and FEF are also found with auditory stimuli (Russo & Bruce, 1994; Stricanne et al., 1996; Cohen & Andersen, 2000; Mullette-Gillman et al., 2005, 2009). Kirchner et al. (2009) reported ultra-rapid sensory responses in the human FEF, with onset latencies to auditory stimuli even smaller than to visual stimuli (24 ms vs. 45 ms, respectively). Recently, Tark & Curtis (2009) found persistent activation in putative human FEF during the maintenance of auditory targets, even for locations behind the head to which it is impossible to make saccades. The authors considered several explanations of their results ranging from that the FEF represents auditory targets in extraretinal coordinates, like head or body coordinates, to that the map of FEF, like the collicular map (Klier et al., 2001), simply extends beyond the oculomotor range (Tark & Curtis, 2009). Future research should further address this question.

In the somatosensory domain, Thura et al. (2010) have shown that hand position influences saccade signals in FEF, indicating that proprioceptive signals reach this area. Likewise, Macaluso et al. (2007) found sustained BOLD signals in both posterior partial cortex and FEFs for visual and tactile stimuli when subjects would later make
an eye movement to these stimuli. All of this evidence suggests that the sensorimotor maps in PEF and FEF encode ‘supramodal’ representations to guide attention and behaviour.

To code a gaze-centred sensorimotor map from signals in other reference frames requires a rewiring of this information, depending on postural configuration (Macaluso et al., 2002; Ren et al., 2006). For example, the direction of a saccade to a somatosensory target presented to the right hand depends on the position of the hand relative to current gaze direction. Evidence for these transformations has been reported. For example, Russo & Bruce (1994) showed that FEF discharge before aurally guided saccades codes the location of auditory target relative to the current direction of gaze, even though sound location cues are sensed in craniotopic coordinates. The neural basis for such transformations could involve gain field mechanisms (Fig. 2), although it is still poorly understood what causes the discharge modulations for different postures. We will briefly touch upon this point below.

### Saccades vs. reaches

Whilst saccades are associated with attentional shifts, they are usually also combined with movements of other effectors, like reaching movements of the arm and hand (Crawford et al., 2004). Tests of effector specificity have been used to examine the nature of the coding in the parietofrontal network. The prevailing view based on monkey neurophysiology is that while PEF and FEF respond to impending eye movements and spatial attention, an analogous link between the parietal reach region (PRR) and the dorsal premotor cortex (PMd) is active for reaching movements. This separation, however, is not strict. Neurons in the various regions also respond for the non-preferred effector (Snyder et al., 1997; Boussaoud et al., 1998; Calton et al., 2002; Lawrence & Snyder, 2006; Oristaglio et al., 2006; Cui & Andersen, 2007; Thura et al., 2008). Lawrence & Snyder (2006), using an effector-instruction task, found a preference for saccades compared with reaches, with the onset of effector-specific modulation about 400 ms later in FEF than PEF. This means that effector-dominant signals in PEF cannot be the result of a top-down influence from FEF. Furthermore, Pesaran et al. (2006, 2010) provided evidence that eye movement and position signals in the PRR–PMd link do not drive eye movements, but rather are used to set up a spatial framework to support visuomotor eye–hand coordination. Likewise, it could be argued that integration of hand position signals in PEF and FEF assist in eye–hand coordination through multimodal integration (Thura et al., 2008).

Recent human fMRI studies are consistent with these observations in monkeys. Many studies noted limited effector specificity in the parietal-frontal network during movement planning (Astafiev et al., 2003; Medendorp et al., 2005a; Beurze et al., 2007, 2009; Connolly et al., 2007; Hagler et al., 2007; Levy et al., 2007; Tosoni et al., 2008; see Filimon, 2010; for review). Beurze et al. (2009) studied the planning and execution of eye and hand movements, by partitioning them over spatial goal, motor effector and time. By using fMRI to characterize the temporal evolution of neural activity, they distinguished the contributions of different portions of the parietofrontal network to the processing and integration of effector and spatial goal information, showing that the degree of spatial and effector selectivity varies gradually over the parietal-frontal cortex, changing over time during the build-up of the movement plan.

The overlap between the cortical circuits for eye and hand movements may suggest that the topology of the parietofrontal network is not based on effector specificity per se, but rather reflects a functional organization as recently suggested for the motor cortex (Graziano & Aflalo, 2007), reflecting the different functional and computational constraints that need to be satisfied when planning eye and hand movements (Beurze et al., 2006, 2010; Vesia et al., 2010). Functionally, eye movements are inseparably bound to visual perception, and serve a different purpose than movements of any other body part. Computationally, the sensory reference frame imposed by the retina for visual target processing is linked to the motor reference frame of the eye. In contrast, the reference frame of a visual target is distinct from the motor reference frame of a limb. Recent observations by Heed et al. (2011), showing differences between eye and limb movement planning, but not between hand and foot movement planning, would be consistent with this idea. Also, from the perspective of parsimonious coding, Levy et al. (2007) suggested that it makes little sense to have separate machinery for coding similar planned movements that only differ in the effector used to execute them; especially for eyes and limbs that so often accompany each other. Future work should further test this hypothesis, perhaps by using new analytic tools such as multivoxel pattern analysis to decode the functional organization of the parietofrontal network (Mur et al., 2009; Leone et al., 2010). Likewise, studies of the neuronal dynamics of this network will help to further understand its contribution to the selectivity and plasticity in the transformations for directing attention and specific motor acts (Van Der Werf et al., 2010).

### Communication

So far, the focus of this paper has been mainly on the increased neuronal firing rates or BOLD signals that are recorded from PEF and FEF during spatially guided behaviour. Interpretations have considered the regions in isolation, but an important piece of information on the functional properties of FEF and PEF lies in their mutual cooperation. Recently, new insights have become available on how the respective neurons in parietofrontal network cooperate and communicate during the processing, storage and exchange of information during such behaviour. Rhythmic neuronal synchronization, within and between areas, has been proposed to provide the circuit with an efficient mechanism to implement intra- as well inter-areal communication, which could change at small time scales (Salinas & Sejnowski, 2001; Buszaki, 2006).

Oscillatory activity can be recorded by the local field potentials from small groups of neurons, or by related oscillations in non-invasive electroencephalographic (EEG) or MEG (EEG/MEG) measurements. Oscillatory activity occurs in various frequency bands, which have been related to different aspects of sensorimotor control in the parietofrontal network (see Fries, 2009; Van Der Werf et al., 2009b; for reviews). Also, interactions among different frequency bands, called cross-frequency coupling, might serve effective communication in the sensorimotor system (see Canolty & Knight, 2010; for review). Oscillatory activity in the alpha band (8–13 Hz) is regarded a gating mechanism that inhibits task-irrelevant regions, thereby routing information to task-relevant regions (Medendorp et al., 2007). At the same time, active processing in the task-relevant sensorimotor areas is reflected by neuronal synchronization in the gamma band (30–100 Hz). Beta band (13–25 Hz) activity has been related to maintaining the current state – the status quo – of the sensorimotor system (see Engel & Fries, 2010, for review).

In monkeys, parietal areas PEF and PRR show direction-selective increases in spectral power of the field potentials in particular
frequency ranges (PEF: 25–90 Hz; PRR: 20–50 Hz; Fig. 3A) when planning saccades and reaches, respectively (Pesaran et al., 2002; Scherberger et al., 2005). In humans, analogous observations have been made using MEG (Fig. 3B; Medendorp et al., 2007; Van Der Werf et al., 2008, 2010; Hinkley et al., 2010) as well as in intracranial recordings (Lachaux et al., 2006). Using a delayed anti-saccade task, Van Der Werf et al. (2008) showed that the gamma band power in human PEF shifts from the initial visual stimulus direction to the direction of the upcoming saccade, the prioritized movement goal, as found in monkey PEF (Zhang & Barash, 2004).

In a further study, Van Der Werf et al. (2009a) studied the role of rhythmic neuronal synchronization in a spatial updating task. By introducing a change of fixation between stimulus presentation and the final memory-guided saccade, their preliminary results indicate that the direction selectivity of the parietal gamma band reflects spatial updating in a gaze-centred reference frame. This suggests that gamma band synchronization reflects a mechanism by which the gaze-centred sensorimotor maps in the parietofrontal cortex encode and amplify the behaviourally relevant goals, providing a putative mechanism to carry along unique sensory information to downstream areas (Tiesinga et al., 2004). Mechanistically, if several inputs are provided simultaneously to a receiving neuron, synaptic integration can induce a rapid change in membrane depolarization, thereby increasing the probability of an action potential. If the receiving neuron fires in coherence with the source neurons, the input could arrive at the right time in the oscillatory cycle, thereby increasing the gain even further (Fries, 2005). In support of this notion, regions along the dorsal visual pathway, including PEF and FEF, have been shown to oscillate coherently in a spatially guided behaviour (Pesaran et al., 2008; Siegel et al., 2008; Gregoriou et al., 2009). Thus, synchrony may set up a functional pathway to route information between parietal and frontal areas.

In a recent study, Buschman & Miller (2007) examined the communication between PEF and FEF during a visual search (involving top-down attention modulation) and a visual pop-out (bottom-up attention) task. While the FEF signalled the target earlier during search, the PEF signalled it earlier during pop-out (Fig. 3C; see also Schall et al., 2007 for a critical comment on this work). Interestingly, the two attentional modulations emphasized coherence between the two regions in different gamma bands, as if the networks ‘tune in’ on different frequencies for different task demands (Roopun et al., 2008). In the human, Van Der Werf et al. (2010) reported recently a difference in power in the human posterior parietal cortex between a delayed saccade task and a delayed reach task, consistent with the notion that different task constraints emphasize spatial goals at different frequencies (Fig. 3D).

Finally, functional communication is not only important to transmit relevant information, but might also play a role in converting information into other reference frames. For example, preliminary evidence of Buchholz et al. (2010) showed a role of oscillatory activity in relaying a somatotopic representation into spatially congruent gaze-centred representation in the maps of PEF and FEF for saccade planning to somatosensory signals. As the information transfer between somatotopic and retinotopic maps depends on body posture, it would be an interesting question for future experimentation how neuronal synchrony relates to the observed gain field mechanisms in PEF and FEF. Likewise, future research should record from different regions simultaneously in various sensorimotor tasks to assess the interplay between action potentials, the BOLD signal, oscillatory activity and inter-areal communication in relation to coordinate transformations, timing issues and making forward predictions.

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**Fig. 3.** Neural synchronization as a means of communication in the frontoparietal network. (A) Power (colour coded) in the local field potential (LFP) recorded from macaque area PEF as a function of time while the monkey is performing a delayed saccade task (adapted from Pesaran et al., 2002; with permission). (B) Power in magnetoencephalography (MEG) sensors overlying the human posterior parietal cortex while subjects are performing a delayed saccade task (adapted from Van Der Werf et al., 2008). Warmer (red) colours, preference to contralateral targets; cooler (blue) colours, bias toward ipsilateral targets. (C) Difference in coherence in a macaque’s frontoparietal network (FEF–PEF) between a visual pop-out and a search task, showing that different task constraints require communication at different frequencies (adapted from Buschman & Miller, 2007; with permission). (D) Difference in power in human posterior parietal cortex between a delayed saccade task and a delayed reach task suggests that different task constraints amplify spatial goals at different frequencies (adapted from Van Der Werf et al., 2010).
Conclusion

The goal of the present review was to integrate recent findings from both human and non-human primate studies that address the signals and cortical mechanisms underlying spatial coding and saccade planning. Our specific focus was on the role of the dynamic sensorimotor maps of PEF and FEF. In both monkey and humans, these maps can be characterized by a gaze-centred topographic organization, have the capacity to store multiple representations and amplify the specific representation that is most relevant to task. This amplification is consistent with the framework of a priority map, which is a crucial concept for many theories of visual attention. But assigning priorities is not the only function of this parietofrontal circuit. Within the maps, representations are also shifted to new locations to compensate for eye movements, or in response to top-down cognitive inputs. Furthermore, representations seem gain modulated by eye and head position signals, which could serve coordinate transformations, also needed when putting information from other modalities that vision on the maps. Finally, studies of effector specificity indicate that the PEF–FEF circuit should not be seen as a solitary network, but overlapping with a larger functionally, not structurally, organized parietofrontal network for different sensorimotor functions. Within this larger structure, networks of smaller regions can be formed for different tasks – attention, saccades, visual search or other – by synchronizing their activity in various frequency bands. Despite all these insights, throughout this review we have listed numerous issues that remain to be addressed in future research. These studies should not only examine the functions of isolated brain regions, without overlooking the functional connectivity between brain areas that serve in goal-oriented behaviour. A major objective is how PEF and FEF, and associated cortical and subcortical regions, act as a circuit, which necessitates studying them simultaneously to reveal timing differences and instantaneous functional connectivity patterns. Future work should also reveal whether our taxonomy, with categories such as attention, intention, memory, priority, effector specificity and internal models, will still suffice to capture the function of the parietofrontal network. All this work should lead to realistic models of the healthy brain, which in the long term may also aid in the development of diagnostic and therapeutic tools for neurological disorders.

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Abbreviations

BOLD, blood oxygen level-dependent; EEG, electroencephalography; FEF, frontal eye field; fMRI, functional magnetic resonance imaging; IPS, intraparietal sulcus; LIP, lateral intraparietal area; MEG, magnetoencephalography; PEF, parietal eye field; PMd, dorsal premotor cortex; PRR, parietal reach region; SEF, supplementary eye field; TMS, transcranial magnetic stimulation.

References


