Frontal Eye Fields

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Location and Connections

The frontal eye field (FEF) was described first in the late 1800s by David Ferrier, who discovered that electrical stimulation of a portion of the frontal lobe of macaque monkeys elicited movements of the eyes. Today we know that the FEF exists in all primates, including humans. A homolog of the FEF has been described in cats and owls too. Thus, the FEF is present in animals that employ visually guided conjugate movements of the eyes or head to locate objects to approach or avoid.

In humans, the FEF is located in the rostral bank of a portion of the precentral sulcus at the caudal end of the middle frontal gyrus (**Figure 1(b)**). In macaque monkeys, the animal of choice for investigations of this part of the brain, the FEF occupies the rostral bank of the arcuate sulcus (**Figure 1(a)**). It occupies the caudal end of the granular prefrontal cortex, with the agranular premotor cortex making up its caudal boundary in the fundus of the arcuate sulcus.

The distinctive cytoarchitecture of the FEF distinguishes it from the surrounding cortex. It contains a high concentration of large pyramidal cells in layer V. This cortex is also characterized by a thinner granular layer 4 compared to the more rostral cortex. The ventrolateral portion of this zone, designated area 45, is distinguished by the presence of large pyramidal cells in layer 3 as well as layer 5. The dorsomedial zone, referred to as area 8A, can be further parcellated based on cytoarchitectonic differences. The cortex within the medial portion of the rostral bank of the arcuate sulcus contains fewer large pyramidal cells in layer 3 and a loosely organized granular layer; it is referred to as area 8Ac. Rostral to area 8Ac medially and area 45 laterally, occupying the convexity of the prearcuate gyrus is a transitional zone, designated area 8Ar, with fewer large pyramidal cells and a thicker, more clearly delineated layer 4. Area 8Ar forms the caudal boundary of area 46 and should probably be considered functionally distinct from the FEF. Curiously, in humans the FEF has been described as being in Brodmann's area 6. However, recent analyses have indicated that this difference between species is more about labels than cortical architecture.

The FEF influences saccade production through four major pathways: (1) a projection to the ipsilateral superior colliculus concentrated in the intermediate layers, (2) a pathway through the basal ganglia via the ipsilateral striatum, (3) a projection to the cerebellum via the pontine nuclei, and (4) a weaker projection to mesencephalic and pontine nuclei that make up the saccade generator circuit (**Figure 2**). The FEF is innervated by nuclei in the thalamus bordering the internal medullary lamina, mainly the lateral part of the mediodorsal nucleus and the medial part of the ventroanterior nucleus. The thalamic zones most heavily connected with the FEF are themselves innervated by oculomotor afferents from the intermediate layer of the superior colliculus, the substantia nigra pars reticulata, and the dentate nucleus of the cerebellum.

The FEF is connected with diverse cortical areas. Within the frontal lobe, the FEF is interconnected with the supplementary eye field, with prefrontal areas 46 and 12, and weakly with anterior cingulate area 24 and the postarcuate premotor cortical areas.

The FEF also receives abundant inputs from a multitude of extrastriate visual cortical areas in both the dorsal and ventral streams (**Figure 3**). In fact, the FEF is unique in the extent of its connectivity with extrastriate visual cortex. Moreover, the FEF provides reciprocal connections to the same diverse areas. Thus, the FEF can influence the activation of neurons in the extrastriate visual cortex. Recent evidence and current models identify the FEF as a source of top-down control on visual processing.

The connectivity of the FEF with visual areas caudal to the central sulcus is topographically organized. The more ventrolateral portion of the FEF, which is responsible for generating shorter saccades, is interconnected with the perifoveal representation in retinotopically organized areas, from areas that represent central vision in the inferotemporal cortex and from other areas having no retinotopic order. In contrast, the mediodorsal FEF, which is responsible for generating longer saccades, is interconnected with the peripheral visual field representation of retinotopically organized areas, from areas that emphasize peripheral vision or are multimodal and from other areas that have no retinotopic order.

Role in Producing Movements of the Eyes

The FEF is a key part of the ocular motor system. Most evidence has been obtained through invasive studies with nonhuman primates, but the human FEF has been located through brain imaging, transdural recording and stimulation, and transcranial magnetic stimulation. The FEF contributes to the generation of rapid saccadic gaze shifts as well as
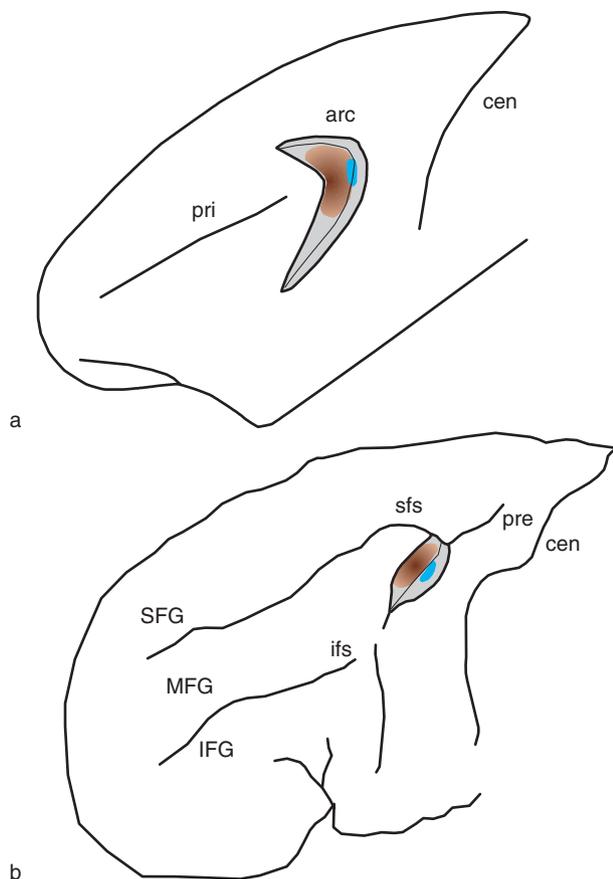
Figure 1 Stylized lateral view of the frontal cortex: (a) of a macaque monkey; (b) of a human. The macaque arcuate sulcus is opened to expose the frontal eye field (brown) on the rostral bank and the frontal pursuit zone (blue) on the fundus. The human precentral sulcus just ventral to the superior frontal sulcus is opened to expose the frontal eye field (red) on the caudal end of the middle frontal gyrus with the pursuit zone (blue) in the fundus. arc, arcuate sulcus; cen, central sulcus; IFG, inferior frontal gyrus; ifs, inferior frontal sulcus; MFG, middle frontal gyrus; pre, precentral sulcus; pri, principal sulcus; SFG, superior frontal gyrus; sfs, superior frontal sulcus.

slow pursuit eye movements and probably also vergence eye movements. In macaques, the zone contributing to the production of smooth pursuit eye movements is located at the fundus of the sulcus, apparently somewhat separate from the area of the FEF that is involved in saccade production (Figure 1(a)).

Electrical Stimulation

Low-intensity electrical stimulation of the FEF in the bank of the arcuate sulcus in monkeys elicits saccadic eye movements directed contralateral to the stimulated hemisphere. Stimulation of the frontal pursuit zone in the fundus elicits pursuit eye movements directed ipsilateral to the stimulated hemisphere. Currents less than 50 µA are sufficient to elicit eye movements, and the movements begin ∼30 ms following the stimulation. The saccades elicited by stimulation of a particular site in the FEF have a particular direction and amplitude that does not vary with the orientation of the eyes in the head. The direction and amplitude of evoked saccades varies gradually as stimulating electrodes are moved through the FEF. The amplitude of the evoked saccade increases laterally to medially along the arcuate sulcus (Figure 4(a)). The FEF also contributes to orienting movements of the pinna in macaques. Recent research has also shown that stimulation of the FEF in monkeys with unrestrained heads can evoke coordinated eye and head gaze shifts.

Inactivation and Ablation

Reversible inactivation of parts of the map in the FEF impairs the production of both visually guided and memory-guided saccades. Monkeys initiate fewer saccades to the retinotopic representation of the inactivated FEF site than to others location in the visual field, and the saccades that are produced are initiated with longer latencies, have lower velocities, and have larger targeting errors than normal. These effects are more pronounced for memory-guided saccades. Also, when tested with memory-guided saccades, monkeys produce more premature saccades to targets in the hemifield ipsilateral to the inactivation. The results from inactivation studies show that the FEF contributes to generating contraversive saccades, especially to locations of remembered targets, maintaining fixation and suppressing inappropriate ipsiversive saccades.

These results complement earlier observations that ablation of the FEF causes an initially severe impairment in saccade production that recovers in some but not all respects over time. If the fundus of the arcuate sulcus is ablated, deficits in pursuit occur; the deficits are most evident in producing pursuit that anticipates the movement of predictable stimuli. Clinical signs of FEF damage in humans include deviation of gaze toward the side of the damage and impaired ability to produce saccades that are more voluntary in character, such as a gaze shift opposite a stimulus (antisaccade) or a saccade to a remembered location.

Functional Brain Imaging

In humans as well as macaque monkeys, the FEFs exhibit increased blood flow and oxygen use when saccadic and pursuit eye movements are produced. The functional magnetic resonance imaging (fMRI) studies locate the human FEF in the precentral sulcus. High-resolution scanning indicates that the upper
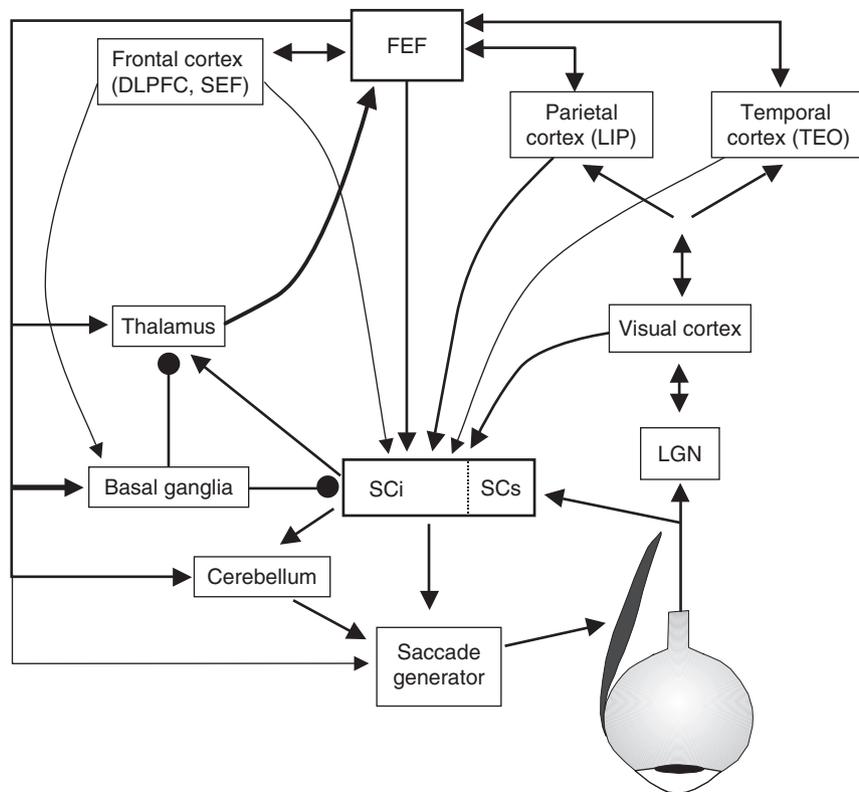
Figure 2 Schematic of brain structures and some of the anatomical pathways involved in saccade generation. Visual input from the retina in the eye is transmitted to the lateral geniculate nucleus (LGN) and the superficial layers of the superior colliculus (SCs). The LGN transmits visual signals to primary visual cortex, where processing proceeds through areas in the temporal lobe (such as area TEO) and the parietal lobe (such as area LIP). Extrastriate visual areas are reciprocally connected with the frontal eye field. The frontal eye field is also connected with areas in the frontal lobe such as dorsolateral prefrontal cortex (DLPFC) and the supplementary eye field (SEF). The frontal eye field influences saccade production through projections to the intermediate layers of the superior colliculus (SCi), the basal ganglia, the cerebellum, and the mesencephalic and pontine brain stem saccade nuclei. FEF, frontal eye field; LIP, lateral intraparietal area; TEO, area TEO.

portion of the anterior wall of the precentral sulcus contributes to saccade production and that a deeper region along the anterior wall extending in some individuals to the fundus or even the deep posterior bank of the sulcus contributes to pursuit production. This localization shows a high degree of homology in the organization of the FEFs in humans and macaque monkeys.

Neuronal Recordings

The influence of the FEF on saccade production is mediated by neurons that are activated specifically before and during saccades. Two kinds of neurons that control gaze have been distinguished. In general, movement neurons contribute to gaze shifting and fixation neurons contribute to gaze holding (**Figure 5(b)**). In other words, an increase in the discharge rate of movement neurons increases the probability that a saccade will be produced. In contrast, elevated discharge rates of fixation neurons occur when gaze is

fixed on a stimulus of interest and reduced discharge rate increases the probability of saccade initiation. Current models of saccade production conceive of movement and fixation neurons as producing signals that are in a reciprocally inhibitory relationship.

Neurons in the FEF that generate movement-related or fixation-related activity are located in layer 5 and innervate the superior colliculus and parts of the neural circuit in the brain stem that generate saccades. Indirect evidence suggests that fixation neurons are smaller than movement neurons. Physiological recordings indicate that these neurons, in concert with a network that includes the superior colliculus, produce signals necessary to produce saccadic eye movements.

Fixation neurons are modulated during saccades in all directions. Movement neurons, on the other hand, are active before saccades of a particular range of directions and amplitudes, referred to as the movement field. The movement fields of neurons in the lateral aspect of the FEF are less eccentric and smaller,
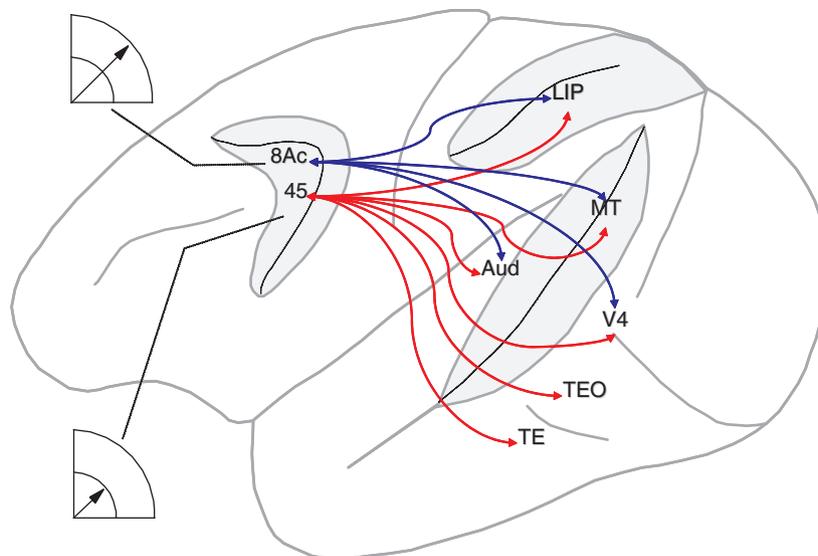
Figure 3 Selective summary of connections of the frontal eye field with extrastriate visual cortical areas. Red lines indicate connections of the ventrolateral frontal eye field in area 45, and blue lines mark connections of the dorsomedial frontal eye field in area 8Ac. Also indicated schematically are connections with belt and parabelt auditory areas (Aud). LIP, lateral intraparietal area; MT, middle temporal area; TE, area TE; TEO, area TEO, V4, area V4.
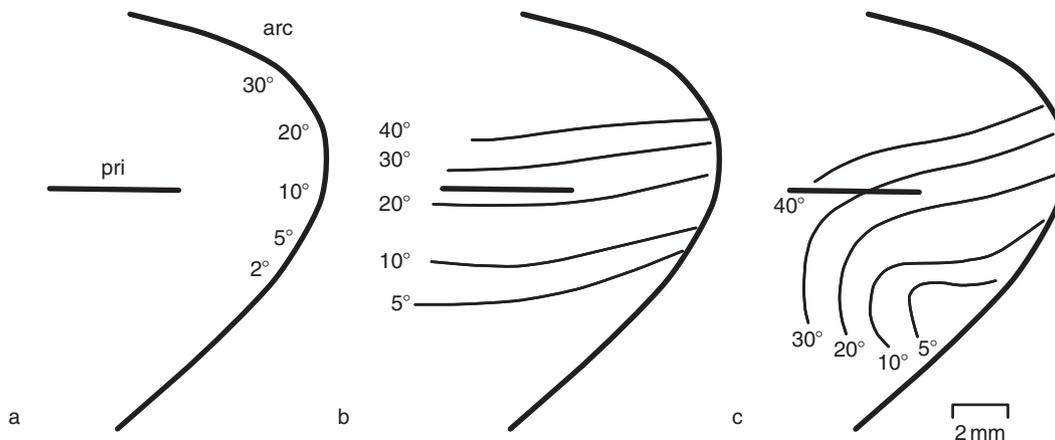

Figure 4 Maps of the frontal eye field and rostrally adjacent cortex: (a) saccade amplitude; (b) visual receptive field eccentricity; (c) receptive field size. arc, arcuate sulcus; pri, principal sulcus.

and movement field eccentricity and size increase medially in the FEF. In direction relative to current fixation, the movement fields are Gaussian shaped. In amplitude, they exhibit a log-Gaussian shape; this means that the outer border of the receptive field extends further than the inner border from the point of peak activity. The more eccentric the movement field, the further the outer border extends. This arrangement corresponds to the mapping of the visual field in the visual pathways and the mapping of saccade direction and amplitude in the superior colliculus.

Saccades are initiated when the activity of fixation neurons decreases and the activity of movement neurons reaches a threshold (**Figure 5(b)**). Variability

in saccade latency can be accounted for by the time taken to reach this threshold. In general, the form of the activation of these neurons in the FEF corresponds to diffusion processes employed in models of response time. If an interrupting stimulus occurs, saccade preparation is canceled if and only if the activity of these neurons is reduced and prevented from reaching the threshold.

Each movement of the eyes causes a shift of the retinal image. A long-standing problem has been understanding how the brain registers whether a movement in the retinal image is due to a movement in the world or a movement of the eyes. The FEF may contribute to maintaining an up-to-date representation
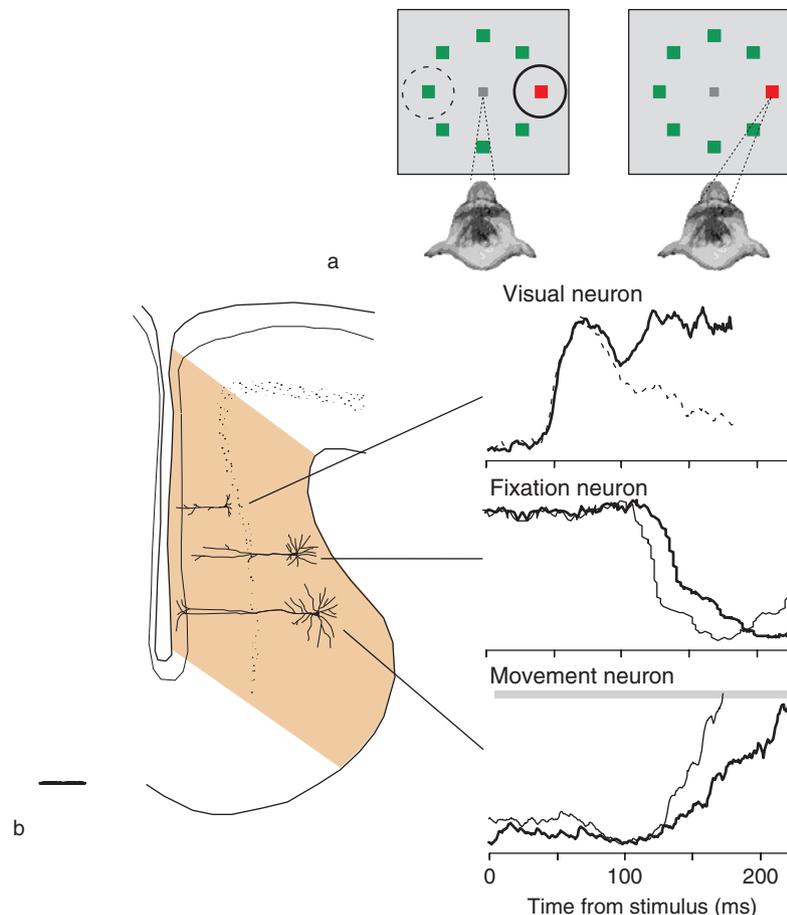
Figure 5 Target selection and saccade preparation by neurons in the frontal eye field: (a) performance of a visual performance task; (b) location and some neural constituents of the frontal eye field and graphs of modulating discharge rates of the main types of neurons found in the frontal eye field. In the visual search task in (a), the gaze must be shifted directly to the uniquely colored target among distractors. Targets for saccades are selected by the pattern of activity of visually responsive neurons in the frontal eye field as part of a distributed network. In (b), the frontal eye field is shown to be distinguished from the surrounding cortex by the large pyramidal cells in layers 3 and 5. In layer 5, pyramidal cells vary in size from smaller to larger. It is likely that each morphological cell type corresponds to a different functional cell type, as indicated in the graphs. The top neural activity graph illustrates the response to the target in the receptive field (thicker solid line) and the response to a distractor (thinner dotted line), superimposed for comparison. After around 100 ms, a selection process transpires that results in an accurate representation of the location of the target that can be used to guide saccade generation. Saccades are produced when the activity of gaze-holding fixation neurons in the frontal eye field, as part of a network, decreases while the activity of gaze-shifting movement-related neurons in the frontal eye field, as part of a network, increases to reach a fixed threshold. Variability in the time of initiation of the saccade originates in the variable time taken for the activity to increase to the threshold. The relation of activity in the frontal eye field to saccade latency is illustrated by portraying activity on trials with shorter (thin) and longer (thick) saccade latencies.

of eye orientation in the head. This is necessary to direct the gaze correctly when confronted with unexpected perturbations resulting in a mismatch between the retinal locus of a target and the angle of the saccade needed to fixate that target.

Role in Selecting Targets and Allocating Attention

Since the discovery of the FEF, research has focused on the contributions of the FEF to the generation of movements of the eyes. In the last 10 years, a wealth of data has demonstrated that the FEF contributes, as well, to the allocation of covert attention.

Neuronal Recordings

By far, most of the neurons sampled by extracellular recordings in the FEF have visual responses. The neurons are not selective for stimulus features except for some particular exceptions (noted later). The receptive fields of FEF neurons are restricted primarily to the contralateral hemifield and scale in size with
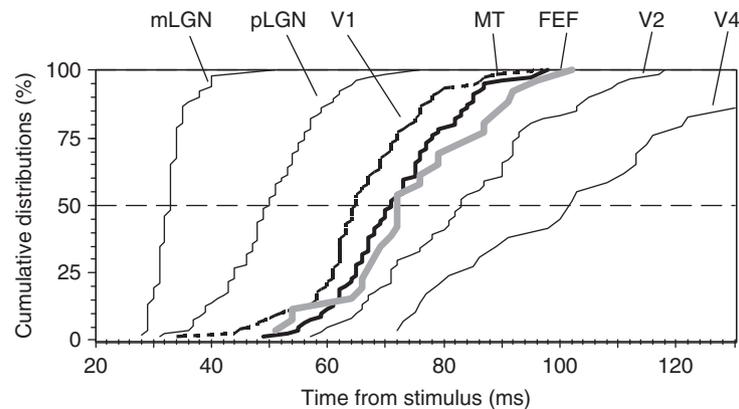
Figure 6 Timing across the visual pathway. Cumulative distributions of visual response latencies are compared for neurons in the magnocellular layers of the dorsal lateral geniculate nucleus (mLGN), neurons in the parvocellular layers of the dorsal lateral geniculate nucleus (pLGN), primary visual cortex (V1), middle temporal visual area (MT), frontal eye field (FEF), visual area 2 (V2), and visual area 4 (V4).

eccentricity. Less eccentric receptive fields are smaller than more peripheral receptive fields. The FEF has a rough map of visual field eccentricity with the central visual field represented laterally and progressively more eccentric visual field represented more medially (**Figure 4(b)**). This topography arises from the pattern of inputs from the extrastriate visual cortex.

The visual responses occur with latencies comparable to those observed in most extrastriate visual areas, averaging around 70 ms (**Figure 6**). Furthermore, the neural signals occurring in the FEF coincide with identical signals occurring in a network of interconnected structures, including the superior colliculus and posterior parietal cortex. Recent evidence indicates that FEF neurons may exhibit some selectivity for disparity and direction of motion. Some neurons in the FEF also respond to acoustic stimuli located preferentially in the contralateral hemifield. These responses contribute to orienting to sound sources.

The FEF contributes to selecting the target and shifting attention before gaze shifts, both saccadic and pursuit. In macaque monkeys trained to shift gaze to the odd-ball target in visual search arrays, most visually responsive cells in the FEF responded initially indiscriminately to the target or the distractor of the search array in their receptive field because neurons in the FEF are not intrisinically feature selective (**Figure 5(a)**). However, before the eyes move, a selection process transpires by which most visually responsive cells in the FEF signal the location of the target stimulus through suppression of the response to nontarget stimuli, leaving only the neurons responding to the target active.

This target selection process occurs if no saccade is made and the target location is signaled by a manual response. The selection process also occurs even if the saccade is directed to a nontarget stimulus. The selection process is influenced by the similarity of the target and nontarget stimuli; if the target is more difficult to distinguish from distractors, then the selection process takes more time and accounts for more of the variability of saccade latency.

The target selection process is influenced by knowledge of target properties acquired over preceding trials or sessions. At one extreme, if monkeys are trained exclusively on one target–distractor pairing, then many neurons in the FEF can appear to acquire immediate selectivity for the overpracticed target. At the other extreme, if monkeys perform a search for one target–distractor pair (e.g., red among green) and then switch to the opposite pair (green among red), they are slower and more error-prone on the first few trials after the switch. Concomitantly, the target selection process in the FEF is later and less certain on the first few trials after the switch.

To investigate more directly the relationship between the allocation of attention and preparation of a saccade, it is advantageous to dissociate at least momentarily the focus of attention from the endpoint of a saccade. This can be accomplished by training macaque monkeys to perform a visual search for an attention-capturing pop-out color target in a search array and then shifting gaze either toward (prosaccade) or opposite (antisaccade) the pop-out target, according to its orientation. Most visually responsive neurons in the FEF initially select the pop-out target while attention is allocated to distinguish its shape, but then these neurons display a strong modulation of the discharge rate whereby they come to select the ultimate endpoint of the saccade. This modulation can be identified with the shift of attention from the pop-out target to the endpoint of the saccade preceding the gaze shift.

These observations motivate the hypothesis that attention is allocated when and to the extent that these neurons in the FEF (and elsewhere in a coordinated network) are active for an object at one (as opposed to any other) location in the visual field. Mechanistically, it can be surmised that these neurons in the FEF (and elsewhere in a coordinated network) make up a salience map guiding covert and overt orienting.

Functional Brain Imaging

Numerous fMRI studies have demonstrated that the FEF and surrounding cortex are involved in the allocation of spatial attention. In fact, current thinking holds that the FEF and areas in posterior parietal cortex make up a network that mediates covert and overt orienting. However, the frontal and parietal areas have distinct roles with the FEF, concerned more with encoding the target of the saccade as such and preparing to execute the saccade, and the parietal cortex, concerned more with representing the visual stimuli.

Several studies have demonstrated the involvement of the FEF in both top-down and bottom-up control of attention. These studies present a cue (such as a small arrow) that instructs observers about some aspect of the forthcoming stimulus (such as the location or visual feature of a target stimulus). While attention is allocated in preparation for the stimulus, activation is observed in the FEF, predominantly in the hemisphere contralateral to the attended location. Studies have also demonstrated fMRI activation in the FEF of participants searching for salient stimuli. Activation is also observed in the FEF when participants maintain a working memory representation. The area of activation overlaps substantially with that activated when saccades are produced.

Inactivation and Ablation

A role for the FEF in the cognitive operations of working memory and allocation of attention is also shown by the effects of ablation or inactivation. Ablation of the FEF in monkeys results in severe deficits in locating a target presented among distractors or maintaining a representation of target location during a delay period. Reversible inactivation of the FEF impaired their detecting a visual target presented among distractors when no eye movements were permitted.

It should be noted that the effects of inactivation of the FEF on search performance are notably different from those seen following inactivation of the lateral intraparietal area in the posterior parietal cortex. Whereas inactivation of the lateral intraparietal area produced deficits that varied in magnitude with task difficulty, inactivation of the FEF produced severe deficits in visual search for single targets that were easy or hard to distinguish from the distractors as well as in search for a target defined by a conjunction of features.

Electrical Stimulation

The contribution of the FEF and surrounding cortex to the allocation of spatial attention has been shown very convincingly using intracortical electrical stimulation in monkeys and transcranial magnetic stimulation in humans. In monkeys trained to locate a single target among conspicuous distractors, stimulation of the FEF increased the probability of locating the target if it was located within the movement field of the site of stimulation. Other work has indicated that this influence may be mediated through a direct influence on the activation of neurons in visual area 4 (V4). In humans, transcranial magnetic stimulation over the FEF can affect attention allocation and awareness of stimuli. Curiously, these effects in humans tend to be specific to the right hemisphere.

These results have been cited in support of the premotor theory of attention, which states that shifting visual spatial attention corresponds to preparing a saccade. The FEF is an ideal region in which to test this theory, being a central node in the network that selects targets and produces saccades. As previously described, the focus of attention can be dissociated momentarily from the endpoint of a saccade when monkeys search for an attention-capturing pop-out color target in a search array and then shift gaze either toward (prosaccade) or opposite (antisaccade) the pop-out target according to its orientation. An experiment used this task and probed the evolution of saccade preparation by measuring the direction of saccades evoked by intracortical microstimulation of the FEF at different times following the search array. The saccades evoked on prosaccade trials deviated progressively toward the target that was the endpoint of the saccade. However, the saccades evoked on antisaccade trials deviated not at all toward the pop-out target but only toward the ultimate endpoint of the saccade opposite the singleton. Recall that, on antisaccade trials, the most visually responsive neurons in the FEF initially select the pop-out target while attention is allocated to distinguish its shape. In contrast, movement neurons are activated but do not produce a directional signal until immediately before the saccade is made. Thus, the FEF can covertly orient attention without preparing a saccade to the locus of attention. These results indicate that the premotor theory of attention must be revised.

In summary, the FEF was discovered over a century ago when it was found that electrical stimulation elicited movements of the eyes. Today, electrical

stimulation of the FEF confirms that it contributes significantly to overt orienting through gaze shift and also to covert orienting through attention shifts.

See also: Attention and Eye Movements; Cortical Control of Eye Movements; Eye and Head Movements; Eye Movement Disorders; Neural Coding of Spatial Representations; Oculomotor Control: Anatomical Pathways; Oculomotor System: Models; Parietal Cortex and Spatial Attention; Prefrontal Cortex: Structure and Anatomy; Prefrontal Cortex; Pursuit Eye Movements; Saccade–Pursuit Interactions; Saccades and Visual Search; Saccadic Eye Movements; Sensorimotor Integration: Attention and the Premotor Theory; Superior Colliculus; Supplementary Eye Fields; Target Selection for Pursuit and Saccades; Visual System: Multiple Visual Areas in Monkeys; Visual Cortex in Humans.

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