

On the Evolution of the Frontal Eye Field: Comparisons of Monkeys, Apes, and Humans

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36.1 Overview

Originally considered only an ocular motor area, interest in frontal eye field (FEF) has increased markedly with its recognition as an anatomical hub region, which is critically involved in covert and overt orienting in monkeys and humans (reviewed by [Squire et al., 2013](#); [Schall, 2015](#)). Thus, FEF is associated with motor, sensory, and cognitive processes, which are mediated in association with neighboring cortical areas.

[Ferrier \(1874\)](#) described an area in the dorsal portion of the arcuate sulcus of anesthetized monkeys where electric stimulation elicited movements of the eyes and head in the direction opposite the stimulated hemisphere. These are referred to as contraversive movements. This finding has been replicated in multiple species including prosimians, New World monkeys, Old World monkeys, apes, and humans. [Förster \(1926\)](#) described the area from which he could evoke eye movement as the “frontales Augenfelder,” which was translated into “frontal eye fields” ([Davidoff, 1928](#); [Förster and Penfield, 1930](#)).

Before proceeding, we introduce our nomenclature. This chapter describes the location of the FEF assessed with a variety of methods. For efficiency we use phrases such as “FEF is located ...,” when we should more clearly state “A region activated during saccades ...” or “A region from which saccades were elicited” We emphasize this here to alert the reader that the location and boundaries of the FEF(s) are uncertain, operational, and have rarely been compared systematically across methods.

Today, the majority of research on FEF is done with macaque monkeys and humans, and this chapter, like previous reviews ([Paus, 1996](#); [Tehovnik et al., 2000](#); [Amiez and Petrides, 2009](#); [Vernet et al., 2014](#); [Percheron](#)

[et al., 2015](#)) is animated by an apparent discrepancy in the location of FEF between monkeys and human. In both macaque and human the FEF is located in a sulcus rostral to the central sulcus, known either as arcuate or precentral (see [Connolly, 1936, 1950](#)). All authors agree that FEF in monkeys is located in the dysgranular region of caudal prefrontal cortex commonly included in Brodmann's area 8; however, most locate FEF in humans in Brodmann's agranular area 6. We address this apparent enigma by highlighting the following observations: (1) particular similarities and differences in eye-, head-, and body-orienting behavior across species, (2) variation of frontal sulcal morphology across species and individuals, (3) the location of FEF at a cytoarchitectonic transition zone between agranular area 6 and granular area 8 in a cortical region with greater than average variation of sulcal pattern, and (4) the embrace of FEF caudally (in premotor cortex) and rostrally (in prefrontal cortex) by areas also contributing to visually guided gaze behavior. These observations are framed by an appreciation of the varying technical limits and spatial resolution of methods used to locate FEF in monkeys, apes, and humans, and of the functional and anatomical position of FEF in a surrounding network of areas contributing to orienting behavior that includes but is not limited to eye movements.

36.2 Gaze Control and Coordination in Prosimians, Monkeys, Apes, and Humans

We briefly review key similarities and major differences in the organization of the eye and head across species. The structure of the neural circuits producing eye movements will naturally vary with differences in the

nature of movement execution dictated by the size and configuration of the eye, head, body, and habitat.

A search for homologies among primates in the cortical and subcortical organization of eye movements is encouraged by the many similarities in gaze behavior observed between monkeys, apes, and humans. Members of each species produce each of the different types of eye movements—fixation maintained by gaze-holding vestibular and visual reflexes, which is interrupted by rapid gaze shifts and slow pursuit eye movements to direct vision in three dimensions. In numerous quantitative respects the eye movements of macaque monkeys and humans are more similar than different in execution but can differ in planning and context (eg, [Martinez-Conde and Macknik, 2008](#); [Baizer and Bender, 1989](#); [Einhäuser et al., 2006](#); [Berg et al., 2009](#); [Shepherd et al., 2010](#)). In a wide range of testing conditions, the advanced cognitive control of eye movements is indistinguishable between humans and macaque monkeys (eg, [Munoz and Everling, 2004](#); [Camalier et al., 2007](#); [Hanes and Schall, 1995](#); [Hanes and Carpenter, 1999](#); [Nelson et al., 2010](#)). Consequently, the macaque has been a faithful source of insights for human clinics of neurology (eg, [Leigh and Zee, 2015](#)) and psychiatry (eg, [Driscoll and Barr, 2016](#)). Comparisons of the eye movements of chimpanzees, gorillas, and orangutans with those of humans also have noted numerous similarities with particular differences ([Kano et al., 2011](#); [Kano and Tomonaga, 2009, 2011](#)). Primates in general are visual creatures with particular ocular, muscular (eg, [Blumer et al., 2016](#)), and neural adaptations including devotion of a large proportion of the brain to visual processing.

Primates execute gaze shifts to scrutinize objects with the high acuity visual resolution afforded by the area centralis or fovea. There are qualitative differences in the organization of central retina between nocturnal and diurnal primates related to their gaze behavior that may be reflected in differences in the ocular motor network. With the exception of the nocturnal owl monkey and Strepsirrhini, all Haplorrhini, including the tarsier, possess a fovea ([Wolin and Massopust, 1967](#)). The absolute size of the fovea is comparable across diurnal primates, and a higher acuity of vision is achieved by increasing the size of the eye; for example, human eyes are about four times larger than marmoset eyes ([Finlay et al., 2008](#)). On the other hand, galagos and owl monkeys have a rudimentary area centralis ([DeBruyn et al., 1980](#); [Stone and Johnston, 1981](#); [Wikler and Rakic, 1990, 1990](#); [Webb and Kaas, 1976](#)). Accordingly, the spatial resolution in galagos and owl monkeys (~ 5 cycles deg^{-1}) is much poorer than in macaques, apes, or humans (~ 50 cycles deg^{-1}) ([Langston et al., 1986](#); [Mitchell and Leopold, 2015](#)). To appreciate this difference, note that when held at arm's length, your finger subtends about 1 degree of arc in the visual field. A

human fingerprint is composed of about 50 ridges, which may be visible to you. A galago or owl monkey could resolve only five large strips across a finger.

The distinctive visual abilities of primates are conferred primarily by a retina equipped with a specialized central region of high resolution that is associated with a sophisticated neural system producing large variety, range, and coordination of eye movements to gather visual information. The large oculomotor range that primates possess appears to be evolutionarily recent. The human oculomotor range spans about ± 50 degrees of visual angle ([Guitton and Volle, 1987](#); [Stahl, 1999](#)) and is nearly matched by that of the macaque monkey ([Tomlinson and Bahra, 1986](#)) and baboon ([Marchetti et al., 1983](#)). In contrast, the oculomotor range of more distantly related primates such as prosimians ([Shepherd and Platt, 2006](#)) or the New World squirrel monkey ([McCrea and Gdowski, 2003](#); [Heiney and Blazquez, 2011](#)) and marmoset ([Mitchell et al., 2014](#)) is limited to <15 degrees. Limited ocular motility is commonly reported in nonhuman primates with small heads and poorly developed fovea, such as tree shrew ([Remple et al., 2006](#)) and cat ([Guitton et al., 1984](#)). Larger gaze shifts are accomplished with a combined rotation of the head and eyes. What qualifies as “larger” varies across species. The greater inertial mass of the larger heads of apes and humans makes head movements more energetically costly, slower, and socially revealing. Thus, while smaller prosimians and New World monkeys naturally make gaze shifts of more than about 5 degrees with a head rotation too (eg, [McCrea and Gdowski, 2003](#)), humans naturally make gaze shifts of more than about 20 degrees with a head rotation too. Moreover, relative to apes and monkeys, the human eye is positioned further forward in the orbit, which expands the effective visual field with horizontal eye movements achieving larger abductions ([Denion et al., 2015a](#)). Such unique orbital morphology is adaptive for bipedal locomotion in a habitat of open planes ([Denion et al., 2015b](#)). Horizontal eye movements are more common for terrestrial species compared with arboreal species ([Kobayashi and Kohshima, 2001](#)).

The eyes may be a window of the soul for humans, but gaze direction is camouflaged in other primates by coloration of the sclera resembling surrounding skin color. Comparing the external features of eyes from 88 primate species, humans are the only primate with a white sclera and the largest amount of exposed sclera relative to the outline of the eye ([Kobayashi and Kohshima, 1997](#)). This morphology affords a clear visual marker of gaze direction that facilitates communication ([Kobayashi and Kohshima, 1997, 2001](#)). Gaze following is observed across primate species ([Rosati and Hare, 2009](#); [Shepherd, 2010](#)), but most often it utilizes the orientation of the head. The reliance on the direction of the eye seems to be

specific to humans (Tomasello et al., 2007). In summary, the specialization of the fovea and the oculomotor range delimit the visual ability of primates and rationalize the amount of cortex dedicated to visual processing.

36.3 Variability of Sulci in the Primate Frontal Cortex

In every primate species including humans FEF is located in a sulcus (or dimple) immediately rostral to the central sulcus. In humans this is referred to as the precentral sulcus, but in monkeys, the arcuate sulcus. Mingazzini (1888) first coined the term arcuate sulcus (“solco arcuato”) to describe the inferior precentral sulcus in the Old World monkey, which others had previously called “sillon courbe” by Gromier or “sillon kypsiloidé” by Broca (see Hervé, 1888).

The location of FEF in standardized coordinates for the individual species can vary in proportion to variability of the morphology of this sulcus. The high variability of sulcal patterns in humans is well known, and a variety of patterns can be identified across individuals (Ono et al., 1990). The precentral sulcus is interrupted into superior and inferior segments in over 50% of individuals; three segments are found in about 30% of individuals, and four segments are found in fewer than 5%. About 30% of individuals also exhibit a longitudinally oriented marginal precentral sulcus, reminiscent of the precentral dimple in macaques. The major superior and inferior segments develop at different times. In more than 90% of individuals the superior precentral sulcus connects with the superior frontal sulcus, and the inferior precentral sulcus connects with the inferior frontal sulcus. None of these tendencies are the same across hemispheres.

The first reference to a sulcus praecentralis referred only to the inferior precentral sulcus (IPrCS) (Ecker, 1869). According to Eberstaller (1890), the superior precentral sulcus was first described as a separate sulcal entity by Jensen (1871). Recent studies have further subdivided these sulci—Germann et al. (2005) distinguished three parts of the IPrCS: a dorsal and a ventral part, and a so-called horizontal extension separating the other two parts. Also, the superior precentral sulcus was subdivided into a ventral and a dorsal part, separated by the superior frontal sulcus (Amiez et al., 2006).

Naturally, the location of FEF and surrounding areas will vary as a function of systematic and random variability of sulcal patterns. In fact, as detailed in the following, Amiez et al. (2006) conducted a subject-by-subject analysis of the locus of eye movement-related functional activity revealed in relation to the detailed morphology of the precentral and superior frontal sulci.

A focus of activation associated with saccadic eye movements was located in the ventral branch of the superior precentral sulcus in both hemispheres. A second focus has been found in the dorsal part of the inferior precentral sulcus. Imaging during a hand response selection task revealed activation focused in the dorsal branch of the superior precentral sulcus close to the caudal end of the superior frontal sulcus. Activation in primary motor cortex was focused in the precentral knob (or Broca’s *pli de passage moyen*). The relationship of FEF to the bordering premotor cortex is elaborated in the following paragraphs.

Compared to humans, the cerebral sulcal pattern is much less variable across Old World monkeys (Cercopithecidae) (Falk, 1978). The frontal lobe consists of an arcuate sulcus rostral to the central sulcus and a longitudinal principal sulcus (known also as sulcus rectus) rostral to the arcuate sulcus (Connolly, 1936, 1950; Walker, 1940). The arcuate sulcus consists of a superior (horizontal) limb or branch and an inferior (vertical); at the genu or curve, typically located caudal to the end of the principal sulcus, some individuals exhibit a posterior extension of the sulcus referred to as a “spur.” Thus, the shape and extent of the arcuate sulcus in monkeys varies. However, no one has systematically characterized the variation of its sulcal morphology. For example, the prevalence of the arcuate spur is unknown in various macaque species. Therefore, we investigated the incidence of an arcuate spur in a sample of 235 hemispheres obtained from nine direct observations before histological processing, 132 magnetic resonance (MR) images, and 109 figures from the literature. This sample consists of 221 left hemispheres and 161 right hemispheres; for 147 brains both hemispheres were available. Samples were obtained from *Macaca fascicularis* ($n = 19$), *Macaca mulatta* ($n = 162$), *Macaca nemestrina* ($n = 7$), and *Macaca radiata* ($n = 21$). We could determine the gender of 54 male and 7 female monkeys. Table 36.1 summarizes the findings. In about one-third of both left and right hemispheres a large spur was present, another one-third exhibited a small spur, and the remaining one-third exhibited no spur. Thus, two-thirds of hemispheres exhibit an arcuate spur. In about two-thirds of hemispheres the spur was symmetric in appearance in both hemispheres.

These values may underestimate the prevalence of an arcuate spur because we found a spur more often in our sample of histological (89%) and MR (86%) images as compared with figures in the literature (57%). We cannot evaluate how faithfully authors portray cortical sulcal patterns. Also, even though the sample of female macaques was small, we found no clear difference in prevalence between females (71%) and males (67%). An arcuate spur was most common in *M. mulatta* (75%) and *M. nemestrina* (71%), only slightly less common in

TABLE 36.1 Prevalence of arcuate spur in macaques

Spur size	Hemisphere	Number	Percentage (%)
Large	Left	65/221	29
	Right	48/161	30
Small	Left	83/221	38
	Right	64/161	40
Absent	Left	73/221	33
	Right	49/161	30
Symmetric	Both	94/147	64

M. radiata (67%), and least common in *M. fascicularis* (53%).

These modest findings have several implications. First, atlases based on averages of macaque brains (eg, Frey et al., 2011; Rohlfing et al., 2012; Calabrese et al., 2015) imply that sulcal patterns are more regular and uniform across individuals than they actually are. Such averaged atlases underestimate the length of the spur observed in many individuals by representing only a small spur (Frey et al., 2011) or none at all (Calabrese et al., 2015; Rohlfing et al., 2012). Likewise, atlases based on a single individual will misrepresent the incidental presence or lack of a spur as standard anatomy (eg, Saleem and Logothetis, 2012). Second, sulcal patterns can serve as reliable landmarks to identify the location of cortical areas. For example, in macaques the location and shape of the arcuate sulcus reliably predicts the location of FEF. Also, the arcuate spur has also been identified as a boundary between functionally and anatomically distinguished dorsal and ventral premotor areas (eg, Gabernet et al., 1999). Third, a variety of mechanisms for cortical folding have been proposed—differential cell proliferation, differential tangential expansion, radial intercalation, axon tension, radial glia, and so on (see for review Striedter et al., 2015; see also Mota and Herculano-Houzel, 2015; Tallinen et al., 2016). These data cannot distinguish among these alternatives, but they offer an opportunity for further exploration. Finally, variation of structure most likely announces variation of function. The common lack of symmetrical occurrences of the spur represents clear evidence for cerebral asymmetry in macaques. While others have reported a rightward bias in the length of the arcuate sulcus in macaques (Sakamoto et al., 2014; Imai et al., 2011), some have reported no asymmetry (Falk et al., 1990; Heilbronner and Holloway, 1989). Whether such asymmetry is systematic and functionally meaningful requires a larger sample. However, behavioral and anatomical evidence for some degree of cerebral asymmetry in macaques has been reported (eg, Hamilton and Vermeire, 1988; Heilbronner and Holloway, 1989; Falk et al., 1990). Perhaps an arcuate spur relates to

individual hand preferences (eg, Lehman, 1980; Mangalam et al., 2014). In any case, when quantified in the MRI atlases of macaque brains, the magnitude of deformation needed to co-register the set of macaque brains varies across the cortex and was noticeably elevated in the region of the spur (Frey et al., 2011; Calabrese et al., 2015). Does this greater variability in the organization of this region provide greater opportunity for natural selection? Further research is needed to determine how the variation of sulcal morphology relates to the location and boundaries of FEF and neighboring areas.

36.4 Location of FEF Across Primate Species

36.4.1 Scandentia

Together with Dermoptera, for which very little is known, Scandentia is the closest mammalian order relative to Primates (Perelman et al., 2011). Most of their visual specializations evolved independently of primates. They inhabit tropical forests of southern Asia. Electrical stimulation mapping of the (small) frontal lobe has not found a discrete FEF, although stimulation of sites in frontal motor areas did elicit eye blinks (Lende, 1970; Remple et al., 2006; Baldwin et al., 2017). This may not be not surprising, because tree shrews have neither a specialized focus of high resolution in the retina nor much range of eye movements. However, they are very visual creatures that orient readily with head and body.

36.4.2 Strepsirrhini: Prosimians

Most prosimians are nocturnal animals. As noted in the earlier section, the retina lacks a clear fovea and instead has only a rudimentary area centralis. Their relatively poor distance vision is compensated by a long snout ending in a moist and touch-sensitive surface, similar to that of dogs. The wet nose provides a conduit for pheromones into the vomeronasal organ.

Prosimians resemble other primates and are distinct from other mammals in the presence of a clear granular prefrontal cortex rostral to the agranular motor cortex. Therefore, prosimians are a good model for the evolution of FEFs, because their frontal cortex is subdivided into a granular and agranular portion, but they do not rely as much on the visual system as simians do.

36.4.2.1 *Lorisoidea* (*Galago*)

Galagos are nocturnal primates living in low forests. Arboreal animals, they move by quadrupedal walking and leaping. Galagos have relatively large eyes with a rudimentary fovea supporting relatively low acuity vision (DeBruyn et al., 1980; Stone and Johnston, 1981). Among primates they rely least on vision. Because of

the relatively large size of the eyes, galagos have a limited range of eye movements and compensate for this with more head movements to explore novel objects (Rogers et al., 1993; Cantalupo et al., 2002). Although their form of locomotion might suggest that they rely on good eye–hand coordination for their agile leaping, they primarily use olfactory and auditory information. Galagos have large ears with great mobility that are continuously moving. As insectivores, they rely on sound to localize their prey (Charles-Dominique, 1977).

Electrical stimulation of a small region medial to the anterior frontal sulcus evokes contraversive eye movements (Wu et al., 2000; Fig. 36.1). This very restricted representation of eye movements was compensated by a larger representation of ear movements in the cortex caudal to FEF (Fogassi et al., 1994). While the more rostral region had cytoarchitectonic characteristics of FEF seen in other species with a granular layer 4 and medium-to-large densely packed layer 5 pyramidal neurons, the caudal region appeared more dysgranular (Preuss and Goldman-Rakic, 1991). Like FEF in macaques the rostral region is connected with the multi-form division of the mediodorsal nucleus and with the intermediate and superficial layers of the superior colliculus (Markowitsch et al., 1980; Preuss and Goldman-Rakic, 1991).

Curiously, a dorsomedial eye field corresponding to the supplementary eye field has not been found (Wu et al., 2000). Research with macaque monkeys and humans has led to the general conclusion that the supplementary eye field contributes to high level, executive control of gaze behavior (eg, Schall and Boucher, 2007). If correct, the absence of a supplementary eye field in galagos could be understood in light of the stimulus-bound simplicity of galago behavior relative to that of macaques and humans. Regardless, this reminds us that the number and organization of cortical areas mediating gaze control need not be equivalent across species.

36.4.3 Haplorrhini: Simians

Simians (anthropoids) are all diurnal with the exception of owl monkeys. They have less reliance on olfaction and are primarily visual animals with a well-developed fovea supporting high acuity vision and a suitably matched ocular motor system supporting the control of eye movements in coordination with head, limb, and body movements.

36.4.3.1 *Platyrrhini* (New World Monkey)

Platyrrhini are small to medium size monkeys with flat noses, which distinguishes them from Old World

monkeys. Other than howler monkeys, they lack the typical trichromatic vision of the Old World monkeys.

36.4.3.1.1 *Callitricidae* (Marmoset)

Marmosets are the smallest New World monkeys. Those used in research, *Callithrix jacchus*, naturally live in open forest habitats. Marmosets are very agile and active, moving with quadrupedal walking and leaping. Claw-like nails allow them to cling to trees while foraging. The retina of the marmoset has a well-developed fovea comparable to that found in other diurnal primates (Finlay et al., 2008; Franco et al., 2000). However, marmosets have the smallest eyes among the primates (Wolin and Massopust, 1967) affording less spatial acuity (Finlay et al., 2008). With lightweight heads, marmosets can shift gaze with rapid head movements and so have correspondingly smaller oculomotor range (Mitchell et al., 2014). Marmosets also display head-cocking, rapid head rotations along the longitudinal axis, for visual exploration (Kaplan and Rogers, 2006).

With a lissencephalic (smooth) cortex and an opportunity for genetic studies, marmosets have gained new popularity in research. A review by Bakola et al. (2015) summarizes knowledge about the frontal motor system. Although the frontal cortex of marmosets is overall a smooth surface, some individuals exhibit an arcuate dimple. Eye movements with and without head movements are elicited from the rostral frontal lobe with electrical stimulation (Mott et al., 1910; Blum et al., 1982; Fig. 36.2). Such movements were also elicited by stimulation of the rostral frontal lobe in prosimian lemurs (Mott and Halliburton, 1908). Subsequent research with marmosets has verified visual and ocular motor connectivity of these regions (Reser et al., 2013; Lyon and Kaas, 2001; Spatz and Tigges, 1972; Rosa et al., 2009; Krubitzer and Kaas, 1990; Collins et al., 2005). Areas 8aV and 45, which might correspond to the frontal visual (FV) area described by Krubitzer and Kaas (1990), show similar patterns of connections with parietal and extrastriate visual areas. This observation suggests that FEF in the marmoset spans area 8 and perhaps partially area 45 (Reser et al., 2013). The cytoarchitecture of the FEF region is characterized by larger neurons in layer 5, higher myelin density, and a granular layer 4 (Burman et al., 2006; Krubitzer and Kaas, 1990), similar to other species examined. The locally elevated density of myelin was also found with structural MRI techniques (Bock et al., 2009). Information about the neurophysiology of FEF in particular or prefrontal cortex in general in marmosets is lacking. However, an fMRI study reported elevated BOLD signal within the location of area 8aV when visual stimuli were presented (Hung et al., 2015).

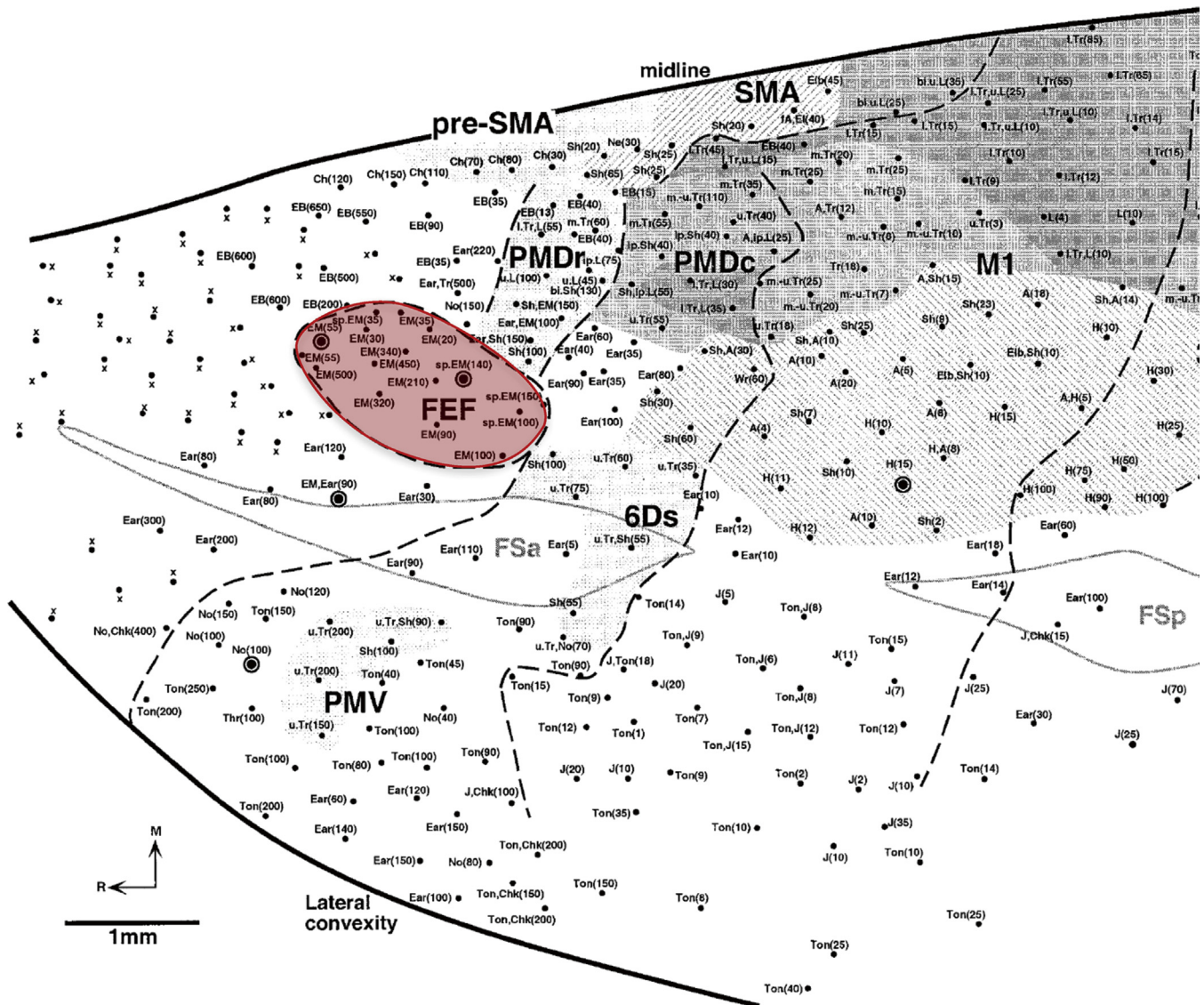


FIGURE 36.1 Map of eye and body movements elicited by intracortical microstimulation in *Galago garnetti*. The frontal eye field (FEF) is highlighted red, located rostral to premotor cortex. Smooth pursuit eye movements were evoked at more caudal sites, and saccadic eye movements, more rostral. Curiously, a supplementary eye field was not found. *Reproduction from Wu, C.W., Bichot, N.P., Kaas, J.H., 2000. Converging evidence from microstimulation, architecture, and connections for multiple motor areas in the frontal and cingulate cortex of prosimian primates. J. Comp. Neurol. 423, 140–177.*

Eye movements with and without head movements were also elicited by stimulation caudal to the FEF (Mott et al., 1910); sites eliciting pinna movements were not found, contrasting with prosimian lemurs (Mott and Halliburton, 1908). In marmosets, an additional caudal area 8 (area 8C) was described at the junction between dorsal and ventral premotor cortex (Paxinos et al., 2012; Burman et al., 2014, 2015; Bakola et al., 2015), which is distinguished by denser myelination. This area has a connectivity pattern like area 6Va, but lacks some of the somatosensory connections and instead receives input from area 8aV and is interconnected with visual areas (Bakola et al., 2015; Burman

et al., 2015; Palmer and Rosa, 2006; Rosa et al., 2009). Burman et al. (2015) consider area 8C as part of the premotor network rather than as a prefrontal area because it lacks a distinct layer 4. However, they also suggest that this region might be specialized for visually guided movements and suggest that it might correspond to a region where Preuss et al. (1996) evoked eye and neck movements in the owl monkey. Marmoset area 8C might correspond to the PMvr spur described by Gabernet et al. (1999) for the macaque monkey as is described in the following section. Burman et al. (2015) point out that area 8C might be similar to area 6Va involved in head movements. Because marmosets compensate for

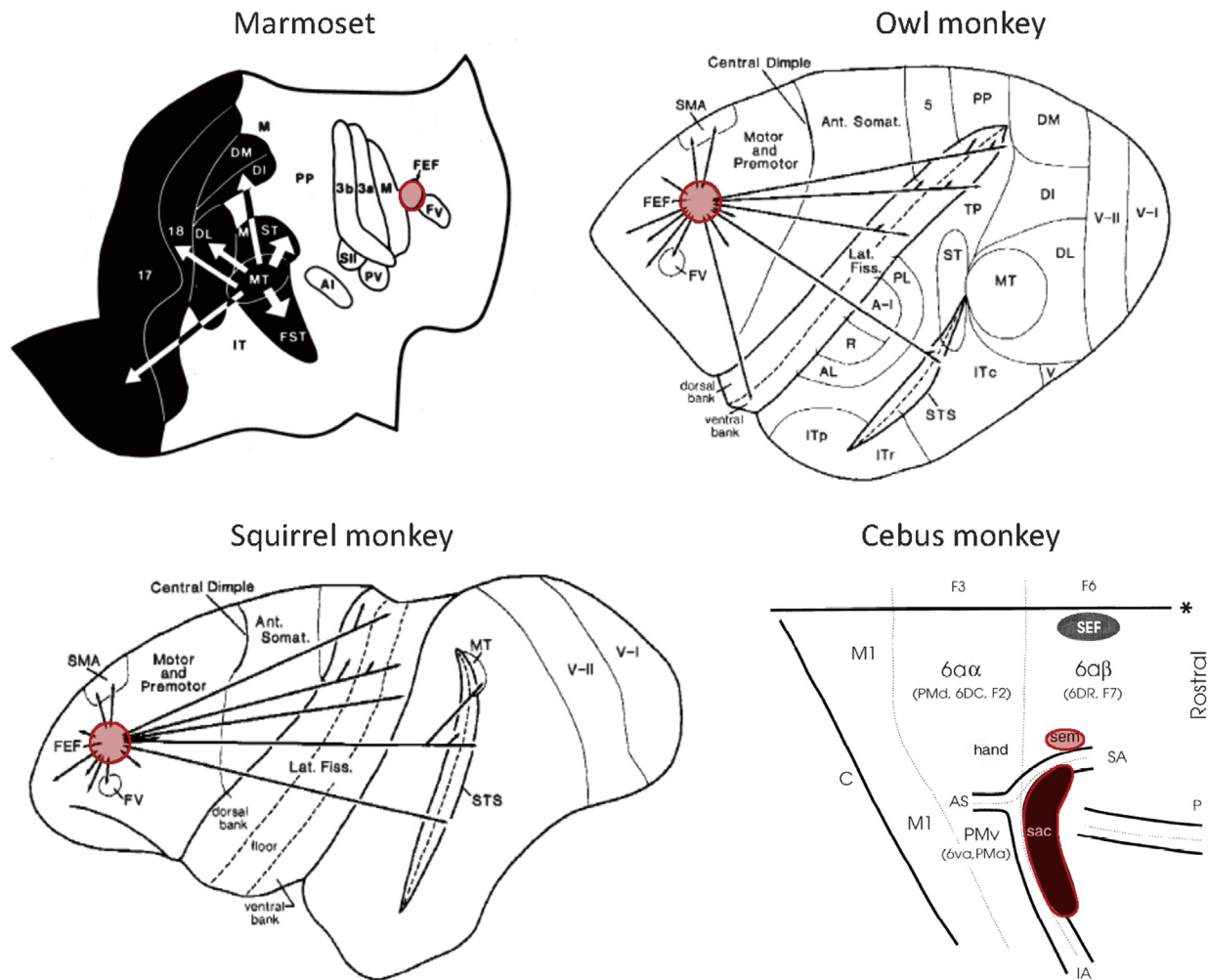


FIGURE 36.2 Location and connectivity of frontal eye field defined by microstimulation and intracortical connectivity in marmoset, owl monkey, and squirrel monkey with map of saccadic and smooth pursuit eye movements elicited by intracortical microstimulation in *Cebus*. Reproduced from Krubitzer, L., Kaas, J., 1990. *The organization and connections of somatosensory cortex in marmosets*. *J. Neurosci.* 10, 952–974; Huerta, M., Krubitzer, L., Kaas, J., 1987. *Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys. II. Cortical connections*. *J. Comp. Neurol.* 265, 332–361; Tian, J., Lynch, J., 1996. *Corticocortical input to the smooth and saccadic eye movement subregions of the frontal eye field in Cebus monkeys*. *J. Neurophysiol.* 76, 2754–2771.

their limited oculomotor range with rapid head movements, an area linked with FEF that is involved in directed head movements is not surprising.

36.4.3.1.2 Aotidae (Owl Monkey)

Owl monkeys are nocturnal. They live in higher elevations in forests and tropical environments of Central America and northern South America (Groves, 2001). They feed upon small fruit, insects, leaves, and flowers. They are able to snatch flying insects out of the air or off of a branch, unlike foragers or tool users who exploit holes and spaces in the tree bark (Wright, 1989). Even though the nocturnal environment would be a disadvantage for animals dependent upon vision, owl monkeys have been able to thrive in the niche. They possess large eyes without a fovea and a nearly pure

rod retina (Woollard, 1927; Jacobs et al., 1993). These structural features provide for better low-light spatial resolution that improves their night vision, but leaves the owl monkey with monochromatic vision.

Owl monkeys are lissencephalic anterior to the central sulcus, only rarely with an arcuate dimple. FEF was identified with microstimulation at low currents around the arcuate dimple, and because of the smaller prefrontal FEF appears located relatively more rostral (Fig. 36.2; Gould et al., 1986; Huerta et al., 1986, 1987). Caudal to FEF is an expanded region where head movements are represented (Gould et al., 1986). Gould et al. (1986) describe another eye field that is located more dorsal and also has a caudally adjacent region representing head movements and likely corresponds to SEF of macaque monkeys (Preuss et al., 1996). Huerta et al.

(1986, 1987) also characterize an FV field located ventral to FEF. Saccadic eye movements could be evoked with higher currents in area 8B—referred to it as dorsal oculomotor area—as well as in the dorsal premotor cortex (Stepniewska et al., 1993; Preuss et al., 1996). Stimulation in the cortex surrounding FEF at higher currents also leads to ear, eyelid, or vibrissa movements (Huerta et al., 1986).

FEF in owl monkeys shows a connectivity pattern comparable to squirrel monkeys and macaque monkeys with connections to the upper temporal lobe, the dorsomedial visual area, and posterior parietal cortex as well as the superior colliculus and the lateral band of the mediodorsal nucleus (Kaas and Morel, 1993; Weller et al., 1984; Krubitzer and Kaas, 1993; Kaas et al., 1977; Collins et al., 2005; Huerta et al., 1986, 1987). However, the FEF region of owl monkeys apparently lacks strong connections with the middle temporal visual area that are found in diurnal monkeys (Huerta et al., 1987; Weller et al., 1984; but see Cerkevich et al., 2014). A connectivity pattern similar to FEF is shared by the more ventral FV area.

36.4.3.1.3 Saimiriinae (Squirrel Monkey)

Squirrel monkeys live in Central and South America in the midlevel tangled layers of branches, vines, and trees of tropical forests. Squirrel monkeys use all four limbs to move but will occasionally walk short distances on two limbs. Squirrel monkeys predominantly eat fruits and insects. They rarely reach for insects in motion, but prefer finding insects on leaves. They engage in long periods of visual observing behavior (Glickman and Sroges, 1966); however, they tend to show notably less visual investigative behavior relative to other primates (DuMond, 1968; Glickman and Sroges, 1966; but see Haude and Ray, 1974). Male squirrel monkeys are dichromatic, while females can be either dichromatic or trichromatic. The eye movements of squirrel monkeys are in general comparable to macaque monkeys, but they have a much narrower oculomotor range of about 10–15 degrees horizontally (Heiney and Blazquez, 2011; McCrea and Gdowski, 2003). Interestingly, the oculomotor range is larger for the vertical axis (about 25 degrees); this asymmetry contrasts with terrestrial species in which horizontal eye movements are more frequent and of larger average amplitude. Like other monkeys, squirrel monkeys communicate with visual signals and social behaviors, including facial expressions, as well as signaling with their ears.

In squirrel monkeys, gyral variations of the frontal lobe range from no sulcus to a small inferior arcuate dimple to a small arcuate sulcus (Emmers and Akert, 1963; Blum et al., 1982; Huerta et al., 1987). FEF was identified with electric stimulation near the dimple, with considerable variation between individuals (Huerta et al., 1986; Fig. 36.2).

FEF of squirrel monkeys is connected with visual areas in the superior temporal sulcus including area MT in addition to subcortical structures paralleling macaques (Huerta et al., 1987; Tigges et al., 1981).

36.4.3.1.4 Cebidae (Capuchin)

Capuchin monkeys are considered to be the most intelligent of New World monkeys, possessing a relatively large brain relative to their body size. They have coordinated movements between hands, tail, feet, and mouth. They perceive objects, movements, and surfaces in much the same way humans do. They have a large repertoire of visual signals and gestural behaviors to communicate, including submissive grins, raising eyebrows, head tilt, play face, threat face, and lip smacking. Capuchins are found commonly in northern parts of Argentina but are also distributed around North and South America. They live in different regions of trees—some very high and others in the lower regions. They spend most of their waking hours foraging for a variety of types of food. They eat a greater variety of food types than any other type of monkeys. They exhibit rudimentary tool use, for example, using stones to access food.

The capuchin (*Cebus apella*) shows a clearly defined gyral pattern (Connolly, 1936, 1950), resembling that of macaque monkeys with an arcuate sulcus that is usually accompanied by a principal sulcus (Sanides, 1970; Tian and Lynch, 1997).

FEF as identified with microstimulation is found along the anterior bank of the arcuate sulcus (Lynch et al., 1994) at a location comparable to that of macaque monkeys. It shows a comparable connectivity pattern as described for other monkeys, with connections to MT and to the posterior parietal cortex as well as subcortically to the superior colliculus and the mediodorsal nucleus of the thalamus (Tian and Lynch, 1997; Leichnetz and Gonzalo-Ruiz, 1996; Rosa et al., 1993; Lynch et al., 1994).

In addition to FEF in the anterior bank of the arcuate sulcus, two more eye fields have been characterized in *Cebus*. One is located dorsomedially and likely corresponds to the supplementary eye field of macaque monkeys (Tian and Lynch, 1995) and another one is located in the posterior bank of the superior limb of the arcuate sulcus (Tian and Lynch, 1996). In contrast to FEF where microstimulation evokes saccadic eye movements, stimulation at the later more dorsomedial location results in smooth eye movements. This location might correspond to the smooth pursuit zone described for macaque monkeys (Gottlieb et al., 1993, 1994); however, in macaque monkeys it is in the posterior bank of the arcuate sulcus adjacent to FEF and not located dorsomedially as in *Cebus* (Fig. 36.2). This illustrates that a common function can be mediated by cortical areas in different relative locations across species.

36.4.4 Cercopithecidae (Old World Monkey)

36.4.4.1 *Macaca* (Macaque)

Macaque monkeys are the most common nonhuman primate used in research to gain insights into human brain function (Passingham, 2009). Hence, the most detailed knowledge about the organization and location of the primate FEF has been obtained from various macaque species (*M. mulatta*, *M. fascicularis*, *M. radiata*, *M. nemestrina*, *Macaca sinica*, and *Macaca fuscata*). Given the relatively minor known differences in the brain organization across macaque species, many studies have used more than a single species or some do not specify clearly what macaque species was used.

Macaques are generally acknowledged as terrestrial, but some (eg, *M. fascicularis*) are also arboreal. Macaques are mostly quadrupedal animals; however, they also are very dexterous in using their hands for visually guided reaching and grasping behavior. Macaques use saccadic and smooth pursuit eye movements to explore the visual field, including vergence movements to explore both far and near locations. Macaques are social animals that usually live in hierarchical groups. Gaze direction is a behaviorally relevant cue, and macaques show gaze-following behavior as directed by the head direction. Gaze direction is also an important signal in the social structure; direct staring at an animal higher in the hierarchy is an offensive behavior that could trigger retribution. Accordingly, macaques covertly observe other animals.

Following the groundbreaking experiments of Fritsch and Hitzig (1870) demonstrating that electric stimulation of certain locations in the cerebral cortex evoked specific body movements in a dog, Ferrier, (1874) carried out a thorough mapping to localize motor functions in the cortex of macaque monkeys. Based on his maps of the frontal cortex, Ferrier located a region in which stimulation evoked contraversive movements of the eyes and head as well as other ocular movements such as vergence and blinks (Fig. 36.3). Numerous subsequent investigators mapped locations eliciting orienting movements in macaque monkeys resolving over time the effects of anesthesia, eye movement recording sensitivity, electrode size, and electrical current levels (Horsley and Schäfer, 1888; Mott and Schäfer, 1890; Russell, 1894; Levinsohn, 1909; Smith, 1949; Crosby et al., 1952; Henderson and Crosby, 1952; Wagman et al., 1957, 1958, 1961; Robinson and Fuchs, 1969; Bruce et al., 1985). The evolution of FEF location across these studies has been reviewed elsewhere (Schall, 1997). The current definition of FEF is the region where currents less than 50 μ A evoke short latency saccades, which restricts FEF in the rostral bank and fundus around the genu of the arcuate sulcus. Within this region saccade amplitude, but not direction, is topographically organized;

shorter (<2 degrees) saccades are represented ventrolaterally, and progressively longer saccades (15–20 degrees) are represented dorsomedially.

The macaque FEF is well known to be highly visually responsive with pronounced modulation according to the allocation of attention and other cognitive demands (reviewed by Squire et al., 2013; Schall, 2015). Visually responsive neurons are found in cortical areas extending rostral to FEF. Indeed, the map of saccade amplitude is paralleled by a map of visual receptive field eccentricity described in the prearcuate gyrus (Suzuki and Azuma, 1983).

A region related to slow tracking pursuit eye movements is located at the fundus of the arcuate sulcus immediately caudal to the principal sulcus (MacAvoy et al., 1991; Gottlieb et al., 1994; Fukushima et al., 2002; Tanaka and Lisberger, 2002; Fig. 36.3). Low-intensity electrical stimulation of FEF in head-free monkeys also elicits contraversive head movements and natural eye-with-head gaze shifts (Tu and Keating, 2000; Knight and Fuchs, 2007; Monteon et al., 2010, 2013). Medial to FEF in the dorsomedial cortex is an anatomically separate and functionally distinct supplementary eye field (Schlag and Schlag-Rey, 1987; Schall, 1991). Along the superior limb of the arcuate is a region that represents orienting movements of the pinna (Bon and Lucchetti, 1994; Lucchetti et al., 2008; Lanzilotto et al., 2013) with a gradual transition from eye movements and ear movements that also correspond to the eccentricity of localized events (Barbas and Mesulam, 1981; Lanzilotto et al., 2013). Finally, neurons in the rostral convexity of the arcuate sulcus are active during vergence and accommodation for perception of objects at different distances (Gamlin and Yoon, 2000).

The location of FEF has a distinctive cyto- and myeloarchitecture (Walker, 1940; von Bonin and Bailey, 1947; Stanton et al., 1989; Preuss and Goldman-Rakic, 1991). Not unexpectedly, it is distinguished by a concentration of large pyramidal cells in layer 5 higher than surrounding areas. It has a thin granular layer 4 distinct from the agranular area 6 at its caudal boundary but noticeably thinner than the rostrally bordering area referred to now as 8Ar. Area 8Ar should probably be considered as functionally distinct from FEF; it may correspond to the area FV that has been distinguished from the heavily myelinated part of FEF in owl monkeys based on patterns of connectivity with prestriate visual areas (Weller and Kaas, 1987; Krubitzer and Kaas, 1990). The medial aspect of FEF has relatively fewer large pyramidal cells in layer 3 and a loosely organized granular layer and has more connectivity with cortical areas representing the peripheral visual field. The dorso-medial border of FEF transitions into area 8B. The ventral aspect of FEF has a higher density of larger pyramidal cells in layer 3 and has more connectivity with

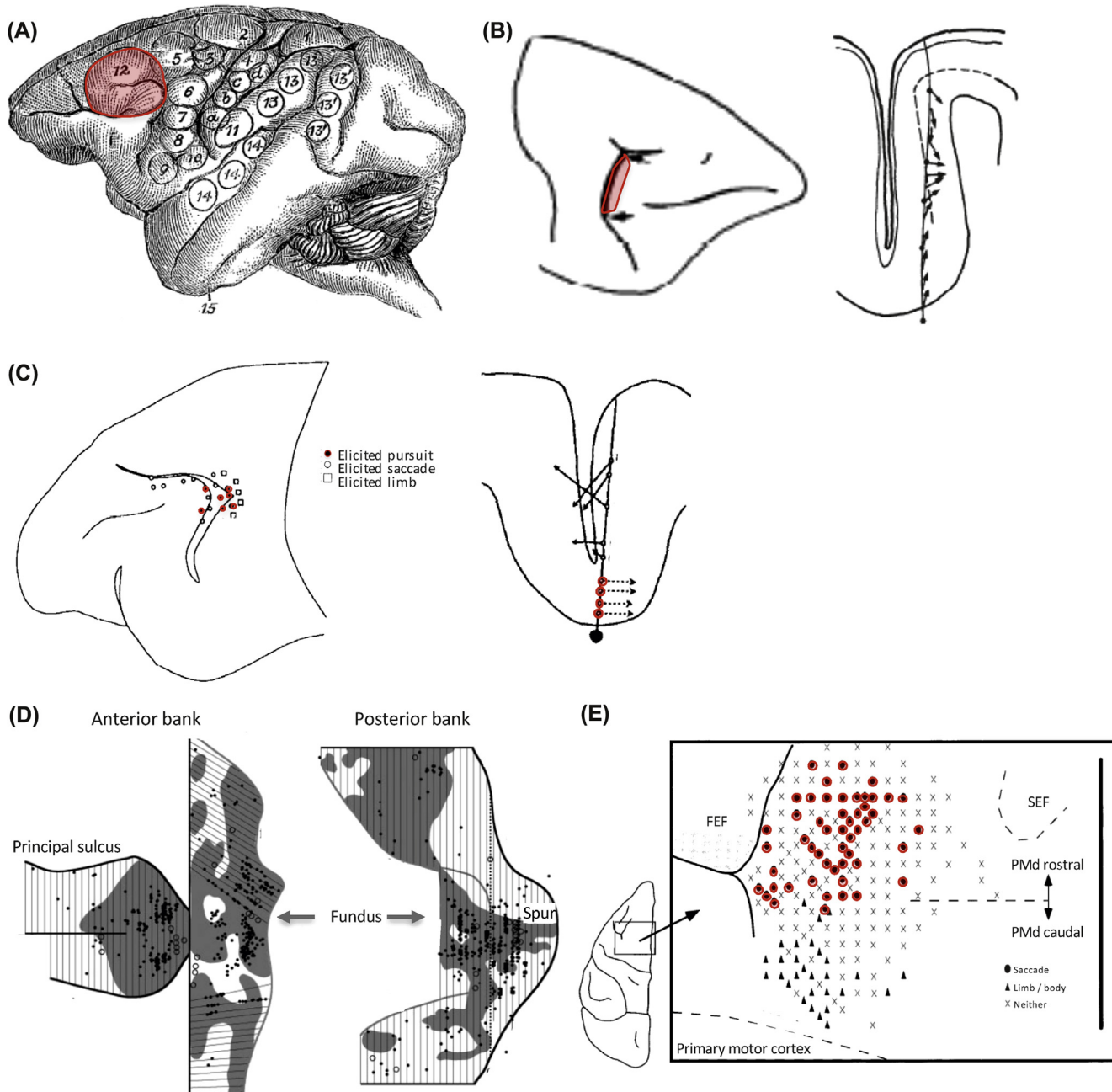


FIGURE 36.3 Representative maps of the frontal eye field (FEF) across eras, methods, and eye movements. (A) Map of body movements elicited by electrical stimulation. Stimulation within the region numbered 12 produced “Elevation of the eyebrows and the upper eyelids, turning of the eyes and head to the opposite side, and great dilatation of both pupils.” Reproduced from Ferrier, D., 1874. Experiments on the brain of monkeys. No. I. Proc. R. Soc. Lond. 23, 409–430. (B) Location of FEF in the rostral bank of the arcuate sulcus extending from the convexity to the fundus defined by saccades evoked with the lowest currents of intracortical microstimulation in awake, behaving macaques. Reproduced from Bruce, C.J., Goldberg, M.E., Bushnell, M.C., Stanton, G.B., 1985. Primate frontal eye fields. II. physiological and anatomical correlates of electrically evoked eye movements. *J. Neurophysiol.* 54, 714–734. (C) Location of pursuit zone in FEF at the fundus of the arcuate sulcus shown in a surface view (left) and cross section (right). Reproduced from MacAvoy, M.G., Gottlieb, J.P., Bruce, C.J., 1991. Smooth-pursuit eye movement representation in the primate frontal eye field. *Cereb. Cortex* 1, 95–102; Gottlieb, J.P., Bruce, C.J., MacAvoy, M.G., 1993. Smooth eye movements elicited by microstimulation in the primate frontal eye field. *J. Neurophysiol.* 69, 786–799. (D) Unfolded arcuate and principle sulci showing locations of neurons transneuronally labeled by rabies virus injected into an extraocular muscle (black dots) and regions of metabolic activation during saccade production (gray). Reproduced from Moschovakis, A.K., Gregoriou, G.G., Ugolini, G., Doldan, M., Graf, W., Guldin, W., Hadjidimitrakis, K., Savaki, H.E. 2004. Oculomotor areas of the primate frontal lobes: A transneuronal transfer of rabies virus and [14C]-2-deoxyglucose functional imaging study. *J Neurosci*, 24, 5726–5740. (E) Map of body movements evoked by intracortical microstimulation of a cortical region caudal to the arcuate sulcus, showing a region from which saccades were evoked in awake behaving macaques. Reproduced from Fujii, N., Mushiaki, H., Tanji, J., 2000. Rostrocaudal distinction of the dorsal premotor area based on oculomotor involvement. *J. Neurophysiol.* 83, 1764–1769.

cortical areas representing the central visual field. The ventrolateral border transitions into area 45. The medial and lateral parts of FEF in the arcuate sulcus are also distinguished by connectivity; they are connected with many common but several distinct cortical areas (Schall et al., 1995; Markov et al., 2014). The lateral segment, which is responsible for generating short saccades, receives visual inputs from the foveal representation in retinotopically organized areas, from areas that represent central vision in inferotemporal cortex and from other areas having no retinotopic order. Meanwhile, the medial segment, which is responsible for generating longer saccades coupled with head and also pinna movements, is innervated by the peripheral representation of retinotopically organized areas, from areas that emphasize peripheral vision or are multimodal and from other areas that have no retinotopic order or are auditory. Convergence from the dorsal and ventral visual processing streams occurs in lateral but not in medial FEF. These differences of connectivity must have corresponding differences of functionality, but they are unknown at this time.

The location of FEF in macaques has also been investigated with a variety of neuroimaging techniques. One approach used 2-deoxyglucose imaging to locate activated areas in both the anterior and posterior banks of the arcuate sulcus, the prearcuate convexity, dorsomedial frontal, caudal principal and periprincipal, anterior cingulate, and even some of the orbitofrontal cortex (Moschovakis et al., 2004; Savaki et al., 2015). The relation of these diverse cortical areas to eye movement production was reinforced by retrograde transneuronal labeling by rabies virus that was injected into the lateral rectus muscle (Moschovakis et al., 2004; Fig. 36.3D).

FEF has also been localized using fMRI with macaques. Early studies identified an involvement of FEF in visual motion processing in awake behaving monkeys (Vanduffel et al., 2001). Subsequent primate fMRI studies characterized involvement of FEF in visually guided saccade tasks (Koyama et al., 2004; Baker et al., 2006; Premereur et al., 2015), memory guided saccade tasks (Kagan et al., 2010), antisaccade tasks (Ford et al., 2009), visual search tasks (Wardak et al., 2010), and spatial attention tasks (Caspari et al., 2015). The connectivity found in resting state fMRI of the macaque FEF corresponds very well to the connectivity pattern found with anatomical tract tracers (Babapoor-Farrokhran et al., 2013).

Finally, the location of FEF in the arcuate sulcus has been confirmed through inactivation (eg, Sommer and Tehovnik, 1997) and lesion studies demonstrating temporary impairments in eye movements (Schiller et al., 1980, 1987; Keating, 1993; Morrow and Sharpe, 1995; Heide et al., 1996) and in eye–head movements (van

der Steen et al., 1986). Inactivation of FEF also impairs visual search (Latto, 1978; Wardak et al., 2006).

While there is no disputing the location of the FEF in the rostral bank of the arcuate sulcus of macaques, multiple studies have described visual- and saccade-related function in areas surrounding the arcuate sulcus. For example, visually responsive, eye movement, and eye position–related neural activity is found in premotor cortex caudal to the arcuate sulcus around the arcuate spur (Boussaoud, 1995; Boussaoud et al., 1993, 1998; Fujii et al., 1998, 2000). Neural activity recorded in this general region is also modulated during tasks requiring visually guided selection of targets for action (eg, Cisek and Kalaska, 2005; Song and McPeck, 2010). Also, measurements of 2-DG uptake during production of saccades of various directions and amplitudes defined two maps, one running between area 44 and ventral area 6, and the other spanning areas 8 and 45 in the anterior bank of the arcuate sulcus and extending onto the prearcuate convexity (Savaki et al., 2015). Finally, fMRI measurements in macaque monkeys reveal saccade-related activation in areas 45A, 45B, and 46 outside the conventional FEF (eg, Premereur et al., 2015).

Thus, numerous studies in macaques agree on the core location of FEF in the rostral bank of the arcuate sulcus, surrounded by areas associated with pursuit and vergence movements. Many other studies demonstrate that neural activity associated with visual responses and eye movement production is found in areas surrounding FEF both caudally in premotor cortex and rostrally in prefrontal cortex. Thus, defining the boundaries of “FEF” in the macaque is a matter of specifying criteria.

36.4.4.2 *Papio (Baboons)*

The frontal lobe of baboons resembles that of macaques although with somewhat more complexity in the relationship of the arcuate and principal sulci and the presence of more dimples or partial sulci (Connolly 1936, 1950).

Less is known about the properties of FEF in baboons. Confidence in its location in the rostral bank of the arcuate sulcus, though, has guided studies of the effects of FEF lesions (eg, Pribram, 1955). Some evidence from cytoarchitecture and connectivity reinforces this confidence (Watanabe-Sawaguchi et al., 1991).

36.4.5 Hominoidea

The evolution of visually guided reaching and grasping is closely associated with primate ecology and the need to move through the forest canopy. Apes and monkeys that use brachiation rely upon vision to select, reach for, and secure their grip onto appropriate branches. These actions are often rapid and coordinated

with other self-generated movements that strongly affect the visual input, such as the motion of the body, turning of the head, and frequent saccades. Since a miscalculation can have fatal consequences, primates have evolved under a strong selective pressure for accuracy in this domain. The origins of precise manual behavior may stem from specific aspects of the feeding behaviors of early primates. One influential hypothesis holds that early primates were nocturnal predators who were aided by a wide field of stereoscopic vision for catching insects in their hands (Cartmill, 1992). An alternative view is that precision reaching and grasping evolved for the purposes of extracting small fruits from terminal branches of angiosperms (Bloch and Boyer, 2002; Sussman et al., 2013).

36.4.5.1 *Pongo (Orangutan), Gorilla (Gorilla), and Pan (Chimpanzee and Bonobo)*

Relative to the Cercopithecidae brain, major changes have occurred in the cerebral cortex of hominids, especially in the frontal lobe (Connolly, 1936, 1950). Apes have no sulcus resembling the arcuate sulcus of Cercopithecidae (eg, Bogart et al., 2012). The chimpanzee frontal lobe consists of a prominent superior precentral sulcus and an inferior frontal sulcus, both with multiple limbs. The inferior precentral sulcus branches off of the inferior frontal sulcus. Ventrolaterally is found a fronto-orbital sulcus. Differential studies carried out on a large number of chimpanzee brains show considerable individual variation, particularly in the inferior precentral region (Sherwood et al., 2003).

Classic studies used electrical stimulation of the cortical surface under anesthesia to map sites eliciting movements of the body and eyes in chimpanzees (Grünbaum and Sherrington, 1901; Leyton and Sherrington, 1917; Hines, 1940; Dusser de Barenne et al., 1941; Bailey et al., 1950), orangutan (Beevor and Horsley, 1890; Leyton and Sherrington, 1917), and gorilla (Grünbaum and Sherrington, 1901; Leyton and Sherrington, 1917). Leyton and Sherrington (1917) mapped body and eye movements elicited by electrical stimulation of the cortical surface in 22 chimpanzees, 3 orangutans, and 3 gorillas. In chimpanzees, they showed that conjugate contraversive ocular rotations were elicited at a range of sites around the middle and inferior sulci with some sites eliciting eye opening as well (Fig. 36.4). Most of the rotations were horizontal, but some sites elicited rotations with upward or more often downward components. A few sites elicited convergence movements. They noted that higher currents were needed to elicit eye movements as compared to limb movements from the precentral gyrus. They further showed that contraversive ocular rotations were not a primary movement from the precentral gyrus and occurred only associated with head movements.

In a sample of 38 chimpanzees Bailey et al. (1950) located regions from which ocular deviations could be elicited in 11. Their results indicate two general regions from which ocular deviation was evoked with greatest frequency. One was located ventrolaterally straddling the inferior frontal sulcus, and the other was located dorsomedially ventral to and straddling the superior frontal sulcus. In most of the chimpanzees, eye movements were elicited much more rostral than the precentral sulci, and in many cases stimulation of the cortex rostral to the regions from which ocular deviations were elicited resulted in no movements. When explored, stimulation of the cortex caudal to the eye fields often elicited skeletal movements and other eye movements such as eye blinks and pupil size changes. The dorsomedial locations eliciting ocular rotations most commonly were located in area FC, which is described as transitional between agranular and prefrontal cortex having a slight granular layer. The ventrolateral locations appeared most commonly located in the weakly granular area FC and possibly extending into granular areas FDΔ and FDF. By the way, note that the summary figure offered by the authors seems not to most accurately portray their findings because it identifies an eye movement region more ventral than was observed (Fig. 36.4C).

In orangutan and gorilla, Leyton and Sherrington (1917) found sites eliciting ocular rotations similarly situated about the middle frontal sulcus (Figs. 36.5 and 36.6). Thus, the site most clearly identified with FEF is located comparably in chimpanzee, orangutan, and gorilla, distant from primary motor cortex and centered rostral to the inferior principal sulcus around the inferior frontal sulcus.

36.4.5.2 *Human*

Readers of this chapter need no introduction to the importance of visually guided eye movements coordinated with ongoing manual, locomotor, and social behavior. They will also know that the human cerebral sulcal pattern is noticeably elaborated from that of apes and appreciate how the significant individual gyral variation, sometimes even between hemispheres, can obscure descriptions of the location of cortical areas. We should also remind the reader that different investigators have arrived at somewhat different descriptions of the organization of cortical areas (Fig. 36.7). In considering which cortical areas in the human are homologous to areas in the brains of nonhuman primates, the FEF provides an interesting test case. The novice is surprised how far caudal FEF is until appreciating how much frontal lobe is in the human brain.

FEF has been located in humans using electrical stimulation in various forms for many years. To summarize, most studies have evoked ocular rotations by

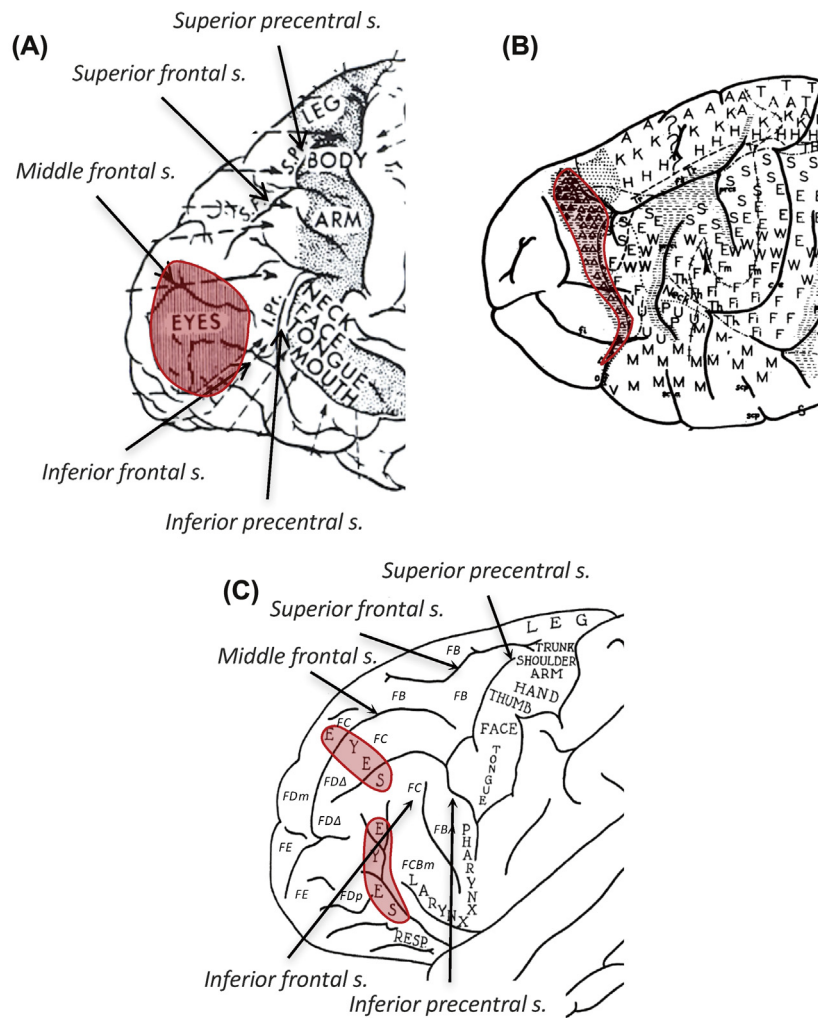


FIGURE 36.4 Location of frontal eye field based on electrical stimulation in the chimpanzee. Reproduced from (A) Grünbaum, A., Sherrington, C.S., 1901. Observations on the physiology of the cerebral cortex of some of the higher apes. *Proc. R. Soc. Lond.* 69, 206–209; (B) Dusser de Barenne, J., Garol, H., McCulloch, W., 1941. Functional organization of sensory and adjacent cortex of the monkey. *J. Neurophysiol.* 4, 287–303; (C) Bailey, P., von Bonin, G., McCulloch, W.S., 1950. *The Isocortex of the Chimpanzee*. University Illinois Press.

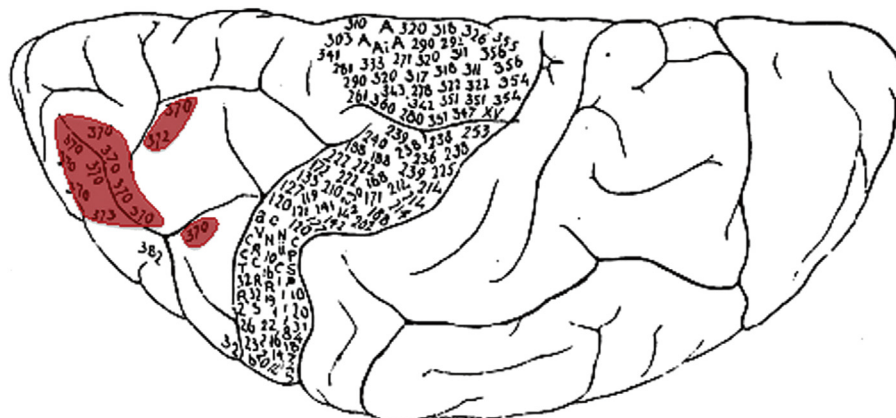


FIGURE 36.5 Location of frontal eye field based on electrical stimulation in the orangutan. From Leyton, A.S., Sherrington, C.S., 1917. Observations on the excitable cortex of the chimpanzee, orangutan, and gorilla. *Q. J. Exp. Physiol.* 11, 135–222.

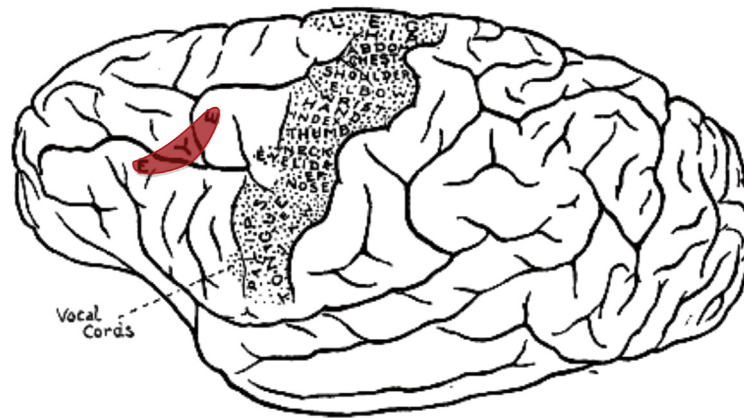


FIGURE 36.6 Location of frontal eye field based on electrical stimulation in the gorilla. From Leyton, A.S., Sherrington, C.S., 1917. *Observations on the excitable cortex of the chimpanzee, orangutan, and gorilla*. *Q. J. Exp. Physiol.* 11, 135–222.

stimulation of the caudal end of the middle frontal gyrus, but results disagree about the extent of surrounding cortex that also elicits eye movements and whether it extends to the skeletal motor representation in the precentral gyrus. Dejerine and colleagues located a region, which they called “area D,” from which conjugate deviation of the head and eyes were evoked (Dejerine and Roussy, 1906; Dejerine, 1914). Förster (1931, 1936) identified FEF as the region from which contraversive ocular rotation was elicited at the caudal end of the middle frontal gyrus (Fig. 36.8) in a region designated $8\alpha\beta\gamma$ by Vogt and Vogt (1926) (Fig. 36.7A). Förster also reported coordinated contraversive eye, head, and trunk rotation following stimulation of a dorsomedial region designated $6\alpha\beta$, corresponding to Dejerine’s area D. Subsequently, Penfield and coworkers evoked eye movements over a wider area of frontal cortex, extending caudally onto the precentral gyrus; however, most

sites were rostral to the precentral sulcus at a location Penfield identifies as Vogts’ $8\alpha\beta\gamma$ (Penfield and Boldrey, 1937; Rasmussen and Penfield, 1947). Subsequently, Lemmen et al. (1959) reported conjugate and divergent eye movements from stimulation of the posterior end of the middle frontal gyrus rostral to sites in the precentral gyrus that elicited limb and lip movements (Fig. 36.9); these authors noted a particular absence of eye movements elicited by stimulation of the precentral gyrus.

Later studies used subdural electrode arrays implanted over the frontal lobe of patients and found FEF in a zone rostrally contiguous with the motor cortex representation of head and forelimb (Godoy et al., 1990). More recent work has located FEF in the posterior part of the middle frontal gyrus, just below the intersection of the precentral sulcus and the superior frontal sulcus (Blanke et al., 2000; Blanke and Seeck, 2003; Lobel

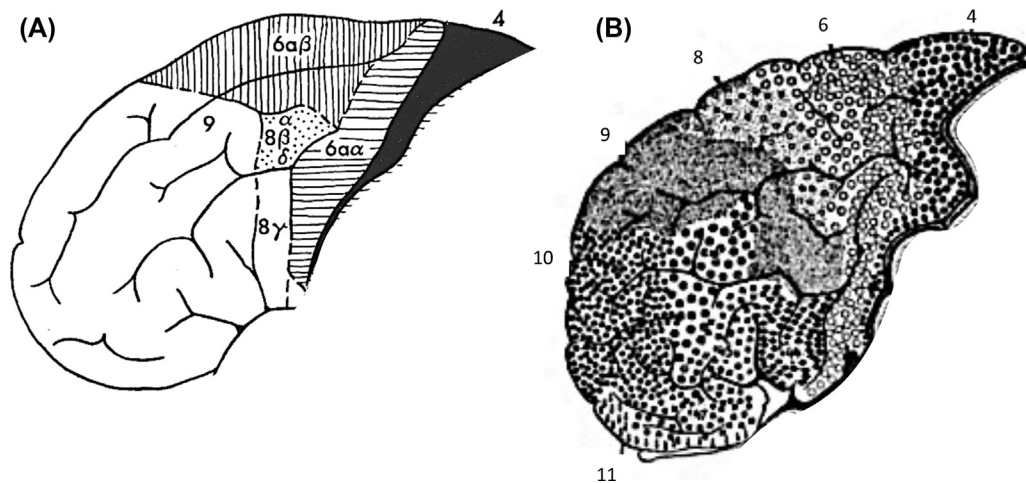


FIGURE 36.7 Frontal lobe areas identified by Vogt and Vogt (1926) (A) and Brodmann (1909) (B). Reproduced from (A) Vogt, C., Vogt, O., 1926. *Die vergleichend-architektonische und die vergleichend-reizphysiologische Felderung der Großhirnrinde unter besonderer Berücksichtigung der menschlichen*. *Naturwissenschaften* 14, 1190–1194; (B) Brodmann, K., 1909. *Localisation in the Cerebral Cortex*. Springer, US.

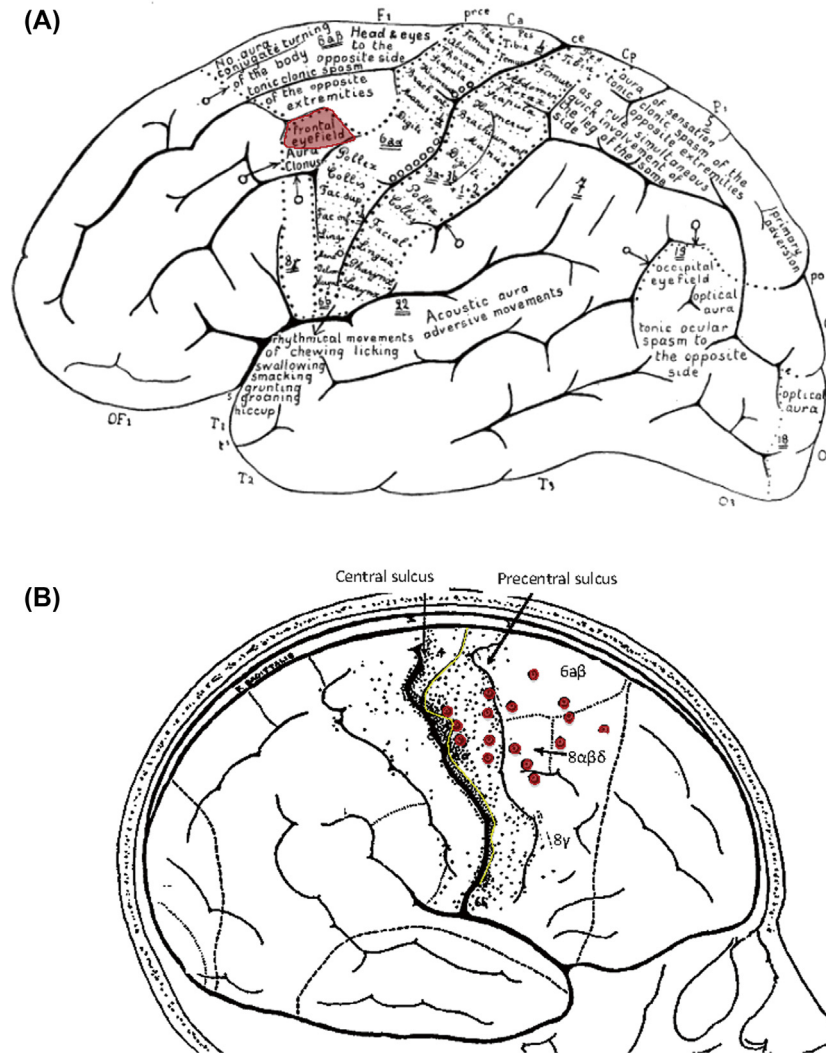


FIGURE 36.8 Location of frontal eye field based on surgical electrical stimulation in the human. (A) Red highlights location of FEF rostral to precentral sulcus. Reproduced from Förster, O., 1931. The cerebral cortex in man. *Lancet* 2, 309–312. (B) Summary of sites eliciting conjugate movements of the eyes (red) superimposed on summary map of sites eliciting movements of other parts of the body (small points). Yellow line marks rostral border of area 4. The remainder of the convexity of the precentral gyrus is made up of area 6 α . From Penfield, W., Boldrey, E., 1937. *Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation*. *Brain* 60, 389–443.

et al., 2001; Milea et al., 2002; Yamamoto et al., 2004; Thurtell et al., 2009; Kaiboriboon et al., 2012; Montemurro et al., 2016; Fig. 36.10). Some studies have also located a more lateral region associated with eye movement production close to the surface of the precentral gyrus (Lobel et al., 2001). The reader should note that these electrical stimulation studies typically can explore only the cortical surface not buried in sulci and that spatial localization is difficult to interpret because of current spread influencing remote sites.

FEF has also been localized using transcranial magnetic stimulation (eg, Wessel and Kömpf, 1991; Müri et al., 1991; Olk et al., 2006; Neggers et al., 2007). Transcranial magnetic stimulation does not elicit ocular rotations,

so the influence is inferred through indirect measures of influence on saccade latency or accuracy. Such studies point toward the caudal end of the middle frontal gyrus at the intersection of the superior frontal sulcus and the superior precentral sulcus. Some investigators also locate FEF relative to the motor hand area (eg, Ro et al., 1999), on average 5 cm lateral of the sagittal midline and 3–4 cm rostral of each subject's motor hand area.

Human FEF has been located through specific deficits in eye movements observed after focal lesions (reviewed by Pierrot-Deseilligny, 1994). Early studies noted gaze deficits with damage involving large parts of frontal cortex; however, more recent studies of patients with more restricted lesions have converged on the precentral

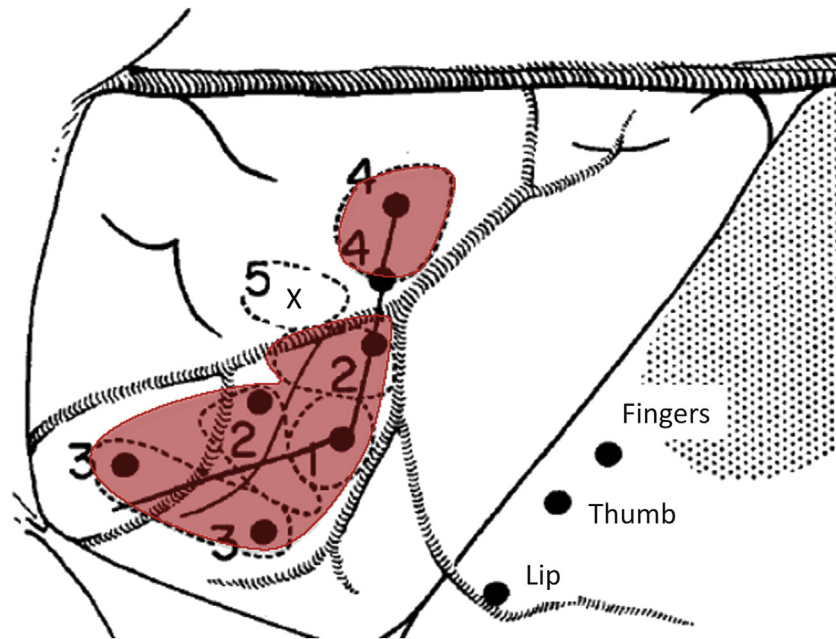


FIGURE 36.9 Red highlights sites from which cortical stimulation resulted in conjugate deviation of the eyes. Stimulation at site 5 had no effect. Stimulation at more caudal sites elicited movements of the indicated parts. From Lemmen, L.J., Davis, J.S., Radnor, L.L., 1959. Observations on stimulation of the human frontal eye field. *J. Comp. Neurol.* 112, 163–168.

sulcus ventral to the superior frontal sulcus (Rivaud et al., 1994; Fig. 36.11).

Human FEF has been described in numerous PET and fMRI studies (reviewed by Grosbras et al., 2005; see also

Luna et al., 1998; Petit et al., 1997, 1999; Neggers et al., 2012; Ford et al., 2005; Amiez et al., 2006; Kastner et al., 2007; Ikkai and Curtis, 2008; Derrfuss et al., 2012; Thakkar et al., 2014). Execution of saccadic eye movements is accompanied by relatively strong and consistent bilateral activation in the superior precentral sulcus and by relatively weaker and less consistent activation in the superior segment of the inferior precentral sulcus. Pursuit eye movements are accompanied by activation in the superior precentral sulcus occupying a smaller region that tends to be inferior and slightly lateral to that occupied during saccades, closer to the fundus. Within individuals, the activation in both precentral sulci is restricted to the banks and does not extend onto the surface convexity, even though maps of average activation give that appearance. High-resolution imaging locates the most active voxels on the rostral bank of the superior precentral sulcus. The dorsal activation is located at the junction of the precentral sulcus and the superior frontal sulcus.

Amiez et al. (2006) conducted a subject-by-subject analysis of the locus of eye movement–related functional activity revealed in relation to the individual morphology of the precentral and superior frontal sulci (Fig. 36.15). A focus of activation associated with saccadic eye movements was located in the ventral branch of the superior precentral sulcus in both hemispheres. A second focus has found in the dorsal part of the inferior precentral sulcus. Imaging during a hand response selection task revealed activation focused

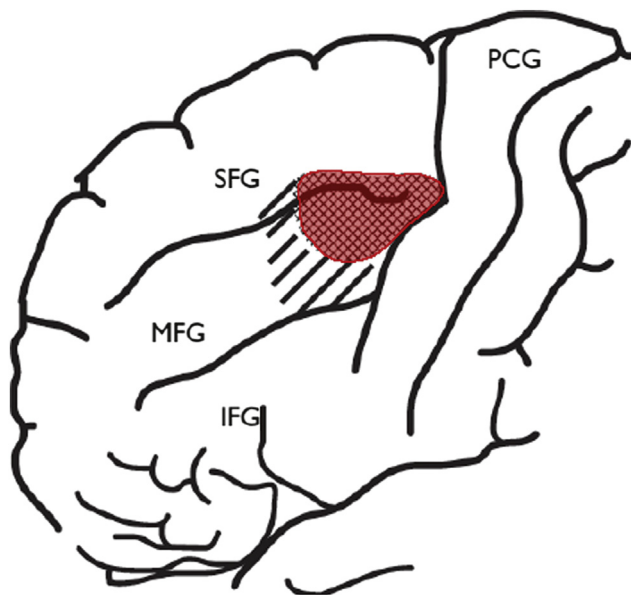


FIGURE 36.10 Red highlights location where conjugate eye movements were elicited with the lowest currents using subdural electrode arrays. From Blanke, O., Spinelli, L., Thut, G., Michel, C.M., Perrig, S., Landis, T., Seeck, M., 2000. Location of the human frontal eye field as defined by electrical cortical stimulation: anatomical, functional and electrophysiological characteristics. *Neuroreport* 11, 1907–1913.

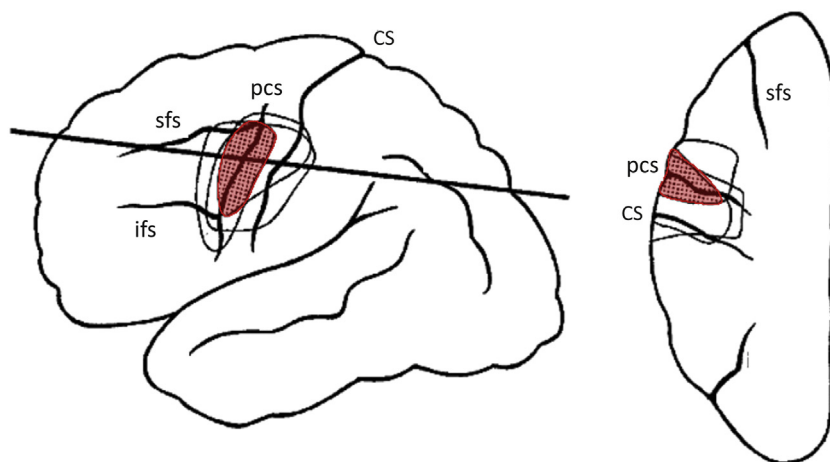


FIGURE 36.11 Lesions of frontal eye field. Lateral (left) and cross-sectional (right) views of the lesions of three patients (*thin outline*) that extend caudally to the central sulcus (cs) intersect (*stippled*) on the precentral sulcus (pcs) ventral to the superior frontal sulcus (sfs) and dorsal to the inferior frontal sulcus (ifs). The patients exhibited a range of deficits in producing saccadic eye movements. From Rivaud, S., Müri, R., Gaymard, B., Vermersch, A., Pierrot-Deseilligny, C., 1994. *Eye movement disorders after frontal eye field lesions in humans. Exp. Brain Res.* 102, 110–120.

in the dorsal branch of the superior precentral sulcus close to the caudal end of the superior frontal sulcus. The relative magnitude of activation in the superior and inferior precentral sulci varies with the nature of the eye movement (eg, saccade or pursuit, in light or dark) and task demands (eg, prosaccade or antisaccade) (Fig. 36.12A; eg, Neggers et al., 2012). Medial and lateral foci are also observed during covert attention tasks as well (Beauchamp et al., 2001). Furthermore, two regions recruited in auditory attention tasks were reported to be interdigitated with these two visual attention regions (Fig. 36.12B; Michalka et al., 2015).

The interpretation of the location of BOLD activation during eye movements can be complicated by other factors. First, eye blinks are commonly associated with saccades (eg, Evinger et al., 1994; Gandhi, 2012). Since the original electrical stimulation mapping it has been clear that cortical regions caudal to the arcuate sulcus in monkeys produce other ocular movements including blinks. Thus, some of the BOLD activation during eye movement tasks could arise from regions producing eye blinks. However, an fMRI study of spontaneous eye blinks in macaque monkeys did not report activation in or around FEF, calling into question whether this is an actual confounding factor for FEF localization (Guipponi et al., 2015). Second, saccades may be associated with neck contractions to rotate the head (eg, Goonetilleke et al., 2015). Thus, some of the BOLD activation during eye movement tasks could arise from premotor cortical areas that contribute to head movements (eg, Preuss et al., 1996). Third, in the macaque areas rostral and caudal to the arcuate sulcus have visually responsive neurons, which are modulated by attention tasks. If the human FEF is similarly surrounded, then BOLD activation would occupy a larger region than FEF

proper. Also, as noted earlier, in the macaque areas caudal to the arcuate sulcus include neurons active during saccade tasks. We suggest alternative hypotheses concerning the relation of the monkey and human FEF and premotor region in the following section.

36.5 Is FEF Located Differently Across Species?

In this section we consider from multiple perspectives whether the FEF can be regarded as homologous across primate species, including humans.

36.5.1 Comparative Neuroimaging

Several studies compare directly macaque and human fMRI data (Koyama et al., 2004; Baker et al., 2006; Ford et al., 2009; Kagan et al., 2010). For example, Koyama et al. (2004) compared fMRI activation patterns in humans and macaques performing visually guided saccades. BOLD activation in macaques was found in the rostral bank of the arcuate sulcus, and also in premotor cortex caudal to the arcuate sulcus. In humans a large domain of activation occupied the banks of the precentral sulcus. The authors propose that the peak of activation near the junction of the precentral and the superior frontal sulci corresponds to the FEF in monkeys. They observed another focus of activation in the inferior precentral sulcus (Fig. 36.14). Resting-state fMRI connectivity of FEF has been compared in macaques and humans (Hutchison et al., 2012; Babapoor-Farrokhran et al., 2013). These studies have found consistent functional connections of the FEF with frontal and parietal cortical areas in humans and macaques (Fig. 36.14). However, the analysis also revealed more lateralization of

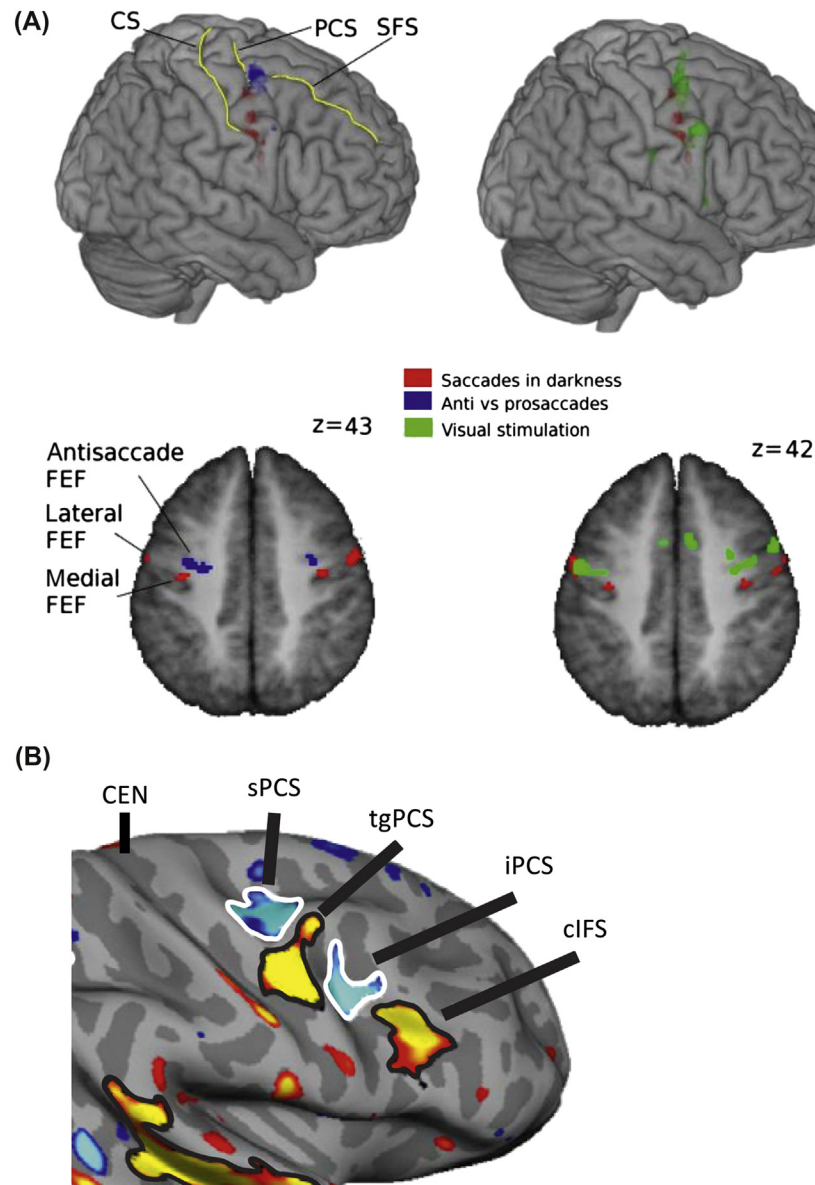


FIGURE 36.12 Functional activation observed in attention and saccade tasks. (A) Activation maps for three tasks. The location of greater activation for saccades in the dark (*red*) is compared with that for antisaccades as compared to prosaccades (*blue*) and that for visual stimulation (*green*) (from [Neggers et al., 2012](#)). (B) Map of the right frontal lobe of an individual subject performing a task requiring sustained attention to sequences of visual or auditory stimuli. The *colors* highlight regions with statistically significantly greater BOLD activation during auditory attention (*hot colors*) or visual attention (*cool colors*). The cortex was inflated to reveal interior of sulci (*dark gray*) between gyri (*light gray*). Note the interdigitated pattern of auditory and visual biases in the caudal lateral frontal cortex. CEN, central sulcus; sPCS, superior precentral sulcus; tgPCS, transverse gyrus intersecting the precentral sulcus; iPCS, inferior precentral sulcus; cIFS, caudal inferior frontal sulcus (from [Michalka et al., 2015](#)). (A) Reproduced from [Neggers, S.F.W., Diepen, R.M., van Zandbelt, B.B., Vink, M., Mandl, R.C.W., Gutteling, T.P., 2012. A functional and structural investigation of the human fronto-basal volitional saccade network. PLoS One 7, e29517](#). (B) Reproduced from [Michalka, S.W., Kong, L., Rosen, M.L., Shinn-Cunningham, B.G., Somers, D.C., 2015. Short-term memory for space and time flexibly recruit complementary sensory-biased frontal lobe attention networks. Neuron. 87, 882–892](#).

connectivity of the region identified as FEF in humans than in monkeys.

The homology or at least comparability of the cortical region in and rostral to the arcuate sulcus in macaques and the superior precentral sulcus in humans has also been revealed in quantitative

functional connectivity maps ([Sallet et al., 2013](#); see also [Goulas et al., 2012](#)). Of note, in macaques a particular hot spot of connectivity with this arcuate region was caudal to the arcuate, dorsal to a spur in the region overlapping that associated with visually guided saccades described previously.

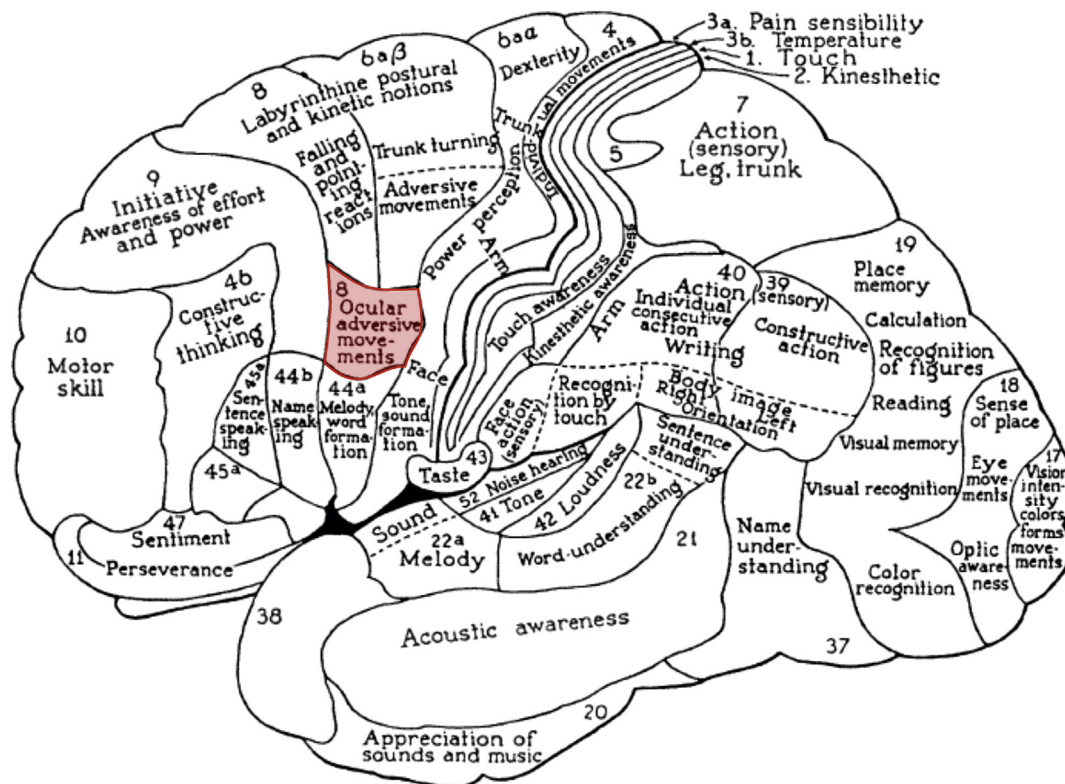


FIGURE 36.13 Lateral view of the human cerebral hemispheres, showing the localization of functions in the cerebral cortex. The numbers list Brodmann's (1909) cytoarchitectonic areas. Note that the domain for "ocular adversive movements" is identified as area 8. From von Kleist, K., 1934. *Gehirnpathologie*. J.A. Barth, Leipzig.

36.5.2 Comparative Architecture

As noted earlier, the FEF in macaque monkeys is centered in the rostral bank of the arcuate sulcus at the caudal end of prefrontal cortex. The cytoarchitecture of the area is included as Brodmann's area 8, generally. Likewise, the FEF mapped in other monkeys is recognized as being located in granular prefrontal cortex. The FEF in apes also appears to be in prefrontal cortex, although we have less specific information about the cytoarchitecture of the regions mapped. However, many authors describe the human FEF as being located in Brodmann's agranular area 6. Here we address this apparent discrepancy.

The literature on the location of FEF in humans has referred exclusively to Brodmann's cytoarchitectonic map (1909). Of course this is not the only or the last description, nor does it correspond to modern descriptions in many respects (Zilles and Amunts, 2010; Nieuwenhuys, 2013). In Brodmann's map area 6 occupies a very large amount of the frontal lobe, but contemporaneous as well subsequent maps by other investigators subdivide Brodmann's area 6 into many more areas. For example, myeloarchitectonic studies have

distinguished the caudal end of the middle frontal gyrus as distinct from surrounding areas (eg, Nieuwenhuys et al., 2015). While other authors locate the caudal end of the middle frontal gyrus in area 6 (Sarkissov et al., 1955), it has also been labeled area FB (von Economo and Koskinas, 1925), area 4s (von Bonin, 1949), the boundary of FA and FB (Bailey and von Bonin, 1951), and 8 $\alpha\beta\gamma$ (Vogt and Vogt, 1926). Penfield, with Förster, described the majority of stimulation sites eliciting eye movements as being in 8 $\alpha\beta\gamma$ (Penfield and Rasmussen, 1950), and the exceedingly elaborate map of von Kleist (1934) identifies ocular adversive movements with Brodmann's area 8 (Fig. 36.13).

Of note, the structure of the cortex occupied by FEF has been reevaluated more recently. Human FEF can be distinguished from surrounding areas by MRI myelin mapping (Glasser et al., 2016). In addition, a recent anatomical study reexamined the architecture of this region using modern chemoarchitectonic methods in post-mortem tissue from six subjects (Rosano et al., 2003; see also Schmitt et al., 2005). The histological structure of the superior precentral sulcus was distinct from adjacent rostral and caudal regions. A thin granular layer 4 was observed in sections labeled with neuronal nuclear

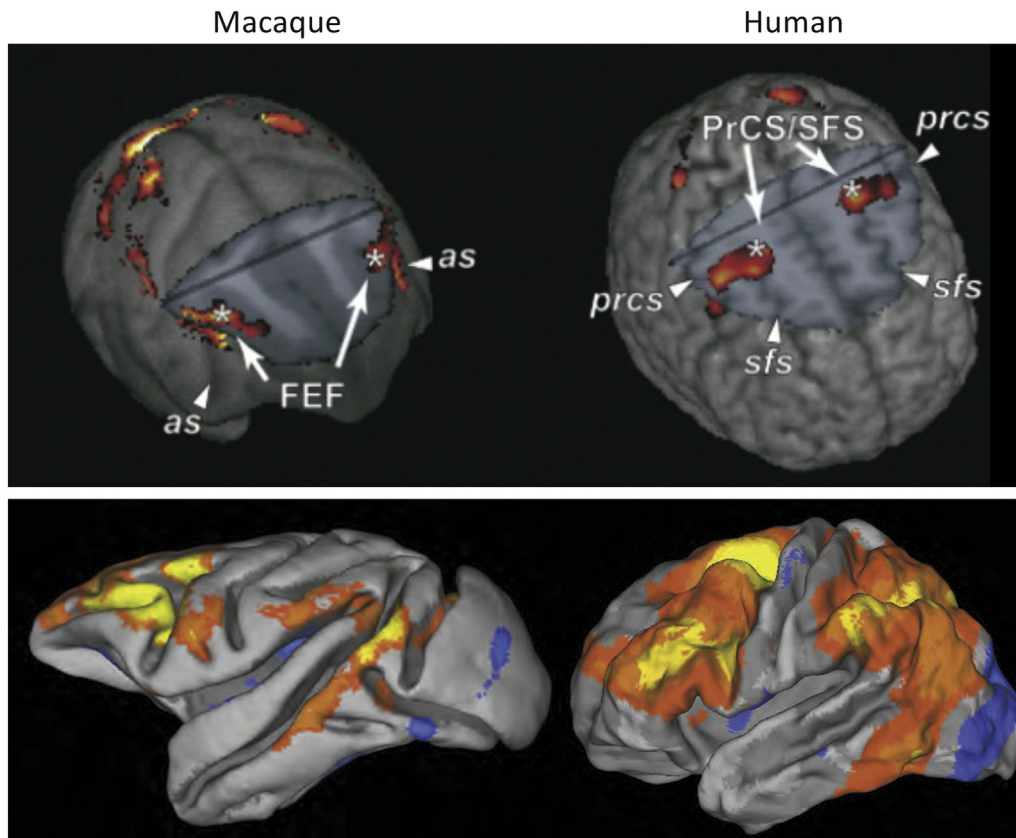


FIGURE 36.14 Direct comparison of monkey and human FEF. Top panel shows fMRI activation in the monkey (left) and human (right) brains during visually guided saccades. From Koyama, M., Hasegawa, I., Osada, T., Adachi, Y., Nakahara, K., Miyashita, Y., 2004. Functional magnetic resonance imaging of macaque monkeys performing visually guided saccade tasks: comparison of cortical eye fields with humans. *Neuron* 41, 795–807. Bottom panel compares resting state connectivity with a seed in FEF for monkey (left) and human (right). From Hutchison, R.M., Gallivan, J.P., Culham, J.C., Gati, J.S., Menon, R.S., Everling, S., 2012. Functional connectivity of the frontal eye fields in humans and macaque monkeys investigated with resting-state fMRI. *J. Neurophysiol.* 107, 2463–2474.

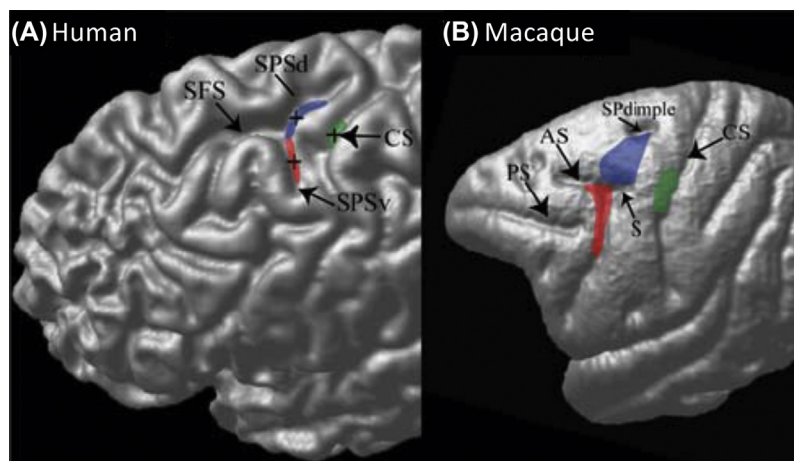


FIGURE 36.15 Location of frontal eye field relative to premotor and motor cortex in human (A) and macaque monkey (B). In humans the FEF is in the ventral limb of the superior precentral sulcus (SPSv) (red) relative to premotor cortex in the dorsal limb of the superior precentral sulcus (SPSd) (blue) and the hand representation of primary motor cortex (green) in the central sulcus (CS). In macaque monkeys the FEF is in the rostral bank of the arcuate sulcus (AS) caudal to the principal sulcus (PS). Dorsal premotor cortex is bounded by the arcuate sulcus and a precentral dimple (SPdimple). The hand representation in primary motor cortex is at the indicated level in the central sulcus. From Amiez, C., Kostopoulos, P., Champod, A.-S., Petrides, M., 2006. Local morphology predicts functional organization of the dorsal premotor region in the human brain. *J. Neurosci.* 26, 2724–2731.

protein (NeuN), and the nonphosphorylated neurofilament triplet protein (NNFP). Also, clusters of large, intensely immunoreactive pyramidal cells were located in deep layers 3 and 5. In sections labeled for calcium-binding proteins, the two walls of the sulcus were characterized by higher density of calretinin-labeled interneurons, lower density of calbindin-labeled pyramidal neurons, higher density of calbindin-labeled interneurons in layers 2–3, and higher density of large parvalbumin-labeled interneurons in deep layer 3. These histological features resemble the macaque FEF more than agranular area 6. These immunohistochemistry methods highlighted distinctions across this cortical region that are obscured in Nissl-stained section. Based on this analysis of cytoarchitectural, myeloarchitectural, and histochemical studies, one can conclude that Brodmann's description is unlikely to be correct because it misplaced the caudal boundary of area 8 of humans rostrally.

This characterization seems to resolve the discrepancy. However, questions remain. As described earlier, BOLD activation is also observed in the inferior precentral sulcus, near areas 44 and 45. In nonhuman primates tested, the FEF in the arcuate sulcus is bordered ventrally by areas 44 and 45. Also, the macaque has a region caudal to the FEF in agranular premotor cortex with visual responsiveness and from which saccadic eye movements can be elicited by intracortical microstimulation. Does this area have a homologue in humans? To motivate future experimental work, we suggest for consideration the hypothesis that the "FEF" in the inferior precentral sulcus is homologous with the "FEF" in the arcuate sulcus, while the "FEF" in the superior precentral sulcus is homologous with the premotor eye movement region caudal to the arcuate sulcus of macaques. We note that this assignment is opposite that featured in a recent comprehensive mapping of human cerebral cortical areas (Glasser et al., 2016; see also Amiez and Petrides, 2009). Is it conceivable that premotor cortex in humans takes over functions that are performed by prefrontal cortex in monkeys? The emergence of language, for example, may entail such a phylogenetic displacement. We find it instructive to consider the finding that cortical control of the larynx in monkeys is located in area 6, while in humans it is located in area 4, presumably to provide for articulated speech (Simonyan, 2014).

Identification of the FEF region in the superior precentral sulcus as a premotor area can provide rationale for the findings of a recent study that compared diffusion tractography of corticostriatal pathways in humans and macaques (Neggers et al., 2015). In macaques a seed region in the rostral bank of the arcuate sulcus had connectivity primarily with the head of the caudate and also the anteromedial putamen, while a seed in primary

motor cortex in the rostral bank of the central sulcus was connected with more posterior sections of caudate and mainly putamen. These observations replicate neuroanatomical tract tracing findings in macaques. In humans, though, the medial region of activation associated with saccadic eye movements was connected primarily to putamen and only a small portion of the caudate. Moreover, the region of striatum connected with the dorsal FEF in humans overlapped substantially the region of striatal connectivity with a point in primary motor cortex in the rostral bank of the central sulcus. We look forward to a future study examining the connectivity of the FEF region in the inferior precentral sulcus.

36.5.3 Comparative Sulcal Patterns

Another way to compare the location of FEF across species involves analyzing the topographic pattern of sulci (Fig. 36.16). The FEF in lissencephalic species is located in the rostral frontal lobe, sometimes around a cortical dimple. In monkeys with an arcuate and principal (previously known as rectus) sulcus, the saccade-related FEF is consistently located in the rostral bank of the arcuate sulcus. Curiously, the smooth pursuit-related region has been found dorsal to the arcuate in *Cebus* and at the fundus of the arcuate in macaques. Another region associated with visually guided saccades has been located immediately caudal to the arcuate sulcus around the arcuate spur (when it exists).

The sulcus pattern in the apes and human is notably more complex than that in monkeys, but particular associations have been described (eg, Hervé, 1888; Owen, 1900; Connolly, 1936, 1950; Rizzolatti and Arbib, 2002; Falk, 2014). First, there is general agreement that the arcuate sulcus, or at least the ventral (vertical) branch, of monkeys corresponds to the inferior precentral sulcus in apes and humans. Second, the superior frontal sulcus and superior precentral sulcus of apes and humans may be derived from the precentral dimple of monkeys. Alternatively, they may correspond to the superior (horizontal) limb of the macaque arcuate sulcus. Third, early authors identified the macaque principal sulcus (also referred to as rectus sulcus) with the hominid inferior frontal sulcus, but later analyses conclude that the inferior frontal sulcus of apes and humans has no counterpart in monkeys and instead the principal sulcus of monkeys corresponds to the middle frontal sulcus of humans. Thus, the ventral frontal lobe of humans has expanded relative to apes and monkeys. Such an expansion could lead to a relatively more dorsal location of the FEF in humans relative to apes and monkeys.

These topological identifications of sulci can guide a perspective on the location of FEF in nonhuman primates and humans. Hence, if the FEF of monkeys is in the arcuate sulcus, and the arcuate sulcus is homologous

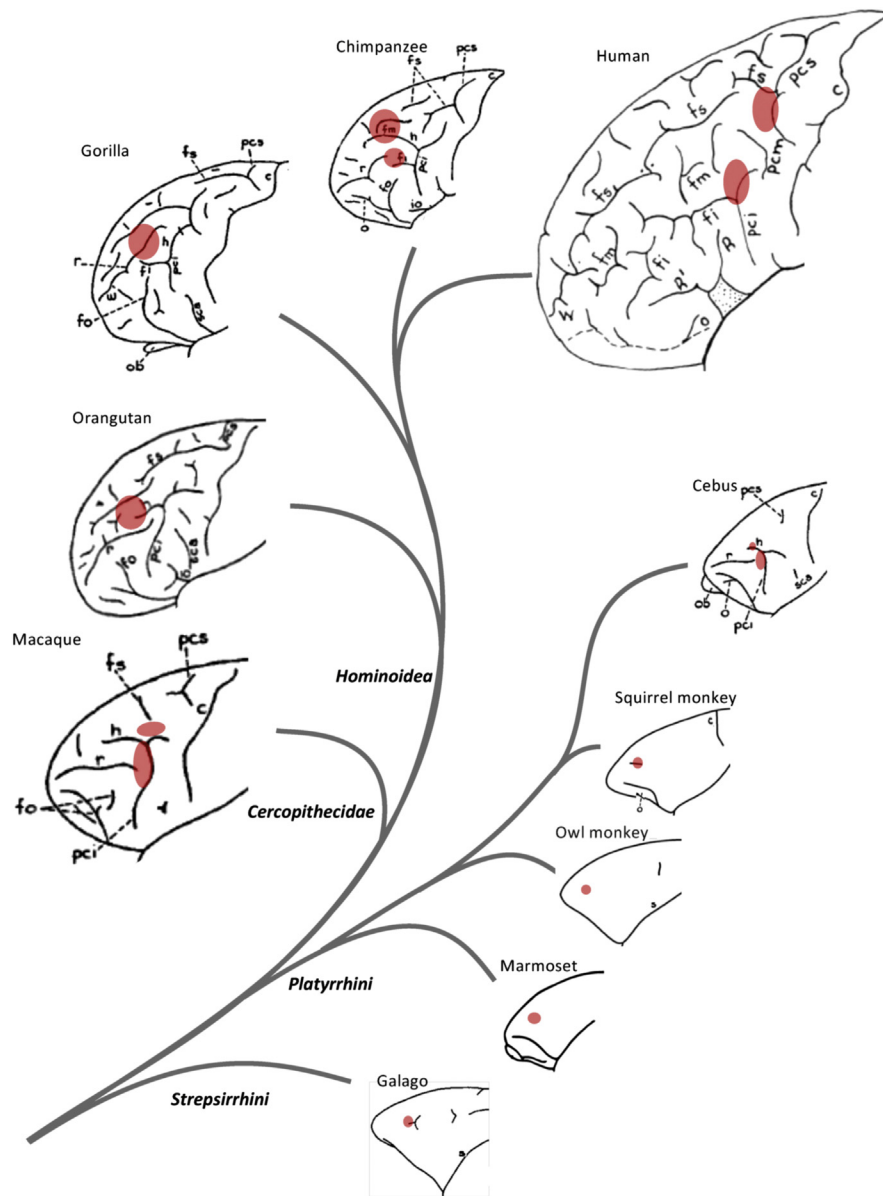


FIGURE 36.16 A frontal cortex cladogram to illustrate the location of FEF in a range of prosimian and primate species. The diagrams are not to scale. Sulcal labels are as follows: *c*, central; *fi*, frontal inferior; *fm*, frontal medius; *fo*, frontal orbital; *fs*, frontal superior; *h*, horizontal ramus of precentral inferior sulcus; *io*, inferior orbital; *o*, orbital; *ob*, olfactory bulb; *pci*, precentral inferior; *pcm*, precentral medius; *pcs*, precentral superior; *r*, rectus; *R*, ramus ascendens fissurae Sylvii; *sca*, subcentral anterior; *W*, frontomarginal of Wernicke. Note the use of the label “rectus” for the macaque and *Cebus* principal sulcus and of the labels “pci” and “h” for the macaque and *Cebus* arcuate sulcus. Two regions are highlighted in *Cebus*, macaque, chimpanzee, and human based on evidence for at least two discrete zones. Reproduced from Connolly, C.J., 1936. *The fissural pattern of the primate brain*. *Am. J. Phys. Anthropol.* 21, 301–422; Connolly, C. J., 1950. *External Morphology of the Primate Brain*. CC Thomas.

with the inferior precentral sulcus, then does it follow that the FEF of humans is located in the inferior precentral sulcus? Such reasoning can account for the lateral BOLD activation observed in imaging studies. If this reasoning is sound and valid, then what is the status of the FEF region at the intersection of the superior frontal sulcus and the dorsal precentral sulcus? One possibility is that this dorsal region is homologous to the premotor eye field of macaques. On the other hand, if the dorsal region is correctly understood as the homologue of the

macaque FEF, based on evidence reviewed previously, then what is the proper relation of the ventral FEF region? Perhaps it is a premotor eye field as suggested earlier. Confusing all of this, though, is the evidence that the eye movement region in orangutans, gorillas, and chimpanzees is located clearly rostral to the precentral sulci. We note, though, that in spite of the similar appearance of the frontal sulci of humans and chimpanzees the precentral sulcus of chimpanzees does not mark the border between premotor and prefrontal cortex as it may in

humans; instead it marks the border between motor and premotor cortex (Preuss, personal communication). This can explain why the FEF is located on the middle frontal gyrus of the apes, but it cannot help us understand the apparent caudal migration of the FEF in humans. Clearly, many questions remain.

36.6 Conclusion

We end this chapter with more questions and cautions than conclusions. First, should the term “frontal eye field” be singular or plural? Shall we regard “FEF” (now in scare quotes to remind the reader of the uncertainty) as a collection of distinct areas that can be of different sizes (and locations) in different species? Or shall we regard “FEF” as a single area with multiple modules adapted according to the lifestyle and habitat of the respective species? Under either hypothesis the apparent location of “FEF” might appear to differ across individuals and species as one function is emphasized over another. In the macaque, for example, we have described both arcuate and post-arcuate regions from which saccades are elicited with weak electrical stimulation. Interposed between these is a pursuit region. Rostral to the saccade map in the arcuate sulcus is a vergence region. The medial and lateral segments within the arcuate sulcus support very different patterns of cortical connections. More dorsomedially in the macaque is a region concerned with ear movements and orienting to sounds. Evolutionary specialization of any (or all of these) could result in elaboration of at least five or six subregions or areas.

Next, across primate species does the size (and complexity) of “FEF” scale with total neocortical area? With the area of visual cortical areas in the parietal and temporal lobes? Does it scale with changes in the subcortical network mediating orienting such as the mediodorsal thalamus, basal ganglia, and—in particular—the superior colliculus. Does it scale with the degree of elaboration of extrastriate visual areas and other sensory systems? Does it scale with the complexity of the musculature used for orienting and associated visually guided behaviors (eye, head, eye + head, eye + head + hand)? Does it scale with the complexity of cognitive control over gaze behavior (eg, dissociation of gaze from visual salience for social deception tested by an ability to make antisaccades)? We cannot answer these questions because precise boundaries of FEF are uncertain, especially in humans. For this reason, it remains essential that the human imaging studies identify the anatomical landmarks and full extent of any activation interpreted as corresponding to FEF.

The size and location of “FEF” is a matter of operational definition with resolution specified by technique.

Consider, for example, mapping based on the eye movements elicited by electrical stimulation. Results differ according to state of consciousness (anesthetized or alert), electrode size (surface or intracortical), stimulation parameters (brief or long stimulation trains), method of movement inspection (simple observation or quantitative eye tracking), and inclusion of coordinated orienting movements (head free or fixed). Until common methods are applied across all species, including humans, ground truth comparisons cannot be made. Therefore, seeking convergence of criteria across methods seems the only viable approach. Ultimately, a comparative analysis of the location, architecture, and connectivity of “FEF” should be framed by an appreciation of the interaction of gaze control with the body size, posture, locomotion, and reaching behavior, plus the elaborated relevance of gaze for communication in monkeys, apes, and humans living in larger social groups.

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References

- Amiez, C., Petrides, M., 2009. Anatomical organization of the eye fields in the human and non-human primate frontal cortex. *Prog. Neurobiol.* 89, 220–230.
- Amiez, C., Kostopoulos, P., Champod, A.-S., Petrides, M., 2006. Local morphology predicts functional organization of the dorsal premotor region in the human brain. *J. Neurosci.* 26, 2724–2731.
- Babapoor-Farrokhran, S., Hutchison, R.M., Gati, J.S., Menon, R.S., Everling, S., 2013. Functional connectivity patterns of medial and lateral macaque frontal eye fields reveal distinct visuomotor networks. *J. Neurophysiol.* 109, 2560–2570.
- Bailey, P., von Bonin, G., 1951. *The Isocortex of Man*. University of Illinois Press.
- Bailey, P., von Bonin, G., McCulloch, W.S., 1950. *The Isocortex of the Chimpanzee*. University of Illinois Press.
- Baizer, J., Bender, D., 1989. Comparison of saccadic eye movements in humans and macaques to single-step and double-step target movements. *Vis. Res.* 29, 485–495.
- Baker, J.T., Patel, G.H., Corbetta, M., Snyder, L.H., 2006. Distribution of activity across the monkey cerebral cortical surface, thalamus and midbrain during rapid, visually guided saccades. *Cereb. Cortex* 16, 447–459.
- Bakola, S., Burman, K.J., Rosa, M.G.P., 2015. The cortical motor system of the marmoset monkey (*Callithrix jacchus*). *Neurosci. Res.* 93, 72–81.

- Baldwin, M.K., Cooke, D.F., Krubitzer, L., 2017. Intracortical microstimulation maps of motor, somatosensory, and posterior parietal cortex in tree shrews (*Tupaia belangeri*) reveal complex movement representations. *Cereb* 27 (2), 1439–1456.
- Barbas, H., Mesulam, M., 1981. Organization of afferent input to subdivisions of area 8 in the rhesus monkey. *J. Comp. Neurol.* 200, 407–431.
- Beauchamp, M.S., Petit, L., Ellmore, T.M., Ingeholm, J., Haxby, J.V., 2001. A parametric fMRI study of overt and covert shifts of visuospatial attention. *Neuroimage* 14, 310–321.
- Beever, C.E., Horsley, V., 1890. A record of the results obtained by electrical excitation of the so-called motor cortex and internal capsule in an orangutang (*Simia satyrus*). *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 181, 129–158.
- Berg, D.J., Boehnke, S.E., Marino, R.A., Munoz, D.P., Itti, L., 2009. Free viewing of dynamic stimuli by humans and monkeys. *J. Vis.* 9, 19.1–19.15.
- Blanke, O., Seeck, M., 2003. Direction of saccadic and smooth eye movements induced by electrical stimulation of the human frontal eye field: effect of orbital position. *Exp. Brain Res.* 150, 174–183.
- Blanke, O., Spinelli, L., Thut, G., Michel, C.M., Perrig, S., Landis, T., Seeck, M., 2000. Location of the human frontal eye field as defined by electrical cortical stimulation: anatomical, functional and electrophysiological characteristics. *Neuroreport* 11, 1907–1913.
- Bloch, J.I., Boyer, D.M., 2002. Grasping primate origins. *Science* 298, 1606–1610.
- Blum, B., Kulikowski, J., Carden, D., Harwood, D., 1982. Eye movements induced by electrical stimulation of the frontal eye fields of marmosets and squirrel monkeys. *Brain Behav. Evol.* 21, 34–41.
- Blumer, R., Maurer-Gesek, B., Gesslbauer, B., Blumer, M., Pechriggl, E., Davis-López de Carrizosa, M.A., Horn, A.K., May, P.J., Streicher, J., de la Cruz, R.R., Pastor, Á.M., 2016. Palisade endings are a constant feature in the extraocular muscles of frontal-eyed, but not lateral-eyed, animals. *Invest. Ophthalmol. Vis. Sci.* 57, 320–331.
- Bock, N.A., Kocharyan, A., Liu, J.V., Silva, A.C., 2009. Visualizing the entire cortical myelination pattern in marmosets with magnetic resonance imaging. *J. Neurosci. Methods* 185, 15–22.
- Bogart, S.L., Mangin, J.-F., Schapiro, S.J., Reamer, L., Bennett, A.J., Pierre, P.J., Hopkins, W.D., 2012. Cortical sulci asymmetries in chimpanzees and macaques: a new look at an old idea. *Neuroimage* 61, 533–541.
- Bon, L., Lucchetti, C., 1994. Ear and eye representation in the frontal cortex, area 8b, of the macaque monkey: an electrophysiological study. *Exp. Brain Res.* 102, 259–271.
- von Bonin, G., 1949. Architecture of the precentral motor cortex and some adjacent areas. In: Bucky, P.C. (Ed.), *The Precentral Motor Cortex*. University of Illinois Press, pp. 7–82.
- von Bonin, G., Bailey, P., 1947. *The Neocortex of Macaca mulatta*. University of Illinois Press.
- Borrell, V., Götz, M., 2014. Role of radial glial cells in cerebral cortex folding. *Curr. Opin. Neurobiol.* 27, 39–46.
- Boussaoud, D., 1995. Primate premotor cortex: modulation of preparatory neuronal activity by gaze angle. *J. Neurophysiol.* 73, 886–890.
- Boussaoud, D., Wise, S., 1993. Primate frontal cortex: effects of stimulus and movement. *Exp. Brain Res.* 95, 28–40.
- Boussaoud, D., Barth, T., Wise, S., 1993. Effects of gaze on apparent visual responses of frontal cortex neurons. *Exp. Brain Res.* 93, 423–434.
- Boussaoud, D., Joffrais, C., Bremner, F., 1998. Eye position effects on the neuronal activity of dorsal premotor cortex in the macaque monkey. *J. Neurophysiol.* 80, 1132–1150.
- Brodman, K., 1909. *Localisation in the Cerebral Cortex*. Springer, US.
- Bruce, C.J., Goldberg, M.E., Bushnell, M.C., Stanton, G.B., 1985. Primate frontal eye fields. II. Physiological and anatomical correlates of electrically evoked eye movements. *J. Neurophysiol.* 54, 714–734.
- Burman, K.J., Palmer, S.M., Gamberini, M., Rosa, M.G.P., 2006. Cytoarchitectonic subdivisions of the dorsolateral frontal cortex of the marmoset monkey (*Callithrix jacchus*), and their projections to dorsal visual areas. *J. Comp. Neurol.* 495, 149–172.
- Burman, K.J., Bakola, S., Richardson, K.E., Reser, D.H., Rosa, M.G., 2014. Patterns of afferent input to the caudal and rostral areas of the dorsal premotor cortex (6DC and 6DR) in the marmoset monkey. *J. Comp. Neuro.* 522, 3683–3716.
- Burman, K.J., Bakola, S., Richardson, K.E., Yu, H.-H., Reser, D.H., Rosa, M.G.P., 2015. Cortical and thalamic projections to cytoarchitectural areas 6Va and 8C of the marmoset monkey: connectionally distinct subdivisions of the lateral premotor cortex. *J. Comp. Neurol.* 523, 1222–1247.
- Calabrese, E., Badaea, A., Coe, C.L., Lubach, G.R., Shi, Y., Styner, M.A., Johnson, G.A., 2015. A diffusion tensor MRI atlas of the postmortem rhesus macaque brain. *Neuroimage* 117, 408–416.
- Camalier, C., Gotler, A., Murthy, A., Thompson, K., Logan, G., Palmeri, T., Schall, J., 2007. Dynamics of saccade target selection: race model analysis of double step and search step saccade production in human and macaque. *Vis. Res.* 47, 2187–2211.
- Cantalupo, C., McCain, D., Ward, J.P., 2002. Function of head-cocking in Garnett's greater bush baby (*Otolemur garnettii*). *Int. J. Primatol.* 23, 203–221.
- Cartmill, M., 1992. New views on primate origins. *Evol. Anthr.* 1, 105–111.
- Caspari, N., Janssens, T., Mantini, D., Vandenberghe, R., Vanduffel, W., 2015. Covert shifts of spatial attention in the macaque monkey. *J. Neurosci.* 35, 7695–7714.
- Cerkevich, C.M., Collins, C.E., Kaas, J.H., 2014. Cortical inputs to the middle temporal visual area in New World owl monkeys. *Eye Brain* 2015, 1–15.
- Charles-Dominique, P., 1977. *Ecology and Behaviour of Nocturnal Primates: Prosimians of Equatorial West Africa*. Columbia University Press.
- Cisek, P., Kalaska, J.F., 2005. Neural correlates of reaching decisions in dorsal premotor cortex: specification of multiple direction choices and final selection of action. *Neuron* 45, 801–814.
- Collins, C.E., Lyon, D.C., Kaas, J.H., 2005. Distribution across cortical areas of neurons projecting to the superior colliculus in new world monkeys. *Anat. Rec.* 285, 619–627.
- Connolly, C.J., 1936. The fissural pattern of the primate brain. *Am. J. Phys. Anthropol.* 21, 301–422.
- Connolly, C.J., 1950. *External Morphology of the Primate Brain*. CC Thomas.
- Crosby, E.C., Yoss, R.E., Henderson, J.W., 1952. The mammalian midbrain and isthmus regions. Part II. The fiber connections. D. The pattern for eye movements on the frontal eye field and the discharge of specific portions of this field to and through midbrain levels. *J. Comp. Neurol.* 97, 357–383.
- Davidoff, L.M., 1928. A visit to professor Förster's clinic in Breslau with special observation of his treatment of epilepsy. *Psychiatric Quart* 2, 307–313.
- DeBruyn, E., Wise, V., Casagrande, V., 1980. The size and topographic arrangement of retinal ganglion cells in the galago. *Vis. Res.* 20, 315–327.
- Dejerine, J., 1914. *Sémiologie Des Affections Du Système Nerveux*. Masson et cie.
- Dejerine, J., Roussy, G., 1906. Le syndrome thalamique. *Rev. Neurol.* 14, 521–532.
- Denion, E., Hitier, M., Guyader, V., Dugué, A.-E., Mouriaux, F., 2015. Unique human orbital morphology compared with that of apes. *Sci. Rep.* 5, 11528.
- Denion, E., Hitier, M., Levieil, E., Mouriaux, F., 2015. Human rather than ape-like orbital morphology allows much greater lateral visual field expansion with eye abduction. *Sci. Rep.* 5, 12437.

- Derrfuss, J., Vogt, V., Fiebach, C.J., von Cramon, D.Y., Tittgemeyer, M., 2012. Functional organization of the left inferior precentral sulcus: dissociating the inferior frontal eye field and the inferior frontal junction. *Neuroimage* 59, 3829–3837.
- Driscoll, C.A., Barr, C.S., 2016. Studying longitudinal trajectories in animal models of psychiatric illness and their translation to the human condition. *Neurosci. Res.* 102, 67–77.
- DuMond, F.V., 1968. The squirrel monkey in a semi-natural environment. In: Rosenblum, L.A., Cooper, R.W. (Eds.), *The Squirrel Monkey*. Academic Press, pp. 87–145.
- Dusser de Barenne, J., Garol, H., McCulloch, W., 1941. Functional organization of sensory and adjacent cortex of the monkey. *J. Neurophysiol.* 4, 287–303.
- Eberstaller, O., 1890. *Das Stirnhirn*. Urban & Schwarzenberg.
- Ecker, A., 1869. *Die Hirnwindungen des Menschen*. Vieweg, Braunschweig.
- von Economo, C.F., Koskinas, G.N., 1925. *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen*. Springer, Berlin, Wien.
- Einhäuser, W., Kruse, W., Hoffmann, K.-P., König, P., 2006. Differences of monkey and human overt attention under natural conditions. *Vis. Res.* 46, 1194–1209.
- Emmers, R., Akert, K., 1963. *A Stereotaxic Atlas of the Brain of the Squirrel Monkey *Saimiri sciureus**. University of Wisconsin Press, Madison.
- Van Essen, D., 1997. A tension-based theory of morphogenesis and compact wiring in the central nervous system. *Nature* 385, 313–318.
- Evinger, C., Manning, K., Pellegrini, J., Basso, M., Powers, A., Sibony, P., 1994. Not looking while leaping: the linkage of blinking and saccadic gaze shifts. *Exp. Brain Res.* 100, 337–344.
- Falk, D., 1978. Cerebral asymmetry in old world monkeys. *Acta Anat.* 101, 334–339.
- Falk, D., 2014. Interpreting sulci on hominin endocasts: old hypotheses and new findings. *Front. Hum. Neurosci.* 8, 134. <https://doi.org/10.3389/fnhum.2014.00134>.
- Falk, D., Hildebolt, C., Cheverud, J., Vannier, M., Helmkamp, R., Königsberg, L., 1990. Cortical asymmetries in frontal lobes of rhesus monkeys (*Macaca mulatta*). *Brain Res.* 512, 40–45.
- Ferrier, D., 1874. Experiments on the brain of monkeys. No. I. *Proc. R. Soc. Lond.* 23, 409–430.
- Finlay, B.L., Franco, E.C.S., Yamada, E.S., Crowley, J.C., Parsons, M., Muniz, J.A.P.C., Silveira, L.C.L., 2008. Number and topography of cones, rods and optic nerve axons in New and Old World primates. *Vis. Neurosci.* 25, 289–299.
- Fogassi, L., Gallese, V., Gentilucci, M., Luppino, G., Matelli, M., Rizzolatti, G., 1994. The fronto-parietal cortex of the prosimian Galago: patterns of cytochrome oxidase activity and motor maps. *Behav. Brain Res.* 60, 91–113.
- Ford, K.A., Goltz, H.C., Brown, M.R.G., Everling, S., 2005. Neural processes associated with antisaccade task performance investigated with event-related fMRI. *J. Neurophysiol.* 94, 429–440.
- Ford, K.A., Gati, J.S., Menon, R.S., Everling, S., 2009. BOLD fMRI activation for anti-saccades in nonhuman primates. *Neuroimage* 45, 470–476.
- Förster, O., 1926. Zur operativen Behandlung der Epilepsie. *J. Neurol.* 89, 137–147.
- Förster, O., 1931. The cerebral cortex in man. *Lancet* 2, 309–312.
- Förster, O., 1936. The motor cortex in man in the light of Hughlings Jackson's doctrines. *Brain* 59, 135–159.
- Förster, O., Penfield, W., 1930. The structural basis of traumatic epilepsy and results of radical operation. *Brain* 53, 99–119.
- Franco, E., Finlay, B., Silveira, L., Yamada, E., Crowley, J., 2000. Conservation of absolute foveal area in New World monkeys. a constraint on eye size and conformation. *Brain Behav. Evol.* 56, 276–286.
- Frey, S., Pandya, D.N., Chakravarty, M.M., Bailey, L., Petrides, M., Collins, D.L., 2011. An MRI based average macaque monkey stereotaxic atlas and space (MNI monkey space). *Neuroimage* 55, 1435–1442.
- Fritsch, G., Hitzig, E., 1870. Über die elektrische Erregbarkeit des Grosshirns. *archives für Anatomie Physiologie und Wissenschaftliche Medizin* 37, 300–332.
- Fritsch, G., Hitzig, E., 2009. Electric excitability of the cerebrum (Über die elektrische Erregbarkeit des Grosshirns). *Epilepsy Behav.* 15, 123–130.
- Fujii, N., Mushiake, H., Tanji, J., 1998. An oculomotor representation area within the ventral premotor cortex. *Proc. Natl. Acad. Sci.* 95, 12034–12037.
- Fujii, N., Mushiake, H., Tanji, J., 2000. Rostrocaudal distinction of the dorsal premotor area based on oculomotor involvement. *J. Neurophysiol.* 83, 1764–1769.
- Fukushima, K., Yamanobe, T., Shinmei, Y., Fukushima, J., Kurkin, S., Peterson, B.W., 2002. Coding of smooth eye movements in three-dimensional space by frontal cortex. *Nature* 419, 157–162.
- Gabernet, L., Meskenaite, V., Hepp-Reymond, M.C., 1999. Parcellation of the lateral premotor cortex of the macaque monkey based on staining with the neurofilament antibody SMI-32. *Exp. Brain Res.* 128, 188–193.
- Gamlin, P., Yoon, K., 2000. An area for vergence eye movement in primate frontal cortex. *Nature* 407, 1003–1007.
- Gandhi, N.J., 2012. Interactions between gaze-evoked blinks and gaze shifts in monkeys. *Exp. Brain Res.* 216, 321–339.
- Germann, J., Robbins, S., Halsband, U., Petrides, M., 2005. Precentral sulcal complex of the human brain: morphology and statistical probability maps. *J. Comp. Neurol.* 493, 334–356.
- Glasser, M.F., Coalson, T.S., Robinson, E.C., Hacker, C.D., Harwell, J., Yacoub, E., Ugurbil, K., Andersson, J., Beckmann, C.F., Jenkinson, M., Smith, S.M., Van Essen, D.C., 2016. A multi-modal parcellation of human cerebral cortex. *Nature* 536, 171–178.
- Glickman, S.E., Sroges, R.W., 1966. Curiosity in zoo animals. *Behaviour* 26, 151–187.
- Godoy, J., Lüders, H., Dinner, D., Morris, H., Wyllie, E., 1990. Versive eye movements elicited by cortical stimulation of the human brain. *Neurology* 40, 296–299.
- Goonetilleke, S.C., Katz, L., Wood, D.K., Gu, C., Huk, A.C., Corneil, B.D., 2015. Cross-species comparison of anticipatory and stimulus-driven neck muscle activity well before saccadic gaze shifts in humans and nonhuman primates. *J. Neurophysiol.* 114, 902–913.
- Gottlieb, J.P., Bruce, C.J., MacAvoy, M.G., 1993. Smooth eye movements elicited by microstimulation in the primate frontal eye field. *J. Neurophysiol.* 69, 786–799.
- Gottlieb, J.P., MacAvoy, M.G., Bruce, C.J., 1994. Neural responses related to smooth-pursuit eye movements and their correspondence with electrically elicited smooth eye movements in the primate frontal eye field. *J. Neurophysiol.* 72, 1634–1653.
- Goulas, A., Uylings, H.B., Stiers, P., 2012. Unravelling the intrinsic functional organization of the human lateral frontal cortex: a parcellation scheme based on resting state FMRI. *J. Neurosci.* 32, 10238–10252.
- Gould 3rd, H., Cusick, C., Pons, T., Kaas, J., 1986. The relationship of corpus callosum connections to electrical stimulation maps of motor, supplementary motor, and the frontal eye fields in owl monkeys. *J. Comp. Neurol.* 247, 297–325.
- Grosbras, M.-H., Laird, A.R., Paus, T., 2005. Cortical regions involved in eye movements, shifts of attention, and gaze perception. *Hum. Brain Mapp.* 25, 140–154.
- Groves, C., 2001. *Primate Taxonomy*. Smithsonian Series in Comparative Evolutionary Biology. Smithsonian, Washington, p. 1.
- Grünbaum, A., Sherrington, C.S., 1901. Observations on the physiology of the cerebral cortex of some of the higher apes. *Proc. R. Soc. Lond.* 69, 206–209.

- Guipponi, O., Odouard, S., Pinède, S., Wardak, C., Ben Hamed, S., 2015. fMRI cortical correlates of spontaneous eye blinks in the nonhuman primate. *Cereb. Cortex* 25, 2333–2345.
- Guitton, D., Volle, M., 1987. Gaze control in humans: eye-head coordination during orienting movements to targets within and beyond the oculomotor range. *J. Neurophysiol.* 58, 427–459.
- Guitton, D., Douglas, R.M., Volle, M., 1984. Eye-head coordination in cats. *J. Neurophysiol.* 52, 1030–1050.
- Hamilton, C., Vermeire, B., 1988. Complementary hemispheric specialization in monkeys. *Science* 242, 1691–1694.
- Hanes, D., Carpenter, R., 1999. Countermanding saccades in humans. *Vis. Res.* 39, 2777–2791.
- Hanes, D., Schall, J., 1995. Countermanding saccades in macaque. *Vis. Neurosci.* 12, 929–937.
- Haude, R.H., Ray, O.S., 1974. Visual observing behavior in the squirrel monkey. *Anim. Learn. Behav.* 2, 138–140.
- Heide, W., Kurzdin, K., Kömpf, D., 1996. Deficits of smooth pursuit eye movements after frontal and parietal lesions. *Brain* 119 (Pt 6), 1951–1969.
- Heilbronner, P., Holloway, R., 1989. Anatomical brain asymmetry in monkeys: frontal, temporoparietal, and limbic cortex in *Macaca*. *Am. J. Phys. Anthropol.* 80, 203–211.
- Heiney, S.A., Blazquez, P.M., 2011. Behavioral responses of trained squirrel and rhesus monkeys during oculomotor tasks. *Exp. Brain Res.* 212, 409–416.
- Henderson, J.W., Crosby, E.C., 1952. An experimental study of optokinetic responses. *AMA Arch. Ophthalmol.* 47, 43–54.
- Hervé, G., 1888. *La Circonvolution de Broca*. A. Delahaye & E. Lecrosnier, Paris.
- Hines, M., 1940. Movements elicited from precentral gyrus of adult chimpanzees by stimulation with sine wave currents. *J. Neurophysiol.* 3, 442–466.
- Hopkins, W.D., Meguerditchian, A., Coulon, O., Bogart, S., Mangin, J.-F., Sherwood, C.C., Grabowski, M.W., Bennett, A.J., Pierre, P.J., Fears, S., Woods, R., Hof, P.R., Vauclair, J., 2014. Evolution of the central sulcus morphology in primates. *Brain Behav. Evol.* 84, 19–30.
- Horsley, V., Schäfer, E.A., 1888. A record of experiments upon the functions of the cerebral cortex. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 179, 1–45.
- Huerta, M.F., Krubitzer, L.A., Kaas, J.H., 1986. Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys: I. subcortical connections. *J. Comp. Neurol.* 253, 415–439.
- Huerta, M., Krubitzer, L., Kaas, J., 1987. Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys. II. Cortical connections. *J. Comp. Neurol.* 265, 332–361.
- Hung, C.-C., Yen, C.C., Ciuchta, J.L., Papoti, D., Bock, N.A., Leopold, D.A., Silva, A.C., 2015. Functional MRI of visual responses in the awake, behaving marmoset. *Neuroimage* 120, 1–11.
- Hutchison, R.M., Gallivan, J.P., Culham, J.C., Gati, J.S., Menon, R.S., Everling, S., 2012. Functional connectivity of the frontal eye fields in humans and macaque monkeys investigated with resting-state fMRI. *J. Neurophysiol.* 107, 2463–2474.
- Ikkai, A., Curtis, C.E., 2008. Cortical activity time locked to the shift and maintenance of spatial attention. *Cereb. Cortex* 18, 1384–1394.
- Imai, N., Sawada, K., Fukunishi, K., Sakata-Haga, H., Fukui, Y., 2011. Sexual dimorphism of sulcal length asymmetry in the cerebrum of adult cynomolgus monkeys (*Macaca fascicularis*). *Congenit. Anom.* 51, 161–166.
- Jacobs, G.H., Deegan 2nd, J.F., Neitz, J., Crognale, M.A., Neitz, M., 1993. Photopigments and color vision in the nocturnal monkey. *Aotus. Vis. Res.* 33, 1773–1783.
- Jensen, J., 1871. *Die Furchen und Windungen der menschlichen Grosshirn-Hemisphären*. Allgemeine Zeitschrift für Psychiatrie. Druck und Verlag von Georg Reimer.
- Kaas, J., Morel, A., 1993. Connections of visual areas of the upper temporal lobe of owl monkeys: the MT crescent and dorsal and ventral subdivisions of FST. *J. Neurosci.* 13, 534–546.
- Kaas, J., Lin, C., Wagor, E., 1977. Cortical projections of posterior parietal cortex in owl monkeys. *J. Comp. Neurol.* 72, 387–408.
- Kagan, I., Iyer, A., Lindner, A., Andersen, R.A., 2010. Space representation for eye movements is more contralateral in monkeys than in humans. *Proc. Natl. Acad. Sci.* 107, 7933–7938.
- Kaiboriboon, K., Lüders, H.O., Miller, J.P., Leigh, R.J., 2012. Upward gaze and head deviation with frontal eye field stimulation. *Epileptic Disord.* 14, 64–68.
- Kano, F., Tomonaga, M., 2009. How chimpanzees look at pictures: a comparative eye-tracking study. *Proc. R. Soc. Lond.* 276, 1949–1955.
- Kano, F., Tomonaga, M., 2011. Species difference in the timing of gaze movement between chimpanzees and humans. *Anim. Cogn.* 14, 879–892.
- Kano, F., Hirata, S., Call, J., Tomonaga, M., 2011. The visual strategy specific to humans among hominids: a study using the gap-overlap paradigm. *Vis. Res.* 51, 2348–2355.
- Kaplan, G., Rogers, L.J., 2006. Head-cocking as a form of exploration in the common marmoset and its development. *Dev. Psychobiol.* 48, 551–560.
- Kastner, S., DeSimone, K., Konen, C.S., Szczepanski, S.M., Weiner, K.S., Schneider, K.A., 2007. Topographic maps in human frontal cortex revealed in memory-guided saccade and spatial working-memory tasks. *J. Neurophysiol.* 97, 3494–3507.
- Kato, M., Miyauchi, S., 2003. Human precentral cortical activation patterns during saccade tasks: an fMRI comparison with activation during intentional eyeblink tasks. *Neuroimage* 19, 1260–1272.
- Keating, E., 1993. Lesions of the frontal eye field impair pursuit eye movements, but preserve the predictions driving them. *Behav. Brain Res.* 53, 91–104.
- von Kleist, K., 1934. *Gehirnpathologie*. J.A. Barth, Leipzig.
- Knight, T.A., Fuchs, A.F., 2007. Contribution of the frontal eye field to gaze shifts in the head-unrestrained monkey: effects of microstimulation. *J. Neurophysiol.* 97, 618–634.
- Kobayashi, H., Kohshima, S., 1997. Unique morphology of the human eye. *Nature* 387, 767–768.
- Kobayashi, H., Kohshima, S., 2001. Unique morphology of the human eye and its adaptive meaning: comparative studies on external morphology of the primate eye. *J. Hum. Evol.* 40, 419–435.
- Koyama, M., Hasegawa, I., Osada, T., Adachi, Y., Nakahara, K., Miyashita, Y., 2004. Functional magnetic resonance imaging of macaque monkeys performing visually guided saccade tasks: comparison of cortical eye fields with humans. *Neuron* 41, 795–807.
- Krubitzer, L., Kaas, J., 1990. The organization and connections of somatosensory cortex in marmosets. *J. Neurosci.* 10, 952–974.
- Krubitzer, L., Kaas, J., 1993. The dorsomedial visual area of owl monkeys: connections, myeloarchitecture, and homologies in other primates. *J. Comp. Neurol.* 334, 497–528.
- Langston, A., Casagrande, V., Fox, R., 1986. Spatial resolution of the Galago. *Vis. Res.* 26, 791–796.
- Lanzilotto, M., Percivalle, V., Lucchetti, C., 2013. A new field in monkey's frontal cortex: premotor ear-eye field (PEEF). *Neurosci. Biobehav. Rev.* 37, 1434–1444.
- Latto, R., 1978. The effects of bilateral frontal eye-field, posterior parietal or superior collicular lesions on visual search in the rhesus monkeys. *Brain Res.* 146, 35–50.
- Lehman, R., 1980. Distribution and changes in strength of hand preference of cynomolgus monkeys. *Brain Behav. Evol.* 17, 209–217.
- Leichnetz, G., Gonzalo-Ruiz, A., 1996. Prearcuate cortex in the *Cebus* monkey has cortical and subcortical connections like the macaque

- frontal eye field and projects to fastigial-recipient oculomotor-related brainstem nuclei. *Brain Res. Bull.* 41, 1–29.
- Leigh, R.J., Zee, D.S., 2015. *The Neurology of Eye Movements*. Oxford University Press, New York.
- Lemmen, L.J., Davis, J.S., Radnor, L.L., 1959. Observations on stimulation of the human frontal eye field. *J. Comp. Neurol.* 112, 163–168.
- Lende, R., 1970. Cortical localization in the tree shrew (*Tupaia*). *Brain Res.* 18, 61–75.
- Levinsohn, G., 1909. Über die Beziehungen der Grosshirnrinde beim Affen zu den Bewegungen des Auges. *Graefes Arch. Clin. Exp. Ophthalmol.* 71, 313–378.
- Leyton, A.S., Sherrington, C.S., 1917. Observations on the excitable cortex of the chimpanzee, orangutan, and gorilla. *Q. J. Exp. Physiol.* 11, 135–222.
- Lobel, E., Kahane, P., Leonards, U., Grosbras, M.-H., Lehericy, S., Bihan, D.L., Berthoz, A., 2001. Localization of human frontal eye fields: anatomical and functional findings of functional magnetic resonance imaging and intracerebral electrical stimulation. *J. Neurosurg.* 95, 804–815.
- Love, S.A., Marie, D., Roth, M., Lacoste, R., Nazarian, B., Bertello, A., Coulon, O., Anton, J.-L., Meguerditchian, A., 2016. The average baboon brain: MRI templates and tissue probability maps from 89 individuals. *Neuroimage* 132, 526–533.
- Lucchetti, C., Lanzilotto, M., Bon, L., 2008. Auditory-motor and cognitive aspects in area 8B of macaque monkey's frontal cortex: a premotor ear-eye field (PEEF). *Exp. Brain Res.* 186, 131–141.
- Luna, B., Thulborn, K.R., Strojwas, M.H., McCurtain, B.J., Berman, R.A., Genovese, C.R., Sweeney, J.A., 1998. Dorsal cortical regions subserving visually guided saccades in humans: an fMRI study. *Cereb. Cortex* 8, 40–47.
- Lynch, J., Hoover, J., Strick, P., 1994. Input to the primate frontal eye field from the substantia nigra, superior colliculus, and dentate nucleus demonstrated by transneuronal transport. *Exp. Brain Res.* 100, 181–186.
- Lyon, D., Kaas, J., 2001. Connectional and architectonic evidence for dorsal and ventral V3, and dorsomedial area in marmoset monkeys. *J. Neurosci.* 21, 249–261.
- MacAvoy, M.G., Gottlieb, J.P., Bruce, C.J., 1991. Smooth-pursuit eye movement representation in the primate frontal eye field. *Cereb. Cortex* 1, 95–102.
- Mangalam, M., Desai, N., Singh, M., 2014. Division of labor in hand usage in free-ranging bonnet macaques, *Macaca radiata*. *Am. J. Primatol.* 76, 576–585.
- Marchetti, E., Gauthier, G.M., Pellet, J., 1983. Cerebellar control of eye movements studied with injection of harmaline in the trained baboon. *Arch. Ital. Biol.* 121, 1–17.
- Markov, N.T., Vezoli, J., Chameau, P., Falchier, A., Quilodran, R., Huissoud, C., Lamy, C., Misery, P., Giroud, P., Ullman, S., Barone, P., Dehay, C., Knoblauch, K., Kennedy, H., 2014. Anatomy of hierarchy: feedforward and feedback pathways in macaque visual cortex. *J. Comp. Neurol.* 522, 225–259.
- Markowitsch, H., Pritzel, M., Wilson, M., Divac, I., 1980. The prefrontal cortex of a prosimian (*Galago senegalensis*) defined as the cortical projection area of the thalamic mediodorsal nucleus. *Neuroscience* 5, 1771–1779.
- Martinez-Conde, S., Macknik, S.L., 2008. Fixational eye movements across vertebrates: comparative dynamics, physiology, and perception. *J. Vis.* 8, 28.1–28.16.
- McCrea, R.A., Gdowski, G.T., 2003. Firing behaviour of squirrel monkey eye movement-related vestibular nucleus neurons during gaze saccades. *J. Physiol.* 546, 207–224.
- Michalka, S.W., Kong, L., Rosen, M.L., Shinn-Cunningham, B.G., Somers, D.C., 2015. Short-term memory for space and time flexibly recruit complementary sensory-biased frontal lobe attention networks. *Neuron* 87, 882–892.
- Milea, D., Lobel, E., Lehericy, S., Duffau, H., Rivaud-Péchoix, S., Berthoz, A., Pierrot-Deseilligny, C., 2002. Intraoperative frontal eye field stimulation elicits ocular deviation and saccade suppression. *Neuroreport* 13, 1359–1364.
- Mingazzini, G., 1888. *Intorno ai solchi e le circonvoluzioni cerebrali dei primati e del feto umano* (Estratto dagli Atti della R. Accademia medica di Roma, anno XV, vol. IV, serie II). Tipografia Fratelli Centenari, Roma.
- Mitchell, J.F., Leopold, D.A., 2015. The marmoset monkey as a model for visual neuroscience. *Neurosci. Res.* 93, 20–46.
- Mitchell, J.F., Reynolds, J.H., Miller, C.T., 2014. Active vision in marmosets: a model system for visual neuroscience. *J. Neurosci.* 34, 1183–1194.
- Montemurro, N., Herbet, G., Duffau, H., 2016. Right cortical and axonal structures eliciting ocular deviation during electrical stimulation mapping in awake patients. *Brain Topogr.* 29.
- Monteon, J.A., Constantin, A.G., Wang, H., Martinez-Trujillo, J., Crawford, J.D., 2010. Electrical stimulation of the frontal eye fields in the head-free macaque evokes kinematically normal 3D gaze shifts. *J. Neurophysiol.* 104, 3462–3475.
- Monteon, J.A., Wang, H., Martinez-Trujillo, J., Crawford, J.D., 2013. Frames of reference for eye-head gaze shifts evoked during frontal eye field stimulation. *EJNS* 37, 1754–1765.
- Morrow, M., Sharpe, J., 1995. Deficits of smooth-pursuit eye movement after unilateral frontal lobe lesions. *Ann. Neurol.* 37, 443–451.
- Moschovakis, A.K., Gregoriou, G.G., Ugolini, G., Doldan, M., Graf, W., Guldin, W., Hadjilimitrakis, K., Savaki, H.E., 2004. Oculomotor areas of the primate frontal lobes: a transneuronal transfer of rabies virus and [14C]-2-deoxyglucose functional imaging study. *J. Neurosci.* 24, 5726–5740.
- Mota, B., Herculano-Houzel, S., 2015. Brain structure. Cortical folding scales universally with surface area and thickness, not number of neurons. *Science* 349, 74–77.
- Mott, F.W., Halliburton, W.D., 1908. Localisation of function in the lemur's brain. *Proc. R. Soc. Lond.* 80, 136–147.
- Mott, F.W., Schäfer, E.A., 1890. On associated eye-movements produced by cortical faradization of the monkey's brain. *Brain* 13, 165–173.
- Mott, F.W., Schuster, E., Halliburton, W.D., 1910. Cortical lamination and localisation in the brain of the marmoset. *Proc. R. Soc. Lond.* 82, 124–134.
- Munoz, D.P., Everling, S., 2004. Look away: the anti-saccade task and the voluntary control of eye movement. *Nat. Rev. Neurosci.* 5, 218–228.
- Müri, R., Hess, C., Meienberg, O., 1991. Transcranial stimulation of the human frontal eye field by magnetic pulses. *Exp. Brain Res.* 86, 219–223.
- Neggers, S.F.W., Huijbers, W., Vrijlandt, C., Vlaskamp, B.N.S., Schutter, D.J.L.G., Kenemans, J., 2007. TMS pulses on the frontal eye fields break coupling between visuospatial attention and eye movements. *J. Neurophysiol.* 98, 2765–2778.
- Neggers, S.F.W., Diepen, R.M., van Zandbelt, B.B., Vink, M., Mandl, R.C.W., Gutteling, T.P., 2012. A functional and structural investigation of the human fronto-basal volitional saccade network. *PLoS One* 7, e29517.
- Neggers, S.F., Zandbelt, B.B., Schall, M.S., Schall, J.D., 2015. Comparative diffusion tractography of corticostriatal motor pathways reveals differences between humans and macaques. *J. Neurophysiol.* 113, 2164–2172.
- Nelson, M.J., Boucher, L., Logan, G.D., Palmeri, T.J., Schall, J.D., 2010. Nonindependent and nonstationary response times in stopping and stepping saccade tasks. *Atten. Percept. Psychophys.* 72, 1913–1929.
- Nieuwenhuys, R., 2013. The myeloarchitectonic studies on the human cerebral cortex of the Vogt-Vogt school, and their significance for the interpretation of functional neuroimaging data. *Brain Struct. Funct.* 218, 303–352.

- Nieuwenhuys, R., Broere, C.A., Cerliani, L., 2015. A new myeloarchitectonic map of the human neocortex based on data from the Vogt–Vogt school. *Brain Struct. Funct.* 220, 2551–2573.
- Olk, B., Chang, E., Kingstone, A., Ro, T., 2006. Modulation of antisaccades by transcranial magnetic stimulation of the human frontal eye field. *Cereb. Cortex* 16, 76–82.
- Ono, M., Kubik, S., Abernathy, C.D., 1990. *Atlas of the Cerebral Sulci*. Thieme Medical Publishers, New York.
- Owen, R., 1900. *Descriptive and Illustrated Catalogue of the Physiological Series of Comparative Anatomy Contained in the Museum of the Royal College of Surgeons of England*. Taylor & Francis, London.
- Palmer, S.M., Rosa, M.G.P., 2006. Quantitative analysis of the corticocortical projections to the middle temporal area in the marmoset monkey: evolutionary and functional implications. *Cereb. Cortex* 16, 1361–1375.
- Passingham, R., 2009. How good is the macaque monkey model of the human brain? *Curr. Opin. Neurobiol.* 19, 6–11.
- Paus, T., 1996. Location and function of the human frontal eye-field: a selective review. *Neuropsychologia* 34, 475–483.
- Paxinos, G., Watson, C., Petrides, M., Rosa, M., Tokuno, H., 2012. *The Marmoset Brain in Stereotaxic Coordinates*. Elsevier.
- Penfield, W., Boldrey, E., 1937. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* 60, 389–443.
- Penfield, W., Rasmussen, T., 1950. *The Cerebral Cortex of Man; a Clinical Study of Localization of Function*.
- Percheron, G., François, C., Pouget, P., 2015. What makes a frontal area of primate brain the frontal eye field? *Front. Integr. Neurosci.* 9, 33.
- Perelman, P., Johnson, W.E., Roos, C., Seuánez, H.N., Horvath, J.E., Moreira, M.A., Kessing, B., Pontius, J., Roelke, M., Rumpler, Y., Schneider, M.P., Silva, A., O'Brien, S.J., Pecon-Slattery, J., 2011. A molecular phylogeny of living primates. *PLoS Genet.* 7 (3), e1001342.
- Petit, L., Clark, V.P., Ingeholm, J., Haxby, J.V., 1997. Dissociation of saccade-related and pursuit-related activation in human frontal eye fields as revealed by fMRI. *J. Neurophysiol.* 77, 3386–3390.
- Petit, L., Dubois, S., Tzourio, N., DeJardin, S., Crivello, F., Michel, C., Etard, O., Denise, P., Roucoux, A., Mazoyer, B., 1999. PET study of the human foveal fixation system. *Hum. Brain Mapp.* 8, 28–43.
- Pierrot-Deseilligny, C., 1994. Saccade and smooth-pursuit impairment after cerebral hemispheric lesions. *Eur. Neurol.* 34, 121–134.
- Premereur, E., Janssen, P., Vanduffel, W., 2015. Effector specificity in macaque frontal and parietal cortex. *J. Neurosci.* 35, 3446–3459.
- Preuss, T., Goldman-Rakic, P., 1991. Myelo- and cytoarchitecture of the granular frontal cortex and surrounding regions in the strepsirrhine primate Galago and the anthropoid primate *Macaca*. *J. Comp. Neurol.* 310, 429–474.
- Preuss, T.M., Stepniewska, I., Kaas, J.H., 1996. Movement representation in the dorsal and ventral premotor areas of owl monkeys: a microstimulation study. *J. Comp. Neurol.* 371, 649–676.
- Pribram, K.H., 1955. Lesions of “frontal eye fields” and delayed response of baboons. *J. Neurophysiol.* 18, 105–112.
- Rasmussen, T., Penfield, W., 1947. Further studies of the sensory and motor cerebral cortex of man. *Federation Proceedings*, pp. 452–460.
- Remple, M.S., Reed, J.L., Stepniewska, I., Kaas, J.H., 2006. Organization of frontoparietal cortex in the tree shrew (*Tupaia belangeri*). I. architecture, microelectrode maps, and corticospinal connections. *J. Comp. Neurol.* 497, 133–154.
- Reser, D.H., Burman, K.J., Yu, H.-H., Chaplin, T.A., Richardson, K.E., Worthy, K.H., Rosa, M.G.P., 2013. Contrasting patterns of cortical input to architectural subdivisions of the area 8 complex: a retrograde tracing study in marmoset monkeys. *Cereb. Cortex* 23, 1901–1922.
- Rivaud, S., Müri, R., Gaymard, B., Vermersch, A., Pierrot-Deseilligny, C., 1994. Eye movement disorders after frontal eye field lesions in humans. *Exp. Brain Res.* 102, 110–120.
- Rizzolatti, G., Arbib, M.A., 2002. Language within our grasp. In: Cacioppo, J.T., et al. (Eds.), *Foundations in Social Neuroscience*. MIT Press, Cambridge, Mass.
- Ro, T., Cheifet, S., Ingle, H., Shoup, R., Rafal, R., 1999. Localization of the human frontal eye fields and motor hand area with transcranial magnetic stimulation and magnetic resonance imaging. *Neuropsychologia* 37, 225–231.
- Robinson, D.A., Fuchs, A.F., 1969. Eye movements evoked by stimulation of frontal eye fields. *J. Neurophysiol.* 32, 637–648.
- Rogers, L., Stafford, D., Ward, J., 1993. Head cocking in galagos. *Anim. Behav.* 45, 943–952.
- Rohlfing, T., Kroenke, C.D., Sullivan, E.V., Dubach, M.F., Bowden, D.M., Grant, K.A., Pfefferbaum, A., 2012. The INIA19 template and neuroMaps atlas for primate brain image parcellation and spatial normalization. *Front. Neuroinform.* 6, 27.
- Rosa, M., Soares, J., Fiorani Jr, M., Gattass, R., 1993. Cortical afferents of visual area MT in the *Cebus* monkey: possible homologies between New and Old World monkeys. *Vis. Neurosci.* 10, 827–855.
- Rosa, M.G.P., Palmer, S.M., Gamberini, M., Burman, K.J., Yu, H.-H., Reser, D.H., Bourne, J.A., Tweedale, R., Galletti, C., 2009. Connections of the dorsomedial visual area: pathways for early integration of dorsal and ventral streams in extrastriate cortex. *J. Neurosci.* 29, 4548–4563.
- Rosano, C., Krisky, C.M., Welling, J.S., Eddy, W.F., Luna, B., Thulborn, K.R., Sweeney, J.A., 2002. Pursuit and saccadic eye movement subregions in human frontal eye field: a high-resolution fMRI investigation. *Cereb. Cortex* 12, 107–115.
- Rosano, C., Sweeney, J.A., Melchitzky, D.S., Lewis, D.A., 2003. The human precentral sulcus: chemoarchitecture of a region corresponding to the frontal eye fields. *Brain Res.* 972, 16–30.
- Rosati, A.G., Hare, B., 2009. Looking past the model species: diversity in gaze-following skills across primates. *Curr. Opin. Neurobiol.* 19, 45–51.
- Russell, J.R., 1894. An experimental investigation of eye movements. *J. Physiol.* 17, 1.
- Sajad, A., Sadeh, M., Keith, G.P., Yan, X., Wang, H., Crawford, J.D., 2015. Visual-motor transformations within frontal eye fields during head-unrestrained gaze shifts in the monkey. *Cereb. Cortex* 25, 3932–3952.
- Sakamoto, K., Sawada, K., Fukunishi, K., Noritaka, I., Sakata-Haga, H., Yoshihiro, F., 2014. Postnatal change in sulcal length asymmetry in cerebrum of cynomolgus monkeys (*Macaca fascicularis*). *Anat. Rec.* 297, 200–207.
- Saleem, K.S., Logothetis, N.K., 2012. *A Combined MRI and Histology Atlas of the Rhesus Monkey Brain in Stereotaxic Coordinates*. Academic Press.
- Sallet, J., Mars, R.B., Noonan, M.P., Neubert, F.X., Jbabdi, S., O'Reilly, J.X., Filippini, N., Thomas, A.G., Rushworth, M.F., 2013. The organization of dorsal frontal cortex in humans and macaques. *J. Neurosci.* 33, 12255–12274.
- Sanides, F., 1970. Functional architecture of motor and sensory cortices in primates in the light of a new concept of neocortex evolution. In: Noback, C.R., Montagna, W. (Eds.), *The Primate Brain*. Appleton-Century-Crofts., New York, pp. 137–208.
- Sarkissov, S., Filimonoff, I., Kononowa, E., Preobraschenskaja, I., Kukuev, L., 1955. *Atlas of the Cytoarchitectonics of the Human Cerebral Cortex*. Medgiz, Moscow.
- Savaki, H.E., Gregoriou, G.G., Bakola, S., Moschovakis, A.K., 2015. Topography of visuomotor parameters in the frontal and premotor eye fields. *Cereb. Cortex* 25, 3095–3106.

- Schall, J.D., 1991. Neuronal activity related to visually guided saccadic eye movements in the supplementary motor area of rhesus monkeys. *J. Neurophysiol.* 66, 530–558.
- Schall, J.D., 1997. Visuomotor areas of the frontal lobe. In: Rockland, K.S., Kaas, J.H., Peters, A. (Eds.), *Extrastriate Cortex in Primates*. Springer, Boston, MA, US, pp. 527–638.
- Schall, J.D., 2015. Visuomotor functions in the frontal lobe. *Annu. Rev. Vis. Sci.* 1, 469–498.
- Schall, J., Boucher, L., 2007. Executive control of gaze by the frontal lobes. *Cogn. Affect. Behav. Neurosci.* 7, 396–412.
- Schall, J.D., Morel, A., King, D.J., Bullier, J., 1995. Topography of visual cortex connections with frontal eye field in macaque: convergence and segregation of processing streams. *J. Neurosci.* 15, 4464–4487.
- Schiller, P., True, S., Conway, J., 1980. Deficits in eye movements following frontal eye-field and superior colliculus ablations. *J. Neurophysiol.* 44, 1175–1189.
- Schiller, P., Sandell, J., Maunsell, J., 1987. The effect of frontal eye field and superior colliculus lesions on saccadic latencies in the rhesus monkey. *J. Neurophysiol.* 57, 1033–1049.
- Schlag, J., Schlag-Rey, M., 1987. Evidence for a supplementary eye field. *J. Neurophysiol.* 57, 179–200.
- Schmitt, O., Modersitzki, J., Heldmann, S., Wirtz, S., Hömke, L., Heide, W., Kömpf, D., Wree, A., 2005. Three-dimensional cytoarchitectonic analysis of the posterior bank of the human precentral sulcus. *Anat. Embryol.* 210, 387–400.
- Shepherd, S.V., 2010. Following gaze: gaze-following behavior as a window into social cognition. *Front. Integr. Neurosci.* 4, 5.
- Shepherd, S.V., Platt, M.L., 2006. Noninvasive telemetric gaze tracking in freely moving socially housed prosimian primates. *Methods* 38, 185–194.
- Shepherd, S.V., Steckenfinger, S.A., Hasson, U., Ghazanfar, A.A., 2010. Human-monkey gaze correlations reveal convergent and divergent patterns of movie viewing. *Curr. Biol.* 20, 649–656.
- Sherwood, C.C., Broadfield, D.C., Holloway, R.L., Gannon, P.J., Hof, P.R., 2003. Variability of broca's area homologue in African great apes: implications for language evolution. *Anat. Rec.* 271, 276–285.
- Simonyan, K., 2014. The laryngeal motor cortex: its organization and connectivity. *Curr. Opin. Neurobiol.* 28, 15–21.
- Smith, W.K., 1949. The frontal eye fields. In: Bucy, P.C. (Ed.), *The Precentral Motor Cortex*. University of Illinois Press.
- Sommer, M., Tehovnik, E., 1997. Reversible inactivation of macaque frontal eye field. *Exp. Brain Res.* 116, 229–249.
- Song, J.H., McPeck, R.M., 2010. Roles of narrow- and broad-spiking dorsal premotor area neurons in reach target selection and movement production. *J. Neurophysiol.* 103, 2124–2138.
- Spatz, W., Tigges, J., 1972. Experimental-anatomical studies on the “middle temporal visual area (MT)” in primates. I. Efferent cortico-cortical connections in the marmoset *Callithrix jacchus*. *J. Comp. Neurol.* 146, 451–464.
- Squire, R.F., Noudoost, B., Schafer, R.J., Moore, T., 2013. Prefrontal contributions to visual selective attention. *Annu. Rev. Neurosci.* 36, 451–466.
- Stahl, J.S., 1999. Amplitude of human head movements associated with horizontal saccades. *Exp. Brain Res.* 126, 41–54.
- Stanton, G.B., Deng, S.Y., Goldberg, M.E., McMullen, N.T., 1989. Cytoarchitectural characteristic of the frontal eye fields in macaque monkeys. *J. Comp. Neurol.* 282, 415–427.
- van der Steen, J., Russell, I., James, G., 1986. Effects of unilateral frontal eye-field lesions on eye-head coordination in monkey. *J. Neurophysiol.* 55, 696–714.
- Stepniewska, I., Preuss, T.M., Kaas, J.H., 1993. Architectonics, somatotopic organization, and ipsilateral cortical connections of the primary motor area (M1) of owl monkeys. *J. Comp. Neurol.* 330, 238–271.
- Stone, J., Johnston, E., 1981. The topography of primate retina: a study of the human, bushbaby, and new- and old-world monkeys. *J. Comp. Neurol.* 196, 205–223.
- Striedter, G.F., Srinivasan, S., Monuki, E.S., 2015. Cortical folding: when, where, how, and why? *Annu. Rev. Neurosci.* 38, 291–307.
- Sun, T., Hevner, R.F., 2014. Growth and folding of the mammalian cerebral cortex: from molecules to malformations. *Nat. Rev. Neurosci.* 15, 217–232.
- Sussman, R.W., Tab Rasmussen, D., Raven, P.H., 2013. Rethinking primate origins again. *Am. J. Primatol.* 75, 95–106.
- Suzuki, H., Azuma, M., 1983. Topographic studies on visual neurons in the dorsolateral prefrontal cortex of the monkey. *Exp. Brain Res.* 53, 47–58.
- Tallinen, T., Chung, J.Y., Rousseau, F., Girard, N., Lefèvre, J., Mahadevan, L., 2016. On the growth and form of cortical convolutions. *Nat. Phys.* 12.
- Tanaka, M., Lisberger, S.G., 2002. Role of arcuate frontal cortex of monkeys in smooth pursuit eye movements. I. basic response properties to retinal image motion and position. *J. Neurophysiol.* 87, 2684–2699.
- Tehovnik, E.J., Sommer, M.A., Chou, I.H., Slocum, W.M., Schiller, P.H., 2000. Eye fields in the frontal lobes of primates. *Brain Res. Brain Res. Rev.* 32, 413–448.
- Thakkar, K.N., van den Heiligenberg, F.M.Z., Kahn, R.S., Neggers, S.F.W., 2014. Frontal-subcortical circuits involved in reactive control and monitoring of gaze. *J. Neurosci.* 34, 8918–8929.
- Thompson, K.G., Bichot, N.P., Sato, T.R., 2005. Frontal eye field activity before visual search errors reveals the integration of bottom-up and top-down salience. *J. Neurophysiol.* 93, 337–351.
- Thurtell, M., Mohamed, A., Lüders, H., Leigh, R., 2009. Evidence for three-dimensional cortical control of gaze from epileptic patients. *J. Neurol. Neurosurg. Psychiatry* 80, 683–685.
- Tian, J., Lynch, J., 1995. Slow and saccadic eye movements evoked by microstimulation in the supplementary eye field of the *Cebus* monkey. *J. Neurophysiol.* 74, 2204–2210.
- Tian, J., Lynch, J., 1996. Corticocortical input to the smooth and saccadic eye movement subregions of the frontal eye field in *Cebus* monkeys. *J. Neurophysiol.* 76, 2754–2771.
- Tian, J., Lynch, J., 1997. Subcortical input to the smooth and saccadic eye movement subregions of the frontal eye field in *Cebus* monkey. *J. Neurosci.* 17, 9233–9247.
- Tigges, J., Tigges, M., Ansel, S., Cross, N., Letbetter, W., McBride, R., 1981. Areal and laminar distribution of neurons interconnecting the central visual cortical areas 17, 18, 19, and MT in squirrel monkey (*Saimiri*). *J. Comp. Neurol.* 202, 539–560.
- Tomasello, M., Hare, B., Lehmann, H., Call, J., 2007. Reliance on head versus eyes in the gaze following of great apes and human infants: the cooperative eye hypothesis. *J. Hum. Evol.* 52, 314–320.
- Tomlinson, R.D., Bahra, P.S., 1986. Combined eye-head gaze shifts in the primate. I. Metrics. *J. Neurophysiol.* 56, 1542–1557.
- Tu, T.A., Keating, E.G., 2000. Electrical stimulation of the frontal eye field in a monkey produces combined eye and head movements. *J. Neurophysiol.* 84, 1103–1106.
- Vanduffel, W., Fize, D., Mandeville, J., Nelissen, K., Van Hecke, P., Rosen, B., Tootell, R., Orban, G., 2001. Visual motion processing investigated using contrast agent-enhanced fMRI in awake behaving monkeys. *Neuron* 32, 565–577.
- Vernet, M., Quentin, R., Chanes, L., Mitsumasa, A., Valero-Cabré, A., 2014. Frontal eye field, where art thou? Anatomy, function, and non-invasive manipulation of frontal regions involved in eye movements and associated cognitive operations. *Front. Integr. Neurosci.* 8, 66.
- Vogt, C., Vogt, O., 1926. Die vergleichend-architektonische und die vergleichend-reizphysiologische Felderung der Großhirnrinde unter besonderer Berücksichtigung der menschlichen. *Naturwissenschaften* 14, 1190–1194.
- Wagman, I.H., Werman, R., Feldman, D.S., Sugarman, L., Krieger, H.P., 1957. The oculomotor effects of cortical and subcortical stimulation in the monkey. *J. Neuropathol. Exp. Neurol.* 16, 269–278.

- Wagman, I.H., Krieger, H., Bender, M., 1958. Eye movements elicited by surface and depth stimulation of the occipital lobe of *Macaque mulatta*. *J. Comp. Neurol.* 109, 169–193.
- Wagman, I.H., Krieger, H.P., Papatheodorou, C.A., Bender, M.B., 1961. Eye movements elicited by surface and depth stimulation of the frontal lobe of *Macaque mulatta*. *J. Comp. Neurol.* 117, 179–188.
- Walker, A.E., 1940. A cytoarchitectural study of the prefrontal area of the macaque monkey. *J. Comp. Neurol.* 73, 59–86.
- Wardak, C., Ibos, G., Duhamel, J.-R., Olivier, E., 2006. Contribution of the monkey frontal eye field to covert visual attention. *J. Neurosci.* 26, 4228–4235.
- Wardak, C., Vanduffel, W., Orban, G.A., 2010. Searching for a salient target involves frontal regions. *Cereb. Cortex* 20, 2464–2477.
- Watanabe-Sawaguchi, K., Kubota, K., Arikuni, T., 1991. Cytoarchitecture and intrafrontal connections of the frontal cortex of the brain of the hamadryas baboon (*Papio hamadryas*). *J. Comp. Neurol.* 311, 108–133.
- Webb, S., Kaas, J., 1976. The sizes and distribution of ganglion cells in the retina of the owl monkey. *Aotus trivirgatus*. *Vis. Res.* 16, 1247–1254.
- Weller, R.E., Kaas, J.H., 1987. Subdivisions and connections of inferior temporal cortex in owl monkeys. *J. Comp. Neurol.* 256, 137–172.
- Weller, R., Wall, J., Kaas, J., 1984. Cortical connections of the middle temporal visual area (MT) and the superior temporal cortex in owl monkeys. *J. Comp. Neurol.* 228, 81–104.
- Wessel, K., Kömpf, D., 1991. Transcranial magnetic brain stimulation: lack of oculomotor response. *Exp. Brain Res.* 86, 216–218.
- Wikler, K., Rakic, P., 1990. Distribution of photoreceptor subtypes in the retina of diurnal and nocturnal primates. *J. Neurosci.* 10, 3390–3401.
- Wolin, L., Massopust Jr., L., 1967. Characteristics of the ocular fundus in primates. *J. Anat.* 101, 693–699.
- Woollard, H., 1927. The differentiation of the retina in the primates. *Proc. Zool. Soc. Lond.* 97, 1–18.
- Wright, P.C., 1989. The nocturnal primate niche in the New World. *J. Hum. Evol.* 18, 635–658.
- Wu, C., Bichot, N., Kaas, J., 2000. Converging evidence from microstimulation, architecture, and connections for multiple motor areas in the frontal and cingulate cortex of prosimian primates. *J. Comp. Neurol.* 423, 140–177.
- Yamamoto, J., Ikeda, A., Satow, T., Matsushashi, M., Baba, K., Yamane, F., Miyamoto, S., Mihara, T., Hori, T., Taki, W., Hashimoto, N., Shibasaki, H., 2004. Human eye fields in the frontal lobe as studied by epicortical recording of movement-related cortical potentials. *Brain* 127, 873–887.
- Zilles, K., Amunts, K., 2010. Centenary of Brodmann's map—Conception and fate. *Nat. Rev. Neurosci.* 11, 139–145.