

A Preparatory Cranial Potential for Saccadic Eye Movements in Macaque Monkeys

Steven P. Errington¹ and Jeffrey D. Schall²

¹Biosciences Institute, Newcastle University, Newcastle-upon-Tyne NE2 4HH, United Kingdom and ²Centre for Vision Research, Centre for Integrative & Applied Neuroscience, Vision: Science to Applications Program, Connected Minds, Department of Biology, York University, Toronto, Ontario M3J 1P3, Canada

Abstract

Response preparation is accomplished by gradual accumulation in neural activity until a threshold is reached. In humans, such a preparatory signal, referred to as the lateralized readiness potential (LRP), can be observed in the EEG over sensorimotor cortical areas before execution of a voluntary movement. Although well described for manual movements, less is known about preparatory EEG potentials for saccadic eye movements in humans and nonhuman primates. Hence, we describe a LRP over the frontolateral cortex in macaque monkeys. Homologous to humans, we observed lateralized electrical potentials ramping before the execution of both rewarded and nonrewarded contralateral saccades. This potential parallels the neural spiking of saccadic movement neurons in the frontal eye field (FEF), suggesting that it may offer a noninvasive correlate of intracortical spiking activity. However, unlike neural spiking in the FEF, polarization in frontolateral channels did not distinguish between saccade generation and inhibition. These findings provide new insights into noninvasive electrophysiological signatures of saccadic preparation in nonhuman primates, highlighting the potential of EEG measures to bridge invasive neural recordings and noninvasive studies of eye movement control in humans.

Key words: EEG; event-related potential; macaque; readiness potential; saccade

Significance Statement

Exploring the neural processes that underpin movement preparation is central to linking brain activity with motor behavior. This study describes a lateralized readiness potential (LRP) for saccades observed over the frontolateral cortex of macaque monkeys, analogous to human EEG signals previously observed during movement preparation. These observations set the foundation for future work to understand the neural generators of the LRP and offer a noninvasive tool to explore eye movement control. These insights could inform clinical and technological applications involving eye movement monitoring and control.

Introduction

Intentional control over our actions emerges from preparatory processes that ensure coordinated and purposeful interactions with our surroundings. This preparatory activity manifests neurally through a slow buildup in activity, which accumulates over time (Tanji and Evarts, 1976; Weinrich et al., 1984; Riehle and Requin, 1989; Hanes and Schall, 1996). In humans, this process has been well described through the lateralized readiness potential (LRP; de Jong et al., 1988; Gratton et al., 1988; Smulders et al., 2012). The LRP is a gradual buildup of electrical polarization observed in EEG signals over the motor cortex. This potential occurs 100 or 200 ms before a voluntary movement is executed and is thought to reflect the preparatory processes in the motor cortex for generating an action (Deecke et al., 1976).

Received Jan. 16, 2025; accepted March 2, 2025.

The authors declare no competing financial interests.

Author contributions: S.P.E. and J.D.S. designed research; J.D.S. performed research; S.P.E. analyzed data; S.P.E. and J.D.S. wrote the paper.

This work was supported by National Eye Institute R01-EY019882 and P30-EY08126 and by Natural Sciences and Engineering Research Council of Canada (RGPIN-2022-04592) and Canada Research Chairs.

Correspondence should be addressed to Jeffrey D. Schall at schalljd@yorku.ca.

Copyright © 2025 Errington and Schall. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International license, which permits unrestricted use, distribution and reproduction in any medium provided that the original work is properly attributed.

Although the LRP is usually described in the context of a voluntary body movement, such as an arm or leg, similar lateralized EEG components have been observed during the preparation of saccadic eye movements (Kurtzberg and Vaughan, 1982; Brickett et al., 1984; Balaban and Weinstein, 1985; Thickbroom and Mastaglia, 1985; Moster and Goldberg, 1990; Evdokimidis et al., 1991, 1992; Everling et al., 1997a,b). Interestingly, these noninvasive event-related potentials (ERPs) show similar dynamics to spiking activity observed in invasive neurophysiological studies of the macaque frontal eye field (FEF)—a region in the frontal cortex of the brain that plays a crucial role in the preparation and execution of saccadic eye movements (Bruce and Goldberg, 1985; Hanes et al., 1998). FEF neurons show a specific type of ramping activity known as “ramp-to-threshold” which is interrupted when saccades are inhibited (Hanes and Schall, 1996; Hanes et al., 1998). This movement-related activity occurs prior to both externally cued saccades (Bruce and Goldberg, 1985) and spontaneous, voluntary saccades (Sendhilnathan et al., 2021, but see Bizzi, 1968).

Previous work has demonstrated that monkeys have homologs of human cognitive ERP components, such as N2pc (Woodman et al., 2007; Cohen et al., 2009; Heitz et al., 2010; Purcell et al., 2013), contralateral delay activity (Reinhart et al., 2012), ERN/Pe (Godlove et al., 2011; Sajad et al., 2019), and N2/P3 (Sajad et al., 2022). These observations have helped establish animal models that can be used to investigate the neural mechanisms underlying these ERPs (Herrera et al., 2022, 2023, 2024). Here, we expand on this literature to describe a presaccadic LRP in EEG signals recorded over the frontolateral cortex.

Materials and Methods

Experimental models and subject details. Data were collected from one male bonnet macaque (Eu, *Macaca radiata*, 8.8 kg) and one female rhesus macaque (X, *Macaca mulatta*, 6.0 kg) performing a countermanding task (Hanes and Schall, 1995; Godlove et al., 2014). All procedures were approved by the Vanderbilt Institutional Animal Care and Use Committee in accordance with the United States Department of Agriculture and Public Health Service Policy on Humane Care and Use of Laboratory Animals.

Animal care and surgical procedures. Surgical details have been described previously (Godlove et al., 2011). Briefly, magnetic resonance images were acquired with a Philips Intera Achieva 3 T scanner using SENSE Flex-S surface coils placed above or below the animal's head. T1-weighted gradient-echo structural images were obtained with a 3D turbo field echo anatomical sequence (TR, 8.729 ms; 130 slices; 0.70 mm thickness). These images were used to ensure that Cilux recording chambers were placed in the correct area (Crist Instruments). Chambers were implanted normal to the cortex (Monkey Eu, 17°; Monkey X, 9°; relative to stereotaxic vertical) centered on the midline, 30 mm (Monkey Eu) and 28 mm (Monkey X) anterior to the interaural line.

EEG processing and data acquisition. EEG electrodes were placed over area of the skull approximating Cz, FCz, F3 and F4. Electrophysiology data were processed with unity-gain high-input impedance head stages (HST/32025-36P-TR, Plexon). All data were streamed to a single data acquisition system (MAP, Plexon). Time stamps of trial events were recorded at 500 Hz. Eye position data were streamed to the Plexon computer at 1 kHz using an EyeLink 1000 infrared eye-tracking system (SR Research).

Stop-signal task. The saccade stop-signal (countermanding) task utilized in this study has been widely used previously (Hanes and Schall, 1995; Hanes and Carpenter, 1999; Cabel et al., 2000; Colonius et al., 2001; Kornylow et al., 2003; Morein-Zamir and Kingstone, 2006; Walton and Gandhi, 2006; Thakkar et al., 2011, 2015; Godlove and Schall, 2016; Wattiez et al., 2016; Verbruggen et al., 2019). Briefly, trials were initiated when monkeys fixated on a central point. Following a variable period, the center of the fixation point was removed leaving an outline. At this point, a peripheral target was presented simultaneously on either the left or right hand of the screen. In this study, one target location was associated with a larger magnitude of fluid reward. The lower-magnitude reward ranged from 0 to 50% of the higher-magnitude reward amount. This proportion was adjusted to encourage the monkey to continue responding to both targets. The stimulus-response mapping of location-to-high reward changed across blocks of trials. Block length was adjusted to maintain performance at both targets, with the number of trials in each block determined by the number of correct trials performed. In most sessions, the block length was set at 10–30 correct trials. Erroneous responses led to repetitions of a target location, ensuring that monkeys did not neglect low-reward targets in favor of high-reward targets—a phenomenon demonstrated in previous implementations of asymmetrically rewarded tasks (Kawagoe et al., 1998).

In most of the trials, the monkey was required to make an eye movement toward this target (no-stop trials). However, in a proportion of trials, the center of the fixation point was reilluminated (stop-signal trials); this stop signal appeared at a variable time after the target had appeared (stop-signal delay; SSDs). An initial set of SSDs, separated by either 40 or 60 ms, were selected for each recording session. The delay was then manipulated through an adaptive staircasing procedure in which stopping difficulty was based on performance. When a subject failed to inhibit a response, the SSD was decreased by a random step to increase the likelihood of success on the next stop trial. Similarly, when subjects were successful in their inhibition, the SSD was increased to reduce the likelihood of success on the next stop trial. This procedure was employed to ensure that subjects failed to inhibit action on ~50% of all stop-signal trials. On no-stop trials, the monkey

was rewarded for making a saccade to the target. In stop-signal trials, the monkey was rewarded for withholding the saccade and maintaining fixation on the fixation spot. Following a correct response, an auditory tone was sounded 600 ms later and followed by a high- or low-fluid reward, depending on the stimulus–response mapping.

Data collection protocol. An identical daily recording protocol across monkeys and sessions was carried out. In each session, the monkey sat in an enclosed primate chair with their head restrained 45 cm from a CRT monitor (Dell P1130, background luminance of 0.10 cd/m²). The monitor had a refresh rate of 70 Hz, and the screen subtended 46 × 36° of the visual angle. Eye position data were collected at 1 kHz using an EyeLink 1000 infrared eye-tracking system (SR Research). This was streamed to a single data acquisition system (MAP, Plexon) and amalgamated with other behavioral and neurophysiological data. After advancing the electrode array to the desired depth, they were left for 3–4 h until recordings stabilized across contacts. This led to consistently stable recordings. Once these recordings stabilized, an hour of resting-state activity in near-total darkness was recorded. This was followed by the passive presentation of visual flashes followed by periods of total darkness in alternating blocks. Finally, the monkey then performed ~2,000–3,000 trials of the saccade-countermanding (stop-signal) task.

Bayesian modeling of stop-signal performance. As performance on the stop-signal task can be considered as the outcome of a race between a GO and STOP process, then a stop-signal reaction time (SSRT) can be calculated (Logan and Cowan, 1984). This value can be considered as the latency of the inhibitory process that interrupts movement preparation. SSRT was estimated using a Bayesian parametric approach (Matzke et al., 2013a,b). Compared with classical methods of calculating SSRT (integration-weighted method; Logan and Cowan, 1984), this approach allows for a distribution of SSRT to be derived by using the distribution of reaction times on no-stop trials and by considering reaction times on noncanceled trials as a censored no-stop response time (RT) distribution. Furthermore, this model also allows for the estimation of the probability of trigger failures for a given session (Matzke et al., 2017). Individual parameters were estimated for each session. The priors were bounded uniform distributions [μ_{Go} , μ_{Stop} , $U(0.001, 1,000)$; σ_{Go} , σ_{Stop} , $(1, 500)$; t_{Go} , t_{Stop} , $U(1, 500)$; pTF , $U(0,1)$]. The posterior distributions were estimated using Metropolis-within-Gibbs sampling, and we ran multiple (three) chains. We ran the model for 5,000 samples with a thinning of 5.

Results

Monkeys produced planned saccades to targets and inhibited them when instructed

We acquired 33,816 trials across 29 sessions from two macaques (Eu, 11,583; X, 22,233) performing the saccade stop-signal (countermanding) task (Fig. 1A). In the majority of these trials (~60%), monkeys were required to make a saccade to a target on the left- or right-hand side of the screen. Across all sessions, the median RT to left ($m = 267.7 \pm 6.8$ ms) targets was significantly slower than that to right ($m = 248.0 \pm 5.8$ ms) targets (Mann–Whitney U test, $z = 2.131$; $p = 0.033$). To account for these differences, we only included trials in which the RT was in a mutual range for both directions.

In a small proportion of trials, the appearance of a visual stop signal instructed the monkey to inhibit the planned saccade. Both monkeys exhibited typical sensitivity to the stop signal: firstly, response latencies on noncanceled (error) trials were faster than those on no-stop trials (Fig. 1B, top); secondly, the probability of failing to cancel and executing an erroneous saccade was greater at longer stop-signal delays (Fig. 1B, bottom). These two observations validated the assumptions of the independent race model (Logan and Cowan, 1984), allowing us to estimate the SSRT, the time needed to cancel to partially prepared saccade.

In addition to rewarded, goal-directed saccades (Fig. 1C, left), monkeys also generated spontaneous saccades (Fig. 1C, right) during the intertrial interval (ITI), when no visual stimuli were displayed and no rewards could be earned. Here, we limit our analyses to saccades in this period that shared similar kinematic characteristics to the goal-directed saccades: namely, we included saccades that were directed toward the left ($180 \pm 45^\circ$) or right ($0 \pm 45^\circ$) from their point of initiation, which exceeded an amplitude of 15° . Although nongoal-directed saccades exhibited higher variability in their characteristics, both types of saccades displayed notable similarities, allowing for comparison of neural signals between the two types.

ERPs over lateral frontal cortex ramp until saccade execution

ERPs were recorded with frontolateral electrodes, homologous to F3 and F4 in the human 10–20 system, during the stop-signal task (Fig. 1D). These contacts were located over the dorsal limb of the arcuate sulcus. Like the LRP reported in humans prior to a voluntary manual movement, we observed a progressive polarization of the EEG in trials in which a goal-direct saccade toward a target was correctly generated (Fig. 2A). This preparatory saccade potential shows a clear potential shift beginning ~300 ms prior to saccade onset, which reaches peak amplitude at the time of saccade execution.

Figure 2A displays the grand-average ERP waveforms for contralateral and ipsilateral saccades, plotted separately for electrode F3 and F4, locked on the time of saccade. A positively accumulating potential was observed prior to the execution of a saccade in the contralateral direction, and a negatively accumulating potential was found prior to the execution of a saccade in the ipsilateral direction (Fig. 2B; repeated-measure ANOVA; electrode × laterality interaction; $F_{(1, 28)} = 3,645.950$; $p < 0.001$). The pattern of polarization was apparent in individual trials (Fig. 2C). An ROC analysis

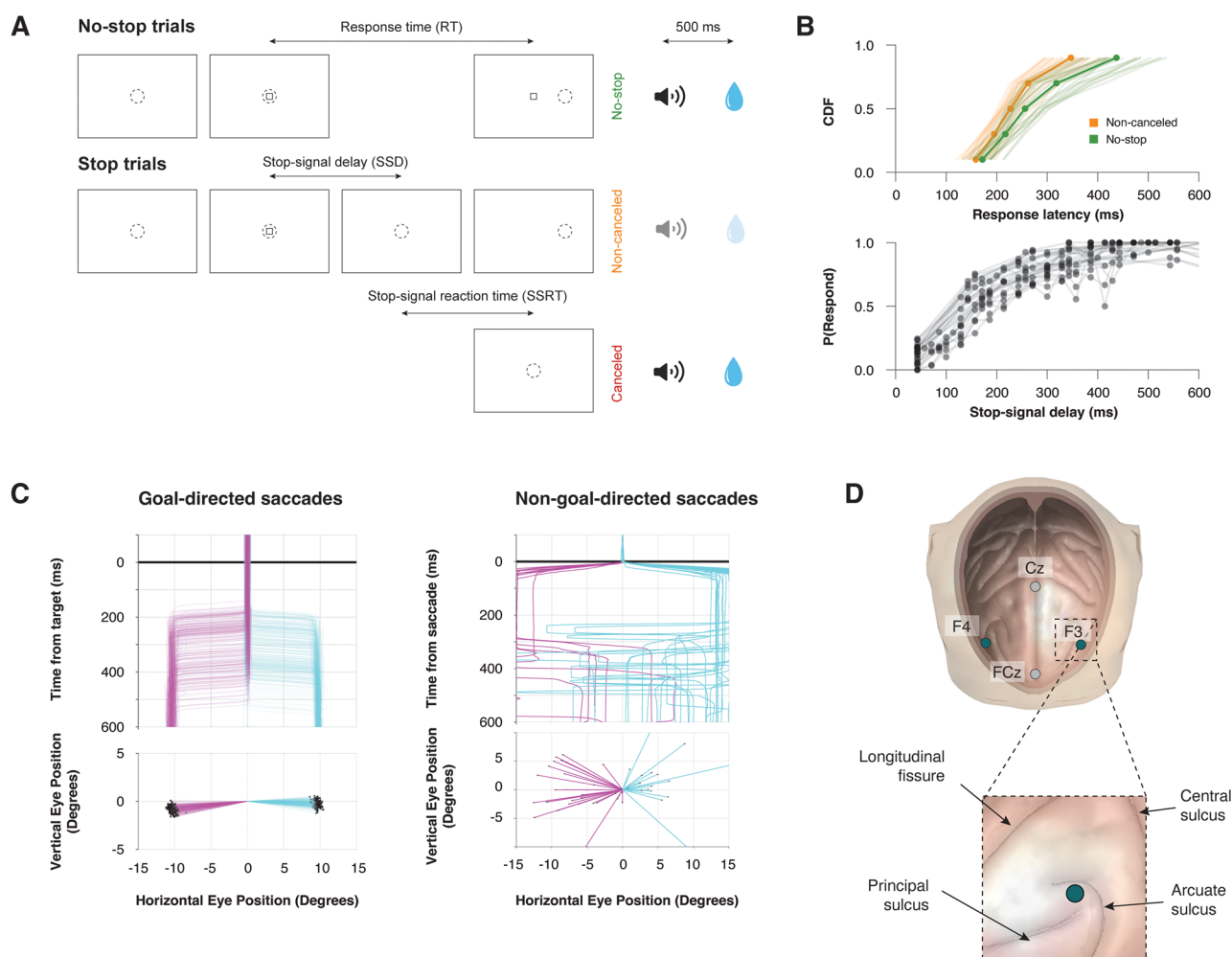


Figure 1. Experimental procedures. **A**, A saccade-countermanding task. Monkeys initiated trials by fixating on a central point. After a variable time, the center of the fixation point was extinguished. A peripheral target was presented simultaneously at one of two possible locations. On no-stop signal trials, monkeys were required to shift gaze to the target, whereupon after 600 ms, a high-pitched auditory feedback tone was delivered, and 600 ms later, fluid reward was provided. On stop-signal trials (~40% of trials), after the target appeared, the center of the fixation point was reilluminated after a variable stop-signal delay, which instructed the monkey to cancel the saccade in which case the same high-pitched tone was presented after a 1,500 ms hold time, then followed 600 ms later by fluid reward. Stop-signal delay was adjusted such that monkeys successfully canceled the saccade in ~50% of trials. In the remaining trials, monkeys made noncanceled errors which were followed after 600 ± 0 ms by a low-pitched tone, and no reward was delivered. Monkeys could not initiate trials earlier after errors. **B**, Countermanding behavior. Top, Cumulative distribution function of response latencies on no-stop (green) and noncanceled (yellow) trials. Response latencies on noncanceled trials were faster than those on no-stop trials. Bottom, Inhibition function plotting the probability of responding across stop-signal delays. **C**, Goal and nongoal-directed saccades. Monkeys made both leftward (magenta) and rightward (cyan) saccades with similar properties, in response to the target (goal-directed, left) and spontaneously (nongoal-directed, right). Examples are plotted from one representative example session. Goal-directed saccades are shown relative to a central fixation spot and aligned on the target onset. Nongoal-directed saccades are shown relative to the presaccade eye position, aligned on the time a saccadic eye movement was detected within the ITI. **D**, EEG electrode position. Monkeys were fitted with four EEG electrodes located over the central sulcus (Cz), the medial frontal cortex (FCz), and the frontolateral cortex (F3 and F4). The position of the F3/F4 electrode is estimated to lie over the FEF.

showed that polarization in both electrodes was larger for contralateral saccades, distinguishing this preferred direction from the onset of the preparatory polarization (one-way independent group t test; F3, $t_{(28)} = 22.254$; $p < 0.001$; F4, $t_{(28)} = 24.758$; $p < 0.001$).

Frontolateral ramping polarization varies with response latency

We observed frontolateral ramping polarization that varied with saccade response latency. Polarization aligned to the target onset revealed clear differences based on upcoming saccade time: trials with earlier saccades exhibited larger polarizations after the target in both electrode sites (Fig. 3A,B, left; repeated-measure ANOVA; F3, $F_{(1,28)} = 22.236$; $p < 0.001$; F4, $F_{(1,28)} = 56.042$; $p < 0.001$). However, polarization aligned to saccade execution showed mixed results. At F3, slower saccades were associated with higher polarization, whereas no significant differences were observed at F4 (Fig. 3A,B, right; repeated-measure ANOVA; F3, $F_{(1,28)} = 15.168$; $p < 0.001$; F4, $F_{(1,28)} = 1.191$; $p = 0.284$).

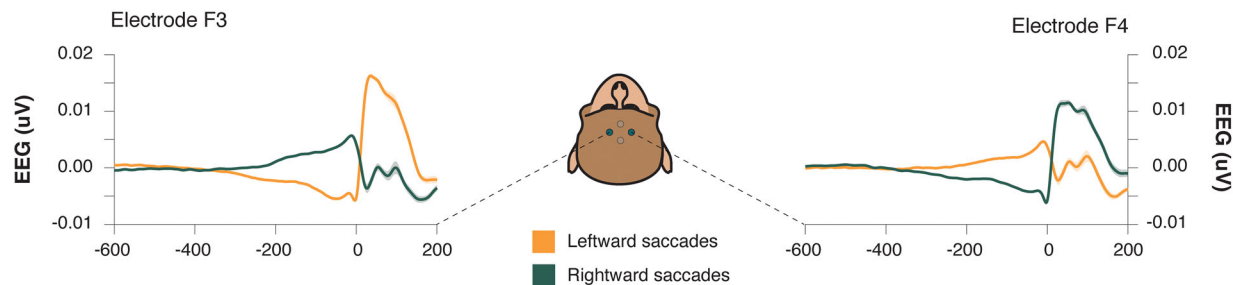
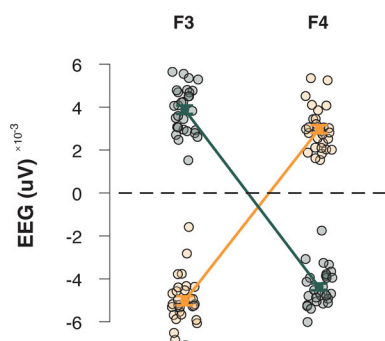
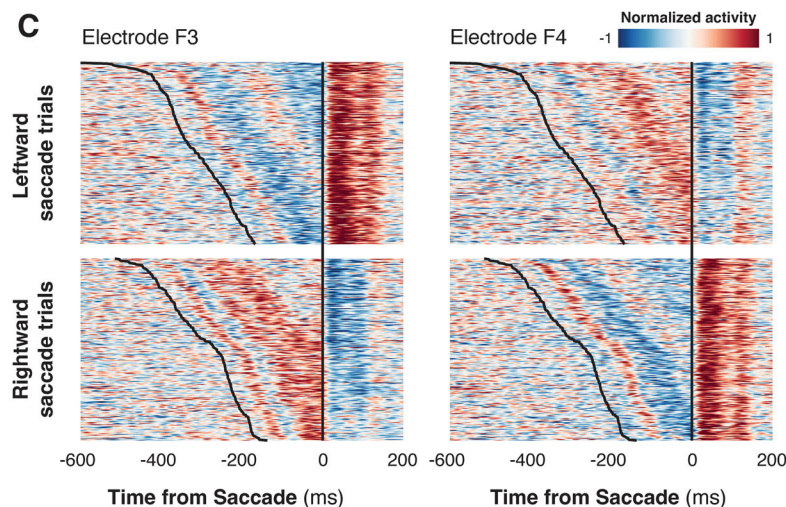
A Goal-directed saccades**B****C**

Figure 2. A LRP for goal-directed saccades. **A**, Trial-averaged ERPs from an example session for left (F3) and right (F4) frontolateral electrodes during leftward (orange) and rightward (green) goal-directed saccades. **B**, A scatterplot illustrating mean EEG amplitudes prior to the saccade at left (F3) and right (F4) frontolateral electrode sites, highlighting lateralization in saccadic activity. **C**, Heatmaps of normalized activity aligned within an example, representative session. Activity is aligned to saccade onset for left (F3) and right (F4) frontolateral electrodes, for leftward (top) and rightward (bottom) saccades.

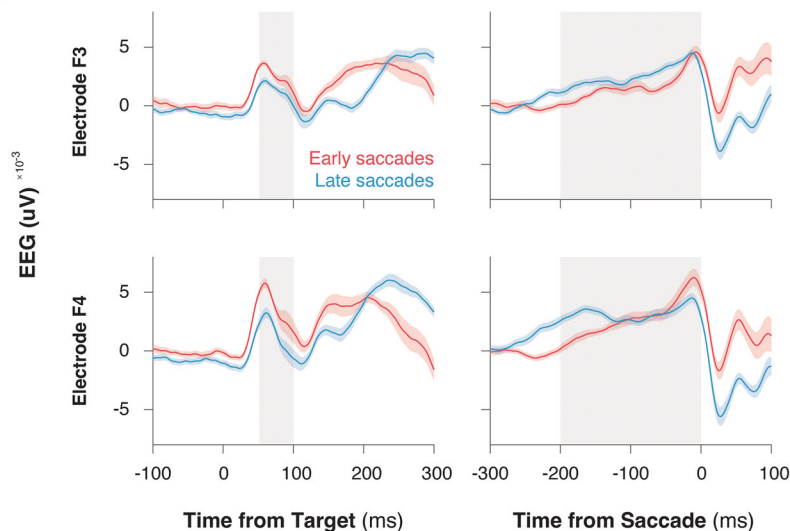
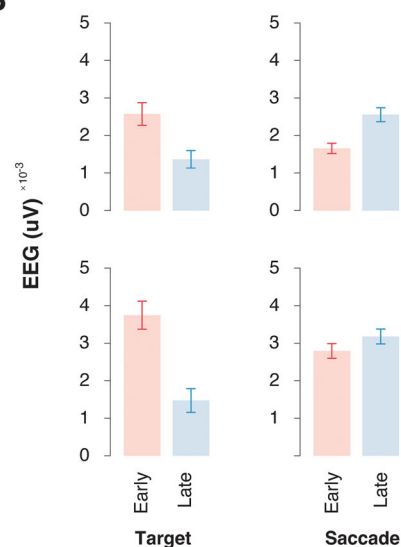
A**B**

Figure 3. Ramping of the LRP is modulated by response latency. **A**, The LRP observed at electrodes F3 and F4, aligned to the target onset (left) and saccade onset (right), for early saccades (red) and late saccades (blue). **B**, Bar plots comparing mean EEG amplitudes for early and late saccades during the target onset and saccade epochs. Error bars represent standard error of the mean (SEM).

Saccade readiness potential precedes nongoal-directed saccades

To understand the function of this preparatory potential, we considered three alternative hypotheses. First, if these preparatory potentials reflected goal-directed saccade planning processes specifically, then they should only be present for saccades to a cued target and not to other saccades that may have occurred during the session. Alternatively, if these signals are specific to self-initiated movement, then the signal should only be present during saccades that occur with no cues. Finally, if this signal is simply a saccade preparation signal, then it should be evident before both goal-directed and nongoal-directed saccades.

Here, we defined goal-directed saccades as eye movements that are directed toward the target—this target served as a cue to initiate the voluntary movement (Fig. 1C, left)—and nongoal-directed saccades were eye movements of approximately the same amplitude and direction that are uncued and not rewarded (Fig. 1C, right). These saccades were sampled from the ITI during which the monkey could move gaze *ad libitum* around the screen. No stimuli or other events occurred during this time. We observed saccades with such parameters in 26 out of 29 sessions.

We observed preparatory polarization in frontolateral electrodes during nongoal-directed saccades (Fig. 4A) that mirrored the preparatory polarization observed during goal-directed saccades (Fig. 2A): differential polarization began 300 ms prior to the saccade execution and was lateralized for contralateral saccades (repeated-measure ANOVA; electrode \times laterality interaction; $F_{(1, 25)} = 1,906.544$; $p < 0.001$). This suggests that the signal we observed in EEG is congruent with the saccade preparation hypothesis and is not sensitive to the motivation of the saccade.

ERPs over the frontolateral cortex do not distinguish between stopping and going

So far, we have demonstrated that ERPs over the frontolateral cortex ramp until the execution of a saccade, much like FEF neurons (Hanes and Schall, 1996; Hanes et al., 1998). However, earlier work has also demonstrated that FEF also contributes to response inhibition—the cancellation of a planned saccade (Hanes et al., 1998). This earlier work demonstrated that separate populations in the FEF are considered to contribute to the generation and inhibition of a saccadic eye movement.

First, we compared polarization between those trials in which movements were inhibited (canceled) and those in which movements were generated but would have been inhibited had a stop signal appeared (latency-matched no-stop trials). We limited our analyses to trials in the preferred direction for each electrode. Stopping occurs following a stop signal and is completed within the SSRT. Resultantly, if neural signals differentiate between going and stopping, it should occur within this timeframe. Figure 5A shows the grand-average ERP for no-stop and canceled trials. Although polarization appeared to differentiate between trial types ~ 200 ms after the stop signal, polarization during the STOP period for both F3 and F4 electrodes did not differentiate between trials in which a movement was generated or inhibited (Fig. 5A, right; one-way repeated-measure ANOVA; F3, $F_{(1, 28)} = 0.426$; $p = 0.519$; F4, $F_{(1, 28)} = 0.540$; $p = 0.469$).

However, although comparisons between these trial types are valid in the context of the race model, they are confounded by task design. Within our task, the stop signal was the reillumination of the central fixation spot; as such, signals on canceled trials are contaminated by visual artifact which was not present in no-stop trials. To address this, we compared polarization during the STOP period between noncanceled and canceled trials. While this approach is confounded by RT differences as formulated by the race model (Logan and Cowan, 1984), a visual stop signal is displayed in both trial types. Figure 5A shows the grand-average ERP for noncanceled trials and latency-matched no-stop trials. Regardless of this potential confound, we observed no significant difference between these trial types (Fig. 5B; one-way repeated-measure ANOVA; F3, $F_{(1, 28)} = 4.858$; $p = 0.036$; F4, $F_{(1, 28)} = 0.115$; $p = 0.737$). These findings suggest that frontolateral EEG may not be a useful index of saccade response inhibition.

A Non-goal-directed saccades

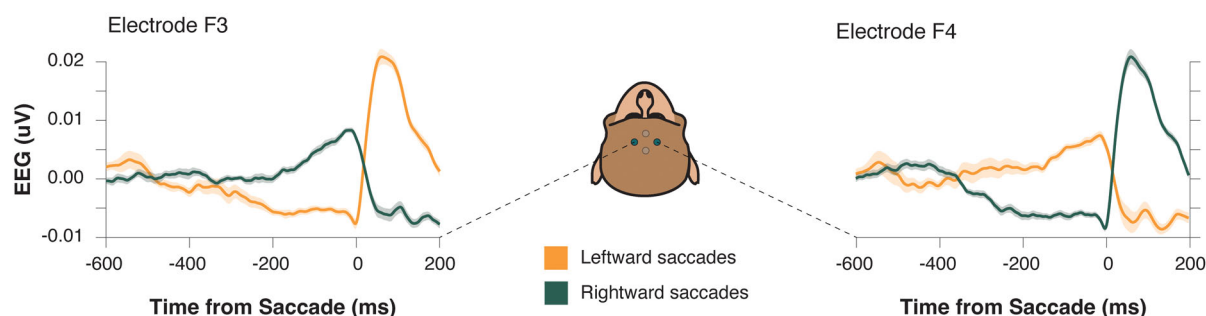


Figure 4. Preparatory activity occurs for nongoal-directed saccades. **A**, Trial-averaged ERPs from an example session for left (F3) and right (F4) frontolateral electrodes during leftward (orange) and rightward (green) nongoal-directed saccades. Shaded areas represent SEM.

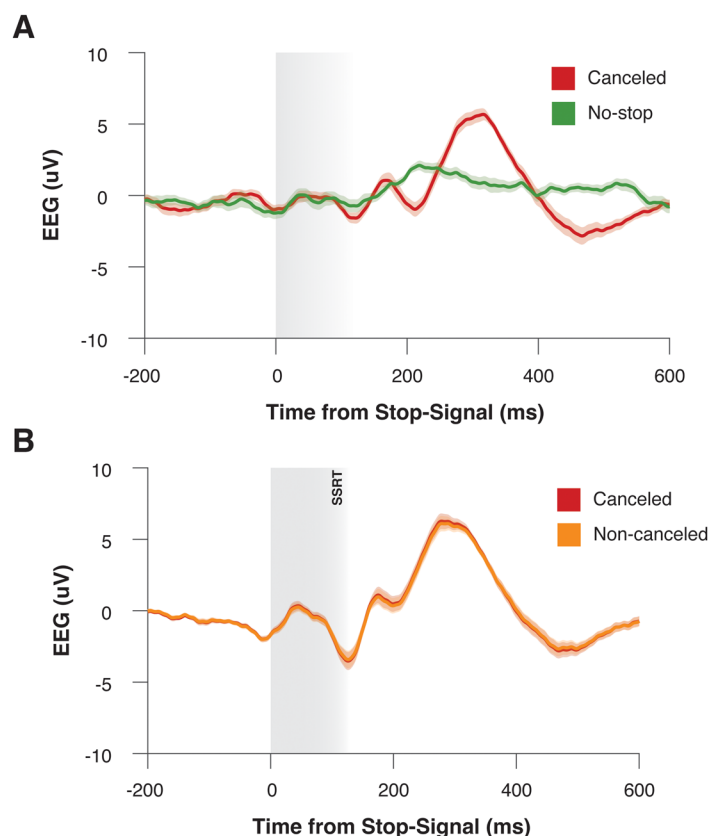


Figure 5. LRP does not index stopping. **A**, Trial-averaged ERPs from an example session, during instances of saccade generation (green) and saccade inhibition (red). Data are aligned on the time at which the stop signal appeared (in canceled trials) or would have appeared (on no-stop signal trials). Data are collapsed across both electrodes for the preferred saccade direction. Shaded areas represent SEM. **B**, Trial-averaged ERPs from an example session, during instances in which a saccade was successfully inhibited (red) or incorrectly generated (yellow) after the presentation of a stop signal. Data are aligned on the time at which the stop signal appeared and is collapsed across both electrodes for the preferred saccade direction. Shaded areas represent SEM.

Discussion

Summary of findings

In this study, we investigated saccadic eye movements in monkeys and made several key findings. We observed that monkeys were able to produce planned saccades to targets and could inhibit them when instructed. Monkeys also made nongoal-directed saccades during the ITI, with a portion of these saccades exhibiting characteristics similar to goal-directed saccades. ERPs recorded over the frontolateral cortex showed a gradual ramping polarization prior to saccade execution, consistent with the readiness potential observed in humans. This preparatory potential was present for both goal-directed and nongoal-directed saccades. However, the ERPs we observed could not distinguish between stopping and going, suggesting limited utility for differentiating saccade generation and inhibition.

Ramping polarization and saccade preparation

Previous work has identified several presaccadic potentials in the EEG signal, providing insight into the neural mechanisms underlying saccade preparation. Two primary ramping or preparatory potentials that have been extensively studied are the contingent negative variation (CNV) and the LRP. The CNV, a slow negative-going waveform, emerges during the interval between a warning signal and a subsequent imperative cue. It signals general anticipatory and preparatory processes leading up to saccade initiation, reflecting broad attentional and cognitive preparation. This potential is observed as a wide distribution of polarization across frontal, central, and parietal regions (Walter et al., 1964; Klostermann et al., 1994). In contrast, the LRP indexes more specific motor preparation, as it captures the buildup of lateralized motor activity over the contralateral cortex before saccade initiation. The LRP is a more localized signal, occurring 200–300 ms before the saccade onset, and reflects the selection and readiness of the motor system to execute the movement (Kurtzberg and Vaughan, 1982; Brickett et al., 1984; Balaban and Weinstein, 1985; Thickbroom and Mastaglia, 1985; Moster and Goldberg, 1990; Evdokimidis et al., 1991, 1992; Everling et al., 1997a,b). Thus, while the CNV is primarily associated with broad attentional preparation, the LRP specifically reflects the motor response preparation and the

readiness of the motor system to initiate the saccade. Together, these two potentials represent the ramping of neural activity in anticipation of a forthcoming action—one related to general readiness (CNV) and the other to motor-specific readiness (LRP).

In this study, both monkeys exhibited a clear ramp in polarization at frontolateral electrode sites following an initial visual transient and prior to the execution of a saccade, with the potential showing a clear lateralization—stronger positivity contralateral to the saccade. These observations are similar to those made by [Sander et al. \(2010\)](#), who reported strongest positivity contralateral to the saccade. Interestingly, in contrast to humans, where saccade readiness potentials are typically characterized by a posterior negativity ([Thickbroom and Mastaglia, 1985](#); [Moster and Goldberg, 1990](#); [Everling et al., 1997a](#)), the monkey data suggest a distinct frontolateral positivity. This flipped polarity of ERPs between humans and macaques has been observed with other signals such as the N2pc ([Woodman et al., 2007](#)). Differences in the organization of sulci and gyri, patterns of cortical folding, and the timing of neural signal propagation between humans and macaques are likely sources of the variation in ERP polarity.

Interestingly, the onset of this potential in monkeys at ~300 ms before the saccade onset aligns with the buildup polarization previously observed in FEF neurons during the saccade-countermanding task ([Hanes et al., 1998](#)). In saccade-countermanding tasks, neurons in the FEF exhibit a ramping increase in activity in the period leading up to the saccade, and this increase is thought to reflect the process of accumulating evidence to make a motor decision (i.e., to initiate a saccade). If the decision to move is inhibited, the buildup of activity is halted, and the saccade does not occur. Similarities in the timing between EEG and FEF ramping activity have also been noted by [Sander et al. \(2010\)](#) who describe their positive potential in monkeys beginning to ramp ~100 ms prior to the saccade onset. Although earlier than those observed here, these latencies were also described as similar to those of FEF neurons during pro- and anti-saccade trials recorded in the same lab ([Everling and Munoz, 2000](#)). As such, the potential we have observed in our EEG signal may reflect the synchronized activity of a network of neurons, including those in the FEF, as they ramp up toward threshold for generating a saccade.

After establishing this signal in saccade preparation, we set out to determine if these signals only occur for goal-directed saccade planning, self-initiated movement, or general saccade preparation. Goal-directed saccades are intentional, targeting specific locations, while nongoal-directed saccades occur reflexively or spontaneously. If tied to goal-directed planning, these signals should appear only during saccades to a cued target. If specific to self-initiated movements, they should occur only during uncued saccades. Alternatively, if they represent general saccade preparation, they should be present for both goal-directed and nongoal-directed saccades. Supporting these distinctions, previous work has shown that macaque FEF neurons discharge before visually guided and memory-guided saccades ([Bruce and Goldberg, 1985](#)), even in darkness, but not before spontaneous saccades in similar conditions ([Bizzi, 1968](#)). However, recent work challenged this latter finding demonstrating that FEF neurons do discharge before nongoal-directed saccades, though were more variable in their trial-to-trial firing rate, had unchanged beta-band power, and demonstrated shorter timing from direction selection to the saccade onset compared with goal-directed saccades ([Sendhilnathan et al., 2021](#)). Supporting this, we also observed preparatory polarization in the EEG signals for both goal-directed and nongoal-directed saccades, suggesting that this polarization may serve as a general index of saccade preparation.

Although indirectly tested in this study, there are clear parallels between preparatory ramping activity within the FEF and the polarization observed in frontolateral EEG contacts. Identifying such markers of intracranial activity are important, as these methods are less invasive and do not require any surgical intervention, reducing the risk and discomfort for the participants. This is particularly important when studying human subjects, as invasive measurements may not be feasible or ethically justifiable. Furthermore, noninvasive techniques are typically more widely accessible and can be applied to a larger population, including individuals with certain health conditions or those who cannot undergo invasive procedures. However, future studies should validate such methods by simultaneously recording intracranial and extracranial signals and investigating the biophysical relationship between them.

Frontolateral ERPs do not distinguish between stopping and going in monkeys

Interestingly, although we found preparatory polarization for generating a saccade, we were unable to demonstrate activity that distinguished between stopping and going. When studying motor responses to visual cues, visual-evoked potentials (VEPs) can contaminate the ERP signal, as the onset of the visual cue triggering the motor response also elicits a VEP. This can lead to the contamination of the motor ERP by the VEP, making it difficult to isolate and interpret the neural polarization associated specifically with the motor response. First, although not a valid approach in the context of the race model, if signals from these frontolateral electrodes could differentiate between stopping and going, we may have expected to have seen some distinction between canceled and noncanceled trials. In both instances, a visual stop signal was presented, but in one instance this stop signal resulted in successfully halting the planned saccade, and the other instance resulted in a saccade being executed. Despite these two outcomes sharing the VEP confound, there was no significant difference between the two conditions during the period in which a saccade could be inhibited. Second, there may be biophysical parameters that constrain the contribution of one population of neurons within FEF to the EEG signals recorded over the scalp. Notably, stopping may be achieved by fixation neurons reactivating after the stop signal is presented, exerting strong inhibition over movement neurons within FEF. The limited contribution of these fixation neurons is twofold: first, fixation neurons are small and may be inhibitory interneurons, as such, their small size and biophysical

properties make it unlikely that they can meaningfully contribute to the EEG signal; second, fixation neurons may be located within the fundus of FEF, as such, even if they were larger pyramidal cells, their dipoles will be orthogonal to movement neurons which are located within the dorsal bank and thus may not be captured as efficiently by EEG.

Interestingly, in human studies of countermanding, several EEG markers have been identified to differentiate between stopping and going and have helped form the basis of neurocognitive models of response inhibition (Diesburg and Wessel, 2021). After sensory processing in the right inferior frontal gyrus, a cascade of activity leads to the inhibition of motor plans, with frontocentral low-frequency activity (theta band; ~2–8 Hz) reflecting increased activity in medial frontal areas like the anterior cingulate cortex and pre-SMA during inhibition (Nigbur et al., 2011). The P3, a prominent frontocentral ERP, is particularly notable in studies of stopping (Sajad et al., 2022), with earlier P3 onset latencies correlating with faster SSRT and better stopping performance (Kok et al., 2004; Ramautar et al., 2004; Wessel and Aron, 2015). Other studies show a clear relationship between P3 amplitude and motor activity, with larger P3s associated with lower levels of prepotent motor activity and more successful inhibition (Wessel, 2018). Perhaps most relevant, β -bursts over medial frontal and sensorimotor cortices have also been linked to inhibition of motor plans. Wessel (2020) demonstrated that β -bursting decreases steadily over bilateral sensorimotor sites during motor preparation, signaling the inhibition of the motor system that must be overcome to execute the movement. In contrast, during successful movement cancellation, β -bursts increase over frontocentral sites, followed by a short-latency rise in sensorimotor β -bursts, indicating the rapid reinstatement of motor inhibition by frontal areas. However, although others observed an increase in frontocentral β -bursts during stopping, it was concluded that they are unlikely to contribute to reactive inhibition due to their incidence and lack of specificity (Errington et al., 2020). Given the new findings of sensorimotor readiness potentials in frontolateral sites, future work could reexamine this line of research to determine if β -bursts are more closely linked to distinguishing between stopping and going within these areas instead.

Through this manuscript, we have established compelling evidence for the presence of a preparatory potential in general saccade production, which is a promising finding for understanding the neural mechanisms underlying motor planning. Similar approaches establishing ERPs in the macaque model have been fruitful previously. In such studies, it has been established that monkeys exhibit other ERPs such as the ERN and an N2/P3 complex over the medial frontal cortex during the saccade-countermanding task (Sajad et al., 2019; Sajad et al., 2022). By combining this data with intracranial laminar recordings, biophysical models of these processes have been developed that allow us to understand how single neurons can contribute to larger-scale dynamics (Herrera et al., 2022, 2023). Although such approaches for the medial frontal cortex are more straightforward due to the favorable geometry of the cortex relative to the EEG sensors, we hope that our findings will drive future research to simultaneously record from the FEF while capturing EEG to further our understanding of saccade generation and inhibition.

References

- Balaban CD, Weinstein JM (1985) The human pre-saccadic spike potential: influences of a visual target, saccade direction, electrode laterality and instructions to perform saccades. *Brain Res* 347: 49–57.
- Bizzi E (1968) Discharge of frontal eye field neurons during saccadic and following eye movements in unanesthetized monkeys. *Exp Brain Res* 6:69–80.
- Brickett PA, Weinberg H, Davis CM (1984) Cerebral potentials preceding visually triggered saccades. *Ann N Y Acad Sci* 425:429–433.
- Bruce CJ, Goldberg ME (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. *J Neurophysiol* 53:603–635.
- Cabel DW, Armstrong IT, Reingold E, Munoz DP (2000) Control of saccade initiation in a countermanding task using visual and auditory stop signals. *Exp Brain Res* 133:431–441.
- Cohen JY, Heitz RP, Schall JD, Woodman GF (2009) On the origin of event-related potentials indexing covert attentional selection during visual search. *J Neurophysiol* 102:2375–2386.
- Colonius H, Ozyurt J, Arndt PA (2001) Countermanding saccades with auditory stop signals: testing the race model. *Vision Res* 41:1951–1968.
- Deecke L, Grozinger B, Kornhuber HH (1976) Voluntary finger movement in man: cerebral potentials and theory. *Biol Cybern* 23:99–119.
- de Jong R, Wierda M, Mulder G, Mulder LJ (1988) Use of partial stimulus information in response processing. *J Exp Psychol Hum Percept Perform* 14:682–692.
- Diesburg DA, Wessel JR (2021) The pause-then-cancel model of human action-stopping: theoretical considerations and empirical evidence. *Neurosci Biobehav Rev* 129:17–34.
- Errington SP, Woodman GF, Schall JD (2020) Dissociation of medial frontal beta-bursts and executive control. *J Neurosci* 40:9272–9282.
- Evdokimidis I, Liakopoulos D, Papageorgiou C (1991) Cortical potentials preceding centrifugal and centripetal self-paced horizontal saccades. *Electroencephalogr Clin Neurophysiol* 79:503–505.
- Evdokimidis I, Mergner T, Lucking CH (1992) Dependence of presaccadic cortical potentials on the type of saccadic eye movement. *Electroencephalogr Clin Neurophysiol* 83:179–191.
- Everling S, Krappmann P, Flohr H (1997a) Cortical potentials preceding pro- and antisaccades in man. *Electroencephalogr Clin Neurophysiol* 102:356–362.
- Everling S, Krappmann P, Spantekow A, Flohr H (1997b) Influence of pre-target cortical potentials on saccadic reaction times. *Exp Brain Res* 115:479–484.
- Everling S, Munoz DP (2000) Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. *J Neurosci* 20:387–400.
- Godlove DC, Garr AK, Woodman GF, Schall JD (2011) Measurement of the extraocular spike potential during saccade countermanding. *J Neurophysiol* 106:104–114.
- Godlove DC, Maier A, Woodman GF, Schall JD (2014) Microcircuitry of agranular frontal cortex: testing the generality of the canonical cortical microcircuit. *J Neurosci* 34:5355–5369.
- Godlove DC, Schall JD (2016) Microsaccade production during saccade cancellation in a stop-signal task. *Vision Res* 118:5–16.
- Gratton G, Coles MG, Sirevaag EJ, Eriksen CW, Donchin E (1988) Pre- and poststimulus activation of response channels: a psychophysiological analysis. *J Exp Psychol Hum Percept Perform* 14:331–344.

- Hanes DP, Carpenter RH (1999) Countermanding saccades in humans. *Vision Res* 39:2777–2791.
- Hanes DP, Patterson WF 2nd, Schall JD (1998) Role of frontal eye fields in countermanding saccades: visual, movement, and fixation activity. *J Neurophysiol* 79:817–834.
- Hanes DP, Schall JD (1995) Countermanding saccades in macaque. *Vis Neurosci* 12:929–937.
- Hanes DP, Schall JD (1996) Neural control of voluntary movement initiation. *Science* 274:427–430.
- Heitz RP, Cohen JY, Woodman GF, Schall JD (2010) Neural correlates of correct and errant attentional selection revealed through N2pc and frontal eye field activity. *J Neurophysiol* 104:2433–2441.
- Herrera B, Sajad A, Errington SP, Schall JD, Riera JJ (2023) Cortical origin of theta error signals. *Cereb Cortex* 33:11300–11319.
- Herrera B, Schall JD, Riera JJ (2024) Agranular frontal cortical microcircuit underlying cognitive control in macaques. *Front Neural Circuits* 18:1389110.
- Herrera B, Westerberg JA, Schall MS, Maier A, Woodman GF, Schall JD, Riera JJ (2022) Resolving the mesoscopic missing link: biophysical modeling of EEG from cortical columns in primates. *Neuroimage* 263:119593.
- Kawagoe R, Takikawa Y, Hikosaka O (1998) Expectation of reward modulates cognitive signals in the basal ganglia. *Nat Neurosci* 1:411–416.
- Klostermann W, Kompf D, Heide W, Verleger R, Wauschkuhn B, Seyfert T (1994) The presaccadic cortical negativity prior to self-paced saccades with and without visual guidance. *Electroencephalogr Clin Neurophysiol* 91:219–228.
- Kok A, Ramautar JR, De Ruiter MB, Band GP, Ridderinkhof KR (2004) ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology* 41:9–20.
- Kornylo K, Dill N, Saenz M, Krauzlis RJ (2003) Cancelling of pursuit and saccadic eye movements in humans and monkeys. *J Neurophysiol* 89:2984–2999.
- Kurtzberg D, Vaughan HG Jr (1982) Topographic analysis of human cortical potentials preceding self-initiated and visually triggered saccades. *Brain Res* 243:1–9.
- Logan GD, Cowan WB (1984) On the ability to inhibit thought and action - a theory of an act of control. *Psychol Rev* 91:295–327.
- Matzke D, Dolan CV, Logan GD, Brown SD, Wagenmakers EJ (2013a) Bayesian parametric estimation of stop-signal reaction time distributions. *J Exp Psychol Gen* 142:1047–1073.
- Matzke D, Love J, Wiecki TV, Brown SD, Logan GD, Wagenmakers EJ (2013b) Release the BEESTS: Bayesian estimation of ex-Gaussian stop-signal reaction time distributions. *Front Psychol* 4:918.
- Matzke D, Love J, Heathcote A (2017) A Bayesian approach for estimating the probability of trigger failures in the stop-signal paradigm. *Behav Res Methods* 49:267–281.
- Morein-Zamir S, Kingstone A (2006) Fixation offset and stop signal intensity effects on saccadic countermanding: a crossmodal investigation. *Exp Brain Res* 175:453–462.
- Moster ML, Goldberg G (1990) Topography of scalp potentials preceding self-initiated saccades. *Neurology* 40:644–648.
- Nigbur R, Ivanova G, Sturmer B (2011) Theta power as a marker for cognitive interference. *Clin Neurophysiol* 122:2185–2194.
- Purcell BA, Schall JD, Woodman GF (2013) On the origin of event-related potentials indexing covert attentional selection during visual search: timing of selection by macaque frontal eye field and event-related potentials during pop-out search. *J Neurophysiol* 109:557–569.
- Ramautar JR, Kok A, Ridderinkhof KR (2004) Effects of stop-signal probability in the stop-signal paradigm: the N2/P3 complex further validated. *Brain Cogn* 56:234–252.
- Reinhart RM, Carlisle NB, Kang MS, Woodman GF (2012) Event-related potentials elicited by errors during the stop-signal task. II: human effector-specific error responses. *J Neurophysiol* 107:2794–2807.
- Riehle A, Requin J (1989) Monkey primary motor and premotor cortex: single-cell activity related to prior information about direction and extent of an intended movement. *J Neurophysiol* 61:534–549.
- Sajad A, Godlove DC, Schall JD (2019) Cortical microcircuitry of performance monitoring. *Nat Neurosci* 22:265–274.
- Sajad A, Errington SP, Schall JD (2022) Functional architecture of executive control and associated event-related potentials in macaques. *Nat Commun* 13:6270.
- Sander V, Soper B, Everling S (2010) Nonhuman primate event-related potentials associated with pro- and anti-saccades. *Neuroimage* 49:1650–1658.
- Sendhilnathan N, Basu D, Goldberg ME, Schall JD, Murthy A (2021) Neural correlates of goal-directed and non-goal-directed movements. *Proc Natl Acad Sci U S A* 118:e2006372118.
- Smulders FT, Miller JO, Luck S (2012) *The lateralized readiness potential*. New York, NY: Oxford University Press.
- Tanji J, Evars EV (1976) Anticipatory activity of motor cortex neurons in relation to direction of an intended movement. *J Neurophysiol* 39:1062–1068.
- Thakkar KN, Schall JD, Boucher L, Logan GD, Park S (2011) Response inhibition and response monitoring in a saccadic countermanding task in schizophrenia. *Biol Psychiatry* 69:55–62.
- Thakkar KN, Schall JD, Logan GD, Park S (2015) Cognitive control of gaze in bipolar disorder and schizophrenia. *Psychiatry Res* 225:254–262.
- Thickbroom GW, Mastaglia FL (1985) Cerebral events preceding self-paced and visually triggered saccades. a study of presaccadic potentials. *Electroencephalogr Clin Neurophysiol* 62:277–289.
- Verbruggen F, et al. (2019) A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. *Elife* 8:e46323.
- Walter WG, Cooper R, Aldridge VJ, McCallum WC, Winter AL (1964) Contingent negative variation: an electric sign of sensorimotor association and expectancy in the human brain. *Nature* 203:380–384.
- Walton MM, Gandhi NJ (2006) Behavioral evaluation of movement cancellation. *J Neurophysiol* 96:2011–2024.
- Wattiez N, Poitou T, Rivaud-Pechoux S, Pouget P (2016) Evidence for spatial tuning of movement inhibition. *Exp Brain Res* 234:1957–1966.
- Weinrich M, Wise SP, Mauritz KH (1984) A neurophysiological study of the premotor cortex in the rhesus monkey. *Brain* 107:385–414.
- Wessel JR (2018) Prepotent motor activity and inhibitory control demands in different variants of the go/no-go paradigm. *Psychophysiology* 55.
- Wessel JR (2020) β -bursts reveal the trial-to-trial dynamics of movement initiation and cancellation. *J Neurosci* 40:411–423.
- Wessel JR, Aron AR (2015) It's not too late: the onset of the frontocentral P3 indexes successful response inhibition in the stop-signal paradigm. *Psychophysiology* 52:472–480.
- Woodman GF, Kang MS, Rossi AF, Schall JD (2007) Nonhuman primate event-related potentials indexing covert shifts of attention. *Proc Natl Acad Sci U S A* 104:15111–15116.