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## Spatio-temporal mapping of motor preparation for self-paced saccades

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### ABSTRACT

We investigated the movement related cortical potentials (MRCPs) associated with self-paced horizontal voluntary saccades and evaluated their cortical sources by applying dipole model. A fixation point and two targets (6° of eccentricity in the left and right fields) were continuously displayed on a screen. A first group (15 subjects) performed a saccade toward one of the lateral targets immediately followed by a re-centering saccade. A second group (15 subjects) performed a saccade followed by a long fixation (few seconds) before a re-centering. Results showed a sequence of activities in contralateral Intra-Parietal Sulcus (IPS), Supplementary Eye Fields and Frontal Eye Fields. In the case of long-fixation-saccades, an additional source in ipsilateral IPS was detected in the planning phase. The amplitude and timing of the planning phase, associated with BP components, were influenced by task demands. Similarity and difference between MRCPs for eyes and limbs movements are also presented.

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### 1. Introduction

The visual guidance of saccadic eye movements represents one form of sensory to motor transformation that has improved our knowledge of motor control and sensorimotor processing (Munoz, 2002). Saccades are used both to direct the fovea from one target to another and to shift the focus of attention (Dorè-Mazars and Collins, 2005).

One of the most investigated types of saccadic eye movement is the externally triggered saccade also called reflexive or reactive saccade (Johnston and Everling, 2008), which is characterized by the stimulus guidance. However, most of our everyday saccades are not triggered by the abrupt onset of a target, and we intentionally decide when to start a saccade and where to move the eyes next. This large category of saccadic eye movements is called self-paced saccade, also known as intentional, voluntary or volitional saccade. Although the self-paced paradigm is an ecologically valid procedure to study the neural bases of the saccadic control, it was less frequently employed. Indeed the literature on saccadic eye movements counts only sparse information for spontaneous self-paced saccades (Klostermann et al., 1994; Kurtzberg and Vaughan, 1982; Moster and Goldberg, 1990; Thickbroom and Mastaglia, 1985) when compared to externally triggered saccades (e.g. Papadopoulou et al., 2010).

A bulk of single experiment on monkey (Wurtz, 1969; see also Tehovnik et al., 2000 for a review) and neuroimaging

studies on humans (Schraa-Tam et al., 2009) have revealed that many areas of frontal and parietal cortices are involved in the generation of self-paced saccades, such as the Frontal Eye Field (FEF), the Supplementary Eye Field (SEF), the Parietal Eye Field (PEF) in the intraparietal sulcus as well as the superficial layer of superior colliculus (see Schiller and Tehovnik, 2005 for a review).

On the other hand, few electrophysiological human studies on the spontaneous self-paced saccades used the movement-related cortical potentials (MRCPs) recording. Compared to neuroimaging techniques, this approach has lower sensitivity for the localization of cortical activity, but much higher temporal resolution allowing to measure the time-course of the neural activity. The MRCPs components have been extensively studied for limbs movement (finger, hand and foot, see Shibasaki and Hallett, 2006 for a review), but much less for eye movements (e.g. Evdokimidis et al., 1992; Everling et al., 1997; Moster and Goldberg, 1990; Richards, 2003). The few studies on MRCPs for spontaneous self-paced saccades showed quite similar results to those obtained for limb movements (Yamamoto et al., 2004). The MRCPs for self-initiated saccades may begin several seconds before the movement onset with a gently rising negativity (ramp-like potential also called pre-motor or pre-saccadic negativity, or negative shift). This activity is considered as an analogue of the Bereitschaftspotential (BP) preceding limb movements (Wauschkuhn et al., 1997). According to various reports (Klostermann et al., 1994; Moster and Goldberg, 1990; Thickbroom and Mastaglia, 1985), this negative wave has larger amplitude over parietal areas of the hemisphere contralateral to the saccade direction, and has been related to saccade motor programming. This pre-saccadic negativity has been usually described as single phenomena, except for one study employing epicortical

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recording of saccadic MRCPs. Although recording from frontal sites only, Yamamoto et al. (2004) unequivocally showed that the pre-saccadic negativity is actually formed by two sub-activities called BP and negative slope (NS') as for hand and foot movements. The NS' can be separated from the BP as it shows a steeper gradient negativity starting around 800 ms before the beginning of the eye movement. The source of the NS' was located on the medial surface of SEF.

An earlier study (Moster and Goldberg, 1990) reported that pre-saccadic negativity is followed by a positive activity starting 200–100 ms before the saccadic onset called pre-motor positivity, but other studies on self-paced saccades failed to find similar results (Yamamoto et al., 2004; Papadopoulou et al., 2010). This pre-motor positivity was more consistently found before externally triggered saccades onset and may be a correlate of visuomotor transformations (Thickbroom and Mastaglia, 1985). Concomitant to saccade onset a sharp potential (or spike potential) is present; for some authors this potential might reflect the maximal recruitment of the oculomotor muscle units and ocular motor neurons (Moster and Goldberg, 1990; Thickbroom and Mastaglia, 1986), while for others it might be generated by the involvement of cortical frontal and parietal areas (Kurtzberg and Vaughan, 1982; Balaban and Weinstein, 1985; Weinstein et al., 1991; Pierrrot-Deseilligny et al., 2003a). More recently, monkey data confirmed the contribution of the contralateral FEF to this potential (Johnston and Everling, 2008; Sander et al., 2010). After the saccade onset another sharp component is present, the so-called occipital wave complex or Lambda responses which is correlated with the input of new visual information into the primary visual cortex (Csibra et al., 2000; Jagla et al., 2007).

Previous studies on self-paced saccades showed inconsistent results about the onset of the BP, reporting timing that varied between 3 s (Klostermann et al., 1994), 1 s (Moster and Goldberg, 1990), 800 ms (Thickbroom and Mastaglia, 1985) and 650 ms (Kurtzberg and Vaughan, 1982) prior to saccade onset. These differences might be due to different instructions and participants' capacity to maintain attention (Klostermann et al., 1994). A relevant disagreement also exists over the presence of the pre-motor positivity, which has not been found in most of previous self-paced studies, as well as on the discussed muscular vs. cortical origin of the sharp potential. Overall, spatio-temporal characteristics of self-paced saccadic MRCPs are not yet entirely described.

The first aim of the present study was to fill this gap, extending previous investigations with the support of methodological instruments such as high-density EEG recordings, fine scalp topography and source analysis with realistic head models.

Furthermore, considering that in the everyday life (for instance, during driving) a saccade towards a lateral target is often followed by a re-centring saccade, we evaluated saccade programming for this type of task and compared it with a different saccadic behavior, such as when we saccade to an object of interest (e.g. a face) and steadily fixate it for some seconds, before returning to the earlier fixation point. Comparing these two different saccadic tasks, one requiring a saccade followed by a short fixation and a quick return to the fixation point, and another task where the first saccade was followed by a longer fixation time, and a return to the fixation point at will, we may evaluate whether the preparation for the first centrifugal saccade is modulated by the delay of the next centripetal saccade. It is likely that these actions engage different neural mechanism especially in the dorsal parietal cortex, where the saccade planning mainly occurs. Both human (e.g. Sereno et al., 2001) and monkey (e.g. Gnadt and Mays, 1995) studies showed that the cortical activity observed during the planning phase of a saccade in some specific areas along the intraparietal sulcus (as area LIP) reflects the remapping of the space (and particularly the future position of the actual fixation point) anticipating the eyes position

before the first saccade's landing. Thus, the parietal activity could be differently modulated during the motor preparation phase of a saccade followed by a long fixation, which may require different programming in the re-centering saccade. So far, the only study that addressed this issue did not report important differences of cortical activity between the two tasks (Thickbroom and Mastaglia, 1985).

## 2. Materials and methods

### 2.1. Participants

The experiment was conducted on 30 healthy adult volunteers (fourteen men, mean age 26.3 years  $\pm$  4.1) with normal or corrected-to-normal vision. After a full explanation of the procedures, all subjects provided written informed consent. The study was approved by the local ethical committee. The group was divided into two cohorts ( $N = 15$ ), which were matched for age and gender. Each cohort executed one of the two tasks described below.

### 2.2. Stimuli and procedure

Participants were seated on a comfortable chair in a dimly illuminated room. Stimuli were continuously displayed throughout the whole experiment on a 24-in. CRT computer monitor at a viewing distance of 114 cm. On a black background (luminance 0.5 cd/m<sup>2</sup>), a central red cross over imposed on a light-grey spot (0.3°) served as fixation point (mean luminance 64 cd/m<sup>2</sup>). Two green disks (0.5° diameter) located one on the right and one on the left side of the fixation point at an eccentricity of 6° served as targets (luminance 64 cd/m<sup>2</sup>).

Two self-paced horizontal eye movement tasks were employed: (a) saccade followed by short-fixation and (b) saccade followed by long fixation, hereafter called 'short-fixation saccade' and 'long-fixation saccade'. The task aimed at mimicking two frequent scanning patterns, such as a quick look to an object (i.e. short-fixation saccade) and a long inspection of an object before making the re-centring second saccade (i.e. long-fixation saccade). In the long-fixation saccade task, participants were instructed to move their eyes to the left or to the right (at will) from the fixation point (first saccade), to hold their gaze laterally for a time of their choosing (longer than two seconds), and then to return (by a re-centring second saccade) to the central position and prepare for the new saccade. A total of 2718 long-fixation saccades were recorded (i.e. 1346 toward the right target and 1372 toward the left target). In the short-fixation saccade task, participants were asked to maintain the fixation on the central cross and then, at will, to saccade to the target either on the left or on the right and then to quick re-center the gaze to the fixation point. A total of 2884 short-fixation saccades were recorded (i.e. 1451 toward the right target and 1433 toward the left target). For both tasks, participants were told not to count or engage in any other rhythmic activity during the session and to keep the eye on the central fixation point for more than 5 s before starting a saccade. Recordings were made in blocks of about 5-min period. The subject was given a 1–2 min rest period between blocks, over a total time of 60 min.

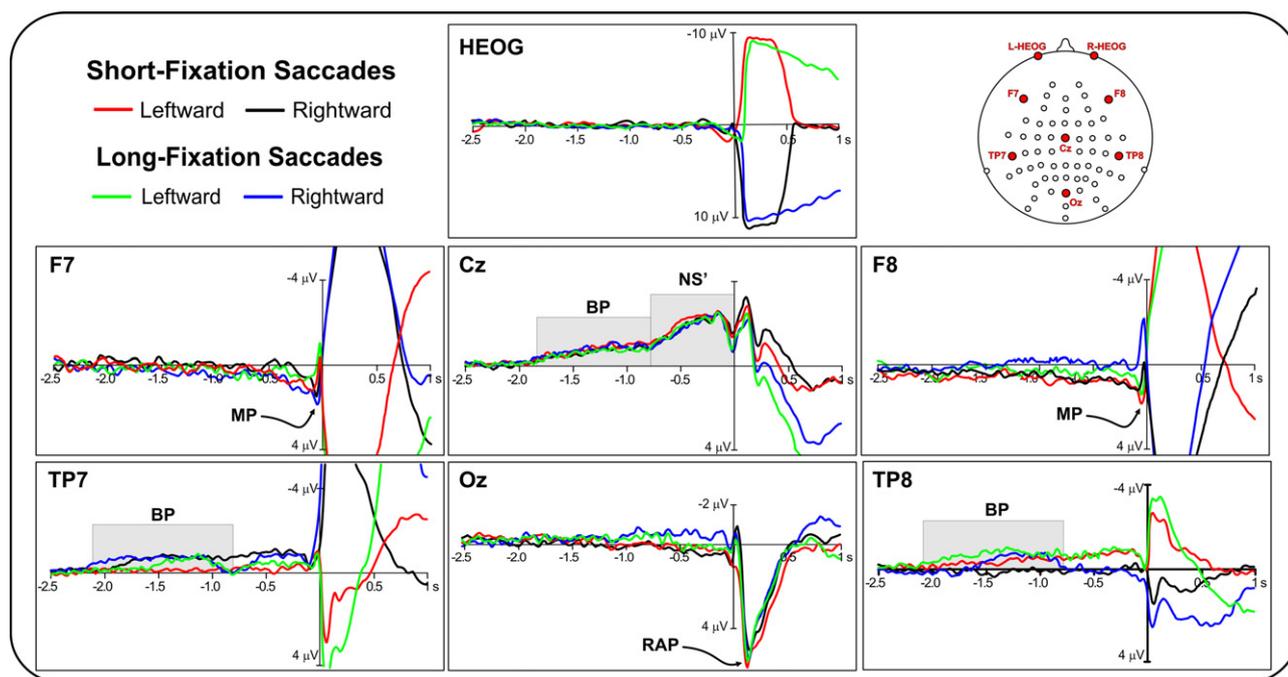
### 2.3. EEG recording

The EEG was recorded using a BrainVision™ 64-channel A/C system (Brain Products GmbH, Munich, Germany). Electrodes were placed according to the 10–10 system montage. All scalp channels were initially referenced to the left mastoid (M1). Horizontal eye movements were monitored by electrooculogram (EOG) with a bipolar recording from electrodes at the left and right outer canthi. Blinks and vertical eye movements were recorded with an electrode below the left eye, which was referenced to site Fp1. The EEG was digitized at 250 Hz with an amplifier band-pass of 0.016–60 Hz together with a 50 Hz notch filter and was stored for off-line averaging. Trials with artifacts (e.g. blinks or gross movements) were excluded from averaging.

### 2.4. Data analysis

The study analyzed MRCPs associated only to the first centrifugal saccade, because the successive re-centering saccade in the long-fixation condition was not detectable with reliability on the EOG. The main reason is the use of A/C amplifiers that reject the noise more easily, but slowly bring the signal back to the baseline during a steady voltage (e.g. Yagi et al., 2000). To our knowledge there are no studies that measured the MRCPs for the second re-centering saccade.

During off-line analysis, data were re-referenced to averaged mastoids, and ocular channel were mounted bipolarly. EOG traces were visually inspected to discriminate onset and directions of the first saccades. Eye movements' artifacts have been reduced throughout the Gratton et al. algorithm (1983). The averaging comprised the epoch of 3500 ms before and 1000 ms after saccade onset. Averaging was performed only in relation to the initial decentering saccade. For each data set, grand average was calculated. A baseline was defined by the mean voltage over the initial 1000 ms of the averaged epochs. To further reduce high-frequency noise, the time averaged MRCPs were low-pass filtered (i.e. Butterworth, second order) at 8 Hz. The period used for statistical analysis started 2500 ms prior and lasted to saccade onset.



**Fig. 1.** Grand average MRCPs for representative electrodes. The traces from long- and short-fixation saccades, as well as for leftward and rightward saccades are superimposed. The MP is more evident on frontal electrodes. The BP is prominent on temporo-parietal electrodes and the NS' on medial central sensors. The RAP peaks on occipital site.

Significant differences in the saccade-related cortical preparation amplitudes for two experimental conditions (long-fixation vs. short-fixation saccades) across leftward and rightward saccades were assessed by using a running paired *t*-test. The BP onset latency was calculated as the first time value showing amplitude larger than 1.5 times the baseline and compared by *t*-test. The overall alpha level was set at  $p < 0.05$  after Bonferroni correction.

To model the intracranial sources of the saccade-related cortical potentials components, the Brain Electrical Source Analysis system (BESA 2000 version 5.18, MEGIS Software GmbH, Grärfelfing, Germany) was used. For this analysis, data were low-pass filtered at 20 Hz. This algorithm calculated the cerebral areas involved in the saccades cortical preparation. The spatio-temporal dipole analysis of BESA estimated the location and orientation, as well as the time course, of multiple equivalent dipolar sources by calculating the scalp distribution obtained for any given dipole model (forward solution). This distribution was then compared with actual MRCPs. Interactive changes in the location and orientation of dipole sources led to the minimization of residual variance (RV) between the model and the observed spatio-temporal distribution of MRCP. The position of the electrodes was digitized and averaged across subjects. The 3D coordinates for each dipole of the BESA model were determined with respect to the Talairach axes (Talairach and Tournoux, 1988) and scaled according to brain size. In these calculations, BESA utilized a realistic approximation of the head (which was based on MRI of 24 subjects), and the radius was obtained from the group average (86 mm). To limit the number of parameters to be estimated, symmetry constraints were applied for each bilateral dipole pair in the scalp distributions that indicated bilateral foci. The possibility that dipoles would interact was reduced by selecting solutions with relatively low dipole moments with the aid of an "energy" constraint (which was weighted 20% in the compound cost function as opposed to 80% for the RV). The optimal set of parameters was identified in an interactive manner by searching for a minimum in the compound cost function. Dipoles were fitted sequentially. Latency ranges for fitting were chosen (see results) to minimize overlap among successive, topographically distinct components. To minimize cross-talk and interactions between sources, dipoles that accounted for earlier portions of the waveform were left in place as additional dipoles were added. The goodness of the dipole model was evaluated by measuring its RV as a percentage of the signal variance, as described by the model, and by applying residual orthogonality tests (ROT; e.g. Bocker et al., 1994). The resulting individual time series for the dipole moments (the source waves) can also be subjected to an orthogonality test, which will be referred to as a source wave orthogonality test (SOT; Bocker et al., 1994). All *t*-statistics were evaluated for significance at the 5% level.

### 3. Results

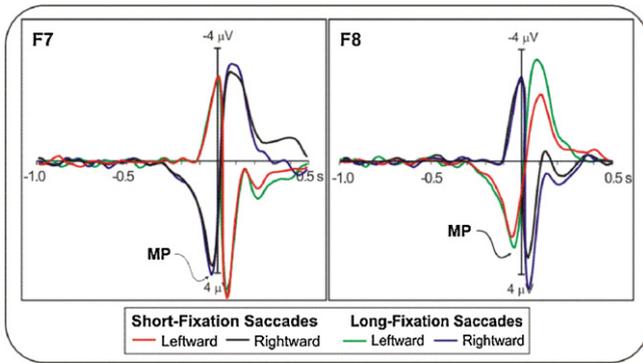
#### 3.1. Waveform analysis

The terminology employed to describe the MRCPs components for saccades is still a matter of debate. However, there is a good

agreement between the terms used in the MRCP studies on saccades with those on limbs movement. Thus, we confirm the terms previously used by Yamamoto et al. (2004) to describe the MRCPs components for eye movements, as follows: BP for the early negativity, NS' for the later negative slope, motor potential (MP) for the activity concomitant the saccade onset and re-afferent potential (RAP) for the visual activity following the saccade.

Fig. 1 shows the grand average waveforms of saccade-related cortical potentials plotted for seven relevant electrodes sites (HEOG, F7, Cz, F8, TP7, Oz and TP8). Traces for leftward and rightward saccades, as well as saccades followed by long and short fixation are superimposed for each electrode. The brisk diverging of the HEOG from its baseline shows the onset of saccade from the central fixation point. In the short-fixation saccade task, on average subjects fixated the lateral target for 250 ms (SD 44 ms) and then returned to the central fixation point 560 ms (SD 115 ms) after the saccade onset, the mean interval between the first and the following centrifugal saccade was 7.86 s (SD 2.27 s). The mean latency between the onset of the centrifugal and that of the centripetal saccade was 380 ms (SD 72 ms). In the long-fixation saccade task, subjects fixated the lateral target for more than 2 s and then returned to the central fixation point, the mean interval between the first and the following centrifugal saccade was 11.84 s (SD 3.47 s). The exact fixation duration and consequently the onset of the re-centering saccade were not detectable (see Section 2). The timing of saccades toward the left and the right visual field were not different at *t*-test.

The MRCPs waveforms reported in Fig. 1 began with the typical gently rising negativity (the BP), first evident in both contralateral temporal-parietal sensors (see TP7 and TP8) and then in medial central sensors (see Cz). The BP was 400 ms earlier in temporal-parietal sensors when compared to central sensors. For long-fixation saccades the BP onset was detectable at temporal-parietal sites 2140 ms (SE = 12) before saccade and for short-fixation saccades it was later ( $t_{39} p < 0.01$ ), at around -1800 ms (SE = 40). The amplitude of the BP in the time window -2100 to -1790 ms was larger for long-fixation saccades than short-fixation saccades ( $t_{19} p < 0.05$ ). Differences between tasks



**Fig. 2.** Grand average MRCPs from lateral frontal sites using 3–20 Hz filters. The MP is characterized by a sharp positivity contralateral to the saccade direction, respectively peaking on F7 for rightward saccades and on F8 for leftward saccades.

hold true for both leftward and rightward saccades. The BP was followed by a steeper negative rise appearing around 750 ms before saccade onset (here called NS'). The NS' component was symmetrical and maximal on the vertex (Cz sensor). For this component no difference was found between conditions.

The last component identified just prior to the beginning of saccades was a sharp positive wave peaking on frontal sites contralateral to the saccade direction (F7/F8), hereafter called MP. The MP component was partially covered by the slower negativity of the NS', thus, for a better visualization a low frequency filter (3–20 Hz) was applied (see Fig. 2). At F7 and F8 sites the MP component was characterized by a contralateral positive wave arising at around –300 ms and peaking 20 ms before saccade. The MP component was not statistically different between conditions. Following the MP, a very sharp ipsilateral negativity was detected more anteriorly. The onset of this negativity was at around –100 ms and peaked

simultaneously to saccades onset. This wave did not differ between conditions.

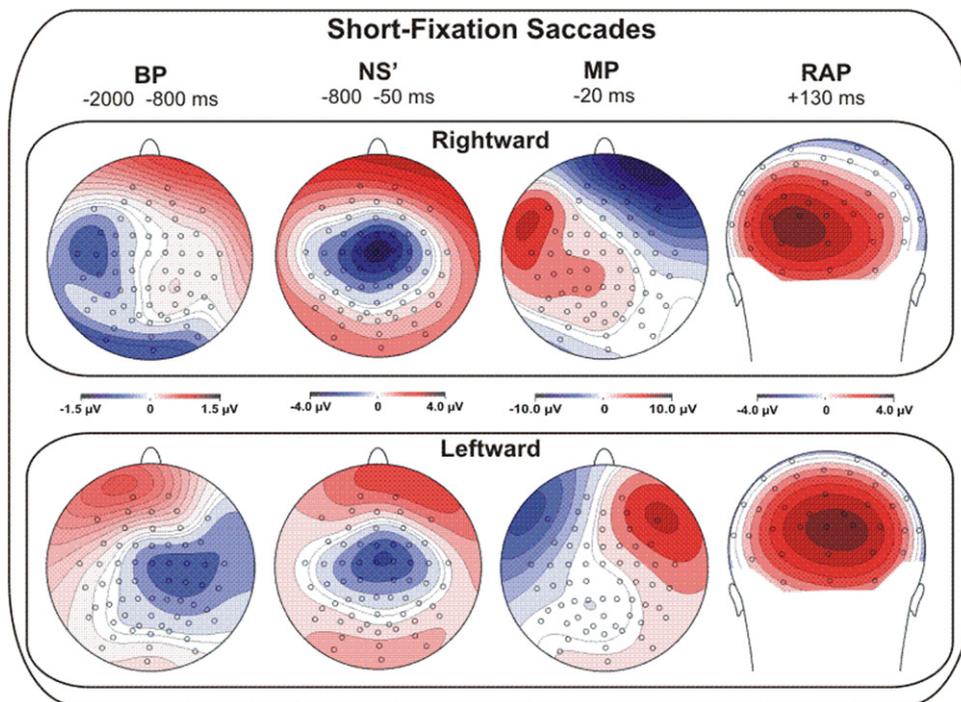
After the saccade, we observed a positive component, hereafter called RAP, peaking on occipital sites (see Oz in Fig. 1) between 130 and 140 ms post-movement, slightly contralateral to the saccade direction. The RAP latency and amplitude did not differ between conditions.

### 3.2. Scalp topography

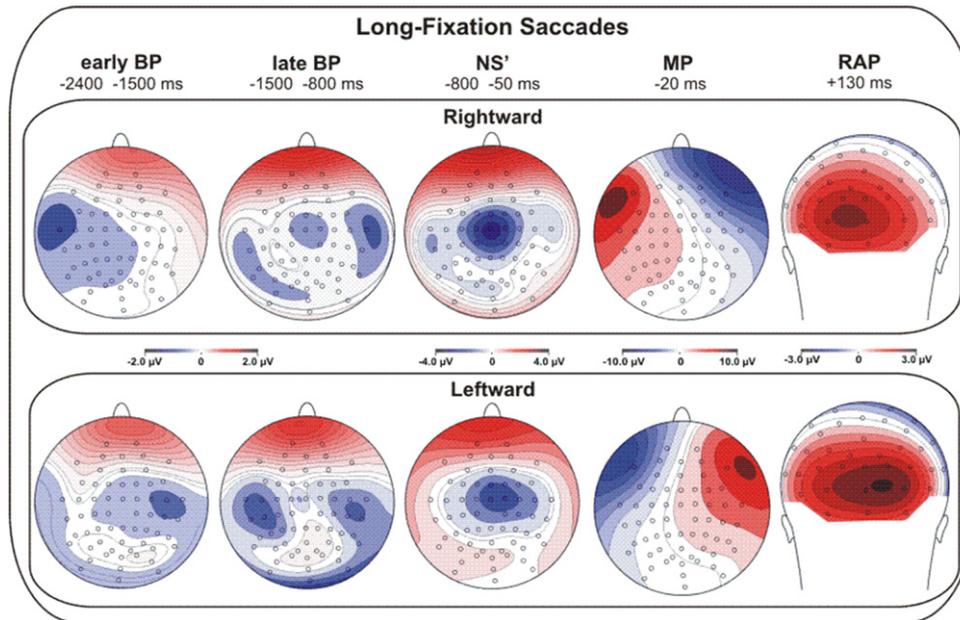
Fig. 3 shows a top-flat-view of the MRCPs scalp distribution for rightward (top panel) and leftward (bottom panel) saccades in the short-fixation saccades task. The BP distribution focuses over temporal-parietal cortex contralateral to the saccade direction. The NS' showed a widespread medial distribution over the central-frontal areas. The MP showed a focal positive distribution over lateral prefrontal regions contralateral to the saccade direction. At that latency the ipsilateral negativity peaked more anteriorly than the MP. After the saccade, the RAP component was present over contralateral occipital areas.

Fig. 4 shows the MRCPs topography for rightward (top panel) and leftward (bottom panel) saccades in the long-fixation saccades task. Similarly to the short-fixation saccades, the early phase of the BP focused, up to –1500 ms, over temporal-parietal cortex contralateral to the saccade direction. Later, up to –800 ms, the topography became bilateral involving also ipsilateral temporal-parietal regions. The bilateral negative activation in temporal-parietal regions between –1500 and –800 ms represents the main difference between the brain activities in the two tasks.

The NS' component showed a medial distribution over the central-frontal areas. The MP component showed a positive distribution over lateral prefrontal regions contralateral to the saccade direction. The ipsilateral negativity peaked more anteriorly than



**Fig. 3.** Topographical scalp potential distribution for the grand average MRCPs across rightward (top panel) and leftward (bottom panel) saccades for short fixation saccades task. The maps are decomposed into four time windows corresponding to each component, aligned from the left to the right. The first maps display the BP over posterior temporo-parietal cortex contralateral to the saccade direction; the second maps show the NS' over the centro-frontal areas; the third maps show the MP with a focal positive distribution over prefrontal regions contralateral to the saccade direction and ipsilateral negativity; the last maps display the RAP as a slightly contralateral positivity over occipital areas.



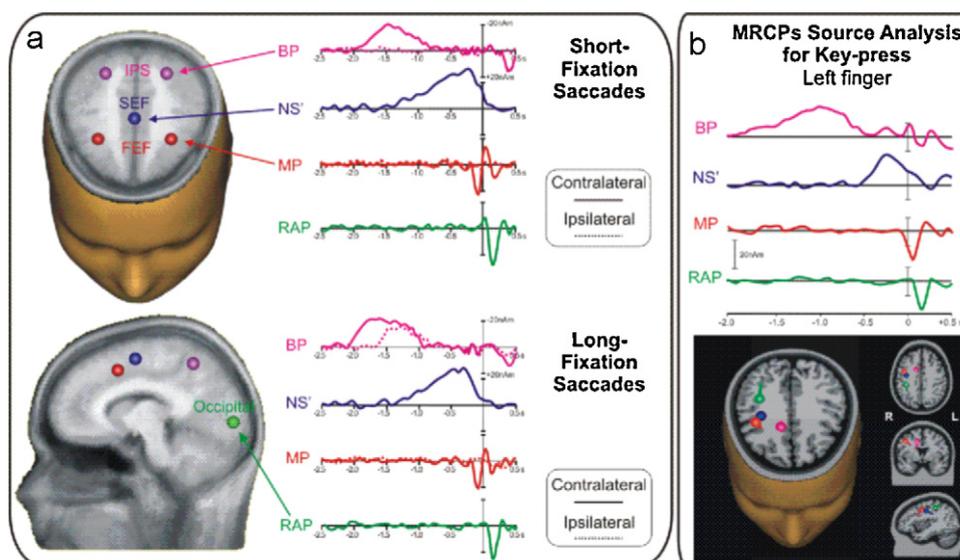
**Fig. 4.** Topographical scalp potential distribution for the grand average MRCPs across rightward (top panel) and leftward (bottom panel) saccades for long fixation saccades task. The maps are decomposed into five time windows corresponding to each component, aligned from the left to the right. The first maps display the BP over posterior temporo-parietal cortex contralateral to the saccade direction; the second maps show bilateral activity in posterior parietal cortex; the third maps show the NS' over the centrofrontal areas; the fourth maps show the MP with a focal positive distribution over prefrontal regions contralateral to the saccade direction and ipsilateral negativity; the last maps display the RAP as a slightly contralateral positivity over occipital areas.

the MP. After the saccade, the RAP component focused over contralateral occipital areas.

### 3.3. Source localization

Fig. 5a shows the source model of the MRCPs of the short and long-fixation saccades conditions. Comparing the scalp topography of the four conditions (Figs. 3 and 4), it is clear that all components had similar spatial distributions, except for the BP component. To increase the signal to noise ratio (typically low in this kind of potentials), waveforms were collapsed across left and right saccades and averaged between the short and long-fixation saccades.

averaged data allowed calculating a general model of the cortical sources of the MRCPs (left side of Fig. 5a). The BP component was fit using a pair of mirror dipoles in the interval between  $-2000$  and  $-1000$  ms and was localized in parietal lobe within the IPS (Talairach coordinates  $\pm 26, -53, 50$ ). The NS' was fit using a single dipole in the interval between  $-800$  and  $-50$  ms and was localized in the medial frontal gyrus within the Supplementary Eye Fields (SEF) region (Talairach coordinates  $0, -4, 54$ ). The MP was fit using a pair of mirror dipole in the interval between  $-50$  and  $-10$  ms and was localized in middle frontal gyrus within the Frontal Eye Field (FEF) region (Talairach coordinates  $\pm 31, -11, 44$ ). Finally, the RAP was fit using a single dipole in the  $100$ – $150$  ms interval and was



**Fig. 5.** Source model of the MRCPs components projected of a realistic model of the brain. (a) Left: Source location of the MRCPs for saccades in the IPS, SEF, FEF and occipital areas. Right: Time course of the cortical sources modeled for short- (top) and long-fixation saccades (bottom). (b) Source location (bottom) and time course (top) of the MRCPs components for finger movements (re-plotted from Di Russo et al., 2005). The time course of the MRCPs for saccades and limbs are quite similar.

localized in occipital extrastriate areas (Talairach coordinates  $\pm 25$ ,  $-87$ ,  $0$ ).

The right side of Fig. 5a shows the time course of the aforementioned sources, modeling separately the waveforms of short and long-fixation saccades. Continuous lines indicate contralateral activity and dashed line the ipsilateral. For the short-fixation saccades the contralateral IPS source started its activity around 2 s before saccades, peaked 500 ms later, and became inactive approximately 700 ms before the saccades. About 300 ms after the saccades, a brief activity was again detectable at the IPS source. The ipsilateral IPS source was not active during this task. The SEF (medial) source started its activity around 1 s before saccades, peaked 800 ms later, and became inactive just after the saccades. The contralateral FEF source started its activity around 200 ms before saccades, peaked 180 ms later, and peaked again after the saccades. The ipsilateral FEF source was not active. The contralateral occipital source started its activity around 80 ms and peaked 120 ms after the saccades.

For the long-fixation saccades the time-course was quite similar for all sources except for the contralateral IPS activity that began earlier (2.2 s before saccade) and an additional ipsilateral activity starting around 1.6 s before saccades and ending about 800 ms later. The residual variance of the models for both short- and long-fixation saccades was lower than 5% in the interval from  $-2000$  to 150 ms.

For ROT, none of the channels pointed to a significant residual signal, which indicated that there was no failure in any channel associated with the model. For SOTs, the sources fail to reach significance over the whole interval of fit; this indicates that the dipole moments do not show systematic time courses.

For comparison, Fig. 5b shows the MRCPs source model for left finger movements taken from a previous study (Di Russo et al., 2005). It's evident that the temporal structure of the two MRCPs is quite similar although the involved brain areas are obviously different.

#### 4. Discussion

The main aim of the present study was to estimate the cortical sources of self-paced saccadic MRCPs using state-of-the-art EEG recordings (high-density electrodes, fine scalp topography and source analysis). We described four main components (labeled BP, NS', MP and RAP). In the short-fixation saccades task, cortical activity initiated around 1.8 s before the eye movement as reflected by the slow rising BP in temporal-parietal regions. The spatial distribution of this component suggested a possible origin in contralateral parietal lobe within the IPS where the area LIP is located. As demonstrated in monkey (e.g. Snyder et al., 2000) and human (e.g. Sereno et al., 2001; Galati et al., 2011) studies, this area plays a critical role in saccadic motor preparation.

Partially overlapping with the BP, the NS' component started about 1300 ms before saccades onset and declined concomitantly to the eye movement. This component particularly large over the central-frontal sites may be generated by activity in the Supplementary Motor Area (SMA), which is crucial for the control of self-initiated movements. The SMA is involved in the planning and preparation of internally motivated, self-initiated limb or eye movements (Goldberg, 1985), perhaps regulating when a goal-directed eye movement will occur. SMA activation in saccades is consistent with single unit data in monkeys (Schall, 1991). Moreover, epicortical recordings in humans (Yamamoto et al., 2004) identified the Supplementary Eye Fields (SEF) in the rostral part of the SMA-proper, which became active in preparation for horizontal saccades. The SEFs are involved in motor program of

several successive saccades (Merriam et al., 2003), as confirmed by Stuphorn et al., 2010 on monkeys.

Previous studies reported two potentials immediately before the saccade onset: the pre-motor positivity and the spike potential. The pre-motor positivity was not found in the present and in several previous self-paced studies (Yamamoto et al., 2004; Papadopoulou et al., 2010). This result could be explained by the task employed (i.e. self-generated saccade), since the pre-motor positivity seems related to stimulus presentation in externally triggered saccades (Thickbroom and Mastaglia, 1985).

Peaking 20 ms before saccades, we found the anterior MP component which was localized in the contralateral middle frontal gyrus within the FEF region, in accordance with previous studies that identified the FEF as crucially involved in triggering an intentional saccade and in guiding visual fixation (e.g. Pierrot-Deseilligny et al., 2003b; Sander et al., 2010). Due to its frontal scalp distribution and timing, the MP might be associated to the spike potential whose neural generator is still controversial. Indeed, some findings support the notion that this wave might reflect the recruitment of the oculomotor muscle units and ocular motor neurons (Moster and Goldberg, 1990; Thickbroom and Mastaglia, 1986), while other studies showed the involvement of cortical areas (e.g. Weinstein et al., 1991; Pierrot-Deseilligny et al., 2003b). Present results might shed light onto this controversy showing the presence of an ipsilateral negativity immediately after the positive MP (recorded at leads contralateral to saccade direction) peaking at saccade onset even more anteriorly than the MP. Given its latency and distribution, this potential may be generated by the muscle activity. Thus, here we found that the FEF and the ocular muscles might have generated two potentials, which are partially overlapped in time and space.

Several studies investigated the post-movement RAP component for saccades often called lambda activity (Billings, 1989; Ogawa et al., 2005. See also Jagla et al., 2007 for a review), present also for microsaccades (Dimigen et al., 2009). We localized this positive activity in occipital extrastriate areas at around 130 ms after saccades onset; it is likely that this activity is triggered by the vision of targets, reflecting the encoding of new foveal information (Jagla et al., 2007).

Overall, present data update the previous literature on self-paced saccades and adopt a terminology close to that used for limb movements (e.g. Yamamoto et al., 2004). This approach allows appreciating the similarity and differences between eyes and limbs self-paced movements (Fig. 5). All components described for limb movements were also detected for eye movements, within similar temporal windows, but, as expected, with different cortical sources.

The second aim of the study was to evaluate the possible MRCPs differences between short- and long-fixation saccades. Results showed that the cortical activity associated with the two saccades was quite similar except for the BP component. Specifically, both onset latency and amplitude of this activity were influenced by the task demands. The BP at temporal-parietal sensors for long-fixation saccades initiated about 300 ms earlier and was larger than short-fixation saccades. Moreover, topographic distributions and underlying cortical sources were different. Until 800 ms before the saccadic onset, activity was present in the contralateral IPS during both tasks and afterwards, only during the long-fixation saccades, activity became bilateral, involving also the ipsilateral IPS. The differences observed on the BP component in the two saccadic tasks differ from Thickbroom and Mastaglia (1985) data showing almost identical BP for short- and long-fixation saccades. The only reliable difference that the authors described was the lower amplitude of the BP for short- than long-fixation saccades at frontal recordings, even though their topographical findings suggested a more central and posterior origin for the BP, and larger BP amplitude on the side contralateral to the eye direction. The authors did not place much significance on the aforementioned

results, because the contribution of the EOG fields with the two types of saccades might have influenced its topography. In the present study, the higher number of recording sites and the source analysis helped us to more precisely estimate the origin of the signal, and to subsequently unearth and discuss such findings.

The differences found in the spatial and temporal dynamics of the activity preceding the two saccadic tasks may be interpreted in several ways. In general terms, the long-fixation saccades planning could be more complex than the short-fixation saccades. The delaying of the re-centering saccade and the need of keeping the fixation for several seconds on the lateral target support the higher complexity of the long-fixation task. Even though the modulation of the BP by task complexity is well known for limb movements, i.e. the BP starts earlier and it increases amplitude as a function of the task's load (Klostermann et al., 1994), the effect of the task complexity for saccades has been reported only in studies using externally triggered saccades (Everling et al., 1997). Within this framework, our findings are the first to show the task complexity effect with self-paced saccades task.

Furthermore, the involvement of ipsilateral parietal cortex during the preparation phase well before the onset of the first saccade might reflect the remapping of the space (and particularly the future position of the actual fixation point) anticipating the eyes position before the first saccade's landing. The source of the BP component in the ipsilateral parietal regions is consistent with the anatomical location of area LIP. Studies in monkey parietal cortex were the first to reveal activity in LIP neurons related to the spatial remapping of the visual world across saccades. LIP neurons have visual receptive fields, which, like classical receptive fields throughout the visual system, are tied to retinal coordinates (Kusunoki and Goldberg, 2003; Johnston and Everling, 2008). Thus, whenever a stimulus is flashed in that part of the visual field that constitutes a neuron's receptive field, it fires, regardless of where the eyes are looking. Duhamel et al. (1992) found that the visual receptive fields of some LIP neurons appeared to shift just before a saccade, from their normal retinal location to the location that the receptive field would occupy after the saccade. Moreover, the neural activity is maintained for several seconds after the cue offset, such as for a delayed saccade. The enhanced response during the delay preceding a saccadic movement is thought to reflect the intention to move the eye (see Calton et al., 2002). Along with this view, the ipsilateral activity, recorded here only during the long-fixation task preparation, could reflect the "intention" to execute a delayed re-centering saccade.

Supporting this interpretation, some fMRI experiments investigating brain regions involved in spatial remapping in humans pointed to a role of dorsal parietal regions, perhaps homologous to monkey area LIP, in such a function (Medendorp et al., 2003; Merriam et al., 2003). These studies suggest remapping of remembered spatial locations across the hemispheres, from one parietal region to its contralateral homologue, when an intervening saccade reverses the position of a remembered location relative to fixation. Thus, if saccade location was initially on the left of the fixation point, it would be encoded within the right parietal cortex. However, if a large leftward gaze shift occurred, the original fixation point was then to the right of the current position, and consequently it would be remapped within the left parietal cortex. Note that the presence of a retinotopic map of the remembered saccadic targets in area LIP as shown in Sereno et al. (2001) fits well with the proposed interpretation of our findings. A compatible location was found in many other studies on saccadic eye movements and spatial attention, and often described as posterior IPS or Parietal Eye Field (PEF) (e.g. Corbetta and Schulman, 2002; Culham and Valyear, 2006).

In conclusion, present study provides novel information on the sources and time-course of activities preceding and concomitant to self-generated saccades. These saccades are first programmed

in contralateral IPS, then in the SEF, and finally the execution processing is performed by FEF structures. Furthermore, we showed that the motor preparation of saccades followed by long fixations is more complex and involves also the ipsilateral IPS. Further investigations with the simultaneous recording of the EEG with D/C amplifiers and eye tracker measures would provide additional validation of the current findings.

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