The Effect of Saccadic Eye Movements on the Sensor-Level Magnetoencephalogram

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Abstract

Objective: We used a combination of simulation and recordings from human subjects to characterize how saccadic eye movements affect the magnetoencephalogram (MEG).

Methods: We used simulated saccadic eye movements to generate simulated MEG signals. We also recorded the MEG signals from three healthy adults to 5-degree magnitude saccades that were vertical up and down, and horizontal left and right.

Results: The signal elicited by the rotating eye dipoles is highly dependent on saccade direction, can cover a large area, can sometimes have a non-intuitive trajectory, but does not significantly extend above approximately 30Hz in the frequency domain. In contrast, the saccadic spikes (which are primarily monophasic pulses, but can be biphasic) are highly localized to the lateral frontal regions for all saccade directions, and in the frequency domain extend up past 60 Hz.

Conclusions: Gamma band saccadic artifact is spatially localized to small regions regardless of saccade direction, but beta band and lower frequency saccadic artifact have broader spatial extents that vary strongly as a function of saccade direction.

Significance: We have here characterized the MEG saccadic artifact in both the spatial and the frequency domains for saccades of different directions. This could be important in ruling in or ruling out artifact in MEG recordings.

Keywords:

MEG

Magnetoencephalography

Saccade

Saccadic Spike

Saccadic Spike Field

Gamma Band

1. Introduction

For both electroencephalography (EEG) and magnetoencephalography (MEG) eye movements are a major signal source **which could easily be confused with other brain-related signals. There are two primary factors which we consider here: the rotation of the eye dipoles, and the synchronous activation of the extraocular muscles.**

Each eye acts like a strong current dipole, and its rotation due to saccadic eye movements can produce massive electrical and magnetic signals. This is the source of the electro-oculogram (EOG), but this signal is strong and can be easily seen at sensors across a large fraction of the scalp surface and not just near the eyes.

At the beginning of a saccade there is also a short-duration synchronous activation of the extraocular muscles (Van Gisbergen et al., 1981). This results in the so-called “saccadic spike,” a brief transient at the beginning of a saccadic eye movement that has a frequency composition extending up into the gamma band (Boylan and Doig, 1989; Keren et al. 2010; Kovach et al., 2011; Moster and Goldberg, 1990; Riemslag et al., 1988; Thickbroom and Mastaglia, 1985; Yuval-Greenberg et al., 2008). This saccadic spike can be seen in human patients that have intact extraocular muscles moving a prosthetic eyeball (Thickbroom and Mastaglia, 1985), thus ruling out any sort of retinal or other eyeball-localized source.

Thus, eye movements can have **strong** effects on extracranial electric and magnetic recordings, and a clear understanding of how eye movements affect EEG and MEG signals is critical for interpreting these measures of brain function. Because of the recent interest in gamma-band brain activity, and because **saccade timing and incidence** can vary with the cognitive task, *even on non-visual tasks*, and *even when the eyes are closed*, (Ehrlichman et al., 2007), the properties of the saccadic spike are of especial current relevance.

As mentioned previously, there are extensive studies on the effects of saccadic eye movements on the EEG, but relatively few on the MEG. One recent study on the effects of saccades on the MEG found that the saccadic spike artifact in the MEG (which is sometimes but not always referred to in the MEG as the “spike field”) was most prominent in the gamma frequency band, and as expected localized to the extraocular muscles (Carl et al., 2012). However, that study only examined horizontal saccades, aligned saccade onsets using the EOG instead of an eye tracker, used bandpass filtering to isolate the saccadic spike, and averaged their data over multiple subjects. In this study we looked at both horizontal and vertical saccades in both directions in individual subjects, modeled the effect of rotating eye current dipoles on the MEG signals, and did not use either narrow bandpass nor line noise notch filters to identify saccadic spike artifacts in the time domain.

We find that the saccadic spike artifact is typically a monophasic pulse, although it can sometimes be strongly biphasic. It begins before the start of a saccadic eye movement, and can extend up past 60 Hz in the frequency domain. In contrast, the effect of the moving dipoles in the frequency domain is primarily below 30 Hz (going down to alpha, theta, and lower frequencies), and has a more widespread spatial distribution that varies strongly with the direction of the eye movement. We also find that the effects of rotating eye current dipoles can in principle be completely accounted for with only three independent components, although in practice this is not so simple. These results may prove useful for ruling in or ruling out saccadic artifacts in MEG recordings, especially as visual inspection of the raw data from individual subjects remains such an important aspect of MEG studies.

2. Materials and Methods

2.1.1 Simulations: Single Saccades

When an eye moves during a saccade, it can be modeled as a single rotating current dipole. The rotating current dipole creates a rotating magnetic field. As the rotating magnetic field sweeps across magnetometer sensors that are located at different positions around the head, it is possible that the magnetic field as a function of time that is picked up by any given magnetometer may not be a simple scaled version of the eye position as a function of time. Determining the possible effect of the geometry of a rotating eyeball on the signals picked up by fixed magnetometers is therefore critical to understanding how saccades may affect the recorded MEG signal.

Of course in the real world current must flow in continuous loops: it is impossible to have a single isolated segment of flowing current without there also being *return* currents. So if the eye is modeled as a current flowing from the front of the eye to the rear, there must also be currents flowing in the orbit and surrounding tissue that is moving from back to front. As is common practice we assume here that the return currents are so dispersed that they can be ignored. It is conceivable that the return currents may change their distribution due to a change in the relative position of the cornea in the orbit, which may add second-order effects, but this possibility is not explored here.

We took the positions and orientations of the magnetometers from the manufacturer-supplied coordinates of the 4-D Systems Magnes 148 WH MEG system. We modeled the two eyes as unit current dipoles at coordinates X (anterior-posterior) 80 mm, Y (medio-lateral) 32 mm, and z (superior-inferior) 25 mm for the left eye, and XYZ 80,-32, and 25 mm for the right

eye (simulated intraocular distance 64 mm). We varied these positions over a range of +/- 3 cm anterior-posterior and +/- 2 cm superior-inferior to verify the robustness of the results.

The saccades were simulated using as a basis the change in angular position over time of the human critically damped 12 degree saccade of Bayhill et al. 1975. **It was surprising to us that we were unable to find any other plots of angle vs. time for normal human saccades: for now, Bayhill et al. 1975 may be the only such example in the published literature, and we use it as a reference standard.** For every millisecond of the saccade simulation, both the left and the right eye dipoles were each rotated by the same amount as the saccade from Bayhill et al. 1975 at that point in time. This rotation was performed in the horizontal plane for simulated horizontal saccades, and in the vertical plane for simulated vertical saccades. The simulation was written in Matlab and run at discrete intervals of 1 msec. The magnetic field at each magnetometer was computed using the Biot-Savart law:

$$B \propto \frac{I dl \times r'}{|r'|^3}$$

Where B is the magnetic field, I is unit current, dl is a unit vector pointing in the direction of the eye, and r' is the full displacement vector from the eye dipole to the location of each magnetometer. The simulated magnetometer signal was computed by taking the dot product of the magnetic field at each magnetometer location with the magnetometer normal vector. The eye velocities are slow enough that magneto-quasistatic conditions are assumed.

We also performed simulations with different sized saccades and verified that, as one might expect, the effects of the rotating eye dipoles on the mEG signal scale linearly with the size of the eye movement for saccades less than 12 degrees in magnitude.

2.1.2: Simulations: Multiple Saccades and Independent Components Analysis

We used a simulation to determine how many ICA components would be required to handle the eye-dipole artifacts in a dataset where the eyes could move in any direction and over a large range of amplitudes. We first created a simulated set of horizontal and vertical eye movements, where saccades occurred at intervals of between 250 and 400 msec. Each simulated saccade was to a random position ± 25 degrees from the central position both horizontally and vertically. The simulation lasted five minutes (300,000 milliseconds). The simulation parameters were as in section 2.1.1 above, as was the process of going from simulated eye position to simulated MEG signals. The variance in this simulated data set will be completely due to eye dipole rotation, and therefore any method that can completely account for this variance could, in principle, completely eliminate this artifact.

The simulated MEG signals were high-pass filtered, and the FastICA algorithm used to extract independent components (Hyvarinen 1999). As there are 148 simulated sensors for 300,000 msec, the input to the FastICA algorithm consisted of 148 signals and 300,000 points, although the signals were first compressed to 20 via a principle components pre-processing step.

2.2 Human studies: recording.

Three normal human subjects ages 24 to 57 were used. The MEG recordings were made in a 4-D Systems Magnes 148 WH (“Whole Head”) magnetometer in a shielded room below ground level. Subjects lay on their backs with their eyes open. A visual target was placed 57 cm

from their eyes. This consisted of three small fiber-optic cables glued into a piece of cardboard, and each of which produced a small point of white light. There was a central fixation point, and a point below the fixation point, and a point to the right of the fixation point. Subjects were instructed to make self-timed saccades from the fixation point to the right and then back, and then from the fixation point downwards, then back up. An average of 77 successful trials were recorded for each saccade direction and subject (range 52 – 86).

Eye movements were recorded using an ISCAN RK716 video tracker (Woburn, MA). The tracker sampled eye position at a rate of 60 Hz. The mean delay between when eye position was sampled and the eye tracker output a change in analog voltage (recorded by the MEG system) was determined by having the tracker focus on a hole cut out in a piece of paper with an LED on the edge of the hole. When the LED was turned on this resulted in a small but detectable change in measured eye position. The delay between a change in eye position and a change in recorded eye tracker signal was determined to be 33 msec, and was corrected for in the results. In order to improve the temporal precision of the eye tracking data, the 60Hz sampled eye position was fit with a cubic spline curve and resampled to 1 kHz. Because the saccadic signal is strongly band-limited to below 30 Hz this should result in minimal loss of temporal resolution. Saccade onset time was determined as the point at which the eye position has moved 20% of the distance from the initial to the final position.

Because the video camera created significant noise if placed next to the MEG sensors, it was positioned approximately three meters away in a far corner of the room near the door, and a 500 mm telephoto lens whose optical path was bounced off a first-surface mirror was used to zoom in on the left eye of each subject. The computer running the eye tracker was outside the

shielded room, and output analog signals representing horizontal and vertical eye position that were recorded by an A/D integrated and synchronized with the MEG recording system.

A recording run was five minutes in duration. Signals were digitized at a rate of 1 kHz, and bandpass filtered from 0.1 to 200 Hz. No notch filters were used in the recording. Analysis was done offline using custom-written MATLAB routines.

2.3 Human studies: analysis.

Data were first imported into matlab. The ballistocardiogram was removed using a template-based time-domain technique. The onset of saccades was determined by hand, choosing the first step of the recorded eye position signal that was visibly different from the baseline. Regions of the data that were visibly corrupted with blinks or motion artifacts were excluded from the analysis. MEG signals from 200 msec before to 200 msec after each hand-identified saccade were extracted for analysis. Because we already know that the eye dipoles are located in the eyes, and the saccadic spike artifacts originate in the extraocular eye muscles, there is no point to doing inverse source modeling (and many inverse source methods can potentially introduce significant artifacts of their own). Therefore all analyses were done at the level of the magnetometers themselves.

Spectrograms were computed using sliding 50 msec-width Hamming windows with 10 msec overlap. The 50 msec chunks were symmetrically padded with 470 zeroes before the Fourier transform was calculated, in order to increase the smoothness of the spectra at lower frequencies. Data were zero-measured within the sliding window.

The data from one subject was partitioned up into 400 msec chunks centered around the onset time of a saccade, all saccade directions mixed together, and 16 independent components

were extracted using the FastICA algorithm (Hyvarinen 1999). The resulting independent component waveforms were then averaged time-locked to saccade onset.

All experiments were performed with the understanding and written consent of the subjects, and were approved by the UAB Institutional Review Board.

3. Results

***** **FIGURE 1 AROUND HERE** *****

3.1 Simulations

Fig.1A shows the baseline saccade as a function of angle and time. This was digitized from Bayhill et al. 1975, and is slightly faster than the human average but still well within the natural range of variation (Leigh and Zee 1991). Fig.1B shows superimposed traces of simulated magnetometer signals overlaid, and normalized to the same range. Depending on the magnetometer location, there are a wide variety of trajectories. The MEG signals are not just scaled copies of the eye position trajectory, although they do tend to cluster around the shape of the eye position trajectory. They are not, of course, anti-causal – they cannot start before the eye actually begins to move nor change after the eye has stopped moving. Plots of the spatial distribution of these simulated signals across the scalp surface are given in **Supplementary Figure S1**. Simulations verify that these results scale linearly with decreasing saccade magnitude, e.g., a 1.2 degree saccade would produce exactly the same pattern of MEG response as the illustrated 12 degree saccade, but scaled to 10% of the amplitude.

Fig.1C shows the same data but with no scaling, and the polarity of the signal change forced to be positive. Without scaling it appears that the most unusual **MEG sensor** trajectories are small in absolute magnitude. **Specifically, the ‘reversing’ trajectories E and F cover 4.8% and 0.2% of the signal range as the more regular trajectory D, respectively.** Thus, the larger magnitude MEG signals appear to be qualitatively similar, **although not identical, to a saccade trajectory, while the ‘reversing’ trajectories are much smaller in relative magnitude.**

Fig.1 D-F show time-frequency spectrograms from three selected exemplar waveforms as labeled in Fig.1B. These three waveforms were selected to span the range of behavior: D is a typical waveform that closely matches the eye movement trajectory, E shows a waveform that partially reverses during the saccade, and F shows a waveform that strongly reverses during the saccade. Even though these waveforms look different, none of them create activity in the higher frequency bands.

******* FIGURE 2 AROUND HERE *******

3.1 Human Studies – Overall Topography

Fig.2 illustrates the average MEG signal from a single subject to a 5 degree horizontal leftwards saccade, positioned as if looking down on the top of the MEG sensor array. Data for each sensor was set to zero in the interval from 200 to 150 msec prior to saccade onset. The deflections are strongest around the frontal sensors. See Supplementary Figure S2 for pdf versions of these and other figures for different directions and subjects: because these are in vector format they can be zoomed in on in the electronic version of this paper for more detail. Small pulses just before saccade onset can be seen in lateral frontal and parietal sensors. These are typically monophasic, but can be strongly biphasic, **as for example seen on the fourth page of Supplementary Figure S2.** The slower patterns of activation seen in the posterior occipital

sensors are most likely due to the visual evoked potential created from a shift in the retinal image from both the current and the preceding saccade (Gawne et al. 2011). This pattern of activity is qualitatively similar to that obtained from the simulations (see again [Supplementary Figure S1](#)), and a rightward horizontal saccade produces qualitatively the opposite pattern of response ([Supplementary Figure S2](#)). The responses from four exemplar sensors have been outlined in dashed circles (A71, A83, A131, and A148) and are considered in more detail later.

***** [FIGURE 3 AROUND HERE](#) *****

Fig.3 illustrates the average MEG signal from a single subject to a 5 degree downwards vertical saccade, laid out as in Fig.2. In contrast to the horizontal saccade, a vertical saccade produces very little signal over central frontal sensors, and is strongest laterally. Again, small pulses just before saccade onset can be seen in lateral frontal sensors. This pattern of activity is also qualitatively similar to that obtained from the simulations ([Supplementary Figure S1](#)), and an upwards vertical saccade produces qualitatively the opposite pattern of response ([Supplementary Figure S2](#)).

***** [FIGURE 4 AROUND HERE](#) *****

Fig.4 illustrates more detail from the selected exemplar sensors from the single subject illustrated in Fig.2. The top row (A) shows that at frontal lateral sites (A131 and A148) there is a monophasic pulse that is similar in timing but opposite in polarity left vs. right. The frontal central sensor (A71) does not have this spike, but only the large excursion signal caused by the rotation of the eye dipole. The posterior site (A83) shows nothing specifically like this. The middle row (B) shows the spectrogram of the average signal traces, and the bottom row (C) shows the average of the spectrograms of the individual trials. These latter are greater in

magnitude, especially in the higher frequency bands, most likely because frequency components of different phases will not average out. We don't see 60 Hz in the spectrogram of the average, but do in the average of the spectrograms, because averaging in the time domain will tend to cancel the 60 Hz line noise. The variable amount of sustained 60 Hz activity in the bottom row is because the amount of line noise varied with sensor location.

Note that the channels that get the saccadic spike show a strong burst of broad-band activity extending up past 60 Hz, while the saccadic artifact away from the extraocular muscles is band-limited to mostly below 30 Hz. This is slightly lower in frequency than the results of the stimulation (see again Fig.1E-F), likely because the saccade in the simulation was slightly faster than the human average, although still well within the range of normal variation (Leigh and Zee, 1991).

The activity in these spectrograms falls off below 20 Hz because the moving window was 50 msec in width and thus the Raleigh frequency was 20 Hz, and also because the data was zero-measured at each epoch. However, it is important to realize that the real frequency spectrum of the moving dipole artifact will have significant power in alpha, theta, and delta bands – effectively, down to DC. Granted it can be easier to remove these lower-frequency components from a recording using independent components or other methods, because less temporal precision is required. **Nevertheless** one should always bear in mind the potential of an eye movement to contaminate a signal across a very broad range of frequencies, not just the gamma band.

Simulations have determined that the amplitude of the saccade is unlikely to significantly change the frequency composition of the time-frequency spectrogram (see Supplementary Figure S3). There is a wide range of variation in the saccade speed of normal human subjects (Leigh

and Zee 1991), but it does not appear that the moving dipole effect would ever produce the kind of short-duration broadband signatures seen in Fig. 4C.

***** FIGURE 5 AROUND HERE *****

***** FIGURE 6 AROUND HERE *****

Fig.5 shows the topographic distribution of 50 Hz gamma band activity around the time of saccadic onset for all four directions of eye movements and all three subjects. There is variability, but it is fairly consistent that the saccadic artifact in the gamma band is localized to lateral frontal sites, and is often roughly symmetrical left vs. right. Fig.6 shows the same thing only at 20 Hz beta band activity, although this distribution will be consistent down to alpha and theta frequencies and lower. Here the artifact is consistently lateral frontal for vertical saccades of either direction, but for horizontal saccades they are more frontally located, and vary more strongly as a function of direction.

Supplementary Figure S4 shows the results of applying ICA analysis to a continuous series of simulated saccades of arbitrary direction and a range of magnitudes. Just three components completely accounted for all of the variance in the simulated MEG signals. Curiously two of the components qualitatively looked like eye movements, but the third had rapid ‘reversals’ during the saccades. It should also be noted that, because the different time-slices in ICA do not interact (e.g., you could shuffle the data between different time points and not change the ICA decomposition) these results will also hold even if the saccades vary in speed, temporal profile, or with any degree of linear temporal filtering.

***** FIGURE 7 AROUND HERE *****

Unfortunately when applied to the real physiological data, this clean result does not hold up, and the effects of saccades appear to be spread across a large number of independent components. Fig.7 illustrates the results of applying independent components analysis to the data from the subject whose data was shown in Fig.2 and 3 (all four directions). Looking at the time domain in panel A, we see ICA5 accounts for some of the saccadic spike, and looking at the topographic distribution in panel B, we see that it is located in the lateral frontal sensors as expected. However, for ICA6, the saccadic spike has also been confounded with activity in the left posterior sensors, and the moving dipole artifact seen in ICA 7 is present in the central frontal right sensors, and also in the left posterior sensors. The independent components of physiological saccade-generated MEG data appears to be spread out and mixed with a variety of other signals, and is not cleanly isolated.

***** FIGURE 8 AROUND HERE *****

It must be pointed out that the data in fig. 2-6 are averaged across multiple saccades. Visual inspection of the raw MEG traces did not show evidence of saccades on single trials. Fig.8 is the result of taking the average spectrogram across the 12 MEG sensors that had the largest saccadic spike amplitudes, for the first 25 single trials of the data from Fig.3 and 4. One can see evidence of the saccade, but it is inconsistent. We tried several different temporal filtering and spatial weighting functions and were not able to find any technique that could reliably detect individual saccades of this magnitude using only the MEG signals.

4. Discussion

Because of the geometry of the MEG sensors and the moving eye current dipoles, MEG sensor traces, while mostly similar to each other, are nevertheless not precisely scaled copies of either the eye movement trajectory or each other. In the gamma band, the saccade artifact was localized in the lateral frontal regions for all classes of eye movements and all subjects. If this pattern is seen, saccadic artifact should be at least considered, but **in this frequency band** saccadic artifact can likely be ruled out for other topographic spatial patterns. In the beta and lower frequency bands the saccadic artifact was more **spatially** widespread, and varied **more** strongly as a function of the direction of the saccade. Given that awake subjects move their eyes in ways that can depend on the cognitive task, even when their eyes are closed or during non-visual tasks (Ehrlichman et al. 2007), the different topography of MEG saccadic artifacts in the different frequency bands should be kept in mind.

The signal space separation method (Taulu and Kajola 2005) cannot be used to remove saccade artifact from MEG data (at least not as typically performed) because it can only reject sources outside the sensor helmet, and both the eyes and the extraocular eye muscles are inside the helmet. Independent Components Analysis (ICA) is routinely used to remove saccadic artifacts, but has typically only been evaluated for saccades of limited directions and magnitudes. Our results show that while just three components are in theory needed to completely account all of the variance in the MEG signal caused by eye dipole rotation for any combination of saccades of any directions or magnitudes (see again **Supplementary Figure S4**), in practice with real saccades saccade-related signals appear to be spread out over a large number of independent components (see again Fig.7).

One is reminded that independent components are statistically independent, but this does not mean that they are physiologically independent. For example, suppose that an eye movement tended to occur slightly more frequently during a specific phase of the alpha rhythm. Then ICA analysis would mix one aspect of the alpha signal in with one aspect of the saccadic artifact. In the final analysis, ICA is just a simple linear unmixing algorithm and it is not omnipotent. At least when applied in a direct manner, our results suggest that saccadic artifacts can be spread over a large number of different components and conflated with other signals.

We were not able to reliably detect microsaccades in this study, however, simulations show that the eye dipole effect will scale linearly with saccade amplitude. Thus, for a saccade of 0.5 degree amplitude the eye dipole artifact will have the same topographical distribution as for the 5 degree saccades used in this study, only scaled to one-tenth the magnitude. The saccadic spike is due to the initial burst of extra-ocular muscle activity at the start of a saccade, and as this initial burst (“pulse”) of extraocular muscle activity scales linearly with saccade amplitude (Leigh and Zee, 1991), one should expect that the MEG saccadic spike should scale linearly with saccade amplitude as well. This linear relationship has been previously demonstrated for the EEG (Keren et.al. 2010, Fig.4).

It should be noted that there are other possible ways that an eye movement could affect the MEG signal. For example, if the eyes are open a saccade could change the retinal image thus activating the cortical visual system. Importantly, this could include effects from preceding saccades, because saccades tend to occur with an irregular rhythm about every 200 to 300 msec and visual cortical processing of an image change can often last this long (for example, see Gawne et al., 2011). We do not address this issue here, but only point out that any MEG study involving saccades with the eyes open should consider the visual environment both before and

after the saccade, as well as the during the previous saccade. Saccade-related signals could also arise from the cortical frontal eye fields (McDowell et al., 2005), although in principle this could be considered as a legitimate task-related brain function, and not an artifact per se.

***** FIGURE 9 AROUND HERE *****

These results may also prove of use when combined with other techniques for automatically identifying eye movement artifacts. We reconfirm that the frequency band from 30 to 70 Hz will be relatively specific for the saccadic spike artifact (Carl et al 2012). However, the saccadic spike artifact is much broader band than this: therefore, using a bandpass filter will distort its true shape. Also, the extremely broad spectrum of the saccadic spike artifact in time-frequency space may be a more reliable indicator of the presence of a saccade than just the activity in the band from 30 to 70 Hz. Consider the cartoon in Fig.9. If saccades are aligned in time about an event of interest, there will be a temporally brief and broad-band in frequency pattern of activity in the time-frequency spectrogram (as seen in Fig.4C, two leftmost panels). If the saccades are misaligned with respect to an event of interest, you will get a more diffuse pattern of response in the time-frequency spectrogram, which might be mistaken for non-phase-locked gamma band (‘induced’) brain activity, but there will still be a broadband pattern across frequencies (assuming that one is not narrow-band filtering the data, of course). On the other hand, narrow-band gamma activity that does not correspond in time with lower-frequency activity is not likely to be due to saccades, especially if it is not localized to the lateral-frontal sensors.

Conclusions

In the gamma band, ruling out saccadic artifact is potentially easy. We have demonstrated that the movements of the eye dipoles cannot create any significant power in the gamma band, and so it is only the saccadic spike that can contaminate the gamma signal. This spike will be localized over the eyes regardless of saccade direction, and because it is a pulse, it will be spectrally broad-band. Therefore, if you find a pattern of gamma band activity that is not associated with a spatial peak over the eyes, you can rule out saccadic artifact. Also, if you find gamma-band activity that is not simultaneously associated with lower-frequency activity, you can also rule out saccadic artifact.

However, in the alpha and lower frequency bands, saccadic artifacts are potentially harder to rule out. That is because the movement of the eye dipoles does create strong signals in these lower frequency bands, and these are both spatially more widespread and this spatial distribution varies strongly with saccade direction. We could not find any obvious means of detecting saccades in single trials from the raw MEG signals. While the eye dipole artifacts have subtly varying shapes as a function of sensor and saccade direction, in principle just three independent components can account for all eye-dipole related activity for an arbitrary combination of saccade directions and magnitudes. However, we point out that when independent component analysis is applied to real data the algorithm could potentially spread the effects of saccades over a large number of components. We would suggest that MEG studies exploring alpha-band and lower frequency signals in the anterior sensors should use eye tracking of some sort. This should be done even when the eyes are closed, although the relative insensitivity of the EOG to microsaccades could be an issue. Alternatively, if directed saccades are part of the experimental design one might optimize the direction to minimize contamination

in specific regions of interest: using vertical saccades to minimize artifact in central frontal regions, and horizontal saccades to minimize artifact in more lateral temporal regions.

Conflict of Interest

None of the authors have potential conflicts of interest to be disclosed.

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Figure Legends

Fig.1. Results of simulations of a rotating current dipole on the MEG field strength normal at the different magnetometers. A: Time course of the rotation of the simulated eye dipoles, based on a real digitized human saccade (Bayhill et al. 1975). B: The signals at all 148 MEG sensors, normalized to range between 0 and 1. The red line is the normalized eye position trace from panel A. In addition to the red line, three specific MEG waveforms have been given different colors and labels and are considered in more detail later. C: The signals at all 148 MEG sensors, flipped to be positive in magnitude but not normalized. D-F: Time-frequency spectrograms (50 msec windows) from the three exemplar waveforms identified in the different colors in panel B, over a longer period of time. As with panel B, these plots are normalized: the absolute magnitude of the more unusual reversing waveforms in panels E and F are smaller than the more

typical one seen in panel D (see text). The more unusual ‘reversing’ temporal waveforms do not obviously increase the peak frequency.

Fig. 2. Average MEG signal response to a 5 degree leftwards saccade from a single subject.

Each small plot is the signal from a single magnetometer, averaged time-locked to saccade onset (indicated by vertical red bars). The individual sensor plots are arranged as if looking down on the top of the subject’s head, with the nose pointed up. The individual sensor plots are not arranged as a 2D projection of the 3D sensor positions, but are spread out so that the individual plots do not overlap. Four exemplar sensors have been outlined in dashed circles and are considered in more detail later.

Fig. 3. Average MEG signal response to a 5 degree downwards vertical saccade from a single subject.

The figure is arranged as in Fig.2, where each small plot is the time-averaged signal from a single magnetometer aligned about saccade onset (indicated by vertical red bars). The individual sensor plots are arranged as if looking down on the top of the subject’s head, with the nose pointed up. The individual sensor plots are not arranged as a 2D projection of the 3D sensor positions, but are spread out so that the individual plots do not overlap.

Fig. 4. Each column is taken from an exemplar magnetometer sensor from Fig. 2, a 5 degree left horizontal saccade. From left to right, sensor A131 is a left frontal sensor, A148 is a right frontal sensor, A71 is a midline frontal sensor, and A83 is an occipital midline sensor. Row A.

Expanded views of the individual sensor signal as a function of time. A131 and A148 both show strong saccadic spikes. Sensor A71, located in the frontal midline, shows a strong saccade-

related signal that is probably due to the rotating eye dipoles, but no saccadic spike. Sensor A83, from the occipital cortex, shows no clear saccade-related activity. Row B. The time-frequency spectrogram of the average MEG signal, using sliding 50 msec windows. The two frontal-lateral sensors (A131 and A148) show a burst of activity around saccade onset, as does A71, although the peak frequency in A71 is less. The occipital sensor A83 shows negligible activity in this space. Row C. The average of the spectrograms of the individual trials. Here it is much clearer that the saccadic spike produces a burst of activity extending up past 60 Hz, while sensor A71, which has only the eye dipole effect, is more strongly band-limited. Because averaging the spectrograms does not average out non phase-locked signals, these plots can have relatively constant horizontal bands to either 60 Hz noise or spontaneous brain rhythms.

Fig. 5. Contour plots of peak magnitude of the time-frequency spectrogram at 50 Hz for all four saccade directions (columns) and all three subjects (rows) in the study. As with Fig.2, these plots are arranged as if looking down on the top of each subject's head, with the nose pointing up. While activity in this frequency band does vary between subjects and saccade directions, spatially it is narrowly localized and always in roughly the same positions.

Fig. 6. Arranged as in Fig.5., contour plots of peak magnitude of the time-frequency spectrogram for all conditions and all three subjects in the study, only looking at the peak of the time-frequency spectrogram at 20 Hz. While the activity in this lower frequency band is still mostly localized around the eyes, it is generally more broadly distributed than for the higher-frequency 50 Hz data shown in Fig.5, and can vary more with saccade direction. In particular, horizontal saccades can produce a lot of activity at the low frequency bands over the frontal

midline (left two columns), while vertical saccades produce activity that is restricted to the lateral frontal regions (right two columns).

Fig. 7. A. The first 16 independent components taken from the raw time series data from the subject whose data was illustrated in Figs.2 and 3 (all saccade directions included), and then averaged time-locked to the time of saccade onset. The number of the component is given in each sub-panel. Saccade onset was at $t=200$ msec, the middle of each plot B. Topographic distribution of the weights of the independent components shown in panel A. The effects of a saccade appear to be spread out over a large number of independent components.

Fig. 8. The time-frequency spectrograms taken from the first 25 single trials of the subject and saccade direction in Figs. 3 and 4. Time 0 is the time of saccade onset. A 50-msec wide moving windows was used to compute the spectrogram. The contour plots are the average of the 12 individual MEG sensors that had the largest saccadic spike activity. While one can often clearly see evidence of saccade in the time-frequency domain in a single trial, this does not appear to be strong enough to reliably detect saccades in single trials.

Fig. 9. Cartoon of the signature of a saccade both as a function of time (left column) and in the time-frequency spectrogram space (right column). Row A. Saccades aligned in time, and the spectrogram shows a brief broad-band burst. Row B. Saccades misaligned in time, the spectrogram shows a longer-duration but still broad-band pattern of activity. This could occur if saccades were elicited around the time of another event, but were not precisely phase-locked to it. Row C. Narrow-spectral gamma band activity with no temporally corresponding lower-

frequency activity. This pattern could not likely be due to a saccadic artifact, because a saccadic artifact extends to lower frequencies

Supplementary Material

Supplementary Figure S1. Simulated effect of a vertical and a horizontal saccade on the MEG signal across all 148 magnetometer sensors, as a function of time. The data are laid out as in Fig.2 and 3 in the main text. Each small plot is the simulated signal from a single magnetometer over a 400 msec interval, with simulated saccade onset in the middle indicated by the vertical red bar. The plots are laid out as if looking down on the top of the subject's head with the nose pointing up. The plots are not a 2D projection of the 3D magnetometer locations but are spread out for clarity.

Supplementary Figure S2. Actual MEG signal traces for all 148 magnetometers, for all four directions of saccades, and all three subjects. The plots are arranged as in Fig.2 and 3 in the main text, and Supplementary Figure S1. Vertical red bars represent time of saccade onset, and their height is 200 femtotesla.

Supplementary Figure S3. A. Three different magnitude saccades (scaled according to Leigh and Zee, 1991, where saccades with twice the amplitude have twice the peak velocity) plotted as a function of time. B-D. Time-frequency spectrograms of the three different magnitude

saccades. The larger magnitude saccades have a higher peak velocity, but a longer duration. The peak frequency response of this range of saccades is little changes, i.e., the larger size and peak velocity of the larger amplitude saccades does not result in a greatly increased peak temporal frequency.

Supplementary Figure S4. A. Simulated multiple saccades of variable direction and magnitude (5000 msec excerpt from a 300,000 msec simulation). B. Simulated high-pass filtered MEG signals in a ‘butterfly plot.’ C. The three independent components that, together, accounted for all of the variance in the simulated MEG signals (vertical offsets added to two of the components for clarity).

References

- Bayhill, A.T., Clark, M.R., Stark, L. 1975. The main sequence, a tool for studying human eye movements. *Math. Biosci.* 24: 191-204.
- Boylan, C., Doig, H.R. 1989. Effect of saccade size on presaccadic spike potential amplitude. *Invest. Ophthalmol. Vis. Sci.* 30: 2521-2527.
- Carl, C. Acik, A., König, P., Engel, A.K., Hipp, J.F. 2012. The saccadic spike artifact in MEG. *Neuroimage* 59: 1657-1667.
- Ehrlichman, H., Micic, D., Sousa, A., Zhu, J. 2007. Looking for answers: eye movements in non-visual tasks. *Brain Cogn.* 64: 7-20.
- Gawne, T.J., Osbourne, T.S., Risner, M.L. 2011. Robust sensory gating in the cortical visual evoked potential to two spatially separated stimuli. *Clin. Neurophysiol.* 122: 588-593.
- Hyvärinen, A. 1999. Fast and robust fixed-point algorithms for independent component analysis. *IEEE Trans. Neural Netw.* 10: 626-634.
- Keren, A.S., Yuval-Greenberg, S., Deouell, L.Y. 2010. Saccadic spike potentials in gamma-band EEG: Characterization, detection and suppression. *Neuroimage* 49: 2248-2263.

Kovach, C.K., Tsuchiya, N., Kawasaki, H., Oya, H., Howard III, M.A., Adolphs, R. 2011. Manifestation of ocular-muscle EMG contamination in human intracranial recordings. *Neuroimage* 54: 213-233.

Leigh, J.R., Zee, D.S. 1991. *The Neurology of Eye Movements*, Edition 2, F.A. Davis Co.

McDowell, J.E., Kissler, J.M., Berg, P., Dyckman, K.A., Gao, Y., Rockstroh, B., Clementz, B.A. 2005. Electroencephalography/magnetoencephalography study of cortical activities preceding prosaccades and antisaccades. *Neuroreport* 16: 663-668.

Moster, M.L., Goldberg, G. 1990. Topography of scalp potentials preceding self-initiated saccades. *Neurology* 40: 644-648.

Riemsagel, F.C., Van der Heijde, G.L., Van Dongen, M.M., Ottenhoff, F. 1988. On the origin of the presaccadic spike potential. *Electroencephalogr. Clin. Neurophysiol.* 70: 281-287.

Taulu, S., Kajola, M. (2005) Presentation of electromagnetic multichannel data: The signal space separation method. *J. Appl. Phys.* 97: 124905. <http://dx.doi.org/10.1063/1.1935742>

Thickbroom, G.W., Mastaglia, F.L. 1985. Presaccadic 'spike' potential: investigation of topography and source. *Brain Res.* 339: 271-280.

Van Gisbergen, J.A., Robinson, D.A., Gielen, S. 1981. A quantitative analysis of generation of saccadic eye movements by burst neurons. *J. Neurophysiol.* 45: 417-442.

Yuval-Greenberg, S., Tomer, O., Keren, A.S., Nelken, I., Deouelli, L.Y. 2008. Transient induced gamma-band response in the EEG as a manifestation of miniature saccades. *Neuron* 58: 429-441.

Real Human Saccade Dynamics

5 Degree Left Horizontal Saccade

Gawne10 MT1

200 femtotesla

A71 Frontal

A131

A148

Left

Right

400 msec

A83

Posterior

5 Degree Down Vertical Saccade

Gawne10 MT1

Frontal

200 femtotesla

Left

Right

400 msec

Posterior

Horizontal Right

Horizontal Left

Vertical Down

Vertical Up

Subject 1

Subject 2

Subject 3

A **B**

Frequency (Hz)

100

50

0

-175 0 +175

Time (msec)

A

Saccades Aligned
in Time

Spectrogram

B

Saccades Misaligned
in Time

Spectrogram

C

Pure Brain Gamma-
Band Activity

Spectrogram