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Detection of very high correlation in the alpha band between temporal regions of the human brain using MEG

K.S. Cover,[a,*] C.J. Stam,[b] and B.W. van Dijk[a]

[a] *MEG Centre, VU University Medical Centre, Amsterdam 1007 MB, The Netherlands*
[b] *Clinical Neurophysiology, VU University Medical Centre, Amsterdam, The Netherlands*

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It is generally believed that alpha band (8–12 Hz) electric and magnetic activity in the area of the left and right temporal regions in the human brain are at best poorly correlated. There are no previous reports of very high alpha band correlation between left and right temporal regions by magnetoencephalography (MEG) or electroencephalography (EEG). We present whole head magnetoencephalography (MEG) results that demonstrate that, for temporal channels in the majority of healthy subjects tested, the alpha band signals are highly to very highly correlated and are antiparallel in direction. A correlation as high as −0.97 was found for a limited time in one subject. We suggest that the correlation found may be the consequence of strong direct or indirect coupling between homologue areas in left and right temporal regions rather than a common source. The correlation may provide a valuable index of loss of connectivity in the brain due to disease as well providing valuable insight to brain function and deserves further investigation.

Keywords: Magnetoencephalography; Alpha band; Temporal regions

Introduction

Highly correlated anterior–posterior electroencephalography (EEG) signals in the alpha band (8–12 Hz) have been reported for some time (e.g. Leocani et al., 2000; Manshanden et al., 2002; Nunez et al., 1997). In some cases, correlations as high as 0.9 have been measured. But there have been no reports of high or very high correlation between left and right temporal signals in the alpha band. Indeed, although there are many publications on synchronization measures between various regions of the brain, there are few publications by any sort of synchronization measures—be it coherence, phase synchronization, correlation or any one of a host of other synchronization measures—between the temporal regions.

A few publications do discuss results from inter-temporal region synchronization measures using EEG. Duffy et al (1996) studied the age effects of interhemispheric EEG coherence including between temporal regions in the alpha band for both eyes-open and eyes-closed brain states. They found the alpha band inter-temporal region coherence to be weak. Winterer et al (2001) studied EEG coherence with eyes closed as part of a genetic risk for schizophrenia study. They reported very high coherence in the delta band between posterior temporal lobe regions but did not report similarly high coherence for the alpha band. Moorehouse et al. (2002) found low inter-temporal coherence during sleep in adolescent girls at high risk for depression in the EEG theta and delta bands. Knyazeva et al (1999) found that a single grating that extended across the vertical meridian significantly increased the EEG interhemispheric coherence in normal adult subjects in the gamma band.

As is well known, there are several sources of alpha band signals in the human brain. The most familiar is probably the alpha rhythm, which emanates from the visual cortex. However, the mu and tau rhythms are also in the alpha band. Detection of reactive magnetic rhythm near 10 Hz in the human auditory cortex has also been reported but signal correlation between different magnetoencephalography (MEG) channels was not considered and the frequency range (6.5–9.5 Hz) is different than the one used herein (Lehtela et al., 1997).

Using MEG, we have detected epochs of high to very high correlation between at least a few left and right temporal MEG channels in most of 10 healthy controls during an eyes-closed no-task condition. In two of the subjects (204 and 210), the correlation was very high for extended periods and extended superior to the temporal regions. With further study, the detected correlation between temporal regions may be useful in understanding the communication between temporal regions in healthy individuals. Also, loss of correlation can be indicative of loss of connectivity in the brain. Loss of connectivity can be an indication of disease and other sources of neurological deficits. Thus, the detected high correlation may be of help in studying and monitoring when loss of connectivity is a problem including diseases such as multiple sclerosis.

Methods

Ten healthy volunteers (age 23–48 years, four females) were scanned for 5 min with eyes closed and then for 3 min with eyes open. They were seated in a 151-channel MEG scanner (CTF

* Corresponding author. MEG Centre VUmc, VU University Medical Centre, -1 OBC, k2, Reception C, PO Box 7057, Amsterdam 1007 MB, The Netherlands. Fax: +31-20-444-4816.
E-mail address: Keith@kscover.ca (K.S. Cover).
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Systems, Vancouver, Canada; Vrba, 1996). The no-task eyes-closed data were acquired after 15 min of visually evoked field data using the standard reversing checkerboard pattern (Niedermeyer and Lopes da Silva, 1993). Electrooculography (EOG) data were acquired simultaneously on all subjects.

The subjects were scanned as healthy controls in a cross-sectional study of correlation in multiple sclerosis. The high correlation between temporal regions was discovered during analysis of the data. Ethics approval was granted for this study by the VU University Medical Centre and written informed consent was obtained from all subjects.

As the time series recorded from sensors above the left and right temporal regions are predominately phase shifted by approximately either 0° or 180° with respect to each other, a good choice to measure the synchronization between the channel pairs was the correlation coefficient (Press et al., 1992; Priestley, 1981). With this type of synchronization, the correlation coefficient has several advantages over the more commonly used coherence measure. These advantages include and (1) a simple and widely applied calculation procedure and (2) the distinction between 0° and 180° phase shifts are clearly expressed in the sign of the correlation coefficient. The expression used to calculate the coefficient for two time series, x_i and y_i, was

$$\frac{\sum_i (x_i-\bar{x})(y_i-\bar{y})}{\sqrt{\sum_i (x_i-\bar{x})^2(y_i-\bar{y})^2}}$$

Statistical analysis showed (presented below) that the correlation coefficients for the channel pairs of interest were highly significant when calculated over epochs as short as 4 s. The choice of a 4-s epoch also allowed the study of how the correlations vary over time using a sliding window. We will refer to two signals as highly correlated when the absolute value of the correlation coefficient is between 0.7 and 0.9. When the absolute value of the correlation coefficient is between 0.9 and 1.0, we will refer to the two signals as very highly correlated.

For analysis MEG, data were band-pass filtered in the 8- to 12-Hz band and down sampled to 625 Hz. The correlation between symmetric left–right channel pairs was calculated over 4-s epochs over the eyes closed and eyes open scans of the subject. Maps of the correlation over the MEG channels were then generated. The maps are left–right symmetric by definition since the correlation coefficient of left–right channel pairs was plotted at both left and right channel location.

An artifact-free epoch at least 30 s from the start of each subject's scan was extracted from the time series such that no artifacts were included. No other information was used to guide the selection of epochs. For each of these epochs, correlation maps were plotted.

To study the variation of the correlation over the full 8-min scan, the correlation coefficient for a temporal MEG channel pair (T34) was calculated at 4-s epochs over the whole scan for each of three subjects. Two of the subjects (204 and 210) were selected for their very high correlation while the third was selected as an example of more typical correlation coefficients (208). Also, for two subjects (204 and 210), the correlation maps and root-mean-square (RMS) over time amplitude maps where plotted for six different 4-s epochs sampled roughly uniformly throughout the scan to show the time evolution of the correlation map over the scan.

To study the correlation between a temporal channel and the rest of the head, the correlation coefficients between channel LT34 and all channels were calculated and mapped. Subjects 204 and 210 were used again with the same 4-s epochs used for the correlation coefficient and RMS amplitude maps.

Finally, as an additional confirmation that the very high correlation between the left and right temporal regions we were seeing was due to sources in the brain rather than to some sort of instrumental artifact, subject 204 was recalled for an additional scan. During the scan, the subject placed his head in the scanner with his eyes closed for 90 s and then withdrew it for 90 s. This pattern was repeated three times. The results were examined with CTF's DataEditor software so only CTF hardware and software was used in the acquisition and analysis of the data. Symmetric left and right temporal channels LT34, LT43, RT34 and RT43 were displayed simultaneously in the alpha band (8–12 Hz) and visually compared.

Results

Fig. 1 shows the correlation maps for each of the subjects for the 4-s epochs extracted from near the start of each subject's scan. An expected feature common to all the subjects is a high positive correlation along the midline of each map. This high positive correlation is at least in part due to physical adjacent coils picking up the same signal (similar to the volume conduction effect).

Moving away from the midline, the correlations change from positive values to negative ones. The map for subject 204 shows particularly high negative correlations over a large temporal region. The other subjects show a high negative correlation between at least some temporal region channels with the exceptions of 201, 203 and 211. Subject 211 had a particularly low correlation between temporal regions.

The statistical significance of the correlation is easy to calculate (Altman, 1991). The parameters needed are the correlation coefficient and the degrees of freedom of the data used to calculate it. As the band-pass-filtered data have bandwidth of 4 Hz, it follows from the Nyquist theorem that there will be 8 degrees of freedom per second. Therefore, over the 4-s epoch there is a total of 32 degrees of freedom. From Altman (1991), for 32 degrees of freedom, the null hypothesis that the correlation is zero can be rejected with a two-sided P value of 0.05 if the absolute value of the correlation exceeds 0.3494. All the correlation coefficients of interest in this paper easily exceed this value.

Fig. 2 shows a very good example of how strong the correlation between temporal channels can be. It happens to be the first epoch selected for subject 204, but examination of the data over the whole scan displayed in Fig. 3 shows several other similar epochs existed during the scan. Fig. 2 shows a substantial drop in the alpha band signal and correlation between the start of the eyes-closed and eyes-open periods for subject 204.

Figs. 4 and 5 show the evolution of the correlation coefficient and RMS amplitude maps for subjects 204 and 210 during the scan. The correlation maps show a gradual decrease in the area of very high correlation between the temporal regions over the scan for subject 204. For subject 210, the very high correlation and the RMS amplitude both drop when the eyes are open.

The eyes-closed and eyes-open states for subjects 204 and 210 were confirmed by examination of the MEG and EOG data. The

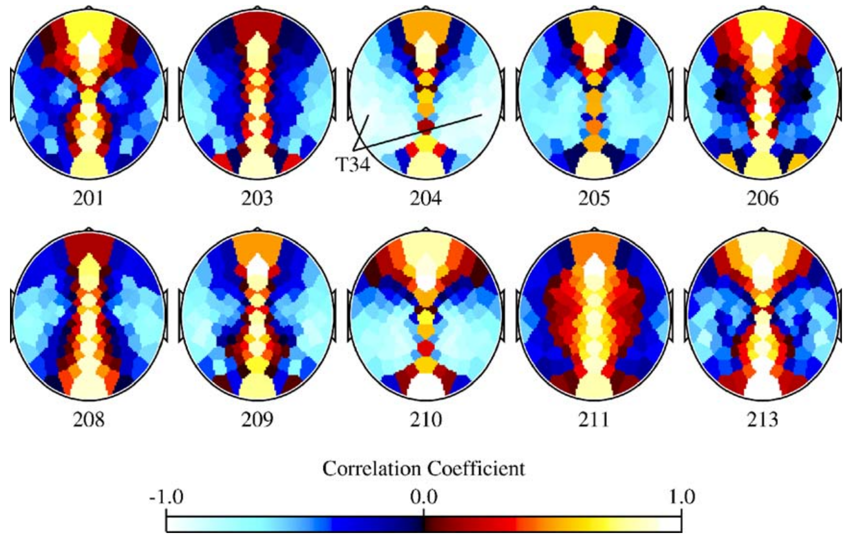

Fig. 1. Each of the 10 correlation maps shows the correlation for the left–right channel pairs of eyes-closed data for a subject. The correlation for each map is calculated over a 4-s epoch of magnetic field data, which has been band-pass filtered (8–12 Hz). The T34 label locates the LT34 and RT34 channels that are used in Figs. 2 and 3. Each correlation map is labeled with the subject's ID.

MEG and EOG data confirmed subject 204 fell asleep during the eyes-closed period but was awake for the eyes open period. This finding was consistent with subject 204 report of feeling drowsy during the scan. The MEG and EOG indicated subject 210 was awake through the whole scan.

Fig. 6 shows the evolution of the correlation coefficients between channel TL34 and all other channels. As channel TL34 is correlated with itself, it has the highest correlation coefficient in each of the maps.

For the early times, the correlation coefficients between TL34 and the right temporal region are closed to −1. The alpha band correlation coefficients between TL34 and the frontal and posterior regions is much closer to zero, suggesting the left–right alpha band correlation is largely independent of anterior and posterior alpha band signals.

The examination of channels LT43, LT34, RT43 and RT34 in the alpha band from the rescan of subject 204 gave the expected results for the left–right temporal region correlation. When the subject's head was not in the scanner, all that was seen was instrumental noise. When the subject's head was in the scanner, the left two channels had highly correlated (near +1) waveforms as did the right two channels. Also, the left channels were very similar to the right channels except that their polarities were opposite as would be expected from a correlation coefficient near −1.

Discussion

When left and right temporal channels of the MEG scanner produce signals which are nearly mirror images of each other, such

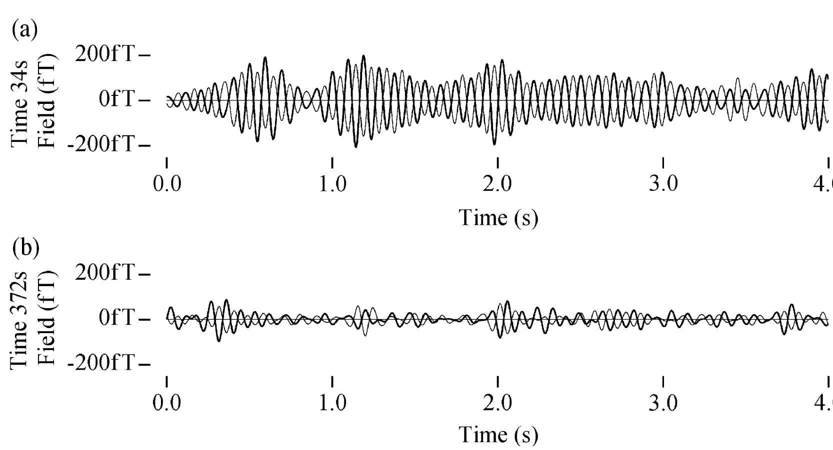

Fig. 2. Figure (a) is an example of the very high correlation in the alpha band between left and right temporal regions in the human brain as detected by MEG. The 4-s epoch was acquired 34 s into the scan while the subject's eyes were closed. The thick line represents the magnetic field strength at left temporal channel MLT34 and the thin line is the same signal for right temporal channel MRT34. The correlation over this 4-s epoch between the two channels is −0.97. Figure (b) shows eyes-open data acquired at 372 s into the scan. As might be expected, the alpha band signal is substantially reduced. All channels are band-pass filtered (8–12 Hz) and are from subject 204.

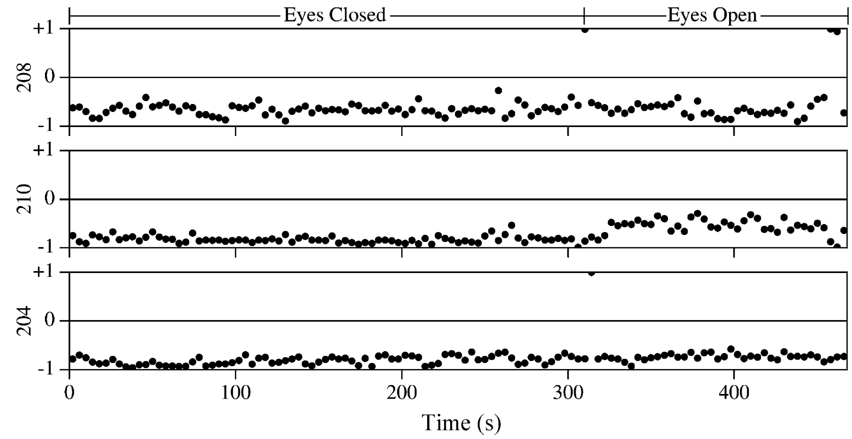

Fig. 3. The correlation for subjects 204, 210 and 208 between channels MLT34 and MLT34 for 4-s epochs over the full 476 s of eyes-closed and eyes-open acquisition. The eyes-closed data extend from 0 to 312 s. The eyes-open data extend from 320 to 460 s. The correlation pulses in the subjects at 316 and 464 s are due to an artificially induced magnetic field used for head localization. In the 8- to 12-Hz band for eyes-closed data, the correlation for subject 204 is consistently near − 1 as would be expected from Fig. 2. Of the three subjects, only 210 shows a response to eyes open in these plots.

as in Fig. 2, it is natural to ask if the correlation could be due to some sort of artifact.

However, many characteristics of the data demonstrate the correlation is physiological in nature:

(1) the alpha band power and correlation drops substantially when the eyes are opened as shown in Figs. 2–4;
(2) weekly calibrations of our MEG scanner show negligible cross talk between any channels;
(3) the high correlation was detected for every setting of the gradient formation on the CTF MEG scanner;
(4) the position of the subject was monitored in the scanner so movement of the subject could not have been a source of the correlation;
(5) repetitively inserting subject 204 into and removing him from the scanner showed only instrumental noise when the subject was not in the scanner and high inter-temporal region correlation when the subject was in the scanner;
(6) as mentioned in the Introduction, very high correlation in the alpha band between anterior and posterior of the brain are well documented demonstrating very high correlation is possible over distances comparable to the size of the skull.

When all these characteristics are taken together, we are very confident that the very high left–right correlation is physiological in nature.

The detection of temporal correlation in MEG raises many questions for further research. These questions include: (1) is there any way to induce very high left–right correlation in subjects that are not currently demonstrating it when asked to close their eyes? (2) In subjects that produce the very high left–right correlation, what tasks will cause the correlation to decrease? (3) How does the correlation vary with sleep state?

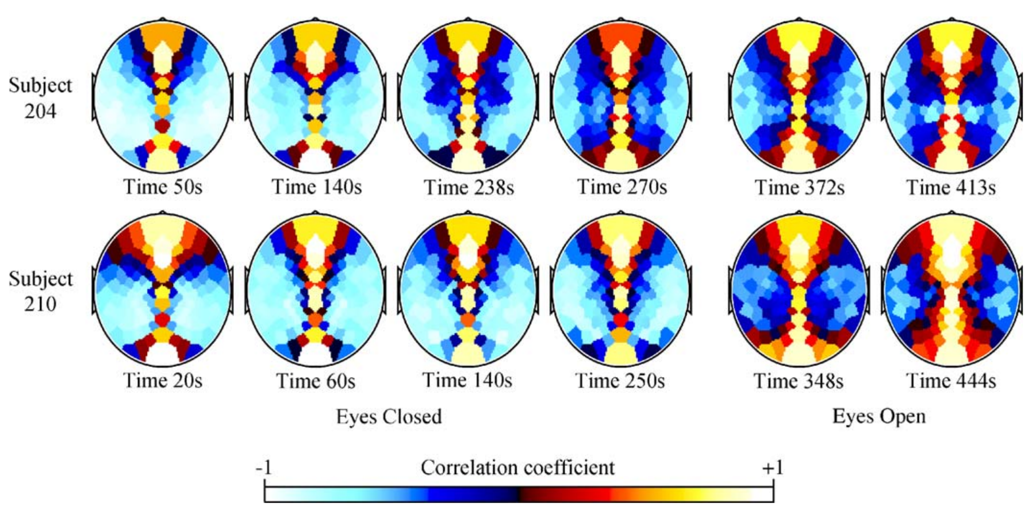

Fig. 4. The evolution of the left–right correlation coefficients map over time for subjects 204 and 210 during the MEG scan. The epoch for the maps is again 4 s. The first four correlation maps are during the eyes-closed period while the last two maps are over the eyes-open interval.

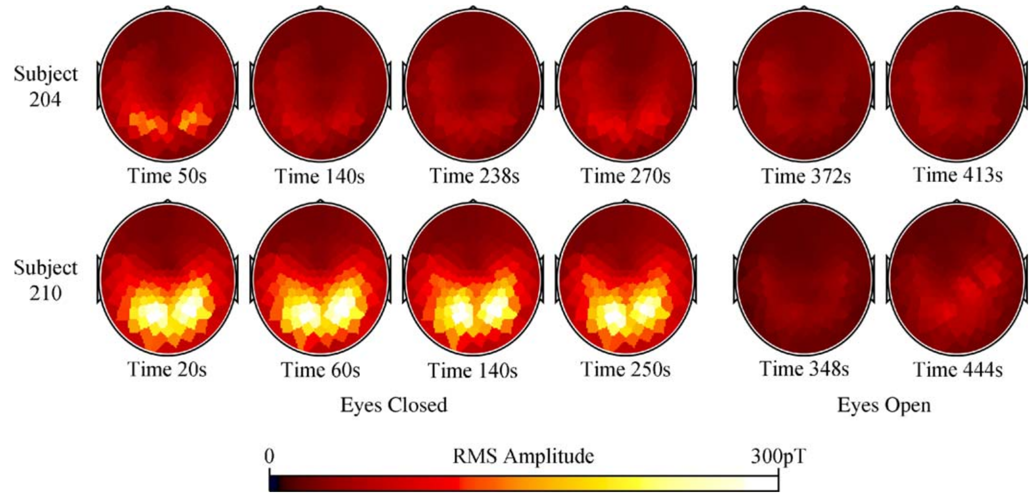

Fig. 5. The evolution of the RMS amplitude over time map using the same data as Fig. 4. The average RMS amplitude over the map is shown beneath the map. Comparison of the correlation maps (Fig. 4) with the RMS amplitude maps demonstrates they give very different information about the brain.

(4) How does the correlation change in neurological disorders that affect functional connectivity? The relation between neurological disorders accompanied by cognitive dysfunction and disturbed synchronization is one of the key research lines at VUMC's MEG center. (5) How much does the position of the subjects head in the MEG scanner affect the correlation results? 6) What is the prominent physiological mechanism underlying the observed temporal correlation? Finding reliable answers to any of these questions will take a great deal more work but we would like to speculate as to question 6.

Although many sources of the high correlation are possible, especially when the nature of the correlation varies between subjects and over time within subjects (Figs. 1 and 4), two classes of hypotheses present themselves. The first is a single anterior-pointing current dipole, or perhaps spatial distribution of anterior-pointing current dipoles, located deep in the brain near the interhemispheric fissure. We think this explanation unlikely but cannot completely rule it out. The probable locations of such deep current dipoles are not known to host structures capable of generating the required signals.

The second hypothesis, and our preferred one, involves two anterior-pointing current dipoles, one in each temporal region. Again, instead of a single current dipole, there could be a spatial distribution of anterior-pointing current dipoles in each temporal region and symmetric about the brain's midline (Nunez et al, 2001). The left and right dipoles are assumed to be tightly coupled by inter cortical connection and in phase. The coupling could be due to a connection directly between the dipoles via the corpus callosum. But it is possible that a third source supplies correlation signals to both temporal regions or that the connection is through several intermediaries.

Although the currents in the current dipoles are in phase, the sources can generate a pair of 180° out of phase MEG signals because of the geometry of the current dipoles and magnetic field.

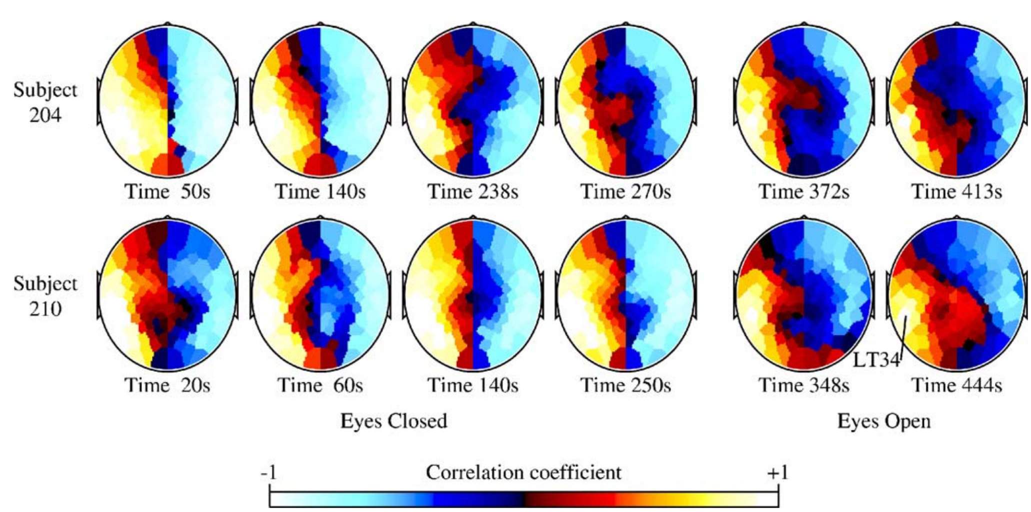

Fig. 6. The evolution of the correlation coefficients between channel TL34 and all the channels over time. The same data are used as for Fig. 4. Channel TL34 has the highest correlation coefficient because it is correlated with itself.

By the right-hand rule, the magnetic field superior to each anterior-pointing current dipole would point right. By standard definition for the CTF MEG scanner, all magnetic fields pointed out the head are considered positive. Thus, the left and right temporal MEG channels would see magnetic fields of opposite signs from the two temporal dipoles. As the direction of the current dipoles changes with time, so to will the sign of the magnetic fields.

Magnetic field inferior to a current dipole would have a direction opposite to those superior for the temporal region dipoles hypothesis. But the directions should be the same for the midline dipoles hypothesis. Unfortunately, the MEG helmet of our system cannot see lower part of the temporal lobe (Leijten et al, 2003) and thus this hypothesis cannot be tested with the current data.

The change in the inter-temporal correlation between the eyes-open and eyes-closed state indicates the correlation is modulated by the state of the eyes. Figs. 5 and 6 show only weak correlation during eyes closed between the left temporal region and high alpha RMS amplitude. Thus, it is unlikely that the inter-temporal region correlation we are seeing is primarily due to the visual cortex.

Determining the source of the alpha band correlation from MEG measurements alone could prove to be difficult. There are many sources of alpha band signals in the brain including the visual cortex; thus, no simple model will fit the alpha bands signals when correlation is not taken into account. And including correlation information is bound to complicate the localization of sources even more. But Fig. 6 suggests the primary source is not from the frontal or occipital lobes as signals from the sensors above these regions are not well correlated with signals from sensors above the temporal regions.

Conclusions

Most of the 10 healthy volunteers undergoing a MEG scan with eyes closed clearly demonstrated high correlation between left and right temporal channels. It is suggested the temporal correlation may be due to anterior-pointing current dipoles in each superior temporal gyrus and adjacent regions that are tightly correlated by direct or indirect cortical–cortical interconnections. Monitoring the loss of correlation between the temporal lobes may provides a valuable way of monitoring disease and other causes of neurological deficits especially those that effect connectivity.

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