Increased variability of the period duration for waveforms in Epochs of MEG data as a function of arousal state

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Introduction

In clinical evaluation of spontaneous magnetoencephalography (MEG) or EEG time series data, the state of arousal is assigned of one of 5 NREM scores (awake, stages 1-4) based on visual examination if the data for the presence of specific waveforms and the general amplitudes and frequencies of these waveforms[1]. However, this method of quantifying the state of arousal is not linearly related to changes in the spectrum of the data and totally insensitive to small shifts of arousal state. These deficiencies required us to develop a new system to quantify changes of arousal for our long duration MEG studies. Our arousal measurement parameters are based on a spectrum of period duration versus power, generated by our DPA (dynamic period analysis) technique. DPA spectra are not complete spectra, such as produced by FFT methods. We found FFT spectra to be ill suited for quantifying arousal state because of large subject to subject spectral differences dominated arousal spectral change. In our DPA spectra, spectral differences between individuals are relatively small compared to spectral changes associated with the state of arousal. Further, a DPA spectrum for any state of arousal can be divided into a linear combination of just two unique DPA spectra. One of these unique spectra is identical to a typical awake DPA spectrum and the other we have been able to identify as the time averaged power spectrum of a highly random component of the MEG data which is only present during states of arousal other than awake. We established these two unique DPA spectra by applying a principal component analysis of a large set of DPA period spectra and obtaining the two unique principal component spectra[2]. During shifts from awake to stages 2, 3, and 4 arousal states the fraction of the awake principal component DPA spectrum is significantly decreased while the proportion of the drowsy/sleep principal component DPA spectrum increases from the zero amplitude awake value. We have found the drowsy/sleep principal component DPA spectrum to exhibit changes in amplitude and amplitude variability which make it especially useful for distinguishing fluctuations of the awake state from a transition state of arousal that signifies the onset of stage 2 sleep. Also, we have established a relationship of our arousal parameters to the traditional classification system such that the results of our system can be related to this familiar and widely used scale of arousal state.

Methods

MEG recordings of spontaneous cortical activity obtained from six subjects were used to develop the two principal component DPA arousal state spectra. The MEG data were acquired with a 7 channel Neuromagnetometer (BTi model 607) equipped with second order gradiometers. The center channel was positioned at P3 of the international 10-20 EEG measurement system and 45 minutes of data was acquired from each subject lying on his/her side. For these subjects, the data was partitioned into 100 second epochs and DPA spectra generated for each epoch. For two additional subjects, included in this report, simultaneous EEG recordings were made with electrode placements, P3-A2 and Cz-F2. The 45 minutes of EEG and MEG data were partitioned into 25 second epochs. DPA spectra were produced for the center channel of the sensor array and the epochs of EEG data were scored for arousal state (awake, stages 1 - 4). For each DPA spectra, the amplitudes for the awake principal component spectrum and the drowsy/sleep principal component spectrum were generated.

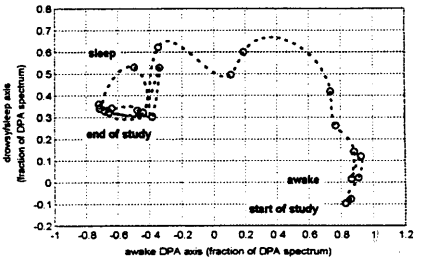

Figure 1 DPA spectral composition during 45 minute study, awake to sleep.

With these amplitudes plotted as X-Y coordinates, the angle from the horizontal (awake) axis was used to relate our two new parameters for quantifying arousal state to the existing system (see Fig. 1).

During subsequent analysis, these two arousal coordinate amplitudes were generated for DPA produced from epochs of durations 4, 8, 16, 32, 64, and 128 seconds. Since DPA spectra are time averaged spectra, these data were used to investigate changes in both the amplitude and amplitude variability of our principal component arousal parameters as a function of data epoch length and arousal state. The standard deviation of the amplitude of both the awake and drowsy/sleep components during extended data segments of a specific state of arousal were used to quantify the amplitude variability associated with the state of arousal and DPA epoch duration. The average amplitude for these same data segments was used to quantify the amplitude of the awake and drowsy/sleep components of the composite DPA spectra.

Results

The DPA spectra of the two principal components extracted from the DPA data using a principal component analysis are shown in Fig. 2. Our data indicates the onset of drowsiness gives rise to a shift in cortical function which introduces progressively greater durations of activity characterized by high variability in both frequency and amplitude. In Fig. 3, we demonstrate that the drowsy/sleep principal component is the time average spectrum of this random cortical process. For this Figure, 17 epochs (25 second epochs used to generate DPA spectra), recorded during stage 1 and 2 arousal states were averaged after subtracting the awake DPA spectral component. This averaged spectrum is nearly identical to the drowsy/awake spectrum in Fig. 3. The single epoch DPA spectrum plotted in Fig. 3 reflects the low rate of occurrence and random amplitude of these waveforms.

In Fig. 4, the amplitude and amplitude variability of the fraction of the a DPA spectrum corresponding to the awake DPA principal component is graphed as a function of both arousal state and epoch duration used to generate the DPA spectrum. For both awake and stage 2 arousal states this fractional amplitude of the awake principal component requires a relatively short epoch of data before reaching a stable value with very low variability. In Fig. 4, both the amplitude and amplitude variability are nearly constant, especially for DPA epochs longer than 16 seconds. Relative to the awake state, the amplitude of the awake principal component of a stage 2 DPA spectrum is less and amplitude variability increased. These amplitude differences are nearly the same for all epoch durations, such that, the graphs of awake and stage 2 are almost parallel.

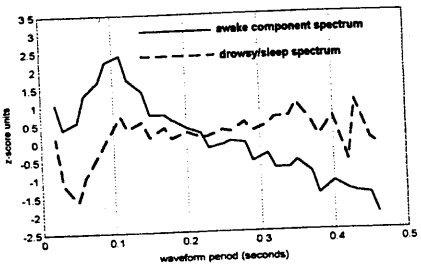

Figure 2 Awake and drowsy/sleep DPA spectra.

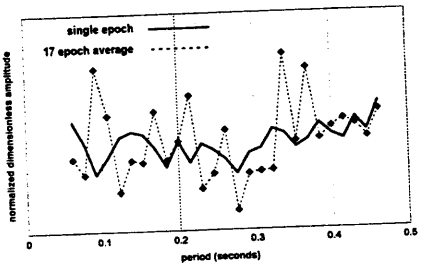

Figure 3 Single epoch DPA spectrum and 17 epoch average spectrum, after removal of awake spectral component.

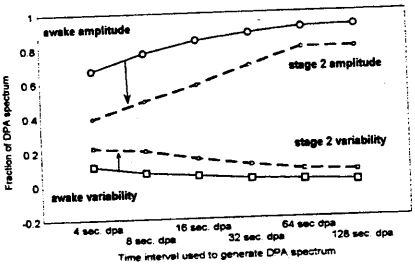

Figure 4 Change in the awake component of the DPA spectrum during transition from awake to stage 2 arousal state.

However, the amplitude and amplitude variability of the drowsy/sleep component content of awake and stage 2 DPA spectra demonstrate a more complex relationship to the state of arousal and the epoch duration used to generate the DPA spectra. As a result, this component is especially useful for recognizing the onset of sleep. This relationship allows the DPA epoch duration to be optimized for recognizing and quantifying changes of arousal. In Fig. 5, the drowsy/sleep content of the awake DPA spectra is nearly zero for all DPA epoch durations. However, for stage 2 DPA spectra, the amplitude of the drowsy/sleep fraction of the DPA spectrum is significantly increased when a longer epoch duration is used to generate these DPA spectra. Therefore, a larger amplitude difference of the drowsy/sleep component between awake and stage 2 arousal states is created when a longer DPA epoch duration is used. Even more interesting and potentially useful is the amplitude variability of the drowsy/sleep component as a function of the duration used to generate the DPA spectra. An adequate sample of the waveforms contributing to the awake DPA spectrum is obtained with a short epoch of data. Thus, random variability of the awake DPA spectrum is reduced when a longer epoch duration is used to generate DPA spectra. However, a very long epoch of data must be used to acquire all waveforms contributing to the stage 2 arousal state DPA spectrum. As a result, the variability of the drowsy/sleep component remains nearly constant until greater than 60 second epochs are used (see Fig. 6). Therefore, the difference in amplitude variability of the drowsy/sleep component between awake and stage 2 arousal states also increases when longer epoch durations are used. During sleep onset, the epoch duration effect on amplitude variability of the drowsy/sleep DPA component can be more dramatic than changes of the mean amplitude. In Fig. 7, a large increase in the variability of the drowsy/sleep component is easy to detect during the stage 1 sleep recorded just prior to the transition to stage 2 (1400 seconds to 1700 seconds). Notice, during this interval, the amplitude variability of the drowsy/sleep component is the nearly same as after the transition to stage 2 (1700 seconds to 2100 seconds). However, during this stage 1 epoch, the amplitude of the drowsy sleep component has an average amplitude identical to the awake state and abrupt increases with stage 2 onset. This sustained increase in amplitude variability is absent during other epochs of stage 1 sleep which alternated with epochs of awake. For this graph, a 32 second epoch duration optimized the compromise between maximizing the drowsy/sleep component amplitude difference between awake and sleep arousal states and the ability to resolve temporal changes of the arousal state. In actual application of this technique, the time series of drowsy/sleep amplitudes for more than one DPA epoch duration are examined for arousal state changes.

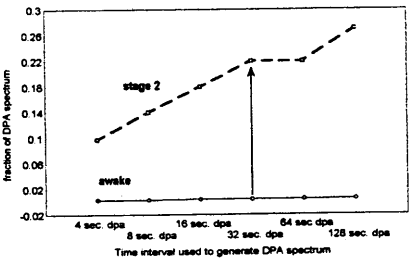

Figure 5 Amplitude of drowsy/sleep component of the DPA spectrum. Awake versus stage 2 arousal.

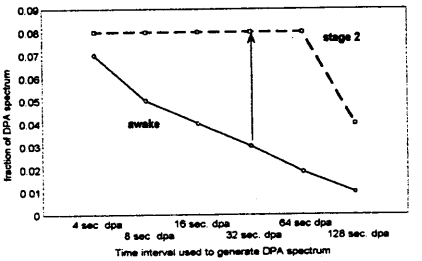

Figure 6 Variability of the drowsy/sleep component of the DPA spectrum. Awake versus stage 2 arousal.

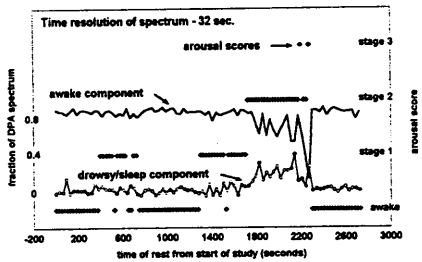

Figure 7 Time series of clinical arousal scores versus amplitudes of awake and drowsy/sleep fraction of the DPA spectra.

Discussion

Our results indicate that during the transition from awake to sleep some portion of the cortex begins to function in a mode distinctly different than the awake state cortex. The time average spectrum of the MEG waveforms arising from this drowsy/sleep mode of cortical function is identical to the DPA drowsy/sleep principal component we extracted. This spectrum has the property that the same time average power occurs at all period durations less than 0.46 seconds, included in our DPA spectra (see Fig. 2). DPA spectra are formed by counting the number of waveforms with each specific period duration and the corresponding waveform power. Therefore, during this mode of cortical function, for each period duration, the number of waveforms multiplied by the time average power of the waveform is equal to a constant for all period durations. If the power and duration of a waveform are on average proportional to the area of cortex generating the recorded activity, then this result implies that the number of waveforms arising from cortex of specific area is inversely proportional to the size of that area for this mode of cortical function.

Compared to awake state waveforms, drowsy/sleep waveforms occur infrequently and are characterized by large amplitude variability. Thus, a very long epoch duration is required to accumulate enough waveforms of all periods to produce a completely stable DPA spectra during sleep arousal levels. As a result, both the amplitude of the drowsy/sleep DPA component and the amplitude variability increase when longer epochs are used for DPA spectra generated from less than 60 seconds of data. Therefore, the amplitude variability of the drowsy/sleep fraction of DPA spectra can be used to detect the switch from awake to sleep cortical function (see Figs. 5, 6 and 7).

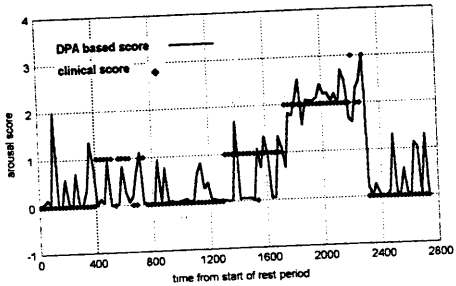

Fig. 8 The time series of DPA based and clinical arousal scores for 45 minute study of single subject.

Also, we have developed a mathematical formula which relates our new arousal parameters to the present clinical scores. This was done to facilitate the use of our new parameters which provide a continuous parameter of changes in the spectrum of MEG data associated with arousal state. As previously described, the amplitude of the awake and drowsy/sleep content of each DPA spectra can be used as X, Y coordinates (see Fig. 1). The angle from the awake coordinate axis was used to develop the relationship. We found the relationship is best described by;

log(DPA angle / 140) = 1.15 (clinical arousal score) - 3.6 angle in degrees

Using this formula on a time series of DPA spectra the same trend in arousal change and approximately the same arousal level is predicted as found in the actual time series of clinical scores (see Fig 8).

References

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