Age Distribution of MEG Spontaneous Theta Activity in Healthy Subjects

Monica Puligheddu*, Jan C. de Munck+, Cornelis J. Stam^, Jeroen Verbunt*, Arent de Jongh*, Bob W. van Dijk*, and Francesco Marrosu*

Summary: This study investigates the possible relevance of distribution and age variation of spontaneous theta activity (4-8 Hz) in normal subjects using magnetoencephalography (MEG) recordings. Spontaneous theta was recorded with a 151-channel MEG in healthy subjects, and a group of 10 subjects simultaneous MEG-EEG was recorded in order to compare the two methods. Theta was divided into two sub-bands: \( T_A \) (4-6 Hz) and \( T_B \) (6-8 Hz). The pre-processed data were transformed into the frequency domain by Fast Fourier Transform (FFT) based software by subdividing the data in epochs of 5 sec, on which FFT amplitudes are computed. Moreover, on all trials a simple model of a single electric current embedded in a spherically symmetric conductor was fitted automatically to the magnetic fields and projected onto an averaged MRI. The results obtained show that FFT-based theta power spectrum was distributed in adults with the highest power over the posterior parietal and occipital areas with \( T_B \) dominance. The dipole analysis resulted in a mid-sagittal distribution, though the youngest group displayed theta dipoles fitting more posteriorly respect to the adults and the elderly. These results suggest that spontaneous theta activity is a diffuse and pervasive rhythm which shows some different topographical distribution among the age groups. Whether the prevalent posterior distribution of theta is the expression of distinct networks or the outcome of complex dynamics are questions of possible relevance in the organization of higher order processes.

Key words: Magnetoencephalography (MEG); Theta rhythms; Electroencephalogram (EEG); Power spectrum; Dipoles.

Introduction

Theta activity is represented by 4-8 Hz rhythmical oscillations first recorded in the hippocampus of mammals and regarded as one of the most distinguished forms of electroencephalographic (EEG) activity in this brain area given the high voltage expressed in comparison with the background EEG. Such rhythm has been experimentally correlated with purposeful exploratory motor activity (Green and Arduini 1954; Bennet 1971) and with the paradoxical sleep (Bland 1986). Hippocampal EEG frequencies in theta range have been classified into two categories: a regular rhythmic slow activity (RSA), characterized by a patterned frequency which is more evident when animals are involved in exploratory tasks or engaged in voluntary motor programs (Robinson 1980; Vanderwolf and Robinson 1981), and a less organized large irregular activity (LIA), recorded when the animal stands still and is apparently disengaged from motor and exploratory tasks (Bland 1986).

Cortical theta was described in humans in relation with temporal epilepsy (Cigànek 1961) as well as in other pathological non-epileptical conditions (Mokrân et al., 1971). Furthermore, other studies have observed theta rhythms during physiological conditions (Westmoreland and Klass, 1986, Mizuki et al. 1980), while most recent reports have related variations in theta rhythms with attentive processes such as episodic encoding (Sarnthein et al. 1998; Klimesh et al. 2001) and retention intervals of working memory (Stam et al. 2002).

Though the use of indwelling electrodes in humans have convincingly established the hippocampal contribution to the genesis of cortical theta activity (Miller 1991; O'Keefe and Burgess 1999), experimental studies supported the hypothesis that theta rhythms are also organized as a system involving large areas of the brain (O'Keefe 1993) and several generators well beyond the hippocampus (Tesche 1996) and includes areas such as the cingulate gyrus (Leung and Borst 1987), the entorhinal cortex (Blaszyk et al. 1996) and other less defined neocortical regions (Biedenbach 1966; Nakamura...
et al. 1992) modulated by thalamo-cortical relays (Buzsaki 1996). However, since these studies are performed during the execution or the retention of traditional neuro-psychological tests, theta rhythms differ in their amplitude and location given that different areas are instructed by different specific trials (Klimesh et al. 1999; 2001a). In contrast, the investigation of spontaneous theta activity, which is unrelated to a particular task, might account for the basic values of the power spectrum of this rhythm and shows whether their bands display a sparse or a locally structured organization.

Since EEG investigations are biased by a large distortion of electric signals and are more sensitive to differences in conductivities of the various compartments of the head with large differences from subject to subject (Gonçalves et al. 2003), it is important that theta activity be studied using appropriate approaches. Intra-cranial EEG seems to offer an optimum solution to these problems. However, this procedure, usually applied prior to surgical treatment of tumors or in refractory epilepsy, may present further pitfalls, e.g. the field explored by indwelling electrodes could be "myopic" as it explores only a limited surface and fails to account for complex and extended relationships bioelectrical activities (Kahana et al. 1999). On the contrary, the whole head MEG seems to be ideally suited to our purpose; this technique is not as invasive and allows for smooth easy gauging of a large neuronal population at the same areas. Since MEG sensors are unaffected by the non-homogeneous media, this type of recording enhances the processes of identification of the areas involved in generating brain rhythms (Salmelin and Hari 1994; Hari et al. 1977; Stam et al. 2003). The combination of magnetic resonance imaging (MRI) with MEG and the use of appropriate coordinates can also account for the strength and direction of the magnetic field and can be visualized as equivalent current dipole (ECD).

**Methods**

**Subjects**

For the present study 42 healthy subjects, 23 male and 19 female, 96% of them right handed were selected from a homogeneous ethnic and linguistic community similar for gender and educational status. After the nature of the experimental procedure has been reviewed and approved by the Institutional Ethics Committee, all subjects selected to this study gave their informed consent. Participants had no history of neurological and vascular disorders. Among the selected population, 9 individuals aged from 7 to 10 years (mean age 8.6), 25 subjects aged from 21 to 58 (mean age 46.1) and 8 subjects aged from 64 to 83 years (mean age 73.5).

**Recordings**

Five minutes, represented by 30 repeated 10 second trials, of spontaneous MEG data obtained by a 151-channel MEG whole head System (CTF System Inc., Port Coquitlam, Canada) were acquired in a magnetically shielded room while subjects were awake in a sitting position with eyes closed. Since the protocol deals with spontaneous activity and did not employ tasks, the control vigilance level of the subject during recording time was a basic selection criterion. For this purpose, an off-line double blind examination of the sample tracing was done by two experienced neurophysiologists in order to rule out epochs showing possible drowsiness. As result, eight records were discarded on the basis of a sporadic abrupt alpha fragmentation and self reporting of short episodes of possible drowsiness by the subjects investigated.

MEG data were digitally acquired with a sampling rate of 125 Hz, a 0.1-40 Hz band pass filter and a notch filter around 50 Hz. In order to compare MEG and EEG data, a simultaneous 64-channel EEG-recording at sampling rate of 312.5 was performed in ten adult subjects (aged 23 to 38). The whole head CTF MEG system is extensively described by Vrba et al. (1998).

**Power Spectra Analysis**

For the purpose of the present study we calculated the range of theta (4 to 8 Hz) into two separated computational sets by dividing this activity in two sub-bands represented by a "slow theta" termed $T_A$ (4-6 Hz), which is more contiguous with the optimal rhythms involved in the long term potentiation (Larson and Linch, 1989) and a "fast theta" termed $T_B$ (6-8 Hz) a frequency closed to the oscillations involved in sensory processing (Montoya et al. 1989).

The pre-processed data were transformed into the frequency domain by Fast Fourier Transform (FFT)-based software with a Hanning window (Frigo and Johnson, 1997), which computes the power spectra of each MEG/EEG channel. Calculation is based on a subdivision of the data in epochs of 5 sec, on which FFT amplitudes are computed. The spectrum was calculated by averaging FFT amplitudes of each epoch, together with FFT amplitudes of epochs consisting of the last 2.5 sec of each epoch concatenated with the first 2.5 sec of the subsequent. The unit of the output numbers is $\text{ft}^2$ in case of MEG data, or $\mu\text{V}^2$ in case of EEG. The total power in theta activity band in the entire frequency spectrum was automatically calculated and summated over five minutes of recordings. Spectrum files of all subjects were then analyzed by reading the spectrum from each channel label, storing the average spectrum and grouping EEG electrodes and MEG sensors for each hemisphere in five areas (frontal, temporal, parietal, occipital, and posterior).