Magnetoencephalography and magnetocardiography in neonates. Our experience in Greece

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Summary

This study reports our experience in the application of magnetoencephalography (MEG) and magnetocardiography (MCG) in neonates. Results gained from our studies, lead us to believe that MEG and MCG could provide clinical practice with non-invasive, rapid and easy to perform methods, which could be adjuncts to conventional methods for the evaluation of neonatal brain and heart function.

Key words: Neonates; MEG; MCG.

Introduction

Early assessment of the degree of the resulting hypoxic-ischaemic encephalopathy (HIE) is essential for the clinical management and is considered a prognostic factor for the newborn's neurodevelopmental outcome. Preeclampsia is a complication of pregnancy that can cause birth asphyxia at or near term, due to the influence on the uteroplacental circulation, resulting in brain damage [1-3].

Conventional neurological examination does not provide specific information of the neonate's neurological status as clinical signs of HIE may have a latency time of even 12 hours after birth [2]. Moreover, perinatal variables such as Apgar score and umbilical cord pH have not been strongly correlated with a poor prognosis [4]. Electroencephalography (EEG), ultrasound (US) examination (including Doppler flow velocity measurements and two dimensional imaging), computed tomography (CT) and magnetic resonance imaging (MRI) have been widely applied in high-risk infants for prognostic purposes, but they are time and money consuming, and need experienced personnel for the interpretation of their results [5-12]. Magnetoencephalography (MEG) has been investigated as an alternative method for assessing brain function in adults [13] as well as in fetuses [14, 15]. It directly records the extremely weak magnetic fields associated with the electrical activity of cortical and subcortical neuronal groups, has high temporal and spatial resolution and is completely safe and non-invasive, since the instrument used acts as a receiver and not as a transmitter.

Magnetocardiography (MCG) is a promising, completely noninvasive method to obtain functional information about electrical activation in the human heart. The electrophysiological activity is associated with a magnetic field detectable without contact to the body surface. Roth and Wikswo [16] presented calculations of a theoretical example of electrically silent magnetic fields. They showed that for tissues with an assumed complex conductivity, some information was lost in the electric potential, but was detectable with a biomagnetic sensor. Van Oosterom and co-workers [17] concluded from measurements and simulations of MCG and ECG that, for the ventricular depolarization, the contribution of electrically silent magnetic fields is only marginal. In contrast MacAuley *et al.* [18] suggested that MCG signals of the QRS offer information that is not available in the ECG.

This study reports our experience in the application of MEG and MCG in neonates in Greece.

Methods

Biomagnetic recordings were acquired using a commercial one-channel SQUID (Superconducting Quantum Interference Device – DC SQUID, model 601, second order gradiometer, Biomagnetic Technologies), of high sensitivity (95 pTesla/Volt at 1,000 Hz). Mechanical vibrations, which could induce intolerable interfering signals, are avoided by mounting the shielded room and the support of the measurement system on a specially designed concrete foundation. The field sensor is located in cryostat filled with liquid helium (4°K), which can be tilted in two directions so as to be adjusted vertically and have access to any part of the body. Informed consent was obtained from the parents prior to the procedure.

MEG recordings were obtained from the temporal region bilaterally, from four specified points on each side of the scalp, with the babies lying prostrate. The selection of the measurement points was based on the 10-20 International Electrode Placement System [24], with the T3-T4 standard EEG recording positions being the centers of two respective circles, and all four measurement points on each side being placed diametrically opposite on two vertical diameters going through T3-T4, 1 cm in distance from the center. The SQUID sensor was placed 3 mm above each particular point. Thirty-two consecutive MEG measurements of 1 sec duration each were taken and digitized, with a sampling frequency of 250 Hz, and a bandwidth between 1 and 128 Hz. The MEG records were digitized with an analog-to-digital converter and stored in an IBM-PC computer for off-line Fourier statistical analysis. In all cases the frequency bands were 2-7 Hz.

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The MCG was recorded digitally for 10 min. We digitized the signals using 12-bit precision analog to digital converter with a sampling frequency of 256 Hz. The MCG signals were band-pass filtered with cut-off frequencies of 0.1-100 Hz. The associated Nyquist frequency limit with the above-mentioned sampling frequency was 128 Hz, which was well above the constituent frequency components of interest in MCG recordings and avoids artifacts. The tip of the single channel biomagnetometer was placed 2-3 cm above the infants' hearts at the position where the QRS signal was found to be at its maximum.

Neonatal magnetoencephalography

Anastasiadis *et al.* [19] performed a prospective study on neonatal brain function on 44 respective term neonates who were delivered normally without any clinical signs of brain damage. Fourteen neonates were the result of preeclamptic pregnancy whereas 30 were associated with a normal pregnancy with normal values of Apgar scores, umbilical cord pH and birth weight. The MEG spectral amplitudes ranged from 132.5 Ft\√Hz to 248 Ft\√Hz. Specifically, the MEG recordings from neonates corresponding to normal pregnancies were of lower magnetic power spectral amplitudes (mean: 163.2 ± 22.57) compared with those gained from neonates corresponding to preeclamptic pregnancies (mean: 211.6 ± 37.74). The difference between the two groups was statistically significant ($p < 0.005$). There was a strong correlation between the degrees of preeclampsia, birthweight and MEG values. The 30 neonates in the normal group had birth weights > 75th percentile, umbilical cord pH > 7.25 and Apgar scores > 7. Therefore, there were three neonates in this group with comparatively high MEG recordings, who were delivered by vacuum extraction. In the preeclamptic group there were five neonates with low MEG recordings (155Ft\√Hz - 175 Ft\√Hz) who corresponded to mild preeclampsia. The five neonates had birth weights between the 75th and 90th percentile, cord-pH between 7.18 and 7.19 and 1 min Apgar score between 5 and 7. The remaining nine neonates with the high amplitudes had cord pH between 7.14 and 7.19 and 1 min Apgar score between 5 and 7. There were no significant differences in this subgroup regarding the initial Apgar scores, probably because the Apgar score is a subjective variable, estimated by different individuals.

Kotini *et al.* [20] investigated the complexity of brain activity using MEG recordings in neonates born to preeclamptic and uncomplicated pregnancies, in order to determine whether nonlinear MEG dynamics measured by dimensional complexity and first Lyapunov exponent could be able to find changes in these groups. They performed a prospective study on 40 neonates (birth weight 2,250-4,100 grams) who were delivered normally between 37-41 weeks of gestation. Maternal age ranged from 16 to 39 years. Ten neonates had preeclamptic pregnancies while 30 neonates had clinically uncomplicated pregnancies randomly selected in the same time period. The authors applied nonlinear analysis in order to investigate the difference in the complexity underlying the dynamics characterizing the MEG activity of preeclamptic and normal neonates. MEG recordings from neonates corresponding to preeclamptic pregnancies were of higher magnetic power spectral amplitudes (236.7 ± 8.9 fT/√ Hz) compared with those gained from neonates corresponding to normal pregnancies (163.2 ± 22.6 fT/√Hz). This difference was statistically significant ($p < 0.005$). There was a strong correlation between the severity of preeclampsia with birth weights ($p = 0.003$) and MEG values ($p = 0.002$). The 30 neonates in normal pregnancies had low amplitudes, birth weights > 75th percentile, umbilical cord pH from 7.25-7.50 and Apgar scores from 7-9. Neonates from the preeclamptic pregnancies had lower values of D at the right ($p < 0.0001$) and left ($p < 0.0001$) temporal regions compared with the ones from normal pregnancies. The correlation dimension D determines the number of independent variables, which are necessary to describe the dynamics of the central nervous system (CNS). The preeclamptic infants had lower values of L1 compared with the controls at the right ($p = 0.0002$) and left ($p = 0.05$) temporal lobes, which means lower information processing.

Neonatal magnetocardiography

Anastasiadis *et al.* [21] investigated the validity of MCG in the estimation of neonatal cardiac rhythm. Their study population consisted of 50 neonates who were delivered normally between 37-41 weeks of gestation from clinically uncomplicated pregnancies. There was also a neonate included in the study in which the diagnosis of "hypoplastic left heart syndrome" was demonstrated by US Doppler examination. Maternal age ranged from 18 to 39 years (mean = 29.15, SD = 6.13). The results revealed 44 neonates with normal cardiac rhythm, four with ventricular tachycardia (VT), one with ventricular tachycardia (VT) and extrasystolic beats, and one with bradycardia. The neonate with the hypoplastic left heart syndrome presented frequent episodes of ventricular bigeminy in the MCG trace. M-mode echocardiography confirmed the diagnosis of the seven cases of arrhythmia in the study group.

Anninos *et al.* [22] studied the relationship between heart rate variability (HRV) and respiration in healthy and probably asphyxiated infants using MCG recordings. Ten healthy and eight infants from pregnancies complicated by preeclampsia with indications of mild perinatal asphyxia were included from the study. All were near term. Maternal age ranged from 16 to 39 years (mean = 29.05, SD = 6.13). Spectral analysis was used to find out any association between respiration and HRV. Respiratory sinus arrhythmia (RSA) was reduced in preeclamptic infants with indications of mild perinatal asphyxia. This difference was statistically significant ($p < 0.0002$, t-test), whereas the heart rate of the two groups was not statistically significant ($p = 0.1$, t-test). The results suggested that infants with indications of mild preeclampsia differ from controls in respiratory activity and this difference is independent of basal heart rate. Thus, spectral analysis could be useful to estimate the influence of mild perinatal asphyxia in the RSA rhythm of newborns.

Discussion

Several techniques are now available for use at the cotside in the first few hours of life, to assess the extent of HIE due to perinatal asphyxia and, accordingly, provide prognostic information. Conventional methods such as EEG, US, CT and MRI present certain disadvantages in everyday practice. EEG provides a reliable prognostic indicator of the neonate's neurodevelopmental outcome [10] but it is time-consuming, presents difficulty in performance (sometimes it can not be performed on neonates obtunded or receiving sedative anticonvulsant drugs), an experienced neonatologist is needed for the accurate interpretation of the data gained and, generally, electric fields are more distorted by the brain, skull and scalp than magnetic fields are [10, 12, 24]. Diagnostic accuracy, interobserver variability and prognostic value of US, CT, and MRI depend on the kind, localization and

extension of brain damage, and differ in preterm and term newborns. US is a practical and low cost method, but it has low sensitivity in detecting brain impairment. CT and MRI provide better diagnostic and prognostic values, but they are time and money consuming, need experienced personnel for performance and interpretation and are not suitable for screening or follow-up techniques [5, 6, 9-12]. Modern methods for the assessment of HIE after perinatal asphyxia like CFM and VEP, though with promising values (CFM is given a sensitivity of 0.93 and negative predictive value of 0.90), are still under investigation and their contribution to the prediction of outcome has not yet been established [2, 23].

A number of studies reported in the past refer to certain advantages that MCG presents compared to other diagnostic techniques such as M-mode echocardiography, two dimensional imaging, pulsed Doppler and color flow Doppler [11, 12, 23, 25]. All the above-mentioned studies confirm the diagnostic accuracy of MCG, especially regarding functional heart disorders like cardiac arrhythmias. Several authors have demonstrated that MCG is useful for the investigation of clinical arrhythmias, non-invasively, and for the identification of patients at risk for sudden death through the detection of magnetic fields. The detection of serious arrhythmias is of a great importance and especially in the patients at risk for sudden death. Thus any new non-invasive method, reliable, with predictive accuracy has potential importance. MCG provides a method of investigating normal and abnormal cardiac rhythm with high temporal and spatial resolution, applicable in the last decade. Its accuracy and reliability has been established with electrophysiology and cardiac pacing [26]. Fujino *et al.* [27] have reported a higher sensitivity of MCG as compared to ECG in the detection of left ventricular hypertrophy. Makijarvi *et al.* [28] concluded that MCG mapping provides accurate localisation of overt atrioventricular accessory pathways and some atrial arrhythmias, as focal atrial tachycardia can probably be localised by MCG mapping.

Biomagnetism is not yet a widely applicable method due to certain drawbacks such as the large size and cost of the device, and the need for sedation and an electrically shielded room. Further improvement of the equipment and software used for biomagnetic recordings, so as to become feasible at the cotside, would provide clinical practice with a useful alternative or adjunct tool, suitable for assessing neonatal brain and heart function. Of course, more studies in large series of infants and further technological innovation of the equipment used need to be done before the method can be established as a screening procedure in clinical practice.

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