Clinical Neurophysiology 125 (2014) 1353–1359

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Quantification of fetal magnetoencephalographic activity in low-risk fetuses using burst duration and interburst interval

Srinivasan Vairavan [a,1], Rathinaswamy B. Govindan [b], Naim Haddad [c], Hubert Preissl [d,e], Curtis L. Lowery [d], Eric Siegel [f], Hari Eswaran [d,*]

[a] Graduate Institute of Technology, University of Arkansas at Little Rock, AR, USA
[b] Division of Fetal and Transitional Medicine, Children's National Medical Center, Washington, DC, USA
[c] Weill Cornell Medical College in Qatar, Education City, Doha, Qatar
[d] SARA Fetal MEG Center, Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR, USA
[e] Fetal MEG Center, University of Tuebingen, Tuebingen, Germany
[f] Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR, USA

ARTICLE INFO

Article history:
Accepted 23 November 2013
Available online 1 December 2013

Keywords:
Magnetoencephalography
Fetus
EEG
Quantification
Burst duration
Interburst interval
Brain activity

HIGHLIGHTS

- Examined fetal neurological maturation indices in normal pregnancies using magnetoencephalographic recordings.
- Interburst interval (IBI) decreases with gestational age – a trend similar to EEG findings in premature neonates.
- Tracking IBI in quiet sleep state could provide valuable insight into fetal neurological maturation.

ABSTRACT

Objective: To identify quantitative MEG indices of spontaneous brain activity for fetal neurological maturation in normal pregnancies and examine the effect of fetal state on these indices.
Methods: Spontaneous MEG brain activity was examined in 22 low-risk fetal recordings with gestational age (GA) ranging from 30 to 37 weeks. As major quantitative characteristics of spontaneous activity, burst duration (BD) and interburst interval (IBI) were studied in correlation with GA and fetal state.
Results: IBI showed a decrease with gestational age (-0.21 s/week, $P = 0.0031$). This trend was only maintained in the quiet-sleep state. With respect to BD, no significant trends were detected with GA and state.
Conclusion: IBI can be quantified as a fetal brain maturational parameter. The decrease in IBI over gestation was similar to the trend reported in the preterm neonatal EEG studies. Quiet sleep could be the optimal state to study such MEG maturational indices.
Significance: With further investigation, indices extracted from spontaneous fetal brain activity may serve as an early warning for fetal neurological distress.

1. Introduction

Although it has been common practice to evaluate the structure of the fetal brain using ultrasound (Awoust and Levi, 1983), the measurement of fetal electrocortical signals would open new horizons complementing the anatomical parameters of neurological maturation with new parameters for evaluating physiology and function.

Electroencephalography (EEG) has long been used to study neurological maturation and cerebral dysfunction in neonates (Parmelee et al., 1969) but its usefulness could not be extended to the fetal stage. Besides EEG, magnetoencephalography (MEG) (Hari and Salmelin, 2012) has been established during recent decades for the recording of human brain activity. This technique is non-invasive and records the magnetic fields corresponding to the electric currents generated by neurons in the brain. Unlike EEG, the MEG technique is not dependent on intervening tissue impedances, which makes it uniquely suited to study the magnetic fields generated in the fetal brain.

---

[*] Corresponding author. Address: University of Arkansas for Medical Sciences, 4301 W. Markham Slot 518, Little Rock, AR 72205, USA. Tel.: +1 501 686 5847; fax: +1 501 603 1544.

E-mail address: eswaranhari@uams.edu (H. Eswaran).

[1] Currently with Philips Research North America, Briarcliff Manor, NY, USA.

1388-2457/$36.00 © 2013 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.clinph.2013.11.018

Since the ontogeny of spontaneous brain activity of the premature infant has been well-studied using EEG (Clancy et al., 2003; Scher, 2004; Mizrahi et al., 2004; Lamblin et al., 1999; André et al., 2010), we postulated that these trends occur even in the fetal stage of life and can be documented using fetal MEG (fMEG). Since its feasibility was reported by Rose and Eswaran (2004), significant progress has been made towards evaluating spontaneous fMEG as a potentially viable technique to study fetal neurological maturation. fMEG patterns have been shown to share many similarities with established EEG features in premature infants at comparable ages. Some fMEG findings include (Rose and Eswaran, 2004; Eswaran et al., 2007; Haddad et al., 2011) (1) Signals equivalent to delta brushes and sharp transients of the neonatal EEG, (2) a decrease in the percentage of discontinuous epochs with advancing gestational age (GA), especially in quiet sleep, and (3) abundance of discontinuous epochs in quiet compared to active sleep, mainly before 35 weeks' GA.

Spontaneous fetal MEG has also been explored in potentially pathological conditions (Eswaran et al., 2012; Kotini et al., 2002). Using spectral analysis and computing relative power between the frequency bands for both low-risk and intrauterine growth restricted (IUGR) fetuses, we have shown that the average relative power was highest in the lowest-frequency delta band, and decreased monotonically in higher frequency bands (Eswaran et al., 2012). Furthermore, when compared to fetuses exhibiting normal growth, the IUGR fetuses showed a significant difference in relative power only in the early part of the third trimester (28–31 weeks), suggesting that growth restriction may have a more pronounced effect on the fetal brain in early rather than the late stage of the third trimester (Eswaran et al., 2012).

To further enhance the utility of fMEG, in the current study we proposed to identify quantitative indices from the selectively identified discontinuous epochs in the recordings from fetuses in normal healthy pregnancies. A discontinuous pattern is characterized by the occurrence of bursts of MEG activity alternating with periods of quiescence. We investigated the interburst interval (IBI) and burst duration (BD) as quantitative indices for neurological maturation in low-risk pregnancies (Neimarkt et al., 2008) . We studied the dependence of these parameters on GA and fetal state – mainly quiet and active sleep.

2. Materials and methods

2.1. Instrument and recording procedures

The measurements in this study were performed using a non-invasive 151-channel SQUID (Superconducting Quantum Interference Device) fMEG system called SARA (SQUID Array for Reproductive Assessment). SARA, built by CTF Systems Inc., Port Coquitlam, BC, Canada, was specifically designed to study different aspects of maternal and fetal physiology (Preissl et al., 2004; Lowery et al., 2009). The sensors in the SARA system are arranged in a concave array. The mother simply sits and leans forward against the smooth surface of the array, allowing the SQUID sensors to receive signals from the anterior maternal abdomen. To reduce the effects of environmental noise, SARA is installed in a magnetically shielded room (Vakuumschmelze, Germany).

An ultrasound examination (GE Voluson 730) was performed prior to the fMEG recording to document general fetal position, head localization, and biometric measurements. The fMEG data were recorded in continuous mode at a sampling rate of 312 Hz with a bandwidth of 0–100 Hz. The recording times ranged from 10 to 30 min and were performed without any stimulation to the mother and the fetus.

2.2. Subjects

A total of 22 low-risk fetal recordings with GA ranging from 30 to 37 weeks were included in the study. The study protocol was approved by the Institutional Review Board at the University of Arkansas for Medical Sciences (UAMS), and a signed consent for participation was obtained from each mother. Maternal demographics including age, weight, height, race and maternal medical conditions were recorded. Only pregnant women with no known maternal or fetal complications at the time of recruitment were included. The GA of the fetus was based on their last clinical visit as determined by their physician. The GA along with the position and distance of the fetal head from the maternal abdomen is shown in Table 1. The distance from the fetal head to the maternal abdomen ranged from 1.0 to 8.5 cm; thus, it is within adequate range of the SARA sensors for fMEG recordings.

Table 1
Fetal head position and distance as recorded by ultrasound prior to MEG recordings.

Subject ID	GA wk	Distance to from the maternal abdomen head (cm)	Head position relative to maternal abdomen determined by US
ntlr29	36w5d	5.7	Low midline
ntlr15	37w2d	2.8	Low midline
spont-pat23	32w6d	6.4	Low midline
spont-pat05	32w	5.1	Low right
ntrl21	36w1d	5.5	Low midline
spont-pat12	37w	4.1	Low midline
ntlr27	36w1d	2.4	High right
ntlr05	33w5d	5.7	Low midline
spont-pat11	36w3d	4.0	Low midline
spont-26	33w5d	7.0	Low midline
spont-27	30w2d	6.4	Low midline
ntlr14	35w2d	9.1	Low left
ntlr18	36w2d	5.2	Low midline
spontpat01	35w	7.5	Low midline
spont-21	34w	1.0	High right
spont03	32w	4.3	Low left
spontpat02	37w	3.7	Low left
spont-pat04	32w	3.3	Low left
spont-pat24	36w4d	8.5	Low midline
ntlr08	34w2d	5.2	Low midline
ntlr01	37w3d	6.1	Low right
ntlr17	35w6d	5.5	Low midline