

EEG Polysomnographic Study of Maturation Differences between Twins

Mirjana Vučinović¹, Anita Ursić², Biserka Rešić³ and Vesna Čapkun⁴

¹ University of Split, Split University Hospital Centre, Clinic of Obstetrics and Gynecology, Neonatology Intensive Care Unit, Split, Croatia

² University of Split, School of Medicine, Children Sleep Laboratory, Split, Croatia

³ University of Split, Split University Hospital Centre, Pediatric Clinic, Split, Croatia

⁴ University of Split, Split University Hospital Centre, Department of Nuclear Medicine, Split, Croatia

ABSTRACT

The purpose of this pilot study is to assess the effects of multiple pregnancies on the maturation of the developing brain using the polysomnographic EEG recordings. Data from prospectively recorded 10 twin sets, born prematurely (mean 36 gestational week; range 33 – 38 GW) in the Split University Hospital Center, were analysed. We compared sleep architecture parameters in the twins at 37th and 44th postmenstrual age (PMA) with parameters that were expected at that PMA. The same parameters were compared within each twin pair using the Man Whitney test. At first measurement indeterminate sleep (IS) proportion was greater in the first twin than in the second one. The IS sleep proportion was 1.6 fold greater in the first twin ($p=0.028$), and 1,8 fold less percentage of quiet sleep (QS) than the second twin ($p=0.054$). The length of sleep stages among the twins was similar at the second measurement. Measures of sleep architecture were not significantly different within the twins in second recording. The results of this study obtained on a relatively small number of twins (longer IS and shorter QS in the first twin at the 38th week recordings), showed that the maturational differences among twins exist in utero and shortly after birth, and then disappear until the end of the first month of the postnatal life.

Key words: EEG polysomnography, twin, immature brain

Introduction

Structural maturation and functional development of the central nervous system (CNS), is a dynamic process, the result of continuous interactions between environment and genome of the fetus, infant and child¹. It has become clear recently that in some human fetuses with placental insufficiency or multiple pregnancies, acceleration of maturation may occur in the brain and lungs as an adaptation to stress. These adaptive changes could represent a life saving answer to moderate stress with resultant earlier birth of more mature newborn, and increased survival as long as the unfavorable fetal environment is not too early or too severe^{2,3}. Multifetal gestations are stressed during the third trimester because of intrauterine crowding and limited uteroplacental supply^{4,5}. The influence of multifetal gestations on rate of maturation or complications of prematurity has been controversial.

There is a widespread clinical impression that twin fetuses may experience more rapid pulmonary maturation than singleton fetuses^{6,7}. Although there is no ideal method with which the neuromaturational changes within population could be compared over time, sleep studies could be used for the assessment of functional brain maturation. Specific EEG – sleep behaviors may suggest an acceleration of brain maturation than expected for that gestational age⁸.

The purpose of this study is to assess the effect of multiple pregnancies on the maturation of the developing brain through first month of life. We compared sleep architecture parameters in the twins at 37th and 44th postmenstrual age (PMA) with parameters that were expected at that PMA. The same parameters were compared within each twin pair using the Man Whitney test.

Material and Methods

Data from prospectively recorded 10 twin sets, born prematurely at the Split University Hospital Center during the period from December 2008 to June 2009 were analyzed.

EEG polysomnographic recordings were obtained at 37th week (range 36–38) of postmenstrual age and at 44th week (range 44–45) postmenstrual age (PMA).

The group consisted of 9 males and 11 females selected according to the following criteria: normal pregnancy and birth, gestation age (GA) between 33 and 38 weeks (mean 35.58;SD+/-1.97), birth weight from 1550 g to 2680 g (mean 2177.98 g; SD+/-378.84), 1 min Apgar ≥7; 5 min Apgar ≥9; normal postnatal physical and neurological status. Gestational age was based on the last menstrual period, ultrasonography examination and neurological assessment according to Amiel-Tison neurological criteria.

Before recording all of them have passed through brain ultrasound, clinical and neurological examination. Seriously ill newborns with sepsis, respiratory distress, prenatal intracranial damage and congenital anomalies were excluded.

EEG-sleep studies were carried out between 10 and 12 a.m. as a part of an interfeeding interval, starting with the patient awake and lasting through an entire sleep period until the baby again showed a sustained period of wakefulness.

All recordings were obtained in an environmentally controlled setting in which sound, light, humidity and tactile stimulation were carefully monitored. All infants were studied while slept in the supine position in open beds.

Second recordings were obtained in the afternoon to coincide with the usual nap time.

All recordings were made on TG Nervus 3 Valor T40; 40-channel EEG.

The EEG electrode array was as follows: Fp1, Fp2, C3, Cz, C4, T3, T4, O1 and O2. The recording included 12 channels of EEG, two channels of electrooculogram (EOG), one channel of submental electromyogram (EMG), one channel of respirogram and pulse oxymeter.

Prior to testing, written informed consent was obtained from the parents of participants. Ethic approval for the study was obtained from the Ethics Committee Clinical Hospital Split.

The six EEG sleep measures were selected as followed: total sleep time (TTS), length and proportion of active sleep (AS), quiet sleep (QS), indeterminate sleep (IS), trace alternant (TA) and delta brushes (DB). TTS, QS, AS and IS times were calculated in minutes and percentage.

To facilitate discussion the term »perinatale patterns« (according to Ellingson, 1979.) will be used to designate patterns which predominate in the EEGs of babies from about 36 to 46 weeks conceptional age (CA).

Each recording was interpreted clinically by the two independent pediatricians.

After completion of the sleep recording portion of the study, all infants were followed clinically for at least one month and judged to be healthy, including age appropriate neurodevelopmental milestones.

Results

Forty EEG polysomnographic recordings obtained at 37 weeks (range 36–38) of postmenstrual age (PMA), and at 44 weeks (range 44–45) were analyzed. The mean duration of sleep cycle, sleep, stage lengths (in minutes) and proportion of the sleep stages (%) in the twins at both recordings were showed at the Table 1.

There were no statistical differences when lengths of sleep cycle and AS were compared between first and second recording and between both babies during one re-

TABLE 1
COMPARISON BETWEEN TWO RECORDINGS OF THE TWIN

Polysomnographic recording	I			II		
	36.58			44.11		
PMA (weeks)	I twin	II twin		I twin	II twin	
Sleep cycle (min)	78.60	77.00	NS*	62.70	53.40	
AS min	51.70	47.30	NS*	34.00	34.00	NS*
AS %	66.23	62.09	NS*	55.05	64.20	NS*
QS min	13.00	22.05	NS*	22.70	14.60	NS*
QS %	15.28	27.47	NS*	35.47	25.73	NS*
IS min	12.10	6.60	p=0.05	6.10	6.60	NS*
IS %	16.07	9.88	p=0.028	9.92	13.51	NS*
Trace alternant (TA)	20/20			8/20		
Delta brush (DB)	20/20			0/20		

NS – non significant

cording, except in duration and percent of IS and QS when two twins were compared.

Significant difference between first and second twin were noted for percentage for indeterminate sleep (IS) in the first measurement. First baby twin showed 1,6 fold greater percentage of IS (16.07% vs. 9.88%; $p=0.005$; $Z=-2.81$), and 1,8 fold less percentage of quite sleep (QS) than the second baby twin (15.28% vs. 22.05%; $p=0.054$; $Z=-1.928$).

In the second measurement percentage of QS was 1,4 fold longer for second baby twin (35.47 % vs. 25.79%; $p=0.082$; $Z=-1.739$).

It is notable that the duration of total sleep time (TTS), percentage of active sleep (AS), and presence of trace alternant (TA) and delta brushes (DB) were not significantly different between the twins.

Discussion

Although the belief persists that twin fetuses experience earlier brain maturation than singleton fetuses do, little has been written to support or refute this claim^{6,7}. In the current sleep study we have found differences between first and second twin in the length of IS and QS. Percentage of IS (16.07 %) in the first twin was slightly beyond values expected for that PMA⁹. Elevation of the IS proportion with proportionally decreased QS, and QS/IS inversion may be attributed to the transition between sleep stages and can constitute a quantitative measure of disturbed sleep, reflecting dissociation of the physiological variables which ordinarily vary during the normal sleep cycle¹⁰. At the time of the first recording, approximately 60% of TST of both twin babies was occupied by AS and there was strong tendency for sleep onset in AS (100% sleep episodes). AS sleep onset decreased rapidly over the next 6 weeks, but 30% (6/20) of sleep episodes were still initiated by AS during the 44th and 45th week of life (Table 1).

Discontinuous pattern of the QS (trace alternant – TA) was present during QS in 100% of newborns in the first records. After 6 weeks, it was still present during QS in the 40% (8/20) of newborns. TA is most striking in prematures and becomes increasingly difficult to distinguish after term. It can no longer be identified at 47th week PMA^{10–12}.

There were not interindividual differences in the appearances of delta brushes in the both recordings. They are salient feature of the EEG of premature, where they may be the dominant features of the tracings^{9,13}. In the full term newborn they are usually infrequent and disappear between 43rd and 46th week PMA^{9,10}. All of these findings are in accordanc with the EEG values described as a perinatal EEG pattern, which is used to designate pattern which predominate in the EEGs of babies from

about 36 to 46 weeks PMA¹⁰. Whether an EEG is to be classified as immature or accelerated depends upon the types of wave forms present and their abundance and prominence. Since clinical EEG interpretation is still impressionistic, only experience will enable the electroencephalographer to make valid and reliable judgments¹⁴.

We do not consider an EEG to be significantly accelerated in the first instance unless the patterns are clearly those characteristics of the infantile pattern¹². This term is used to designate EEG pattern which predominates after 52nd week PMA and is similar to those exemplified in the manual of Rechtschaffen and Kales¹⁵. Comparing two EEG records for each twin baby performed during the neonatal period, we could not found any evidence of accelerated brain maturation.

The concept of acceleration of brain maturation was described in infants with intrauterine growth retardation who exhibited advanced neurological examinations during the neonatal period as well as shorter brainstem evoked response latencies during infancy than expected for their postconceptional ages^{16–18}. Even asymptomatic neonates exhibited precocious or advanced sleep behaviors within a day of birth with predicted delayed neurodevelopment⁸.

Several shortcomings of this study are recognized. Firstly, our study included only two measurements during the perinatal period, before the transition into infantile sleep pattern begin. Secondly, we had a small sample of patients. Fewer studies were obtained at older ages beyond 44 weeks PMA; persistent sleep differences might be present at 1–6 months of age, but were not detectable based on our limited sample sizes at this age. Finally, other physiologic measurements may more accurately reflect differences in state regulations between twin babies as recently described using instantaneous heart rate and respiratory measures.

In conclusion, we have found no evidence to support the view that twinning *per se* accelerates maturation.

Longitudinal EEG sleep studies are needed to substantiate the presence of acceleration of brain maturation at older ages.

Conclusion

The results of this study obtained on a relatively small number of twins (longer IS and shorter QS in the first twin at the 37 weeks recordings), showed that first-born twin showed more immature EEG polysomnographic pattern compared with the second twin at 37 weeks of postmenstrual age but not at 44 weeks. It might be suggested that the maturational differences among twins exist in utero and shortly after birth, and then disappear until the end of the first month of the postnatal life.

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M. Vučinović

University of Split, Split University Hospital Centre, Clinic of Obstetrics and Gynecology, Neonatology Intensive Care Unit, Spinčićeva 1, 21000 Split, Croatia
e-mail: mirjana.vucinovic@yahoo.co.uk

PRAĆENJE MOŽDANE MATURACIJE BLIZANACA EEG POLISOMNOGRAFIJOM

SAŽETAK

Svrha ovog istraživanja je pomoću EEG polisomnografije usporediti moždanu maturaciju u blizanaca. U studiju su uključeni deset pari blizanaca, prijevremeno rođenih (srednja gestacijska dob 36; raspon 33–38) u rodilištu Kliničkog bolničkog centra Split. Usporedili smo arhitekturu spavanja u blizanaca u 37. i 44. tjednu postmenstrualne dobi (PMA – postmenstrual age). Za statističku obradu koristio se Man Whitney U test. U prvom snimanju postotak IS stanja (%) u ciklusu spavanja je značajno veći u prvog blizanca nego u drugog blizanca. Udio mirnog spavanja je 2,5 puta veći u drugom nego u prvog blizanca. Tijekom drugog snimanja nije bilo statistički značajne razlike između prvog i drugog blizanca. Mjere arhitekture spavanja kod oba blizanca u oba mjerjenja nisu se značajno razlikovali od očekivanih za dob. Rezultati dobiveni ovom studijom na manjem broju uzoraka upućuju na činjenicu da najveće razlike u maturacionim postupcima kod blizanaca postoje u prvom mjesecu života i nakon toga nestaju.