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Pilot study of EEG in neonates born to mothers with gestational diabetes mellitus

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ABSTRACT

Background: The goal was to evaluate whether there was neurodevelopmental deficits in newborns born to mothers with gestational diabetes mellitus (GDM) compared to control newborns born to healthy mothers.
Methods: Forty-six pregnant women (21 controls and 25 GDM) were recruited. Electroencephalogram (EEG) was recorded in the newborns within 48 h after birth. The EEG signal was quantitatively analyzed using power spectral density (PSD); coherence between hemispheres was calculated in paired channels of frontal, temporal, central and occipital regions.
Results: The left centro-occipital PSD in control newborns was 12% higher than in GDM newborns ($p = 0.036$) but was not significant after adjustment for gestational age. While coherence was higher in the frontal regions compared to the occipital regions ($p < 0.001$), there was no difference between the groups for the fronto-temporal, frontal-central, centro-occipital and tempo-occipital regions.
Conclusion: Our results support that EEG differences between groups were mainly modified by gestational age and less by GDM status of the mothers. However, there is a need to confirm this result with a higher number of mother-newborns. Quantitative EEG in GDM newborns within 48 h after birth is feasible. This study emphasizes the importance of controlling blood glucose during GDM to protect infant brain development.

1. Introduction

Over the last 10 years, prevalence of childhood psychiatric disorders has increased dramatically (Atladottir et al., 2015). This phenomenon is linked to multiple conditions. Among them, gestational diabetes mellitus (GDM) is an increasingly common pregnancy condition (Jiwani et al., 2012) continuously associated with poorer behavioural and intellectual development, even with good control of blood glucose levels as reflected by glycated hemoglobin (A_{1C}) in the normal range (Castro Conde et al., 2013; Rizzo et al., 1991). In a study on > 230,000 deliveries, GDM was reported as an independent risk factor for long-term neuropsychiatric morbidity in their offspring (Nahum Sacks et al., 2016).

Abnormalities of electroencephalography (EEG) patterns were reported in infants of diabetic mothers compared to infants of control mothers (Castro Conde et al., 2013; Jabes et al., 2015; Deregnier et al., 2000). From birth to one year of age, two studies described EEG patterns of newborns or infants born to diabetic mothers compared to infants born to control mothers. At 10 years old, one study found subtle information processing differences between children of diabetic mothers compared to children of control mothers. Unfortunately, little data has been collected in newborns of diabetic mothers that could have helped to prevent further behavioural deficits during infancy.

The power spectral density function (PSD) produces the complete frequency distribution of the EEG signal. It indicates if the EEG signal contains more or less energy for every frequency present in the signal. The PSD calculation can be applied to a few seconds of continuous EEG data. With this method, it is also possible to evaluate functional cortical

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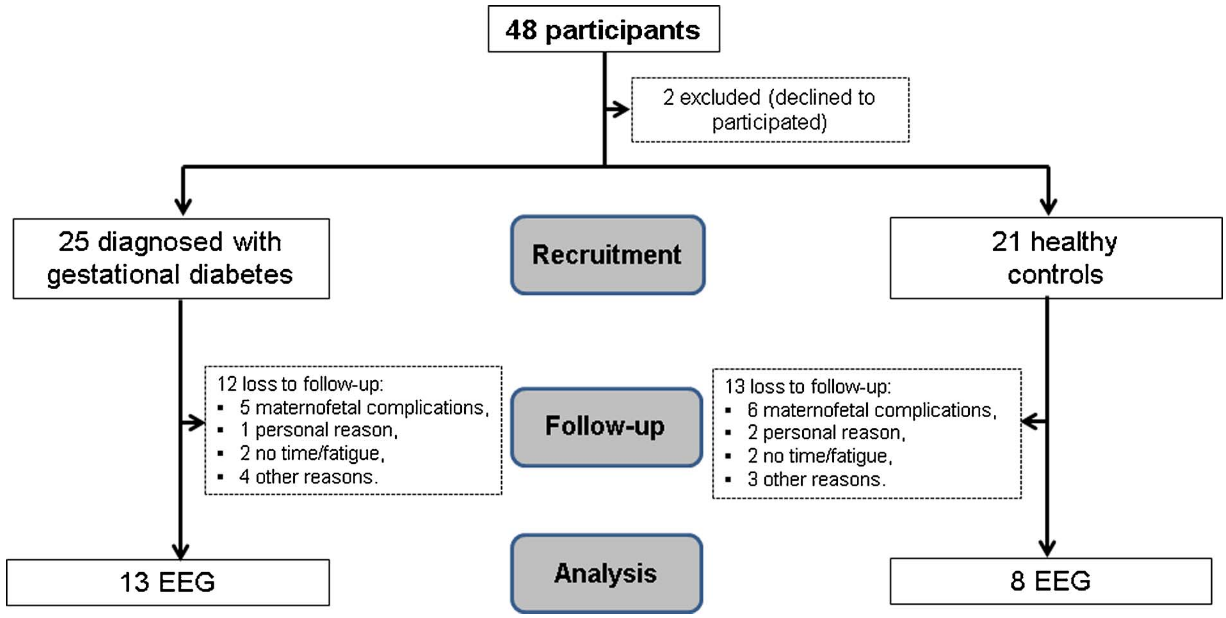

Fig. 1. Flow chart of study participants.

connections between brain hemispheres using a correlation coefficient of oscillations in the left and right hemisphere. EEG coherence in newborns is indicative of the neural network at birth. It is possible to detect subtle changes in EEG such as delayed maturation using these analytical techniques.

Here, we present a pilot study in newborns using a quantitative EEG analysis method to evaluate whether subtle neurodevelopmental alterations can be detected in newborns from mothers with GDM, compared to controls. We hypothesize that PSD and coherence are altered in newborns from GDM compared to control newborns due to under development of brain connectivity.

2. Material and method

2.1. Participants

Pregnant women (n = 46, 18–40 years of age, with singleton pregnancy) were recruited at the Centre Hospitalier Universitaire de Sherbrooke (CHUS) at 24–28 weeks of gestation between December 2013 and May 2014 while they were performing 50-g glucose loading test (GLT) (Fig. 1). Exclusion criteria were: smoking, illicit drug or omega-3/6 consumption, liver or renal disease, cancer, or any medical conditions affecting glucose/lipid metabolism.

GDM was diagnosed using plasma glucose (PG) cut-offs of the American Diabetes Association (ADA): fasting PG ≥ 5.1 mmol/l; 1h-PG ≥ 10.0 mmol/l; 2h-PG ≥ 8.5 mmol/l (American Diabetes Association, 2010). After GDM diagnosis, all women with GDM were recommended dietary intervention, physical activity, and self-monitoring of blood glucose. Individualized insulin therapy was initiated if lifestyle interventions failed.

Our study (Clinical Trial Registration: NCT02779452) was approved by the Human Ethics Research Committee of the Centre hospitalier de l'Université de Sherbrooke; women gave informed written consent before delivery for themselves and their newborns.

2.2. Data collection

Prepregnancy maternal weight was self-reported and maternal weight close to delivery was measured. Pregnancy weight gain and prepregnancy BMI were calculated. Birth weight, length, head circumference, Apgar score and glycaemia of the newborn were recorded at birth. A maternal blood sample was collected at admission to measure A_{1C} using HPLC (Bio-Rad VARIANT, Hercules, CA). EEG was recorded in the newborn within 48 h after birth (Fig. 2A).

2.3. EEG montage and data acquisition

EEG data was recorded using a 14-channel bi-polar montage based on the 10–20 System (Grass Technologies, Warwick, RI). The montage was identified as follows: left and right fronto-temporal channels, Fp_1-T_3; Fp_2-T_4, left and right fronto-central channels, Fp_1-C_3; Fp_2-C_4; left and right central channels, C_3-Cz; C_4-Cz, left and right centro-temporal channels, C_3-T_3; C_4-T_4, left and right tempo-central channels, T_3-Cz; T_4-Cz, left and right centro-occipital channels C_3-O_1; C_4-O_2, and left and right tempo-occipital channels; T_3-O_1; T_4-O_2 (Fig. 2B). Silver–silver chloride electrodes were placed on the newborn's scalp using a conductive water-soluble fixative paste and secured using adhesive tape. Two shoulder electrocardiogram electrodes were used to record a single channel heart rate signal. Respiratory movements were measured using a thoracic respiratory band. Acquisition of the EEG signal was performed at 200 Hz sampling rate for 12.5 min and processed using in-house Matlab scripts (Mathworks). All recordings were performed in awake newborns: sleeping newborns were awoken before data acquisition. In order to remove movement artifacts, the continuous EEG signal was converted to z-scores using a built-in Matlab function and divided into non-overlapping 5s windows. Windows with z-score > 10 were considered as artifacts and discarded from the analysis. The recordings were visually inspected to ensure all electrodes were connected and not saturated. A PSD was computed on remaining windows for every electrode pair using Welchs' approach as implemented in Matlab ('pwelch.m'). The function was setup to compute each 5s window individually and perform a 2048 points PSD using a non-overlapping window of 500 points. Coherence (using 'mscohere.m') was computed using the same parameters used with 'pwelch' between channels in the left and right hemispheres (Fig. 2C).

2.4. Statistical analysis

Descriptive statistics were used to report characteristics of the mothers and newborns. Chi-square tests were used to compare categorical variables and Mann-Whitney *U* tests were used to compare means (SPSS software, version 12.0; SPSS Inc., Chicago, IL). Simple regression