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Development of Emotional Face Processing in Premature and Full-Term Infants: A Quantitative EEG Study

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Abstract

The rate of premature births has increased in the past 2 decades. Ten percent of premature birth survivors develop motor impairment, but almost half exhibit later sensorial, cognitive, and emotional disabilities attributed to white matter injury and decreased volume of neuronal structures. The aim of this study was to test the hypothesis that premature and full-term infants differ in their development of emotional face processing. A comparative longitudinal study was conducted in premature and full-term infants at 4 and 8 months of age. The absolute power of the electroencephalogram was analyzed in both groups during 5 conditions of an emotional face processing task: positive, negative, neutral faces, non-face, and rest. Differences between the conditions of the task at 4 months were limited to rest versus non-rest comparisons in both groups. Eight-month-old term infants had increases ($P \leq .05$) in absolute power in the left occipital region at the frequency of 10.1 Hz and in the right occipital region at 3.5, 12.8, and 16.0 Hz when shown a positive face in comparison with a neutral face. They also showed increases in absolute power in the left occipital region at 1.9 Hz and in the right occipital region at 2.3 and 3.5 Hz with positive compared to non-face stimuli. In contrast, positive, negative, and neutral faces elicited the same responses in premature infants. In conclusion, our study provides electrophysiological evidence that emotional face processing develops differently in premature than in full-term infants, suggesting that premature birth alters mechanisms of brain development, such as the myelination process, and consequently affects complex cognitive functions.

Keywords

neonate, pediatric, oscillations, children, electroencephalogram (EEG), electroencephalography

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Introduction

In the past 2 decades, the rate of very premature births (delivery before 32 weeks of gestation) and very low birth weights (<1500 g) has increased.[1] Almost 50% of premature infants develop some type of perinatal brain injury (PBI); the most common are diffuse periventricular leukomalacia, intraventricular hemorrhage and periventricular hemorrhagic infarction.[2,3] PBI is tightly related to a decreased volume of neuronal structures, such as the thalamus and basal ganglia,[4] and to the impaired development of white matter.[3] Although only 10% of premature and low birth weight infants develop a motor disability, almost half exhibit later sensorial, cognitive, and social-emotional disabilities.[5-10]

Emotional face processing is a cognitive function that depends on the integrity of a complex cerebral network, which includes cortical regions implicated in perceptual processing of faces, such as the fusiform gyrus[11] and superior temporal sulcus[12]; structures related to emotion, orbitofrontal cortex, and amygdala[13]; and attentional networks in the dorsolateral prefrontal cortex, such as the anterior cingulate gyrus.[14]

Developmental studies have shown that infants have the ability to discriminate different facial-emotional stimuli as early as 4 months of age, when the stimulus is presented in the audiovisual mode.[15] However, unimodal visual stimulus discrimination seems to develop later, between 5 and 7 months of age.[15-18]

Neural correlates of emotional face processing in infants have been assessed in some functional studies.[19-23] A near-infrared spectroscopy study reported the activation of the

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Table 1.

	4 Months Old					8 Months Old				
Mean trials	Positive	Negative	Neutral	No-Face	Rest	Positive	Negative	Neutral	No-Face	Rest
Preterm	23.3	23.0	23.3	22.6	22.3	23.9	24.3	24.3	24.8	24.6
Term	21.9	22.0	22.0	21.9	21.2	24.0	23.7	24.0	23.9	23.8
P	.26	.46	.43	.56	.48	.97	.79	.83	.72	.73

orbitofrontal cortex in 9- to 13-month-old infants viewing their mother's smile.[19] Event-related potentials (ERPs) have been used to assess the development of emotional face processing in infants. It has been found that in 7-month-old infants, the negative component of the ERPs is larger in amplitude when seeing fearful compared with happy/neutral faces.[20,21] This finding was observed in 2 principal regions: frontal and central derivations, showing allocated attentional resources, and in occipital and temporal derivations, supporting the visual processing of faces. Moreover, Grossmann et al[22] argue that familiarity with happy faces at this age could explain the larger amplitude in the negative component of the ERPs in frontal derivations found in response to happy faces compared with fearful ones. They also extended this study, adding that in the occipital derivations of 12-month-old infants, ERPs have a larger negative amplitude in response to fearful than to happy faces, explained as enhanced visual processing after a recent experience with negative emotions.

In premature infants, PBI disturbs the early development of the brain, altering its structural and functional integrity. Although premature birth sequelae in cognitive functions, such as learning, language and memory, have been investigated, there are few studies about deficits in emotion processing. Therefore, the aim of the present study was to test the hypothesis that premature infants differ from full-term infants in their development of emotional face processing.

Materials and Methods

Infants at the "Dr Augusto Fernández Guardiola" Neurodevelopmental Research Unit were prospectively selected to participate in the longitudinal study and were divided into 2 groups. The healthy group consisted of 15 infants who were born full-term (>37 gestational weeks) and had normal birth weight (>2500 g), no risk factors for PBI, and normal neurological and ophthalmological examinations. The premature group contained 20 infants who were born prematurely (<35 gestational weeks) with risk factors for PBI and who had a normal ophthalmological examination but an abnormal neurological examination. The infants were evaluated by the Bayley Scale of Infant Development (BSID-II)[24] at 4 months to assess mental and motor development. Ten healthy and 17 premature infants were studied longitudinally at 4 and at 8 months (corrected age for prematures) by registering brain electrical activity during an emotional face processing task. Informed written parental consent for participation in this study was obtained for all subjects. The Ethics Committee of the Instituto de Neurobiología, Universidad Nacional Autónoma de México approved this study, which also complies with the Ethical Principles for Medical Research Involving Human Subjects established by The Declaration of Helsinki.

Electroencephalographic Recording

Continuous electroencephalogram (EEG) was carried out in infants using a 19-channel cap (Electro Cap International, Inc, Eaton, OH, USA) with a Medicid System (Neuronic Mexicana, SA, México City, México). The sampling rate was 200 Hz, with an amplifier gain of 10,000 and a band-pass filter of 0.5 to 30 Hz. Mastoid electrodes (M1, M2) were used as a reference, and impedances in all electrodes were kept under 5 kohms. The data were analyzed offline with EP Workstation software 1.4 (Neuronic Mexicana, SA, México City, México). Windows of 2560 ms were selected 300 ms after stimulus onset. EEG was analyzed with an expert electrophysiologist (S-R.E.), and trials with extracerebral activity or artifacts were excluded. There were no differences between groups in the number of analyzed trials among the conditions (Table 1). Windows were quantified using a fast Fourier transform to calculate absolute power in the narrow band from 0.7 to 19.1 Hz with a spectral resolution of 0.3 Hz.

Emotional Face Processing Task

The EEGs were recorded while the infants were seated on their parent's lap viewing a black-and-white picture of a face with a neutral, negative, or positive emotion or a non-face picture for 3000 ms, followed by a dark screen for 3000 ms. Rest condition windows were taken from dark screen period after non-face pictures. Each type of stimulus was presented 25 times, comprising a total of 100 trials. Face pictures were selected from the Pictures of Facial Affect (POFA) system[25] and non-face pictures from the International Affective Picture System (IAPS).[26] Stimuli were generated by Mind Tracer Software (Neuronic Mexicana, SA, México City, México) and projected on a 37 × 30 cm computer monitor with a resolution of 1024 × 768 pixels and color quality of 32 bits. Pictures were 21 × 13 cm; the infants were 50 cm from the monitor and had a visual angle of 22.7°. The infant's eye movements were monitored by an infrared camera on top of the monitor.

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Table 2. Risk Factors of Preterm Infants.

Characteristic	n (%)
Prematurity	20 (100)
Respiratory distress syndrome	16 (80)
Requiring ventilation	16 (80)
Neonatal sepsis	12 (60)
Hyperbilirubinemia	11 (55)
Maternal urinary infection	9 (45)
Premature rupture of membranes	8 (40)
Threatened abortion	6 (30)
Oligohydramnios	6 (30)
Preeclampsia	6 (30)
Retinopathy of prematurity	5 (25)
Intrauterine growth restriction	2 (10)
Neonatal seizures	2 (10)

Data Analysis

We examined differences between groups in gestational age and birth weight using the 2-tailed *t* test. Differences in absolute power of the EEG between groups and between conditions were calculated in the 19 derivations and for each of the 48 narrow-band frequencies with Neuronic Estadistic 3.0 Software (Neuronic Mexicana, SA, México City, México) using 2-way analysis of variance (ANOVA). ANOVA factors were group (premature with risk factors for PBI and full-term) and condition (rest, non-face, neutral, positive, and negative face). When ANOVA indicated that any factor or interaction was significant, post hoc comparisons using FDR (false discovery rate) Newman-Keuls–corrected Student's *t* test for multiple comparisons were performed. The statistical significance threshold was .05 in all analyses.

Results

The preterm group had a lower gestational age (30.9 ± 2.73 weeks) and lower birth weight (1665 ± 589.61 g) than did the full-term group (38.66 ± 1.04 weeks, 3430 ± 505 g) ($P < .0001$). The MDI scores (BSID-II Mental Developmental Index) were lower in the preterm (93.35 ± 7.52) than the full-term group (99.5 ± 5.27) ($P = .03$). Risk factors and magnetic resonance imaging findings in the premature group are shown in Tables 2 and 3, respectively.

Four-Month Analysis

The final 4-month-old groups consisted of 15 full-term infants with mean age of 4.56 ± 0.38 (6 females and 9 males) and 20 preterm infants with mean age of 4.54 ± 0.34 ($P = .8$) (8 females and 12 males).

Group Factor. Significant differences between full-term and preterm groups were found in the most of frequencies but especially in the following frequencies and regions: the bifrontal and bitemporal regions at frequencies from 0.7 to 5.0 Hz; in the bifrontal, biparietal, and bicentral regions at frequencies from 5.8 to 13.6 Hz, and finally in the right frontopolar and left frontal and bitemporal regions at frequencies from 14.0 to 19.1 Hz ($P < .05$).

Group Post Hoc Analysis. Preterm infants had higher absolute power than full-term infants in the left frontopolar and right frontal regions at frequencies from 0.7 to 4.3 Hz in all 5 conditions of the task (rest, non-face; neutral, positive, and negative face). Preterm infants also had lower absolute power than full-term infants in the left frontal region at frequencies from 6.6 to 7.8 Hz in the neutral, positive, and negative face conditions ($P < .05$).

Condition Factor. Significant differences between the 5 conditions of the task were found in the right central and occipital regions at frequencies from 7.0 to 14.0 Hz and in the bitemporal regions at frequencies from 11.3 to 17.9 Hz ($P < .05$).

Condition Post Hoc Analysis. In the left temporal regions, both groups had lower absolute power at frequencies from 13.2 to 19.1 Hz (full-term infants) and at 11.3 Hz (preterm infants) during non-face, neutral, and positive face conditions in comparison to rest. The full-term group also had higher absolute power in the right occipital region at frequencies from 8.9 to 9.3 Hz during non-face, neutral, and positive face conditions than at rest ($P < .05$).

No significant interactions were observed between groups and conditions in the 4-month analysis.

Eight-Month Analysis

Longitudinal 8-month-old groups consisted of 10 full-term infants with mean age of 8.62 ± 0.5 months (3 females and 7 males) and 17 preterm infants with mean age of 8.47 ± 0.27 months ($P = .3$) (6 females and 11 males).

Group Factor. Significant differences between the preterm group and full-term group were found in the frontocentral and bioccipital regions at frequencies from 0.7 to 3.1 Hz, in the right frontopolar, temporal, and the left occipital region at frequencies from 7.0 to 14.0 Hz, and in the left frontal and occipital regions and right temporal region at frequencies from 14.8 to 19.1 Hz ($P < .05$) (Figure 1A).

Group Post Hoc Analysis. The preterm group had higher absolute power than the full-term group in the right frontopolar and left frontal regions at frequencies from 10.1 to 19.1 Hz. Additionally, the preterm group had lower absolute power in the left temporal and bioccipital regions at frequencies from 0.7 to 1.9 Hz and from 8.2 to 19.5 Hz. These results were found during all task conditions, and significant differences were observed at more frequencies for the positive face condition ($P < .05$) (Figure 2A).

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Table 3. Magnetic Resonance Imaging in the Preterm Group.

Subject	Postconception Age[a]	Lateral Ventricle Dilation	Subarachnoid Space Enlargement	Corpus Callosum Hypoplasia	Others
1	54	Both	Frontoparietal		
2	57	Right			
3	56	Both	Frontoparietal	Present	
4	51		General		
5	51	Both		Present	
6	49	Both	General	Present	
7	50	Both	General		
8	57	Both	General		
9	49		General		
10	56	Both			
11	51				Normal
12	52	Both	General		
13	58	Both			
14	51	Both			
15	50		General		Germinal matrix hemorrhage
16	51		General		
17	53	Right			
18	51	Both			
19	53		General		
20	50	Both			
Total	Mean: 52.5	14 (70%)	11 (55%)	3 (15%)	1 (5%)

[a]Postconception age in weeks when magnetic resonance imaging was performed.

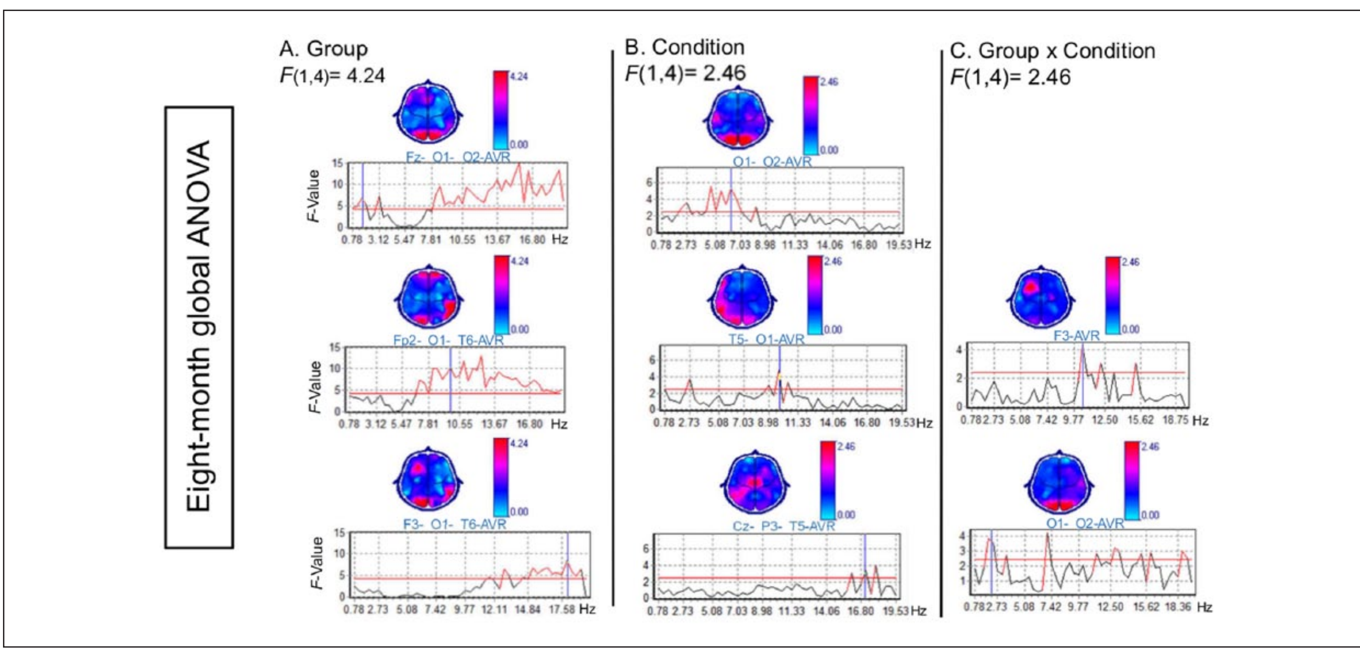

Figure 1. Global analysis of variance (ANOVA) results for analysis of 8-month-olds. *F*-value topographic maps of representative frequencies (top), red represents *F*-values larger than threshold ($P \leq .05$); and frequency graphs of representative derivations (bottom), *X*-axis represents all electroencephalogram narrow-band frequencies, *Y*-axis represents *F*-value, and the red line is the *F*-value threshold. A, B, and C represent the ANOVA group, condition, and interaction factor, respectively. Rows represent low, middle, and high electroencephalogram frequencies. The vertical blue line represents the frequency of the topographic map.

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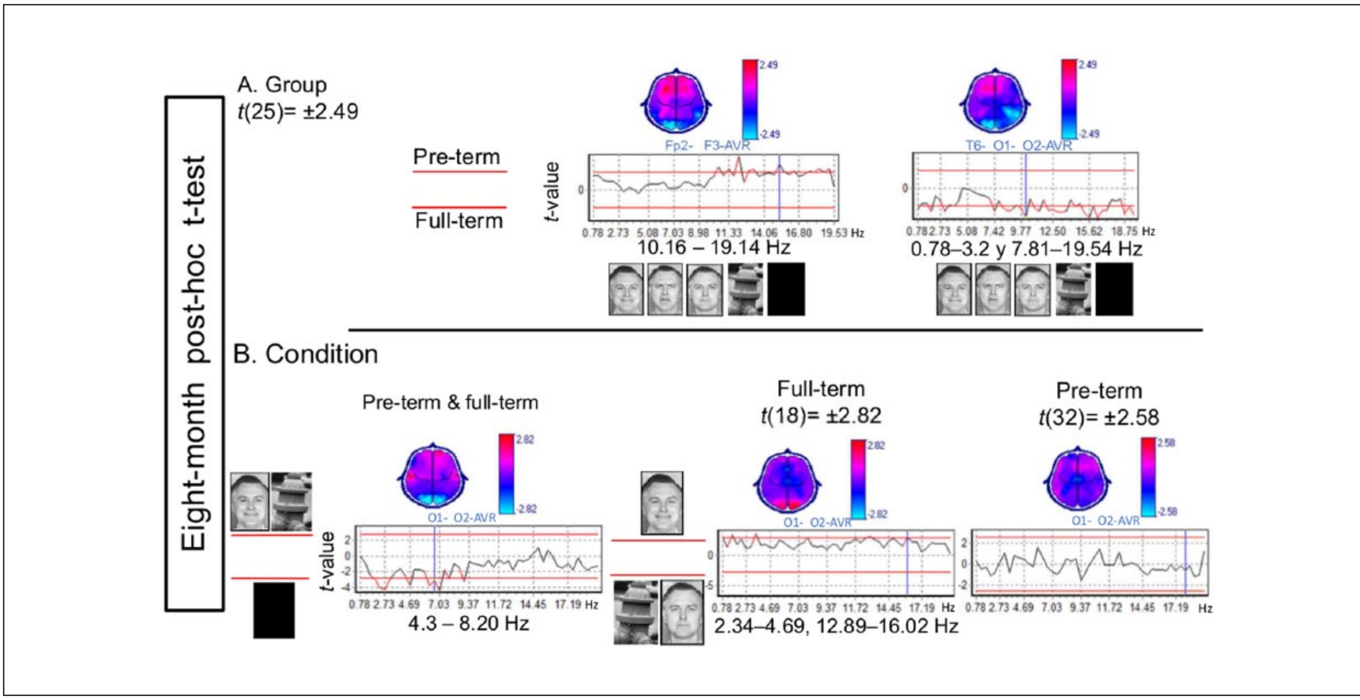

Figure 2. Post hoc *t* test in the analysis of 8-month-olds for group and condition differences. Top: Differences between groups. Positive *t*-values above the red line showed significantly higher electroencephalogram absolute power in the pre-term group, as represented in the topographic map in red. Negative *t*-values below the red line showed lower absolute power in the preterm group, represented in light blue (topographic maps and graphs were taken from positive condition representing similar results in all conditions). Bottom: Differences between conditions. Left, negative *t*-values below the red line show lower absolute power during non-rest than in rest conditions, as represented in light blue. Right, positive *t*-values above the red line show higher absolute power during positive in comparison to neutral and non-face conditions, represented in red (first topographic map and graph was taken from preterm group representing similar results in term group analyzed).

Condition Factor. Significant differences between task conditions were found in the bilateral occipital region at frequencies from 0.7 to 7.0 Hz, in the left frontal temporal and occipital region at frequencies from 8.2 to 11.3, and in the left parieto-temporal and in central regions at frequencies from 13.2 to 18.7 Hz ($P < .05$) (Figure 1B).

Condition Post Hoc Analysis. Both groups had lower absolute power in the bioccipital regions at frequencies from 2.3 to 9.3 Hz during all conditions in comparison to rest.

In contrast to the results at 4 months, significant differences between face stimuli (positive, negative, and neutral) were detected at eight months. The full-term group had higher absolute power in the right occipital region at frequencies from 2.3 to 4.6 Hz while observing positive in comparison with neutral and non-face stimuli ($P < .05$). The preterm group did not show this increase of absolute power (Figure 2B).

Interaction. Preterm infants showed no differences between neutral, negative, and positive face conditions. On the other hand, full-term infants had higher absolute power in the left occipital region at 10.1 Hz and in the right occipital region at 3.5, 12.8, and 16.0 Hz in response to a positive compared with neutral face stimuli ($P < .05$). In addition, the full-term group had higher absolute power in the left occipital region at 1.9 Hz and in the right occipital region at 2.3 and 3.5 Hz when viewing a positive compared with a non-face stimulus ($P < .05$), but the preterm group did not (Figure 3).

Discussion

The aim of the present study was to test the hypothesis that emotional face processing develops differently in full-term than in preterm infants. The main finding of our study was that 8-month-old full-term infants showed an increase of absolute power in the occipital region at 10.1 Hz on the left side and at 3.5, 12.8, and 16.0 Hz on the right side during exposure to a positive face compared with a neutral face. Additionally, absolute power increased in the left occipital region at 1.9 Hz and at 2.3 and 3.5 Hz on the right side when a positive face was compared to a non-face stimulus. In contrast, preterm infants did not show these changes. These results are analyzed below.

Our preterm sample has clinical characteristics that are typical of premature infants: lower birth weight, risk factors for PBI, such as respiratory distress syndrome, neonatal sepsis, and hyperbilirubinemia; worse motor and mental performance, as evidenced by lower MDI score (BSID-II Mental Developmental

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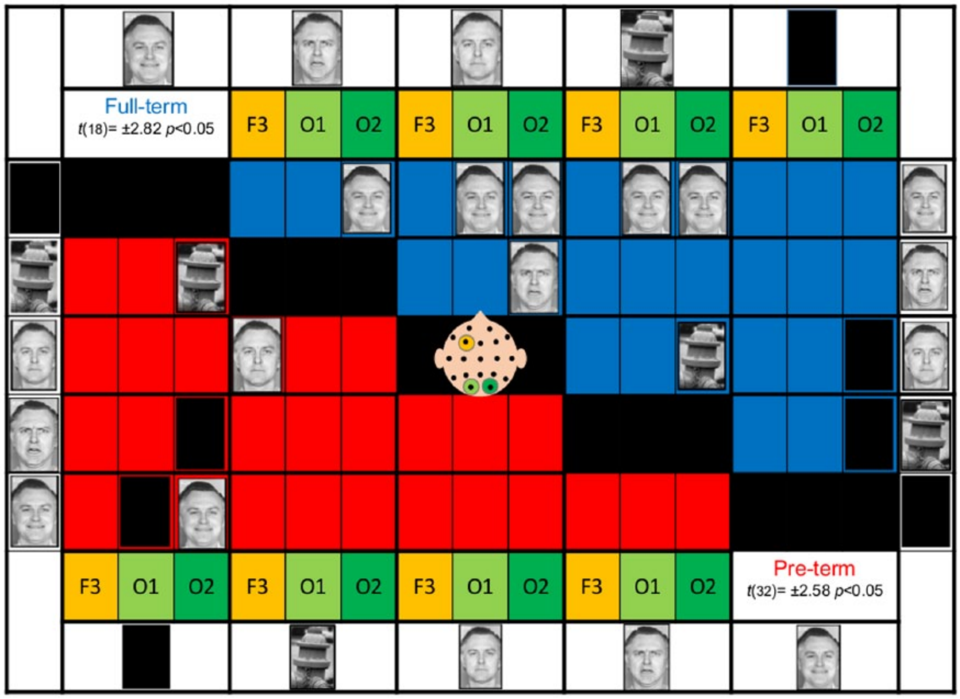

Figure 3. Interaction analysis. All possible comparisons between task conditions (positive, negative, and neutral faces, non-face, and rest) in full-term (blue rows) and preterm infants (red rows). Derivations with 3 or more significant frequencies are shown. The results between the right column and the upper row correspond to full-term comparisons. The results between the left column and the lower row correspond to preterm comparisons. Images in the chart represent significantly higher absolute power during that condition in the corresponding derivation.

Index scale), and abnormal neurological examination.[27,28] Furthermore, most preterm infants had magnetic resonance images with lateral ventricle dilation and subarachnoid space enlargement, findings associated with the white matter injury present in almost 40% of premature infants.[2,29]

The preterm group analyzed at 4 months had higher absolute power at frequencies from 0.7 to 4.3 Hz, while the full-term group had higher absolute power at major frequencies from 6.6 to 7.8 Hz; this difference was observed in the frontal regions, regardless of the condition. This pattern of differences between preterm and term infants has already been reported in other sample comparisons as well as in toddlers with antecedents of periventricular leukomalacia compared with healthy toddlers[9] and even in school-age infants with unspecific learning disabilities compared with healthy peers.[30] It has been observed that the maturation process of brain oscillations during the first year of life as measured by quantitative electroencephalography consisted of increased power in beta and alpha frequencies and a decrease in lower delta and theta frequencies.[31] The differences between preterm and full-term infants support the idea that prematurity alters the brain maturation of electrical oscillations.

At 4 months, differences in absolute power of electrical brain oscillations were only detected between rest versus non-rest conditions in both groups. Compared with the rest condition, the absolute power during most of the picture-viewing conditions was higher in the right occipital region at frequencies from 8.9 to 9.3 Hz in full-term infants and lower in the left temporal region at frequencies from 11.3 to 19.1 Hz in both groups. This result can be attributed to the simple processing of visual stimuli, regardless of their emotional content or valence.[32] Previous behavioral and electrophysiological studies have confirmed that the identification of emotional features in visual stimuli begins between 5 and 7 months old specially with negative emotions as fearful ones.[15-17] Differences between groups were more evident at 8 months. Preterm infants had higher absolute power in frontal regions at high frequencies (10 Hz and higher), while full-term infants had higher absolute power in occipital regions in almost all frequency bands. Given that these differences were evident during an emotional task regardless of the condition, we believe that higher absolute power in the frontal regions of preterm infants could be indicative of attention allocation that fails to improve the processing of emotional faces,[14] while the full-term infant's higher occipital power represents a major allocation of sensorial and perceptual resources to processing emotional faces.[21,33]

Our main result was found in the interaction analysis of 8-month-old infants. Full-term infants had higher absolute power in occipital regions during the positive face condition

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than during the neutral and non-face conditions. Indeed, previous electrophysiological studies using ERPs with healthy infants showed a similar occipital pattern of activation during the processing of visual emotional stimuli at similar ages.[21,22] On the other hand, premature infants with risk factors for PBI had no differences between positive-, negative-, and neutral-face conditions. This result suggests impaired or altered emotional stimulus processing in premature infants. This alteration could be the prelude to the later social and emotional problems reported previously in preterm infants.[34,35] Most of the premature infants in this sample had an initial magnetic resonance imaging with lateral ventricle dilation and white matter injury, a very common characteristic of preterm infants.[2,29] White matter injury may explain an impaired connectivity between cortical regions implicated in emotional face processing, as reported in previous studies.[6-10]

There were some limitations to our study, one of which was the use of scalp EEG for the localization of abnormalities in preterm infants. Future studies should consider larger samples, more precise techniques as electrical source analysis and the effect on brain oscillations of the anatomical differences between preterm and full-term infants.

In conclusion, differences between preterm and full-term infants in the processing of emotional faces are evident at 8 months old, when preterm infants had no absolute power differences between positive, negative, and neutral face conditions, while full-term infants had higher absolute power in the bilateral occipital regions at frequencies between 3 and 16 Hz during the positive face than during the neutral face and non-face conditions. This result suggests that premature birth alters brain development and consequently complex cognitive functions, including emotional face processing.[6-10]

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Author Contributions

Conceived and designed the experiments: CCC-V, ES-R. Performed the experiments: CCC-V ES-R. Analyzed the data: CCC-V, ES-R, TH, GL-Q. Wrote the paper: CCC-V, ES-R, TH, GL-Q.

Declaration of Conflicting Interests

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