Perception of optic flow and random visual motion in preterm and full-term infants: A longitudinal EEG study

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May 2015

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ACKNOWLEDGEMENTS

ABSTRACT

Electroencephalogram (EEG) was used in preterm and full-term infants at 5 and 12 months of age to longitudinally study brain electrical activity as a function of perception of structured forward optic flow, structured reversed optic flow, and non-structured random visual motion. This study aimed to investigate how developments in neuronal maturation and locomotion are related to changes in brain activity. Analyses of visual evoked potentials (VEPs) and temporal spectral evolution (TSE, time-dependent amplitude changes) were performed on EEG data recorded with a 128-channel Geodesic Sensor Net 200 (GSN). In full-term infants, VEP results revealed a significant decrease in latencies for forward and reversed optic flow, but not for random visual motion with age. At 12 months, full-term infants were also found to significantly differentiate between the three motion conditions, with shortest latencies for forward optic flow, and longest latencies for random visual motion. When the TSEs of the three motion conditions were compared to the TSEs of a static non-flow control condition, full-term infants at 5 and 12 months showed significant differences in induced activity. A decrease in amplitudes at 4.6-7.9 Hz was observed as desynchronized theta-band activity at both ages in full-term infants, while an increase in amplitudes at 13-21 Hz was observed as synchronized beta-band activity only at 12 months. Preterm infants showed a different developmental trend to full-term infants, as the VEP results revealed that they did not decrease their latencies with age, nor were able to significantly differentiate between the motion conditions at 12 months. When the TSEs of the motion conditions were compared to the TSEs of the static non-flow condition, preterm infants at 5 and 12 months showed significant differences in induced activity. A decrease in amplitudes at 4.9-7.2 Hz was observed as desynchronized theta-band activity at both ages in preterm infants. Although some preterm infants showed an increase in amplitudes at 13-21 Hz that was observed as synchronized beta-band activity, it was not as prevalent as that observed in their full-term peers. It was concluded that the preterm infants' atypical responses could be related to brain anomalies related to dorsal stream vulnerability, while full-term infants' progression in visual motion perception could reflect increased neuronal maturation and locomotion experience. More follow-up research is required to investigate the long-term effects of dorsal stream impairment.

1. INTRODUCTION

Due to advances in obstetric and neonatal care over the past decades, the survival rate of infants born prematurely has significantly increased (MacKay et al., 2005). In this regard, a extremely preterm infant is understood as an infant born before week 28, or with birth weight less than 1000 grams (Torvik Griffiths et al., 2013). Although severe developmental disabilities are more common in preterm infants born before 26 weeks of gestation, research suggests that even less premature infants without major disabilities exhibit minor impairments related to attentional, cognitive, and behavioural functioning (Aarnoudse-Moens, Weisqlas-Kuperus, van Doudoever & Oosterlaan, 2009; Bhutta, Cleves, Casey, Cradock & Anand, 2002; de Jong, Verhoeven & van Baar, 2012; Johnson, 2007; Marlow, Wolke, Bracewell & Samara, 2005). The impact of these subtle problems becomes even more apparent when considering the high incidence of prematurely born children requiring additional educational resources at school (Bhutta et al., 2002; Torvik Griffiths et al., 2013), and their long-term effects on educational and occupational attainment (Johnson, Hennesy, Smith, Trikic, Wolke & Marlow, 2009; Moster, Lie & Markestad, 2008). Most children with a history of premature birth appear to handle the demands of everyday life quite well but when introduced to tasks of increased complexity a substantial proportion demonstrate reduced functioning (Torvik Griffiths et al., 2013). Up to this date, there are no good predicators of these more subtle problems that can be identified during infancy or preschool age, but due to the recent advancements in science of visual development, there is now reason to believe that vision can provide us with important insights into the typically and atypically developing infant that might eventually lead us in that direction (Braddick & Atkinson, 2011).

Radial optic flow provides us with important cues for where we are heading, and is thus important for perceiving and controlling motion (Gibson, 1979; Vaina & Rushton, 2000). This large-scale structured pattern appears on the retina as a result of self-produced motion or approaching objects, and is detected by the observer as expanding or contracting patterns (Shirai & Imura, 2014). As such, forward motion is characterised by expanding patterns, while reversed or backwards motion is characterised by contracting patterns. When considering the importance of motion perception for effective functioning in the environment and not least survival (Snowden & Freeman, 2004), it makes obviously one of the most primary tasks of the visual system. Consequently, processing of optic flow is an important area of research for developmental studies.

Already as newborns, infants show a preference for moving objects over static objects. However, research (Regal, 1981) suggests that this may rather reflect sensitivity to temporal modulation than to motion as such, since full use of motion information involves sensitivity to speed and direction, which necessitates the involvement of higher-level motion processing (Brosseau-Lachaine, Casanova & Faubert, 2008; Wattam-Bell, 1996). The first stage of motion analysis is therefore believed to consist of basic quantities by directionally selective low-level mechanisms that provide the foundation for global perceptual processes at an older age. This corroborates with the findings of a recent EEG study in infants. Rosander, Nyström, Gredeback and von Hofsten's (2007) findings showed that infants younger than 6-8 weeks did not discriminate motion direction, and did not smoothly pursue small moving objects. However, a significant improvement in discriminating direction and following moving objects was observed in infants between 6-14 weeks of age (ibid.). According to Shirai and Yamaguchi (2010) this observed improvement is indicative of important developmental trends, as perception of single directional motion is found to emerge at around 2 months, while perception of radial motion develops between 3-4 months of age. Surprisingly, radial-flow sensitivity does not change significantly between the ages of 3-4 months and 6-8 months (Brosseau-Lachaine et al., 2008; Gilmore, Baker & Grobman, 2004; Gilmore & Rettke, 2003), but is shown to rapidly develop hand in hand with the development of locomotion skills such as crawling and independent walking, approaching adult levels by 4 years of age at the earliest (Anderson et al., 2001; Campos et al., 2000; Johnson, 2000; Kaufmann, 1995). Although there has been common agreement that sensitivity to optic flow develops as a result of experience with real-flow experience through self-produced motion (Anderson et al., 2001; Campos et al., 2000; Johnson, 2000), a recent study suggests that it is rather the developmental change in optic flow perception that allows further development of locomotion. In a combined cross-sectional and longitudinal study in infants, Shirai and Imura (2014) found preference for expanding patterns over contracting patterns just before the onset of self-produced locomotion. Since locomotion is typically experienced through forward motion and not reversed this may suggest that changes in optic flow perception trigger normative locomotion abilities. This finding also highlights early appearance of the dominant asymmetric response to forward optic flow that also has been found in adults (Gilmore, Hou, Pettet & Norcia, 2007), that supports the notion of ecologically shaping of human perception. Additionally, as the ecological approach holds that the environment appears to us as structured entities (Gibson, 1979) greater sensitivities have also been reported for structured optic flow than for unstructured random visual motion (van der Meer, Fallet & van der Weel,

2008).

Moreover, as the visual system is crucial for perceiving motion, several physiological studies have sought to map the cortical areas that are involved in processing visuo-spatial information. Evidence points to the involvement of the dorsal or parietal visual stream where neurons from the primary visual cortex lead to the medial temporal (MT) and area V5 of the occipito-temporal cortex, and medial superior temporal dorsal (MSTd), which collectively has been referred to as V5/MT+ (Graziano, Andersen & Snowden, 1994; Newsome & Paré, 1988; Probst, Plendl, Paulus, Wist & Scherg, 1993; Smith, Wall, Williams & Singh, 2006). Studies using positron emission tomography (PET) (Lagae, Maes, Raiguel, Xiao & Orban, 1994) and functional magnetic resonance imaging (fMRI) (Smith et al., 2006) suggest that MST cells are more selective to radial motion than MT cells. However, transcranial magnetic stimulation (TMS) studies have pointed towards the involvement of area MT/V5 in motion perception where perception was impaired when applied over area MT/V5 at 130-150 ms post-stimulus (Sack, Kohler, Linden, Goebel & Muckli, 2006). The dorsal stream is one of two visual pathways, and while the dorsal stream is involved in recognition of motion or visual-spatial information, the ventral or temporal stream is suggested to be involved in recognition of objects or colours (Milner & Goodale, 2008). These streams work in a separate, yet interactional way with several cross talks between the streams (Blatt, Andersen & Stone, 2990; Johnson, Mareschal & Csibra, 2001; Maunsell & van Essen, 1983) and project both to the frontal lobe (Goodale, 1993). Deficits of radial motion perception have been found in developmental disorders related to perinatal brain anomalies following premature birth. The division between the dorsal and ventral stream has therefore proved an increasingly important area of research with respect to the effects of prematurity, leading to the proposal of general 'dorsal stream vulnerability' (Braddick & Atkinson, 2011; Grinter, Maybery & Badcock, 2010).

Neuroimaging studies (Counsell & Broadman, 2005; Hüppi et al., 1998; Inder, Warfield, Wang, Hüppi & Volpe, 2005; Nagy et al., 2003) have revealed a number of brain abnormalities in the brains of infants born preterm, even in the absence of major cerebral lesions that are otherwise undetectable by ultrasonography. Accordingly, diffusion tensor imaging (DTI) has shown that white matter fibers in areas of the brain through which the dorsal stream flows are shorter, thinner, and less organized in preterm than full-term control infants at 40 weeks gestational age (Hüppi et al., 1998). At 11 years of age, DTI has suggested that the white matter in these brain areas in preterm children are characterised by reduced thickness, fewer axons and/or poorer myelination compared to that of the full-term control

children (Nagy et al., 2003). Furthermore, a number of studies has suggested that (very) premature birth affects more significantly the dorsal stream or the magnocellular (M) pathway than the ventral stream or the parvocellular (P) pathway in children (Guzetta et al., 2009; Hammarrenger et al., 2007; Tremblay et al., 2014; Weinstein et al., 2011). In a behavioural study, Guzetta and colleagues (2009) investigated perception of global motion (optic flow) and form (shapes, outlines) in school-aged preterm born children. They found that preterms with and without brain lesions performed worse than their full-term peers when introduced to global motion perception, however when form information was embedded in the stimulus, preterm children with brain lesions performed significantly worse than preterm children without brain lesions. As a result, they concluded that while ventral stream impairments were more related to the presence of periventricular brain injury, dorsal stream impairments were more related to prematurity per se, that is irrespective of brain damage. Disorders of attention are one of the major implications of (very) premature birth, and considering the close relation between dorsal stream visual processing and attentional systems, there is reason to believe that more research within this area can provide an early functional window to improve the prospects of children born prematurely (Braddick & Atkinson, 2011; Mulder, Pitchford, Hagger & Marlow, 2009; van de Weijer-Bergsma, Wijnroks & Jongmans, 2008).

Electroencephalogram (EEG) recordings offer a complimentary technique in the study of the cortical areas involved in motion perception on a millisecond scale (Probst, Plendl, Paulus, Wist & Scherg, 1993). In EEG, visual motion stimuli result in the generation of visual evoked potentials (VEPs) that can be detected by averaging techniques. VEPs are dominated by a negative peak component (N2), which occurs around 270-350 ms post-stimulus in 12 month-old full-term infants (Agyei, Holth, van der Weel & van der Meer, 2015), and around 140-200 ms post-stimulus in adults (van der Meer, Fallet & van der Weel, 2008). The N2 peak is suggested to be originating from the area V5/MT+ which corresponds to occipital and parietal areas that lie in the posterior part of the brain (Probst et al., 1993). The latency and the amplitude associated with N2 peak gives us an indication of the time and effort involved in processing the motion stimuli, and arises as a result of post-synaptic response from main cortical pyramidal neurons to changes in afferent activities (Pfurtscheller & Lopes da Silva, 1999). Previous studies (van der Meer et al., 2008) have reported that the N2 peak is longer in latency and larger in amplitude in infants compared to adults, which indicates that adults show greater sensitivity and specialization in processing motion. Latency is known to be a highly sensitive measure that is both stimulus- and age-dependent, and latency delays inappropriate for either stimulus or age are suggested to reflect visual pathway abnormalities (Apkarian,

1996). Accordingly, VEPs offer a useful tool in studying dorsal stream vulnerability. However, it should be noted that ERP only represents a certain aspect of the event-related EEG-signal (Bastiaansen, Mazaheri & Jensen, 2012). Visual events can also result in frequency specific changes in the ongoing EEG that are time-locked but not phase-locked to the events (Pfurtscheller & Lopes da Silva, 1999). These frequency changes are observed as event-related desynchronisation (ERD) or event-related synchronization (ERS) oscillations and may suggest either an increase or a decrease in amplitude or power of given frequency bands, an indication of an increase or a decrease in synchrony of underlying neuronal populations (Hoechstetter, Bornfleth, Weckesser, Ille, Berg & Scherg, 2004). It has been suggested that while VEPs represent responses of cortical neurons to changes in afferent activity (van der Meer et al., 2008) event-related time-frequency responses represent local cortical neuronal interactions that control the frequency components of an ongoing EEG (Pfurtscheller & Lopes da Silva, 1999).

EEG studies in the time-frequency domain have only recently been given attention, and although several studies (Carmeli, Knyazeva, Innocenti & De Feo, 2005; Hoogenboom, Schoffelen, Ostenveld, Parkes & Fries, 2006; Krishnan, Skosnik, Vohs, Busey & O'Donell, 2005; Pfurtscheller & Lopes da Silva, 1999) have found evidence for the modulation of the natural frequencies by motion stimuli in adults, little evidence for such activity is known in infants. In adults, motion-induced power increases in gamma band (30-80 Hz) activity (Hoogenboom et al., 2006) and beta band (12-30 Hz) activity (Carmeli et al., 2005) have been observed over occipital electrodes. In infants, low frequency rhythms have been reported, which have been interpreted as signs of immaturity (Orekhova, Stroganova, Posikera & Elam, 1999; Thierry, 2004). Factors such as efficient task performance and increased task complexity are suggested to contribute to enhancement in low-amplitude theta (4-8 Hz) and alpha (8-12 Hz) activities in infants, which have been found to undergo systematic development from early childhood to adulthood (Stroganova, Orekhova & Posikera, 1999). Furthermore, van der Meer and colleagues (2008) observed low-amplitude values in the theta-band activities over visual areas in 8-month-old full-term infants when motion stimuli were compared with a static dot pattern, an observation that indicated desynchronized theta-band activity in processing motion in infants, particularly since synchronization was shown when infants were presented with static stimuli. Similar findings have also been reported in a recent study (Agyei et al., 2015) in full-term infants at 3-4 and 11-12 months of age. However, in addition an increase in amplitudes at 9-13 Hz was reported, which was shown as synchronized alpha-band activity when the TSE results of motion conditions were compared to those of a

static dot pattern, but only at 11-12 months. This transition of EEG spectral amplitudes from lower to higher frequencies during development is attributed as a sign of maturation (Hudspeth & Pribram, 1992).

The aim of the present longitudinal study was to study brain electrical activity during the first year of life with a focus on the effects of prematurity. Preterm and full-term infants at 5 and 12 months of age were presented to structured forward optic flow, structured reversed optic flow and non-structured random visual motion by employing a combination of VEP and time-frequency analyses using high-density EEG. It was hypothesised that perception of optic flow would rapidly improve in infants due to increased neuronal maturation and increased locomotion experience with no marked difference in perception of random visual motion, and that an induced amplitude decrease in low frequencies would be observed. Differences between preterm and full-term infants in evoked and induced activities were also explored to investigate whether atypical responses could be indicative of dorsal stream impairment.

2. METHODS

2.1 Participants

Ten normally developing preterm infants (seven boys) and ten normally developing full-term infants (four boys) were recruited for the study. The preterm infants were recruited with help from the pediatrician in charge at the Neonatal Intensive Care Unit at St Olav's University Hospital (Trondheim, Norway). The preterm infants were born at ≤ 33 weeks of gestation with an average birth weight of 1622 grams (SD = 453) with a range of 1000-2670 grams. The neurological status of the infants was not known to the experimenter. The full-term infants were recruited by contacting parents through birth announcements in the local newspaper, or by parents' own interest and request for their baby's involvement in the study. The full-term infants were born at term with an average birth weight of 3642 grams (SD = 608) with a range of 3085-5120 grams.

Preterm and full-term infants were matched according to their age in full months. To attain a valid matching, age corrected for prematurity was calculated for the preterm infants. One of the preterm infants was very restless during the second testing and this prevented the experimenters from collecting any data on this infant. Consequently, this infant and his matched full-term control were excluded from the longitudinal analysis. As such, longitudinal analyses were carried out on nine preterm and nine full-term infants only.

Testing followed a longitudinal design. First, infants were tested at 5 months followed by a second testing when the infants were 12 months of age. For the first session, the mean (corrected) age of the preterm infants was 4 months and 24 days (SD = 11 days), and the mean age of the full-term infants was 4 months and 29 days (SD=29 days). Most of the infants could roll over from back to stomach at this time, but none of the infants had any crawling experience. For the second session, the mean (corrected) age of the preterm infants was 11 months and 20 days (SD = 11 days), and the mean age of the full-term infants was 11 months and 20 days (SD = 16 days). Full-term infants had a history of crawling acquisition at around 9 months. One of them was able to walk independently at the time of the second testing, three of them had taken some independent steps, whereas the others with the exception of two were able to cruise with support. Motor development of the preterm infants was similar to that of the full-term infants except for three of the preterm infants, who had not started crawling yet and were bottom shuffling instead.

Electroencephalogram (EEG) recording as a psychological procedure is known to cause no harmful effects to the participant. The parents gave their informed consent prior to

the testing, and understood that they were free to withdraw from the study at any given time. Ethical permission for the experimental procedure was provided by the Norwegian Regional Ethics Committee and the Norwegian Data Services for the Social Sciences.

2.2 Experimental stimuli and paradigm

To simulate movement in space, the stimuli was programmed in E-prime (a psychological software tool) and mirror-reversed projected onto a wide white screen (108 cm × 70.5 cm) by means of an ASK M2-projector. The width and the height of the display subtended a visual angle of 68° and 47°, which was placed at a distance of 80 cm from the infants. In order to discriminate between structured and non-structured radial motion, three motion stimuli were employed: forwards optic flow, reversed optic flow and random visual motion. The forwards optic flow condition simulated movements towards the infant, whereas the reversed optic flow simulated movement away from the infant. The random motion condition presented a display of randomly moving dots. The duration of presentation for each motion stimulus was 1500 ms, and the order was randomly chosen. To suppress the effect of motion adaptation, each motion condition was followed by a control condition, a static dot pattern lasting for 1500 ms (Müller, Göpfert & Hartwig, 1986). However, this static dot pattern was not subject to further analysis. Stimulus consisted of 100 randomly placed dot particles, 5 mm in virtual radius, on a white background. Dot size increased gradually about 0.025 pixels per pixel as a function of their distance to the centre of the screen, where a red fixation point the size of one pixel was located to direct attention to the screen. Stimulus contrast was around 99.5% with mean luminance of 68 cd/m².

In the three motion conditions the dots appeared to move toward the infant with constant velocity (30 mm per frame), with image resolution of 593 pixels per meter at a refresh rate of 60 Hz. For forward optic flow the movement was parallel to the z-axis towards the eye with a constant negative velocity in the z-direction, while velocities in the x- and y-axis were zero (see Figure 1). The reversed optic flow condition was analogous to forwards optic flow, and the only difference between the conditions was that the dots moved in the opposite direction. Moreover, in the reversed optic flow condition the dots moved parallel to the z-axis towards the eye with a constant positive velocity, while velocities in the x – and y-axis were zero. In the random motion condition, the dots moved with a constant velocity, but were different to the two other motion conditions in that the direction was completely random in space. In the static non-flow condition the dots were the same as in the three other
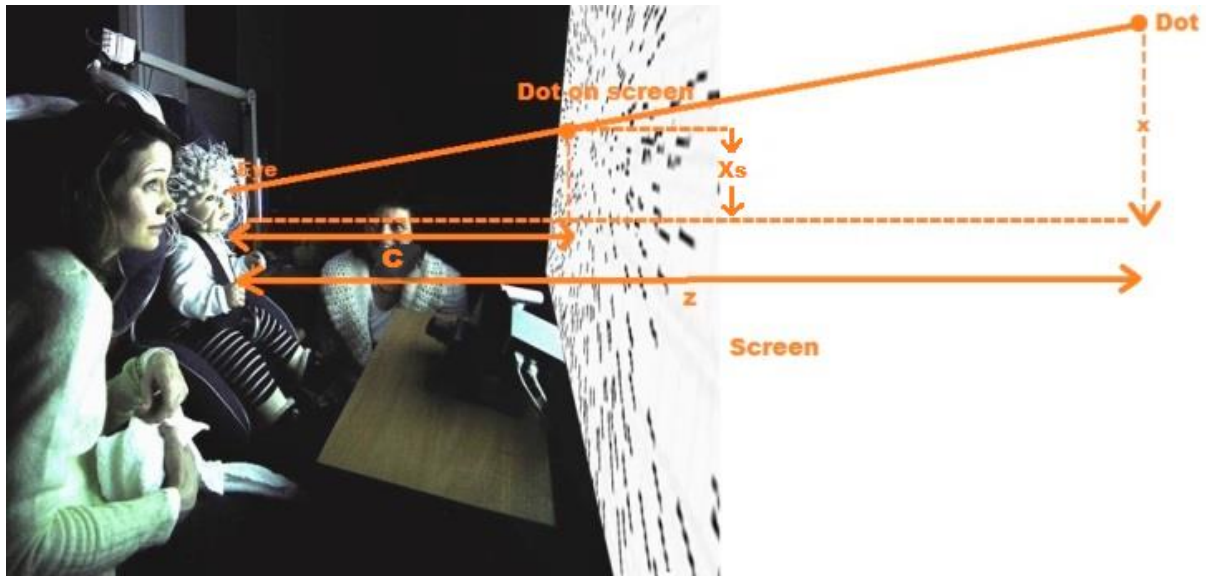
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Figure 1. *Illustration of the projection from a three-dimensional virtual space on to a two-dimensional screen, where 'x' and 'z' are position variables, 'Xs' is the position in the x-direction, and 'c' is the constant distance (80 cm) of the infant's eye to the screen.*

conditions, but the dots remained in the same position for the whole duration of the trial with zero velocity in all directions. Assuming a virtual space pyramid is created from the eye to the four corners of a rectangular screen where the probability of placement for each particle at any point in virtual space was made the same for all points in the pyramid, then dot particles that moved outside the pyramid and the range of sight on the rectangular screen had an equal probability of placement when they were automatically repositioned on the screen.

2.3 Data acquisition

A Geodesic Sensor Net (GSN) 200 (Tucker, 1993) provided the means of recording the EEG activity. This consisted of an array of 128 sensors that were evenly distributed on the infant's head. A high-input EGI amplifier connected to the GSN 200 ensured amplification of signals at impedance set to a maximum of 50 kΩ as recommended for an optimal signal-to-noise ratio (Budai, Contento, Locatelli, & Comi, 1995; Ferree, Luu, Russell, & Tucker, 2001; Picton et al., 2000). Net Station software on a Macintosh computer recorded the amplified EEG signals at 500 Hz.

Furthermore, the infant's gaze was tracked using an infrared Tobii X50 camera. The visual feed was processed with Clear View software on an HP computer. To track off-line the behaviour of the infant during the experiments, digital videos were recorded with two cameras

positioned at different angles in front of the infants. Recorded data were thereafter stored for off-line analyses.

2.4 Procedure

The parents arrived with their infant several minutes prior to the experiment. The necessary information for signing the consent form was then made available to the parents, while the infant was allowed some time to get familiar with the laboratory environment. In the process, an assistant measured the infant's head circumference to allow for the correct size of the GSN 200. After immersing the appropriate electrode net in a saline electrolyte solution to optimize electrical conductivity, it was partially dried and mounted on the head of the infant. The infant sat on the parent's lap and was distracted with toys while the electrode net was mounted on the scalp. Immediately after mounting the net, the infant was moved into a sound attenuated, dimly lit experimental room along with a parent and an assistant. The room was separated with a transparent glass partition from a control room where an assistant managed the computers necessary for the data acquisition. The infant was placed in a baby seat facing the screen (see Figure 1). The net was connected to the amplifier and the impedance of the electrodes was checked. If necessary, contact of electrodes was improved by adding saline electrolyte to the electrodes or simply adjusting their positions. For the entire duration of the experiment, a parent was present in the experimental room to reduce any stressful effect an absent parent may have, while the presence of an assistant was required to monitor the experiment and help the infant focus on the screen.

An experimental session began immediately after calibrating the infant's eye movement in virtual space to the Tobii X50 camera. In a random sequential order, generated stimuli were presented on the screen for a varying number of trials, typically 60-100 trials per infant. Data acquisition was carried out in one block. However, the presentation was paused if the infant showed signs of boredom or disinterests at which time the assistant and/or the parent played for a short period of time with the infant to revive the level of interest. A considerable level of distress, tiredness or fussiness on the part of the infant signaled the end of the experiment. The optic flow experiment, which took about 4-6 minutes on average, was usually the first of three of visual motion experiments that were performed by each infant during an experimental session.

2.5 Data Analyses

EEG raw data were analyzed with Brain Electrical Source Analysis (BESA) research software version 5.3. As an initial pre-processing step, recordings were segmented with the Net Station software and exported as raw files. Appropriate auxiliary files that contained trigger and sensor information were then imported and attached. Epochs around the triggers of stimuli were set such that the averaging epoch was at -200 ms to 800 ms at a baseline definition of -100 ms to 0 ms. Notch filter was set at 50 Hz to remove 50 Hz lines interference from the recorded data. Low cut-off filter was set at 1.6 Hz to remove slow drift in the data while a high cut-off was set at 60 Hz. Band pass was disabled for averaging. By visual inspection, artefact-contaminated channels and epochs resulting from head or body movements were excluded from further analyses or interpolated where necessary. In scanning for artefacts, threshold values for gradient and low signal were set at 75 µV and 0.1 µV, respectively, while maximum amplitude was at 220 µV. As EEG signals are usually contaminated by physiological artefacts such as blinking and eye movements (Lindsen & Bhattacharya, 2010; Pham, Croft, Cadusch, & Barry, 2011; Shao, ShenOng, Wilder-Smith & Li, 2009), a manual form of artefact correction (Berg & Scherg, 1994; Ille, Berg, & Scherg, 2002) designed to separate brain activity from artefacts using spatial filters was further employed.

For the VEP peak analysis, data on each participant were averaged over whole EEG files and interpolated to 81 standard electrodes after re-referencing to an artificial reference calculated from the average potentials over the scalp such that individual averages were obtained. The individual averages for the participants were then combined into grand averages. The N2 components of the VEP waveforms were identified and values for peak latencies and peak amplitudes of the individual averages were recorded and subjected to further VEP analyses. Peak latency was measured as the time from stimulus onset to the peak of each scalp N2 component with peak amplitude recorded relative to the pre-stimulus baseline.

2.6 Time-frequency analyses in brain space

Time-frequency analyses were performed in brain space using multiple source dipoles that modeled the main brain region of interest, the visual cortex. The source models were used to calculate source montages and source waveforms of the single trials, which were then

transformed into time-frequency domains. The regional sources which were applied are believed to be involved in the visual processing of motion stimuli (van der Meer et al., 2008; Probst et al., 1993; van der Weel & van der Meer, 2009) and were the visual cortex lateral left (VClL), visual cortex lateral right (VClR) and the parietal midline (PM). In analyzing these sources, a 4-shell ellipsoidal head model (Berg & Scherg, 1994; Hoechstetter et al., 2004) was created for each infant and the source dipoles (Figure 2) were inserted in the head models while the artefact corrected coordinate files were attached. In line with recent recommendations (Grieve, Emerson, Fifer, Isler & Stark, 2003), bone thickness was adjusted for infants at 3.0 mm and conductivity at 0.02 σ.
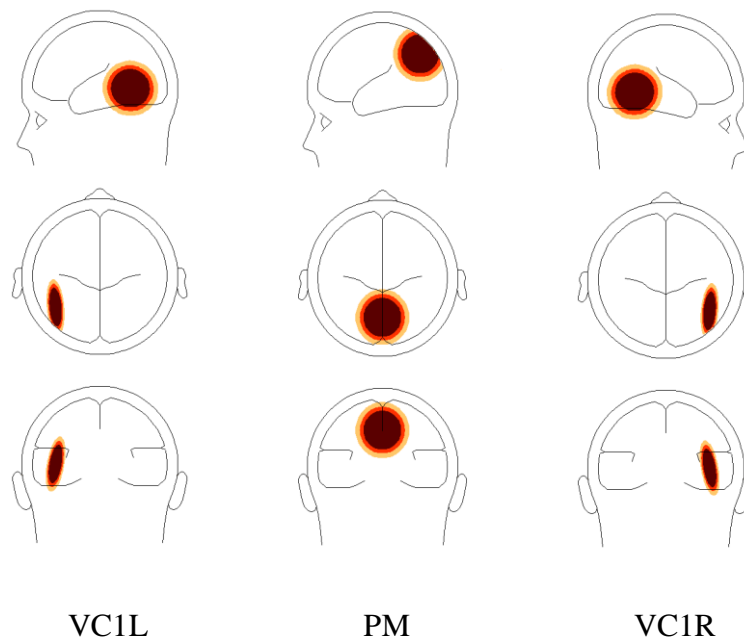

| VC1L | PM | VC1R |

Figure 2. *Head models of associated brain regions in visual cortical areas VC1L and VC1R, and visual parietal area PM. The approximate Talairach coordinates for the sources are x = - 45.2, y = - 57.2, z = 6.5 for VC1L; x = 45.2, y = - 57.2, z = 6.5 for VC1R and; x = 0.0, y = - 72.3, z =37 for PM.*

Time-frequency displays, which represented the change in amplitude over time (TSE, temporal spectral evolution), were generated from the single trials by averaging spectral density amplitudes over trials such that each displayed graph plotted the spectral amplitude density of one montage channel over time and frequency which were normalized to the baseline for each frequency in displaying ERD/ERS plots (Hoechstetter et al., 2004; Pfurtscheller, Neuper & Mohl, 1994; Pfurtscheller, Stancak & Neuper, 1996). To focus on

only induced oscillatory brain activity, average evoked response signals were removed from the single trial time series before computing a TSE. TSE displays were limited between frequency cut-offs of 4 Hz and 30 Hz, while frequency and time sampling were set at 1 Hz, 50 ms, respectively. All other traces of regional sources were also searched and analysed. A comparison between the three motion conditions of forwards optic flow, reversed optic flow and random visual motion and the static non-flow control condition was computed for each participant. Bootstrapping was used to generate a two-sided permutation test, which displayed the probability of significance in amplitude values and frequency ranges between the motion conditions and the static non-flow condition at the significance level p<0.05.

Paired samples t-tests were conducted in BESA Statistics 1.0 (BESA, GmbH), to test for significant differences between conditions in the time-frequency domain. In this analysis the TSE data from all participants were averaged and analysed together. BESA statistics uses a combination of permutation testing and data clustering (Bullmore et al., 1999; Maris & Oostenveld, 2007; Ernst, 2004) to avoid the multiple comparisons problem. There were 256 permutations for each t-test (forwards optic flow – static, reversed optic flow - static and random motion – static). Frequency ranges and epochs were the same as in the time-frequency analysis.

3. RESULTS

The respective mean numbers of accepted trials for preterm infants for forward optic flow, reversed optic flow, random motion and the static control conditions at 5 months were 19 (SD = 6), 19 (SD = 5), 20 (SD = 4), and 56 (SD =20), and at 12 months 17 (SD=5), 19 (SD = 5), 18 (SD = 6) and 56 (SD=14). In full-term infants the respective mean trials for forward optic flow, reversed optic flow, random motion and the static non-flow at 5 months were 24.4 (SD = 4.3), 19 (SD = 4.7), 19.7 (SD = 4.7), and 56.6 (SD = 13.8), and at 12 months 19.2 (SD=4.1), 15.7 (SD = 4.4), 15.4 (SD = 4.2) and 48.7 (SD=11.1).

3.1 VEP responses

Four posterior electrodes for each of the participant groups and ages were selected for further analysis (see Figure 3). The electrodes POz, PO4, PO8, and O2 were selected for the preterm infants at 5 months of age, while PO10, O10, Oz, and Iz were selected for the same group at 12 months of age. Moreover, the electrodes POz, PO4, Oz and O2 were selected for the full-term infants at 5 months of age, while POz, PO4, PO8 and O2 were selected for the same group at 12 months of age. These electrodes were selected as they showed the highest mean activation values in the forward optic flow condition of the grand average VEPs, and is thus equivalent with the method used in previous studies (Agyei et al., 2014; van der Meer et al., 2008).

Latencies and amplitudes of the VEPs were analysed separately using repeated measures ANOVAs in a 2 (group) X 2 (age) X 3 (motion condition) factor design. Within-subject factors were motion condition (forward optic flow, reversed optic flow and random visual motion) and age (5 and 12 months), while between subject factor was participant group (preterm and full-term). Adjustment for multiple comparisons was made by Bonferroni correction. The electrode showing largest N2 amplitude in the forward optic flow condition was used in the ANOVA. The electrode used varied across participants, but was always one of the four posterior electrodes shown in Figure 3, and was the same for the three motion conditions in each infant for each session. Grand average VEPs are presented in Figure 4 and show one typical electrode for each of the participant groups and ages. Similar grand average VEPs were observed across the other selected electrodes.
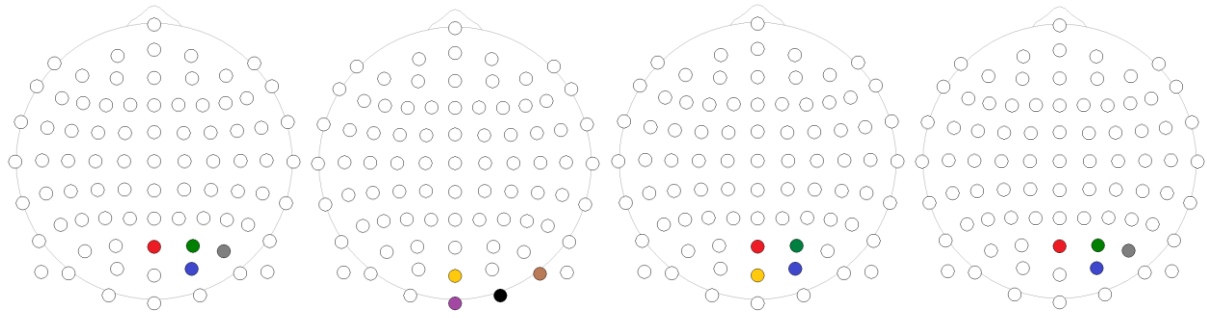
Figure 3. *Head drawings (nose up) show the scalp localization of the 81 standard electrodes. From left to right: preterm infants 5 months, preterm infants 12 months, full-term infants 5 months, and full-term infants 12 months. The four electrodes of interest are indicated with colour-filled circles: POz (**red**), PO4 (**green**), PO8 (**grey**), O2 (**blue**), PO10 (**brown**) O10 (**black**), Oz (**yellow**) and Iz (**purple**).*

For latency, a significant three-way interaction of condition, age and group $F(2,32) =$ 5.56, $p < 0.01$ was found, indicating that latency differences between the motion conditions were found only in full-term infants at 12 months of age. The results revealed that full-term infants showed shorter latencies for forward optic flow than for reversed optic flow, and shorter latencies for reversed optic flow than random visual motion at 12 months (see Figure 5). The preterm infants, on the other hand, did not differentiate between the three visual motion conditions, neither at 5 nor at 12 months. In addition, the ANOVA revealed a significant two-way interaction of age and group, $F(2, 32) = 23.66$, $p < 0.001$, indicating that at 5 months of age, the preterm infants had significantly shorter N2 latencies than the full-term infants irrespective of visual motion condition, but at 12 months, the full-term infants had significantly shorter N2 latencies than the preterm infants. Finally, the two-way interaction of age and group indicated that only the full-term infants significantly reduced their N2 latencies with age, particularly for the two optic flow conditions.
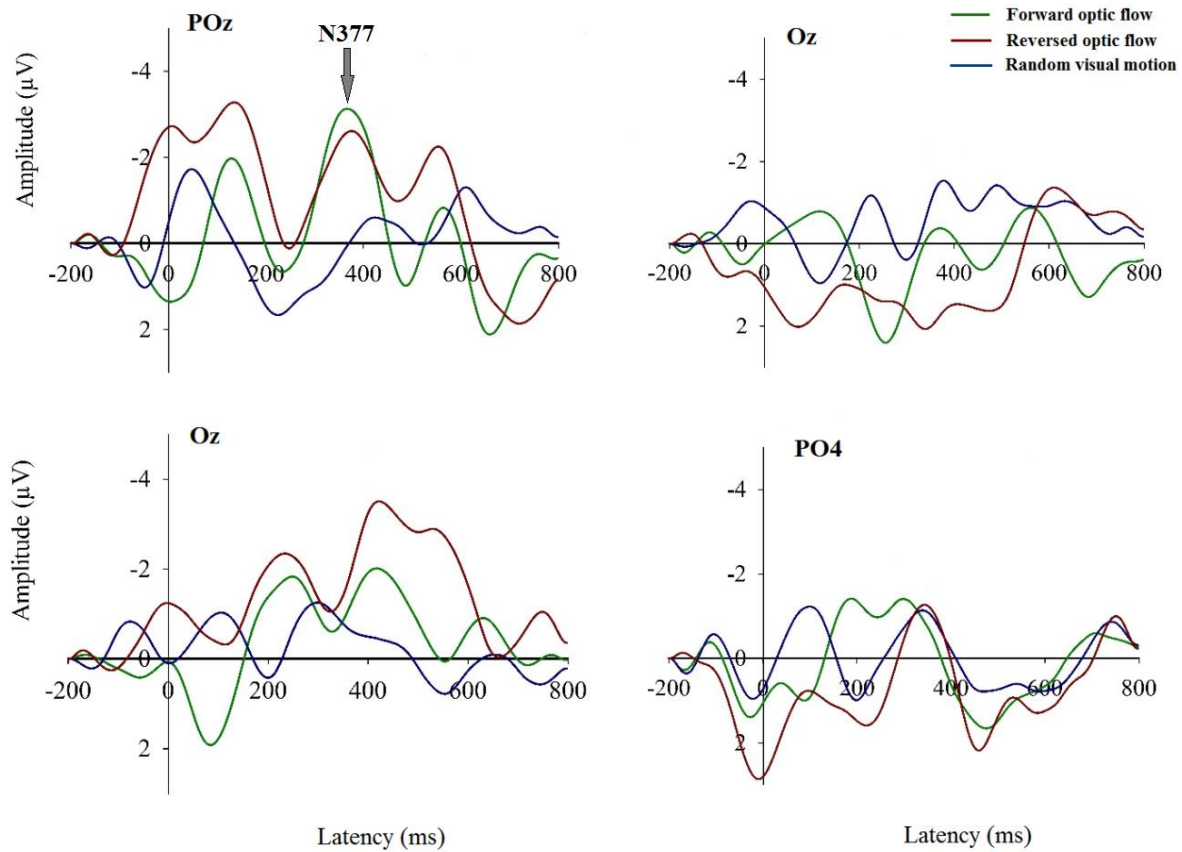
Figure 4. *Grand average motion VEPs of one typical electrode in preterm infants at 5 months at the top left, preterm infants at 12 months at the top right, full-term infants at 5 months at the bottom left, and full-term infants at 12 months at the bottom right for forward optic flow (green), reversed optic flow (red), and random motion (blue). The N2 peak for forward optic flow is marked with actual latency at the POz electrode for preterm infants at 5 months. The epoch is from -200 ms to 800 ms.*

Mean N2 peak amplitudes in preterm infants at 5 months of age were calculated to be 5.7 µV (SD = 5.2) in forward optic flow, 3.7µV (SD = 2.8) in reversed optic flow, and 3.65 µV (SD = 3.4) in random visual motion while the amplitudes in the same group at 12 months of age were 3.7 µV (SD = 2.4), 0.9 µV (SD=2.6), and 0.1 µV (SD=1.4), respectively. For full-term infants at 5 months of age mean N2 peak amplitudes were calculated to be 3.78 µV (SD = 2.7) in forward optic flow, 4.7 µV (SD = 1.9) in reversed optic flow, and 1.4 µV (SD = 2.7) in random visual motion while those in the same group at 12 months of age were 5.4 µV (SD = 2.6), 1.9 µV (SD = 3.8), and 1.2 µV (SD = 2.2). No significant main effects for motion condition or age or group were found, nor were there any significant interactions, demonstrating that peak amplitudes in preterm and full-term infants at 5 months were about the same as at 12 months.
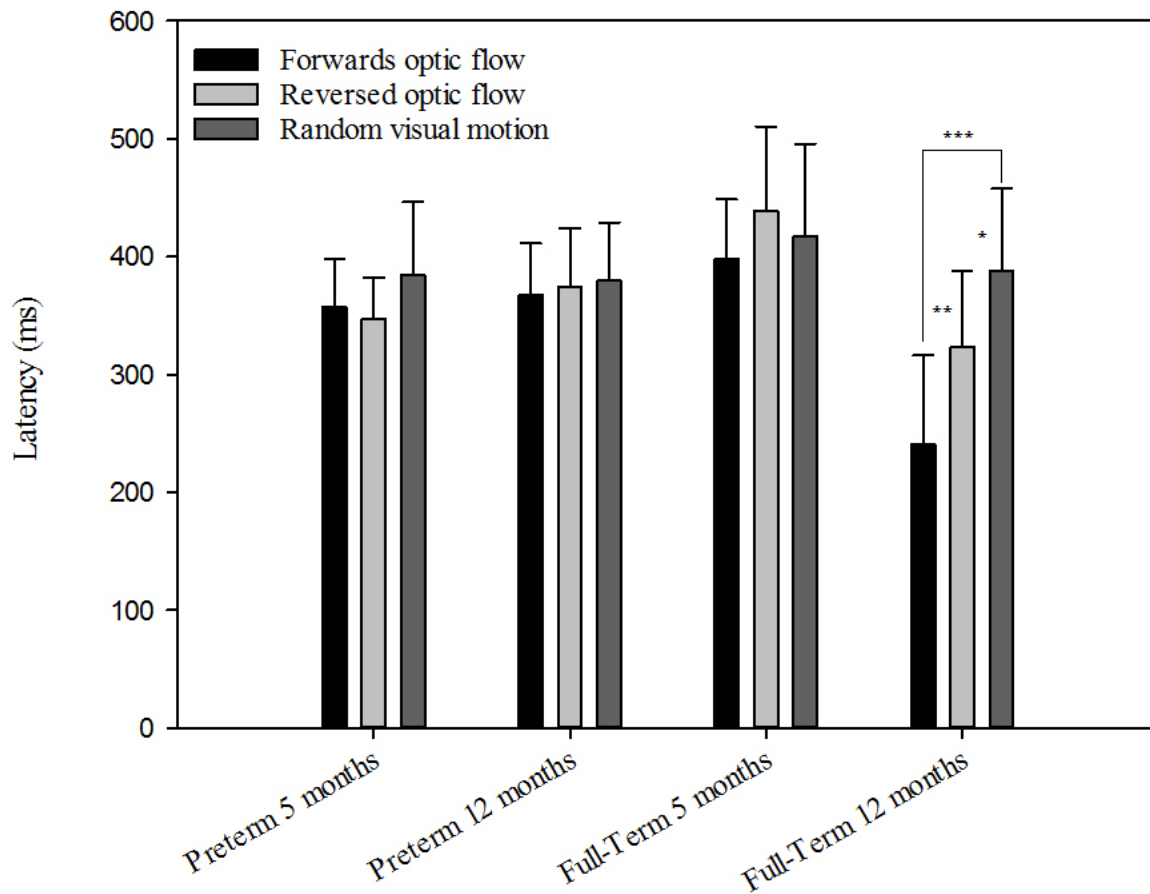
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Figure 5. *Group mean peak latencies (and SDs) of the motion conditions for the preterm and full-term infants at 5 and 12 months of age. * Significant at p < .05. ** Significant at p < .01. *** Significant at p < .05*

3.1.1 Individual analysis of VEPs

The latency data from the preterm and full-term infants at 12 months were further explored to investigate whether some preterm infants showed remarkably long latencies in their responses to optic flow and thus struggling to perceive visual motion efficiently. An outlier can be formulated a value larger or smaller than mean ± SD*2 (Field, 2005; Miller, 1991). Due to the fact that preterm infants at 5 months of age were found to have significantly shorter latencies than full-term infants, only criterion values for the 12-month-old full-term infants' latencies were computed based on the mean and standard deviation values for the three visual motion conditions, and the 12-month-old preterm infants who showed latencies above these criterion values were marked (see Table 1). The application of the criterion pointed to three preterm infants, namely ES, MS and WI, who at 12 months of age showed

remarkably long latencies for forward optic flow. However, none of these three preterm infants showed delayed motor development or were bottom shufflers at the time of the second testing session.

Full-term	Forward	Reversed	Random	Preterm	Forward	Reversed	Random
AS	366	366	466	AL	356	424	362
BI	146	198	322	DD	352	362	356
CA	308	344	414	DI	270	412	348
GR	194	304	268	ES	416	442	476
JE	264	358	396	FI	376	418	368
MA	210	266	320	MS	398	316	402
SI	284	348	434	SO	388	340	314
SU	140	304	416	TA	406	336	356
VI	258	422	460	WI	344	318	434
Mean	241	323	388				
SD	75	65	69				
Mean +SD*2	391	453	526				

Table 1. *VEP latencies (ms) for the three visual motion conditions for 12-month-old full-term and preterm infants. The yellow markings indicate the preterm infants who showed latency values greater than mean + SD*2 of the VEP latency values of the full-term group. Preterm infants ES, MS and TA stood out with their remarkably long latencies for forward optic flow.*

3.2 Time-frequency analyses

The permutation test for the average of all infants in each testing session and each participant group when comparing the TSEs of forward optic flow with the TSE of the static non-flow condition are presented in Figure 6. The permutation test for the average of all infants revealed significant negative clusters, with at least one significant negative cluster found in the visual areas VC1L, PM and VC1R for preterm infants at 5 (Figure 6a) and 12 months of age (Figure 6b), and for full-term infants at 5 (Figure 6c) and 12 months of age (Figure 6d). The results of the permutation test for the comparison of the forward optic flow and static condition showed negative clusters in the visual areas of interest indicating that
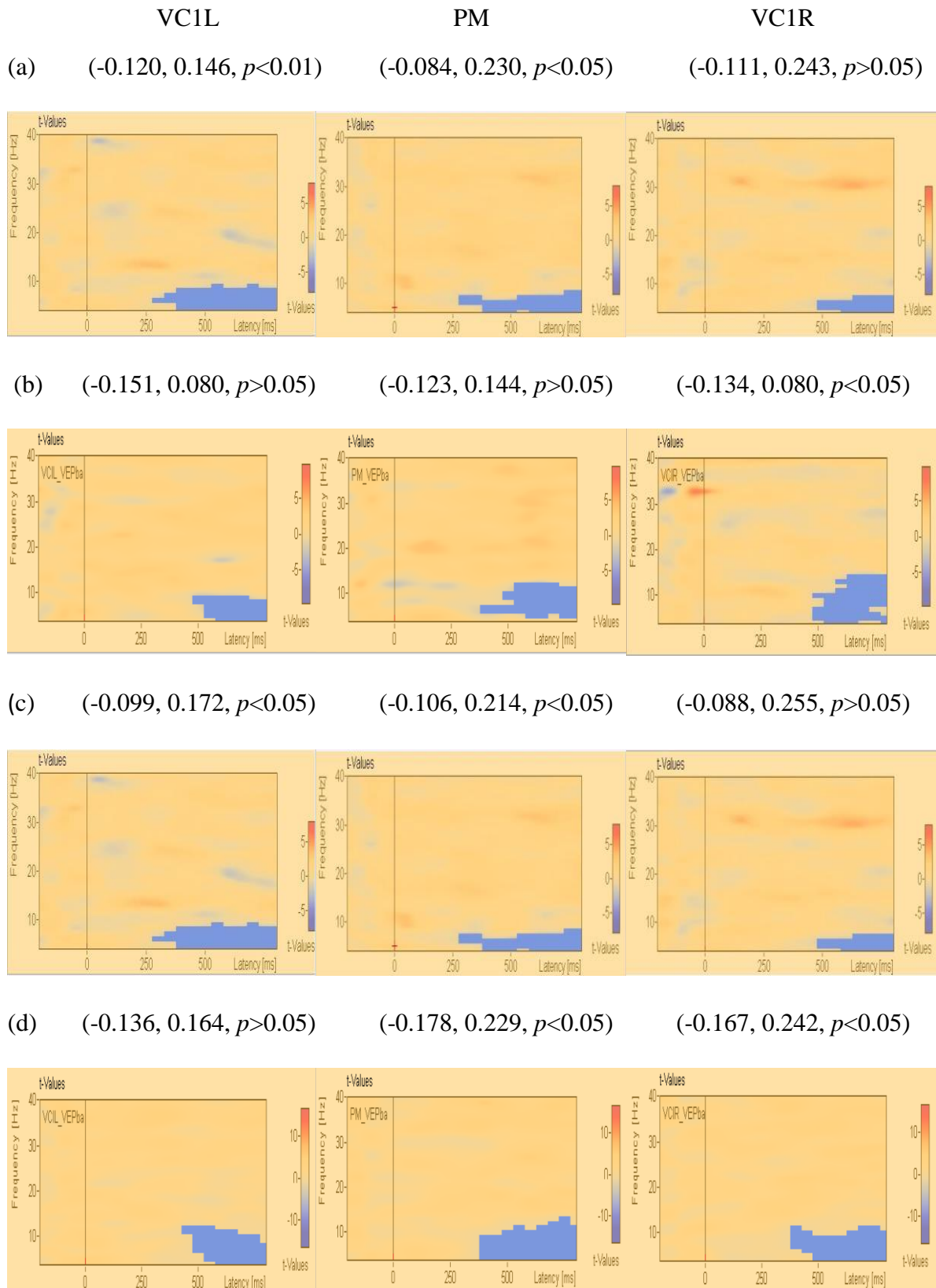
	VC1L	PM	VC1R
(a)	(-0.120, 0.146, *p*<0.01)	(-0.084, 0.230, *p*<0.05)	(-0.111, 0.243, *p*>0.05)

	VC1L	PM	VC1R
(b)	(-0.151, 0.080, *p*>0.05)	(-0.123, 0.144, *p*>0.05)	(-0.134, 0.080, *p*<0.05)

	VC1L	PM	VC1R
(c)	(-0.099, 0.172, *p*<0.05)	(-0.106, 0.214, *p*<0.05)	(-0.088, 0.255, *p*>0.05)

	VC1L	PM	VC1R
(d)	(-0.136, 0.164, *p*>0.05)	(-0.178, 0.229, *p*<0.05)	(-0.167, 0.242, *p*<0.05)

Figure 6. *The average visualization of significant data clusters in the visual sources of interest (VClL, PM, VClR) when forward optic flow was compared with static non-flow in preterm infants at 5 months (a), in preterm infants at 12 months (b), in full-term infants at 5 months (c), and in full-term infants at 12 months (d). Negative clusters are indicated with light blue (i.e. forward optic flow had smaller t-values than static non-flow), while*

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forward optic flow had significantly lower amplitude values in the theta-band range than in the static condition. In addition, the results showed that theta-band activity was more prevalent in both participant groups at 5 months (Figure 6a, 6c) compared to a shorter period at 12 months (6b, 6d). Similar permutation results were found when the TSEs of reversed optic flow and random visual motion were each compared with the TSE of the static non-flow condition. No significant differences were observed when the TSEs were compared between the motion conditions.

Furthermore, the decrease in low-frequency amplitudes was desynchronized with activity induced by each of the motion conditions at both ages where suppression of 4.9-7.2 Hz theta-band activity was observed in the visual areas of interest, with maximum activity around 500-750 ms post-stimulus in preterm infants, while in full-term infants suppression of 4.6-7.9 Hz was observed in the visual areas of interest, with maximum activity around 500-750 ms post-stimulus.

3.2.1 Individual analysis

Analyses of TSE maps across the visual areas of interest when forward optic flow was compared with static non-flow were conducted for each infant. Theta-band activity was observed as desynchronized oscillatory activity in the TSEs of preterm and full-term infants at 5 months of age (Figure 7a, 7c, 7e) around 250-800 ms, and was thus in accordance with the estimates from the grand average for both groups (Figure 6a, 6c). At 12 months, desynchronized theta-band activity between 400-800 ms was observed in full-term infants (Figure 7b) and three preterm infants (trend 1, see Figure 7c). In the remaining six preterm
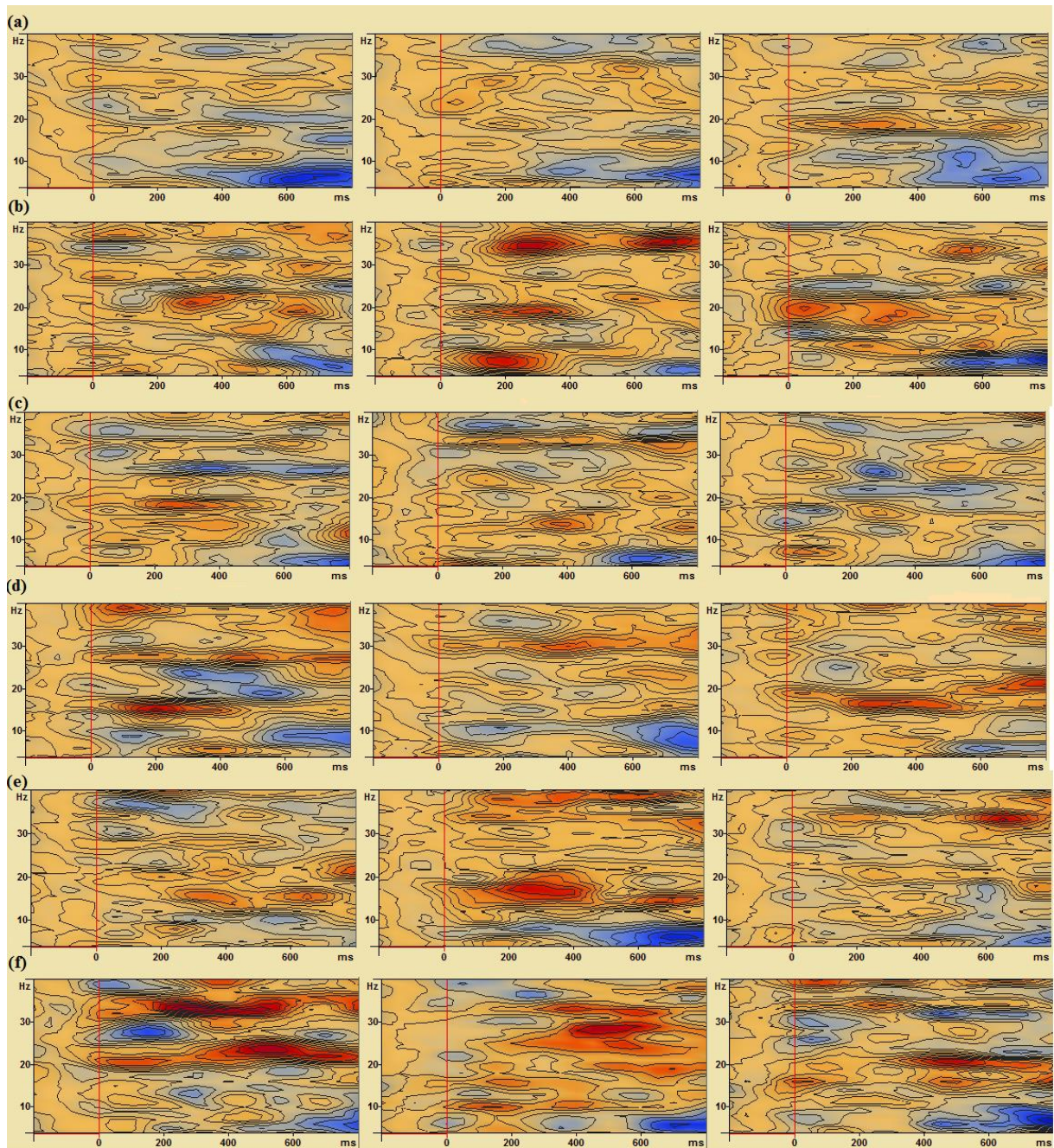
Figure 7. *TSE maps across the visual areas of interest when forward optic flow was compared with static non-flow in a typical full-term infant at 5 months (a) and at 12 months (b), in a typical preterm infant (trend 1) at 5 months (c) and 12 months (d) and in a typical preterm infant (trend 2) at 5 months (e) and at 12 months (f) VC1L, PM and VC1R represent visual areas of interest. Induced synchronized activity (increased spectral amplitude) is revealed as red colored contours, while induced desynchronized activity (decreased spectral amplitude) is revealed as blue colored contours. Induced theta-band desynchronized activities are observed in all visual areas of interest at both 5 (a,c,e) and 12 months (b,d,f). Synchronization in the beta-band frequency, however, can be observed in two or more visual areas but only at 12 months (b,d). Similar TSEs were observed when reversed optic flow and random visual motion were compared to the static non-flow control condition.*

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infants on the other hand, desynchronized theta-band activity was more widespread and was observed around 250-800 ms, and thus showing similar responses to what was observed in both groups at 5 months (trend 2, see Figure 7e-f for example for typical infant DD). Hence, six preterm infants revealed more immature developmental manifestations in the TSE maps when compared to that of the other preterm infants and full-infants at 12 months of age (see Figure A4 for TSE maps for the five other preterm infants at 12 months).

In addition to the observed theta-band desynchronized activities, further statistical analyses were conducted for each infant comparing the TSE of the respective motion condition with the TSE of the static non-flow condition. These statistical analyses revealed significant high-amplitude oscillatory activities consistently found in one or more of the visual areas of interest in full-term infants, but only at 12 months as shown in Figure A1e-f for a typical infant. TSE of forward optic flow had significantly larger amplitudes ($p < .05$) in induced beta-band activity than static non-flow over one or more of the visual areas of interest in most of the full-term infants (7 out of 9) at 12 months. Moreover, these observed amplitude increases were synchronized with induced expression of lower beta-band rhythm at peak latencies between 200-400 ms post-stimulus in two or more of the visual areas of interest for full-term infants at 12 months of age in the forward optic flow condition (Figure A1c). These induced higher frequency synchronizations occurred within the same frequency range as the desynchronizations observed in the TSEs of the static non-flow condition (Figure A1d). Similar oscillatory activities were observed in the TSEs for reversed optic flow and random visual motion. However, no significant differences were found when comparing the TSEs between motion conditions in each infant. TSEs of forward optic flow and static non-flow at 5 and 12 months in a typical full-term infant are presented in Appendix 1. In preterm infants, statistical analyses revealed significant high-amplitude oscillatory activities consistently found in one or more of the visual areas of interest in addition to the observed desynchronized theta-band activity, but only at 12 months as shown in Figure A2e-f for a typical preterm infant. However, a split group trend was revealed, similar to the one found in the observed desynchronized activity for the same preterm group, in that only three out of nine infants in the TSE of forward optic flow had significantly larger amplitudes ($p < .05$) in induced beta-band activity than static non-flow over one or more of the visual areas of interest. The six

preterm infants who did not reveal significant induced synchronized lower beta- band activity in the forward optic flow condition were mostly the same as the six preterm infants that showed more widespread desynchronized theta activity (see Figure A3e-f for an example of a typical preterm infant DD) at 12 months. Moreover, these observed amplitude increases were synchronized with induced expression of lower beta-band rhythm at peak latencies between 200-400 ms post-stimulus for the three preterm infants at 12 months of age in the forward optic flow condition (Figure A2c). These induced higher frequency synchronizations occurred within the same frequency range as the desynchronizations observed in the TSEs of the static non-flow condition (Figure A2d). Similar oscillatory activities were observed in the TSEs for reversed optic flow and random visual motion. However, no significant differences were found when comparing the TSEs between motion conditions in each infant. TSEs of forward optic flow and static non-flow at 5 and 12 months for a typical preterm infant (trend 1-2) are demonstrated in Appendices 2-3. Isolated desynchronized and synchronized activity in the higher frequencies did also appear in individuals at both ages, but the activity did not follow a trend and most of the time it was not significant in the statistical analyses.

Finally, it is important to note that although some preterm infants at 12 months (3 out of out of 9) revealed significant induced synchronized beta-band activity in the forward optic flow condition, the trend was still not as prominent as the one found in the full-term infants at 12 months of age.

4. DISCUSSION

In this longitudinal study, high-density EEG was used in preterm and full-term infants at 5 months and 12 months to study brain electrical activity as a function of perception of structured optic flow and random visual motion. The study attempted to investigate the development of radial motion perception in infants, and explore whether there are any differences between normally developing preterm and full-term infants. VEP and TSE analyses were conducted to investigate whether there were differences in brain activity in preterm and full-term infants when they were introduced to two conditions of structured radial motion, i.e., forward and reversed optic flow, and to non-structured random visual motion.

4.1 VEP responses

Comparisons of the motion-specific N2 component of the VEP waveform revealed that only full-term infants showed a significant improvement in latencies from 5 to 12 months of age. Hence, full-term infants became more sensitive to structured radial motion: forward and reversed optic flow, by demonstrating shorter latencies at 12 months of age compared to that of 5 months of age. These results corroborate the findings of a similar study using the same experimental paradigm (Agyei et al., 2015). Ongoing neurobiological development could be one major contributing factor to the observed improvement in processing of radial motion, in that it allows for more effective processing of visual motion stimuli, as infants get older. Research (Bourgeouis, Goldman-Rakic & Rakic, 1994; Huttenlocher & Dabholkar, 1997; Rakic, Bourgeuis, Eckenhoff, Zecevic & Goldman-Rakic, 1986) suggests that cortical synapse overproduction takes place within the first two years of life, with synaptic density of the visual cortex reaching its peak around 9-15 months of age. Synaptogenesis is therefore an important aspect in understanding brain development and plasticity in the first year of life. Additionally, increase in local glucose metabolic rates have been found in motion-sensitive areas, namely the occipital, parietal and temporal lobe after 3 months and in association visual cortex and frontal cortex after 6-8 months of age (Chugani, Phelps, Mazziotta, 1987; Gilmore et al., 2004; Klaver et al., 2011). Higher rates of metabolism would allow for readily available neuronal energy for efficient information transmission. As such, rapid development in the processing of functional networks between 5 and 12 months along with increased neuronal myelination of white matter tracts (Grieve et al., 2003; Webb et al., 2005) could explain the

improved latencies in full-term infants at 12 months.

Full-term infants at 12 months could differentiate between the three motion conditions, as latencies were found to significantly decrease from random visual motion to reversed optic flow, and then to forward optic flow. Their N2 latency at 12 months for the unstructured random visual motion was longest and showed inferior improvement from 5 months when compared to the structured motion conditions: forward and reversed optic flow. This could suggest that it is easier for full-term infants at 12 months to detect the structured coherence in the optic flow as opposed to the non-coherence in the random visual motion condition, which could reflect the importance of optic flow for moving around efficiently in the environment (Brosseau-Lachaine et al., 2008; Bruggeman & Warren, 2007). Several studies (Anderson et al., 2001; Campos et al., 2000; Johnson, 2000) have suggested that sensitivity to optic flow develops hand in hand with locomotor experience, and that infants are more dependent on coherent visual motion for controlling posture. Even though infants would have experienced passive locomotion prior to crawling, either in the arms of their parents or in a stroller, self-produced locomotion is found to be a superior contributor to the normal development of visual motion perception (Gilmore et al., 2004; Hein & Held, 1963). In the present study, the full-term infants at 12 months had been crawling for approximately 3 months prior to the second testing session. As a result, of increased experience with real-life structured optic flow the full-term infants may have become reliant on structure for perceiving motion, and thus become negatively affected by the lack of structure in the random visual motion condition.

The responses to forward and reversed optic flow in full-term infants at 12 months, revealed an expansion bias as the infants showed greater sensitivity towards forward optic flow than reversed optic flow (contraction), as demonstrated by shorter N2 latencies. This asymmetry has been extensively reported and has been linked to the more ecological egomotion, which is mostly experienced in the forward direction (Agyei et al., 2015; Brosseau-Lanchaine et al., 2008; Gilmore et al., 2007). Hence, the greater sensitivity to forward optic flow could be interpreted to mean that infants rely more on visual information, particularly during forward motion for efficiently manoeuvring in the environment. Research has proposed that there may be multiple functional systems detecting radial expansion and contraction in the visual system. As such, in line with the ecological notion that humans usually move forwards rather than backwards, it has been suggested (Shirai et al., 2009) that detectors of motion that are biased towards radial expansion may tap expansion-sensitive mechanisms that are important for ecological egomotion as compared to contraction-sensitive mechanisms that are involved with controlling hand-reaching actions (Edwards & Badcock,

1993). This proposition corroborates with Ptito and colleagues' (2001) finding using positron emission tomography, which demonstrated larger activation of the visual occipital-parietal areas when normal human adults were stimulated with forward optic flow compared to reversed optic flow. There is therefore reason to believe that expansion-sensitive mechanisms in normal infants at 12 months may have been prioritized more than contraction-sensitive mechanisms, particularly since an approaching object imposes more potential danger than a receding one.

Furthermore, the findings of the present study suggested that preterm infants neither showed improved N2 latencies between 5 and 12 months, nor demonstrated significantly different latency responses between the three motion conditions. Although most of the preterm infants had equivalent crawling experience to that of their peers at the time of the second testing session, they still did not differentiate between the motion conditions like full-term infants did. Latency has been shown to be a highly sensitive measure that is both stimulus- and age-dependent (Apkarian, 1996). Consequently, latency delays inappropriate for either stimulus or age have been suggested to reflect visual pathway abnormalities (ibid). Since preterm and full-term infants were presented with the same visual motion stimuli at comparable ages, the present findings support the notion of dorsal stream impairment following premature birth, that has been suggested by previous research involving global motion comparable to the motion conditions used in the present study (Guzetta et al., 2009; Mutaf, 2012). The dorsal stream or the M pathway is known to be highly vulnerable to injury in the perinatal period, and it is has been shown that premature birth affects more significantly the M pathway than the P pathway or the ventral stream (Guzetta et al., 2009; Hammarrenger et al., 2007; Tremblay et al., 2014; Weinstein et al., 2011). This vulnerability may be explained by differences in developmental periods for each visual pathway. As such, the M pathway development is believed to occur during the third trimester of the pregnancy, whereas the P system is believed to develop several weeks later, after birth during neonatal period (Hammarrenger et al., 2003; Klaver et al., 2011), an idea that is also supported by recent research (Neuringer et al., 1986) on docosahexaenoic acid (DHA). DHA is an omega 3 long chain polyunsaturated fatty acid that is transferred from the mother to the fetus during the last three months of pregnancy and in the early neonatal period, and is regarded as an important component for synthesis of brain tissue, synaptogenesis, metabolism of neurotransmitters and cellular differentiation (Neuringer et al., 1986; Sabel et al., 2009). MRI studies suggests that M cells need a high amount of polyunsaturated fatty acids to preserve their membrane flexibility crucial for allowing physiological processes (Stein, 2001). Thus,

insufficient supply of DHA is suggested to lead to impaired functioning associated with the M pathway (Carlson & Werkman, 1996; O'Connor et al., 2001). The preterm infants in the present study were all born before 33 weeks of gestation, and it is therefore possible that the observed latency delay is related to deprivation of this essential fatty acid. Additionally, diffusion tensor imaging (DTI) has shown that white matter fibers in areas of the brain through which the dorsal stream flows are shorter, thinner, and less organized in preterm than full-term control infants at 40 weeks gestational age (Hüppi et al., 1998). At 11 years of age, DTI has suggested that the white matter in these brain areas in preterm are characterised by reduced thickness, fewer axons and/or poorer myelination compared to that of the full-term control children (Nagy et al., 2003). Together these studies (Carlson & Werkman, 1996; Hüppi et al., 1998; Nagy et al., 2003; O'Connor et al., 2001) indicate that dorsal stream impairment is irreversible, and that a history of premature birth before 33 weeks of gestation may lead to reduced synaptic efficiency as revealed by longer latencies when processing motion (Duffy, McAnulty, Jones & Albert, 1993).

Surprisingly, preterm infants at 5 months of age demonstrated significantly shorter latencies regardless of visual motion condition when compared to their full-term peers. This finding could reflect preterm infants' longer exposure to real-world visual flow experiences, since they were tested corrected for prematurity. If this were the case, one would expect full-term infants at the age of 7 months to show similar latency responses to that of preterm at 5 months. Thus, this finding leaves an interesting focus for future research.

High activation values were recorded for preterm and full-term infants at both 5 and 12 months. This could be a due to infants' relatively thinner skulls compared to adults (Grieve et al., 2003), and thus involving less impedance in measuring cortical electrical activity. No significant amplitude differences were found for the motion conditions between the participant groups and ages, which could be indicative of no marked increase in skull thickness in preterm and full-term infants between 5 and 12 months of age. However, since amplitude of oscillations is suggested to be proportional to the number of synchronously active neural elements (Elul, 1971; Pfurtscheller & Lopes da Silva, 1999), the large amplitudes could further suggests a generally large activation and less specialization of cortical areas when processing motion stimuli in preterm and full-term infants during the first year of life.

An individual analysis of the preterm infants were conducted to explore the developmental trajectories of visual motion perception and the effects of prematurity. Consequently, in an attempt to identify individuals that might be at risk of developmental

disorders, an outlier criterion was suggested for detecting preterm infants who demonstrated remarkably long latency responses at 12 months. Although the application of the criterion pointed to three preterm infants, the longer latencies could also reflect a normal developmental delay to be recovered as they grow older.

4.2 Time-frequency responses

Differences in induced activities in preterm and full-term infants at 5 and 12 months when perceiving visual motion were also investigated. When the TSEs of the three motion conditions were each compared with the static non-flow control condition over the visual areas of interest, it was found that preterm infants at 5 and 12 months showed low-amplitude values in the 4.9-7.2 Hz theta-range, while full-term infants at 5 and 12 months showed low-amplitude values in the 4.6-7.9 Hz theta range. The low-amplitude values were observed as desynchronisation in the TSE plots.

At 5 months, desynchronized theta-band activity was more widespread and /or increased in full-term infants and some preterm infants (3 of 9) than at 12 months. This is in accordance with the findings of Agyei et al. (2015), who also suggested that this could be due to involvement of relatively larger networks or more cell assemblies when processing radial motion at a younger age compared to at an older age, an idea that corroborates previous pioneering studies in adults (Pfurtscheller & Lopes da Silva, 1999; Pfurtscheller et al., 1994). Since comparable results were found in the present study for full-term infants at 5 months to what has been found in full-term infants at 3-4 months (Agyei et al., 2015) this could indicate that cortical activity in typically developing infants does not change much between 3-5 months of age. However, it is important to note that most preterm infants (6 of 9) did not show this trend at 12 months and instead they revealed similar responses to what they did at a younger age by showing widespread desynchronized theta-band activity for both testings. Further, the present study observed significant high-amplitude values in the 13-21 Hz beta range in full-term infants and in some preterm infants in the same visual areas of interest only at 12 months, which was revealed in the TSE plots as synchronisation. Interestingly, most of the preterm infants that did not show significant beta-band synchronization at 12 months were also amongst the same infants that did not show change with respect to theta desynchronisation between 5 and 12 months of age. Synchronized beta-band activity has also been demonstrated in adult studies as a result of processing motion stimuli, indicating that this is representing more adult-like activity (Carmeli et al., 2005; van der Meer et al., 2008). In

full-term infants, at 11-12 months of age, Agyei and colleagues (2015) also found desynchronised theta activity to be accompanied by synchronized alpha-band activity when processing motion stimuli compared to a static dot pattern, but this was not observed in the present study. It is possible that the large amplitudes of the signal with low frequency masked other less mature components, and that this could explain why this activity was not found in the current study (Ceponiene, Rinne & Näätänen, 2002). Another explanation could be the low-signal-to-noise ratio obtained for infants. When considering the short attention span in infants and the general challenges it involves when collecting data, this must be overcome by experimental design.

Previous research suggests that amplitude of oscillations is proportional to the number of neurons firing in synchrony (Elul, 1971; Pfurtscheller & Klimesch, 1992; Pfurtscheller & Lopes da Silva, 1999; Singer, 1993), and therefore slower oscillating cell assemblies as revealed by theta-band activity would generally involve more neurons than faster oscillating cell assemblies, as revealed by beta-band activity. Because beta-band activity was only observed at an older age, this could reflect gradual progression from less specialised and relatively immature larger oscillatory cell assemblies to a more adult-like pattern of specialisation in processing motion where cell assemblies have fewer but more specialised neurons (Agyei et al., 2015). This developmental trajectory becomes even more obvious when considering that adult studies have found increased gamma-band activity in the visual cortex (Hoogenboom et al., 2006; Krishnan et al., 1993; Singer, 1993), especially since this appears to be a more efficient way of establishing rapid coupling between cell assemblies that are spatially segregated (Singer, 1993). One possible explanation for the present findings could be that while full-term infants and some preterm infants progressed into employing a smaller and more specialised network in processing motion stimuli at an older age, most preterm infants continued to use a larger and less specialised network, which could be related to the notion of dorsal stream impairment following premature birth. Several studies (Carmeli et al., 2005; Pfurtscheller et al., 1994; Orekhova et al., 2006; Thierry, 2005) have found EEG in infants to be dominated by low-frequency activity of large amplitudes, an observation that has been suggested to reflect general signs of immaturity in infants. On the other hand, considering that ongoing rapid cortical synapse overproduction takes place within the first two years of life (Bourgeouis et al., 1994; Huttenlocher & Dabholkar, 1997; Rakic et al., 1986) it is likely that cortical theta-band activity may act as an mechanism for synaptic plasticity (Kahana, Seelig & Madsen, 2001). As such, DTI studies (Mullen, Vohr & Katz, 2011) suggest that effects of prematurity could result in enhancement of alternative pathways. In line with this notion of

alternative pathways, another DTI study (Eikenes, Løhaugen, Brubakk, Skranes, & Håberg, 2011) observed increased white matter fibers in areas different to term born control peers at 20 years of age. Other studies (Smyser et al., 2010) also reported grey matter injury in preterm infants without major cerebral lesions. It is believed that damage to white matter might disturb these connections directly, while injury to grey matter may alter these connections (ibid.). The prevalent theta-band activity found in most preterms at 12 months in the present study could thus reflect ongoing synaptogenesis and myelination related to alternative pathways. The spilt group trend that was observed in preterm infants at 12 months of age could possibly reflect different developmental stages of an alternative pathway involved in processing motion. This could again be due to different developmental stages in self-produced motion, as some of the preterm infants that showed more immature manifestations of cortical activity had not started crawling at the time of the second testing, and were bottom shuffling instead. The bottom shuffling strategy is associated with delayed onset of independent walking (Størvold, Aarethun & Bratberg, 2013), and research (Shirai & Imura, 2014) implies that this could be related to inadequate development of processing visual motion. On the other hand, it is possible that the practice of age-correction in preterm infants may mask minor impairments (Aylward, 2002). Even though some preterm infants showed synchronised beta-band frequencies when motion conditions were compared to static at 12 months of age, it was still not as prevalent as demonstrated in full-term infants.

When induced theta-band desynchronisation was observed in the TSEs for the three motion conditions in the infants, induced theta-band synchronisation was observed in the TSEs of the static condition. This implies that neuronal assemblies fired in synchrony under the perception of the static pattern, while this synchronised activity was suppressed when the infants perceived the motion conditions. Consequently, desynchronisation in the theta band frequency could be an oscillatory mechanism for communication between underlining cortical networks when processing motion stimuli in infancy. This finding corroborates another longitudinal study (Agyei et al., 2015). It is believed that increased task complexity can contribute to the enhancement of theta desynchronisation (Pfurtscheller et al., 1994). Because task complexity is increased from the relatively simple static non-flow condition to more complex motion conditions, the observed oscillatory differences when processing the static pattern compared to the motion stimuli could be attributed to differences in task-complexity.

On the other hand, since amplitude enhancement in an ERS is based on the coupled or synchronised behaviour of a large number of neurons (Pfurtscheller & Lopes da Silva, 1999; Pfurtscheller et al., 1996), the 13-21 Hz synchronised activity observed in the TSEs when the

older infants perceived motion stimuli could be attributed to synchronised behaviour of large cortical neuronal networks that were activated when perceiving motion, but not the static dot pattern which rather elicited desynchronised activity within the same frequency band. As such, the synchronized beta-band oscillatory activities observed in the full-term infants and (some) preterm infants at 12 months of age could reflect the involvement of subsets of activated cortical areas when processing motion, indicating the involvement of higher cortical structures in the perception of motion. This corroborates findings of another study that suggests the necessity of higher-level processing in detecting radial motion (Brosseau-Lachaine et al., 2008). Consequently, as infants get older it is possible that a progressive shift in cortical coupling occurs such that a slower theta-band desynchronized network communication gradually makes way for a faster and more efficient cortical coupling using synchronized high-frequency oscillations especially in the beta-band when processing radial motion.

Two preterm infants were detected as showing atypical responses for age and stimulus in both VEP and TSE analysis. Further longitudinal follow-up on these preterm infants is necessary in order to apply EEG data as an early screening tool for dorsal stream vulnerability. Since subtle impairments may not be detectable before preterm born children start school, it would therefore be interesting to call these two preterm infants back for follow-up testing at 6 years of age to evaluate the reliability of previous findings.Finally, future research should also involve greater samples to allow for greater statistical power for findings.

In conclusion, the present longitudinal study has demonstrated that full-term infants follow a developmental trend where they increase their sensitivities to optic flow, and become capable of processing structured optic flow more effectively than unstructured random visual motion with age. When comparing the TSEs of forward optic flow, reversed optic flow, and random visual motion with the TSEs of static non-flow, full-term infants showed desynchronisation in theta-band frequencies, with synchronisation in beta-band frequencies, but only at 12 months of age. These enhancements in full-term infants have been attributed to neuronal maturation coupled with locomotion experiences. Preterm infants, on the other hand, were found to follow a different developmental trend where they did not increase their sensitivities to optic flow with age nor became capable of detecting structured optic flow more effectively than unstructured random visual motion. When comparing the TSEs of forward optic flow, reversed optic flow, and random visual motion with the TSE of static non-flow, preterm infants showed widespread desynchronised theta-band frequencies at both ages. This difference in functional motion processing in preterm infants could be attributed to brain

anomalies related to dorsal stream vulnerability. More longitudinal research is warranted to gain a better understanding of the developmental progress of visual motion perception in preterm and full-term infants, before EEG measures can be used to aid an early detection.

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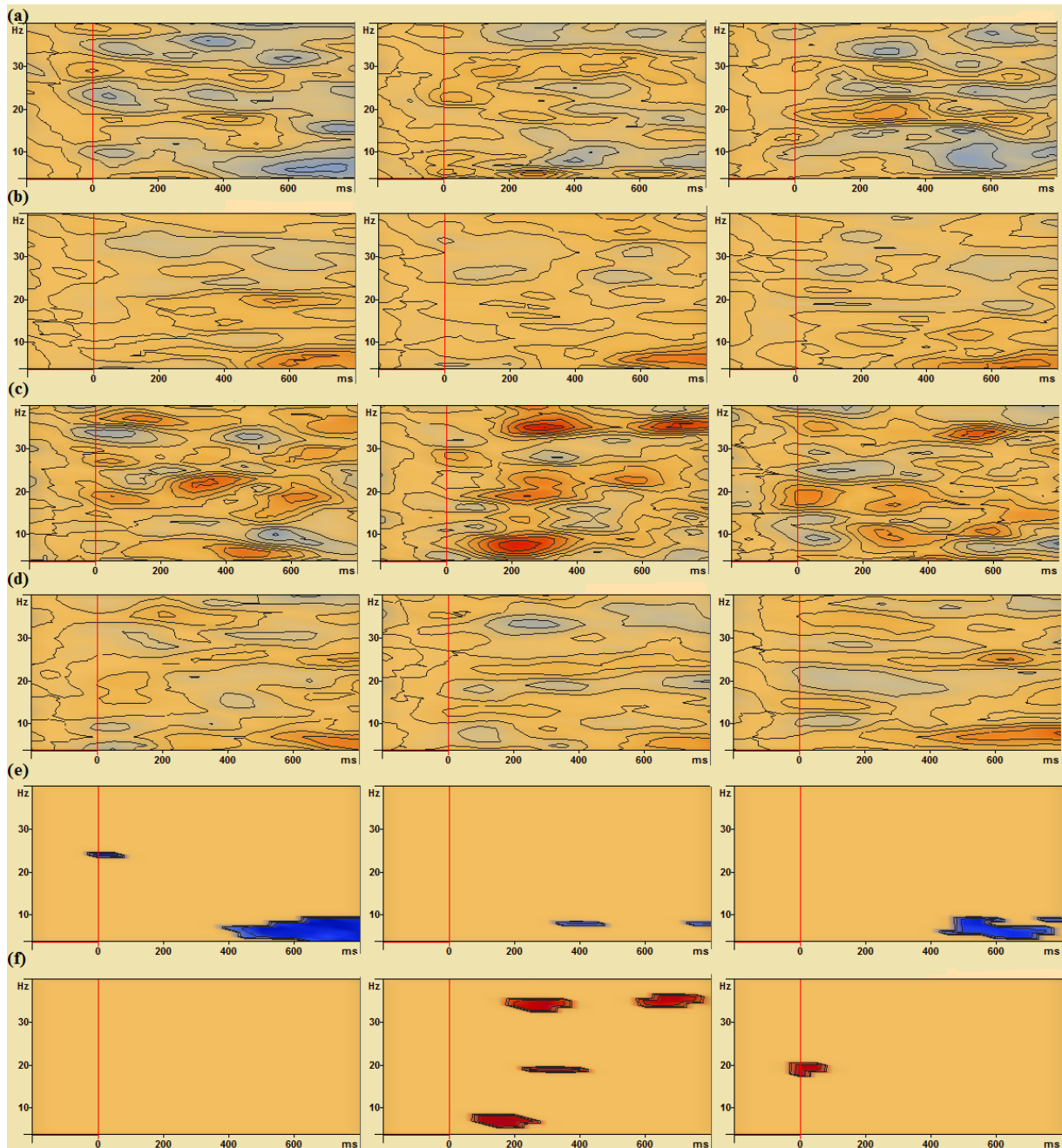VC1L   PM   VC1R

Figure A1. *TSE maps for typical full-term infant in visual areas VC1L, PM and VC1R (a-d.). TSE maps at 5 months for forward optic flow (a) and static non-flow (b), and at 12 months for forward optic flow (c) and static-non-flow(d). Induced synchronized and desynchronized and desynchronized activities are shown in red and blue contours respectively. Desynchronization in theta-band frequency is observed in visual areas of interest in the forward optic flow at both ages with theta-band synchronization observed in the static condition at the same time as the respective desynchronizations in the forward optic flow. Induced synchronizations at higher frequencies in the beta-range are observed only in (c) with induced desynchronizations in the same frequencies seen in (d) at the same time as synchronizations observed in (c). TSE probability maps (p <0.05) at 5 months (e) and at 12*

months (f) when forward optic flow was compared with static non-flow. Significant increase and decrease of TSE forward optic flow with respect to static non-flow is shown with red and blue colors where negative p-values indicate decrease (blue colors) and positive p-values indicate increase (red colors). TSE of forward optic flow showed significantly decreased amplitudes in induced theta-band activity than non-flow in (e). In (f), significantly induced amplitude increases in the beta-range can be observed. Stimulus onset is marked with a vertical line at 0 ms. Epoch is from – 200 ms to 800 ms at baseline -100 ms to 0 ms.

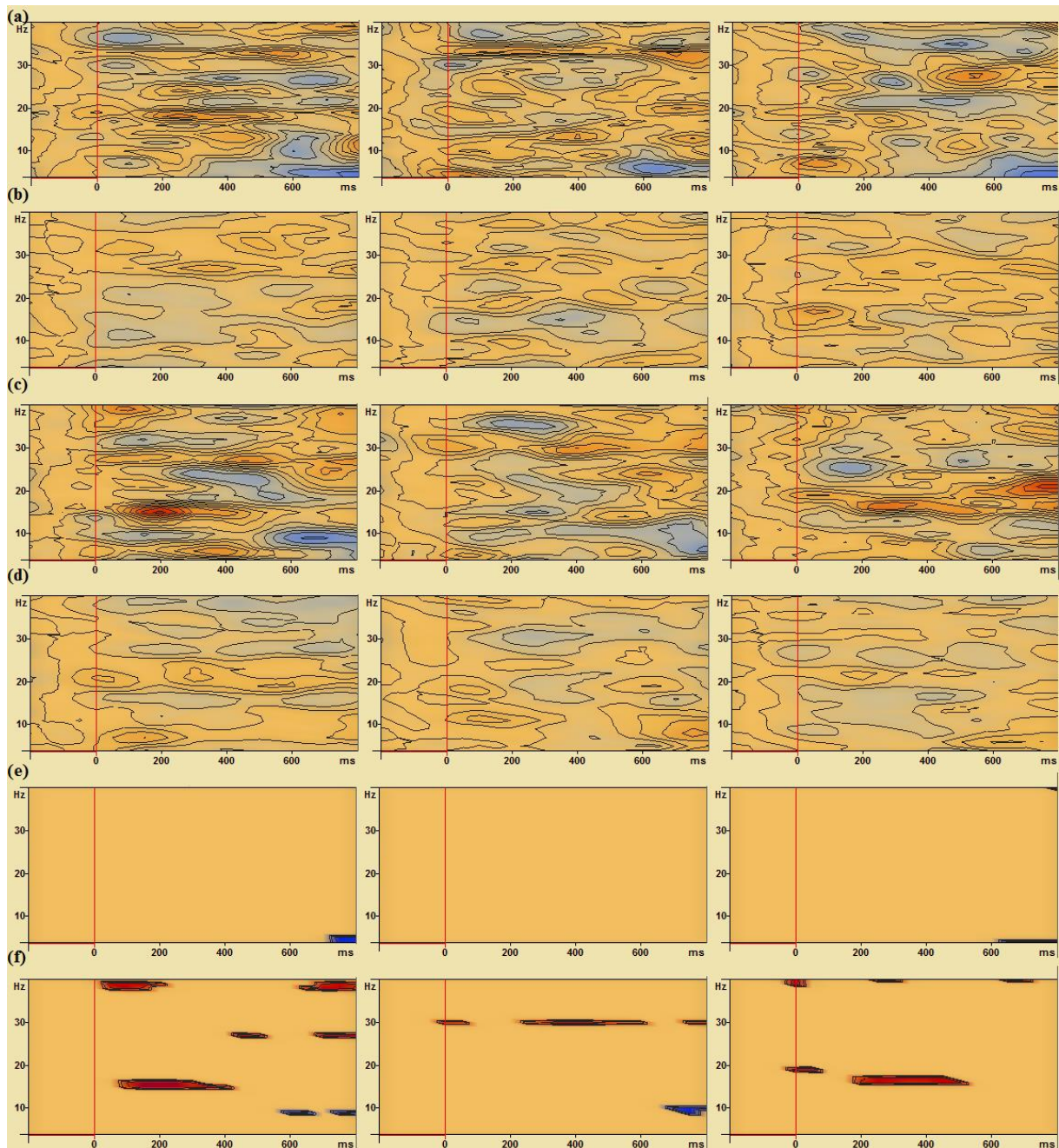VC1L   PM   VC1R

Figure A2. *TSE maps for preterm infant (trend 1) in visual areas VC1L, PM and VC1R (a-d.). TSE maps at 5 months for forward optic flow (a) and static non-flow (b), and at 12 months for forward optic flow (c) and static-non-flow (d). Induced synchronized and desynchronized and desynchronized activities are shown in red and blue contours respectively. Desynchronisation in theta-band frequency observed in visual areas of interest in the forward optic flow at both ages with theta-band synchronization is observed in the static condition at the same time as the respective desynchronizations in the forward optic flow. Induced synchronizations at higher frequencies in the beta-range are observed only in (c) with induced desynchronizations in the same frequencies seen in (d) at the same time as synchronizations observed in (c). TSE probability maps (p <0.05) at 5 months (e) and at 12 months (f) when forward optic flow was compared with static non-flow. Significant increase and*

decrease of TSE forward optic flow with respect to static non-flow is shown with red and blue colors where negative p-values indicate decrease (blue colors) and positive p-values indicate increase (red colors). TSE of forward optic flow showed significantly decreased amplitudes in induced theta-band activity than non-flow in (e). In (f), significantly induced amplitude increases in the beta-range can be observed. Stimulus onset is marked with a vertical line at 0 ms. Epoch is from – 200 ms to 800 ms at baseline -100 ms to 0 ms.
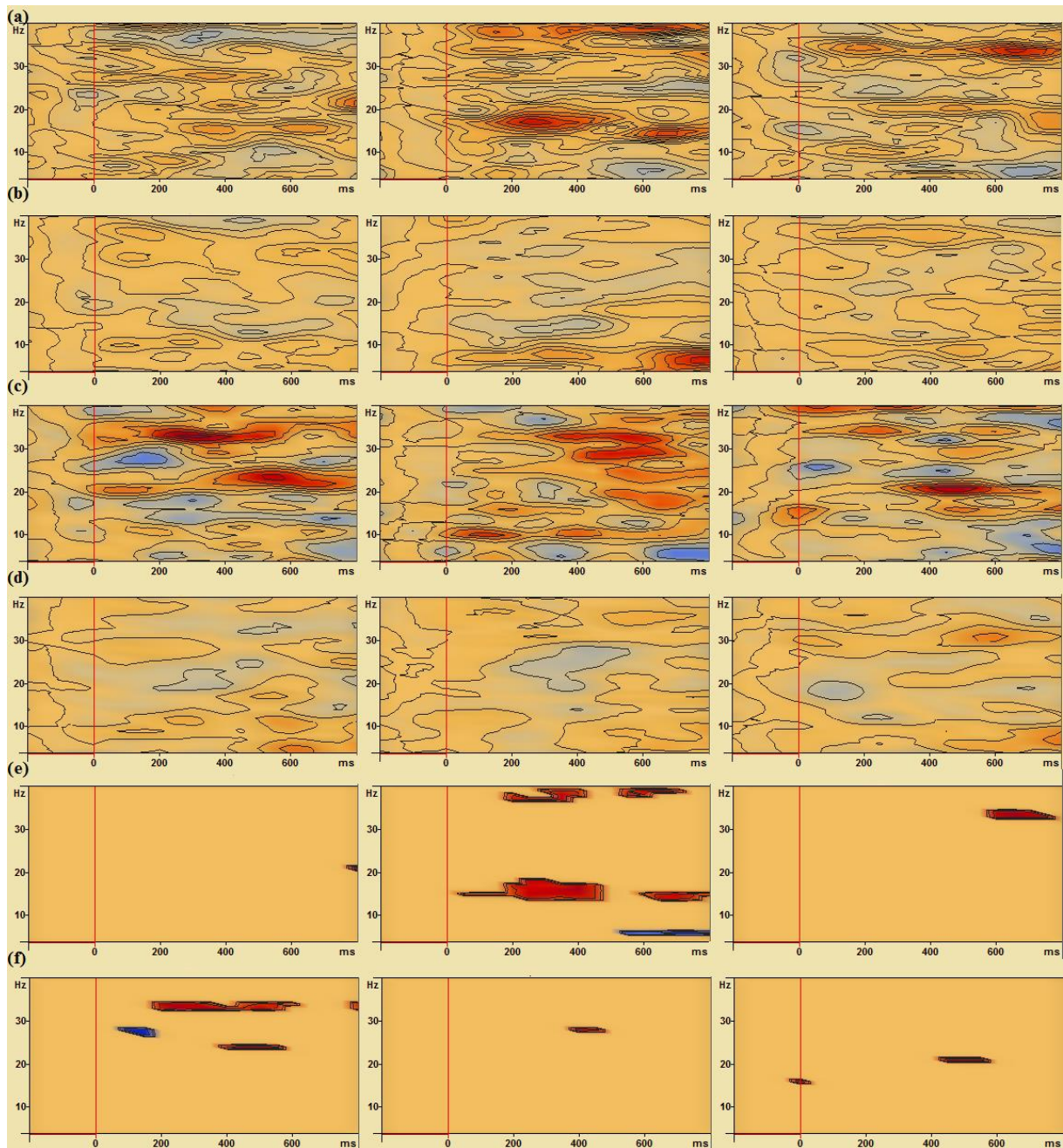
Figure A3. *TSE maps for preterm infant (trend 2) in visual areas VC1L, PM and VC1R (a-d.). TSE maps at 5 months for forward optic flow (a) and static non-flow (b), and at 12 months for forward optic flow (c) and static-non-flow (d). Induced synchronized and desynchronized and desynchronized activities are shown in red and blue contours respectively. Widespread desynchronisation in theta-band frequency is observed in visual areas of interest in the forward optic flow at both ages with theta-band synchronization observed in the static condition at the same time as the respective desynchronizations in the forward optic flow. Significant beta-band synchronizations is not observed between 200-400 ms at 12 months (c, f). TSE probability maps (p <0.05) at 5 months (e) and at 12 months (f) when forward optic flow was compared with static non-flow. Significant increase and decrease of TSE forward optic flow with respect to static non-flow is shown with red and blue colors where negative p-values indicate decrease (blue colors) and positive p-values indicate increase (red*

colors). TSE of forward optic flow showed significantly decreased amplitudes in induced theta-band activity than non-flow in (e). Stimulus onset is marked with a vertical line at 0 ms. Epoch is from – 200 ms to 800 ms at baseline -100 ms to 0 ms.
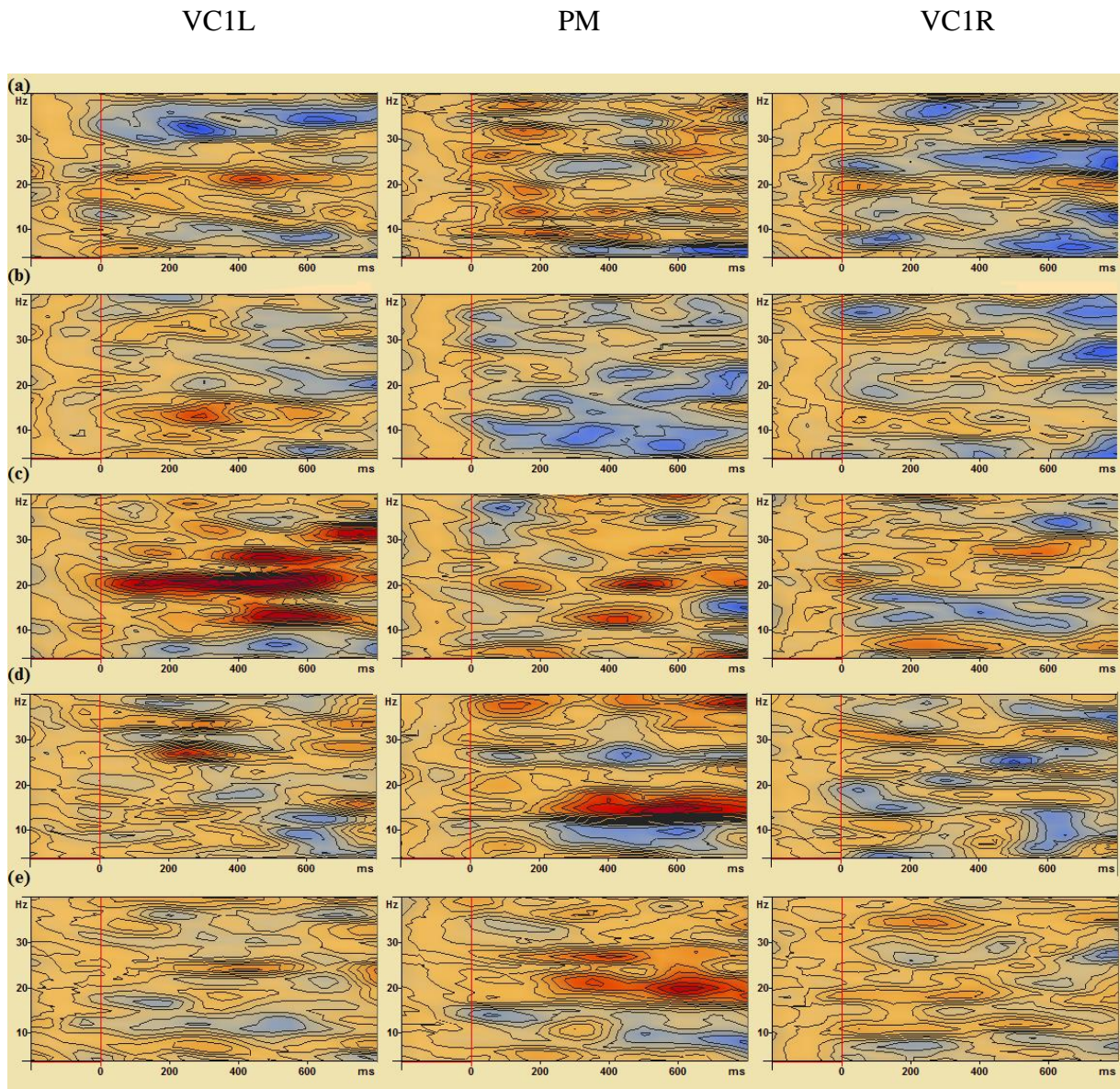
VC1L   **PM**   **VC1R**

Figure A4. *TSE maps across the visual areas of interest when forward optic flow was compared to static non-flow at 12 months in the other five preterm infants who showed more immature developmental manifestations (trend 2), namely FI (a), DI (b), TA (c), WI (d) and MS (e). VC1L, PM and VC1R represent visual areas of interest. Desynchronized activity (decreased spectral amplitude) is revealed as blue colored contours, while induced synchronized activity (increased spectral amplitude) is revealed as red colored contours. Induced theta-band activity is prevalent in all infants at 12 months (a-e).*