学位論文

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Original article

Do low birth weight infants not see eyes? Face recognition in infancy

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Abstract

Background: Progress in neonatal medicine has dramatically improved the survival rate of preterm births, but the evidence suggests that these low-birth weight infants (LBWIs) go on to develop pervasive development disorders and attention deficit hyperactivity disorder (ADHD) at greater rates than the general population. Children with neurodevelopmental disorders are known to suffer from deficits in visual cognition, such as in face perception and attentional functions, the characteristics of which already manifest in early infancy.

Purpose: This study aimed to investigate visual cognition in LBWIs during infancy.

Subjects: 20 LBWIs and 20 normal-birth-weight infants (NBWIs: control) of age 9–10 months (corrected age was used for LBWIs).

Method: Children were held seated in front of an eye tracking system by a parent, and presented with facial photos as visual stimuli. During the familiarization phase, the child was presented with two images of the same human face (familiarization stimulus) on the left and right side of a display screen (5×10 s trials). Next, during the test phase, the child was presented with the same image on one side of the screen, and a photo of a different person's face (novel stimulus) on the other (2×5 s trials). Gaze behavior was assessed in terms of the total time spent looking at either facial stimulus, and specifically at the eyes of the stimuli, as well as the number of attentional shifts between stimuli, and novelty preference.

Results/Discussion: LBWIs spent significant less time looking at facial stimuli overall, and less time at the eye region, than NBWIs. These findings seem to evidence developmental differences in functions related to visual cognition.

Keywords: Low birth weight infant; Facial recognition; Eye tracker

1. Introduction

While recent progress in neonatal medicine has markedly increased the survival rate of low-birth-weight infants (LBWIs), survivors reportedly develop a host of neurological and developmental conditions, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), at higher rates than their normal-birth-weight infants (NBWIs) [1,2]. These include, characterized by social communication difficulties and limited, stereotypic patterns of behavior, and, characterized by inattention and hyperactivity/impulsivity. These behaviors are believed to originate in dysfunc-

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tional processing of visual information in domains such as face perception and attentional functions.

Studies have demonstrated that individuals with ASD have trouble recognizing faces and understanding facial expressions [3–7], and that autistic children exhibit such deficits in facial recognition skills even before verbal communication difficulties, stereotypy, and other characteristic features of the disorder become apparent [7]. The dysfunctional recognition of facial expressions in infants with ASD has been attributed to their utilization of a "face scanning" technique different from that employed by normally developing infants [8]. One study reported that autistic infants tend not to look into the eyes of facial stimuli at two years of age [9]; another has claimed they give preferential attention to the mouth over the eyes [10]. Similarly, Klin and colleagues have observed associations between gaze patterns and sociality [11].

The idea that impaired executive function lies at the root of the core symptoms of ADHD is nothing new, having been purported long ago by Barkley et al. [12]. Executive functions are a collection of processes used to filter and sort important information, guiding and implementing behaviors towards achieving some goal. One subset of these, crucial to normal cognition, are the *attentional functions*, defined as a subset of processes that ensure selectivity in conscious activity by judging the relative importance of competing information, establishing and following an accurate and organized plan of action, and continuously regulating this sequence in the course of its execution [13,14].

Face perception and attentional processes have been demonstrated to be already active in infancy, with Haxby et al. reporting the same for core neurological systems for processing visual information related to faces: notably, constantly changing factors such as facial expressions and eye and mouth movements [15]. Regions involved in attention such as the dorsolateral prefrontal, anterior cingulate, and orbitofrontal cortices begin to function around six months after birth, while higher-level attentional functions (e.g. sustained and selective attention) start to engage around the same period [16]. Children's performance on attention-related tasks in infancy is known to relate with their later executive functioning: Cuevas et al. reported that infants who more efficiently processed information about stimuli at five months of age exhibited superior executive functioning throughout early childhood [17].

Eye trackers are a type of recently developed device, utilized in a variety of fields, which can be used to monitor a subject's gaze easily and highly accurately. Infrared light is shined from the device into a subject's eyes, and their line of sight determined by sensor based on its reflection off their corneas. Eye trackers have made it possible to assess visual cognition in an objective way: in fact, multiple studies have reported their usefulness in detecting neurodevelopment disorders in infancy [18–20]. Konishi et al.'s research on visual cognitive functions in both full- and pre-term infants at three to four months of age has found that at the corrected age of four months, premature infants focus on different areas of the face from full-term infants, evidencing developmental differences in facial recognition [21,22]. One might expect that such differences between preterm and full-term children grow more and more obvious as they grow and develop, yet few studies to date have actually compared the eye movements and gaze patterns of these two groups in a detailed way [23].

Using gaze trackers to identify aspects of visual cognition in infancy typical of preterm infants, and determining how these patterns relate to subsequent manifestation of neurodevelopmental disorders, would help to inform the development of early discovery and early intervention approaches this at-risk population.

This paper details the findings of our investigation of attention and facial perception in LBWIs during infancy, in which the eye movements of LBWIs and NBWIs of corrected age 9–10 months towards images of faces were measured and analyzed in the context of a novelty preference paradigm.

2. Method and materials

2.1. Subjects

LBWIs seen at the Pediatrics Department of the Kagawa University Hospital were enrolled between December 2016 and September 2017, and tested at the corrected age of 9–10 months. NBWIs (control group) were recruited between April 2017 and April 2018, from children aged 9–10 months brought in for health checkups in the town of Shodoshima, Kagawa Prefecture. This study was approved by the Ethics Committee of the Kagawa University School of Medicine (accession no. 2018-025). The study overview was explained to one of the child's parents in writing, and informed consent obtained before they began the experimental protocol.

2.2. Equipment

Eye tracking was performed using the Tobii T60 (Tobii Technologies, Sweden).

The device shines infrared light at the subject's eyes, which is picked up by a sensor set up at the bottom of a (display) screen, allowing users to simply and highly accurately monitor where and for how long a subject's gaze is fixed. During the calibration phase, each subject's gaze was recorded at five points: i.e. when directed towards the center and four corners of the 17″ display screen (31 × 25 cm).

2.3. Procedure

All subjects were examined in a quiet small room in each hospital.

Subjects were held seated on the knee of a parent about 60 cm from the monitor, and presented with visual stimuli—facial photos—on the screen (size: 10 × 15 cm, viewing angle: 95°). Children who obviously did not look at the screen during the task were excluded from analysis, and two participants were excluded for this reason.

After the calibration phase, two facial stimuli were simultaneously presented in a horizontal row across the center of the screen. The respective lengths of time the infant spent looking at each stimulus were recorded for analysis. During the familiarization phase, the same facial photo (i.e. *familiarization stimulus*) was presented on the left and right in successive trials (5 × 10-s trials). During the test phase, one familiarization stimulus was replaced with a photo of a different person's face of the same expressive category (i.e. *novel stimulus*) (2 × 5-s trials) (Fig. 1). We used the photographs of the face from the ATR Facial Expression Image Database (ATR-Promotions Inc, Japan).

2.4. Evaluation items

Children's visual behavior was evaluated using the following measures.

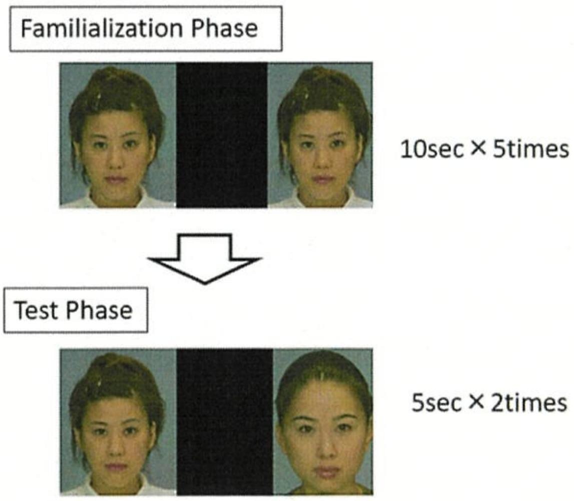

Fig. 1. The experimental task consisted of two phases. During the familiarization phase, subjects were presented with the same stimulus—an image of a face—on both the left and right side of a monitor for 10 s, for five trials in total. Subjects were kept engaged with the task between trials with a short animation presented on the screen. During the test phase, the same stimulus as before was presented on one side of the screen, and the novel stimulus—an image of a different face—on the other.

(1) Gaze timeThe total time a child spent looking at either facial stimulus across all familiarization and test trials.
(2) Eye gaze timeThe time a child spent looking at the eyes of either facial stimulus in familiarization and test trials. *Eye gaze rate*—the ratio of eye gaze time to gaze time—was additionally calculated. We defined the square region that covered both eyes as "eye-field". This region is the same size in both stimuli.
(3) Attention shift frequencyThe number of times a child switched their gaze from one facial stimulus to the other in all familiarization and test trials. Does not include instances where their gaze moved elsewhere on the screen besides the image stimuli. *Gaze time per shift*—total gaze time divided by this value—was additionally calculated.
(4) Novel facial preferenceThe ratio of the time a child spent looking at the novel stimulus to total gaze time in all test trials.
(5) Statistical analysisThe evaluation items above were compared by Wilcoxon test using JMP 14 statistical software (SAS Institute Inc., Cary, NC, USA). All data are reported as median (Interquartile range; IQR) unless otherwise noted. All statistical hypothesis testing employed a significance level of $p < 0.05$.

3. Results

3.1. Subjects

We obtained consent from 20 LBWIs and 22 NBWIs. Two infants of NBWIs were not able to look at the screen for intense crying. Data was analyzed for 20 preterm LBWIs (male:female ratio: 10:10, birth weight: 505–2087 g, gestation length: 23.4–36.9 weeks) and 20 full-term NBWIs (9:11, 2500–4000 g, 37.0–41.6 weeks). All participating children were first examined by a pediatrician, and confirmed to lack neurological abnormalities. LBWIs and NBWIs had a mean post menstrual age (PMA) of 569 ± 12.4 and 574 ± 20.4 d, respectively.

The subjects' characteristics are shown in Table 1.

3.2. Measurement results and analysis findings

(1) Gaze Time

The median of *Gaze time* of LBWIs is 26.75(s) (19.96–35.38) in familialization phase. On the other hand, the *Gaze time* of NBWIs in familialization phase is 36.27 (s) (30.76–39.64), and *Gaze time* of LBWIs was significantly shorter than NBWIs. In test phase, the median of *Gaze time* of LBWIs is 5.64(s) (3.66–7.76), and NBWIs is 7.36 (s) (6.20–8.85). There was no significant difference in the results of both groups (Fig. 2a).

Table 1

	LBWIs (n = 20)	NBWIs (n = 20)	p-value
Male, n (%)	10 (50)	9 (45)	–
Gestational age (weeks)	30.4 ± 3.5	39.2 ± 1.6	<0.0001
Birth weight (g)	1327 ± 464	3066 ± 430	<0.0001
Days after birth (days)	356 ± 25.4	299 ± 17.5	<0.0001
Post menstrual age (days)	569 ± 12.4	574 ± 20.4	0.15

LBWIs: low birth weight infants
NBWIs: Normal birth weight infants

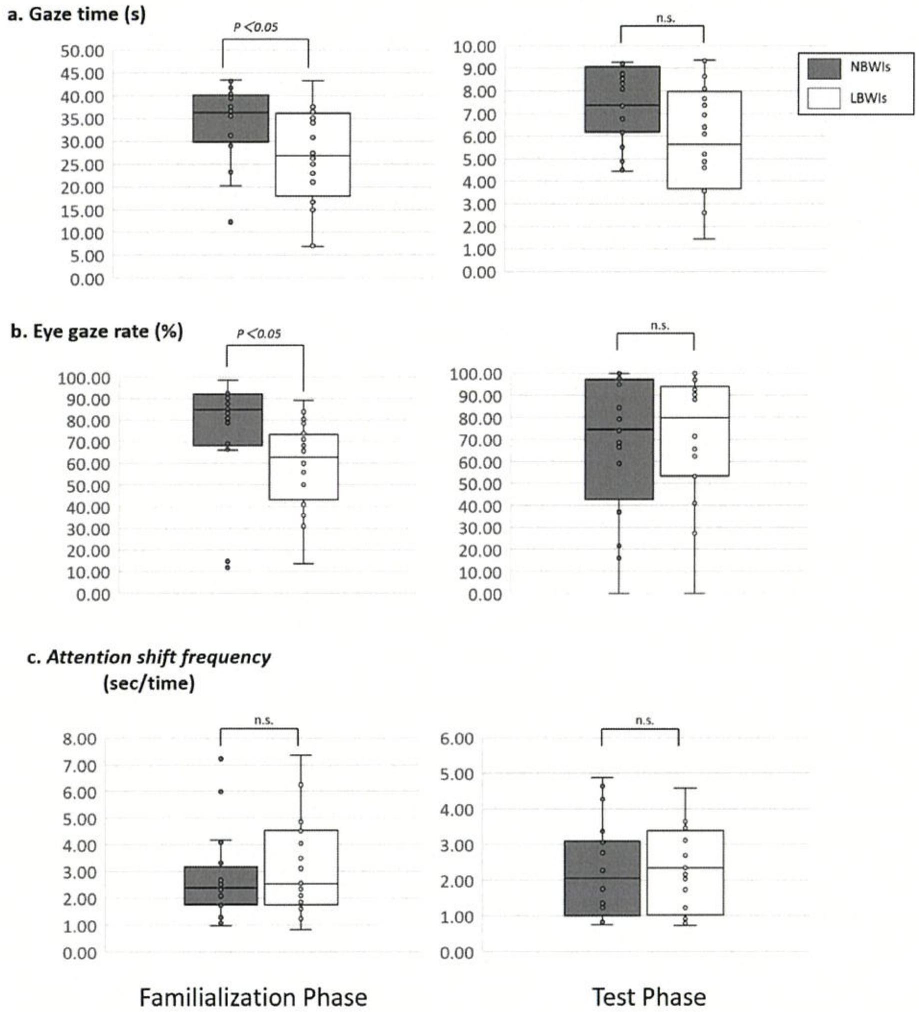

Fig. 2. (a) Total gaze time: Significantly shorter for LBWIs in familialization phase. (b) Eye gaze rate: Significantly lower for LBWIs in familialization phase. (c) Gaze time per shift: Not significantly different between the groups.

(2) Eye gaze rate

The median of *Eye gaze rate* of LBWIs is 62.79 (%) (47.75–71.82) in familialization phase. In the other hand, the gaze rate of NBWIs in familialization phase is 84.88 (%) (68.84–91.74), and *Eye gaze rate* of LBWIs was significantly shorter than NBWIs. In test phase, the median of *Eye gaze rate* of LBWIs is 79.85(%) (54.15–93.98), and NBWIs is 74.49 (%) (53.56–96.66). There was no significant difference in the results of both group (Fig. 2b).

(3) Attention shift frequency

The median of *Attention shift frequency* of LBWIs is 2.38 (sec/time) (IQR1.78–2.84) in familialization phase. In the other hand, the gaze time of NBWIs in familialization phase is 2.53 (sec/time) (IQR1.82–4.53). There was no significant difference in the results of both group. In test phase, the median of *Attention shift frequency* of LBWIs is 2.34 (sec/time) (IQR1.15–3.26), and NBWIs is 2.06 (sec/time) (IQR 1.16–3.08). Similar to results in familialization phase, there were no significant differences between both groups in test phase (Fig. 2c).

(4) Novel facial preference

LBWIs spent no more or less time looking at the novel facial stimuli, as a percentage of the time spent looking at either face, than NBWIs: (58.12 ± 19.44 v. 54.85 ± 19.29%: n.s.).

4. Discussion

Our findings demonstrate that preterm and full-term infants react differently to facial stimuli in early infancy. First, the gaze time of LBWIs was significantly shorter than a term infant in familialization phase. Also, the eye gaze rate in the familialization phase was significantly low in LBWIs. Whereas, as for the gaze time and the eye gaze rate in the test phase, there were no significant differences in both groups. In addition, LBWIs shifted their attention between the facial images less frequently, but there was no difference in the time spent attending to a face per shift. Novelty preference did not differ between the two groups. These results show that both attentional processes and face perception differ in several respects between children born prematurely and their full-term counterparts.

The product of a combination of neural functions, attention can be classified into four key categories related to volitional (dynamic) control [24]. The first, *sustained attention*, refers to the ability to continually maintain one's focus during an activity. The second, *selective attention*, is the ability to select from among competing stimuli to focus on a specific objective. The third and fourth are *switching (shifting) attention*—the ability to flexibly alternate between different cognitive tasks—and *divided attention*—the ability to handle multiple tasks at the same time—both of which fall under the control of attention and executive control.

Several studies have reported on the attentional processes in preterm infants during infancy. Butcher et al. found that at six months of corrected age, preterm infants were less efficient at performing a behavior involving basic attentional processes than full-term controls of the same age [25]. Rose et al. found that in infancy, premature infants take roughly 20–30% longer to develop a novelty preference than full-term infants [23]. This finding accords with our own observation of shorter gaze time in familialization pahse in LBWIs. Sustained attention—or rather, deficits therein—seems most involved in this outcome of the four functions described above. On the one hand, this suggests preterm infants are poorly able to maintain focus; on the other hand, since they did not switch between facial stimuli any more frequently than full-term infants, their abilities to shift and divide their attention appear intact.

But, the results of the test phase were different from familialization phase. There were no differences in gaze time and eye gaze rate in test phase in both groups. In gaze time, there was no significant difference between LBWIs and NBWIs, but the tendency that had a shorter gaze time of LBWIs was seen. Eye gaze rate was similar to both groups in the test phase, and it was shown that LBWIs saw eyes for a long time more in test phase as compared with familialization phase. These findings may indicate that LBWIs does not look to the eyes for maintenance of attention, but look to the eyes for orientation of attention. Konishi et al. reported that 4-month-old preterm infants spent less time gazing at their eyes than normal term infants in a mixed face presentation task [22]. They presented normal and mixed faces to infants and examined which face the child looked at longer. Both normal and preterm infants gazed at normal faces for longer, but preterm infants were less likely to look at eye region. This small amount of time spent gazing at the eyes was shown to be a feature of preterm visual cognitive functioning in infants, and this feature persisted from early infancy.

In this study, there was no novelty preference in both groups. In the habituation method that we used in this study, the time necessary to bring about novelty preference is different by the type of stimuli. In this study, time to show stimulation might be too short to produce novelty preference.

Our study has several limitations. First, our results may be biased by our small sample size. Second, infants' development could not be investigated over time due to our cross-sectional study design. As seen above, the literature is already full of research purporting relationships between novelty preference in face perception in infancy and subsequent manifestation of impaired perception of facial expressions and other sociodevelopmental deficits. Our observations of preterm infants spending less time looking at facial stimuli generally, and at the eyes specifically, should be further investigated in a longitudinal study, to explore their associations with developmental outcomes.

5. Conclusion

LBWIs spent significantly less time looking at facial stimuli, as well as the eye region specifically (in terms of both absolute time and as proportion of total gaze time), in a novelty preference task in late infancy. These observations seem to reflect differences in attentional processes and facial cognition between preterm and full-term infants at an early age. Reluctance to look in the eyes is a characteristic also seen in autistic children; this trait may predict future development of ASD. Our evidence also supports the value of assessing the developmental characteristics of preterm infants based on visual behaviors at an early age, and providing disability rehabilitation as needed. This topic should be further investigated with a greater number of subjects using a longitudinal design.

Conflict of interest disclosures

The authors declare no competing interests.

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