Visual Attention Control Differences in 12-month-old Preterm Infants

ABSTRACT

There have been few previous attempts to assess the development of early markers of executive function in infants born preterm despite well-established deficits reported for older preterm children that have been closely linked to poorer academic functioning. The present study investigates early attention control development in healthy 12-month-old age-corrected pre-term infants who were born less than 30 weeks and compares their performance to full-term infants. Eye-tracking methodology was used to measure attention control. Preterm Infants spent less time focused on the target and were slower to fixate attention, with lower gestational age associated with poorer target fixation and slower processing speed. There were no significant group differences observed for inhibition of return or interference control. These findings suggest that specific emerging deficits in attention control may be observed using eye tracking methodology in very preterm infants at this early stage of development, despite scores within the average range on the Bayley Scales of Infant Development.

Key Words: Preterm, Executive function, Eye-tracking, Attention, Inhibition, Processing Speed

Abbreviations: ADHD= Attention deficit hyperactivity disorder, ASD= Autism spectrum disorder, BSID=Bayley Scales of Infant Development, IOR= Inhibition of return
INTRODUCTION
Deficits in executive skills such as attention, inhibition, and processing speed have been widely reported in preterm children at school age (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Mulder, Pitchford, Hagger, & Marlow, 2009). The extent of these deficits has been linked to factors such as gestational age, birth weight, and gender (Atkinson & Braddick, 2012b; McGrath et al., 2005). Children who are born at less than 32 weeks of gestation are at greatest risk of developing deficits in executive functioning (Anderson & Doyle, 2004; Bayless & Stevenson, 2007; Clark, Woodward, Horwood, & Moor, 2008; Lindström, Lindblad, & Hjern, 2011; Luu, Ment, Allan, Schneider, & Vohr, 2011) and the prevalence may be related to increasing immaturity (Mulder et al., 2009). Despite the accumulating evidence for differences in executive function by school age, there is little known about how these skills emerge in preterm infants (van de Weijer-Bergsma, Wijnroks, & Jongmans, 2008). The identification of early markers of altered or delayed developmental trajectories is important because of the potential for early intervention to promote school readiness and the robust evidence for associations between foundational executive skills and later cognitive and academic ability (Garon, Bryson, & Smith, 2008; Lawson & Ruff, 2004; Rose, Feldman, Jankowski, & Van Rossem, 2008). The utility of eye-tracking methodology in the early detection of markers of potential executive problems warrants further investigation, particularly as widely administered behavioural scales, such as the Bayley Scales of Infant and Toddler Development (BSID) alone, may not pick up on these deficits (Spencer-Smith et al., 2015).

Most studies have relied on behavioural coding measures to investigate early executive development in infants born preterm (Rose, Feldman, & Jankowski, 2001; Ross-Sheehy, Perone, Macek, & Eschman, 2017; Sun, Mohay, & O’Callaghan, 2009). Eye-tracking methodology complements behavioural findings as it is less prone to human error and has higher spatial and temporal resolution than traditional

Anderson’s developmental model of executive function suggests that a more basic attentional control domain emerges first and lays down the foundation for later emerging higher-order skills such as goal setting, cognitive flexibility, and information processing (Anderson, 2002). Foundational executive skills such as selective attention and inhibition are thought to be intact by 12 months of age in typically developing infants (Atkinson & Braddick, 2012a). Early executive skills have been described as integral components of later cognitive development (Diamond, 1990). Lawson and Ruff (2004) found that focused attention at seven months was predictive of both behavioural and parental reports of attention in the toddler and preschool years. Similarly, Cuevas and Bell (2014), reported that attention at 5-months-old was related to executive performance on behavioural tasks at 23-,36-, and 48-months old. Previous research has indicated less optimal development of executive subsystems in preterm infants when compared with full-term controls in the first few years of life, and that these deficits become more evident with time (van de Weijer-Bergsma et al., 2008). However, despite evidence for early attentional delays predicting later executive outcomes, there has been a lack of focus on early emerging markers of executive domains in preterm infants and there have been no eye-tracking studies that have attempted to address this. This is in contrast to the investigation of social attention in preterm infants, which has been more widely investigated using eye-tracking methodology (Imafuku et al., 2016; Peña, Arias, & Dehaene-Lambertz, 2014).

Processing speed, which can be measured by investigating eye movement reaction times to target stimuli, develops rapidly in the first year of life and continues to develop with age, playing an important role in the processing of information and learning (Canfield et al., 1997; Luna, Garver, Urban, Lazar, & Sweeney, 2004). Specific deficits in processing speed have been previously reported for infants and children born preterm (Mulder et al., 2009; Rose, Feldman, & Jankowski, 2002). Aarnoudse-Moens and colleagues reported poorer processing speed in their
population of schoolage preterm children. They also showed that deficits in executive function were independent of poor processing speed (Aarnoudse-Moens, Duivenvoorden, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2012).

Selective attention involves attending to relevant information while simultaneously inhibiting distracting or irrelevant information (Desimone & Duncan, 1995). Studies using behavioural tasks of executive functioning, such as habituation, A not B, object examination, and object permanence paradigms, with infants born preterm, have reported evidence for poorer attention when compared to their full-term counterparts (Ross, Tesman, Auld, & Nass, 1992; Sun, Mohay, & O’Callaghan, 2009).

Interestingly, Anderson and colleagues administered a battery of executive measures to a cohort of preterm children and matched controls at eight years of age and found poorer performance across all attention domains, including selective attention and shifting attention, in their preterm group, except for inhibition (Anderson et al., 2011).

Inhibition of distracting, or irrelevant, information is an important aspect of attention control (Fuchs & Ansorge, 2012). IOR is the natural bias of reducing the likelihood of returning attention to previously attended locations (Johnson & Tucker, 1996). This results in a slowed response towards a location that previously contained an ignored distractor and reflects the ability to inhibit interfering information in the visual scene so that the most relevant information can be processed. It is an important process in the ability to inhibit interfering visual information, so that the most relevant information can be processed. IOR can be observed from infancy and becomes more efficient with increasing age (MacPherson, Klein, & Moore, 2003). Previous research with typically developing nine-month-old infants found longer saccade latencies in the Ignored Repetition (IR) condition, where the target appears in a location that previously held a distractor (Amso & Johnson, 2008). IOR is disrupted in children with cerebral palsy who have anterior and diffuse lesions, and children with neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD) and Tourette’s syndrome, in which there is co-morbid attention deficit hyperactivity disorder or obsessive-compulsive disorder (Schatz, Craft, White, Park, & Figiel, 2001; Yuen, Bradshaw, Sheppard, Lee, & Georgiou-Karistianis, 2005). However, IOR has been found to be intact or even enhanced in children with autism spectrum disorder (ASD) (Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2008).
IOR has not yet been explored in children born preterm using eye-tracking methodology. Children born preterm are at a greater risk for both ADHD and ASD (Johnson et al., 2010), therefore it is of interest to establish which patient group their performance will more closely reflect. A recent study found that interference control was intact in school-age children from four to 12 years born preterm but that there was a significant delay in response inhibition, a group difference that showed gradual catch up with developmental progression (Aarnoudse-Moens et al., 2012).

Early executive markers such as processing speed, attention fixation, distractor suppression, and IOR, have not been previously investigated in healthy infants born preterm with the exception of two studies which looked at visual orienting and attention in preterm infants using behavioural coding measures (Rose, Feldman, & Jankowski, 2001; Ross-Sheehy, Perone, Macek, & Eschman, 2017). Evaluating the development of specific executive skills in very preterm infants with eye-tracking methodology will establish the sensitivity of this research tool with this patient population and demonstrate the potential utility of this tool in future clinical assessment in terms of developing targeted interventions. Attention control is a multifactorial process. It is difficult to determine where the breakdown in an infant’s task performance occurs on a behavioural level. Poor performance on a task at a behavioural level may be due to a deficit or delay in one specific cognitive control process and identifying this process is important in terms of early targeted intervention. Eye-tracking paradigms can separate individual processes of interest, such as processing speed, attention fixation, distractor suppression, and IOR in the case of this study, providing more detailed information on group differences and similarities in markers of emergent executive functioning than behavioural methods.

The primary aim of this study was to compare the visual attention performance of 12-month-old preterm infants born at 30 weeks of gestation or less with full-term infants on an eye-tracking task in order to investigate the emergence of specific attentional processes. The eye-tracking task was developed based upon the task design used by Amso and Johnson (2008) as it has previously been successfully administered to infant groups and it offers the opportunity to simultaneously capture data on selective attention, inhibition (IOR and distractor suppression) and processing speed. Based on previous research, it was predicted that the preterm group would show indices of
slower processing speed, delayed IOR, and would fail to attend to relevant information and inhibit distracting information as efficiently as full-term infants. A secondary objective was to explore associations between task performance on the four variables of interest and gender and gestational age given that these factors have been previously associated with cognitive outcomes in the preterm literature (van de Weijer-Bergsma et al., 2008).

**METHOD**

**Participants**

Ethical approval was obtained from the BLINDED FOR REVIEW. Forty participants were recruited as inpatients on the neonatal unit (19 preterms) and through the maternity service (21 age-matched full-term control infants) between April 2012 and February 2014 at BLINDED FOR REVIEW, as part of the BLINDED FOR REVIEW testing battery at 12 months of age (using corrected age for preterm infants). All infants were healthy with no known co-morbid disorders. Seven infants were excluded due to insufficient data (1 preterm, 4 full-term) and non-compliance (2 preterm). The final sample included 33 datasets to be analysed including 16 preterm and 17 full-term infants. Table 1 shows that both groups were matched for gender, age at assessment, ethnicity, general cognitive ability, socioeconomic status (SES) as indicated by the Index of Multiple Deprivation, and level of maternal education. The preterm population spent 38.25 (SD=20.43) days in the intensive therapy unit at birth and 113 (SD=53.3) total days in hospital. Fifteen of the preterm infants experienced chronic lung disease/bronchopulmonary disease at birth, 11 experienced retinopathy of prematurity and eight experienced white matter damage (intraventricular haemorrhage, n=4; periventricular leukomalacia, n=4).

**TABLE 1 HERE**

**Procedure**

Testing occurred in the BLINDED FOR REVIEW. The eye-tracking task was completed as part of a larger battery of tasks, including the Bayley Scales of Infant
and Toddler Development (BSID), within a larger follow-up study. Infants were seated approximately 65 cm from a monitor used to present the paradigm (Figure 1A). If the infant was not content to sit in the baby seat alone, they could sit on the caregiver’s lap. In this instance, the caregiver was instructed to be passive during the experiment. Data were collected with a Tobii X60 Eye Tracker in conjunction with E-prime software (Psychology Software Tools Inc., PA) for the presentation of stimuli and the collection of data. The tracker has an average gaze position error of 0.5° and a spatial resolution of 0.2°; eye-movements were recorded binocularly at a sampling rate of 60 Hz. Calibration was conducted at the beginning of the experimental session using the 5-point fixation procedure in Tobii Studio software, and repeated if necessary. Fixations were defined as stable looking (+/- 0.5°) for a minimum of 100 milliseconds (ms). Once the best possible calibration was acquired, the experimenter accepted it, and the task began. The task continued until the end (total time: 4 minutes 23 seconds) or earlier if the infant became distressed.

Attention Control Paradigm

The task was chosen and developed based on previous experiments to investigate early markers of executive attention with similar age and patient populations (Amso & Johnson, 2005; Rose, Feldman, & Jankowski, 2009). In line with the original task design there are two conditions in this paradigm, both of which have a prime and a probe display. The probe display, which contains a target stimulus, is presented a short interval after the prime display which contains a target stimulus and a distractor stimulus. In the Ignored Repetition condition (IR), the target appears in a location during the probe that previously contained a distractor stimulus during the prime. In the Control condition, the target appears in a location that was not previously occupied by a distractor (Figure 1B). It is expected, due to IOR, that there will be a slower response latency towards the target in the IR condition as it is in a location that previously contained an ignored distractor. The target stimuli were a selection of animated characters that moved in synchrony with musical sounds. The prime trials contained a distractor (grey diamond) in one of four possible locations that measured 9 cm by 9 cm. At the infant’s 65 cm viewing distance, the visual angle subtended for the distractor and the target stimuli was 6.58 degrees. The distractor was not present
in the probe presentation as it can contribute to more invalid trials (Amso & Johnson, 2005; Milliken, Tipper, Houghton, & Lupiáñez, 2000).

The trials were presented in random order, with the same sequence for each child, for a total of 36 trials. The number of trials feasible for infants to complete was established through a piloting phase with infants prior to the study. Each trial consists of the prime and the probe, which last 2000 ms each. There were three inter stimulus intervals (ISIs) of 67, 200, and 550 ms (between prime and probe presentation). The ISI was manipulated in order to generate an inhibitory temporal profile as an index of selection efficiency and to compare findings with previous research in younger infants that found developmental differences in IOR efficiency dependent on the length of the ISI (Amso & Johnson, 2008). The inter trial interval was 1500 ms.

Gaze variables analysed were proportion of target fixations (focus of attention), proportion of distractor fixations (distractor susceptibility or interference control), the speed of latency to target (processing speed), and IOR. Focus of attention was analysed as the proportion of time spent fixated on the target during the probe display of the control conditions. The probe of the control condition was chosen to measure this variable in order to isolate the attention process from any potential distractor effects related to IOR or the presence of the on-screen distractor. Distractor suppression was analysed as the proportion of time spent fixated on the distractor in the prime display of both the IR and control conditions. The prime display was chosen as both the target and distractor stimuli were present on the screen at the same time. Processing speed was analysed as the saccade latency to the target stimuli in the probe of the control condition. The probe, and not the prime, was used here to isolate saccade latency to target stimuli as the probe did not contain any distractor stimuli. The control condition, rather than the IR condition was chosen to remove any potential impact of the IOR effect on saccade latency. IOR was measured as the difference in latency score between the IR and control conditions across the three ISIs. It is expected that the full-term infants will show the IOR effect at least in the 200 and 550 ms latencies based on previous research with 9-month-olds while the preterm infants may not yet be showing the IOR effect at these latencies (Amso & Johnson, 2008).
Data Analysis

Raw Gaze data files were extracted and analysed using custom written code in Matlab 2012 R2012b (The MathWorks, MA). Data pre-processing was in accordance to criteria described by Amso and Johnson (2005). Thus, individual trials were invalid if the infant fixated the distractor/did not fix the target during the prime presentation, exerted a pre-programmed eye movement toward the target location in probe trials (167 ms or less before appearance of stimulus), or the gaze was not recorded/directed elsewhere. Statistical analyses were conducted using SPSS for Mac version 21.

RESULTS

Table 2 shows that there were a similar number of valid trials for analysis in the preterm (M=22.0; SD=6.9) and full-term infant groups (M=20.5; SD=8.1).

TABLE 2 HERE

Processing Speed

We predicted that, compared to preterm infants, full-term infants would show faster saccade latencies or response times to stimuli in the probe of the control condition. Multivariate ANOVA with group as the between factor and condition (67ms, 200ms, 550ms) as the within subject factor found that processing speed was significantly different between groups ($F(3,26)=4.099, p=.017$). Using univariate ANOVAs, it was observed that the full-term infants tended to have faster latencies, although this was only significant at the 550 ISI (figure 2; $p=.009$; preterms, M=.38, SD=.09; full-term, M=.3, SD=.08).

FIGURE 2 HERE

Inhibition of Return

We predicted that full-term infants would show a greater magnitude of IOR at all ISIs when compared with preterm infants. Multivariate ANOVA with group as the between factor and condition (67ms, 200ms, 550ms) as the within subject factor
found that overall, the IOR was not reliably observed or significantly different between groups.

**Selective Attention**

Selective attention can be conceptualised as a dual process of fixating target information and inhibiting distracting information. The proportion of target fixation was used to measure the focus of attention during the probe of the control condition. Full-term infants attended to the target for a longer period of time than the preterm infants ($t(31)=-4.10, p<.001$). We predicted that reduced interference control during the prime could lead to facilitation in the IR probe for the preterm infants at 67ms (Amso & Johnson, 2008). Interference control, or distractor suppression, was measured by the proportion of time that children fixated on the distractor rather than the target during the prime across all trials. The preterm group showed a similar proportion of distractor fixation as the controls during the prime display (Table 2; figure 3).

**FIGURE 3 HERE**

**Predictors of performance**

The impact of gender and gestational age on eye-tracking variables was investigated using bivariate correlations. Gender had no effect on the eye-tracking variables for each group. Gestational age was strongly correlated with the proportion of target fixation ($r=.590, p<.005$) and processing speed ($r=-.397, p<.05$) across both groups, however these relations did not reach significance when each group was examined separately. On further investigation, only 18.8% (n=3) of the preterm group fixated the target stimuli over 40% of the target presentation time in comparison to 64.7% (n=11) of the control group (figure 4). There was no relation observed between the BSID composite and target fixation or processing speed.

**FIGURE 4 HERE**

**DISCUSSION**

In this study, we examined attentional control, a potential precursor of later executive function, in preterm and full-term infants at 12 months corrected age using eye-
tracking methodology. We found that infants born preterm had slower processing speed or were slower to shift attention and spent less time attending to or fixating on the target. Poorer target fixation was not due to increased distractor fixation in the prime display, as there was no difference between groups on this measure, suggesting that it is not an issue of disengagement or distractor susceptibility, but instead an issue of allocating sufficient attention. Taken together, this can be interpreted as evidence for poorer attention allocation in the preterm infants compared to their full-term counterparts. These findings are in line with what has been reported in studies investigating executive functions in very preterm infants using behavioural tasks and behavioural coding measures (Rose, Feldman, & Jankowski, 2001; Ross-Sheehy, Perone, Macek, & Eschman, 2017; Sun, Mohay, & O’Callaghan, 2009; Stroganova, Posikera, & Pisarevskii, 2005).

Alongside differences on behavioural tasks of executive function, Sun and colleagues (2009) also reported differences on the BSID, however when these group differences between preterm and full-term infants were partialled out, the preterm group still performed significantly poorer on the behavioural measures of executive function. We found no group differences on the BSID in the current study, and similar to Sun and colleagues (2009), both groups had composite scores within the average range. These high scores are consistent with other recent studies of preterm infants leading authors to query the high mean scores obtained on the most recent version of the BSID and call for more cautious interpretation (Lowe, Erickson, Schrader, & Duncan, 2012; Moore et al., 2012; Vohr et al., 2012). Higher BSID scores may reflect improvements in healthcare over time or a bias towards healthy infants and families from a higher socioeconomic status in the current population (the majority of maternal caregivers in this study had third level education). Nevertheless, given that the BSID is not a good predictor of later academic outcomes in preterm infants (Aylward, 2013; Hack et al., 2005), a greater focus on alternate measures of modifiable cognitive domains is warranted.

Preterm infants may show gains in visual attention in the first few weeks of life due to more environmental exposure, but these are not evident by the end of the first post-term year, as observed in the current study and by others (Bonin, Pomerleau, & Malcuit, 1998; Butcher, Kalverboer, Geuze, & Stremmelaar, 2002; Hunnìus, 2005). In
a similar study that utilised a visual expectation paradigm, infants born preterm showed similar proficiency to full-term infants at making anticipatory saccades on the basis of a regular pattern but had more issues with speed of processing and maintaining fixation, similar to findings in the current paradigm (Stroganova, Posikera, & Pisarevskii, 2005). Rose, Feldman, and Jankowski (2002) also reported similar findings for anticipatory eye movements in infants born preterm using a continuous familiarisation task where preterm infants showed markedly slower processing speed. In a further study, infants born preterm not only fixated longer, but also shifted more slowly between targets compared to full-term infants in a paired comparison paradigm and a continuous familiarization task (Rose, Feldman, Jankowski, & Caro, 2002). Thus, after an initial period of comparable alertness, preterm infants show less efficient orienting or shifting of attention, and demonstrate problems with sustaining focused attention (van de Weijer-Bergsma, Wijnroks, & Jongmans, 2008). Preliminary research with older preterm children has reported a greater amount of saccadic intrusions that make it more difficult to fixate attention, attributing these errors to the frontal eye fields (Newsham, Knox, & Cooke, 2005).

Limitations

Despite our small sample size, this is the first time that eye-tracking methodology has been applied to investigate executive functions at this early stage of development in preterm infants. A further limitation is that we did not find group differences in IOR or observe consistent effects in either group. It was expected that the full-term infants would show more efficient IOR than the pre-term infants, whose performance we expected to more closely resemble IOR responses previously shown for younger infants (Amso & Johnson, 2008). These unexpected findings could be attributed to an insufficient duration of prime display, small sample size, task design, or inherent developmental differences between this older cohort and the findings for previous cohorts (Amso & Johnson, 2008). A second limitation is that processing speed was only significantly slower in the preterm infants at 550 ms. It may be that the shorter ISIs are too short for this developmental phase leading to inconsistent results as a result of factors such as sticky fixation or this lack of difference at the other ISIs could be due to low power related to the reduced number of trials as a result of data resulting from invalid trials. Future research should consider these limitations during
the development of eye-tracking paradigms for 12-month olds.

Conclusion

The findings of the current study suggest that eye-tracking methodology could be utilised as an important tool to complement early behavioural assessment in clinical settings. Current findings reveal that processing speed and focus of attention, rather than inhibitory control, may be where performance breaks down in the attention control process of infants born preterm. Future research should further investigate these specific at-risk attentional processes using appropriate marker tasks of executive function, so that the executive development of preterm children can be better supported. Attention control processes emerge at an early developmental stage and form the basis for more complex later emerging executive skills to develop (Anderson, 2002). Given that executive impairments in adults born preterm are predictive of lower achievement across multiple real-life domains, including social, academic, and employment, interventions that target early markers of executive function should be prioritised in future research (Kroll et al., 2017). Early interventions targeted at attentional control may mitigate the development of future deficits in other executive domains, such as planning and working memory (de Haan, Bauer, Georgieff, & Nelson, 2000; Luciana, Lindeke, Georgieff, Mills, & Nelson, 1999; Mulder et al., 2009; Wass, 2015).

References


**List of Tables**

**Table 1. Group Descriptives**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preterm Group (N=16)</th>
<th>Full-term Group (N=17)</th>
<th>P-value*</th>
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<tr>
<td>Female (n)</td>
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<td>9</td>
<td>.43</td>
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<tr>
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<td>Age at Testing (weeks)</td>
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<td>Full-term Group (N=17)</td>
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<td>------------------------</td>
<td>------------------</td>
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<td>-.01 (.08)</td>
<td>.58</td>
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<td>Mean IOR</td>
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<td>Percent distractor fixated Probe</td>
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<td>13.4 (8.1)</td>
<td>.47</td>
</tr>
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</table>

*IOR=Inhibition of Return

Table 2. Mean (standard deviation) for group comparisons for eye-tracking variables of interest

**Fisher’s exact was used for two category variables, chi-square analyses were used for multiple category variables, and t-test was used for continuous variables

** IMD= The Index of Multiple Deprivation (IMD) ranges from 1 (least deprived) to 5 (most deprived)

*** BSID=Bayley Scales of Infant and Toddler Development-third version

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Figure 1. (A) The “Baby Cinema” experimental set-up using a Tobii X60 eyetracker (B) The eye-tracking paradigm consists of a Prime display followed by the Probe display after ISIs of 67, 200, and 550ms. In the control condition of the Probe display, the target appears in a location that was not previously occupied during the Prime, while in the Ignored Repetition, the target appears in a position that was previously occupied by the distractor.
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**Figure 3.** Group difference between proportion of target fixations in the probe control condition but not for distractor suppression/interference control during the prime display across both conditions.
Figure 4. The relation between target fixation and gestational age across groups. The black line illustrates the proportion of children in each group that fixated the target stimuli more than 40% of the time. Differences can be observed between groups in the amount of time that they have attended to the target.