Visual orienting and attention deficits in 5- and 10-month-old preterm infants

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Abstract

Cognitive outcomes for children born prematurely are well characterized, including increased risk for deficits in memory, attention, processing speed, and executive function. However, little is known about deficits that appear within the first 12 months, and how these early deficits contribute to later outcomes. To probe for functional deficits in visual attention, preterm and full-term infants were tested at 5 and 10 months with the Infant Orienting With Attention task (IOWA; Ross-Sheehy, Schneegans and Spencer, 2015). 5-month-old preterm infants showed significant deficits in orienting speed and task related error. However, 10-month-old preterm infants showed only selective deficits in spatial attention, particularly reflexive orienting responses, and responses that required some inhibition. These emergent deficits in spatial attention suggest preterm differences may be related to altered postnatal developmental trajectories. Moreover, we found no evidence of a dose-response relation between increased gestational risk and spatial attention. These results highlight the critical role of postnatal visual experience, and suggest that visual orienting may be a sensitive measure of attentional delay. Results reported here both inform current theoretical models of early perceptual/cognitive development, and future intervention efforts.

Keywords: Attention, preterm, infant cognition, visual orienting, spatial attention

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Visual Orienting and Attention Deficits in 5- and 10-Month-Old Preterm Infants

The development that occurs during the first few postnatal months is foundational, and evidence suggests that the building blocks of cognition are laid in infancy (Cuevas & Bell, 2010, 2011, 2014). Not surprisingly, early deficits in basic cognitive processes can have lasting negative effects well into adolescence and beyond (Rose & Feldman, 1995; Rose, Feldman, Jankowski, & Van Rossem, 2005). Previous research has demonstrated multiple areas of deficit for children born preterm, including spatial attention, working memory, visual recognition memory, processing speed, and executive function (Atkinson & Braddick, 2007; Bhutta, Cleves, Casey, Craddock, & Anand, 2002; Lindström, Lindblad, & Hjern, 2011; Rose et al., 2005; Stroganova, Posikera, & Pisarevskii, 2005). Unfortunately, preterm birth continues to be quite prevalent. In 2015, the March of Dimes reported a preterm infant birth rate of 9.6% in the United States, with even higher rates reported for minority groups. Infant neurocognitive tasks that assess skills such as visual attention, visual orienting, and eye movements are especially critical, because they are well-suited for use in very young and preterm infants, and because they may provide important insights into later individual differences. Thus, we present here data collected using the Infant Orienting With Attention (IOWA) task.

Visual behaviors are stable indices of individual differences in neurocognitive processes (Colombo & Fagen, 1990; Perone & Spencer, 2013b; Rose, Feldman, & Jankowski, 2001). Simple visual behaviors measured by the IOWA task, such as orienting, provide an index of neural development as well. For instance, orienting in a competitive context (e.g., which requires inhibiting a saccade to one location in favor of another) relies largely on frontal cortical development (e.g., frontal eye fields, dorsolateral prefrontal cortex, and supplementary eye

fields) (Johnson, 1990, 2011). As a result, orienting deficits may be sensitive indicators of clinical and sub-clinical neurological damage (Atkinson & Braddick, 2007, 2012), particularly in areas related to attentional control. For example, the “Gap Task” is used to assess an infant’s ability to disengage attention from a salient visual stimulus in favor of a new competing stimulus (Csibra, Tucker, & Johnson, 1998; Hood & Atkinson, 1993; Matsuzawa & Shimojo, 1997). Orienting in a competitive context, such as the Gap Task, has successfully been used as a marker of perinatal neural deficit and injury (Atkinson & Braddick, 2012).

The IOWA task additionally elicits the spatial cueing effect, which may also be an important marker of postnatal neural development. The spatial cueing effect refers to the robust tendency of eye movements to be faster and more accurate to peripheral targets that were preceded by a brief spatial cue than to targets that were not preceded by a cue (Posner & Petersen, 1990). This effect has been theorized to involve a covert shift of attention immediately preceding the eye movement, or saccade (Remington, Johnston, & Yantis, 1992; Theeuwes, 1994; Wolfe, Võ, Evans, & Greene, 2011; S Yantis & Jonides, 1984; Steven Yantis & Jonides, 1990), and the absence of this effect, suggests insufficiently developed parietal, and likely frontal, orienting mechanisms (Johnson, 1990; Posner & Petersen, 1990).

The IOWA task probes infants’ orienting behavior under conditions that involve visual competition like the Gap Task as well as stimuli preceded by a cue and stimuli not preceded by a cue to elicit the spatial cueing effect. Thus, the IOWA task evokes responding across distinct brain areas. The IOWA task also yields several indices of individual differences in attention that may enable us to identify specific attentional deficits in preterm infants. The broad empirical foundation of the IOWA task makes it an ideal means of assessing individual differences in

infant attention. Moreover, even young preterm infants readily engage in orienting behavior. Thus, the IOWA task eliminates the behavioral demands associated with current neurocognitive assessment tools (Bhutta et al., 2002; Glascoe et al., 1992; Harris, Megens, Backman, & Hayes, 2005; Lindström et al., 2011; McGowan, Alderdice, Holmes, & Johnston, 2011), and focuses measurement specifically on visual attention. The present investigation was guided by three central goals. First, we aimed to demonstrate that preterm infants tolerate the IOWA task and contribute enough data to provide robust measures of *individual* differences in attention. Second, we sought to determine if the IOWA task is sensitive enough to detect *developmental* differences in orienting speed, error, and visuospatial attention in preterm infants. Finally, we sought to determine if preterm (age corrected) infants were significantly different from full term infants with respect to accuracy, reaction time, and spatial attention measures.

Method

Participants

We tested 108 infants, 54 preterm infants (gestational age < 37wks), and compared them to 54 full-term infants¹. Preterm infants were divided into two groups based on corrected age (chronological age minus weeks born preterm). This provides the most stringent assessment of preterm risk because it essentially equates preterm and fullterm infants on days since conception, a proxy for physical maturity. Thus, any significant between-group differences are likely to be driven by disruption of developmental processes that typically occur late in gestation, morbidity associated with prematurity, or (as may be the case with visual studies), the effects of increased early sensory experience for preterm infants. We divided preterm and fullterm infants into two age groups, 5 and 10 months (corrected): 5-month-old preterm infants

(mean = 4.44, range = 2.04-6.74, mean gestation age = 32.58 weeks, mean birth weight = 1985.04 grams), 5-month-old full-term infants (mean = 5.22, range = 2.92-6.44), 10-month-old preterm infants (mean = 10.26, range = 7.11-14.57, mean gestation age = 31.11 weeks, mean birth weight = 1941.11 grams), and 10-month-old fullterm infants (mean = 9.94, range = 7.11-14.31). [Note that preterm infants were a sample of opportunity, recruited at various ages during routine high-risk follow-up visits at a large tertiary care children's hospital. Though resulting age ranges are broad, the full-term comparison group was blindly selected to approximate the age distribution of the preterm groups]. Interested parents of preterm infants were consented during their follow-up appointment, and the infants were tested in a nearby lab room. The names of full-term infants were obtained from county birth records, and all parents were contacted by letter and received a follow-up phone call to schedule an appointment at a non-clinical research lab housed within a large local university. Families were not paid for their participation, but infants received a small toy and full-term infants' parents' parking expenses were reimbursed.

Stimuli, Design, and Procedure

All infants were assessed in the IOWA task. All procedures were approved by the BLINDED Institutional Review Board (200701759). A detailed description of the methods are reported elsewhere (Ross-Sheehy, Schneegans, & Spencer, 2015), and will be summarized here. A Macintosh G5 computer was used to present the stimuli on a 37" LCD color monitor. During the experimental session, infants sat on their parents lap 100 cm in front of the monitor. A trained observer sat out of sight and recorded infant and adult eye movements (latency and direction) via live video feed.

The IOWA task consists of a mixture of 3 different cued attention conditions that vary in their degree of cue/target competitiveness, and 2 control conditions that serve as baseline measures of gross orienting speed to the target in lieu of spatial pre-cuing (Fig 1). Each of the three experimental conditions contained a 100ms spatial cue (small black dot measuring 1 degree in diameter) paired with a 500 Hz pure tone. Spatial cues appeared 11 degrees to the left or right of fixation, either in the same location as the target (valid), contralateral to the target (invalid), or on both sides (double). Neither of the two control conditions contained a spatial cue: The tone condition contained only the 100ms tone, and the no cue condition contained neither a spatial nor tone cue. Targets in each condition consisted of colorful images of everyday objects (e.g., cheeseburger, mailbox, coffee mug, etc.) randomly selected from a pool of 182 possible targets. All targets subtended 4.8 degrees (w) by 4.4 degrees (h), and novelty, total area, contour, chromatic and luminance contrast varied randomly across targets.

Before each trial, a fixation stimulus was presented in the center of the monitor to attract attention to that location. Once the infant looked, a key was pressed that ended the fixation stimulus, and initiated a 100ms cue period, followed by a 100ms delay interval, then finally the presentation of the target to the left or right of fixation. This target remained visible until the infant made an eye movement, and the observer made a speeded button press indicating a look to either the left or the right. If an infant did not make an eye movement to the target within 2000ms of the target presentation, the trial was ended and repeated, beginning again with the fixation stimulus. Each infant saw at least 40 trials and up to 7 blocks of 10 trials, for a total of 70 trials. Each block contained two of each cue condition (one with target on left, and one with target on right) presented in random order. The timing and

accuracy of these responses served as the primary dependent measures.

Measures. Reaction times and directional responses were calculated for each trial using frame-by-frame coding. Videos were captured at 30 fps or 33ms per frame, allowing for accurate coding of both directionality and latency of the infant's first saccade. Moreover, frame-by-frame coding is externally verifiable, and tends to produce more data points per infant. Responses were coded as "correct" if the infant's first saccade was to the side of the display that contained the target, and "incorrect" for any other response. Only correct responses were used for reaction time measures. Twenty-five percent of the data were recoded by a second trained observer. Reliability was very high ($r = .98$, Mean Difference = 24.01ms, SD = 11ms). Group reaction time and accuracy scores were calculated for each condition.

Results

Our results are divided into four sections. The first section describes group and developmental differences in reaction time. The second section describes group and developmental differences in accuracy. The third section focuses on group differences in spatial attention, and the last section explores gestational risk and group differences in orienting speed, accuracy and spatial attention.

Reaction Time by Age and Birth Status. Group Reaction Time data were analyzed using a 2x2x5 repeated measures ANOVA, with Age (5mo and 10mo) and Birth Status (preterm and fullterm) as between-subject variables, and Condition (valid, invalid, double, tone only, and no cue) as the within subjects variable. Results revealed a significant main effect of Condition, $F(4, 416)=98.50$, $p<.001$, $\eta p^2=.486$, indicating the cue manipulations significantly influenced RT. There was also a significant main effect of Age, $F(1,104)=11.62$, $p=.001$, $\eta p^2=.100$, and a

significant main effect of Birth Status, $F(1,104)=12.487$, $p=.001$, $\eta^2=.107$, both of which were subsumed by a significant Age by Birth Status interaction, $F(1,104)=5.30$, $p=.023$, $\eta^2=.048$ (Fig 2, top panel). Figure 2 reveals that the effect of prematurity on orienting speed is clearly apparent at 5-months, with effects disappearing by 10-months. To probe this interaction, we conducted follow up simple effect tests, and found preterm infants to be significantly slower than the full-term infants at 5-months, $F(1,104)=17.023$, $p<.001$, $\eta^2=.141$, but not 10-months-of-age, $F(1,104)=.759$, $p=.386$, $\eta^2=.007$. Additionally, an inspection of Figure 2 reveals classic spatial cueing effects. Overall, infants showed the fastest reaction times for the valid cues, $M=221.61$, $SE=7.48$, and slowest reaction times for the invalid cues, $M=315.72$, $SE=7.77$. Means were as follows for the remaining three conditions: double cue, $M=257.52$, $SE=7.28$; no cue, $M=297.69$, $SE=7.53$, tone cue, $M=300.13$, $SE=7.16$. Though 5-month-old preterm infants show *qualitatively* similar spatial cueing effects, they are slower to orient in all cue conditions, indicating relatively slow processing speed, oculomotor orienting responses, or both. We will more closely examine age, birth status, and cue condition effects in our *Spatial Attention* analyses below.

Accuracy by Age and Birth Status. Group accuracy data were analyzed using the same 2x2x5 repeated measures ANOVA, with Age (5mo and 10mo) and Birth Status (preterm and fullterm) as between-subject variables, and Condition (valid, invalid, double, tone only, and no cue) as the within-subjects variable. Results revealed a significant main effect of Condition, $F(4, 416)=142.107$, $p<.001$, $\eta^2=.577$. Results additionally revealed a significant main effect of Birth Status, $F(1, 104)=6.77$, $p=.011$, $\eta^2=.061$, as well as two significant interactions: Condition by Age, $F(4, 416)=2.93$, $p=.021$, $\eta^2=.027$, and Condition by Birth Status, $F(4, 416)=5.82$, $p<.001$,

$\eta p^2=.053$ (Fig 2, bottom panel). Figure 2 once again reveals clear age by birth status effects, with 5-month-old preterm infants showing unusually low error rates for the invalid cue condition. Follow up simple effects tests confirmed this observation, demonstrating preterm infants to be significantly higher in accuracy than the full-term infants at 5-months, $F(1,104)=5.47$, $p=.021$, $\eta p^2=.050$, but not 10-months-of-age, $F(1,104)=1.80$, $p=.183$, $\eta p^2=.017$.

Though this finding may seem counterintuitive, it is important to note that some amount of error is appropriate, and reflects high sensitivity to the spatial cue, and processing speeds that are sufficiently fast to allow an infant to program and initiate a saccade *before* the appearance of the contralateral target (<200ms). If, however, infants are still in the process of planning a saccade when the contralateral target appears, they must *inhibit* the planned saccade to the cue, and program a new saccade to the contralateral target, resulting in a slower RT, and a “correct” response. Previous work suggests error rates for the invalid cue condition increase between 5 and 10 months of age, and then appear to plateau (Ross-Sheehy et al., 2015).

It’s important to consider error rate and orienting speed together. For example, infants with a low error rate (high percent correct) and relatively slow reaction times are likely *slow processors*, whereas infants with a low error rate and relatively fast reaction times are likely *fast processors*, with *good inhibition*. In contrast, infants with high error rates and relatively fast reaction times are likely *fast processors*, with *poor inhibition*. To facilitate these qualitative comparisons, and to make the comparison of individual infants possible, we have created a series of *spatial attention scores*, presented below.

Spatial Attention by Birth Status. Though group reaction time and accuracy means

reveal qualitative similarities between preterm and full term infants, birth status and age clearly interact in complex ways. Ross-Sheehy et al. (2015) developed a series of difference scores that enable us to examine group differences in spatial cueing effects across the various cue conditions. These scores are then normalized using each infants baseline orienting speed (tone only cue condition), so we can examine the specific effects of the cue independent of sometimes large individual differences in orienting speed. Additionally, because spatial attention scores are essentially difference scores, infants' scores should scale with spatial cueing effects, such that strong cue effects produce high attention scores, whereas weak or nonexistent attention scores approach zero. The spatial attention score calculations and analyses are described below.

Cue Facilitation ((baseline RT- valid RT)/baseline RT). Higher scores indicate the infant's RT to the target was substantially reduced by a valid spatial precue. Separate one-way ANOVAs conducted for each age revealed a significant difference between preterm and full term infants at 10-months, $F(1,52)=4.46$ $p=.040$, $\eta^2 = .079$, but not at 5-months, $F(1,52)=1.09$ $p=.302$, $\eta^2=.020$, indicating the preterm 10-month-old infants were significantly lower in facilitation than fullterm 10-month-old infants. When comparing facilitation scores to zero (zero indicating no difference between valid cues and tone only cues), results reveal cue facilitation scores to be significantly greater than zero for every group: 5-month preterm infants, $t(26)=5.89$, $p<.001$, $\delta=2.31$, 10-month preterm infants, $t(26)=7.68$, $p<.001$, $\delta=3.01$, 5-month full term infants, $t(26)=7.88$, $p<.001$, $\delta=3.09$ and 10-month full term infants, $t(26)=12.02$, $p<.001$, $\delta=4.71$, demonstrating that all infants showed significant spatial cueing effects, though 10-month-old preterm infants showed significantly less. This suggests a relatively late appearing deficit in

covert attention and reflexive orienting, processes that are typically developing between 2-6 months (Johnson, 2011)

Cue Interference ((invalid RT- baseline RT)/baseline RT). Higher scores indicate infant's RT to the target was substantially increased by an invalid spatial precue. Separate one-way ANOVAs conducted for each age revealed a marginal difference between preterm and full term infants at 10-months, $F(1,52)=2.84$ $p=.098$, $\eta p^2=.052$, and no difference at 5-months, $F(1,52)=.29$ $p=.591$, $\eta p^2=.006$. Interestingly, comparisons to zero are nonsignificant for every group except 10-month-old preterm infants, $t(26)=3.55$, $p=.001$, $\delta=1.39$. Though previous work (Ross-Sheehy et al., 2015) did find significant interference effects for 10-month-old typically developing infants, the effect was smaller than for 7-month-old infants, likely reflecting increasing frontal cortical involvement at 10-months. Further, the broad age bins of the current sample may have contributed to slightly more mature profile of performance for our full-term 10-month-old infants relative to previous work (Ross-Sheehy et al., 2015). In this sample, only preterm 10-month-old infants demonstrated significant interference effects, suggesting relative deficits in the ability to quickly cancel a saccade plan, shift attention, and reorient the eyes. This pattern of deficits suggests delayed maturation of cortical areas responsible for saccade cancelling, shifting, and/or inhibition, possibly including parietal cortex, frontal eye fields, supplementary eye fields, as well as more frontal areas (Johnson, 2011).

Cue Competition ((double RT- valid RT)/baseline RT). Higher scores reflect a high degree of visual response competition, or saccade inhibition, when presented with two competing attention cues. Separate one-way ANOVAs conducted for each age revealed no significant difference between preterm and full term infants either at 5-months, $F(1,52)=.127$ $p=.723$,

$\eta^2=.002$, or 10-months, $F(1,52)=.194$ $p=.661$, $\eta^2=.004$. When comparing cue competition scores to zero, all groups were significant: 5-month preterm infants, $t(26)=2.43$, $p=.022$, $\delta=.95$, 10-month preterm infants, $t(26)=6.014$, $p<.001$, $\delta=2.36$, 5-month full term infants, $t(26)=2.289$, $p=.030$, $\delta=.90$, and 10-month full term infants, $t(26)=7.35$, $p<.001$, $\delta=2.88$. Thus, all infants were significantly slower in the double cue condition than the valid cue condition, and there was no clear effect of prematurity. These findings suggests all infants are experiencing visual competition from the double spatial cues, presumably requiring cortical involvement to resolve (Atkinson et al., 2008; Johnson, 2011). Cue competition scores near zero suggest infants lack the ability to perceive multiple simultaneous onsets. It is somewhat surprising this comparison was not significant, as previous work has demonstrated a clear effect of prematurity on the development of cortical visual areas (Atkinson et al., 2008).

Mean Reaction Time (mean RT across all conditions). Higher scores reflect relatively slow overall orienting speeds. Separate one-way ANOVAs conducted for each age revealed a significant difference between preterm and full term infants at 5-months, $F(1,52)=12.94$ $p=.001$, $\eta^2=.199$, but not at 10-months, $F(1,52)=1.11$ $p=.297$, $\eta^2=.021$. This is interesting, and suggests that early delays in RT appear to resolve by around 10-months-of age. This implies that speed of orienting reflects both physical maturation (recall we used corrected ages for preterm infants, equating for post-conception age and physical maturation), *and* postnatal visual experience. If RT were driven primarily by physical maturation, we might expect 5-month-old preterm infants to look just like typically developing 5-month-olds, but they do not. Likewise, if RT were driven primarily by postnatal visual experience, we might expect preterm infants to show slightly faster RTs than age-matched controls, as matching on corrected age results in increased visual

experience for preterm infants, ($M = 8.16$ weeks preterm, $SD = 4.21$).

Task Error ($1 - (\text{average of double \% correct \& invalid \% correct})$). Higher scores reflect a higher degree of interference from the invalid spatial cues that were present in both the double % correct and invalid % correct conditions. High task error requires: 1) infants are sensitive to the spatial cue, 2) processing speeds are fast enough to complete saccade planning before presentation of the target, and 3) the ability to inhibit or cancel a preplanned saccade is limited. Separate one-way ANOVAs conducted for each age revealed a significant difference between preterm and full term infants at 5-months, $F(1,52)=11.109$ $p=.002$, $\eta p^2=.176$, but not at 10-months, $F(1,52)=.1.624$ $p=.208$, $\eta p^2=.030$. This task-specific difference in error coupled with significantly slower RTs likely suggests that 5-month-old preterm infants are simply slower to process and respond to spatial cues. Similar to RT, this Task Error appears to reach near typical levels by around 10 months (corrected).

Baseline Error ($1 - \text{average}(\text{valid \% correct, tone \% correct, no cue \% correct})$). Higher scores reflect a high degree of off-task behavior, or non-selective orienting. This is a good measure of vigilance and task engagement, and high baseline errors may further suggest visual deficits such as retinopathy of prematurity. Separate one-way ANOVAs conducted for each age revealed no significant difference between preterm and full term infants either at 5-months, $F(1,52)=.063$ $p=.802$, $\eta p^2=.001$, or 10-months, $F(1,52)=.00$ $p=.983$, $\eta p^2=.000$. The lack of a birth status effect is important, and suggests that preterm infants are able to see the spatial cue, can stay “on task” as well as typically developing infants, and are responding selectively to the visual events.

Gestational Risk and Group Differences. The IOWA Task provides a rich set of

attentional measures at the level of the individual. These individual composite scores reveal some interesting trends, and we see here several possibilities for infant attention style classifications, or *attentional phenotypes*, that may predict cognitive outcome. As a first step toward identifying these differential patterns of attention, we conducted separate Pearson Correlations (two-tailed) for each birth cohort (preterm and full term infants) examining relations between Facilitation, Interference, Competition, Reaction Time, Task Error, Baseline Error, and Age (uncorrected). For preterm infants, we also included Weeks Preterm, and Birthweight (see Table 1). This analysis revealed several significant correlations unique to each cohort. For example, Interference is correlated with Reaction Time ($r = -0.29$), Task Error ($r = 0.47$), and Age ($r = 0.29$) for preterm infants, but not for fullterm infants. These findings suggest that the fastest preterm infants are older, and show high task-specific errors, strengthening our previous suggestion that preterm infants “catch up” in terms of processing and orienting speed, but may be delayed in their ability to inhibit the automatic saccades to the invalid cue. In addition, Mean RT is also related to Baseline Errors for preterm infants ($r = 0.38$), suggesting that the slowest preterm infants may indeed be struggling to stay on task. Finally, the significant relation between Competition and Interference unique to the fullterm infants ($r = 0.37$), suggests the increasing importance of inhibition to help resolve cue/target conflict as in both the double and invalid cue conditions. Interestingly, this analysis produced no evidence of a dose-response effect of gestational age on orienting speed, accuracy, and spatial attention – suggesting that preterm deficits in attention, speed and orienting were distributed across all gestational ages. This counterintuitive finding suggests attentional mechanisms are either developing very late in gestation, or that postnatal developmental trajectories are disrupted by

the events and/or morbidity associated with preterm birth, as even minimal gestational risk appears to influence performance on visual orienting assessments.

In summary, this study had three goals. First, we sought to show that the IOWA task was suitable for use with preterm infants and yielded measures of individual differences in attention. Second, we sought to show that the IOWA task can detect developmental differences in preterm infants' attentional abilities. Third, we sought to test whether the IOWA task could differentiate preterm and term infants based on their attentional abilities. We contend that the present study achieved all three goals. In particular, the IOWA task yielded a number of measures of individual differences in attention. Among other observations, these measures revealed no dose-response relation with respect to gestational age. The IOWA task also revealed specific attentional deficits in preterm infants relative to term infants *that emerged with age*. In the General Discussion, we focus on our observation of attentional deficits in preterm infants, insights into the underlying neurocognitive processes, and the broader implications of this study.

General Discussion

Preterm infants exhibit deficits in foundational attentional and cognitive processes that persist into adolescence (Rose & Feldman, 1995; Rose et al., 2005). There is a need for continued development of innovative early assessment tools that are sensitive enough to detect even subtle attentional and cognitive deficits in preterm infants. Such assessments can help identify individuals who may need early cognitive intervention and, perhaps, help tailor interventions to the specific needs of individual infants. A valuable early assessment tool must be easily administered and meaningfully differentiate individuals based on their visual-cognitive

abilities. One attractive feature of the IOWA task is that it is easily administered. The IOWA task also includes numerous data points across a number of conditions designed to identify specific attentional phenotypes at the level of the individual (e.g., cue interference). Below, we discuss key findings from preterm infants' performance in the IOWA task and their implications for understanding the attentional deficits of preterm infants.

We observed two key findings that characterize preterm infants' attentional deficits over the course of the first year of life. The first finding was that 5-month-old preterm infants exhibited slower RTs across all conditions than similarly aged term infants. By 10 months of age, preterm and term infants exhibited nearly identical patterns of RT across conditions. This pattern of results suggests that preterm infants more slowly process a peripheral stimulus, program and execute an eye movement, or both at 5 months of age but "catch up" by 10 months of age. Interestingly, the slower RTs of 5-month-old infants led them to perform more accurately in the invalid condition, resulting in significantly lower task error. We suspect that this is attributable to preterm infants' slower processing of the precue, which does not result in a saccade plan. This, in turn, enables them to quickly shift attention and execute an eye movement to the target.

The second finding was that a specific attentional deficit emerged in preterm infants by 10 months of age. Specifically, 10-month-old preterm infants exhibited significantly less cue facilitation and marginally more cue interference than term infants. Recall that higher cue facilitation scores indicate the infant's RT to the target are substantially reduced by a valid spatial precue. Preterm infants' cue facilitation scores were significantly lower than similarly aged term infants. This indicates a relatively late appearing deficit in covert attention and

reflexive orienting, processes that are typically developing between 2 and 6 months of age (Johnson, 2011). Ten-month-old preterm infants also exhibited marginally more cue interference than similarly aged term infants. Recall that high cue interference scores indicate infant's RT to the target are substantially increased by an invalid spatial precue. We found that only 10-month-old preterm infants demonstrated significant cue interference, which suggests a deficit in the ability to quickly inhibit a saccade plan, shift attention, and reorient the eyes. This deficit may arise from atypical neural development in cortical areas responsible for saccade cancelling, shifting, and/or inhibition, including parietal cortex, frontal eye fields, supplementary eye fields, and frontal areas (Johnson, 2011).

The aforementioned findings suggest that the IOWA task can detect specific attentional deficits in preterm infants, but what neurocognitive processes might underlie such deficits? We can gain some insight into this issue from a neural process model of visual orienting proposed by Ross-Sheehy et al. (2015). They proposed a dynamic neural field (DNF) model that simulates developmental change in term infants' performance in the IOWA task. Briefly, the model consists of two interactive neuronal layers defined over a single horizontal axis of retinocentric visual space. One layer is an *attention field* that responds to the presence of stimuli at their spatial location (e.g., precue). Strong neural activation in the attention field generates activation in similarly tuned neurons in a *saccade motor field*, which, in turn, generates an eye movement to that location.

Ross-Sheehy et al. (2015) proposed that developmental change in infants' performance was driven by increases in the excitatory and inhibitory interactions governing the processing of stimuli and generation of eye movements within the model (Perone, Simmering, & Spencer,

2011; Perone & Spencer, 2013a, 2013b, 2014). With strong interactions, the spatial attention field responds more robustly to the cue and the target, quickly generating strong activation in the saccade motor field. This leads to increasingly fast eye movements and decreased reaction times over development, as was observed empirically.

Strong interactions also influence the execution of erroneous eye movements (i.e., errors). Consider an example of the invalid condition. In this condition, when the cue appears it selectively activates neurons in the spatial attention field tuned to its location. Importantly, this activation suppresses activation at all other sites via long-range inhibition. Consequently, when a target appears at a different location, activation in the spatial attention field is slow to build and slow to feed into the saccade motor field. This leads to a relatively slower reaction time in the invalid condition. Critically, as neural interactions increase in strength over development, the cue alone is even more likely to drive an eye movement, leading to an erroneous response in the invalid condition. Over development, then, sensitivity to the cue increases and so do the proportion of erroneous responses.

With this understanding of the neural dynamics underlying term infants' performance in the IOWA task, we can begin to gain some insight into what might be driving preterm infants' performance. Perone & Spencer (2013a) simulated the gaze behavior of preterm infants in a different DNF model by weakening excitatory and inhibitory interactions relative to a term infant version of the model. The slow RTs across conditions for the young preterm infants indicates the slow buildup of activation in the spatial attention field and subsequently the saccade motor field, characteristic of weak excitation. What about error rates? The fact that young preterm infants are highly accurate in the invalid condition early in development

indicates that long-range inhibition may also be weak. In particular, the activation associated with the cue in the attention field might not slow activation associated with the target due to weak inhibition, leading to an erroneous fast eye movement to the target (for additional details on the model dynamics, see Ross-Sheehy et al., 2015). The DNF model might provide a fruitful framework for thinking about the neurocognitive deficits that might underlie attentional deficits in preterm infants.

Conclusion

The IOWA task shows promise in identifying unique attentional deficits in preterm infants, which is a crucial first step in unpacking the precursors that contribute to later attentional and cognitive deficits (Bayless & Stevenson, 2007; Botting, Powls, Cooke, & Marlow, 1998; Grunau, Whitfield, & Fay, 2004; Isaacs et al., 2004; Rose et al., 2005; Søltnes et al., 2015; Taylor, Klein, Minich, & Hack, 2000). Interestingly, most deficits in preterm infants have been studied in extremely low birthweight infants (<1000g). Here, we found evidence of delay even in healthy, low risk preterm infants. This highlights the need for early assessments that are sensitive enough to detect subtle deficits in foundational attentional and cognitive processes.

The IOWA task also shows promise as an early assessment tool because it is easily administered and sensitive to individual differences in attentional ability. Critically, more research is needed to understand precisely how attentional deficits that can be identified in the IOWA task influence later cognitive development. Nevertheless, the findings in the present report indicate that preterm infants exhibit attentional deficits and suggest that intervention efforts that train visual behaviors early could capitalize on the plasticity of the brain during the first year of life (Alcauter et al., 2014; Ramenghi et al., 2007; Short et al., 2013). Early

intervention for attentional processes might be especially crucial in light of our observation that there is no dose-response relations with respect to gestational age and attention. Early postnatal interventions that train attention might reshape the trajectory of attentional development in at-risk infants and eliminate the emergent deficits observed here.

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Figure legends

Figure 1: Experimental and control conditions for the Infant Orienting With Attention, or IOWA Task.

Figure 2: Reaction time measures (correct trials only) and proportion correct by condition. Error bars represent ± 1 SEM.

Figure 3: Attention scores for 5- and 10-month-old full- and preterm infants. Note: Asterisks indicate significant Birth Status differences. Significance is indicated as follows: * $p \leq .05$, ** $p \leq .01$, and *** $p \leq .001$. Error bars represent ± 1 SEM.

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Table 1. Correlations examining relations between Facilitation, Interference, Competition, Reaction Time, Task Error, Baseline Error, and Age (uncorrected) for fullterm infants (n = 54) in addition to Weeks Preterm and Birthweight for preterm infants (n = 54). Significance is indicated as follows: * $p \leq .05$, ** $p \leq .01$, and *** $p \leq .001$.

Variables		1.	2.	3.	4.	5.	6.	7.	8.	9.
Preterm	1. Facilitation	-								
	2. Interference	-0.17	-							
	3. Competition	0.52**	0.23	-						
	4. Reaction Time	-0.26	-0.29*	-0.18	-					
	5. Task Error	0.15	.47**	0.12	-0.22	-				
	6. Baseline Error	0.21	-0.11	0.02	0.38**	0.07	-			
	7. Age (Uncorrected)	0.14	0.29*	0.18	-0.48**	0.01	-0.20	-		
	8. Weeks Preterm	-0.02	-0.02	-0.10	-0.14	-0.17	-0.18	0.31*	-	
	9. BW†	-0.06	-0.00	-0.14	0.22	0.13	0.15	-0.18	0.86***	-
Fullterm	1. Facilitation	-								
	2. Interference	-0.12	-							
	3. Competition	0.60**	0.37**	-						
	4. Reaction Time	-0.52**	0.10	-0.19	-					
	5. Task Error	0.53**	-0.10	0.13	-0.23	-				
	6. Baseline Error	0.10	-0.31*	-0.17	-0.10	0.08	-			
	7. Age (Uncorrected)	0.19	-0.14	0.19	-0.24	-0.02	-0.23	-		

† Birthweight data missing for 11 infants

Footnotes

¹ Note, a subset of the full-term infants were reported elsewhere (Ross-Sheehy, Schneegans, & Spencer, 2015) and are were randomly selected to roughly match the Mean and SD of the preterm infant sample ages (corrected).

Reaction time (top panel) and accuracy (bottom panel) by age and birth status

Attention scores (top panel), error and RT (bottom panel) by age and birth status