



CLINICAL RESEARCH ARTICLE

Visual tracking at 4 months in preterm infants predicts 6.5-year cognition and attention

Ylva Fredriksson Kaul¹✉, Kerstin Rosander², Claes von Hofsten², Katarina Strand Brodd^{1,3}, Gerd Holmström⁴ and Lena Hellström-Westas¹

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BACKGROUND: Visual tracking of moving objects requires sustained attention and prediction of the object's trajectory. We tested the hypothesis that measures of eye-head tracking of moving objects are associated to long-term neurodevelopment in very preterm infants.

METHODS: Visual tracking performance was assessed at 4 month's corrected age in 57 infants with gestational age <32 weeks. An object moved in front of the infant with sinusoidal or triangular (i.e. abrupt) turns of the direction. Gaze gain, smooth pursuit gain, and timing of gaze to object motion were analyzed. At 6.5 years the Wechsler Intelligence Scale for Children (WISC-IV), the Brown Attention Deficit Disorder (Brown ADD), and visual examination were performed.

RESULTS: Gaze gain and smooth pursuit gain at 4 months were strongly related to all WISC-IV parameters at 6.5 years. Gaze gain for the triangular and sinusoidal motion patterns related similarly to the cognitive scores. For the sinusoidal motion pattern, timing related to most Brown ADD parameters. There were no statistically significant differences in associations dependent on motion pattern. Visual function did not influence the results.

CONCLUSION: The ability to attend to and smoothly track a moving object in infancy is an early marker of cognition and attention at 6.5 years.

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IMPACT:

- Potential long-term implications of infant visual tracking of moving objects for school-age neurodevelopment has not been previously studied in very preterm infants.
- Early coordination of eye and head movements in gaze gain, smooth pursuit, and timing of gaze to object motion are closely associated with cognition and attention at 6.5 years.
- As related functions at 6.5 years include perceptual and verbal skills, working memory, processing speed and attention, predictive elements in gaze tracking of moving objects might be a suitable target for future intervention studies.

INTRODUCTION

Common cognitive sequelae in children born very preterm include reductions in overall intelligence, deficits in verbal reasoning, perceptual ability, processing speed, and working memory.^{1,2} The prevalence of ADD (attention deficit disorder) and ADHD (attention deficit hyperactivity disorder)-related symptoms is also higher in children born very preterm than in term-born peers.³

Several studies have demonstrated that early visual tracking performance is closely associated with development of higher cognitive functions.^{4–6} The available data indicate that a few basic abilities set the stage for later complex functions of language, thinking, and reasoning,^{5,7} and that one such basic ability could be the ability to effectively visually track objects in motion.

Optimal visual tracking of objects in motion is accomplished by a combination of smooth pursuit eye movements, head

movements and catch-up saccades, together comprising the gaze. Saccades dominate in the newborn infant, while smooth pursuit eye movements develop in early infancy and at around 4 months of age typically developing children perform almost at adult levels.⁸ In addition, smooth visual tracking presumes sustained attention to the moving object.⁹ The ability to focus attention on objects and events in the environment is present at birth¹⁰ and the development of smooth pursuit is intimately associated with the development of attention.¹¹

Visual tracking is supported by a neural network called the dorsal stream, which can be characterized as "vision for action".^{12,13} The dorsal stream is vulnerable to white matter injury,¹⁴ which is prevalent in preterm infants and often compromise the visual pathways.^{4,15,16} In 6- to 7-year-old children born very preterm, white matter injury engaging the dorsal stream

¹Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden. ²Department of Psychology, Uppsala University, Uppsala, Sweden. ³Centre for Clinical Research Sörmland, Uppsala University, Uppsala, Sweden. ⁴Department of Neuroscience/Ophthalmology, Uppsala University, Uppsala, Sweden.

✉email: ylva.fredriksson_kaul@kbh.uu.se

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is related to deficits in attentional control, location memory, visual-cognitive ability, selective attention, and executive function.¹⁷

Deficits in visual tracking ability involving smooth pursuit eye movement and saccades are affected by white matter alterations¹⁶ and have been associated with a number of neurodevelopmental and behavioral disorders such as dyslexia, ADHD, autism, and anxiety.¹⁸

Optimal visual tracking of moving objects also relies on the ability to predict the object's trajectory. The ability to predict upcoming visual stimuli is present at 2 months of age in typically developing infants.⁸ Emberson et al.⁶ showed that whereas very preterm 6-month-old infants had typical responses to presented visual stimuli, they showed substantially reduced neural responses to predicted visual stimuli. The investigators suggested that the inability to predict visual stimuli might result in later neurodevelopmental delays in the preterm infants.

We hypothesized that the ability to predict object motion during smooth visual tracking is part of the engine that drives cognitive development. In order to function in a changing environment, the infant has to focus and move in response to predicted future events.¹⁹ When visually tracking an object, the neurosensory feedback loop takes at least 0.20–0.25 s,²⁰ which means, that if an infants' actions exclusively rely on feedback it will constantly lag the changing surrounding conditions. In contrast, if future events can be predicted the child can prepare for what is going to happen next. The predictive control is facilitated when objects move according to experienced regularities. Human movements are usually performed according to sinusoidal motion patterns, and tend to slow down, turn and accelerate again.²¹ When an object abruptly changes motion (triangular motion pattern), the visual tracking can become predictive if the motion shows some form of regularity or repetitiveness.⁸

Sinusoidal motion patterns allow for prediction at both a local level (the continuous motion change) and at a global level (the periodicity of the motion) while a triangular motion pattern can only be used for prediction at a global level. Rosander and von Hofsten⁸ found that by 17 weeks of age, typically developing infants anticipated repeated abrupt reversals of linear motions. In previous studies, we showed that visual tracking performance at 4 month's corrected age was delayed compared to controls²² and predicted neurodevelopment at 3 years²³ in children born very preterm. The most important tracking parameter for future neurodevelopment was how close the infant's gaze followed the object's motion amplitude. This, in turn, was dependent on the infants' ability to coordinate smooth pursuit eye movements, head movements, and saccades when tracking the object.²³ As in most other goal-directed activities, attention is required both in the tracking and neurodevelopmental tasks.²⁴

In the present study we hypothesized that early visual tracking performance in children born very preterm is a determinant of cognitive development and closely associated to attention. First, we aimed at investigating whether the ability to visually track sinusoidal and triangular (abruptly changing) motion patterns at 4 month's corrected age predicted cognitive abilities at 6.5 years. Secondly, as visual tracking also depends on ability to focus attention, we aimed to investigate how the early visual tracking performance during the two different movement patterns was related to attention at 6.5 years.

METHODS

The LOVIS-study (LOngitudinal multidisciplinary study of VISuomotor capacity in very preterm infants) is a prospective population-based study that aimed to investigate visual perception and its long-term consequences in children born very preterm (gestational age 22–31 weeks) during the years 2004–2007 at Uppsala University Hospital, Sweden. Written parental consent was obtained and the regional ethical committee approved the study (Ups 03-665).

Table 1. Background characteristics of the study population, very preterm infants with gestational age <32 weeks. Values are mean (standard deviations) or number (percentages).

Infant data		
Perinatal data	<i>n</i> = 57	
Antenatal steroids ^a , <i>n</i>		41 (72%)
Cesarean section, <i>n</i>		30 (53%)
Gestational age, weeks		28.1 (2.6)
Birthweight, g		1149 (361)
Small for gestational age ^b , <i>n</i>		9 (16%)
Girl, <i>n</i>		24 (42%)
Neonatal risk factors	<i>n</i> = 57	
Severe brain injury ^c , <i>n</i>		6 (11%)
Bronchopulmonary dysplasia ^d , <i>n</i>		14 (25%)
Severe retinopathy of prematurity ^e , stage ≥3, <i>n</i>		6 (11%)
Tracking parameters	<i>n</i> = 50–54	
Gaze gain sinus		0.90 (0.26)
SP gain sinus		0.44 (0.22)
Head gain sinus		0.30 (0.19)
Number of saccades sinus		1.46 (0.65)
Timing of gaze to object sinus		0.14 (0.16)
Gaze gain triangular		0.91 (0.29)
SP gain triangular		0.47 (0.23)
Head gain triangular		0.27 (0.19)
Number of saccades triangular		1.49 (0.70)
Timing of gaze to object triangular		0.16 (0.19)
6.5-year data		
Ophthalmological assessment	<i>n</i> = 51	
Visual acuity ≤ 0.8		17 (33%)
Contrast sensitivity < 0.5		16 (31%)
Manifest strabismus		7 (14%)
Wechsler scales	<i>n</i> = 54–57	
Full-scale IQ (<i>n</i> = 57)		92.4 (16.2)
Verbal Comprehension Index (<i>n</i> = 57)		98.4 (15.7)
Perceptual Reasoning Index (<i>n</i> = 57)		98.1 (16.1)
Working Memory Index (<i>n</i> = 54)		84.2 (15.1)
Processing Speed Index (<i>n</i> = 57)		89.1 (15.2)
Brown ADD	<i>n</i> = 50	
Organizing, prioritizing and activating to work		50.7 (9.1)
Focusing, sustaining and shifting attention		49.1 (8.9)
Regulating alertness, sustaining effort and processing speed		48.0 (9.0)
Managing frustration and modulating emotions		46.7 (7.2)
		48.1 (10.7)

Table 1. continued

6.5-year data	
Using working memory and accessing recall	
Monitoring and self-regulating action	49.3 (8.8)
ADD inattentional total score	48.7 (8.6)
ADD combined total score	49.0 (9.2)

^aDefined as 1–2 doses of betamethasone more than 12 h before delivery.

^bDefined as birthweight more than 2SD below the mean for gestational age.

^cDefined as intraventricular hemorrhage grade 3–4 according to Papile et al.³³ or periventricular leukomalacia.

^dDefined as the need of at least 25% oxygen for a saturation of 90% at 36 gestational weeks, as a result of lung complications.

^eDefinition based on degree of vascularization of the retina, based on the ETROP criteria.³⁴

Participants

The study cohort has been described previously.²² All infants were born at Uppsala University Hospital in 2004–2007. Out of 113 enrolled infants, 109 survived the first year. Clinical characteristics and neonatal data were prospectively collected.

At 4 months of age, corrected for prematurity, the infants underwent a visual tracking task as previously reported and as described below.²⁵ The children had neurodevelopmental follow-up and visual examinations at 2.5–3 and 6.5 years.^{26,27} Background characteristics and 6.5-year data are presented in Table 1.

Data on both the visual tracking task at 4 months and the 6.5-year follow-up were available for 57 children, which comprised the final study group. The Wechsler Intelligence Scale for Children IV (WISC-IV)²⁸ was used to assess cognitive function at 6.5 years in 54 children. Three children, with previously diagnosed neurodevelopmental problems, were tested with the Wechsler Preschool and Primary Scale of Intelligence—Third Edition (WPPSI-III).²⁹ Data from ophthalmological examinations at 6.5 years were available in 51 children in the final study group.

Study procedure at 4 months' corrected age

The infants were placed in a baby seat in the center of a white cylinder with a diameter and height of 1 m. The baby seat supported the infant's head, but head movements were otherwise unrestricted. A happy face (diameter 0.07 m) moved horizontally back and forth along a slit in the cylinder in front of the child at 0.25 Hz, either according to a sinusoidal or triangular motion pattern (abrupt reversal of the direction). The amplitudes of the object motion were 12.5° and 25°, respectively, for both motion patterns and the means for each tracking parameter were used.

Head and eye movements were recorded at a synchronized frequency of 240 Hz by two complementary systems. A custom-built electro-oculography (EOG) system (G. Westling, Department of Neurophysiology, Umeå University, Sweden) recorded eye movements with a precision of 0.4°. Miniature Beckman electrodes (Ag/AgCl) (Grass Technologies, West Warwick, RI, USA) were placed at the infant's outer canthi, and the ground electrode was positioned on the forehead or earlobe. To improve signal quality, a preamplifier was placed on the top of the infants' head. An optoelectronic camera system (Qualysis Proreflex, Gothenburg, Sweden) recorded the position of small (diameter 5 mm) passive reflective markers placed on the infant's head and on the moving object with a precision of 0.2° of visual angle. After calibration of the EOG, repeated trials of 35 s each were presented in a randomized order of combinations (sinusoidal, triangular, and 12.5° and 25°).

Visual tracking parameters

Using Fourier analysis, the relative proportion to which the infant followed the object was calculated (gain). Gain was obtained through a ratio between the object motion amplitude and a tracking parameter amplitude, and was calculated for smooth pursuit eye movements (smooth pursuit gain) and head movements (head gain), separately. Gaze

was defined as the combined amplitude of saccades, smooth pursuit, and head movements. Thus, the optimal gaze gain was 1, which means that the child followed the entire trajectory of the object and predicted the turn in order not to overshoot at the turning point.

Timing of gaze to object motion was estimated by cross-correlation analysis between the object and the gaze velocity. Finally, the number of saccades, here defined as rapid eye movements $\geq 100^\circ$ of visual angle per second, was determined from the eye velocity record.

Thus, the visual tracking parameters obtained through the coordinates of the eye, head and object positions in this study were *gaze gain*, *smooth pursuit gain*, *head gain*, *timing of gaze to object motion*, and *number of saccades*.

Instruments and protocol at 6.5 years

In the WISC-IV, ten core subtests are organized in four indices: Verbal comprehension, Perceptual reasoning, Working memory, and Processing speed, which together comprise the Full-Scale IQ. In the present study, the Working memory subtest Letter-number-sequencing was substituted by the optional subtest Arithmetic, as the children were too young to have automated the alphabet. The WPPSI-III does not include the Working memory index, and two core subtests in the Verbal comprehension index differ from the WISC-IV (Information replaces Similarities, and Word reasoning replaces Comprehension). All other subtests are the same across the WISC-IV and WPPSI-III tests.

The caregivers replied to the questionnaire Brown Attention-Deficit Disorder Scales (Brown ADD). The Brown ADD covers six clusters of (mainly) executive functions, central for Thomas Brown's model³⁰ of ADD/ADHD and affecting school performance, social functioning, emotions and behavior according to the Swedish manual.³¹ The model views ADHD as a developmental disorder with delays or alterations in executive function, with self-regulation at the core, and executive functions as governed by neurological networks that prioritize, integrate and regulate other processes in the brain.³⁰ The questionnaire contains six subscales: 1. Organizing, prioritizing and activating to work, 2. Focusing, sustaining and shifting attention, 3. Regulating alertness, sustaining effort and processing speed, 4. Managing frustration and modulating emotions, 5. Using working memory and accessing recall and 6. Monitoring and self-regulating action. The subscales 1–5 were combined in the ADD Inattention Total score, and subscales 1–6 combined into an ADD Combined Total score. The Brown ADD was not administered to the children given the WPPSI-III.

Finally, an ophthalmological examination was performed, where linear visual acuity, manifest strabismus, and contrast sensitivity were assessed.²⁶ Subnormal visual acuity was defined as a visual acuity of 0.8 or less and subnormal contrast sensitivity as <0.5 .

Statistical considerations

Associations between infant visual tracking parameters and the 6.5-year Wechsler and Brown ADD variables were explored in univariate regression models. For gaze gain, quadratic regressions were used since optimal tracking is equal to a gaze gain (i.e. the ratio between the moving object and gaze) of 1. For all other tracking parameters, linear associations were used. A two-tailed p value < 0.05 was considered statistically significant.

Based on the univariate analyses, gaze gain was chosen as the most important variable in relation to the Wechsler scores and timing of gaze to object motion was considered the most central in relation to the Brown ADD scores. To compare the tracking performance of triangular and sinusoidal motion patterns, respectively, regression models with interaction terms were used with the Wechsler scale scores or Brown ADD scores as dependent variables. To this end, it was important to handle missing values (Working memory index $n = 3$, Gaze gain sinus $n = 3$, Gaze gain triangular $n = 4$). For this analysis only, we used multiple imputation method of chained equations,³² as implemented in the R package mice.

Except for the analyses above, non-imputed data were chosen as a more conservative alternative, which means that all other analyses concerning the Working memory index or the Brown ADD scores were conducted without the three children tested with the WPPSI-III. When performing these analyses on the imputed data set, the risk of making type 1 errors (p values) decreased, but the pattern of results was not altered.

To control for neonatal risk factors, linear hierarchical regression analyses were conducted. As a rough indicator of illness severity, a variable was created in which the presence of any of the following three neonatal complications were added to a total score of 0–3 (0 meaning no complication): bronchopulmonary dysplasia, retinopathy of prematurity

stage ≥ 3 , and severe brain injury (defined as intraventricular hemorrhage grade 3–4 and/or periventricular leukomalacia assessed by repeated cranial ultrasound). Two variables, i.e. the sum of neonatal risk factors and gestational age in weeks, were entered in the first step in the hierarchical regression model, and gaze gain or timing of gaze to object, respectively, were added in the second step.

Finally, univariate analyses were conducted to assess whether the results of the 6.5-year ophthalmological examination related to the visual tracking and outcome measures.

Statistical analysis was carried out with the IBM SPSS Statistics, version 26.0 (Armonk, NY, USA), and R version 4.0.5. Graphs were created in Matlab (Mathworks Inc, Natick, MA, USA) or Desmos Graphing Calculator (Desmos Inc. San Francisco, CA, USA).

RESULTS

The two main parts of the gaze, head movement and smooth pursuit eye movements, are shown in Fig. 1a, c. Figure 1b, d demonstrates how the gaze follows the object motion. They should ideally add up to a perfect gaze, the number of saccades should compensate for a difference.

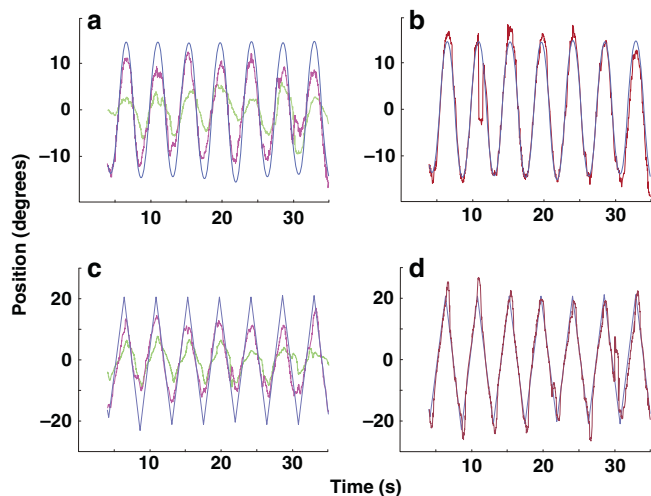


Fig. 1 Examples of visual tracking recordings in a preterm infant (24 weeks) at 4 months corrected age. Panels (a) and (b) depict smooth pursuit (magenta), head (green) and gaze (red), when the object (blue) moved sinusoidally. The number of saccades (>100 deg/s) was 0.19/s. Panels (c) and (d) depict the corresponding recordings for a triangular motion pattern. The number of saccades was 0.81/s. In panels (a) and (b) the gains were: 0.3 (head), 0.7 (smooth pursuit) and 1.05 (gaze). The gaze was lagging the object with 0.05 s. In panels (c) and (d) the gains were: 0.29 (head), 0.63 (smooth pursuit) and 1.08 (gaze). The gaze was lagging the object with -0.108 s.

Tracking related to cognitive test scores at 6.5 years

The associations between the visual tracking results at 4 months and the Wechsler scores are presented in Table 2. Gaze gain, compared to the other tracking parameters, was more strongly associated with the cognitive scores at 6.5 years (explaining 17–30% of variance) and was significantly associated with all Wechsler indices. The quadratic regressions for gaze gain are depicted in Fig. 2, demonstrating that most peaks of the association-curves were close to 1. In the quadratic associations, gaze gains closer to 1 tended to give higher cognitive scores. Furthermore, all linear associations between smooth pursuit gain and the Wechsler scales were positive, showing that the larger the gain the higher the cognitive scores. The associations were similar for the sinusoidal and triangular motion patterns.

There were no significant associations between head gain, number of saccades, or timing of gaze to object in relation to the Wechsler scale scores.

Visual tracking associated to measures of ADHD-related executive function at 6.5 years: Brown ADD

The significant relationships between Brown ADD at 6.5 years and the various aspects of visual tracking at 4 months are shown in Fig. 3 and eTable 1. The magnitude of variance explained ranged from 9 to 17%. For the sinusoidal motion pattern, gaze gain, timing of gaze to object, and saccades were all related to Brown ADD scales. The strongest association was found between timing and the Brown ADD score for Focusing, Sustaining and Shifting Attention. For the triangular motion pattern, only smooth pursuit gain was significantly associated with the Brown ADD scales. The sub score for Regulating alertness, sustaining effort and processing speed showed strong associations with tracking parameters for both sinusoidal and triangular motion patterns.

Comparison of sinusoidal and triangular-shaped motion patterns

Gaze gain for both triangular and sinusoidal motion patterns related similarly to the cognitive scores at 6.5 years (Fig. 2). The largest discrepancy between the two motion patterns were found in relation to the Processing speed index, but the regression models demonstrated no statistically significant interactions between motion pattern and Wechsler scores (all p values between 0.49 and 0.94). Similarly, there were no statistically significant interactions for timing of gaze to object during the sinusoidal versus the triangular motion pattern in relation to the Brown ADD (all p values between 0.25 and 0.90).

Multiple regressions for sinusoidal motion pattern

In the hierarchical regression model, when adding gaze gain in step two, to gestational age and the sum of neonatal risk factors in step one, gaze gain had an independent association with Perceptual reasoning ($\Delta R^2 = 0.095$, $\Delta p = 0.04$) and Processing

Table 2. Results of visual tracking parameters (smooth pursuit gain and gaze gain) at 4 month's corrected age in relation to cognitive test results at 6.5 years (Wechsler Scales), as assessed by linear and quadratic univariate regression models for sinusoidal and triangular motion patterns.

Wechsler Scale Index	Sinusoidal motion pattern				Triangular motion pattern			
	Smooth pursuit gain		Gaze gain ^a		Smooth pursuit gain		Gaze gain ^a	
	R^2	p	R^2	p	R^2	p	R^2	p
Full-scale IQ	0.106	0.016	0.242	0.001	0.080	0.038	0.185	0.007
Verbal comprehension	0.059	0.078	0.179	0.007	0.040	0.146	0.139	0.025
Perceptual reasoning	0.048	0.113	0.285	0.000	0.053	0.095	0.284	0.000
Working memory	0.109	0.018	0.173	0.010	0.075	0.052	0.170	0.014
Processing speed	0.172	0.002	0.306	0.000	0.115	0.014	0.166	0.014

^aQuadratic regressions.

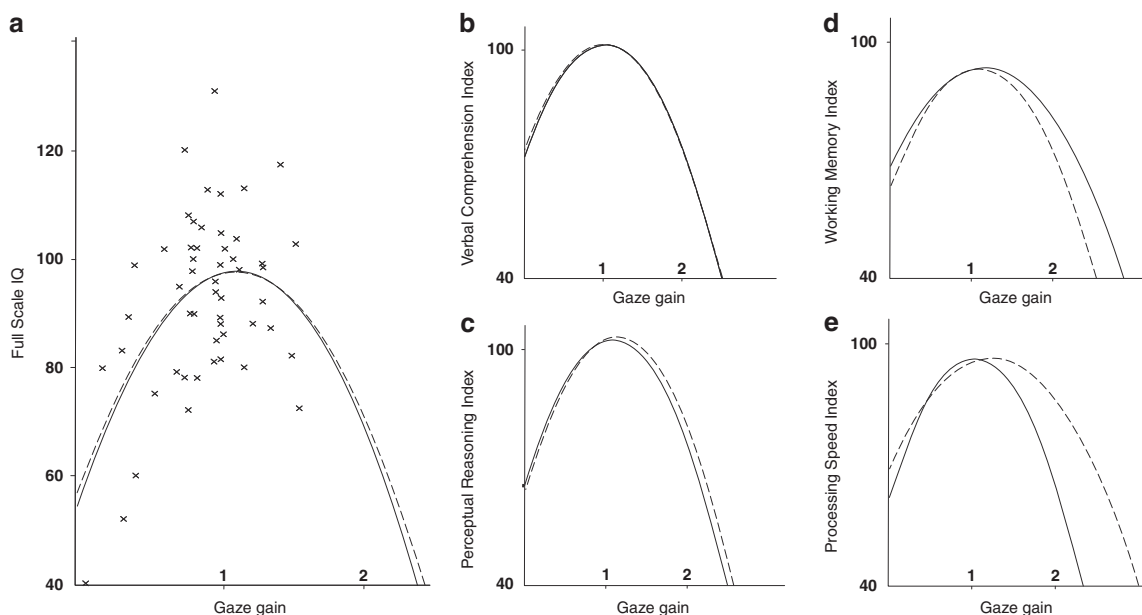


Fig. 2 Relation between gaze gain and Wechsler indices gaze gain in the sinusoidal (solid lines) and triangular (dashed lines) tracking tasks at 4 months' corrected age in relation to the Wechsler indices at 6.5 years. The associations are depicted in separate panels (a–e) for the Wechsler scores. A gaze gain of 1 indicates a perfect ratio between the gaze and the object amplitude, a ratio <1 represent undershoot of the gaze, and a ratio >1 overshoot by the gaze at the turns of the moving object. In panel (a), observations of individual subject data points for the sinusoidal motion pattern only are depicted.

speed ($\Delta R^2 = 0.115$, $\Delta p = 0.02$). Timing of gaze to object did not remain significant after the same procedure was performed in relation to the Brown ADD.

Effect of visual function for the sinusoidal motion pattern

There was no relation between the visual tracking parameters and visual acuity, contrast sensitivity or strabismus at 6.5 years. A decreased visual acuity <0.8 at 6.5 years was related to a lower Full-Scale IQ ($p = 0.036$) and lower scores in Perceptual reasoning ($p = 0.037$). There was no relation between strabismus or contrast sensitivity and the Wechsler indices, or the Brown ADD subscales and total scores.

DISCUSSION

This prospective study was designed to investigate long-term effects of preterm birth on neurodevelopment and cognitive processes. The hypothesis was that if predictive visual tracking of a moving object is important for cognitive development, then disturbances to this system could alter the developmental trajectory, contributing to the neurodevelopmental deficits that are prevalent in children born very preterm. The current results support our hypotheses, both as regards the cognitive and the attentional consequences of early visual tracking performance.

The main results were that early visual tracking performance, at 4 months of age (corrected for prematurity), predicted both cognitive and attentional abilities at 6.5 years in children born very preterm. Gaze gain and smooth pursuit gain were mainly related to cognitive functions while timing of gaze to object motion was more linked to ratings of attention. For perceptual functions and processing speed, gaze gain explained unique variance when risk factors were added to the model. The patterns of associations were similar for the sinusoidal and triangular motion patterns, indicating that both motion patterns measure aspects of global prediction.

Two important determinants affect visual tracking performance, the ability to predictively follow the moving object and the capability to focus attention on it. In typically developing infants,

attentional abilities appear soon after birth^{17,35} and smooth pursuit eye movements start to develop within two months of age.⁸ Sustained attention makes it possible to track the moving object over time and smooth pursuit eye movements enables the gaze to stay on the object predictively. In an earlier study of the preterm group, we showed that visual tracking at 4 months was strongly correlated with cognition, receptive and expressive language and fine motor function assessed with the Bayley-III at 3 years.²³ The present results show that the relation between early visual tracking performance and cognition persists and remains strong also later in the preschool years.

Gaze gain was the variable most closely related to cognitive functions at 6.5 years. For the sinusoidal motion pattern, gaze gain explained 24–30% of the variance for the Full-Scale IQ, Perceptual reasoning and Processing speed, but also demonstrated significant associations to Verbal comprehension and Working memory. The patterns of associations were similar for gaze gain in relation to the triangular-shaped motion pattern, with significant correlations to all Wechsler scores but with lower explained variances. The similarity between relations was further confirmed, as the interaction analyses were non-significant. Thus, both the local and the global changes in the moving object's velocity seemed to be of crucial importance for a number of cognitive abilities that appeared later in development.

Gaze gain was related not only to perceptual cognitive abilities, but also to verbal cognition, working memory and processing speed scores, and explained 17–31% of the variance. The presence of these broad associations suggests that early common mechanisms could be of major importance for global neurodevelopment. Smooth pursuit gain was also associated with the Full-Scale IQ, Working memory and Processing speed indices, explaining 11–17% of variance. Working memory and Processing speed are necessary for effective visual tracking, as the infant must process the visual information continuously and predictively.

The close associations between infant gaze gain and later Perceptual reasoning as well as Processing speed demonstrate the importance of early visual tracking performance since these two cognitive abilities are considered to be especially vulnerable in

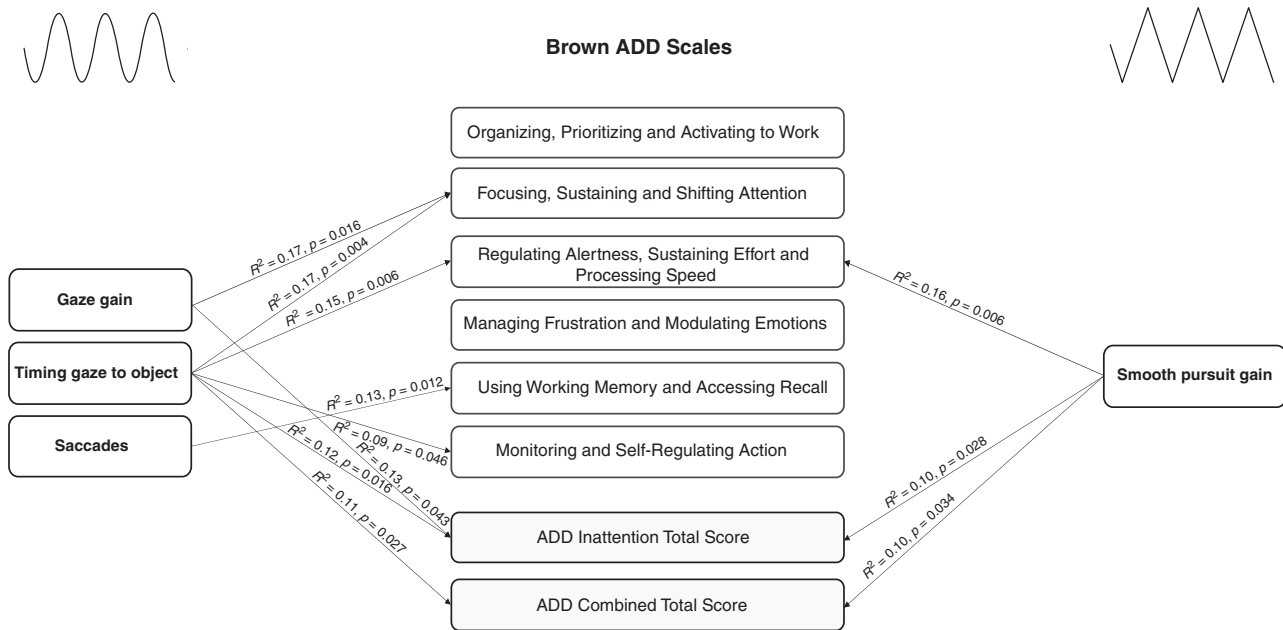


Fig. 3 Relations between visual tracking parameters and Brown ADD scores schematic overview of statistically significant associations between visual tracking parameters at 4 months' corrected age and the results of the Brown ADD questionnaire at 6.5 years in very preterm infants ($n = 50$), with sinusoidal (left) and triangular motion patterns (right). The regression lines demonstrate that a ratio closer to 1 for gaze gain in relation to object motion (quadratic regression), better timing of gaze to object motion and fewer saccades (linear regressions) were associated with less problems, as rated by the parents.

children born preterm.^{36–38} Processing speed allows adequate employment of intellectual functions and has been shown to predict general academic achievement.³⁹ In addition, visuospatial deficits in children born preterm have been associated to poorer academic achievement, especially in mathematics.^{37,40}

Gaze gain, smooth pursuit gain and timing of gaze to object were all associated with the attention-related executive functioning at 6.5 years, further demonstrating that the ability to sustain attention to a moving object in infancy has important implications for later development. Attention serves to select which information that should be considered for further processing of thought and action.⁴¹ Infant attention and smooth pursuit eye movements increase in parallel from 8 to 26 weeks.¹¹ In addition, attention also shares neurological substrates with visual tracking ability.⁴² Comparable to the results in the present study, similar associations are present between attention at 1 year and executive functions at 2 years of age in term-born children.⁴³

Attention deficits are among the most prevalent sequels after preterm birth, and the present results indicate that poor attention in infancy persists during development.^{36,43} Consequently, later attention deficits could potentially also be predicted by early visual tracking performance. Timing of gaze to object was more related to attentional domains than gaze gain. For executive functions measured by the Brown ADD, finely tuned timing is probably of greater importance than when solving the more static problems in the Wechsler tasks. In a social interaction or executive behavior in everyday situations, the fine tuning of the chain of responses to outside events is very important. In typically developing infants, timing of gaze to object develops before gaze gain.²⁵

In line with our previous results,²³ gaze gain displayed the strongest relations to neurodevelopment at 3 years, but smooth pursuit gain was also related to cognition and receptive communication. At 6.5 years, the associations between infant visual tracking performance and verbal functions were weaker. At 3 years, the verbal tasks tapped more basic language abilities, such as word production and understanding, while the tasks at 6.5 years involved higher verbal functions of concept formation,

vocabulary and reasoning. Timing of gaze to object was also primarily related to cognitive and language functions at 3 years, but showed no associations with the Wechsler results at 6.5 years. In adults, saccades interrupting smooth pursuit are often signs of non-specific neurological influence.⁴⁴ For the tasks presented to the infants in this study however, saccades served to catch up and seemed to be more functionally integrated and contributing to more effective visual tracking. In the present study, visual tracking parameters were not predictive for any of the visual variables, i.e. visual acuity, contrast sensitivity or strabismus.

The present results are supported by a study of Stjerna et al.,⁴ although eye movements in that study were rated by an observer and not recorded by an eye-tracking device. Newborn gaze fixation and tracking behavior were investigated in two groups, extremely preterm infants and infants of all gestational ages. The infants' eye tracking and fixation performance correlated to visuomotor ability at 2 years and to visuomotor and visual reasoning abilities at 5 years, respectively.⁴ Also, as already mentioned, Emberson et al.⁶ showed that prediction of visual stimuli but not responses to visual stimuli was altered in preterm infants, but the results were not compared to later neurodevelopmental assessment.

The method used in the study was based on independent and precise recordings of eye and head movements at high frequency (240 Hz) with very few unusable data points. Recent commercially available techniques of recording gaze behavior with cornea reflection do not separate eye and head movements. They have, however, proved to be useful in evaluating gaze shifts in static and dynamic displays.^{45–47}

There were some limitations to the study. There were three impaired children, that were tested with the WPPSI-III and lacked scores for the Brown ADD, which could result in somewhat underestimated strengths of the associations. Cranial ultrasounds were performed according to clinical routines, and no major cerebellar hemorrhages were diagnosed. However, the possibility of minor punctate lesions, that potentially could affect the visual tracking performance, could not be ruled out. Another limitation was that the study did not include full-term controls. Thus, a new

cohort including a control group is currently being planned. In this context recent intervention studies in progress targeting visual tracking ability or attention in both infants and older children^{48–50} are of special clinical interest. The current results propose that the predictive element in visual tracking of moving objects could be a complementary target to consider in future intervention studies.

CONCLUSION

In the present study, early visual tracking performance in very preterm infants was related to cognitive abilities and ratings of attention at 6.5 years. We conclude that preterm birth influences basic processes of visual tracking, with implications for cognitive function and attention in later development. The ability to coordinate one's actions with a moving object is a strong indicator of the proficiency of the infant's visual, attentional predictive systems, and also sets the boundaries for early visual experience. The present results show that relevance of early maturation of visual tracking goes beyond infancy and has strong implications for cognitive functions in the late preschool years.

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AUTHOR CONTRIBUTIONS

Data collection K.R., G.H., K.S.B., Y.F.K.; Statistical analysis Y.F.K.; Interpretation of results Y.F.K., K.R., L.H.-W., C.v.H., G.H.; Study design Y.F.K., K.R., C.v.H., L.H.-W.; Tracking paradigm and data processing K.R., C.v.H.; Drafting and revision of manuscript Y.F.K., K.R., C.v.H., L.H.-W., K.S.B., G.H.

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COMPETING INTERESTS

The authors declare no competing interests.

CONSENT STATEMENT

The caregivers of the children gave oral and written consent both for the clinical data collection and for the experimental visual tracking assessment.

ADDITIONAL INFORMATION

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Correspondence and requests for materials should be addressed to Ylva Fredriksson Kaul.

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