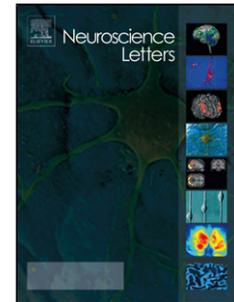# Accepted Manuscript

Title: Global motion perception is associated with motor function in 2-year-old children

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Title: Global motion perception is associated with motor function in 2-year-old children

Authors
Benjamin Thompson[1,2]
Christopher JD McKinlay[3,4]
Arijit Chakraborty[1,2]
Nicola S Anstice[1]
Robert J Jacobs[1]
Nabin Paudel[1]
Tzu-Ying Yu[1]
Judith M Ansell[3]
Trecia A Wouldes[5]
Jane E Harding[3]
For the CHYLD Study Team

1 School of Optometry and Vision Science, University of Auckland, Auckland, New Zealand
2 School of Optometry and Vision Science, University of Waterloo, Waterloo, Canada.
3 Liggins Institute, University of Auckland, Auckland, New Zealand
4 Department of Paediatrics: Youth and Child Health, University of Auckland, Auckland, New Zealand
5 Department of Psychological Medicine, University of Auckland, Auckland, New Zealand

Corresponding author
Benjamin Thompson, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, Canada.

Email: ben.thompson@uwaterloo.ca
Phone: 519 888 4567 x3938

Highlights

- Global motion perception is associated gross motor function at 2 years of age
- Stereopsis is associated with fine motor function at 2 years of age
- Acuity is not associated with motor function at 2 years of age
- Visual and motor dorsal stream sub-components are associated early in development

Abstract

The dorsal visual processing stream that includes V1, motion sensitive area V5 and the posterior parietal lobe, supports visually guided motor function. Two recent studies have reported associations between global motion perception, a behavioural measure of processing in V5, and motor function in pre-school and school aged children. This indicates a relationship between visual and motor development and also supports the use of global motion perception to assess overall dorsal stream function in studies of human neurodevelopment. We investigated whether associations between vision and motor function were present at 2 years of age, a substantially earlier stage of development. The Bayley III test of Infant and Toddler Development and measures of vision including visual acuity (Cardiff Acuity Cards), stereopsis (Lang stereotest) and global motion perception were attempted in 404 2-year-old children (± 4 weeks). Global

motion perception (quantified as a motion coherence threshold) was assessed by observing optokinetic nystagmus in response to random dot kinematograms of varying coherence. Linear regression revealed that global motion perception was modestly, but statistically significantly associated with Bayley III composite motor ($r^2 = 0.06$, $p < 0.001$, $n = 375$) and gross motor scores ($r^2 = 0.06$, $p < 0.001$, $n = 375$). The associations remained significant when language score was included in the regression model. In addition, when language score was included in the model, stereopsis was significantly associated with composite motor and fine motor scores, but unaided visual acuity was not statistically significantly associated with any of the motor scores. These results demonstrate that global motion perception and binocular vision are associated with motor function at an early stage of development. Global motion perception can be used as a partial measure of dorsal stream function from early childhood.

Abbreviations
CHYLD, Children with Hypoglycaemia and their Later Development
NICU, Neonatal intensive care unit

Key words: Hypoglycaemia Infant, newborn Visual perception Motor activity Dorsal stream Motion coherence threshold

Background

The two-systems theory of visual processing describes two interconnected cortical processing streams; the dorsal stream and the ventral stream [10]. The dorsal stream includes V1, motion sensitive area V5 (also known as the middle temporal area or MT) and the posterior parietal lobe. The ventral stream also includes V1 and projects to the inferior temporal lobe via visual areas such as V4. The distinction between these two pathways is based on their function. In general terms, the dorsal stream supports motion perception and visually guided motor function (visuomotor integration), whereas the ventral stream supports form processing and object recognition (see [9] for an overview).

The dorsal stream vulnerability hypothesis proposes that the dorsal stream is more susceptible to the effects of abnormal neurodevelopment than the ventral stream [6]. This is based on evidence that motion integration (a dorsal stream function) but not form integration (a ventral stream function) is impaired in children with conditions such as Williams Syndrome or a history of preterm birth [see 2, 6, 11 for reviews]. In these studies, motion integration, also known as global motion perception, is typically measured using random dot kinematograms that are constructed from two groups of dots; a signal group that move in a coherent direction and a noise group that move randomly. The observer judges the direction of coherent motion and the signal to noise ratio is varied to estimate a motion coherence threshold (the lowest signal to noise ratio required for a particular level of task performance). Combining local motion signals into a coherent, global perception of motion involves area V5 in the dorsal stream [7, 22, 24, 26].

Until recently it has been unclear whether motion coherence thresholds provide an index of overall dorsal stream function or whether they simply reflect motion processing. However, we and others have recently demonstrated modest but statistically significant associations between motion coherence thresholds and motor development in children [5, 8]. We found an association between motion coherence thresholds and standardized clinical measures of visuomotor integration and gross (but not fine) motor function in a group of 606 4.5-year-old children born at risk of abnormal neurodevelopment [8]. Similarly, Braddick et al. [5] found that motion, but not form coherence thresholds were associated with visuomotor integration and posterior parietal lobe development in a group of 154 normally developing 5-12 year olds. Together, these results support the overall concept of a dorsal processing stream and indicate that motion coherence thresholds do provide a partial index of dorsal stream function.

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Building on this prior work, the primary aim of this study was to assess whether a relationship between motion coherence thresholds and motor function is present at an earlier stage of child development, 2 years of age. Such a relationship would suggest that both functions of the dorsal stream develop in parallel and that motion coherence thresholds can be used to estimate dorsal stream function early in life.

Our secondary aim was to assess the strength of association between motor function, stereopsis and unaided binocular visual acuity at 2 years of age. Binocular vision [1], and, to a lesser extent, visual acuity [15] have each been associated with motor function in normally developing pre-school and school age children. In our previous study, we observed a significant association between stereopsis and motor function at 4.5 years of age [8]. Visual acuity was not significantly associated with fine or gross motor function at 4.5 years, but there was an association with overall motor function. It is unknown whether these associations exist at an earlier stage of neurological development.

Methods

Participants

Participants were recruited as part of the Children with Hypoglycaemia and their Later Development (CHYLD) study, a prospective cohort study designed to investigate the relationship between neonatal hypoglycaemia and long-term neurodevelopment. Infants were recruited before or shortly after birth to one of two parallel studies (BABIES, N=102 and Sugar Babies, N=514) if they had one or more risk factors for neonatal hypoglycaemia, including being born to a diabetic mother, preterm (<37 weeks), small ($<10^{th}$ centile or <2500 g) or large ($>90^{th}$ centile or >4500 g) [13, 14]. Infants with serious congenital malformations or terminal conditions were excluded. The cohort was recruited from 2006 to 2010 at Waikato Hospital, New Zealand, a regional public hospital with approximately 5,500 births annually. Cohort characteristics and neonatal glycemic monitoring and management have been reported [12-14]. We anticipated considerable variability in motor development within the CHYLD study cohort because conditions present in the cohort such as neonatal hypoglycaemia [18], late preterm birth [20] and intrauterine growth restriction [17] can influence motor development. Such variability would facilitate the detection of even weak associations between motion coherence thresholds and motor function. The CHYLD study was approved by the Health and Disability Ethics Committee. Written informed consent was obtained at study entry and at follow-up.

Assessment at 2 years of age

At 2 years' corrected age ($\pm$ 4 weeks) all children in the CHYLD Study who were born $\geq$35weeks' gestation were invited to participate in a comprehensive neurodevelopmental assessment, including neurological status, Bayley Scales of Infant Development (Bayley-III), executive function, vision screening and global motion perception, as previously described [21]. Bayley-III provides composite scores for cognitive, language, and motor ability, with standardised means (standard deviation [SD]) of 100 (15) [4]. The motor score is a composite of fine and gross motor subtest scores, each with a standardised mean (SD) of 10 (3). Fine motor tests include reaching and grasping activities whereas gross motor tests include measures of locomotion, coordination and balance.

Vision screening included unaided binocular visual acuity measurement (Cardiff Acuity Cards), stereopsis (Lang Stereotests), alignment and motility (including cover test, 20^{Δ} base-out test), and non-cycloplegic autorefraction (Suresight[TM] Autorefractor, Welch Allyn, Skaneateles Falls, NY) [28]. A Vision Impairment Score assigned one point for each of the following: internal or external ocular health problem, strabismus, abnormal motility, absence of stereopsis, binocular visual acuity worse than 0.5 logMAR. Children were assigned a Refractive Error Score consisting of one point for each of the following: hyperopia (mean sphere

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[M] ≥+4.00 dioptre [D]), myopia (M ≤-1.00 D), astigmatism (cylinder [C] ≤-1.50 D in any meridian), and anisometropia (difference in M between eyes of ≥3.00 D in either the most positive or negative meridian) [25].

Global motion perception was measured from optokinetic nystagmus (OKN) responses to random dot kinematograms (RDK) of varying coherence, as previously described. [28] In brief, RDK stimuli created in Matlab (MathWorks, Matick, MA) were presented within a circular aperture (radius 8.3°) on a cathode ray tube and consisted of 250 white dots (138 cd/m^2, diameter 0.5°, speed of 8°/s) on a grey background (42 cd/m2, dot density = 1.16 dots/deg^2). Signal dot direction (left or right) was randomized and noise dots had a random direction. Dots had a limited lifetime with a 5% chance of being randomly relocated on each frame. Stimuli were presented for 8 seconds at coherence levels of 100%, 84%, 68%, 52%, 36% and 20%, in descending order across consecutive trials. The sequence was repeated until the child could no longer be encouraged to look at the monitor. Eye movements were recorded at 50 Hz using a high definition camera (Sony HDR-CX7EK; Sony Corporation, Tokyo, Japan) and motion coherence threshold corresponding to 63% correct was determined from a Weibull fit to the proportion of correct responses at different coherence levels [28].

A subset of the children who completed the 2-year assessment also completed a 4.5-year assessment. Data from these children were reported in our recent study into the association between global motion perception and motor function at 4.5 years of age [8].

Statistical analysis
Analysis was performed with SAS software, version 9.4 (SAS Institute, Cary, NC). Bayley-III composite and subtest scores, and motion coherence thresholds were converted to z-scores. Socioeconomic status was determined from the New Zealand Deprivation Index [3]. Linear regression was used to assess the relationship between motion coherence and Bayley-III motor z-scores. Multivariate analysis was used to explore for potentially confounding effects of vision problems (Vision Impairment Score ≥1) and Bayley-III language score. The Bayley-III language score was used to represent cognitive ability because many of the tasks involved in assessing the Bayley-III cognitive score include visual-motor activities. Interaction tests were used to investigate if the relationship between motion coherence and Bayley-III motor z-scores was affected by sex, low socioeconomic status (≤3rd decile), neonatal hypoglycaemia (blood glucose concentration <2.6 mmol/L) or being born preterm or small. Linear regression was also used to assess the relationship between stereopsis or binocular visual acuity and Bayley-III motor z-scores, and multivariate analysis was used to assess potential confounding by global cognitive ability (Bayley-III language score). An exploratory analysis was also conducted to assess the univariate correlations between each of our variables. A two-tailed alpha level <0.05 was considered to indicate statistical significance.

Results
Of 528 children eligible for follow up at 2 years, 404 (77%) were assessed [21] and 375 (71%) who completed the Bayley-III, vision screen and global motion perception test were included in the analysis.

Children were assessed at a median (IQR) age of 24 (23-25) months (Table 1). The most common reasons for enrolment in the CHYLD Study were having a diabetic mother (39%) and being born preterm (33%) (Table 1). Just over half of the children were of European ethnicity (52%) and nearly one third were Māori (28%) (Table 1). Mean (SD) Bayley-III composite scores were lower than the standardised mean of 100; cognitive score 93.7 (10.2), language score 95.1 (14.0), motor score 98.8 (9.5), all P<0.01. Children had a mean (SD) motion coherence threshold of 42.2 (13.9) and 22% had one or more problems detected on the vision screen (Table 1). Autorefraction was successful in 195 (52%) children, of whom 9.5% were found to have a significant refractive error (Table 1).

In univariate analysis, there was a significant inverse association between motion coherence threshold and Bayley-III fine, gross and composite motor scores. For each 1 SD increase in motion coherence threshold (indicating worse global motion perception) Bayley-III motor scores decreased by approximately 0.15 SD (all P<0.001) (Table 2). However, the association was modest as motion coherence z-score explained only 4-6% of the variation in motor z-scores (Table 2).

Adjustment for the presence of an ocular problem (Vision Impairment Score ≥1) did not alter the results (Table 2). After adjustment for Bayley-III language score, a significant association remained between motion coherence threshold and Bayley-III composite and gross motor but not fine motor z-scores (Table 2). The relative contribution of each potentially confounding variable to the model can be judged by comparing the R^2 value for the uncorrected model to the R^2 values for the corrected models in Table 2.

The association between motion coherence and Bayley-III composite motor z-scores was not influenced by sex (P=0.54), low socioeconomic status (P=0.21), neonatal hypoglycaemia (P=0.55) or being born preterm (P=0.07) or small (P=0.42).

Stereopsis, measured using the Lang stereotest, was significantly associated with fine and composite motor scores but not gross motor score (Table 3). These associations remained significant when Bayley-III language score was included in the model. Binocular visual acuity was also associated with fine and composite motor scores; however, these associations became statistically non-significant when language score was included in the model (Table 4).

Exploratory univariate correlation analyses (Supplementary Table) were consistent with the regression analyses. In addition, these analyses showed that language score was significantly correlated with all motor and vision variables. Moreover, there was a statistically significant relationship between motion coherence threshold and stereopsis, in agreement with our previous work [28]. An additional regression analysis showed that the association between motion coherence threshold and composite motor score remained significant when the model was adjusted for stereoacuity (β [95% CI] = -0.11 [-0.18, -0.04], R^2 = 0.08, P = 0.001). This indicates that stereopsis and motion coherence threshold have independent relationships with motor function.

Discussion

The similarity between the results we report here for 2 year old children and those we reported previously for 4.5 year old children [8] is striking. In both studies, motion coherence thresholds were modestly but significantly associated with both gross motor and overall motor function, even when controlling for general cognitive ability, as indicated by Bayley-III language scores. Furthermore, the associations were seen across the cohort and were not confined to children born preterm, with neonatal hypoglycaemia or low socioeconomic status. It has recently been reported that visually guided movements recruit dorsal stream areas in children 4-7 years of age, and thus the standardized tests of gross and fine motor function we used in this study were likely to involve dorsal stream processing [16]. Together, these results suggest that the development of dorsal stream functions relating to motion perception and motor function are linked early in life. Our findings, along with others' [5], also support the use of motion coherence thresholds as a partial measure of dorsal stream function in studies of normal and abnormal child development.

Also in agreement with our data from 4.5 year old children [8], when controlling for language score, we observed that stereopsis was associated with fine and composite motor scores whereas binocular visual acuity was not significantly associated with any of the motor scores. These results reinforce the importance

of binocular vision for the development of fine motor skills, and demonstrate that stereopsis and fine motor function are associated early in childhood. However, very few children in this study had impaired visual acuity, which may have obscured any possible association between visual acuity and motor function.

OKN-based measures of motion coherence may involve thalamic processing during early infancy [19]. However, OKN is likely to rely on cortical function by 2 years of age (see [28] for a discussion of this issue). The similarity between the current results and those that we have previously reported for 4.5 year olds with psychophysical measures of motion coherence [8] also support the theory that our OKN based measure reflects cortical processing in 2 year olds.

At 4.5 years of age, stereopsis was associated with all aspects of motor function that were assessed, including gross motor function [8]. However, in this group of 2-year-old children, we did not find a statistically significant association between stereopsis and gross motor function. This may be due to differences in the composition of the standardized tests used at each age, with tests designed for older children requiring more complex gross motor tasks that place greater demands on binocular vision.

The association between motion coherence thresholds and fine motor function was not statistically significant when language score was included in the regression model. This was also the case at 4.5 years of age [8]. It appears that stereopsis, but not the measure of dorsal stream function provided by motion coherence thresholds, is associated with fine motor function up until school-age. Retinal disparity, the visual information required for stereopsis, is encoded in both dorsal and ventral stream areas [23]. It is possible that the fine motor tasks used in standardized tests of child motor function have a greater reliance on the integration of information between the dorsal and ventral streams than the gross motor tasks that may rely primarily on the dorsal stream. For example, the fine motor tests in the Bayley-III involve precision object oriented hand movements which are likely to rely on both dorsal and ventral stream processing [27].

The regression models including language score explained substantially more variance than vision measures alone for the composite and fine motor scores. R^2 values increased by approximately 0.2 when language scores were included for both of these measures. This was not the case for gross motor scores, however, where r^2 values increased by approximately 0.05. It appears that fine and composite motor scores are influenced by a combination of vision and language development, presumably because successful task performance requires the understanding of verbal instructions. Language may not be as important for gross motor performance as the tasks involve more familiar body movements and do not require such precise comprehension of verbal instructions. If this distinction is correct, it may also have contributed to the observation that motion coherence thresholds were associated with gross but not fine motor function when language score was included in the regression model.

In summary, our results indicate that motion perception and motor function develop in parallel from an early age. This may be because both abilities rely on a common neural pathway; the dorsal stream.

Disclosure: The authors have no financial or other conflicts of interest to declare.

Author's roles
JEH, BT, TAW, JMA, NSA and RJJ designed the study; TYY, NSA, JMA and NP assisted with data collection; CJDM and BT performed the analysis and drafted the manuscript. AC edited the manuscript.

All authors contributed to the revision of the manuscript. The CHYLD Study Steering Group had sole responsibility for the decision to publish. CJDM takes responsibility for the integrity of the data analysis. Sponsors had no role in study design, conduct, data analysis or the decision to publish.

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Table 1: Cohort characteristics (N=375)

Baseline characteristics, *mean (SD) [range] unless labelled otherwise*	
Female, *n (%)*	177 (47)
Gestation at birth in weeks	37.8 (1.7) [35.0, 42.7]
Birthweight in grams	3141 (850) [1590, 5770]
Birthweight z-score	0.20 (1.67) [-3.75, 6.12]
Primary risk factor for neonatal hypoglycaemia, *n (%)*	
Diabetic mother	146 (39)
Preterm	122 (33)
Small	56 (15)
Large	42 (11)
Other	9 (2)
Ethnicity, *n (%)*	
Maori	106 (28)
Pacific	13 (3)
Other	62 (17)
European	194 (52)
Socioeconomic decile	4.6 (2.7) [1, 10]
2 year characteristics	
Assessment age in months, *median (IQR) [range]*	24 (23, 25) [22, 37]
Bayley-III score	
Cognitive composite	93.7 (10.2) [55.0, 125.0]
Language composite	95.1 (14.0) [56.0, 144.0]
Motor composite	98.8 (9.5) [73.0, 145.0]
Fine motor subtest	10.1 (2.1) [5.0, 17.0]
Gross motor subtest	9.5 (1.8) [5.0, 19.0]
Motion coherence threshold in percent coherence	42.2 (13.9) [9.0, 94.6]
Stereoacuity in seconds of arc[*]	366 (196) [200, 1200]
Binocular visual acuity in LogMAR[†]	0.06 (0.15) [-0.20, 1.00]
Vision Impairment Score, *n (%)*	
0	290 (77)
1	69 (18)
$\geq$2	16 (4)
Refractive Error Score, *n (%)*[‡]	
0	177 (90.5)
1	17 (9)
$\geq$2	1 (0.5)

[*]314 children completed Lang Stereotest. [†] 330 children completed Cardiff Acuity Cards. [‡] 195 children completed non-cycloplegic autorefraction.

Table 2: Association between z-scores for motion coherence threshold and Bayley-III motor z-scores at 2 years (N=375)

Bayley-III outcome	β (95% CI)	R^2	P
Composite motor	-0.16 (-0.22, -0.09)	0.06	<0.0001
Adjusted for vision impairment score[‡]	-0.14 (-0.20, -0.08)	0.10	<0.0001
Adjusted for language score	-0.09 (-0.15, -0.03)	0.24	0.002
Fine motor subtest	-0.13 (-0.20, -0.06)	0.04	0.0002
Adjusted for vision impairment score[‡]	-0.11 (-0.18, -0.05)	0.08	0.001
Adjusted for language score	-0.06 (-0.12, 0.00)	0.23	0.07
Gross motor subtest	-0.13 (-0.19, -0.07)	0.05	<0.0001
Adjusted for vision impairment score[‡]	-0.12 (-0.18, -0.06)	0.05	<0.0001
Adjusted for language score	-0.09 (-0.15, -0.03)	0.10	0.002

[‡]Vision impairment score ≥1

Table 3: Association between stereoacuity and Bayley-III motor z-scores at 2 years (N=314)

Bayley-III outcome	β (95% CI)	R^2	P
Composite motor	-0.04 (-0.06, -0.02)	0.05	<0.0001
Adjusted for language score	-0.02 (-0.04, -0.00)	0.19	0.02
Fine motor subtest	-0.05 (-0.07, -0.03)	0.06	<0.0001
Adjusted for language score	-0.03 (-0.04, -0.01)	0.21	0.008
Gross motor subtest	-0.02 (-0.04, 0.00)	0.01	0.06
Adjusted for language score	-0.01 (-0.02, 0.01)	0.05	0.36

Stereoacuity measured by Lang Stereotest in minutes of arc.

Table 4: Association between visual acuity and Bayley-III motor z-scores at 2 years (N=330)

Bayley-III outcome	β (95% CI)	R^2	P
Composite motor	-0.65 (-1.08, -0.21)	0.03	0.004
Adjusted for language score	-0.15 (-0.57, 0.27)	0.18	0.49
Fine motor subtest	-0.94 (-1.41, -0.47)	0.04	0.0001
Adjusted for language score	-0.40 (-0.86, 0.06)	0.19	0.09
Gross motor subtest	-0.12 (-0.54, 0.30)	0.001	0.59
Adjusted for language score	0.17 (-0.26, 0.60)	0.06	0.44

Visual acuity measured by Cardiff Acuity Test (binocular) in LogMAR.