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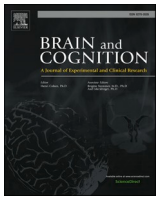

Relationship between maternal biological features, environmental factors, and newborn neuromotor development associated with visual fixation abilities

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ABSTRACT

Newborn visual fixation abilities predict future cognitive, perceptive, and motor skills. However, little is known about the factors associated with the newborn visual fixation, which is an indicator of neurocognitive abilities. We analyzed maternal biological and environmental characteristics associated with fine motor skills (visual tracking) in 1 month old infants. Fifty-one infants were tested on visual tracking tasks (Infant Visuomotor Behavior Assessment Scale/ Guide for the Assessment of Visual Ability in Infants) and classified according to visual conducts scores. Differences between groups were compared considering motor development (Alberta Infant Motor Scale) maternal mental health (Edinburgh Postnatal Depression Scale and Hamilton Anxiety Scale); home environment (Affordances in the Home Environment for Development Scale); maternal care (Coding Interactive Behavior); breastmilk composition (total fatty acids, proteins, and cortisol); and maternal metabolic profile (serum hormones and interleukins). Mothers of infants with lower visual fixation scores had higher levels of protein in breastmilk at 3 months. Mothers of infants with better visual conduct scores had higher serum levels of T4 (at 1 month) and prolactin (at 3 months). There were no associations between visual ability and motor development, home environment, or maternal care. Early newborn neuromotor development, especially visual and fine motor skills, is associated with maternal biological characteristics (metabolic factors and breastmilk composition), highlighting the importance of early detection of maternal metabolic changes for the healthy neurodevelopment of newborns.

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1. Introduction

Neurocognitive and motor development in early life are established by a cascade of basic abilities (Rose et al., 2008). Visual fixation skills represent the ability to accurately target the eyesight to a particular point. This skill is relevant for cognitive neurodevelopmental processes, serving as an early sensitive marker of subtle changes in cognitive, perceptive, and motor functions (Cang & Feldheim, 2013; Sandfeld Nielsen et al., 2008; Stjerna, 2015).

Visual functioning reflects the integrity of cortical and subcortical areas, which appear interconnected for both motor and cognitive abilities (Atkinson, 2017; Stjerna, 2015). At birth, brain structures belonging to the subcortical pathway are more developed than those in the cortical pathway (Mercuri, 2007). In the first few months, subcortical systems involving the superior colliculus in the midbrain sustain important visual capabilities, such as early visual fixation ability, visual attention, visual tracking, and saccadic ocular movements (Kandel, 2014; Mercuri, 2007). The development of visual tracking is determined by two important factors: the ability to predictively follow a moving object and the ability to focus attention on it. In typically developing infants, attention skills emerge shortly after birth, with smooth eye movements developing within the first two months of age (Kaul, 2022). The infant's visual tracking begins with a preference of visual fixation especially for geometric features, such as faces (Atkinson, 2017; Farroni, 2005; Johnson, 2005). Between 2 and 6 months of age, the infant has a predominance of visual contact compared to visual fixation for other regions of the face, such as the mouth, body, or other objects (Farroni, 2005). As time passes, infants start to shift their attention, observing wider regions of the face, body, objects, and environment (Jones & Klin, 2013).

In the first months after birth, the visual system primarily operates at the subcortical level, and becomes progressively integrated, dominated, and modulated by cortical processes during the first year of life (Gilmore, 2012; Kaul, 2016; Stiles & Jernigan, 2010). These subcortical networks, crucial for adequate visual function, also serve as a foundational nucleus for higher cognitive functions later in life (Stjerna, 2015). An important determinant of cognitive and motor development is visuospatial function – the ability to observe, perceive and process visual and spatial information in the environment (Atkinson & Braddick, 2007).

Several studies demonstrate the interconnectedness of early visual abilities with later cognitive skills. Newborn visual fixation skills are associated with cognitive test scores and IQ at 1 and 6 years of age (Boot, 2013; Taanila, 2005; Wallace, 1995). These abilities also relate to visuomotor performance at 2 and 5 years of age, as well as visual reasoning at 5 years of age, where superior performance in visual fixation tasks is related to the development and integrity of white matter (Stjerna, 2015). Compared to motor skills, early visual fixation skills are better predictors of later visuocognitive development (Poranen-Clark, 2015; Stjerna, 2015). Visuospatial attention and movement processing function in the first year of life predict cognitive and motor development at 2 years of age, as reported by Beunders (2021). Visual tracking at 4 months is strongly correlated with cognition, receptive and expressive language, and fine motor function at 3 years (Kaul, 2016), as well as predicts cognitive and attention skills at age 6.5 (Kaul, 2022). These findings suggest that visual tracking plays a quantifiable role in children's early linguistic, thinking, reasoning, and social-cognitive development (Brooks & Meltzoff, 2015; Kaul, 2022). Early development of these visual skills, integrated with cortical maturation, can promote positive long-term cognitive development (Kaul, 2016; Stjerna, 2015).

Although cognitive cascades have been extensively studied in infant cognitive research, mechanisms underlying newborn visual fixation abilities remain poorly understood (Stjerna, 2015). Environmental and biological factors can influence early visual development and subsequently affect infant cognition. Breastfeeding plays a crucial role in optimal visual development, with specific nutrients in human milk critical for preterm infants' visual development (Birch, 1993; Hoffman et al., 2009). There is an intimate dialog leading to biological responses affecting numerous organ systems in the nursing dyad, with both uni- and bidirectional components (Krebs, 2023; Neville, 2023). As breastfeeding influences children visual-motor integration (Smith, 2003), the infant's mental and physical state create subsequent responses in both the lactating parent and infant that affect the brain in both individuals (Krebs, 2023; Neville, 2023).

Maternal metabolism also affect the cognitive function of the progeny by influencing brain development, and thereby visual function (Henrichs, 2010; Min, 2016). Adequate maternal hormone levels are crucial for perinatal brain development, including thyroid hormones, which regulate the development of neural circuits that affect cognition and psychomotor function (Henrichs, 2010; Oken, 2009; Wang, 2014).

The quality of mother-infant interaction is another critical factor influencing infant development and cognition (Shannon et al., 2002). Infants of mothers demonstrating effective interaction quality tend to exhibit higher mental development (Barnard & Eyres, 1979). Impairment of this interaction may be associated with maternal depressive symptoms (Zhang, 2017), which in turn is linked with higher cortisol levels and hypothalamic–pituitary–adrenal (HPA) axis hyperactivity (Liu et al., 2020). Low levels of prolactin, a hormone associated with milk production, have been related to postpartum depression and stress reactivity (Gust et al., 2020). Beyond caregiving, environmental factors that most determine variations in developmental skills are the environmental opportunities, practices during infants' routines, and the home space (Pereira et al., 2016). Environmental enrichment and practices are strongly influenced by parental education and tend to remain stable, although there is an increase in the variety of stimulation as well as fine and gross motor toys offered as the child gets older (Francisco, Graciosa, Pacheco, & Sanada, 2023).

Although visual fixation abilities are important early predictors of later neurodevelopment, little is known about the influence of maternal biological and environmental factors associated with these abilities in newborns, which was central to our research question. The main objective of this study is to compare infants with different levels of visual fixation abilities, investigating the relationship with maternal metabolic and psychological profiles that may affect infants at risk for poorer later neurodevelopmental outcomes. Our hypothesis was that the interindividual differences in visual fixation abilities in infants would be related to maternal behavior and biological characteristics. More specifically, we investigated the association between visual fixation abilities at 1 month of age and a) newborn characteristics (age at evaluation, weight gain in the 1st and 3rd months of life, gross motor skills in the 1st and 3rd months of life); b) breastmilk characteristics (total fatty acids, proteins, and cortisol at 1 and 3 months of age); c) maternal metabolic profile (peripheral cortisol, prolactin, T3, T4 and interleukins at 1 and 3 months of age); d) maternal psychological profile (anxiety and depression at 1 month) and e) environmental variables (maternal care at 1 month and toys available for stimulation measured at 3 months, assuming that the measure reflects the age-appropriate richness of the environment across development).

2. Methods

2.1. Study population

We utilized data from a prospective human cohort study involving 82 mother-infant dyads recruited from Hospital de Clínicas de Porto Alegre and Grupo Hospitalar Nossa Senhora da Conceição in Porto Alegre, Rio Grande do Sul, Brazil. This study was approved by the Human Research Ethics Committee of Hospital de Clínicas de Porto Alegre and Grupo Hospitalar Nossa Senhora da Conceição (GPPG/HCPA 13–0507). It was part of a larger project that examined maternal behavior and variations in maternal care.

Mother-infant dyads were recruited during antenatal consultations

or immediately after birth from February 2015 to January 2016. Participants were selected for analysis based on the following criteria: residing in Porto Alegre, mothers aged over 18 years, absence of abuse or history of drug use, single gestation of at least 37 weeks, no more than four pregnancies, and newborns with no history of congenital disease or hospitalization needs. After signing the Informed Consent Form, mothers were interviewed regarding their basic health history, obstetric data, and economic status. Socioeconomic classification was determined using the ABEP score (Brazilian Association of Research Companies), which accesses socioeconomic status attributing points based on ownership of specific household items (e.g. number of bathrooms, number of automobiles, presence of a personal computer, dishwasher, refrigerator, freezer, washing machine, microwave, etc.), access to piped water, and the educational level of the head of the household (with points ranging from no schooling to higher education degree). Higher scores indicate higher socioeconomic status: Class A – 35 to 46 points; Class B – 23 to 34 points; Class C – 14 to 22 points; Class D – 8 to 13 points and Class E – 0 to 7 points (for more details and the complete table, refer to https://www.abep.org/criterio-brasil) (Rutter, 1988).

After the inital contact, mother-infant dyads were visited at home twice: first between 25–40 days and again between 85–100 days after birth. Each visit was conducted by a trained psychiatrist and a physiotherapist (or undergraduate physiotherapy student). During these visits, questionnaires and tasks were administered to investigate various factors:

- Maternal factors such as age, education level, type of delivery, number of antenatal consultations, breastfeeding type, and smoking habits (categorized as yes or no).
- Biological characteristics of the newborn including sex, gestational age, birth weight, head circumference, and Apgar score at one minute.
- Infant motor tests, maternal psychological profile, environmental variables, and collection of maternal milk and blood samples.

Out of the 82 recruited mother-infant pairs, 26 infants were fully asleep or drowsy during the visit and could not be adequately assessed. Additionally, data from 5 infants were excluded due to active crying during the tasks. Therefore, data from a total of 51 infants were used in this study.

2.2. Measures

2.2.1. Visuomotor and motor behavioural measurement in the infants

The newborn's motor evaluation was performed during each one of the two visits (25–40 days and 85–100 days after birth). Two different instruments were used for the evaluation: the Visuomotor Behavior Assessment Guide for the Infant at 1 month (Gagliardo, 1997) and the Alberta Infant Motor Scale at 1 and 3 months (Piper et al., 1994).

The Infant Visuomotor Behavior Assessment Scale/ Guide for the Assessment of Visual Ability in Infants (Gagliardo, 1997, 2004b; Gagliardo, Gonçalves, & Lima, 2004a) assesses oculomotor (visual fixation, eye contact, smile in response to social contact, visual exploration of the environment, visual exploration of the hand, horizontal and vertical visual tracking) and appendicular functions (increase movement of the upper limb, extension of the arms towards the object displayed). Trained examiners (a physiotherapist and a physiotherapy undergraduate student trained together for consistency) evaluated the children. Infants were tested either lying on supine on a comfortable but firm surface allowing free head movements, or in a sitting position. The assessment consists of 9 tests: 1) eye contact with examiner (examiner's face positioned 30 cm above and aligned with child, smiling and moving the head 4–5 times; a positive response is when the child looks at the examiner for at least 3 s); 2) smile in response to social contact (same setup as number 1; a positive response is when the child smiles or vocalizes); 3) visual fixation (examiner behind the child, holding a bull's eye at the midline 20–30 cm above child's eyes; a positive response is when the child looks to bull's eye for at least 3 s); 4) Horizontal visual tracking (similar setup as 3, but moving the bull's eye slowly left and right; a positive response is when the child can track the bull's eye for a complete excursion, even if deviating the gaze momentarily 1–2 times); 5) Vertical visual tracking (similar setup as 3, but moving the bull's eye slowly up and down; a positive response is when the child can track the bull's eye for a complete excursion, even if deviating the gaze momentarily 1–2 times); 6) Spontaneous visual exploration of the environment; 7) Spontaneous visual exploration of hands; 8) Increased arms movements (similar setup as 3, but using the bull's eye to attract the child's attention and then keeping it still; a positive response is when the child increases arms movements while looking at the object); 9) Attempt to reach (similar setup as 8; a positive response is when the child moves arms in the object's direction).

More mature children demonstrate better ability to sustain eye contact with the examiner/object and perform intentional arm movements. Based on the 9-point scale described above and the median score obtained in our sample, infants were categorized into two groups: those scoring 6 or higher were classified as having a "higher score" while those scoring 5 or lower were classified as having a "lower score" for visual conduct.

The Alberta Infant Motor Scale, a validated instrument (Valentini & Saccani, 2012) and standardized in Brazil (Saccani & Valentini, 2012), evaluates infants' postures (prone, supine, sitting, standing), counter gravity movements, and weight support. Infants were categorized according to the instrument's instructions into three groups: delayed (below 5th percentile), suspected (between 5th and 25th percentile) and normal (above 25th percentile).

2.2.2. Maternal mental health

The maternal psychological profile was assessed using the Edinburgh Postnatal Depression Scale (EPDS) (Santos, 2007; Cox, Holden, & Sagovsky, 1987), a self-report instrument consisting of 10 items referring to the last 7 days. Data collection for the EPDS occurred during the first visit (25–40 days after birth). This instrument was utilized to evaluate the presence and severity of maternal depressive symptoms. The Hamilton Scale for Anxiety (Hamilton-A) (Gorenstein et al., 2000; Hamilton, 1960; Telles-Correia & Barbosa, 2009) was administered during the same visit (25–40 days after birth) by a trained psychiatrist from the home visiting team. This scale assesses anxiety symptoms and comprises 14 items. Responses range from 0 (not present) to 4 (severely present), categorizing scores into levels of anxiety: absence, mild anxiety, mild to moderate anxiety, and moderate to severe anxiety.

2.2.3. Characterization of home environment

The home environment was assessed using the Affordances in the Home Environment for Development scale (AHEMD-IS) (Caçola et al., 2011). This scale was administered during the second visit (85–100 days after birth), as it is validated for use from three months of age onwards, although it broadly reflects newborn environment. The AHEMD-IS evaluates the opportunities for stimulation provided by the home environment to infants. It consists of 32 questions filled out by parents, subdivided into items assessing aspects such as the newborn and the family, physical space of the residence, daily activities, and availability of toys for both fine and gross motor skills within the home.

2.2.4. Maternal care assessment

Maternal care assessment data were collected at 25–40 days postpartum. Mother-infant dyads were filmed for 5 min during free interaction, and the behavior was scored using the Coding Interactive Behavior (CIB) for newborns. This assessment included maternal gaze, affection, vocalization, touch, mother-baby positioning, infant affection, alertness, and vocalization, evaluated every 10 s. Additionally, a global assessment of parental affect, intrusiveness, and acknowledgment was rated on a scale ranging from 1 to 5, with 1 indicating minimal

occurrence of specific behaviors and 5 indicating maximum occurrence. The CIB assessments were conducted by a single psychiatrist trained in the coding system (Feldman et al., 1999); given the single rater, inter-rater reliability was not applicable.

2.2.5. Maternal milk profile

Maternal milk profiles were collected during two visits (25–40 days and 85–100 days after birth). Milk samples were collected between 2 pm and 6 pm, transported refrigerated, and subsequently frozen at −80 °C. Total fatty acids, proteins, and cortisol levels were measured in the maternal milk. Fatty acid methyl esters were identified using gas chromatography with a CG-17A Flame Detector model (FID) from Shimadzu (GC-17A, Kyoto, Japan). Chromatograms were recorded and analyzed using the GC Solution program. Compounds were separated and identified on a Carbowax capillary column (30 m × 0.25 mm). For chromatographic separation, 1 μl of sample was injected using a 10 μl syringe Hamilton (Reno, NV, USA) in Split System = 5. Nitrogen gas served as the carrier gas with a programmed linear velocity of 37.8 cm s^{-1}. The injector and detector temperatures were maintained isothermally at 220 °C and 240 °C, respectively. The initial column temperature was set at 200 °C (held for 2 min), then increased at 4 °C per minute up to 240 °C, in a total analysis time of 20 min. The carrier gas flow rate in the column was 1.0 ml min^{-1}. These analyses were conducted at the Nutritional Biochemistry Laboratory, Universidade Federal de Viçosa, Viçosa, MG, Brazil. Milk protein concentration was quantified using the bicinchoninic acid (BCA) protein assay kit (Pierce Biotechnology, Rockford, IL, USA) and milk cortisol concentration was measured with commercial ELISA kits (ADI 901–071).

2.2.6. Maternal metabolic evaluation

The maternal metabolic profile was assessed by measuring serum hormones (T3, T4, prolactin, and cortisol) and interleukins (Il-10, Il-1β, Il-6, and TNF-α). Blood samples were collected during both visits between 2 pm and 6 pm, transported in cold conditions, and centrifuged at −4 °C for 10 min at the research facility. Serum was aliquoted and stored in −80 °C. Serum hormones (T3, T4, prolactin, and cortisol) were quantified using Centaur XP equipment from Siemens through chemiluminescence methodology. Interleukins (Il-10, Il-1β, Il-6, TNF-α) were measured using the Milliplex® Map Human High Sensitivity T Cell Magnetic Bead Panel on first time-thawed samples (with minimum sensitivity for each interleukin as follows: Il-6 = 0.11 pg / ml; Il-10 = 0.56 pg / ml; Il-1β = 0.14 pg / ml; TNFα = 0.16 pg / ml).

2.3. Statistical analysis

The significance level was set at 5 %, and statistical analyzes were conducted using the Statistical Package for the Social Sciences (SPSS), version 29.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were described as mean and confidence interval, while categorical data were presented as relative frequencies or median and interquartile range. Normality of data distribution was assessed using the Kolmogorov-Smirnov test. For normally distributed data, Student's t-Test and One-Way ANOVA were performed. Fisher Exact Test was used for non-parametric categorical data. Non-parametric data were log trasnformed for subsequent analysis. Multivariate Analysis of Variances (MANOVA) was employed to examine differences between the groups across five dimensions of variables: a) newborn characteristics (age at evaluation, weight gain in the 1st and 3rd month of life, gross motor skills in the 1st and 3rd month of life); b) breastmilk characteristics (total fatty acids and proteins at 1 and 3 months of age, cortisol at 1 month of age); c) maternal metabolic profile (peripheral cortisol, prolactin, T3, T4 and interleukins at 1 and 3 months of age); d) maternal psychological profile (anxiety and depression at 1 month) and e) environmental variables (maternal care at 1 month and availability of toys for stimulation). MANOVA uses the covariance between outcome variables in testing the statistical significance of the mean differences. MANOVA was chosen due to the biological correlations among the groups of outcome variables. No covariates were included in the MANOVA analysis since there were no statistically significant differences in baseline sample characteristics between the higher and lower visual conduct score groups. Additionally, as there were only two groups (higher and lower visual conduct score), post hoc tests were not necessary.

3. Results

The visuomotor behavior was tested in 51 infants at 1 month. The percentage of positive response for each of the nine components of the visual fixation scale were respectively: visual fixation (100 %), eye contact with the examiner (94.1 %), smile in response to social contact (28.0 %), horizontal visual tracking (92.0 %), vertical visual tracking (98.0 %), environmental visual exploration (94.0 %), hand visual exploration (0.0 %), increased arm movements when visualizing object (32.0 %), extends the arm towards the object (8.0 %) and cephalic control (4.1 %). Table 1 compares the groups of infants divided according to the visuomotor behavior score in many confounders. There are no statistically significant differences between the higher and lower score groups for the baseline sample characteristics.

3.1. Newborn characteristics

Infants from higher or lower visuomotor behavior scores groups were compared for age at evaluation in days, weight gain in the 1st and 3rd month of life (in Z-scores according to WHO standards) (World Health Organization, 2006), as well as their gross motor skills at the 1st and 3rd month of life in percentiles according to the local population (Saccani et al., 2016).

The groups did not statistically differ in terms of age at evaluation [Student *t*-test, t(49) = 0.510, P = 0.613]. When adjusting for length at the corresponding age, there were no statistical differences between the groups in weight gain from birth to 1 month [One-Way ANOVA, F(1, 44)

Table 1
Description of the baseline characteristics of the cohort. Infants were classified according to their visual fixation score at 1 month of age.

	Higher score of visual fixation at 1 month of age		Lower score of visual fixation at 1 month of age		P-value
Gestational age (weeks)[a]	39.20	(38.50; 39.90)	39.10	(38.64; 39.56)	0.977
Birth weight (g)[a]	3261.3	(2974.1; 3548.6)	3417.4	(3303.4; 3531.5)	0.191
Head circumference (cm)[a]	33.77	(33.01; 34.52)	34.14	(33.62; 34.66)	0.398
Number of prenatal visits[a]	8.93	(7.64; 10.23)	9.41	(7.99; 10.84)	0.608
Apgar score 1 min[a]	8.27	(7.42; 9.12)	8.69	(8.40; 8.98)	0.311
Maternal age[a]	27.60	(24.54; 30.66)	26.76	(24.67; 28.85)	0.640
Males[b]	52.4	(31.04; 73.76)	50.0	(32.11; 67.89)	1.000
Smoking during gestation[b]	19.0	(2.22; 35.78)	13.3	(1.15; 25.45)	0.702
Maternal Schooling (<8 years)[b]	71.4	(52.07; 90.73)	73.3	(57.47; 89.13)	1.000
SES (Socioeconomic status) Classes C/D/E from ABIPEME[b]	47.6	(26.24; 68.96)	60.0	(42.47; 77.53)	0.408
Exclusive breastfeeding[b]	66.7	(46.54; 86.86)	66.7	(49.84; 83.56)	1.000
Vaginal delivery[b]	57.1	(35.93; 78.27)	60.0	(42.47; 77.53)	1.000

[a] Student *t*-test. Data expressed as mean and 95 % confidence intervals.
[b] Chi-square test. Data expressed as relative frequencies (%) and 95 % confidence intervals.

= 0.174, P = 0.678], and from birth to 3 months [F(1, 35) = 2.211, P = 0.089]. There were also no significant differences in gross motor skills between the two groups at 1 [Fisher's exact test, P = 1.000] and 3 months [P = 0.773] (see Table 2).

A multivariate model including all variables (age at evaluation, weight gain, and gross motor skills) at 1 month (after log transformation of the non-normally distributed variables) was not statistically significant [MANOVA F(3, 19) = 0.186, P = 0.905]. Similarly, no statiscally significant differences were found between groups for the multivariate model including all variables at 3 months [MANOVA F(2, 28) = 0.900, P = 0.418].

3.2. Breastmilk characteristics

Breastmilk from mothers in the two groups were not statiscally significant different regarding the total fatty acids content at 1 [Student *t*-test, t(25) = 0.481, P = 0.635, n = 11–16/group] or 3 months of age [Student *t*-test, t(19) = 0.241, P = 0.812, n = 9–12/group]. There were no significant differences in the breastmilk protein content at 1 month [Student *t*-test t(37) = 0.990, P = 0.328, n = 18–21/group]. However, at 3 months, the group with the lower visual fixation scores had increased levels of milk protein [Fisher's exact test, P = 0.047] (see Table 3). There were no significant differences in the milk cortisol levels between groups [Student *t*-test, t(37) = 0.071, P = 0.944, n = 18–21/group]. A multivariate model including all the variables at 1 month (after log transformation of the non-normally distributed variables) was not statistically significant [MANOVA F(3, 21) = 0.768, P = 0.525]. Similarly, the multivariate model including all the variables at 3 months did not show significance [MANOVA F(2, 18) = 0.484, P = 0.624].

3.3. Maternal metabolic profile

We compared the two groups of infants in terms of the metabolic profile of the mothers. We analyzed different serum hormones (T3, T4, prolactin, cortisol), as well as interleukins (Il-10, Il-1β, Il-6, and TNF-α) at 1 and 3 months postpartum.

Mothers of infants of high and low groups differ statistically in terms of T4 levels at 1 month postpartum [Student *t*-test, t(35) = 2.826, P = 0.008, n = 14–19/group], showing higher levels in the group with higher visual fixation scores. At 3 months postpartum, mothers of the group with higher visual fixation scores had increased prolactin levels [Fisher's exact test, P = 0.031] (see Table 4). There were no statistically significant differences between groups for the other measures. A multivariate model including all variables at 1 month (after the log transformation of the non-normally distributed variables) almost

Table 2
Newborn characteristics in the two groups of infants divided according to the visual fixation score at 1 month of age.

	Higher score of visual fixation at 1 month of age		Lower score of visual fixation at 1 month of age		P-value
Age at evaluation (days)[a]	28.0	(25.51; 30.49)	28.30	(26.13; 30.46)	0.613
Delta Z score weight for age, 1 month – birth [b]	−0.18	(−0.73; 0.37)	−0.26	(−0.61; 0.08)	0.678
Delta Z score weight for age, 3 months – birth [b]	−0.01	(−0.87; 0.84)	−0.28	(−0.90; 0.34)	0.089
Percentile for Alberta Infant Motor Scale – 1 month[c]	37.5	(25–75)	50.0	(25–62.5)	1.000
Percentile for Alberta Infant Motor Scale – 3 months[c]	50.0	(25–75)	50.0	(50–75)	0.773

[a]Student t-test, [b] One-Way ANOVA adjusted by current Z score for length. [c]Fisher Exact Test. Data expressed as mean and 95 % confidence intervals[a,b] or median and interquartile range[c].

Table 3
Breastmilk characteristics in the two groups of infants divided according to the visual fixation score at 1 month of age.

	Higher score of visual fixation at 1 month of age		Lower score of visual fixation at 1 month of age		P-value
Total fatty acids at 1 month (μg/g)[a]	99.02	(98.29; 99.76)	99.24	(96.70; 101.78)	0.635
Total fatty acids at 3 months (μg/g)[a]	98.94	(98.19; 99.69)	98.35	(97.34; 99.35)	0.241
Total protein content at 1 month (μg/ml)[a]	11421.05	(9984.68; 12857.43)	11470.08	(7913.12; 15027.04)	0.328
Total protein content at 3 months (μg/ml)[b]	8688.10	(4134.82)	9930.22	(4843.5)	0.047 *
Cortisol at 1 month (pg/ml)[a]	2949.63	(2365.26; 3533.99)	3350.40	(2473.60; 4227.19)	0.944
Milk collected immediately before or at least 50 min after nursing [c]	58.8	(28.29; 89.31)	50.0	(20.45; 79.55)	0.748

[a]Student *t*-test, [b] Fisher Exact Test, Chi-square test[c]. Data expressed as mean and 95 % confidence intervals[a], median and interquartile range[b] or relative frequencies (%) and 95% confidence intervals[c]
* Statistically significant difference ($p < 0.05$).

Table 4
Maternal metabolic profile in the two groups of infants divided according to the visual fixation score at 1 month of age.

	Higher score of visual fixation at 1 month of age		Lower score of visual fixation at 1 month of age		P-value
Maternal metabolic profile at 1 month postpartum					
T3 (ng/dL)[a]	130.67	(109.84; 151.51)	120.41	(113.37; 127.45)	0.474
T4 (ng/dL)[a]	1.20	(1.06; 1.33)	1.07	(1.03; 1.12)	0.008 *
Prolactin (ng/mL)[a]	215.12	(53.32; 376.92)	147.92	(90.20; 205.65)	0.494
Cortisol (μg/dL)[a]	6.69	(2.90; 10.47)	5.26	(3.77; 6.75)	0.729
Il-10 (pg/mL)[a]	6.18	(−0.17; 12.53)	6.70	(5.19; 8.21)	0.995
Il-1β (pg/mL)[a]	1.30	(0.65; 1.95)	1.13	(0.87; 1.38)	0.644
Il-6 (pg/mL)[b]	1.30	(1.53)	1.36	(0.55)	0.540
TNFα (pg/mL)[a]	3.90	(3.18; 4.62)	4.28	(3.73; 4.82)	0.471
Maternal metabolic profile at 3 months postpartum					
T3 (ng/dL)[a]	128.00	(105.33; 150.67)	111.40	(104.64; 118.17)	0.974
T4 (ng/dL)[a]	1.16	(0.95; 1.37)	1.08	(1.02; 1.14)	0.110
Prolactin (ng/mL)[b]	82.70	(76.95)	33.22	(34.42)	0.031 *
Cortisol (μg/dL)[a]	5.48	(2.40; 8.57)	5.52	(4.41; 6.63)	0.801
Il-10 (pg/mL)[a]	6.49	(−0.76; 13.75)	6.59	(5.05; 8.14)	0.226
Il-1β (pg/mL)[b]	1.17	(1.12)	1.19	(1.11)	0.145
Il-6 (pg/mL)[b]	1.37	(1.83)	1.34	(1.04)	0.192
TNFα (pg/mL)[b]	3.82	(1.05)	4.45	(1.99)	0.839

[a]Student *t*-test, [b] Fisher Exact Test. Data expressed as mean and 95% confidence intervals[a] or median and interquartile range[b].
* Statistically significant difference ($p < 0.05$).

reaches statistical significance [MANOVA F(8, 23) = 2.331, P = 0.054], in which T4 levels were statistically significant [F(1, 31) = 11.422, P = 0.002]. A multivariate model including all variables at 3 months showed that the visual fixation score at 1 month is associated with the maternal metabolic profile observed at 3 months [MANOVA F(7, 21) = 2.988, P = 0.024], in which Il-6 [F(1, 28) = 6.646, P = 0.016] and prolactin [F(1, 28) = 8.948, P = 0.006] were statistically significant.

3.4. Maternal mental health

There were no significant differences in maternal mental health scores between groups of infants from higher and lower visual fixation scores [EPDS median (interquartile range): higher visual fixation score = 7 (7); lower fixation score = 6 (6), Fisher Exact Test P = 0.415]; [Hamilton mean (95 % CI): higher fixation score = 6.33 (3.74; 8.93); lower fixation score = 4.97 (3.09; 6.84), Student's t-Test t(48) = 0.907, P = 0.369]. A multivariate model including all the variables (after log transformation of the non-normally distributed variables) was not statistically significant [MANOVA (2, 44) = 0.210, P = 0.811].

3.5. Environmental variables

The infants's environment was characterized in two "layers" (Dalle Molle, 2017) considering maternal care and the affordances in the home environment for motor development scale (AHEMD-IS). We investigated these two environmental factors since an enriching and stimulating early environment can promote healthy growth and brain development (Valentini & Saccani, 2012). We did not observe significant differences between the groups considering the different components of the Affordance scale (physical space, daily activities, toys for gross motor skills, toys for fine motor skills, total score) and for maternal care (Acknowledgement, Affect and Intrusiveness) (See Table 5). A multivariate model including all the variables (after log transformation of the non-normally distributed variables) was not statistically significant [MANOVA (8, 18) = 0.716, P = 0.675].

4. Discussion

This study elucidated that early neuromotor development, defined by visual fixation abilities in 1-month old infants, correlates significantly with specific maternal biological characteristics. Infants classified in the lower visual fixation group exhibited higher levels of protein in the breastmilk at 3 months of age. Additionaly, mothers of infants with better visual conduct scores had higher serum T4 levels in the first month and prolactin levels in the third month. Our findings indicate that environmental factors, maternal care, and maternal mental health did not influence visual conduct abilities in the first month of life.

Table 5
Environmental variables in the two groups of infants divided according to the visual fixation score at 1 month of age.

	Higher score of visual fixation at 1 month of age	Lower score of visual fixation at 1 month of age	P-value
Affordances in the Home Environment for Motor Development Scale (AHEMD-IS)			
Physical space	5 (4)	4.5 (3)	0.929
Daily activities	7 (6)	7.5 (4)	0.992
Toys gross motor	3 (2)	3.5 (7)	0.345
Toys fine motor	1 (1)	1.5 (1)	0.345
Total score	17 (10)	17 (6)	0.827
Coding Interactive Behavior (CIB)			
Parental acknowledging	2.5 (2)	3.25 (1.5)	0.739
Parental intrusiveness	1.5 (0.5)	1.25 (0.5)	0.352
Parental affect	3.5 (1)	3.5 (1)	0.842

Fisher Exact Test for all comparisons. Data expressed as median and interquartile range.

Visual fixation, including ocular contact with the examiner, vertical and horizontal visual tracking, and visual exploration of the environment, was observed in all infants evaluated at one month. This aligns with previous studies highlighting the maturation of the subcortical system at birth, which underpins these primitive visual functions (Atkinson, 2017; Kaul, 2016; Mercuri, 2007; Mercuri, Ricci, & Romeo, 2012; Ruas, Gagliardo, Martinez, & Ravanini, 2010; Gagliardo, Gonçalves, & Lima, 2004). These primitive functions are fundamental for the subsequent development of fine motor skills (Ricci, 2008a,b; Ruas, Gagliardo, Martinez, & Ravanini, 2010; Stjerna, 2015; Gagliardo, Gonçalves, & Lima, 2004). Notably, our study observed a higher frequency of positive responses in vertical visual tracking compared to previous studies, potentially due to differences in the testing instruments used. Our use of a black and white bull's eye, known to attract infant attention due to contrast sensitivity, likely contributed to these findings. The black and white bull's eye is similar to the one used in the standardization of the "Visual Test Battery" test (Ricci, 2008b), in contrast to the ring suspended by a cord used in the reference study (Gagliardo, Gonçalves, & Lima, 2004). It is known that infants are attracted to toys with contrasting colors (Mercuri, 2007; Ricci et al., 2008a, 2008c) and they have a preference for visual fixation in faces (Farroni, 2005; Johnson, 2005; Pereira, 2017). For that reason, our assessment instrument may have attracted more attention from the infants. This result corroborates the study by Ricci and collaborators (Ricci, 2008b), which found that 95 % of the newborns evaluated were able to follow the bull's eye during the vertical course.

Studies evaluating visual behavior in infants born at various gestational ages have shown a progressive maturation of visual functions with increasing gestational age. Preterm infants with an average of 28.9 gestational weeks (27.0–32.9) evaluated at 31 to 33 post-menstrual weeks showed 90 % visual fixation frequency, horizontal, and vertical visual tracking (Ricci, 2010). Another study evaluated preterm infants with an average of 28.2 gestational weeks (25.0–30.9) at 35 and 40 post-menstrual weeks, where 91 % of the infants had visual fixation at 35 weeks and 97 % at 40 weeks; 97 % demonstrated horizontal and vertical visual tracking at 35 weeks and 100 % at 40 weeks (Ricci, 2008a). In late preterm infants with average 35.2 weeks gestational age (34.0–36.9), 98 % had visual fixation, 98 % visual horizontal tracking, and 58 % vertical visual tracking. When evaluated at full-term age (between 39 and 41 weeks), 100 % showed visual fixation and horizontal visual tracking and 88 % had vertical visual tracking (Romeo, 2012). In relation to full-term newborns, 95 % had visual fixation, horizontal and vertical visual tracking (Ricci et al., 2008a, 2008b). These studies and our findings underscore that both prenatal and extrauterine factors play pivotal roles in the maturation of visual pathways during early infancy.

Other functions assessed in our study, such as visual exploration of the hand, arm extension when viewing objects, and cephalic control, typically develop between 2 to 3 months of age, consistent with established literature (Ferreira, 2011; Gagliardo, 2004; Ruas et al., 2010; Souza, 2011). Our infant participants demonstrated a greater frequency in arms movement when viewing the object. The frequency of the ability to smile during social contact is also in line with the literature, and this capacity is associated with positive social factors, such as parental care (Mendes & Seidl-de-Moura, 2014), and predictors of cognitive, social and emotional development indexes (Atkinson, 2017; Farroni, 2005; Johnson, 2005; Mercuri, 2007; Pereira, 2017).

Despite the potential confounding factors such as gestational age, birth weight, and other perinatal characteristics, we found no correlation with visual skills scores in our study. This contrasts with studies reporting associations between certain perinatal factors and visual behavior impairments, such as low birth weight and length, smaller head circumference, lower gestational age, and male sex (Geldof, 2012; Phadke, 2014). Preterm infants have a high incidence of visual changes, which can be explained not only by retinopathy of prematurity and brain lesions, but also by the development of white matter in optical

radiation (Bassi, 2008). Other studies support that gestational age, rather than birth weight, would be determinant for the maturation of cortical aspects of visual function (Carrara, 2016; Ricci et al., 2008a, 2008b). On the other hand, a study states that being born small for gestational age (SGA) associated or not with prematurity induces changes in axonal processes, leading to neuronal loss of the retinal nerve fibers and consequent brain atrophy, visuomotor difficulties and cognitive dysfunctions (Oros, 2014). However, our community-based sample suggests that variations in birth weight within normal ranges do not significantly impact early visual behavior. Similarly, socio-demographic variables like maternal age, education level, and socio-economic status (SES) did not correlate with visual conduct scores. This finding corroborates previous research indicating that maternal socio-demographic characteristics have minimal influence on newborn visual fixation (Phadke, 2014). There was also no association between visual score at 1 month and the richness of the environment at 3 months. In our analysis, the reasoning for associating the environment richness at 3 months with the behavioral data at 1 month assumes that the tool reflects the age-appropriate richness of the environment across development, although it is expected an increase in the variety of stimulation and fine and gross motor toys offered as the child gets older (Francisco, Graciosa, Pacheco, & Sanada, 2023).

In terms of gross motor function, as assessed by the Alberta Infant Motor Scale, we did not find a significant correlation with early visual conduct data. Fine motor skills are typically more directly linked to visual abilities in newborns, although the successful functional scope does not appear before 4 months of life (Hofsten, 2009). The development of fine motor skills depends on the attention and processing of visual information since fine adjustments to the ability to reach and grasp are visually guided. Due to the characteristics of fine motor development, initial visual abilities are fundamental for fine motor skills and are also predictive of cognition and language (Kaul, 2016; Miquelote, 2012). Conversely, the relationship between visual conduct and gross motor function seems to be more important for the infant's first three months of life, when they start to demonstrate antigravity movements, and alterations in visual behavior may interfere with the feedback from the proprioceptive and vestibular systems over the motor system (Prechtl, 2001). This interdependence is supported by studies describing an inability to walk at 2 years in preterm infants with visual impairment and in blind infants without brain lesions who had inability for cephalic control in prone at 3 months (Phadke, 2014; Prechtl, 2001).

Analyzing maternal biological markers, we observed that higher protein levels in breastmilk at 3 months were associated with lower scores in early visual conduct. Studies indicate that breastmilk contains several types of proteins with specific functions, such as the supply of amino acids necessary for adequate infant growth, the contribution of breastmilk digestion by the immature gastric tract, aiding intestinal iron absorption, optimization function of the immune system and physiological development of the intestine (Huang, 2017; Lönnerdal, 2016; Wada & Lönnerdal, 2014). The amount of protein in breastmilk is high in early life (in colostrum), decreases markedly after the first month, and gradually decreases in the progressive stages of lactation (Gidrewicz & Fenton, 2014; Kreissl, 2016; Lönnerdal, 2016). Breastmilk protein is an essencial nutrient for newborn brain growth and development. Studies report that the average protein in the breastmilk of preterm infants is twice as high compared to the average protein in breastmilk of infants born at an adequate age (Gidrewicz & Fenton, 2014; Kreissl, 2016). Breastfeeding facilitates the child's adjustment to the extrauterine environment, and it appears that changes in macronutrient composition occur in response to the needs of the offspring. We did not find in current literature studies that related maternal milk composition, visual behavior and possible correlations. Our findings may be explained by the demand presented by infants who had alterations in early visual behavior, and the prompt maternal adaptation in response to such demands.

Analyzing the maternal metabolic profile, we found a positive association between maternal T4 serum hormone and the infant's visual conduct scores in the first month of life. During pregnancy, fetal thyroid function is immature and the fetus is completely dependent on maternal thyroxine (Min, 2016). Adequate levels of thyroid hormones during the fetal developmental period are required for axon elongation, dendritic branching, neuronal migration, differentiation and proliferation, and synapse formation (Min, 2016). Several human studies have linked maternal gestational hypothyroidism to developmental changes in infants, such as delayed verbal and non-verbal performance (Henrichs, 2010), mental and psychomotor retardation (Min, 2016), impaired learning abilities (Finken, 2013; Opazo, 2008), poor general cognitive and perceptual-manipulative index, and memory coefficients (Suárez-Rodríguez et al., 2012), impaired motor development (Li, 2010), lower gross and fine motricity scores and lower socialization (Berbel, 2009). In rodents, maternal hypothyroidism models showed structural and functional alterations in different brain regions of the offspring, especially in the hippocampus and cerebellum, regions closely related to cognitive and psychomotor function (Wang, 2014). Our findings suggest that maternal thyroid hormones, essential for fetal neurodevelopment, likely continue to influence visual pathways postnatally. Higher levels of maternal thyroid hormones can modulate the offspring brain development, including visual functioning. These findings demonstrate that the importance of adequate maternal thyroid screening extends beyond the immediate postnatal period, and even subtle variations in T4 (within the normal range) are linked to important developmental abilities in 1-month-old infants.

Similarly, elevated maternal serum prolactin levels were associated with higher visual conduct scores at 3 months. Beyond its role in lactation, prolactin may exert neuroprotective effects and influence neural plasticity in the developing infant brain. Studies report that during gestational and lactation periods, low levels of maternal serum prolactin are related to maternal depressive symptoms, with a consequent increase in the level of serum cortisol and hyperactivity of the HPA axis (Smith, 2011; Zhang, 2017). Maternal depressive symptoms can impair mother-infant interaction, leading to the mother's inability to respond the demands of their offspring, a poor establishment of interaction with the child, and negatively influence the child's neuromotor development (Grattan & Kokay, 2008; Smith, 2011; Zhang, 2017). In our study, prolactin levels were not associated with maternal depressive symptoms and maternal care, since no significant differences were observed between higher and lower visual abilities scores groups for these variables. Possibly, other mechanisms beyond the proper mother-infant interaction and maternal mental health profile are involved in the relationship between maternal prolactin and newborn's visual conduct, such as direct action on neurodevelopment, neural plasticity, and neuroprotection (Cabrera-Reyes, 2017).

These positive associations found between thyroxine and prolactin may also reflect the functioning of the maternal hypothalamus. Studies indicate that thyrotropin-releasing hormone (TRH) in the hypothalamus stimulates the synthesis and release of both thyroid-stimulating hormones (TSH) and prolactin (Kanasaki et al., 2015; Nillni & Sevarino, 1999). Thus, the proper functioning of the maternal hypothalamus seems to be another determining factor for the maturation and development of the offspring's neurological pathways, responsible for the visual conduct and fine motor skills.

4.1. Conclusions

This study contributes novel insights into the multifaceted influences on early visual motor skills, highlighting associations with maternal metabolic factors (T4 and prolactin levels) and breastmilk composition (protein concentration). The findings underscore the importance of postnatal maternal hormonal profiles in shaping early neuromotor development pathways in infants. Future research with larger, prospective studies is needed to further elucidate these mechanisms and identify potential biomarkers for early neurodevelopmental outcomes in

newborns. Early detection of biological and environmental factors affecting neurodevelopment can inform targeted interventions and improve developmental outcomes in infancy.

CRediT authorship contribution statement

Fernanda Rombaldi Bernardi: Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Marta Knijnik Lucion:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Roberta Dalle Mole:** Writing – review & editing, Project administration, Methodology, Investigation. **Tania Diniz Machado:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Bibiana Bolten Lucion Loreto:** Writing – review & editing, Methodology, Investigation, Data curation. **Bruna Luciano Farias:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Tatiane Madeira Reis:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Roberta Sena Reis:** Writing – review & editing, Project administration, Methodology, Investigation. **Solange Mara Bigonha:** Writing – review & editing, Methodology. **Maria do Carmo Gouveia Peluzio:** Writing – review & editing, Methodology, Investigation, Data curation. **Danusa Mar Arcego:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Carla Dalmaz:** Writing – review & editing, Supervision, Resources, Investigation. **Patricia Pelufo Silveira:** Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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