Development of oculomotor control throughout childhood: A multicenter and multiethnic study

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Citation: Pueyo, V., Yam, J. C. S., Perez-Roche, T., Balasanyan, V., Ortin, M., Garcia, G., Prieto, E., Pham, C., Gutierrez, D., Castillo, O., Masia, B., Alejandre, A., Bakkali, M., Ciprés, M., Esteban-Ibañez, E., Fanlo-Zarazaga, A., Gonzalez, I., Gutiérrez-Luna, I. Z. K., Pan, X., Pinilla, J., Romero-Sanz, M., Sanchez-huerto, V., Vilella, M., Tinh, N. X., Hiep, N. X., & Zhang, X. (2022). Development of oculomotor control throughout childhood: A multicenter and multiethnic study. *Journal of Vision*, *22*(13):4, 1–13, https://doi.org/10.1167/jov.22.13.4.

https://doi.org/10.1167/jov.22.13.4 Received December 27, 2021; published December 2, 2022 ISSN 1534-7362

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Although steady fixation is a key aspect of a proper visual function, it is only subjectively assessed in young and uncooperative children. In the present study, we characterize the development of fixational behavior throughout childhood in a large group of healthy children 5 months of age and up, recruited in five geographically diverse sites. In order to do it, we examined 802 healthy children from April 2019 to February 2020. Their oculomotor behavior was analyzed by means of an automated digital system, based on eye-tracking technology. Oculomotor outcomes were gaze stability, fixation stability and duration of fixations (for both long and short fixational tasks), and saccadic reaction time. Ninety-nine percent of all recruited children were successfully examined. Fixational and saccadic performance improved with age throughout childhood, with more pronounced changes during the first 2 years of life. Gaze and fixation tended to be more stable with age ($p < 0.001$ for most the outcomes), and saccades tended to be faster. In a multivariate analysis, including age and ethnicity as independent variables and adjusting by data quality, age was related with most fixational outcomes. Our automated digital system and eye-tracking data allow us to quantitatively describe the development of oculomotor control during childhood, assess visual fixation and saccadic performance in children 5 months of age and up, and provide a normative reference of fixational outcomes for clinical practice.

Introduction

Visual fixation can be defined as periods in which an area of the visual scene is kept on the fovea, while saccades would be periods in which an area of the visual scene is brought onto the fovea (Hessels, Niehorster, Nyström, Andersson, & Hooge, 2018). However, small fixational eye movements are necessary for maintaining optimal vision, since they overcome visual fading due to the stabilization of the image on the retina (Epelboim, 1998). Stable fixation is thus characterized by miniature eye movements: tremor, drifts, and microsaccades, which occur in horizontal, vertical, and torsional directions (Ditchburn & Ginsborg, 1953; Martinez-Conde, Macknik, & Hubel, 2004).

Such stable visual fixation is a prerequisite for proper visual development (Rucci & Casile, 2004). The most frequently used method in clinical practice for estimating global visual function in preverbal children is evaluating the child's ability to fixate and follow an object. As recommended by existing guidelines (American Association of Certified Orthoptists, 2003; Wallace et al., 2018), this is mostly performed by clinical observation, using an attractive visual stimulus, and assessed subjectively by an examiner. However, such simple observation of fixational behavior provides only a qualitative assessment (central or eccentric, steady or not, and maintained or not) and requires a skilled, experienced examiner. Given the capabilities of current eye-tracking technology, however, it may be possible to provide more accurate and objective assessment of visual fixation even for preverbal children.

Visual fixation is not fully developed at birth; instead, it is progressively acquired during the first months of life, as the fovea reaches its adult structure and the central nervous system (CNS) matures (Roucoux, Culee, & Roucoux, 1983). Previous studies have shown that fixational behavior changes throughout childhood, increasing the fixation time and the fixation density around the center of gravity with increasing age, while fixation interruptions seem to decrease (Aring, Grönlund, Hellström, & Ygge, 2007). On the other hand, optimal vision requires a balanced development of eye structures, oculomotor control, and visual cognitive integration. Congenital ocular disorders and certain neurological impairments, such as cerebral visual impairment (CVI), may interfere with oculomotor control development, giving rise to unstable visual fixation (Birch, Wang, Felius, Stager, & Hertle, 2012; Sweeney, Takarae, Macmillan, Luna, & Minshew, 2004). Hence, impaired oculomotor skills may be used as early markers of cognitive development in preterm infants (Kaul et al., 2016; Stjerna et al., 2015) and as accurate and objective measurements for monitoring the follow-up of visual disorders (Fujii et al., 2002; Testa et al., 2014).

However, before considering using oculomotor outcomes as a sign of visual or neurologic dysfunction, normative data should be available for every age group.

Unfortunately, there is a shortage of comparative oculomotor control data from all stages of children development and a lack of objective tools to quantify oculomotor performance throughout childhood in clinical practice. In this study, we use an eye-tracking-based digital device to quantify fixation stability during short and long fixational tasks. From our gathered data, we describe fixational and saccadic performance in a large cohort of children from 5 months to 15 years of age, offer insights into the development of oculomotor control during childhood, and provide normative reference ranges of fixational outcomes to be used in clinical practice.

Materials and methods

Participants

The oculomotor assessment is part of the TrackAI Project, whose protocol has already been described in detail (Pueyo et al., 2020). Its main goal was to develop a system to identify children with visual disorders, for which visual parameters were obtained by means of a single digital vision screening test (named DIVE AI Vision Screening). The test included the assessment of oculomotor control, visual acuity, contrast sensitivity, and color perception.

Participants were recruited from five study sites, located in Spain, China, Vietnam, Russia, and Mexico, coordinated by a coordinating unit (see supplemental data). Candidate children were patients with a clinical appointment at one of the pediatric ophthalmology departments of a tertiary hospital during the recruitment time; all children fulfilling the inclusion criteria of the TrackAI Project were recruited (children aged between 5 months and 15 years, both with normal and abnormal vision) (Pueyo et al., 2020). Among them, only the children born at term (>37 weeks of gestational age), with no known ocular disease (except low ametropia) and no neurological or systemic disorder, were included in this study. All participants with anisometropia (defined by a difference of at least 1 diopter [D] between both eyes) or moderate/severe refractive errors based on cycloplegic refraction were excluded from the study: myopia higher than 3.5 D for children younger than 30 months, 3.0 D between 31 and 48 months, and 1.5 D over 48 months; hyperopia higher than 4.5 D for children younger than 30 months, 4.0 D between 31 and 48 months, and 3.5 D over 48 months; and astigmatism higher than 2.0 D for children younger than 48 months and 1.5 D over 48 months (Donahue & Baker, 2016).

All included participants were divided into five groups based on developmental stages of childhood: infancy (<1 year), toddlerhood (1–2 years), early childhood (3–5 years), middle childhood (6–11 years), and adolescence (≥12 years).

The study protocol was approved by the local ethics committees of every center, and written informed consent was obtained from the parents or guardians of each child. All procedures adhered to the tenets of the Declaration of Helsinki.

Examination

Ophthalmological assessment

All children underwent an ophthalmological assessment, including best-corrected visual acuity, ocular alignment and motility, refraction under cycloplegia, and funduscopy assessment. Monocular and binocular visual acuity was assessed in cooperative participants using optotypes adapted to each participant's age, based on LEA symbols or letters. Grating acuity was obtained using the preferential looking test (LEA paddles) for all infants younger than

Figure 1. DIVE being used by a young patient sitting on his mother's lap. DIVE includes a Huawei Matebook E tablet with a 12-in. tactile screen and an integrated X3-120 Tobii eye tracker.

24 months and older ones who did not cooperate for the previously detailed visual acuity assessments.

Fixation stability assessment

Preparation: The examination was performed in a quiet room under mesopic ambient illumination. Children were positioned in a chair at 65 cm from the screen and were asked to fixate on the different targets on the screen, trying not to move their heads (Figure 1). Children had no head immobilization, and in order to ensure homogeneity of the clinical protocol in all the participating centers, the same instructions were given to all participants. Children younger than 24 months were positioned on a parent's lap, and instructions were given to the parents to keep their eyes closed and their child's head steady. Instructions and feedback throughout the test were delivered by the device in the participant's mother tongue. Whenever they failed doing it, the test was repeated or the child excluded from the study. No eyeglasses were used during the examinations. Visual acuity at 65 cm was confirmed to be adequate for performing the study in all cases.

Equipment: The digital test was performed using a DIVE device (DIVE Medical SL, Zaragoza, Spain). The system is made up of (a) a Huawei Matebook E (Huawei Tech Co., Shenzhen, China) tablet with a 12-in. tactile screen corresponding from 65 cm to a visual angle of 22.04° horizontally and 14.82° vertically with a resolution of 2,160 × 1,440 pixels, regularly calibrated with a Datacolor SpyderX (Luzern, Switzerland) calibrator (gamma 2.20, white dot 6500K, and 120 cd/m^2), as well as (2) an integrated X3-120 Tobii (Stockholm, Sweden) eye tracker sampling at 120 Hz. The manufacturer specifications for binocular accuracy and precision of the eye tracker are around 0.6° and 0.25°, respectively (0.8° and 0.34° for the monocular case). A Bluetooth keyboard is used to

Figure 2. Stimuli used during the long fixational task (left) and during the short fixational task (center and right). Note that the stimuli displayed here are not at the same scale as the one used during the visual tests.

facilitate the interaction with the device. A Huawei P30 smartphone may also be connected to the DIVE device via Bluetooth, to launch the tests and to obtain real-time feedback about progress and the quality of the captured data. A 9-point calibration procedure of the eye tracker was always performed prior to the fixation study. Each individual point was repeated if necessary, until the eye tracker reported a reliable calibration. Moreover, a subsequent validation test showing nine stimuli uniformly distributed across the screen allowed us to quantify the eye tracker's exact accuracy and precision for each subject.

Study: The oculomotor assessment was made up of two parts. First, a *long* fixational task was carried out, consisting of a cartoon of a child of 3° × 1.56° appearing on the center of the screen, which is supposed to draw the participant's attention for 12 s. During the second part of the exam, *short* fixational tasks were introduced. The fixation target consisted of a cartoonish image of an animal, combining three features with binomial categories: size (1° or 2°), sound (on/off), and either static or pulsing. In total, each participant saw eight short fixation targets and one long fixation target.

Stimuli for the long and short fixational tasks are depicted in Figure 2.

The test began with a 2° pulsing stimulus with sound, located at the center of the screen. After that, every 3 s, a peripheral stimulus from the rest of the possible combinations described above was displayed at a random position on the screen, ensuring a fixed distance of 5.96° between consecutive stimuli and no overlap.

Analysis of fixations: Given their low velocity, fixation points tend to cluster closely together. We identify fixations as gaze samples with a dispersion smaller than 3° and within a moving time window of at least 160 ms. We identify fixations using thresholding based on a maximum dispersion and a minimum duration, following common practice and paying special attention to the selection of the threshold. While the mean duration of a fixation seems to depend on the task (Rayner, 1998), there is a common agreement that the minimum falls within the range of 100 to 200 ms for free-viewing tasks. Experiments have compared results for both (100 and 200 ms) and found that only around 12% of fixations fell below 160 ms (Manor & Gordon, 2003); however, note that this experiment was done with complex and large stimuli (up to 15° and 17° in size), while our stimuli are significantly smaller (up to 2° or 3°); it has been shown that mean fixation duration increases with smaller stimulus size (Harris et al., 1988).

Dispersion is calculated by adding the differences between the maximum and minimum x and y values in the window. We obtain fixation stability by computing the bivariate contour ellipse area (BCEA) (Steinman, 1965). which quantifies the area (degrees squared) of the ellipse containing a given percentage of the fixation positions, assuming a normal distribution of the samples. The BCEA encompassing 68.2% of fixation points (corresponding to one standard deviation; we term this percentage P) was obtained as

$$\mathrm{BCEA} = 2 * k * \pi * \sigma_x * \sigma_y * (1 - \mathrm{p}^2)^{1/2},$$

where σ_x and σ_y are the standard deviations of the horizontal and vertical eye positions, p is their Pearson product moment correlation coefficient, and k is obtained from P as $P = 1 - e^{-k}$ (Kulke, Atkinson, & Braddick, 2017). Since the BCEAs are usually not normally distributed, we used a natural log transformation on their values to normalize data (logBCEA).

To assess fixation stability, only data from fixations around the target must be included.

However, while this assessment can be performed in adults prompted to fixate on a target, it may be difficult with young children or patients with attentional difficulties. To overcome this, we additionally analyze gaze stability, which provides valuable complementary information regarding oculomotor control. We thus included data not only from fixations but also between fixations by analyzing data within a centered window during the tasks (11 s for the long fixation task; 2 s for the short task). Figure 3 shows examples of the resulting fixation and gaze stability bivariate contour

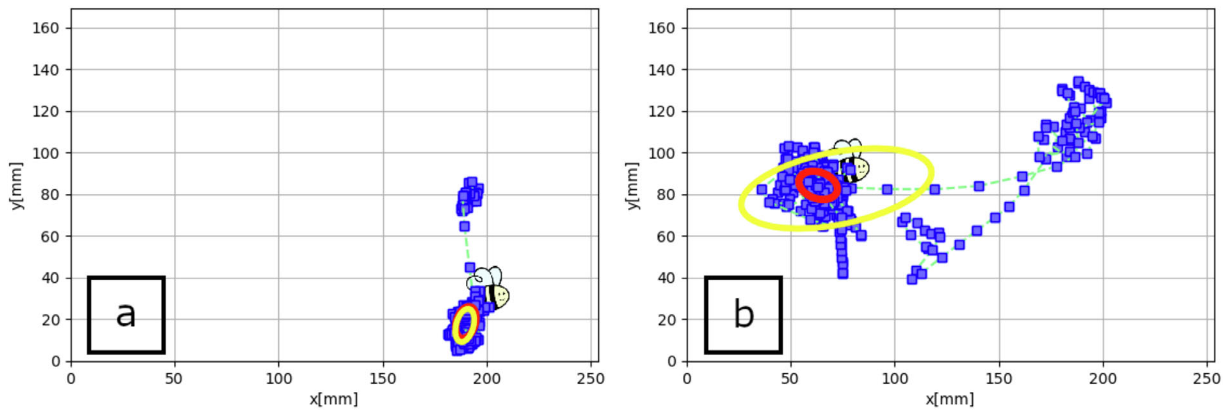

Figure 3. Comparison of oculomotor behavior in a 14-year-old child (left) and a 9-month-old infant (right). The plotted bivariate contour ellipses show fixation stability (red) and gaze stability (yellow). A lower BCEA (smaller ellipse) indicates more stability. Note how the less stable gaze in the infant is captured by their higher BCEA (larger yellow ellipse).

ellipses for both a 14-year-old child and a 9-month-old infant.

Therefore, we evaluated the following fixational outcomes from both short and long fixational tasks: fixation stability (in logdeg^2), gaze stability (in logdeg^2), and duration of fixations (in ms). Since all these outcomes consisted of several measurements, the median of all the valid ones from each participant was considered for the analysis. A minimum of 25% on-screen gaze samples was required to consider a target valid for the fixational study.

Analysis of saccadic performance: We analyzed latency through the saccadic reaction time (SRT) for each stimulus presented during the short fixational tasks. SRT was defined as the time lapse between the presentation of the stimulus and the onset of the saccade toward it. For saccade-related computations, a minimum of 75% on-screen gaze samples are required during the first 800 ms after a new target appears on the screen. Besides, it is ensured that the gaze of the patient is not on top of the target plus a 1° margin at the beginning of the time frame in which a new target appears and a saccade is identified.

For every exam, the quality of the obtained measurements was provided on a scale of 1 to 5, with 1 indicating poor reliability, 3 corresponding to reliable metrics, and values above 3 referring to very reliable metrics. Data quality was calculated based on several parameters collected during the execution of the visual exploration.

To ensure consistency across all study sites, a senior researcher from the coordinating unit (defined in detail in the supplementary material) traveled to each participating center to train and instruct the local researchers involved. Furthermore, all the oculomotor assessments were performed by one of five technicians, who had been trained by the first author of the study and the technician coordinator. Clinical protocol, patient selection, equipment setup, and environmental conditions were, therefore, exactly the same in all the recruiting centers. In all cases, the oculomotor control assessment was performed in a completely dark and quiet room, with no visual distractor behind the digital test.

Statistical analysis

All data were analyzed using SPSS 25.0 statistical software (SPSS, Inc., Chicago, IL, USA) and R software (R Core Team, Vienna, Austria). Descriptive characteristics were reported by the mean, standard deviation, and ranges, while for fixational outcomes, we use the median and 5th and 95th centiles. We compared fixational skills among the different age groups and the influence of gender and ethnicity.

Groups were compared by means of nonparametric tests due to the distribution of fixational outcomes, using the Mann–Whitney U test and Kruskal–Wallis test. Multivariate analyses were performed, including age, ethnicity, and data quality as independent variables and fixational outcomes as dependent variables. Effect size was calculated by partial eta squared and interpreted as recommended: small (partial eta squared around 0.01), medium (partial eta squared around 0.06), and large (partial eta squared > 0.14) (Cohen, 1988).

Normative growth curves were created using the GAMLSS (Generalized Additive Models for Location, Scale, and Shape) package in R (Rigby & Stasinopoulos, 2005). The Akaike information criteria (Akaike, 1974) and Q test were used to evaluate goodness of fit. The models for all the variables included parameters that account for skewness and kurtosis in the distribution of the values.

Additionally, we report the tolerance limits of fixation stability adjusted for age as the range in which

90% of a normally distributed population is found, with a probability of 95%.

Results

In total, 802 patients were included in the study. Only nine children (approximately 1%) had to be excluded due to calibration problems or failure to complete the test. A total of 793 participants were thus finally included in the study (402 female), with ages ranging from 5 months to 15.9 years, with a mean of 6.76 years. From these, 398 children were recruited in Spain, 279 in Hong Kong, 66 in Russia, 36 in Mexico, and 14 in Vietnam. Most children were Caucasian ($n = 404$), 295 were Oriental, 62 were Latin American, 19 were from the Middle East, 10 were African Black, and 3 were Indian.

They were divided into five study groups according to their age, shown in Table 1 together with the descriptive characteristics and visual outcomes for each one. In all the cases, binocular visual acuity at 65 cm was better than or equal to two cycles per degree (when assessed by preferential looking test) and better than or equal to 0.2 in logMAR scale (when using LEA symbols). Mean refractive error was 0.56 spherical diopters and 0.56 cylinder diopters in the right eyes and 0.60 spherical diopters and 0.58 cylinder diopters in the left eyes. As required by the inclusion criteria, all participants presented normal ocular motility and funduscopic examinations.

Fixational outcomes for every age group, during both short and long fixational tasks, are reported in Table 2. Univariate analysis concluded that fixational and saccadic behavior (in terms of latency) differs significantly throughout childhood, except for the median duration during long fixational tasks. Table 2 also provides tolerance limits of fixation stability adjusted for age. It presents the range in which 90% of a normally distributed population is found, with a

Variable	<1 y	1–2 y	3–5 y	6–11 y	>12 y
N	33	104	145	466	45
n of excluded participants	0	0	0	8	1
Gestational age at birth (weeks)	39.30 (1.33)	39.30 (1.05)	39.35 (1.18)	39.45 (1.22)	39.72 (1.17)
Birthweight (g)	3,208.48 (450.88)	3,236.26 (386.46)	3,338.03 (374.19)	3,270.25 (462.37)	3,240.64 (320.79)
Binocular grating acuity (cpd)	5.74 (2.91)	6.84 (3.22)	—	—	—
Binocular visual acuity (logMAR)	—	0.10 (0.11)	0.08 (0.11)	0.06 (0.19)	0.04 (0.18)
Right eye spherical equivalent defect (diopters)	2.15 (1.07)	0.98 (1.06)	1.22 (0.98)	0.35 (1.15)	−0.06 (1.44)
Right eye cylindrical defect (diopters)	0.87 (0.54)	0.68 (0.39)	0.65 (0.37)	0.52 (0.37)	0.44 (0.30)
Left eye spherical equivalent defect (diopters)	2.07 (0.90)	1.02 (1.09)	1.28 (1.00)	0.38 (1.18)	0.06 (1.32)
Left eye cylindrical defect (diopters)	0.82 (0.56)	0.62 (0.38)	0.65 (0.42)	0.55 (0.36)	0.44 (0.41)

Table 1. Demographic and visual outcomes from every study group. *Note:* Data are presented as mean (standard deviation). Spherical defect is reported in spherical equivalent cycloplegic refraction, while cylindrical defect is reported in absolute values.

Variable	< 1 y	1–2 y	3–5 y	6–11 y	> 12 y	*p*
Short fixational task						
Fixation stability (logBCEA; logdeg^2)	−0.210 (−0.436 to −0.069)	−0.310 (−0.527 to −0.078)	−0.366 (−0.558 to −0.144)	−0.405 (−0.628 to −0.186)	−0.408 (−0.613 to −0.213)	<0.001
Gaze stability (logBCEA; logdeg^2)	0.305 (−0.249 to 1.387)	0.136 (−0.476 to 1.041)	−0.092 (−0.479 to 0.609)	−0.131 (−0.569 to 0.593)	−0.275 (−0.623 to 0.184)	<0.001
Duration of fixations (s)	0.317 (0.172–0.530)	0.412 (0.217–0.575)	0.508 (0.233–0.572)	0.496 (0.233–0.603)	0.496 (0.235–0.875)	0.132
Long fixational task						
Fixation stability (logBCEA; log deg^2)	−0.229 (−0.452 to 0.066)	−0.309 (−0.467 to −0.039)	−0.355 (−0.560 to −0.063)	−0.398 (−0.567 to −0.118)	−0.372 (−0.583 to −0.082)	<0.001
Gaze stability (logBCEA; log deg^2)	1.067 (0.221–1.715)	0.880 (0.064–1.524)	0.925 (0.251–1.388)	0.863 (0.290–1.350)	0.686 (0.047–1.250)	0.013
Duration of fixations (s)	0.317 (0.178–2.045)	0.415 (0.209–1.464)	0.508 (0.236–1.363)	0.496 (0.250–1.421)	0.496 (0.220–1.771)	0.002
Saccadic performance						
Saccadic reaction time (s)	0.325 (0.1125–0.4208)	0.283 (0.175–0.442)	0.258 (0.200–0.319)	0.225 (0.179–0.304)	0.216 (0.184–0.298)	<0.001
Test quality (reliability)						
Test quality (1–5 value), mean (standard deviation)	4.24 (0.43)	4.34 (0.49)	4.74 (0.44)	4.83 (0.38)	4.89 (0.32)	

Table 2. Comparison of fixational and saccadic behavior among the different age groups. *Note:* Data are reported as median (p5–p95), while logBCEA refers to the log-transformed bivariate contour ellipse area. Quality values indicating reliability of the metrics are also included (values above 4 indicate *very reliable metrics*, as assessed by independent ophthalmologists not linked to DIVE or this study).

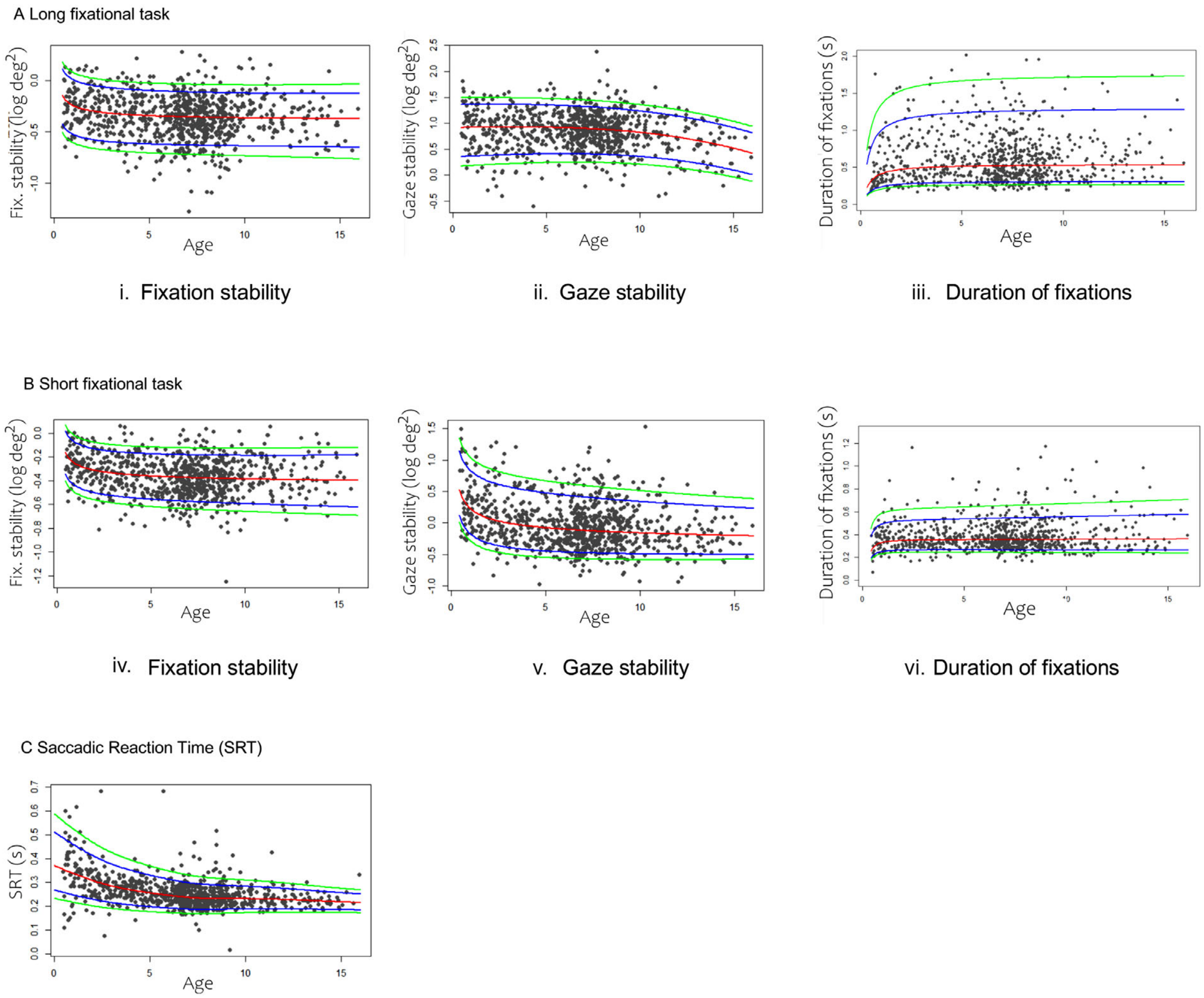

Figure 4. Scatterplots of oculomotor control outcomes versus age for long (A) and short (B) fixation tasks and saccadic performance (C). The gray dots are the observed values, while the curves indicate age-specific fitted percentiles: 5th and 95th (blue), 10th and 90th (green), and 50th percentile (red). Note that lower values of logBCEA correspond to more stable fixations.

probability of 95%. Current mean values for missing gaze data per age group are as follows: 31% for < 1 year, 30% for 1 to 2 years, 18% for 3 to 5 years, 11% for 6 to 11 years, and 8% for > 12 years. Since DIVE is able to compute reliable fixational metrics even with up to 75% of missing gaze data per target, this means that our metrics could not be computed in only 5.3% of all cases.

Figure 4 shows fixational outcomes as a function of age, as well as SRTs. A multivariate analysis including age, ethnicity, and data quality as independent variables (predictors) revealed that age was related to all fixational outcomes, except for duration of fixations during long task, with older children presenting more stable and longer fixations. This tendency was observed during both the long fixation task (fixation stability, $p = 0.009$; gaze stability, $p < 0.001$) and the short task (fixation stability, $p = 0.009$; gaze stability, $p < 0.001$; duration of fixations, $p = 0.001$), as well as in the SRT ($p < 0.001$). Ethnicity of the participants was related to fixational stability during long and short tasks ($p < 0.001$), gaze stability during long and short tasks ($p = 0.003$ and $p = 0.011$ respectively), and with SRT ($p < 0.001$). However, effect size of age and ethnicity was low to moderate, with partial eta squared ranging from 0.009 to 0.109. Partial eta squared and significance of the parameters included in the model are detailed in Appendix.

Discussion

The ability to fixate and follow an object is the most frequently used method in clinical practice to estimate the global visual function in preverbal children (American Association of Certified Orthoptists, 2003; Wallace et al., 2018). Currently, oculomotor skills are mostly evaluated subjectively and qualitatively in clinical practice. In this study, we have described fixational behavior throughout childhood in a quantitative way, using novel automated digital tests coupled with eye-tracking technology. Within the range of our study, fixations tend to be longer and more stable with increasing age, during both long and short fixational tasks, while saccades are faster. Fixational behavior seems to improve mostly during the first 2 years of life but keeps on stabilizing until middle childhood, when most children reach adult outcomes.

We assessed fixation stability, including in the analysis only data sets corresponding to fixations on the visual stimulus. However, gaze data, besides fixational data, also yield valuable information such as intrusive saccades and are affected not only by visual factors but also by attentional or behavioral ones. Thus, both fixational and gaze performance should be analyzed to provide an exhaustive description of the development of oculomotor control in childhood. This joint assessment provides richer information about oculomotor control in daily life, when attention is usually shared between several visual stimuli.

Visual fixation is among the most basic oculomotor skills, with several functional systems involved in the control of eye movements (such as superior colliculus, cerebellum, and reticular formation) (Krauzlis, Goffart, & Hafed, 2017). This ability to steadily fixate on a given stimulus is not fully developed at birth (Roucoux, Culee, & Roucoux, 1983); instead, it requires retinal maturation during the first months of life and accurate control from the CNS. However, the development of oculomotor skills throughout childhood has not yet been fully described. Aring et al. studied fixational behavior in a group of children aged 4 to 15 years (Aring, Grönlund, Hellström, & Ygge, 2007; Ygge, Aring, Han, Bolzani, & Hellström, 2005). They found that the fixation density is more centered around the center of gravity and that fixation time increases with age, while intruding saccades decrease. As far as saccadic performance, Alahyane et al. (2016) reported immature saccades in 7- to 42-month-old infants compared with adults, with longer reaction times and less precise amplitude in young children. Using a saccadic paradigm, Fisher and Hartnegg (2000) reported improvement of fixation stability with age, in both dyslexic and control children, aged 7 to 17 years. Although there has been extensive research focused on visual development in early years in the past decades (Braddick & Atkinson, 2011), there is a lack of eye-tracking assisted tests with normative data from oculomotor control performance throughout childhood starting at only 5 months of age.

Recently, Seemiller, Port, and Candy (2018) carried out a study using eye-tracking technology and proposed that gaze stability may follow an adult-like pattern in infants as young as 4 to 10 weeks of age. However, adult-like saccades were removed from the study before assessing gaze stability, and the eye tracker was not calibrated by every infant but by using the standard adult Hirschberg ratio instead. On the contrary, our work makes no assumptions in terms of fixational or saccadic performance, thus avoiding potential sources of bias. By performing an accurate calibration for each subject, we found that age has an impact on oculomotor skills (i.e., on fixation and gaze stability and saccadic reaction time). However, age is only one of the predictors explaining improvement of oculomotor performance with age, and its effect size is only small to moderate for most of the oculomotor parameters. Attention is known to inhibit microsaccades and increase fixation stability (Denison, Yuval-Greenberg, & Carrasco, 2019), which may contribute to the improvement of visual function during attended times. Furthermore, individual differences in the duration of fixations have also been linked to cognitive processes such as attention, information processing, memory, and anticipation, as well as with later intellectual function in childhood (Munoz et al., 2016; Papageorgiou, et al., 2014).

Most of the patients with functional visual impairment present unstable fixation, even if visual acuity is only slightly reduced (Rohrschneider, Becker, Kruse, Fendrich, & Völcker, 1995). Children with amblyopia due to strabismus present higher saccadic latency and decreased fixation stability, not only in the amblyopic eye but also in the fellow eye (Subramanian, Jost, & Birch, 2013). Fixation stability has shown a good correlation with visual acuity and stereoacuity in patients with amblyopia (Siepmann, Reinhard, & Herzau, 2005; Subramanian et al., 2013). Fixation stability is also reduced in patients with central visual loss and extrafoveal locus of fixation (Castet & Crossland, 2012). A direct correlation has also been found between steady fixation and visual acuity or reading speed in patients with macular disease (Crossland, Kabanarou, & Rubin, 2004). Improving gaze fixation stability is, therefore, the goal of most training programs in macular disease (Vingolo, Salvatore, & Cavarretta, 2009).

Since steady fixation requires accurate control by the CNS, unstable visual fixation and defective saccadic movements can be found in certain neurologic impairments. Salati et al. studied a group of children with CVI aged 2 to 6 years (Salati, Borgatti, Giammari, & Jacobson, 2002). They assessed oculomotor skills by clinical observation and found that 84% of them had unstable fixation, while 93% had defective coordination of saccades, with an increased rate of intruding saccades.

Fixational stimuli have been presented in previous studies using very different durations, from 3 to 30 s. Although fixation stability decreases with longer durations, recent evidence suggests that shorter protocols could be more appropriate for certain study populations (Tarita-Nistor, Gill, González, & Steinbach, 2017). Some studies select manually the period with the best fixational behavior to perform the analysis (Fujii et al., 2002). Different from them, and in order to increase the objectivity and repeatability of our study, we consider a fixed period for gaze stability assessment and only fixation times for fixation stability assessment.

Eye movements can be recorded using different technologies, such as electro-oculography, scanning laser ophthalmoscope, scleral search coil, video-oculography, or pupil tracker. Eye tracking is a noninvasive technology, based on projecting near-infrared light onto the eyes of the subject; gaze direction is then obtained from the vector between the center of the pupil and the resulting corneal reflections. This requires very limited cooperation from children while providing very accurate outcomes despite using no chin or forehead rest. Moreover, since our automated tests leverage the capabilities of modern digital screens, this approach is easily accepted even by young infants. In our study, only 9 subjects in 802 were excluded, yielding a 98.88% success rate.

Measuring fixation stability in preverbal children is a difficult task; to minimize the risk of using invalid data, we include only fixational periods in our measurements analyzing the dispersion of gaze samples. However, although we instructed parents to keep their child's head as stable as possible, gaze and fixation stability may have been affected by the procedure. Another limitation could be the different number of participants included in every age group; to minimize any potential source of bias, all participants fulfilling the inclusion criteria and no exclusion criterion were consecutively included in the study, and we divided them into groups based on the standard developmental stages of childhood. Finally, due to the design of the study as part of the TrackAI project, there could be a selection bias since we recruited healthy participants from children visited in ophthalmology clinics. However, we consider that Berkson's bias has little influence on our results since most of these children were visited as part of universal vision screening programs with no other risk factor.

In conclusion, given that steady visual fixation is a key aspect of a proper visual development, accurate assessment of fixational behavior by means of eye-tracking technology may be a useful tool in pediatric visual examinations. Such assessment may help to understand visual outcomes in certain disorders and to enable an objective follow-up. Since our digital test requires low conscious cooperation and cognitive requirements, it can be performed in most children regardless of age or neurologic impairments. As a result, we have provided reference data of fixational outcomes throughout childhood from 5 months of age, which can be used as an objective reference to assess pediatric patients.

Keywords: childhood, development, oculomotor control, visual fixation, saccades, eye tracking

Acknowledgments

Funding was partially provided by Huawei Technologies Company.

Marta Ortín's contribution is partially funded by Torres Quevedo grant PTQ-010775 from the Ministerio de Ciencia e Innovación of Spain.

Partially funded by the Vicerrectorado de Transferencia e Innovación Tecnológica from Universidad de Zaragoza (project DI 7/2020).

Commercial relationships: Victoria Pueyo, Marta Ortin, Belen Masia, and Diego Gutierrez are cofounders of DIVE Medical Startup, while Marta Ortin, Xian Pan, Adrian Alejandre, and Alvaro Fanlo-Zarazaga work for DIVE Medical startup.
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Appendix

	Age				Data quality	
	Partial eta squared	p	Ethnicity partial eta squared	p	Partial eta squared	p
Short fixational task						
Fixation stability (logBCEA; logdeg^2)	**0.009**	**0.009**	**0.049**	**<0.001**	**0.015**	**0.001**
Gaze stability (logBCEA; logdeg^2)	**0.042**	**<0.001**	**0.017**	**0.011**	**0.138**	**<0.001**
Duration of fixations (sec)	**0.014**	**0.001**	0.008	0.196	0.002	0.260
Long fixational task						
Fixation stability (logBCEA; log deg^2)	**0.009**	**0.009**	**0.056**	**<0.001**	**0.034**	**<0.001**
Gaze stability (logBCEA; log deg^2)	**0.027**	**<0.001**	**0.021**	**0.003**	0.003	0.162
Duration of fixations (sec)	0.002	0.235	0.001	0.930	**0.009**	**0.011**
Saccadic performance						
Saccadic reaction time (sec)	**0.109**	**<0.001**	**0.032**	**<0.001**	0.003	0.163

Table A1. Significance and magnitude of the effect of every predictor included in the model. Significant parameters in the model are highlighted.