Saccade amplitudes and fixation durations measured during static and dynamic fixation tasks in children with retinopathy of prematurity

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Амплітуда сакад і тривалість фіксацій у дітей із ретинопатією недоношених у статичному та динамічному тестах

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Abstract

Purpose. *To compare the distributions of saccade amplitude and fixation duration measured during static and dynamic fixation tasks across five clinical groups of children with and without retinopathy of prematurity (ROP) and to assess the effect of removing blink-related events.*

Methods. *We analyzed eye movements in five groups of children aged 6–13 years (full-term emmetropic children, full-term myopic children, preterm children without ROP, children after laser photocoagulation for ROP and children after spontaneous regression of ROP). Eye movements were recorded at a sampling rate of 2000 Hz using an EyeLink 1000 Plus® eye tracker. Saccade data were available for 119/123 children and fixation data for 113/118 in the static/dynamic fixation tasks. Comparisons accounted for repeated measures in children and were repeated after excluding blink-related events.*

Results. *In the static fixation task, there were between-group differences in the proportions of saccades with an amplitude of 5–10° (p=0.0028) and ≥5° (p=0.0126). The proportion of 5–10° saccades after Holm correction was higher in full-term emmetropic children (18.9%) than in children after spontaneous regression of ROP (6.8%; p=0.0032) and in full-term myopic children (7.7%; p=0.014). For saccades with amplitude of ≥5°, proportions were 32.8% in full-term emmetropic children, 19.9% after laser photocoagulation and 18.8% after spontaneous regression of ROP; no pairwise comparison remained significant after Holm correction. No difference occurred for <1° (p=0.133). After removing blink-related events, overall differences in the proportions of saccades with an amplitude of 5–10° and ≥5° persisted (p=0.0033 and p=0.030). In the dynamic fixation task, no significant differences occurred for the proportions of saccades with an amplitude of ≥5° (p=0.701) or fixation duration categories (p=0.060–0.920).*

Conclusion. *In the static fixation task, between-group differences involved larger saccades and the proportion of 5–10° saccades was higher in full-term emmetropic children than in children after spontaneous regression of ROP and in full-term myopic children. For the proportion of saccades ≥5°, the overall between-group difference was not confirmed in any pair after correction for multiple comparisons. The results need to be adjusted for age; these findings do not establish underlying mechanisms.*

Keywords: *retinopathy of prematurity, retina, eye tracking technology, eye movements, saccades, children, laser photocoagulation, myopia.*

Резюме

Мета. *Порівняти розподіл сакад за амплітудою та фіксацій за тривалістю між п'ятьма клінічними групами дітей без та з ретинопатією недоношених у статичному й динамічному тестах та оцінити вплив виключення записів, пов'язаних із морганням.*

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Матеріал та методи. *Проаналізовано записи рухів очей дітей 6–13 років п'яти груп: доношених з еметропією, доношених з міопією, передчасно народжених без ретинопатії недоношених (РН), дітей після лазерної коагуляції з приводу РН та дітей після самовільного регресу РН. Записи отримано за допомогою EyeLink® 1000 Plus із частотою 2000 Гц. Дані для аналізу сакад були доступні у 119 дітей у статичному тесті та у 123 – у динамічному; для фіксацій – у 113 та 118 дітей. Сакади поділяли за амплітудою, фіксації – за тривалістю. Групи порівнювали з урахуванням кількох вимірювань в однієї дитини. Аналіз повторили після виключення записів, пов'язаних із морганням.*

Результати. *У статичному тесті виявлено міжгрупові відмінності частки сакад амплітудою 5–10° (p=0,0028) та ≥5° (p=0,0126). Для класу 5–10° після поправки Холма доношені діти з еметропією (18,9 %) відрізнялися від дітей після самовільного регресу РН (6,8 %; p=0,0032) та від доношених дітей з міопією (7,7 %; p=0,014). Для класу ≥5° частки становили 32,8 % у доношених дітей з еметропією, 19,9 % після лазерної коагуляції та 18,8 % після самовільного регресу РН; після поправки Холма жодна пара груп статистично значущо не відрізнялася. Відмінностей частки сакад <1° не виявлено (p=0,133). Після виключення записів, пов'язаних із морганням, загальні відмінності для класів 5–10° і ≥5° зберігалися (p=0,0033 і p=0,030). У динамічному тесті відмінностей для сакад ≥5° (p=0,701) та класів тривалості фіксацій (p=0,060–0,920) не виявлено.*

Висновки. *У статичному тесті міжгрупові відмінності виявлено для сакад більшої амплітуди: частка сакад 5–10° у доношених дітей з еметропією була вищою, ніж у дітей після самовільного регресу РН та в доношених дітей з міопією. Для сакад ≥5° загальна відмінність між групами не підтверджувалася в жодній парі після поправки на множинні порівняння. Результати потребують перевірки з урахуванням віку та не встановлюють причини цих особливостей.*

Ключові слова: *ретинопатія недоношених, сітківка, айтрекер-технологія, рухи очей, сакади, діти, лазерна коагуляція, міопія.*

Introduction

Previous studies conducted in Odesa region described changes in incidence rates of retinopathy of prematurity (ROP) in the region [1] and the relationship of the risks of ROP and the need for treatment of ROP with gestational age (GA) and birth weight (BW) [2]. Additionally, age-related changes in refraction and axial length were assessed in preterm infants who received laser photocoagulation (LPC) for ROP [3].

Preterm children exhibited worse fixation stability and longer saccadic reaction times than controls [4, 5]. Microperimetry studies in children with a history of ROP reported contradictory results with regard to fixation stability [6, 7], but they differed, among other things, in the composition of comparison groups.

Even during fixation on the immovable target, the eye performs drifts, tremor and microsaccades [8]. Drifts and microsaccades influence the ability to discriminate fine details [9]. Saccade amplitude is the angular distance the eye traverses during a saccadic eye movement. The average saccade amplitude does not show how often movements of different sizes occur, and may decrease due to a low proportion of large saccades.

We have previously found that average saccade amplitude was smaller in the group of children that had undergone LPC for ROP compared to full-term emmetropic controls. There was no significant difference in median saccade amplitude among five groups [10].

This prompted a comparison of proportions among saccades with different amplitudes. In the static fixation task, the subject has to fixate the gaze on the immovable target, whereas in the dynamic fixation task, on the moving target. Blinking and signal loss may affect the results of both tasks.

The purpose of this study was to compare the distributions of saccade amplitude and fixation duration measured during static and dynamic fixation tasks across five clinical groups of children with and without ROP and to assess the effect of removing blink-related events.

Material and Methods

This single-center observational study with prospective data collection was conducted at SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine". Eye movement records of children aged 6 to 13 years were analyzed. Numbers of participants with suitable data for each type of analysis are presented in the Results and tables.

Participants were distributed into five groups: group 1 (EMMET group; full-term emmetropic children without ophthalmological abnormalities); group 2 (MYOP group; full-term mildly to moderately myopic children without ocular comorbidity); group 3 (NROPP group; preterm children without signs of ROP); group 4 (ROPLC group; preterm children that have undergone LPC of the avascular retina) and group 5 (ROPRG group; children with spontaneous ROP regression).

Inclusion criteria were the age between 6 and 14 years, meeting the criteria for one of the five clinical groups, the ability to understand and perform a visual task, and informed consent from parents or legal guardians. Exclusion criteria were acute eye disorders, marked nystagmus or other conditions making stable gaze recording impossible, neurological or cognitive abnormalities preventing the participant from being able to execute the task, impossibility to follow a standard eye-tracking calibration procedure, or inadequate quality of eye-tracking record.

This study was approved by the Bioethics Committee of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" (Meeting Minutes No.1 dated October 18, 2023), and followed ethical standards as outlined in the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians. Participants' data were anonymized before analysis.

Eye movements were recorded at a sample rate of 2000 Hz using an EyeLink 1000 Plus® eye tracker (SR Research Ltd., Ottawa, Canada). Eye positions were recorded for both eyes simultaneously. The head was stabilized by a chin and forehead rest. Participants followed a 9-point eye-tracking calibration procedure before performing a trial. Illumination level, brightness and contrast of the target, distance to the screen and position of the screen were kept constant for all participants.

In a static fixation task, a participant was asked to fixate gaze on the immovable central stimulus (a round dot-shaped target against a neutral background) for 10 seconds. In a dynamic fixation task, the target was presented sequentially at the center and at the right, at the left, above and below at an angular distance of 12.5° from the central position, for 5 seconds per position.

Gaze position data were decomposed into saccades, fixations, and blinks using the built-in EyeLink algorithm. Saccade amplitude and fixation duration data were exported from Data Viewer for Eyelink to the Web platform IONDS (https://ionds.app/, algorithm v2) developed for automated analysis of saccade and fixation data. The platform categorized saccades by amplitude and fixations by duration using predetermined thresholds uniform for all participants. It calculated the count and proportion of fixations and saccades in respective classes for each child.

Saccades were categorized into five classes (<1°, 1–2°, 2–5°, 5–10° and ≥10°. Saccades with amplitudes less than one degree were defined as microsaccades. Extraction and counts of fixations and saccades depend on the algorithm and parameter settings [11, 12]. Fixations were categorized into five classes (<100, 100–200, 200–400, 400–600 and ≥600 ms.

Saccades with a blink before, during or after the saccade in question were identified by special markers provided by EyeLink software. Initially, the analysis of all events meeting the inclusion criteria was conducted. Thereafter, the analysis was repeated after removing the blink-related events. In this way, we evaluated the extent to which blinking could influence the collected data.

Before the analysis, record identifiers were checked for consistency with the list of participants and records were deduplicated. Only the records of the participants were left for analysis. Events with no amplitude were removed. No significant between-group differences were found with regard to the duration of the available record as assessed by the duration of the last fixation ($p = 0.390$ for the static fixation task and $p=0.899$ for the dynamic fixation task).

Statistics. For each group, the proportion of saccades or fixations of a specific category was calculated relative to the total number of saccades or fixations in the group. For example, the proportion of larger saccades (≥5°) for the group was determined as the number of these saccades divided by the total number of saccades in the group. The participant's contribution to this proportion was proportional to the number of his/her saccades.

In order to take into account several measurements for a child, statistical procedures were carried out at the participant level. To construct 95% confidence intervals (CIs), data from the participants of each group were repeatedly resampled many times, allowing the same child to be selected more than once (cluster bootstrap, 10000 replications). If a child was selected, all his/her events were included in the set for analysis. Group assignments were randomly shuffled to compare the groups (permutation test, 100000 replications). Pairwise comparisons were performed using the permutation test with 50000 replications and Holm's correction for 50 comparisons (correction was not applied to the overall p).

Wilcoxon signed-rank test was used to compare characteristics of the same child before and after the exclusion of blink-related events. Statistical analysis was conducted in Python, using pandas, NumPy and SciPy. All tests were two-tailed and $p < 0.05$ was considered significant. A fixed random seed was used to ensure reproducibility.

Results

The numbers of fixations and saccades analyzed were 1504 and 1552, respectively, for the static fixation task, and 3078 and 3190, respectively, for the dynamic fixation task (totally, 4582 and 4742, respectively). Median fixation count and median saccade count for a child were 13 and 12, respectively, for the static fixation task, and 25 and 25, respectively, for the dynamic fixation task.

Fixations and saccades were available for 113/126 children and 119/126 children, respectively, for the static fixation task, and 118/123 and 123/123, respectively, for the dynamic fixation task. Numbers of participants in groups and numbers of events are presented in Tables 1 and 2.

Median proportions of blink-related events for fixations and saccades were 30.8% and 16.7%, respectively, for the static fixation task, and 17.2% and 9.4%, respectively, for the dynamic fixation task. Median proportions of blink-related events in groups EMMET, MYOP, NROPP, ROPLC, and ROPRG were 36.1%, 35.7%, 34.2%, 39.5% and 35.8 %, respectively ($p = 0.957$), for static fixations, 23.8%, 19.5%, 20.3%, 23.6%, and 22.2 %, respectively ($p = 0.856$), for static saccades, 26.5%, 17.9%, 18.9%, 25.7%, and 17.2% respectively ($p = 0.126$), for dynamic fixations, and 15.6%, 10.3%, 10.9%, 13.2%, and 11.2% ($p = 0.322$), respectively, for dynamic saccades, with no significant between-group differences.

After the removal of blink-related events, the association of saccade amplitude with peak velocity got stronger,

Table 1. Saccade amplitude distribution expressed as proportion, percentage (95% CI)

Static task

Class, °	EMMET	MYOP	NROPP	ROPLC	ROPRG	p
n / N	17 / 238	21 / 235	33 / 431	23 / 312	25 / 324	—
< 1	38.7 [30.7;46.8]	55.3 [46.3;64.3]	41.5 [33.7;49.5]	49.7 [41.3;58.8]	45.7 [36.4;54.8]	0.133
1–2	14.7 [10.2;19.8]	14.0 [9.6;18.9]	16.5 [12.8;20.2]	16.7 [12.7;20.4]	21.3 [16.2;26.8]	0.247
2–5	13.9 [8.4;19.3]	11.1 [6.5;15.9]	13.7 [9.2;18.9]	13.8 [9.5;18.4]	14.2 [8.5;20.4]	0.951
5–10	18.9 [13.7;24.4]	7.7 [4.3;10.9]	13.9 [9.7;18.4]	12.8 [8.5;17.6]	6.8 [3.7;9.9]	0.0028
≥ 10	13.9 [8.1;20.3]	11.9 [6.8;17.7]	14.4 [9.9;18.9]	7.0 [3.5;10.4]	12.0 [7.0;17.1]	0.251
≥ 5 (sum)	32.8 [25.5;40.6]	19.6 [13.2;26.1]	28.3 [22.2;34.0]	19.9 [14.1;25.4]	18.8 [12.5;25.0]	0.0126
After the application of Holm's correction for multiple comparisons, the only significant between-group difference for saccades with amplitudes between 5° and 10° was that between the EMMET and ROPRG groups (p=0.014), but there were no significant between-group differences for saccades with an amplitude ≥5°.						

Dynamic task

Class, °	EMMET	MYOP	NROPP	ROPLC	ROPRG	p
n / N	19 / 483	23 / 453	34 / 912	23 / 687	24 / 644	—
< 1	38.3 [31.5;43.4]	36.0 [29.6;42.3]	35.5 [31.3;39.9]	33.6 [24.9;42.2]	34.9 [28.6;41.4]	0.926
1–2	16.1 [13.3;18.8]	19.0 [15.3;22.5]	17.3 [14.6;20.1]	19.8 [16.8;23.0]	20.0 [16.2;23.8]	0.464
2–5	14.3 [11.2;17.7]	12.1 [8.2;16.9]	13.1 [11.0;15.3]	17.2 [13.7;20.8]	14.1 [10.6;17.3]	0.285
5–10	8.1 [4.5;12.2]	5.3 [2.9;8.0]	9.2 [7.1;11.3]	9.6 [5.8;14.0]	8.8 [5.2;12.9]	0.545
≥ 10	23.2 [20.3;26.1]	27.6 [24.5;30.9]	24.9 [22.2;27.8]	19.8 [16.5;23.6]	22.1 [18.2;26.3]	0.050
≥ 5 (sum)	31.3 [26.5;36.4]	32.9 [30.4;35.7]	34.1 [30.5;37.8]	29.4 [23.8;35.4]	30.9 [24.8;37.6]	0.701

Note: CI, confidence interval; EMMET, full-term emmetropic children; MYOP, full-term myopic children; n, number of children; N, saccade count; NROPP, group of non-retinopathy of prematurity preterm children; ROP, retinopathy of prematurity; ROPLC, group of preterm children that have undergone retinal laser photocoagulation; ROPRG, group of children with spontaneous ROP regression. The proportions were calculated from the total count of saccades in the group before the removal of blink-related events. P is a p-value for the overall comparison among five groups.

and Spearman correlation coefficient (ρ) increased from 0.612 to 0.923 for the static task and from 0.766 to 0.929 for the dynamic task ($p < 0.001$ for both comparisons). For blink-related and non-blink-related events, median peak velocity was 760 and 93 degree/s, respectively, in the static task, and 699 and 128 degree/s, respectively, in the dynamic task, and median saccade duration, 208 and 22 ms, respectively, in the static task, and 212 and 26 ms, respectively, in the dynamic task. The proportions of blink-related and non-blink-related events in which peak velocity exceeded 1000 degree/s were 23.4% and 0.1%, respectively, for the static task, and 18.1% and 0.1%, respectively, for the dynamic task.

Saccade amplitude distribution is presented in Table 1.

For the static task, the proportion of saccades with an amplitude of 1° or less varied from 38.7 % in the EMMET group to 55.3% in the MYOP group, with no significant between-group differences ($p = 0.133$). For saccades of amplitudes 1–2°, 2–5° and >10°, corresponding p-values were 0.247, 0.951 and 0.251, respectively.

For saccades of amplitudes 5–10°, the overall p-value was 0.0028. The proportions of these saccades for the EMMET, ROPLC, and ROPRG groups were 18.9%, 12.8%, and 6.8%, respectively; the respective 95% CIs are presented in Table 1. The between-group difference for the EMMET and ROPRG groups was 12.1 percentage points

Table 2. Fixation duration distribution expressed as proportion, percentage (95% CI)

Static task

Class, ms	EMMET	MYOP	NROPP	ROPLC	ROPRG	p
n / N	15 / 205	20 / 252	34 / 468	22 / 314	22 / 265	—
< 100	5.8 [2.1;10.8]	14.3 [5.1;26.7]	3.2 [1.8;4.7]	8.6 [4.5;13.0]	6.0 [2.9;9.2]	0.050
100–200	16.6 [10.8;21.9]	15.5 [8.9;22.0]	20.1 [16.9;22.9]	17.2 [13.5;20.7]	18.9 [14.2;23.4]	0.597
200–400	32.2 [22.0;41.8]	26.6 [18.8;34.4]	31.0 [25.9;35.9]	24.2 [16.9;30.9]	23.8 [18.6;28.7]	0.334
400–600	9.3 [5.0;13.8]	11.5 [7.5;16.3]	13.7 [9.7;17.7]	13.7 [8.3;19.6]	10.9 [7.2;14.7]	0.695
≥ 600	36.1 [31.2;42.5]	32.1 [26.2;39.3]	32.0 [26.3;38.7]	36.3 [29.5;44.5]	40.4 [34.3;47.8]	0.443

Dynamic task

Class, ms	EMMET	MYOP	NROPP	ROPLC	ROPRG	p
n / N	18 / 476	23 / 476	33 / 921	23 / 670	21 / 535	—
< 100	10.7 [6.7;14.7]	7.8 [4.7;11.4]	9.0 [6.4;12.1]	9.2 [6.6;12.6]	8.4 [4.8;12.7]	0.883
100–200	23.7 [20.0;27.4]	21.9 [18.1;25.5]	22.7 [19.8;25.3]	24.2 [20.7;27.8]	23.2 [19.1;26.7]	0.920
200–400	23.7 [19.3;28.5]	22.1 [16.7;27.9]	25.3 [22.7;27.8]	24.8 [21.1;28.3]	19.8 [16.5;22.9]	0.271
400–600	9.7 [7.0;12.4]	9.9 [7.0;13.0]	11.3 [8.8;13.8]	13.0 [10.7;15.3]	12.2 [9.1;15.1]	0.461
≥ 600	32.1 [27.8;37.6]	38.5 [33.8;43.4]	31.7 [28.0;35.6]	28.8 [24.4;33.8]	36.5 [31.6;42.5]	0.060

Note: CI, confidence interval; EMMET, full-term emmetropic children; MYOP, full-term myopic children; n, number of children; N, fixation count; NROPP, group of non-retinopathy of prematurity preterm children; ROP, retinopathy of prematurity; ROPLC, group of preterm children that have undergone retinal laser photocoagulation; ROPRG, group of children with spontaneous ROP regression. The proportions were calculated from the total count of fixations in the group before the removal of blink-related events. P is a p-value for the overall comparison among five groups.

(unadjusted p-value, 0.0003; adjusted p-value, 0.0032), and EMMET and MYOP groups, 11.3 percentage points (unadjusted p-value, 0.0016; adjusted p-value, 0.014).

Additionally, saccades with an amplitude of 5° or greater were combined into one class (Table 1). Their proportions were 32.8%, 28.3%, 19.9%, 19.6% and 18.8% for the EMMET, NROPP, ROPLC, MYOP and ROPRG groups, respectively (overall p = 0.0126). The between-group difference for the EMMET and ROPRG groups was 14.0 percentage points (unadjusted p-value, 0.0091), and EMMET and ROPLC groups, 12.9 percentage points (unadjusted p-value, 0.0107). However, no significant adjusted between-group difference was observed.

For the dynamic task, the p-value for saccades with an amplitude of 5° or greater was 0.701, and for individual classes varied from 0.050 to 0.926. The lowest p-value was obtained for saccades with an amplitude of more than 10°, and the proportions of these saccades in the MYOP and ROPRG groups were 27.6% and 19.8%, respectively (unadjusted pairwise comparison, p = 0.0052; adjusted pairwise comparison, p = 0.052). The proportions of saccades with an amplitude of 1° or less in groups ranged between 34% and 38% in the dynamic task versus 39% and 55% in the static task, whereas the proportions of saccades with amplitude of more than 10° ranged between 20% and 28% in the dynamic task versus 7% and 14% in the static task. This is a descriptive comparison of different tasks.

With regard to fixation duration, for the static task (Table 2), p-values of between-group differences varied in the range 0.050–0.695, with the lowest value observed for fixation duration of less than 100 ms. For the dynamic task, there was no significant between-group difference with regard to fixation duration (p = 0.060–0.920). The proportion of fixations with duration longer than 600 ms was 38.5% for the MYOP group (95% CI, 33.8–43.4) and varied in the range 28.8–36.5% for other groups. The overall p-value was 0.060; the between-group difference for the MYOP and ROPLC groups was 9.6 percentage points (unadjusted p-value, 0.011).

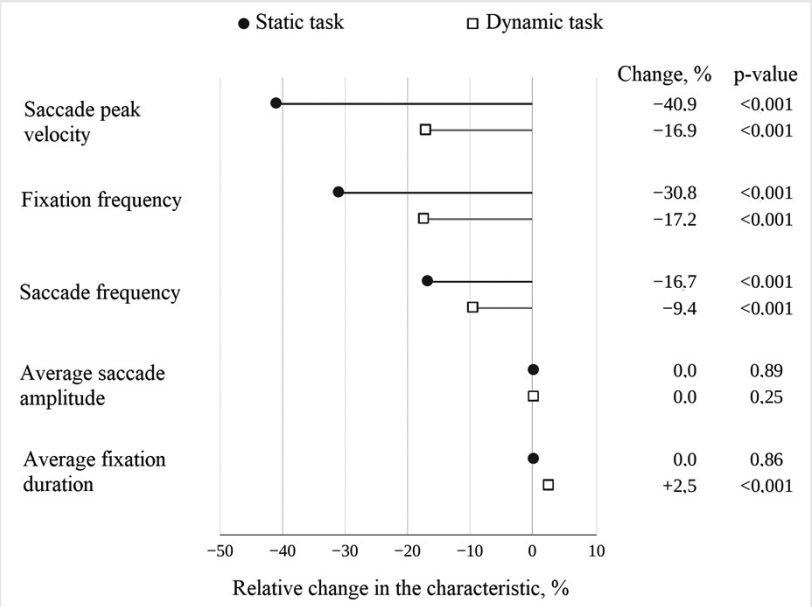


Fig. 1. Changes in characteristics after the removal of blink-related events in static and dynamic fixation tasks. Median individual relative changes were calculated as 100 × (post-removal value — pre-removal value) / pre-removal value. Negative values reflect a decrease in the characteristic. Circles correspond to the static task and squares to the dynamic task. Relative changes expressed as percentage and corresponding p-values are specified at the right.

Median individual relative changes in saccade velocity and fixation frequency after exclusion of blink-related events are presented in Figure 1. For the static and dynamic tasks, peak saccade velocity decreased by 40.9% and 16.9%, respectively, fixation frequency, by 30.8% and 17.2%, respectively, and saccade frequency, by 16.7% and 9.4%, respectively (for all comparisons, $p < 0.001$). For the static and dynamic tasks, median change in average saccade amplitude was 0.0% and 0.0% ($p = 0.89$ and $p = 0.25$), respectively, and median change in average fixation duration, 0.0% ($p = 0.86$) and +2.5% ($p < 0.001$), respectively.

After the removal of blink-related events, the proportions for larger saccades (≥5°) in the static task were 32.4%, 20.0%, 29.8%, 18.8%, and 19.8 % ($p = 0.030$), and for saccades with an amplitude between 5° and 10°, 19.8%, 6.8%, 15.5%, 12.1%, and 7.5% ($p = 0.0033$), for the EMMET, MYOP, NROPP, ROPLC, and ROPRG groups, respectively. The largest proportions were still observed for the EMMET group, but the complete sequence of groups has somewhat changed. No significant difference was found for saccades with an amplitude of 1° or less ($p = 0.104$).

The sequential leave-one-out analyses (119 replications) were conducted, by removing 1 participant at a time, to assess how each individual participant affected the combined result. With these analyses done, overall p-value remained less than 0.05 in 100% of trials, and ranged between 0.001 and 0.006 for saccades with an amplitude 5–10° and between 0.005 and 0.031 for saccades with an amplitude 5° or greater. With a complete sample ($n = 119$ children), p-value was 0.0028 for saccades with an amplitude between 5° and 10°, and 0.0126 for those with an amplitude of 5° or more.

With a threshold of at least 10 saccades ($n = 83$ children), p-values were 0.003 and 0.028, respectively, and with a threshold of at least 15 saccades ($n = 40$ children), 0.147 and 0.272, respectively. The loss of significance may be due to the reduction in the sample size or change in the sample composition. For saccades with an amplitude of 5° or more, the calculation of χ^2 while not taking into account repeated trials yielded $p = 0.00006$; this is just a comparison with the main participant-level analysis ($p = 0.0126$).

Discussion

For the static task, we found significant between-group differences for the proportion of saccades with amplitude of 5° or greater, but not for the proportions of saccades of other classes. This clarifies the description of the distribution of eye movements, but does not prove that the fixation function was similar among all groups.

After correction for multiple comparisons, there were significant differences between the EMMET and ROPRG groups and between the EMMET and MYOP groups in the proportion of saccades with amplitude between 5° and 10°. Consequently, this result cannot be considered specific for children with ROP. A class of larger saccades (≥5°) was additionally analyzed, and the overall between-group difference for the five groups was significant ($p = 0.0126$); however, the difference between any two groups was not significant after Holm's correction. Both these findings should be interpreted within the context of these limitations, rather than as definite evidence of a specific effect of laser treatment.

Microperimetry studies in children with a history of ROP reported contradictory results with regard to fixation stability [6, 7], but these studies differed, among other things, in the composition of comparison groups. Ozen and Idil [6] found no difference in fixation stability among children without ROP, children with spontaneously resolved ROP and children who had laser treatment for ROP. Unlu et al [7] found a significant difference in fixation stability among the three groups (children who

had received LPC for ROP in infancy, prematurely born infants without any ROP diagnosis, and full-term controls) and significantly eccentric fixation in laser-treated infants. The authors of [6, 7] used outcome measures that directly characterize fixation, whereas our analysis describes proportions of saccades with different amplitudes.

In a study by Romero-Sanz et al [4], preterm children exhibited significantly poorer fixation stability and longer saccadic reaction times than full-term controls. Similar differences were described in a multicenter study by Vilella et al [5]. The last two studies are, however, related to prematurity in general, and do not explain the cause of a smaller proportion of larger saccades in our ROPRG and MYOP groups than in the EMMET group of children.

Saccades of different amplitudes are involved in the change in gaze direction [8, 9]. A small proportion of larger saccades during the static task may have different explanations. For example, the subject may less often require to turn gaze back to the target or perform these movements with smaller amplitude. In this work, slow drift was not measured, nor was it determined whether each saccade brought the gaze closer to the target. Therefore, the cause of between-group differences cannot be determined from the amplitude distribution alone, and these differences cannot be interpreted as evidence of impaired corrective refixational saccades from the amplitude distribution alone.

We found no between-group differences in the proportion of larger saccades (≥5°) in the dynamic task. This, however, does not prove that the mechanisms of saccade execution have been completely preserved. Static and dynamic tasks differ in record terms, and, in this study, the results of performance of these tasks were analyzed separately. Making up a conclusion that the detected feature is specific to the static task only requires a direct statistical comparison of the performance of the two tasks taking into account repeated measurements.

Fixation stability and saccade response duration change with age [14]. We did not take age into account in our analysis because its contribution into between-group differences is still unknown. Additionally, contribution to the proportion of saccades of a particular class in the group was greater of participants with a greater number of recorded events. The conclusions should be checked taking into account the age and individual proportions of subjects.

The removal of blink-related events had different effects on different characteristics. It resulted in decreases in peak velocity and movement frequency, but the median change in average saccade amplitude was 0.0%. After this removal, the overall between-group differences for larger saccades in the static task were maintained. Additionally, the positions of groups exchanged.

The increase in the strength of the association of saccade amplitude with peak velocity is in agreement with the effect of events with a blink before or after the event in question on measurements. Re-analysis decreases the probability that the result is explained by these events only. They, however, can neither exclude other types of recording errors nor confirm that any saccade left for analysis is error free.

The relevant guideline [15] requires that a research involving eye tracking should report data processing steps and data loss. This is especially important for comparing studies with regard to peak velocity and movement counts, because these characteristics changed in the analysis after the removal of blink-related events.

Study limitations and prospects for future research

The present study has several limitations. First, the study had a single center design. Second, suitable records were available not for all participants, and there was a difference between the fixation analysis sample count and saccade analysis sample count. Third, because age was not taken into account in the analysis, a proportion of between-group differences may be associated with the age composition of the study sample. Finally, the comparison of the ROPLC and ROPRG groups also does not allow us to separate the effect of treatment from that of the specific features of the ROP course.

We believe it is promising to validate the findings of this study on the basis of individual proportions of saccades, while taking age into account in the direct comparison of static task data and dynamic task data.

Therefore, in the static task, significant between-group differences were found only in the proportion of larger saccades, and saccades of amplitudes between 5° and 10° were more common in full-term emmetropes (18.9%) than in children with spontaneous ROP regression (6.8%) and full-term myopes (7.7%). The overall unadjusted between-group difference in the proportion of saccades ≥5° was significant ($p = 0.0126$), but the difference between any two groups was not significant after the correction for multiple comparisons was applied. We found no between-group differences in the proportion of saccades <1°, fixation duration or characteristics shown in the dynamic task. After the removal of blink-related events, the overall between-group differences for saccades ≥5° and those with an amplitude between 5° and 10° in the static task were maintained, but the peak velocity and movement frequency substantially decreased. Association of the found features with ROP, treatment for ROP, refractive errors and age require a separate evaluation.

Author Contributions

AO: Conceptualization and Design, Data Curation and Processing, Statistical Analysis, Writing – original draft; KS: Conceptualization, Supervision, Writing – review & editing

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mechanisms and approaches to the correction of the disease" (state registration number 0125U002076). No separate external funding was received for the research.

Conflict of interest

No conflict of interest to declare.

Acknowledgements and use of artificial intelligence

ChatGPT and Codex (OpenAI) were used for language editing, manuscript shortening, translating and producing figures based on study results.

Ethical statement and informed consent

Study subjects were children aged 6 to 13 years. This study did not include animal experiments. This study was approved by the Bioethics Committee of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" (Meeting Minutes No.1 dated October 18, 2023), and followed ethical standards as outlined in the Declaration of Helsinki. Informed consent was obtained from parents or legal guardians. Participants' data were anonymized before analysis.

Data Availability Declaration

The anonymized dataset generated and analyzed during the current study is available from the corresponding author on reasonable request.

Abbreviations

CI, confidence interval; EMMET, group of emmetropic children; LPC, retinal laser photocoagulation; MYOP, group of full-term myopic children; NAMS, National Academy of Medical Sciences of Ukraine; NROPP, group of non-retinopathy of prematurity preterm children; ROP, retinopathy of prematurity; ROPLC, group of preterm children that have undergone LPC; ROPRG, group of children with spontaneous ROP regression; SI, state institution

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