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Commentary

Vergence and accommodation disorders in children with vertigo: A need for evidence-based diagnosis

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ABSTRACT

Background: Previous clinical evaluations have demonstrated a difference in eye movements in healthy children compared to children with vertigo without vestibular pathology. It has also been previously shown that accommodation and vergence responses can be measured with remote haploscopic photo refractor (RHP) devices. We have developed a method, called REMOBI (patent US8851669, WO2011073288) that allows us to test eye movements in three-dimensional space without decoupling vergence and accommodation.[1].
Methods: We compared standard clinical testing of vergence and accommodation responses separately, with laboratory simultaneous measurement of vergence and accommodation in healthy children, 31 with vertigo (mean age 11 SD +/- 3.02), and 53 without (mean age 10 SD +/- 3.29). Children diagnosed with vertigo then underwent orthoptic rehabilitation for vergence and accommodation disorders and were re-evaluated twice using laboratory testing: once after 12 sessions and once 3-months after completing the sessions.
Findings: Using the clinical tests, significant differences were found between the vertigo and healthy groups: D' (break point of divergence near), D2 (second measurement of divergence after convergence far), D2' (second measurement of divergence after convergence near), C (break point of convergence far), and C' (break point of convergence near). However, no significant differences in accommodation or vergence were seen between the two groups using laboratory tests (RHP and REMOBI). Further, there was no difference in laboratory measurements in children with vertigo before, after, and 3 months after clinical rehabilitation.
Interpretation: We postulate the difference in these two tests is because the laboratory tests are more accurate and more realistic because they measure accommodation and vergence simultaneously, as it incorporates a stronger binocular coordination response not appreciated by current clinical measurements. Further studies should be conducted to evaluate whether clinicians should consider adding objective measurements, such as using a RHP device, when diagnosing patients with vergence and accommodation disorders, to avoid prescribing costly and timely rehabilitation programs that do not improve accommodative and vergence movements.
Funding: We thank the Fulbright Foundation, along with the University of California, San Francisco, for the research fellowship to Lindsey M Ward. This study is part of the PHRC VERVE, hospital research program, run at the hospital Robert Debré and supported by Direction de la Recherche Clinique, Assistance Publique, France. The funding sources had no involvement in the study design; collection, analysis, and interpretation of data; writing of the manuscript; and in the decision to submit the manuscript for publication.

1. Introduction

Vergence eye movements change the angle between the visual axes of the two eyes: in convergence the angle is increased, in divergence it is decreased. Vergence is one of the most complex eye movements, driven both by retinal binocular disparity as well as by accommodation when focusing on near or far objects. A synergy between these two phenomena occurs: accommodation triggers vergence and vice versa. These relationships are conventionally expressed as the accommodative convergence to accommodation ratio (AC/A ratio). Until recently, objective measurement of vergence and accommodation together while the eyes move in three-dimensional space has been difficult to achieve.

Suryakumar et al. developed a high-speed digital photo refractor (up to 75 Hz) synchronized with a video-based stereo eye tracker to allow a simultaneous assessment of accommodation and vergence, thereby producing more accurate vergence and accommodation values [1,2]. Later, Suryakumar and Bobier developed a mathematical

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Research in context

Evidence before this study

We searched PubMed up until June 1, 2019 for reviews on abnormal eye movements in children with vertigo due to vergence issues. We also searched PubMed for papers published using remote haploscopic photo refractor (RHP) devices in these populations. We searched using the terms "children", "vertigo", "vergence", "accommodation", "orthoptic rehabilitation", "RHP device", "remote haploscopic photo refractor". We searched the reference lists of the retrieved articles. There were no meta-analyses on this topic.

We found that the earlier studies showed the RHP method could be used to study variations in accommodation and vergence with high validity in the laboratory setting. We did not find any articles referring to this technique used to study children with vertigo in a clinical setting.

Added value of this study

Our paper represents the only study that has evaluated children with vertigo using an RHP device that allows for the simultaneous consideration of accommodation, binocular disparity, and vergence movements. Our study is the first to compare this novel method of objective examination to the clinical model of examination of eye movements in children with vertigo. Although clinical examination found some differences in eye movements between children with vertigo and healthy controls, we found there was no significant difference in eye movements between children with vertigo and healthy controls measured by the new, objective method of measurement that incorporates a more realistic measurement in the three-dimensional space, as it is able to account for accommodation and binocular disparity.

Implications of all the available evidence

Our data suggest that this novel method of measuring eye movements may be a more accurate test because it incorporates these additional factors. We postulate it is possible, due to the discrepancy in testing results, that the childrens' naturally coupled vergence and accommodation provide a compensatory mechanism that may be underappreciated by the current clinical evaluation methods. This leads to costly and time-consuming prescribed rehabilitation that may not improve symptoms. We suggest further research to support the argument that children with vertigo who are clinically identified as having abnormal eye movements should be secondarily screened for a more objective, complete evaluation with this novel method before starting a rehabilitation program.

model known as the dynamic photo refraction system (DPRS), which gives an accurate and rapid measurement of accommodation and pupil size from images obtained by the eccentric photo refraction optical technique [3]. Other studies have provided data on accommodation, vergence and their coupling using a remote haploscopic photo refractor (RHP) device (PlusOptix, PowerRefII). Horwood and Riddell demonstrated that the RHP could be considered a reliable method to measure variations in accommodation and convergence and to determine AC/A ratios, compared to clinical prism cover test (measuring Heterophoria Method Stimulus AC/A Ratio, Lens Gradient Method AC/A Ratio), and that the RHP method can be used for measuring accommodation, vergence, and AC/A ratios with high validity [4].

It is important to produce these measurements in the real space without decoupling accommodation and vergence. When using an RHP device to record movements in three-dimensional space, the disparity produced by measuring both eyes together has been shown to produce an augmented response; however, when disparity is absent, blur and proximity cues alone have been shown to produce weaker responses [5–9]. Thus, measuring vergence and accommodation in the real space is the best way to evaluate physiologic function. The present study aims to bridge this gap and provide an objective vergence accommodation measurement in the real space for healthy children and children with vertigo.

Children presenting with vertigo often demonstrate normal vestibular function but abnormal vergence movements [10,11]. It has been suggested that these vergence deficits could contribute to an abnormal gaze stabilization while the body is in motion, causing blurry or double vision, leading to vertigo symptoms. Previous studies have measured vergence eye movements in healthy children and children with vertigo in three-dimensional space. It has been argued that those with vergence deficiencies have abnormal gain adjustments, and therefore have decreased ability to stabilize their fixation on an image while the head or body is moving, thus leading to vertigo symptoms [12].

Currently, children are diagnosed with vertigo by utilizing a series of clinical exam maneuvers which often isolate portions of their visual systems to determine differences from normal children. However, these methods have not been compared to current objective laboratory measurements which allow for simultaneous recordings of accommodation as well as vergence.

Although previous studies have evaluated children with vertigo, to our knowledge, these eye movements have never been studied using an RHP device in this population that allows for the consideration of accommodation and binocular disparity. In the present study, healthy children and children with vertigo were evaluated using traditional clinical examinations and then by using objective laboratory equipment. Given that it has been shown that binocular disparity by these laboratory measurements can augment a provoked response, we were determined to find any differences between the laboratory and clinical eye movement measurements.

2. Methods

2.1. Subjects

Healthy children and children with vertigo were recruited for the experiment through contacts with friends and families. Following criteria exclusion (see below), 53 healthy (mean age 10 +/- 3.29) and 31 vertigo children (mean age 11 +/- 3.02) were investigated. This study was conducted during a Hospital Project of Clinical Research (PHRC Verve) between the Robert Debré Pediatric Hospital and the French National Center of Scientific Research (CNRS). The investigation adhered to the principles of the Declaration of Helsinki and was approved by the institutional human experimentation committee, the "Comité de Protection des Personnes" (CPP) Ile de France V, Saint-Antoine Hospital in Paris, France. Informed parental consent was obtained for each child after the experiment had been explained.

2.2. Clinical examination

All children, with and without a diagnosis of vertigo, underwent a thorough vestibular, ophthalmologic and orthoptic examination. The vestibular exam, to assess the vestibulo-ocular reflex (VOR), was comprised of the Head Impulse Test (HIT), the Fukuda test, and the test of the twelve cranial nerve pairs.

For children with a diagnosis of vertigo, a more thorough clinical examination of the vestibular system was completed to exclude a vestibular cause of their vertigo. An Earth Vertical Axis Rotation (EVAR) and a Caloric test were performed to test the semi-circular canals. An Off Vertical Axis Rotation Test (OVAR) and a Vestibular Evoked Myogenic Potential (VEMP PEOM) test were performed to test the otolith

system. Children with a diagnosis of vertigo who were found to have vestibular problems were excluded from the experiment.

After the vestibular testing, children underwent a complete ophthalmological examination. All children had normal or corrected to normal vision: the range of visual acuities was 8/10 to 12/10.

Finally, all children underwent a complete orthoptic evaluation. The dominant eye was measured with the unilateral cover-test: the child fixated a target at 5 m while the orthoptist alternately covered each eye while observing the viewing eye. If the viewing eye did not move, it was considered the dominant eye. No children had a diagnosis of strabismus. Stereoacuity, measured with the Toegepast Natuurwetenschappelijk Onderzoek (TNO) test for stereoscopic vision, ranged from 30-60 arc sec. The near point of convergence (NPC) was measured by bringing a pen incrementally closer to the patient's face. When the patient saw double, the distance between the pen and the center of the eyes was measured as the NPC. The break point of divergence far (D), break point of divergence near (D'), second measurement of divergence after convergence far (D2), second measurement of divergence after convergence near (D2'), break point of convergence far (C), and break point of convergence near (C') were measured using prisms at near (40 cm) and far (5 m) distances. The accommodative convergence/accommodation (AC/A) ratio was evaluated by inserting spherical lenses of −3, −1, 0, +1, +3 in front of the two eyes and measuring the resulting vergence with a bar of prisms. The AC/A ratio was calculated with the formula (5B-15A)/100 where A represents the accommodation induced and B the vergence measured, expressed in units of prism diopter (vergence change) per diopter (change in refractive power), or PD/D.

Children were excluded from the control group if they had a NPC more remote than 5 cm (i.e., greater than 5 cm), an exophoria at near larger than to 8 ± 2 prism diopters (pD), and range of fusional vergence smaller than 25 pD at near, 20 pD at far for convergence; 14 pD at near and 5 pD at far for divergence. Children with a diagnosis of vertigo were included if they showed an abnormal NPC (distant near point of convergence superior to 8 cm) and abnormal convergence (less than 20 pD at near and 10 pD at far) and divergence amplitudes (less than 14 pD at near and 5 pD at far).

2.3. Laboratory testing

The additional laboratory testing, or the new method tested, also measured vergence and accommodation with novel equipment. Children were asked to stand upright in front of a horizontal table, called REMOBI, with arms placed at either side along the body. Children were asked to make active convergence-divergence movements between two diodes that lit up alternatively with one diode at a distance of 20 cm and the other one at a distance of 70 cm, changing the vergence angle of 13° (18° at 20 cm and 5° at 70 cm) (Fig. 1A). The children made approximately 15 convergence and 15 divergence movements over 30 s. Each diode was lit for 1000 ms, and the second LED was lit once the first LED disappeared. The device used is the laboratory precursor of the REMOBI device (patent US8851669, WO2011073288) [1]. Fig. 1B shows the convergence-divergence eyes positions as well as the associated accommodation-disaccommodation of the eyes, with I and F indicating the beginning and end of each test.

2.4. Vergence and accommodation recording

Vergence and accommodation movements were recorded with the infrared optometer PowerRef II (Plusoptix, Germany). The PowerRef II guarantees an objective measure of both the accommodation (subject refraction) and the vergence for a specific target placed one meters from the child's eyes (see Fig. 1A). A small infrared light, eccentric to the CCD camera aperture, is reflected from the eye and captured as a video image. In this video image, a typical brightness profile is seen within the pupil that provides quantitative measures

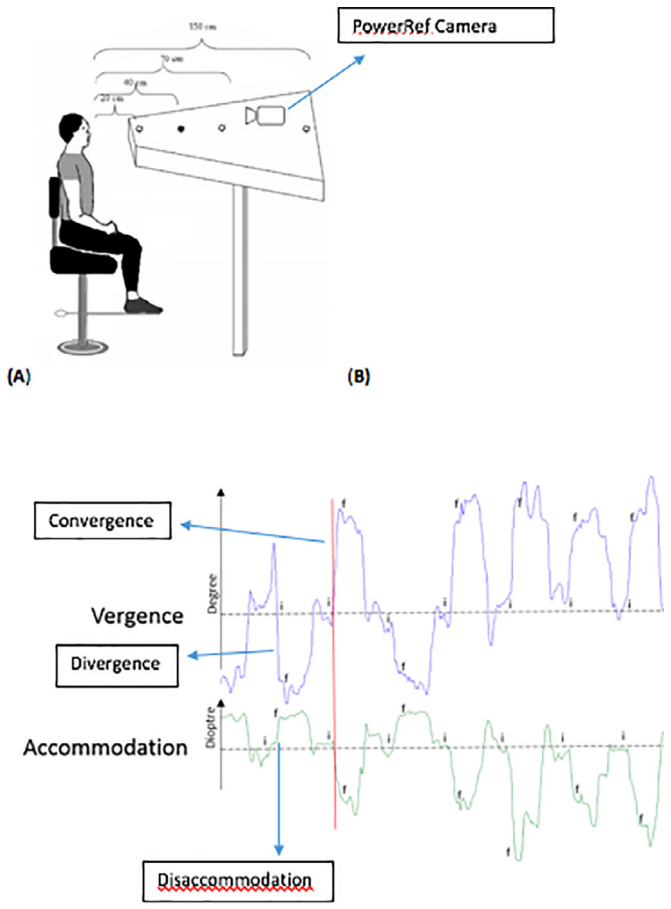


Fig. 1. (A and B): **(A)** Experimental set-up. **(B)** Vergence and accommodation traces recorded with the PoweRef device.

of the direction and degree of the eye's defocus over a defined working range. The slope of the intensity gradient indicates the degree of the eye's defocus. Information on the direction of this defocus (hyperopia or myopia) is provided by the sign characterizing the slope of the intensity gradient.

2.5. Orthoptic follow-up

Each child in the vertigo group received a series of 12 clinical re-education orthoptic sessions (2 sessions / week) conducted by orthoptists outside the hospital. They then repeated the laboratory portion of the experiment (V2). Three months after this re-evaluation, the children with vertigo repeated the laboratory portion of the experiments (V3).

2.6. Laboratory data analysis

The PowerRef II device is traditionally used to study vergence accommodation during stationary fixation. The present study introduces a novel software method, created by the lab, for studying dynamic vergence accommodation. The PowerRef II measures provide the following data: the vergence signal (Gaze Right) and the accommodation signal (Refraction Right) for the right eye, and the vergence signal (Gaze Left) and the accommodation signal (Refraction Left) for the left eye. These data were imported to the laboratory software Analyze32 as four channels. We then marked manually in each trace the highest and the deepest peak of every movement, by the letters 'I' and 'F' respectively, corresponding thus to the vergence movements and the accommodation responses. Thereafter, we deduced

from these data the following parameters: (1) Global time (ms), the time used to execute a cycle of response, from one peak to the next. This global time includes the time to perform a vergence movement and an accommodative response, the time to fixate the target, and the time to prepare the successive movement/accommodative response. (2) Vergence in degrees (°), obtained by a calculation of the mean of 'Gaze L' and 'Gaze R', in absolute value. (3) Mean accommodation in spherical diopters (SD), obtained by a calculation of the mean of 'Refraction L' and 'Refraction R', in absolute value. (4) Vergence-accommodation ratio was evaluated by dividing the change in vergence by the change in the accommodation of the left and the right eye, in absolute value (Vergence / Accommodation). Each parameter was studied in both divergence and convergence movements.

2.7. Statistical analysis

Three main analyses were performed: (1) the difference in clinical examination between children with vertigo and normal, healthy controls; (2) the difference in the laboratory examination between children with vertigo and normal, healthy controls, and (3) for children with abnormal clinical examinations who were recommended for orthoptic rehabilitation, compare the difference in laboratory testing at three points: before, immediately after, and three months after rehabilitation.

In a first analysis, we performed a Shapiro-Wilk-W-test for normality. As the data were not normally distributed, we performed a Mann-Whitney U test with the factor condition (healthy, vertigo) for all clinical examination parameters. In a second analysis, we performed a Mann-Whitney U test with the factor condition (healthy, vertigo) for all laboratory measurements incorporating disparity. Finally, in a third analysis, we performed a Friedman ANOVA and Kendall Concordance test in children with vertigo to compare laboratory measurements taken at time 0 (V1), after 12 sessions of training (V2), and three months after training was completed (V3). For all analyses, the statistical significance was set at $p \leq 0.05$.

2.8. Role of funding

We thank the Fulbright Foundation, along with the University of California, San Francisco, for the research fellowship to Lindsey M Ward. This study is part of the PHRC VERVE, hospital research program, run at the hospital Robert Debré and supported by Direction de la Recherche Clinique, Assistance Publique, France. The funding sources had no involvement in the study design; collection, analysis, and interpretation of data; writing of the manuscript; and in the decision to submit the manuscript for publication.

3. Results

3.1. Orthoptic tests

The clinical evaluation found there to be a significant difference between the children with vertigo and the healthy children in 5 parameters: D' (mean healthy = 2511.5, mean vertigo = 5744.5; $U = 1383.5$; n1 = 47; n2 = 81; $p = 0.01$); D2 (mean healthy = 1619, mean vertigo = 3946; $U = 878$; n1 = 38, n2 = 67; $p = 0.005$); D2' (mean healthy = 1367, mean vertigo = 4198; $U = 626$; n1 = 38, n2 = 67; $p = 0.00001$); C (mean healthy = 2605.5, mean vertigo = 5650.5; $U = 1477.5$; n1 = 47, n2 = 81; $p = 0.03$); and C' (mean healthy = 2281, mean vertigo = 5975; $U = 1153$; n1 = 47, n2 = 81; $p = 0.002$). There was no significant difference in TNO, NPC, D, or AC/A between the two groups after clinical evaluation. Fig. 2 displays means and standard deviations for all clinical evaluation measurements.

3.2. Laboratory evaluation

The laboratory testing with the PowerRef evaluation did not find any significant difference in measurements between healthy children and children with vertigo. Fig. 3 displays means and standard deviations for all laboratory evaluation measurements.

3.3. Evaluation during and after rehabilitation

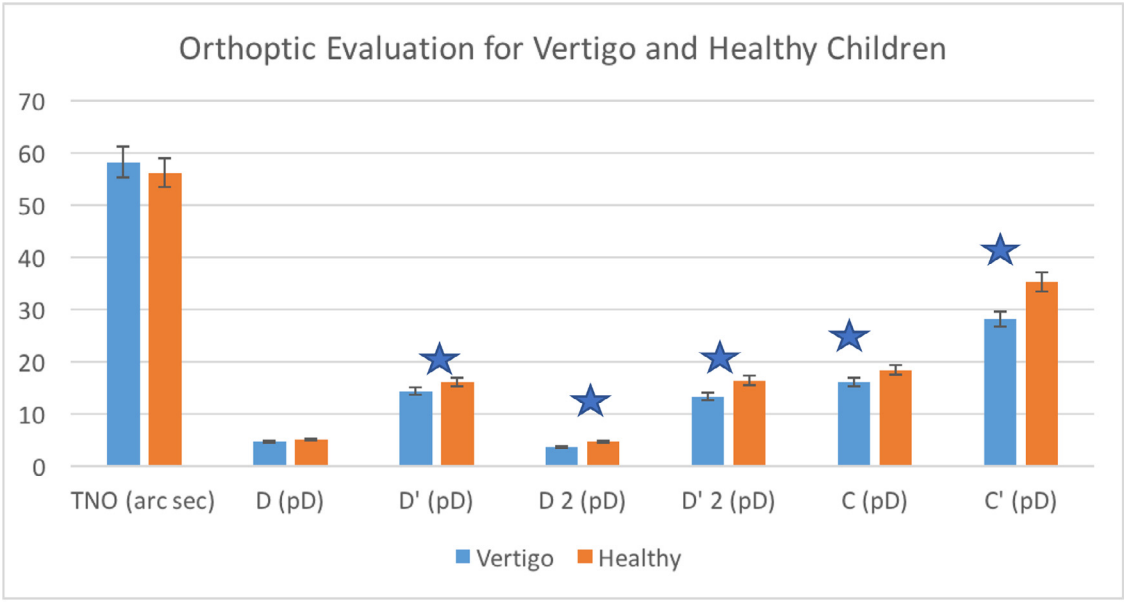
For all parameters on laboratory testing (convergence; divergence; accommodation; disaccommodation; convergence/accommodation ratio; divergence/disaccommodation ratio; time cycle convergence; and time cycle divergence), there was no significant difference in children with vertigo at 0 months (V1), after 12 sessions of rehabilitation (V2), and 3 months after rehabilitation is complete (V3). Fig. 4 displays means and standard deviations for all laboratory evaluation measurements at time 0, after 12 sessions of rehabilitation, and 3 months after the rehabilitation.

4. Discussion

For certain subjective clinical measurements, there was a statistically significant difference between children with vertigo and healthy children. This difference confirms that a subjective orthoptic criteria identifies a difference between children with vertigo and children without vertigo. However, it is notable that there was a significance found in these particular values: D' (break point of divergence near) D2 (second measurement of divergence after convergence far) D2' (second measurement of divergence after convergence near) C (break point of convergence far) C' (break point of convergence near). These measure the evolution of the disparity vergence with the use of prisms, providing a measurement during which vergence and accommodation are uncoupled. The NPC, the unique value that tests how the eyes work together in real three-dimensional space, was not significantly different between the two populations. This suggests that there could be a specific problem recorded when testing the vergence dichoptically (e.g., by using prisms), as such uncoupling does not occur in everyday life.

There were also no statistically significant differences between the two groups for any parameters using the laboratory measurements. This was the case for both accommodation, vergence, and their ratio. The key difference between clinical orthoptic testing and laboratory testing is that laboratory testing allows testing of coupled vergence accommodation movements, simulating what we use in real life. Most of the clinical evaluation separates the disparity from the accommodation evaluation, and therefore produces a limited value relative to how the eyes are behaving in everyday life. As previously mentioned, this decoupling has been found to provoke a smaller accommodation and vergence response [5–9]. It is possible that coupling of vergence and accommodation allows children with vertigo to overcome potential differences such that no objective difference in measurements exists. While these children may have some vergence accommodation deficits, it is possible they are able to overcome them when they make natural gaze shifts using vergence and accommodation together.

Notably, these results differ from previous experiments conducted in children with vertigo, which determined a difference in the gain in vergence between children with vertigo and healthy children [12]. The previous experiment found a difference in the gain in vergence, a measurement we were unable to capture in this study due to our equipment; the resolution of the RHP device is much lower than the equipment used in the previous study. However, the previous equipment was unable to evaluate accommodation; with the RHP device, we are able to measure accommodation with a high resolution and found no accommodation differences between children with vertigo and healthy children.



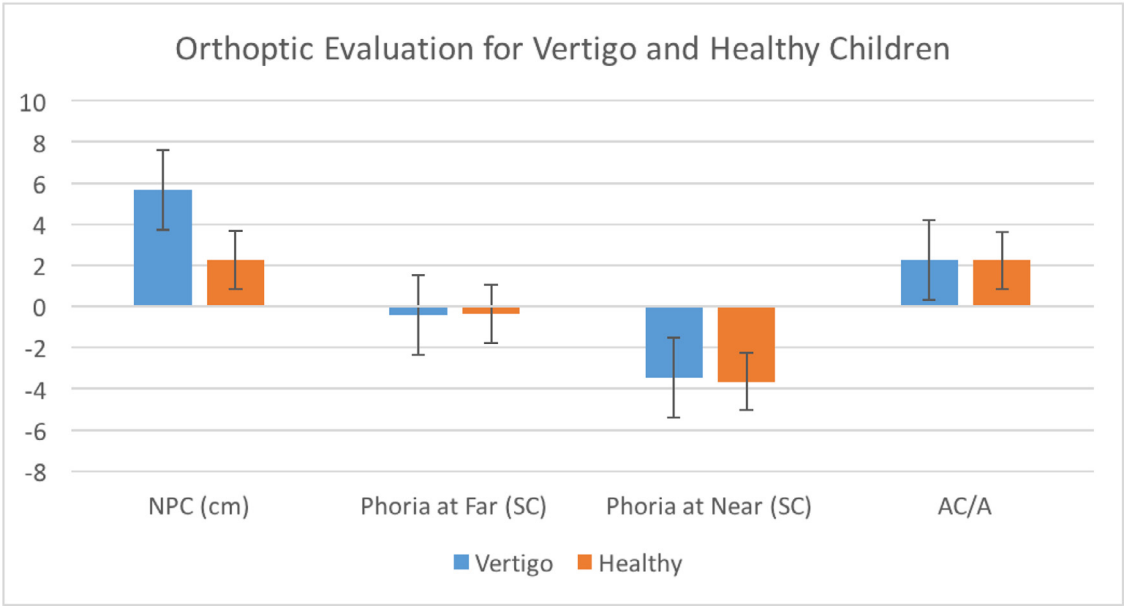


Fig. 2. *Clinical evaluation for vertigo and healthy children:* There was a significant difference found between healthy children and those with vertigo in D' (break point of divergence near), $p = 0.009$; D2 (second measurement of divergence after convergence far), $p = 0.005$; D2' (second measurement of divergence after convergence near), $p = 0.001$; C (break point of convergence far), $p = 0.03$; and C' (break point of convergence near), $p = 0.001$. Error bars represent standard deviation; significant values are marked with stars.

Further, as the clinical orthoptic examination is performed by humans, it is inherently a subjective test; the examination relies primarily on the child's response to the clinician's questions (e.g., "Do you see one object or two?"). The laboratory measurements, calculated by an algorithm that gives an accommodative and vergence response, are more objective and do not rely on the subjectivity of the patient, who, as a young child, may not be able to give a consistently objective answer. Therefore, given the objectivity of the test and the fact that it incorporates natural coactivation of vergence and accommodation, the laboratory measurements may be considered a more accurate measurement of accommodation and vergence in the natural environment.

Finally, it is important to note that children with vertigo did not appear to respond to orthoptic rehabilitation exercises over the course of 6 months as determined by laboratory measurements, as there was no difference in laboratory testing before, after 12 sessions of rehabilitation, and 3 months after the 12 sessions. This finding is possibly explained by the natural compensatory behavior children with vertigo appear to exhibit to overcome their deficits when accommodation and vergence are simultaneously measured.

It is important to note there are several limitations in this study. First, the exclusion criteria for vertigo may not have given a representative sample of children with vertigo secondary to vergence problems alone. Children with psychogenic dizziness or orthostatic dysregulation may not have been excluded with the extensive vestibular testing we conducted. Additionally, although their laboratory exams did not improve over the rehabilitation period, it would have been prudent to clinically re-evaluate each subject at V2 and V3 to see if their clinical exam improved as a result of rehabilitation. Finally, this is relatively small sample size of 84 children (53 healthy,

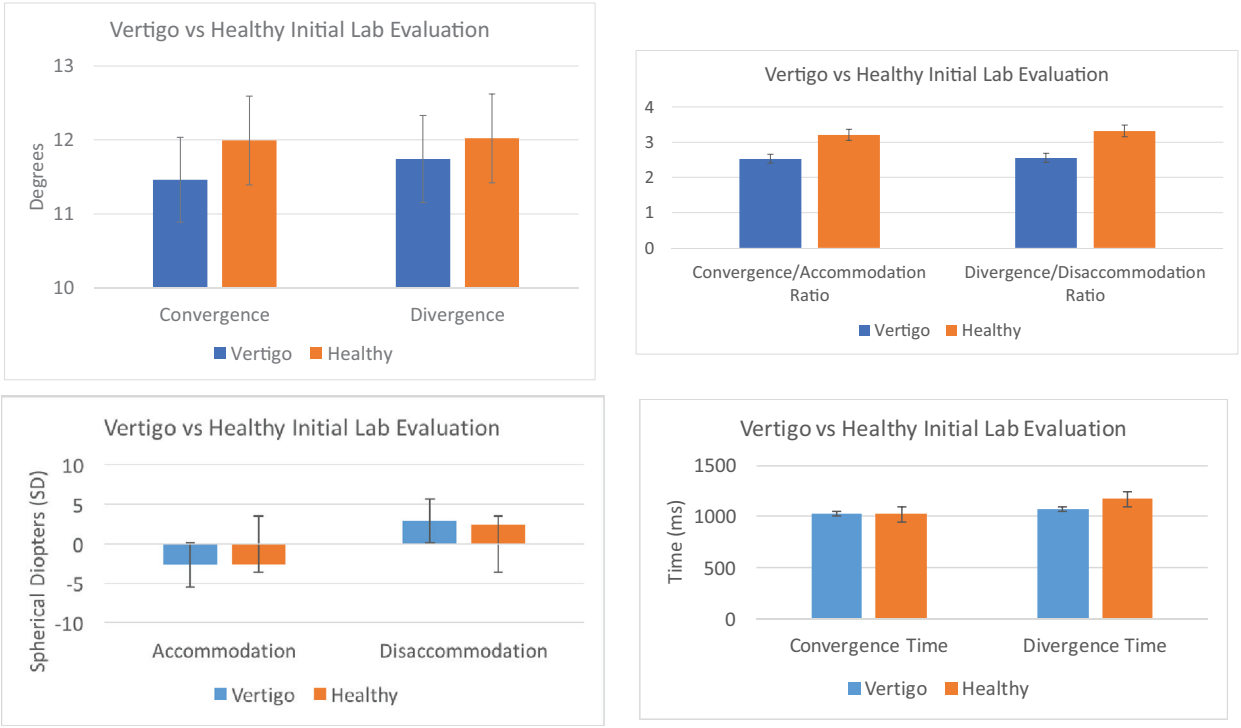


Fig. 3. *Laboratory evaluation for vertigo and healthy children:* There was no significant difference in laboratory evaluation (convergence; divergence; accommodation; disaccommodation; convergence/accommodation ratio; divergence/disaccommodation ratio; time cycle convergence; and time cycle divergence) between healthy children and those with vertigo (all $p > 0.10$). Error bars represent standard deviation.

31 vertigo) recruited through a hospital network, which has an inherent bias. It would be prudent for future research to expand the population in both size and diversity.

In summary, this study utilized for the first time, to our knowledge, a device which measures vergence and accommodation simultaneously in children with vertigo. Our data suggest that the natural coupled vergence and accommodation that allow children with vertigo to compensate for their deficits may be underappreciated by current clinical evaluation. This may lead to potential misdiagnosis and costly, time-consuming rehabilitation. Given our

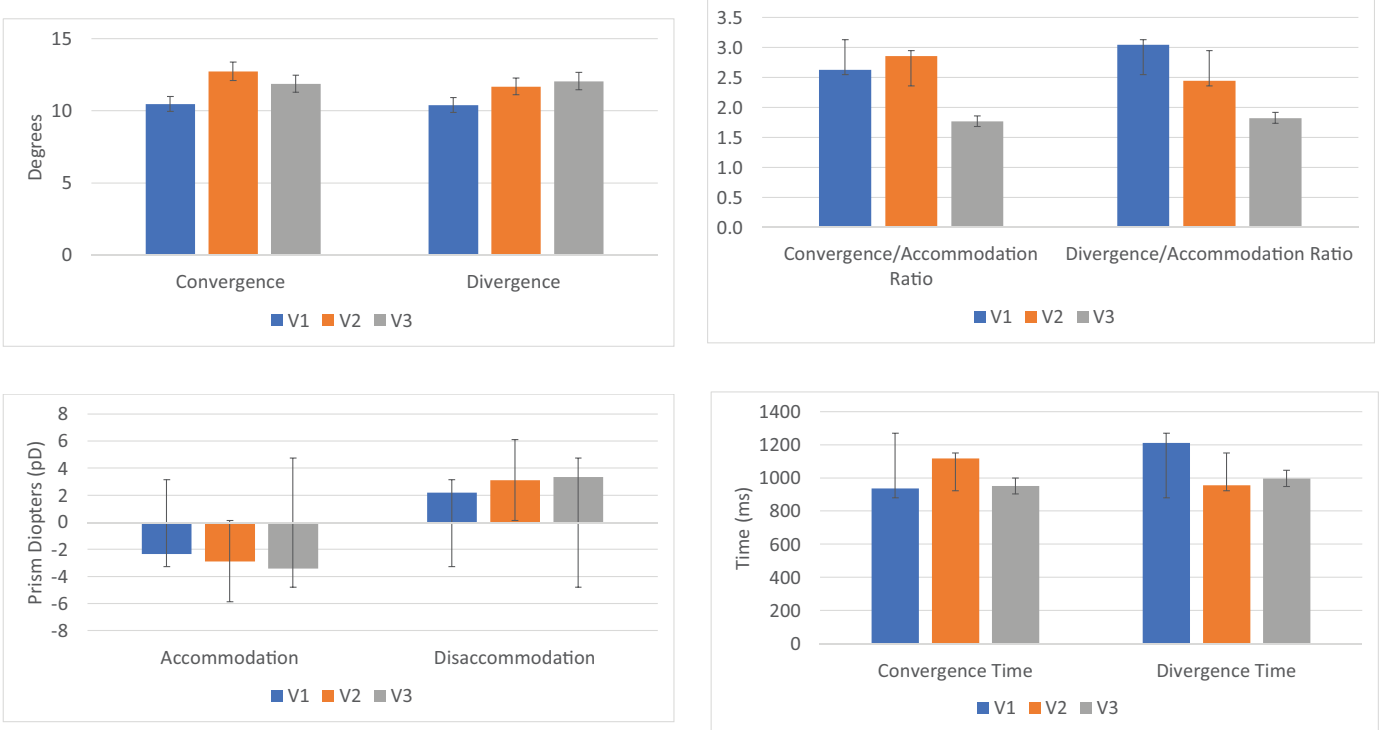


Fig. 4. *Laboratory evaluation for vertigo children at V1 (before rehabilitation), V2 (after 12 sessions of rehabilitation), and V3 (6 months after rehabilitation).* There was no significant difference in any laboratory parameters (convergence; divergence; accommodation; disaccommodation; convergence/accommodation ratio; divergence/disaccommodation ratio; time cycle convergence; and time cycle divergence) for any time point (all $p > 0.10$). Error bars represent standard deviation.

findings, we suggest that further research be conducted to validate the utilization of devices that measure the natural eye movements of children such as the RHP device or other equipment with high resolution in contrast to the traditional clinical exam. If further research validates our results, we suggest that the traditional clinical exam may be more appropriately utilized as a screening tool for which patients who screen positive are referred for more objective measurements before starting a rehabilitation program.

Declaration of Competing Interests

The authors have no potential conflicts of interest.

Acknowledgments

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Author Contribution Statement

Lindsey Ward analyzed the data, performed the statistics, and co-wrote the manuscript.

Chrystal Gaertner and Lucrezia Olivier conducted the experiments and analyzed the data.

Layla Ajrezo conducted the orthoptic evaluation for all children.

Zoi Kapoula conceived and designed the study, developed the algorithms for data analysis, and co-wrote the manuscript.

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