Received: 12 April 2021 | Revised: 26 June 2021 | Accepted: 29 July 2021

DOI: 10.1002/lio2.632

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Normative data for ages 18-45 for ocular motor and vestibular testing using eye tracking

Aura Kullmann PhD[1] | Robin C. Ashmore PhD[1] | Alexandr Braverman PhD[2] | Christian Mazur BS[1] | Hillary Snapp PhD[3] | Erin Williams BS[3] | Mikhaylo Szczupak MD[3] | Sara Murphy PhD[4,5] | Kathryn Marshall PhD[5,6] | James Crawford MD[6] | Carey D. Balaban PhD[7] | Michael Hoffer MD[3,8] | Alexander Kiderman PhD[1]

[1]Neurolign USA LLC, A Subsidiary of Neurolign Technologies Inc. (formerly Neuro Kinetics, Inc.), Pittsburgh, Pennsylvania, USA

[2]The Hebrew University of Jerusalem, Jerusalem, Israel

[3]Department of Otolaryngology, Miller School of Medicine, University of Miami, Miami, Florida, USA

[4]Naval Medical Center, San Diego, California, USA

[5]Department of Defense, Hearing Center of Excellence, San Antonio, Texas, USA

[6]Madigan Army Medical Center, Tacoma, Washington, USA

[7]Department of Otolaryngology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

[8]Department of Neurological Surgery, Miller School of Medicine, University of Miami, Miami, Florida, USA

Correspondence
Aura Kullmann, PhD, Neurolign USA, LLC., 128 Gamma Dr. Pittsburgh, PA, 15238, USA.
Email: aura.kullmann@gmail.com

Funding information
Department of Defense, Grant/Award Numbers: W81XWH-12-C0205, W81XWH-13-C-0008; National Institutes of Health, Grant/Award Numbers: R43DC014611, R44HD100247

Abstract

Objective: Eye tracking technology has been employed in assessing ocular motor and vestibular function following vestibular and neurologic conditions, including traumatic brain injury (TBI). Assessments include tests that provide visual and motion (rotation) stimuli while recording horizontal, vertical, and torsional eye movements. While some of these tests have shown diagnostic promise in previous studies, their use in clinical practice is limited by the lack of normative data. The goal of this study was to construct normative reference ranges to be used when comparing patients' results.

Methods: Optokinetic response, subjective visual horizontal and vertical, and rotation tests were administered to male and female volunteers, ages 18-45, who were free from neurological, vestibular disorders, or other head injuries. Tests were administered using either a rotatory chair or a portable virtual reality-like goggle equipped with video-oculography.

The views expressed in this article reflect the results of research conducted by the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of the Army, Department of Defense, nor the United States Government.

LTC James Crawford was a military service member. Kathryn Marshall and Sara Murphy are contracted employees of the United States government. This work was prepared as part of their official duties. Title 17 U.S.C. 105 provides that 'copyright protection under this title is not available for any work of the United States Government.' Title 17 U.S.C. 101 defines a U.S. Government work as work prepared by a military service member or employee of the U.S. Government as part of that person's official duties.

An abstract of this paper has been accepted for presentation at the 2020 Military Health System Research Symposium (MHSRS) virtual conference August 17-20, 2020.

Results: Reference values for eye movements in response to different patterns of stimuli were analyzed from 290 to 449 participants. Analysis of gender (self-reported) or age when grouped as pediatric (late adolescent; 18-21 years of age) and adult (21-45 years of age) revealed no effects on the test metrics. Data were pooled and presented for each test metric as the 95% reference interval (RI) with 90% confidence intervals (CI) on upper and lower limits of the RI.

Conclusions: This normative database can serve as a tool to aid in diagnosis, treatment, and/or rehabilitation protocols for vestibular and neurological conditions, including mild TBI (mTBI). This database has been cleared by the FDA for use in clinical practice (K192186).

Level of evidence: 2b

KEYWORDS
concussion, eye tracking, mild traumatic brain injury, mTBI, Neurolign Dx 100, neurological conditions, NOTC, rotation tests, vestibular conditions

1 | INTRODUCTION

Vestibular system dysfunctions have been reported in as many as 35% of adults and approximately 18% of children.[1,2] Symptoms include dizziness, blurred vision, and balance issues.[1-5] In recent years, a large body of literature has shown numerous vestibular deficits following mild TBI (mTBI; also known as concussion). It has been reported that vestibular symptoms are present in up to 95% of individuals at the initial presentation following TBI,[3,5,6] can be associated with prolonged recovery after mTBI, and can persist for weeks to months or even years post injury.[5,7-10]

The function of the vestibular system has traditionally been investigated using a battery of assessments that include dynamic and static vestibular testing and ocular motor testing.[11] Dynamic vestibular testing uses motion stimuli provided by a rotational chair and includes tests such as sinusoidal harmonic acceleration (SHA), visual enhancement (VE), visual suppression (VS), and the head impulse test (HIT). The computerized rotational head impulse test (crHIT) is delivered by a computer-controlled rotational chair using brief, whole-body, earth-vertical axis impulsive rotations while subjects are maintaining fixation on an earth-fixed target. Eye movements are measured using video-oculography, overcoming the limitations of manual HIT.[12] Static vestibular testing includes positional/positioning tests, caloric, subjective visual vertical (SVV), and subjective visual horizontal (SVH). Ocular motor tests include spontaneous nystagmus, gaze nystagmus, optokinetic response (OKN), pursuit, saccade, vergence tests, and others.

Many of these tests have been employed traditionally in the evaluation of vestibular conditions such as Meniere's disease (MD) and vestibular neuritis or examination of semicircular canal and otolith function.[12-23] A number of research studies, including several from our group, have employed these tests for evaluation of mTBI and have shown that metrics from these tests can be useful to detect and monitor deficits following mTBI.[24-29] Furthermore, the availability of high-resolution eye-tracking technology, which can accurately measure eye movements on the order of less than 0.1°, makes these tests valuable tools for the assessment of mTBI and other neurological conditions. However, the scarcity of normative data has impeded the wide adoption of these tests in clinical practice. Very few studies include data from healthy subjects; many involve a small number of participants and/or a wide range of ages.[13,14,30-33] A normative database represents the ranges of test performance of a group of medically healthy individuals.[34] Such a database could be useful for diagnostic purposes and for tracking improvements over time, to aid in diagnosis and evaluation of treatment efficacy, rehabilitation, and return to duty/work/activity decisions.

The goal of this study was to construct a normative database (defined as a reference interval to be used to determine if the test result of a subject is in the normal range) for eye-tracking ocular motor and vestibular tests for healthy 18-45-year-old participants.

2 | MATERIALS AND METHODS

2.1 | Study participants

All research activities were approved by Institutional Review Board (IRB) protocols and registered under NCT02486003 and NCT01832714. Participants, male and female volunteers 18-45 years of age (see demographics

TABLE 1 Demographics of the participants included in this study

Age/groups (years)	Mean age (years ± SD)	*N*	Sex M/F
18–45	24.75 ± 6.28	449	294/155
Group 1:18–21	19.62 ± 1.12	196	122/74
Group 2:22–45	28.64 ± 5.77	253	172/81

Abbreviations: M, male; F, female; N, number of participants; SD, standard deviation.

TABLE 2 Battery of ocular motor, reaction time and cognitive tests

	Tests	Metrics
1	*Optokinetic (OKN) 20 deg/s*: Participants see a stimulus consisting of a field of dots moving on the display first to the right, then to the left, with a velocity of 20 deg/s. Each test consists of a stimulus rotating for 10 seconds clockwise (CW) and then 10 seconds counterclockwise (CCW), with 3 seconds of rest between CW and CCW rotation.	a. Average eye velocity CCW (deg/s) = eye velocity during the slow phase of nystagmus for stimuli moving in counterclockwise (CCW) direction b. Average eye velocity CW (deg/s) = eye velocity during the slow phase of nystagmus for stimuli moving in clockwise (CW) direction c. Gain = ratio between average eye slow phase velocity and stimulus for CW and CCW segments d. Gain Asymmetry (%) = represents the difference between gain calculated for CW and CCW segments e. *Area Under Velocity Fit +(30 deg) = proportional to fast beat velocity for CCW stimuli f. *Area Under Velocity Fit (30 deg) = proportional to fast beat velocity for CW stimuli g. Normalized OKN CW velocity gain (normalized at 20 deg/s) h. Normalized OKN CCW velocity gain (normalized at 20 deg/s) *-see details for calculation in the method section
	Optokinetic (OKN) 60 deg/s – same as OKN 20 deg/s, but with the stimulus moving at 60 deg/s.	Same as above
2	*Sinusoidal harmonic acceleration (SHA) 0.02 Hz* (also known as Chair rotation sinusoidal): subject is rotated back and forth sinusoidally in the dark at frequency of 0.02 Hz with a peak velocity of 60 deg/s.	a. Gain = average of gain left and gain right, that is, vestibulo-ocular reflex (VOR) gain, where gain (left or right) is the ratio of the peak slow phase eye velocity to the peak head velocity and is expressed as a percentage b. Asymmetry = represents the percentage difference between gain calculated for left and right gains c. *Phase = temporal relationship between peak eye and peak head velocity, expressed in degrees *see details for calculation in the method section
	Sinusoidal Harmonic Acceleration (SHA) 0.64 Hz	Same as above
3	*Visual enhancement (VE)*: subject is rotated back and forth sinusoidally at frequency of 0.64 Hz with a peak velocity of 60 deg/s. A static optokinetic stimulus is presented during this rotation.	a. Average gain b. Asymmetry c. Phase All values that have similar meaning are calculated similar to those described in the SHA test
4	*Visual suppression (VS)*: subject is rotated back and forth sinusoidally at frequency of 0.64 Hz with a peak velocity of 60 deg/s. Subject is directed to fixate on laser dot that moves with the chair. This allows an individual to suppress the VOR. Suppression is poorer at higher frequencies of rotation.	a. Average gain b. Asymmetry c. Phase All values that have similar meaning are calculated similar to those described in the SHA test
5	*Controlled rotational head impulse test (crHIT)*: subject is rotated briefly in pseudo-random direction (6 CW and 6 CCW) for a total of 12 rotations. An acceleration of 1000 deg/s^2 is included in this test. Participants are directed to fixate on earth-fixed target during rotation. Each stimulus consists of 150 milliseconds acceleration using an "S" type profile (to minimize patient's discomfort), followed by 300-400 milliseconds run at speed up to 180 deg/s and slow "S" type deceleration for 2–3 seconds. Between each stimulus the subject is at rest for 5–8 seconds.	a. *Gain = Average VOR Gain b. *Asymmetry = Average VOR Gain Asymmetry (%) *see details for calculation in the method section
6	*Subjective visual vertical (SVV)*: subject is presented with a non-vertical line and by using the left and right buttons on the handheld control box (Dx 100) or the buttons located on the chair handle (NOTC), orients the line to the vertical (upright) position, and then presses the accept button on the control box (Dx 100), or verbally acknowledges the alignment (NOTC). A total of 6 trials were performed per subject, 3 with a positive and 3 with a negative angle preset, presented randomly.	Mean error (deg) = difference between subject's orientation angle and true vertical. Data are presented as a mean of errors of all measurements.

TABLE 2 (Continued)

	Tests	Metrics
7	*Subjective visual horizontal (SVH)*: subject is presented with a non-horizontal line and by using the left and right buttons on the handheld control box (Dx 100) or the buttons located on the chair handle (NOTC), orients the line to the horizontal position, and then presses the accept button on the control box (Dx 100), or verbally acknowledges the alignment (NOTC). A total of 6 trials were performed per subject, 3 with a positive and 3 with a negative angle preset, presented randomly.	Mean error (deg) = difference between subject's orientation angle and true horizontal. Data are presented as a mean of errors of all measurements.

Note: Description of each test and metrics measured for each test.

in Table 1), were recruited from three different sites: a) University of Miami, Miami, FL, IRB#2015036; b) Naval Medical Center San Diego, San Diego, CA, IRB# NMCSD.2013.0060; and c) Madigan Army Medical Center, Tacoma, Washington, IRB# 393240-1. All participants signed an informed consent. To create a representative sample of the general population, the study included civilians, military service members, and non-professional athletes who participate in intercollegiate athletics. Exclusion criteria were conditions and diseases that could impact the vestibular and ocular motor systems. These include a history of brain injury, repeated blast exposure, presence of severe aphasia, history of diagnosed neuropsychiatric disorders (eg, hypochondriasis, major depression, schizophrenia), neurodegenerative disorders, disorders of hearing and balance (eg, MD, multiple sclerosis, vestibular neuritis, vestibular schwannoma, sudden sensorineural hearing loss), cerebrovascular disorders, history of ear operation other than myringotomy tube, and systemic disorders (eg, chronic renal failure, cirrhosis of the liver). Special populations including women who were pregnant, children under 18 years old, and those with impaired decision-making capacity were also excluded from this study. Data presented here include 300 healthy controls subjects included in earlier papers from this group that described the use of ocular motor and vestibular tests for evaluation of mTBI.[24,27,35] All sites used the same inclusion/exclusion criteria, which are listed in the Supplemental data.

2.2 | Battery of tests

Table 2 describes the tests and metrics measured in this study. These include OKN response, SVV and SVH, SHA, VE, VS, and crHIT.

2.3 | Devices

The devices, eye tracking technology, and software used in this study were developed by Neurolign USA, LLC (formerly known as Neuro Kinetics, Inc.; Pittsburgh, PA). Two FDA-cleared eye-tracking devices were used in this study: a) neurolign Dx NOTC, formerly known as I-Portal Neurotologic Test Center (NOTC) and b) neurolign Dx 100, formerly known as I-Portal Portable Assessment System—Nystagmograph (I-PAS). The study started using the NOTC initially and was later supplemented by the Dx100. These devices are substantially equivalent, that is, they use the same acquisition and analysis software, have the same high-resolution eye tracking capabilities, and data obtained with each device are statistically or clinically equivalent. The only difference is in the type of stimuli that each device can deliver and their size. The Neurolign Dx NOTC is a rotational chair that provides rotational, visual, and auditory stimuli while recording eye movements and reaction time responses. The Neurolign Dx 100 is a portable, compact, 3D, head-mounted display system with integrated eye tracking that provides visual and auditory stimuli while recording eye movements. Both the Neurolign Dx NOTC and the Neurolign Dx 100 use infrared video-oculography. High-resolution eye-tracking images are acquired via two high-speed digital infrared cameras (940 nm illumination; sampling rate 100 frames/sec). Spatial resolution for horizontal, vertical, and torsion eye tracking is <0.1°; eye-tracking range is at least ±24° horizontal, ±20° vertical, and ± 10° torsional. Data were collected using I-Portal software, which captures, time stamps (critical for synchronization), and analyzes digital images of the eye to capture horizontal and vertical eye movement data. VEST™ software was used to operate the hardware, manage and capture the stimulus profiles, integrate I-Portal eye-tracking data, and analyze the data to generate a comprehensive set of metrics. Tests using motion as stimulus were administered only using the NOTC and included: SHA, VE, VS, and crHIT. The remainder of the tests (OKN, SVV, and SVH) were administered using both devices.

2.4 | Data Analysis

Acquired data for each test were inspected for completion and validity and analyzed using VEST software. Data were then exported to IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, USA) and Microsoft Excel for further analysis.

2.4.1 | Treatment of artifacts and outlying samples

Data were calibrated for position by the comparison of eye movement to fixation positions with known displacement. The software detected artifacts such as blinks, recording noise, and temporary failures of eye tracking. These and other artifacts, such as shifting of goggles, erroneous responses, or responses not related to the task, were manually evaluated to separate eye movement signals from other recording

noise. Manual analysis was also performed in some cases to segregate saccadic activity from pursuit activity. The software reported data validity, which is the percentage of data needed to calculate a metric. If this percentage was below 60%, the software had a blinking function to attract attention. In these cases, the software analyzed data from a single eye (left or right), if data for that particular eye met the 60% validity criteria. If not, data from that particular test were discarded. For some participants, individual tests were removed from analysis when the data quality was judged to be inadequate for accurate measurement or produced analytic errors.

2.4.2 | Test metrics calculation

The metrics defined in Table 2 are calculated by VEST software, as described below. The OKN test delivers light stimuli moving rightward (or clockwise, CW, relative to the subject seated at the central axis) and leftward (counterclockwise, CCW) across the visual field and measures eye movements in response to these moving stimuli. The eye movements are composed of slow and fast phase beat movements; the slow phase represents eye movement in the direction of a moving object; and the fast phase represents rapid return of the eye in the opposite direction. For this test, the metric "average eye velocity" represents the average of the slow phase velocity (ASPV; deg/s). The metric "gain asymmetry" was then calculated using ASPV for stimuli moving in the CW and CWW direction:

$$\text{Gain Asymmetry} = \frac{CW\,ASPV - CCW\,ASPV}{CW\,ASPV + CCW\,ASPV} \times 100\%.$$

Normalized OKN CW velocity gain (normalized at 20 deg/s) represents gain CW at 60 deg divided by gain CW at 20 deg. Normalized OKN CCW velocity gain (normalized at 20 deg/s) represents gain CCW at 60 deg divided by gain CCW at 20 deg.

Fast phase eye movements of OKN-induced nystagmus are quantified with peak velocity and beat amplitude. The "main sequence" of fast phase beats represents beat peak velocity as a function of beat amplitude. CW direction of stimulus rotation produces leftward fast phase movements, and CCW direction of stimulus rotation produces rightward fast phase movements. Two separate main sequences are built for leftward and rightward fast phase eye movements. The following model function is used to fit the main sequence data: $y(x) = Ae^{Bx}$-A, where x is the fast phase beat amplitude and y is the fast phase beat peak velocity.[36-38] Nonlinear regression is applied to each main sequence, and A and B coefficients are calculated. Area under velocity fit is then calculated using the following equations: $\int_0^{30} Ae^{Bx} - A$, for fast beat velocity for CCW stimuli and $\int_{-30}^{0} Ae^{Bx} - A$ for fast beat velocity for CW stimuli.

The SHA (0.02, 0.64 Hz) is a test that assesses the vestibulo-ocular reflex (VOR) by rotating the patient in a sinusoidal pattern at various frequencies, with vision denied. In this test, the phase metric represents the temporal relationship between peak eye and peak head velocity. The phase metric is computed as the sinusoidal-cycle difference between the stimulus and eye movement. Phase metrics are reported for eye and stimulus position and for eye and stimulus velocity. The "asymmetry" metric is calculated as the difference between left and right gain divided by the sum of left and right gain. Throughout the test period, the subjects were given verbal tasks, including alphabetically naming things, places, foods, or counting, to maintain a constant level of alertness.

The crHIT delivers a precise, brief, whole-body, earth-vertical axis impulsive rotation, while subjects are maintaining fixation on an earth-fixed target, and eye movements are measured using video-oculography.[12] Data collected are eye position, head and chair velocity, and acceleration in X, Y, and Z planes. The gain is calculated using $Gain = Veye/\ Vhead$, where *Veye* is eye velocity and *Vhead* is head velocity, for L and R, respectively. The gain is calculated for all rightward (L) and leftward (R) impulses, and the average gain is computed as (Gain L + Gain R)/2. Asymmetry represents the VOR gain asymmetry and is computed as [(R-L)/(R + L)] × 100, percentage, where R = mean right VOR gain and L = mean left VOR gain. The VS test is another test of the rotary chair that assesses the VOR, using the reduction in the VOR as an evaluation of the central (cerebellar/brainstem) function. This test involves the patient staring at a target light that moves with the chair, while the chair produces the sinusoidal harmonic rotation. Similar to the SHA, gain, phase, and asymmetry are recorded. The VE test is another test of the rotary chair that assesses the VOR, similar to VS test. This test involves the patient staring at a full field, stationary optokinetic stimulus, while the chair produces the sinusoidal harmonic rotation. Similar to the SHA, gain, phase, and asymmetry are recorded.

The SVV and SVH tests measure the ability of a person to perceive verticality or horizontality, respectively, which involves primarily vestibular and ocular motor system interaction, and a host of other interactions, such as (but not limited to) somatosensory, memory, cognition, and musculoskeletal interactions. In this study, these tests were only performed under static and not head tilt or dynamic rotational conditions. The test presents a line at a certain angle and the subject is asked to place the line either vertical or horizontal. The software measures the mean error (deg) as the difference between subject's orientation angle and true vertical or horizontal, respectively. The SVV test has been performed on both devices, the NOTC (N = 287 subjects) and the Dx 100 (N = 159 subjects). In the NOTC, the stimulus is projected on the wall of the dark enclosure and the subject is asked to press buttons located on the chair arm to adjust the line to their perceived vertical position. The subject's head is positioned between two adjustable arms ensuring the head is aligned to the vertical gravity axis.

In the Dx 100, the stimulus is projected inside the head mounted screen, and the subject is instructed to press the buttons located on a hand-held button box. The Dx 100's head mounted screen has a 6° of freedom (6 DOF) sensor which compares the subject's head position relative to the vertical gravity axis, providing extra information on how well the subject's head is aligned to the vertical gravity axis. Therefore, data from the Dx 100 have confirmatory information of vertical head position, while data from the NOTC rely on the tester

TABLE 3 Descriptive statistics and the effect of age group, gender, and interaction between the two on test metrics

		Descriptive statistics			ANOVA									
					(1)		(2)		(3)					
					Age group		Gender		Age group		Gender		Age × gender	
Test	Metrics	N	Mean	SD	F	*P*-value	F	*P*-value	F	*P*-value	F	*P*-value	F	*P*-value
OKN 20 deg/s	Average eye velocity CCW (deg/s)	286	−16.88	1.91	2.776	0.097	0.395	0.530	4.091	0.044	0.059	0.808	1.744	0.188
	Average eye velocity CW (deg/s)	286	17.66	1.34	1.077	0.300	0.774	0.380	0.908	0.341	0.065	0.799	0.340	0.560
	Gain	286	0.86	0.08	2.440	0.119	0.346	0.557	2.168	0.142	0.832	0.362	0.162	0.687
	Gain asymmetry (%)	286	2.27	4.60	0.114	0.735	0.941	0.333	0.127	0.721	0.337	0.562	3.227	0.074
	Area under velocity fit +(30 deg)	286	8172	1452	0.035	0.853	0.164	0.685	0.017	0.896	0.058	0.810	0.012	0.915
	Area under velocity fit -(30 deg)	286	−8525	1378	0.423	0.516	0.707	0.401	0.346	0.557	0.611	0.435	0.028	0.868
OKN 60 deg/s	Average eye velocity CCW (deg/s)	447	−38.27	8.71	14.709	0.000	0.118	0.731	11.961	0.001	0.004	0.949	0.382	0.537
	Average eye velocity CW (deg/s)	447	41.65	8.85	0.118	0.731	0.247	0.620	18.978	0.000	0.077	0.782	0.180	0.672
	Gain	447	0.68	0.13	24.273	0.000	0.279	0.598	22.025	0.000	0.064	0.801	0.005	0.942
	Gain asymmetry (%)	447	4.02	7.21	0.056	0.813	0.009	0.925	0.437	0.509	0.000	0.998	2.006	0.157
	Area under velocity fit +(30 deg)	447	8564	1461	0.442	0.506	0.680	0.410	0.092	0.762	0.490	0.484	0.834	0.362
	Area under velocity fit -(30 deg)	447	−8499	1315	4.073	0.044	2.211	0.138	3.831	0.051	2.781	0.096	0.071	0.790
SHA 0.02 Hz	Gain average	296	0.42	0.12	0.527	0.468	0.455	0.501	1.112	0.293	0.014	0.906	1.107	0.294
	Asymmetry (%)	296	4.24	10.89	1.861	0.174	0.024	0.878	1.644	0.201	0.030	0.862	0.001	0.978
	Phase (deg)	296	21.37	6.20	0.471	0.493	0.564	0.453	0.444	0.506	1.651	0.200	0.721	0.396
SHA 0.64 Hz	Gain average	295	0.58	0.14	0.119	0.730	0.011	0.915	0.556	0.456	0.487	0.486	1.670	0.197
	Asymmetry (%)	295	−2.57	7.81	0.218	0.641	0.164	0.685	0.658	0.418	0.135	0.713	1.294	0.256
	Phase (deg)	295	4.30	4.60	0.112	0.738	5.172	0.024	0.444	0.506	1.651	0.200	0.721	0.396
VE 0.64 Hz	Gain average	295	0.98	0.08	1.751	0.187	0.026	0.872	2.530	0.113	0.627	0.429	1.308	0.254
	Asymmetry (%)	295	0.34	1.51	1.198	0.275	1.478	0.225	1.535	0.216	1.990	0.159	0.617	0.433
	Phase (deg)	295	0.09	1.75	1.839	0.176	0.092	0.762	0.848	0.358	1.040	0.309	1.477	0.225
VS 0.64 Hz	Gain average	290	0.14	0.04	0.048	0.827	0.122	0.727	0.179	0.672	0.011	0.917	0.390	0.533
	Asymmetry (%)	290	1.29	11.40	2.649	0.105	0.407	0.524	0.003	0.959	3.586	0.059	1.050	0.306
	Phase (deg)	290	12.67	10.05	0.378	0.539	2.382	0.124	0.389	0.533	1.732	0.189	0.038	0.845
crHIT	Gain	299	0.96	0.03	0.702	0.403	3.399	0.066	0.843	0.359	2.096	0.149	0.524	0.470
	Asymmetry (%)	299	−0.17	2.12	0.003	0.953	0.405	0.525	0.333	0.565	2.170	0.142	2.431	0.120
SVV	Mean error (deg)	446	0.09	1.49	1.575	0.210	0.366	0.545	1.102	0.294	0.486	0.486	0.269	0.605
SVH	Mean error (deg)	291	−0.13	1.45	0.697	0.404	0.112	0.738	0.393	0.531	0.007	0.935	0.273	0.602

Note: Mean and standard deviation (SD) are presented for each test metric. Effects of age group (1), gender (2) on test metrics are calculated using one-way ANOVA. Effects of the interaction between the age group and gender (3) are calculated using two-way ANOVA. The *t*-test-based results examining the effect of age and gender are not reported in this paper. However, it should be noted that these results, as expected, are consistent with those of one-way ANOVA.

for ensuring head verticality. Because of these potential differences in the head position evaluation, differences between data (i.e., mean error in aligning the presented line to the vertical axis) collected on each device were compared. The univariate analysis of variance indicated that there is no statistically significant difference between the data collected with each device ($P = 0.161$). Therefore, data were pooled for constructing the normative ranges presented here. In the experiments using Dx100, the subject's head position was adjusted to less than ±2.5 deg.

2.5 | Statistical analysis

Descriptive statistics and results reported were based on raw measurements, using IBM SPSS Statistics for Windows, version 21. Raw measurements were visually and statistically inspected. Values that were potential outliers were individually inspected examining the original data from which the test value was obtained, formulas, and possible human error. Values deemed incorrect were not included in the final analysis. Values deemed correct but still yielding results outside of the expected values were included. To construct a normative database for the test metrics (e.g., computing the reference intervals), we first examined the homogeneity of the participants' test results. We examined whether the test results were affected by the age and/or gender of the participants. For this purpose, the data were grouped by (a) *age* into two populations: pediatric or late adolescent (18-21 years) and adult (22-45 years) and (b) *gender* (ascertained by self-report): female and male. Possible effects of age and gender were tested using the *t*-test (mean difference) for independent samples and by applying univariate one and two-way (with interaction) analysis of variance (ANOVA). The t-test and one-way ANOVA were used to examine each effect separately, whereas a two-way ANOVA was used to test jointly the potential effects of age and gender including their possible dependence measured by interaction (i.e., age group × gender). Levene's test for equal variance was used to decide whether to apply t-test assuming equal variances or not. To construct a normative database, for each test metric we calculated a 95% reference interval (RI) with 90% confidence interval (CI) on the lower and upper limits of the RI assuming a nonparametric distribution, according to the FDA suggested guidelines and other published references.[39,40] To calculate the RI, individual metrics (results) were organized by rank from the lowest to highest values: $y_1, y_2, \ldots, y_N$, where N is sample size. The $100(1-\alpha)\%$ RI is given by the upper and lower limits, R_L and R_U, calculated as follows: $R_L = y_{[N\times(\alpha_2)]}$ and $R_U = y_{[N\times(1-\alpha_2)]}$ with $\alpha = 0.05$. (Square brackets indicate that the number is rounded to the nearest integer.) Next, for each limit of the 95% RI, R_L, and R_U, the 90% CI, R_q and S_q [39,40] were calculated.

The percentiles, 2.5, 5, 10, 25, 75, 90, 95, and 97.5 for each test metric were calculated using a SPSS built in function.

2.5.1 | One sided metrics

The OKN test includes one metric (area under velocity fit, a measure of beat velocity) for which the lower or the upper limits are either

TABLE 4 Normative data for optokinetic (OKN) tests

Test	Metric	RI lower limit	RI upper limit	90% CI for lower limit RI	90% CI for upper limit RI
OKN 20 deg/s	Average eye velocity – for CCW stimuli (deg/s)	−20.05	−12.15	(−20.31) - (−19.84)	(−13.00) - (−11.37)
	Average eye velocity – for CW stimuli (deg/s)	14.56	19.75	13.74-14.66	19.58-20.84
	Gain	0.66	0.97	0.62-0.70	0.96-0.98
	Gain asymmetry (%)	−7.66	10.55	(−10.41) - (−5.42)	9.99-12.01
	Area under velocity fit +(30 deg)	5740	NA	5674-5886	NA
	Area under velocity fit (30 deg)	NA	−6175	NA	(−6359) - (−6060)
OKN 60 deg/s	Average eye velocity CCW (deg/s)	−52.94	−21.15	(−54.01) - (−52.21)	(−22.39) - (−19.69)
	Average eye velocity CW (deg/s)	24.15	55.93	21.22-25.06	54.90-56.71
	Gain	0.40	0.90	0.37-0.42	0.90-0.92
	Gain asymmetry (%)	−14.54	18.10	(−16.13) - (−12.39)	17.46-19.69
	Area under velocity fit +(30 deg)	6491	NA	6390-6642	NA
	Area under velocity fit (30 deg)	NA	−6420	NA	(−6479) - (−6312)
	Normalized OKN CW velocity gain (normalized at 20 deg/s)	0.47	0.98	0.37-0.48	0.95-1.01
	Normalized OKN CCW velocity gain (normalized at 20 deg/s)	0.45	0.95	0.40-0.48	0.92-1.03

Note: The upper and lower limits of the RI and 90% CI for each limit are presented. For one sided metrics, the limit of no interest is marked with not applicable (NA). For description of each metric see Table 2. The OKN 20 deg/s test was performed only in the NOTC device in 290 participants. The OKN 60 deg/s was performed in both devices, NOTC and Dx100, in a total of 449 participants.

TABLE 5 Normative data for rotational tests: sinusoidal harmonic acceleration (SHA), visual enhancement (VE), visual suppression (VS), and controlled rotational head impulse test (crHIT)

Test	Metric	RI lower limit	RI upper limit	90% CI for lower limit RI	90% CI for upper limit RI
SHA 0.02 Hz	Gain average	0.21	0.67	0.2-0.22	0.61-0.73
	Asymmetry (%)	−20	25	(−21) - (−17)	22-29
	Phase (deg)	10.28	34.84	8.6-12.16	31.62-39.26
SHA 0.64 Hz	Gain average	0.29	0.83	0.28-0.32	0.8-0.87
	Asymmetry (%)	−17	15	(−22) - (−15)	11-19
	Phase (deg)	−6.46	13.56	(−8.57) - (−4.15)	12.89-15.15
VE 0.64 Hz	Gain average	0.77	1.08	0.71-0.79	1.08-1.10
	Asymmetry (%)	−2.80	3.97	(−2.94) - (−2.00)	3.16-5.03
	Phase (deg)	−3.51	3.61	(−4.52) - (−2.94)	2.99-4.29
VS 0.64 Hz	Gain average	0.08	0.25	0.07-0.08	0.24-0.27
	Asymmetry (%)	−21.85	22.25	(−23.37) - (−18.11)	19.27-25.68
	Phase (deg)	−7.18	31.74	(−15.21) - (−5.4)	30.48-32.34
crHIT	Gain	0.89	1.03	0.87-0.9	1.02-1.04
	Asymmetry (%)	−4.42	4.35	(−5.07) - (−3.94)	3.91-4.91

Note: The upper and lower limits of the 95% RI and 90% CI for each limit are presented. For one-sided metrics, the limit of no interest is marked with not applicable (NA). For description of each metric see Table 2. These tests have been performed only using the NOTC device, in a total of 290–299 subjects.

TABLE 6 Normative data for subjective visual vertical (SVV) and horizontal (SVH)

Test	Metric	RI lower limit	RI upper limit	90% CI for lower limit RI	90% CI for upper limit RI
SVV	Mean error (deg)	−2.84	3.08	(−3.00) - (−2.64)	2.81-3.35
SVH	Mean error (deg)	−3.00	2.90	(−3.27) - (−2.74)	2.33-3.14

Note: The upper and lower limits of the 95% RI and 90% CI for each limit are presented. For one-sided metrics, the limit of no interest is marked with not applicable (NA). For description of each metric see Table 2. SVV test has been performed in a total of 446 participants, on both devices, the NOTC (N = 287) and the Dx100 (N = 159). SVH test has been performed in the NOTC device only in a total of 291 participants.

meaningless or are not of clinical interest for the general population. For example, the upper limit of beat velocity is not of clinical concern, whereas the lower limit, indicative of a slow beat, may represent a clinical concern. For these metrics, the 5th or 95th percentile was calculated for the limit of interest; the limit of no interest was marked as not applicable (NA).[39,40]

3 | RESULTS

The database presented here includes seven ocular motor and vestibular tests commonly used in conjunction with eye tracking to assess peripheral and central vestibular system function: OKN response, SVV and SVH, SHA, VE, VS, and crHIT (Table 2). These tests are commonly used to evaluate ocular motor and vestibular deficits following mTBI and/or other neurological conditions.[24,27,41-45] Metrics describing different components of eye movement (e.g., gain, phase) for each test were computed (detailed description of each metric is included in Table 2).

3.1 | Age and gender effect

The US FDA considers the pediatric population as being 0 to 21 years of age, and the *Journal of Academy of Pediatrics* terms them as "Late Adolescents".[46] Here, the pediatric or late adolescent participants (ages 18-21 years) and adult participants (ages 22-45 years) were analyzed to determine whether late adolescent vs adult age status had any effect on test results (Table 3). Gender (self-reported) was also examined (Table 3). The findings indicated that age and gender had a statistically significant effect (0.05 level) on only five of the 28 test metrics, and that even for those five metrics, statistical effects did not indicate clinical significance. This is based on the fact that the 95% RIs (with 90% CI) showed great overlap. For example, in the OKN 60 deg/s test, for the metric "Average eye velocity" for clockwise (CW) stimulus, the 95% RIs were (deg/s): [25.64-56.71], [24.12-54.26], and [24.15-55.93] for the 18-21, 21-45, and 18-45-year-old groups, respectively. These small differences with significant overlap of the RI (as well as 90% CI for each upper and lower limit) suggest no clinical significance.

3.2 | Normative database

Following the age and gender analyses, data from all subjects were pooled for the purpose of constructing a normative database. The 95% RI with a 90% CI on the lower and upper limits of the RI are reported in Tables 4, 5, 6 for all tests and metrics. The 2.5, 5, 10, 25, 75, 90, 95, and 97.5 percentile for each metric within each test are presented in Supplemental Tables 1-3, included in the Supplemental data.

4 | DISCUSSION

Vestibular testing in conjunction with eye-tracking represents a non-invasive method of assessing the peripheral and central deficits in the vestibular and ocular motor systems in many neurological conditions, including brain injury. Work from our group and findings from other studies have shown the utility of ocular motor and vestibular testing in the detection, diagnosis, and monitoring of mTBI,[24,27,28,44,47,48] vestibular, neurotological, and neurological conditions.[12,21-23,35]

Appropriate tools for diagnosis and monitoring of the mTBI/concussion have gained significant interest in recent years. Impairments in the optokinetic response have been reported in acute and chronic mTBI patients.[28,49] In conjunction with metrics from ocular motor and cognitive tests (e.g., smooth pursuit, antisaccades, predictive saccades), metrics from the crHIT test (gain, gain asymmetry) and the optokinetic response test have been shown as reliable indicators of acute mTBI.[24] These same metrics have been found useful in monitoring the progress of patients following mTBI.[27] Tests including SHA, VE, VS, SVV, and SVH, have been used to screen for acute concussion in athletes[26] and military service members.[49] Metrics such as VOR suppression gain and variance of SVV and SVH errors were found to differ between healthy and concussed subjects [26]; deficits in many of these test metrics (e.g., SHA, SVV, and visual fixation) were found in a large percentage of service members.[49]

Vestibular testing using a rotary chair and static tests like SVV and SVH have long been used in clinical practice for patients who present with dizziness and balance complaints due to conditions including MD, chronic otitis, vascular disorders, BPPV, vestibular neuritis, migraines, acute labyrinthitis, cochlear hydrops, sudden deafness, otosclerosis, perilymphatic fistula, and other vestibular lesions.[12-23,50-56] SHA is considered one of the cornerstone tests in the evaluation and understanding of the peripheral and central aspects of the vestibular system. A large study (6000 patients) showed that the temporal pattern of asymmetry can reliably differentiate peripheral from central vestibular dysfunction and by combining phase and symmetry metrics, the side of the lesion can also be reliably determined.[19] Similarly, asymmetry was frequently seen in patients suffering from migraines[50] and unilateral vestibular loss.[51] Patients with unilateral vestibular loss demonstrated low gains at frequencies below 0.02 Hz and large phase shifts at frequencies below 0.32 Hz.[51] Another study found that a selection of the 0.01, 0.05, and 0.1 Hz SHA rotations creates an ideal rotatory test protocol that when combined with caloric and VEMP testing provides comprehensive evaluation of patients diagnosed with unilateral peripheral vestibular pathology, including Meniere's disease, vestibular neuritis, labyrinthitis, acoustic neuroma, superior canal dehiscence, and post traumatic vertigo.[52]

OKN has also been employed in the evaluation of patients with various conditions. For example, several studies have shown impairment of the OKN response in patients with cerebral palsy and Parkinson's disease (slow-phase optokinetic nystagmus).[53,54] OKN was employed in the evaluation of patients with ocular diseases, such as generalized retinal diseases, media opacity, refractive errors, glaucoma, maculopathies, and optic neuropathies.[55] OKN gain and asymmetry are associated with the development of binocular vision and have been helpful to identify patients with binocularity or binocular potential in strabismus.[56]

Collectively, these studies, as well as many other publications, indicate the utility of ocular motor and vestibular testing not only in mTBI/concussion but also in many other vestibular disorders. By providing an FDA-cleared normative ocular motor and vestibular database, our study enables wide adoption of these tests in clinical practice.

Data from healthy subjects have been previously published for various vestibular tests. For example, SHA test metrics (gain, phase, and asymmetry) were reported in healthy volunteers 6-81 years of age,[13,30-32,57] OKN gain data in subjects 1-89 years of age,[33] and SVV data in subjects 4-89 years of age.[14] A number of studies report normative values for SHA metrics including gain, phase, and asymmetry, with the majority of data presented as mean and SD. For example, Peterka et al.[57] report VOR gain, phase, and asymmetry at 0.05, 0.2, and 0.8 Hz (216 subjects ages 7-81), Maes et al.[31] report gain, phase, and asymmetry at 0.01-0.16 Hz (150 subjects ages 18-40), Chan et al.[30] present VOR gain at 0.01-0.64 Hz (100 subjects ages 6-78, reported by age groups 6-12, 13-17, 18-30, 31-50, and >50.[30] Other papers report data from smaller cohorts, including Wall[58] (50 subjects ages 20-59; 0.005-1.0 Hz), Moller[59] (50 subjects ages 17-39; 0.01-0.32 Hz), Li[13] (41 subjects ages 21-67, 0.01-0.64 Hz). Collectively, these studies reflect the importance of this test and need for normative data. The results presented here add to previous studies, providing normative data from a larger group of subjects presented in the format that is typical for clinical laboratory tests, that is, reference ranges.

Although the age ranges, age groupings, metrics, and values reported (mean ± SD vs RI ± 90% CI) vary between studies and cannot be directly compared to our data, the relationship between test metrics and age and gender can be examined. The normative data presented here indicated no clinically significant differences for age or gender between the ages of 18 and 45. These results are in line with previous publications, which have reported stable OKN gain in subjects 10-45 years old,[33] no influence of age on SVV in subjects ages 20-49,[14] and no effect of age on SHA metrics in subjects younger than 50 years old.[16,32] In another study, participants over the age of 40 showed some differences for phase and gain.[13] Comparisons of five age groups (6-12, 13-17, 18-30, 31-50, and > 50 years, 20 subjects per group) indicated that VOR gain was

mostly influenced by age in the preadolescent and geriatric groups.[30] Gender did not have an effect on SHA metrics,[13,31,57] or on SVV.[14] Together, these data are consistent with our findings of stable metrics for the 18-45-year-old group. Future studies are required for the pediatric population younger than 18 years of age, as well as for populations older than 45. Additionally, a present limitation of the current database is that some tests, such as OKN or SHA, have a limited number of outcome metrics. Future studies will need to focus on adding more granularity to these tests.

ACKNOWLEDGMENTS

The authors thank J. Howison Schroeder for his editorial and conceptual contributions to the grants that funded this research, discussions of the study results, as well as ensuring device availability and maintenance throughout the study.

CONFLICT OF INTEREST

Aura Kullmann, Robin C. Ashmore, Christian Mazur, and Alexander Kiderman are/have been employees of Neurolign (formerly known as Neuro Kinetics Inc). The remainder of the authors do not have any conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Aura Kullmann, Alexander Kiderman, Michael Hoffer. Data Curation: Robin Ashmore, Aura Kullmann, Alexander Kiderman, Michael Hoffer. Formal Analysis: Aura Kullmann, Alexander Kiderman, Robin C. Ashmore, Christian Mazur, Alexandr Braverman. Funding Acquisition: Alexander Kiderman, Michael Hoffer, Aura Kullmann, Carey Balaban. Investigation: Hillary Snapp, Mikhaylo Szczupak, Erin Williams, Sara Murphy, Kate Marshall, James Crawford, Michael Hoffer. Methodology: Alexander Kiderman, Robin C. Ashmore, Alexandr Braverman, Michael Hoffer, Carey Balaban. Project Administration: Alexander Kiderman, Michael Hoffer, Robin C. Ashmore. Resources: Alexander Kiderman, Michael Hoffer. Software: Alexander Kiderman, Robin C. Ashmore. Supervision: Alexander Kiderman, Michael Hoffer. Validation: Aura Kullmann, Alexander Kiderman, Michael Hoffer. Visualization: Aura Kullmann, Alexander Kiderman, Michael Hoffer. Writing – Original Draft Preparation: Aura Kullmann, Alexander Kiderman, Michael Hoffer. Writing – Review & Editing: Aura Kullmann, Alexander Kiderman, Michael Hoffer, Hillary Snapp, Sara Murphy, Kate Marshall, James Crawford, Carey Balaban, Christian Mazur, Alexandr Braverman, Mikhaylo Szczupak, Erin Williams.

ETHICS STATEMENT

The study protocol was approved by the Naval Medical Center San Diego (NMCSD) Institutional Review Board (IRB), the University of Miami IRB, and Madigan Army Medical Center (MAMC) IRB in compliance with all applicable federal regulations governing the protection of human participants. Research data were derived from approved NMCSD IRB protocol number NMCSD.2013.0060, University of Miami IRB#2015036, and MAMC IRB protocol number 393240-1. The investigators have adhered to the policies for protection of human participants as prescribed in 45 CFR 46.

ORCID

Aura Kullmann https://orcid.org/0000-0001-6625-2946
Hillary Snapp https://orcid.org/0000-0002-2000-5357
James Crawford https://orcid.org/0000-0001-7599-647X
Carey D. Balaban https://orcid.org/0000-0002-3570-3844
Michael Hoffer https://orcid.org/0000-0002-5574-4387

BIBLIOGRAPHY

1. Agrawal Y, Ward BK, Minor LB. Vestibular dysfunction: prevalence, impact and need for targeted treatment. *J Vestib Res*. 2013;23(3):113-117. https://doi.org/10.3233/VES-130498
2. Gioacchini FM, Alicandri-Ciufelli M, Kaleci S, Magliulo G, Re M. Prevalence and diagnosis of vestibular disorders in children: a review. *Int J Pediatr Otorhinolaryngol*. 2014;78(5):718-724. https://doi.org/10.1016/j.ijporl.2014.02.009
3. Hoffer ME, Szczupak M, Kiderman A, et al. Neurosensory symptom complexes after acute mild traumatic brain injury. *PLoS One*. 2016;11(1):e0146039. https://doi.org/10.1371/journal.pone.0146039
4. Crampton A, Teel E, Chevignard M, Gagnon I. Vestibular-ocular reflex dysfunction following mild traumatic brain injury: a narrative review. *Neurochirurgie*. 2021;67(3):231-237. https://doi.org/10.1016/j.neuchi.2021.01.002
5. Wallace B, Lifshitz J. Traumatic brain injury and vestibulo-ocular function: current challenges and future prospects. *Eye Brain*. 2016;8:153-164. https://doi.org/10.2147/EB.S82670
6. Hoffer ME, Balaban C, Gottshall K, Balough BJ, Maddox MR, Penta JR. Blast exposure: vestibular consequences and associated characteristics. *Otol Neurotol*. 2010;31(2):232-236. https://doi.org/10.1097/MAO.0b013e3181c993c3
7. Fife TD, Kalra D. Persistent vertigo and dizziness after mild traumatic brain injury. *Ann N Y Acad Sci*. 2015;1343:97-105. https://doi.org/10.1111/nyas.12678
8. Akin FW, Murnane OD, Hall CD, Riska KM. Vestibular consequences of mild traumatic brain injury and blast exposure: a review. *Brain Inj*. 2017;31(9):1188-1194. https://doi.org/10.1080/02699052.2017.1288928
9. Chandrasekhar SS. The assessment of balance and dizziness in the TBI patient. *NeuroRehabilitation*. 2013;32(3):445-454. https://doi.org/10.3233/NRE-130867
10. Sharp DJ, Jenkins PO. Concussion is confusing us all. *Pract Neurol*. 2015;15(3):172-186. https://doi.org/10.1136/practneurol-2015-001087
11. Zalewski CK. *Rotational Vestibular Assessment*. San Diego, CA: Plural Publishing; 2018.
12. Furman JM, Shirey I, Roxberg J, Kiderman A. The horizontal computerized rotational impulse test. *J Vestib Res*. 2016;26(5–6):447-457. https://doi.org/10.3233/VES-160595
13. Li CW, Hooper RE, Cousins VC. Sinusoidal harmonic acceleration testing in normal humans. *Laryngoscope*. 1991;101(2):192-196. https://doi.org/10.1288/00005537-199102000-00016
14. Toupet M, Van Nechel C, Grayeli AB. Subjective visual vertical tilt attraction to the side of rod presentation: effects of age, sex, and vestibular disorders. *Otol Neurotol*. 2015;36(6):1074-1080. https://doi.org/10.1097/MAO.0000000000000771
15. Gordon CR, Kuritzky A, Doweck I, Spitzer O, Shupak A, Hering R. Vestibulo-ocular reflex in migraine patients: the effect of sodium valproate. *Headache*. 1993;33(3):129-132. https://doi.org/10.1111/j.1526-4610.1993.hed3303129.x
16. Lee MY, Kim MS, Park BR. Adaptation of the horizontal vestibuloocular reflex in pilots. *Laryngoscope*. 2004;114(5):897-902. https://doi.org/10.1097/00005537-200405000-00021
17. Olson JE, Wolfe JW, Engelken EJ. Symposium on low frequency harmonic acceleration, the rotatory chair. Responses to low-frequency harmonic acceleration in patients with acoustic neuromas. *Laryngoscope*. 1981;91(8):1270-1277. https://doi.org/10.1288/00005537-198108000-00008

18. Probst R, Aoyagi M, Pfaltz CR. Diagnosis of peripheral and central vestibular lesions by the harmonic acceleration test. *Adv Otorhinolaryngol*. 1983;30:159-164. https://doi.org/10.1159/000407630
19. Hamid MA. Clinical value of sinusoidal harmonic acceleration test results. Site of lesion and side of lesion. *Neurol Clin*. 1990;8(2):287-295.
20. Suzuki M, Pulec JL, Smith JC. The sinusoidal harmonic acceleration test in vestibular disorders. Comparative study with caloric test results. *Acta Otolaryngol Suppl*. 1989;468:317-322. https://doi.org/10.3109/00016488909139068
21. Zalewski CK, Chien WW, King KA, et al. Vestibular dysfunction in patients with enlarged vestibular aqueduct. *Otolaryngol Head Neck Surg*. 2015;153(2):257-262. https://doi.org/10.1177/0194599815585098
22. Chien WW, Leiding JW, Hsu AP, et al. Auditory and vestibular phenotypes associated with GATA3 mutation. *Otol Neurotol*. 2014;35(4):577-581. https://doi.org/10.1097/MAO.0000000000000238
23. Cohen HS, Mulavara AP, Sangi-Haghpeykar H, Peters BT, Bloomberg JJ, Pavlik VN. Screening people in the waiting room for vestibular impairments. *South Med J*. 2014;107(9):549-553. https://doi.org/10.14423/SMJ.0000000000000017
24. Balaban C, Hoffer ME, Szczupak M, et al. Oculomotor, vestibular, and reaction time tests in mild traumatic brain injury. *PLoS One*. 2016;11(9):e0162168. https://doi.org/10.1371/journal.pone.0162168
25. Casto KL. Auditory, vestibular and cognitive effects due to repeated blast exposure on the warfighter; 2012.
26. Christy JB, Cochrane GD, Almutairi A, Busettini C, Swanson MW, Weise KK. Peripheral vestibular and balance function in athletes with and without concussion. *J Neurol Phys Ther*. 2019;43(3):153-159. https://doi.org/10.1097/npt.0000000000000280
27. Hoffer ME, Balaban C, Szczupak M, et al. The use of oculomotor, vestibular, and reaction time tests to assess mild traumatic brain injury (mTBI) over time. *Laryngoscope Investig Otolaryngol*. 2017;2(4):157-165. https://doi.org/10.1002/lio2.74
28. Kelly KM, Kiderman A, Akhavan S, et al. Oculomotor, vestibular, and reaction time effects of sports-related concussion: video-Oculography in assessing sports-related concussion. *J Head Trauma Rehabil*. 2019;34:176-188. https://doi.org/10.1097/HTR.0000000000000437
29. Cochrane GD, Christy JB, Almutairi A, et al. Vestibular, oculomotor, and balance functions in children with and without concussion. *J Head Trauma Rehabil*. 2021;36(4):264-273. https://doi.org/10.1097/HTR.0000000000000651
30. Chan FM, Galatioto J, Amato M, Kim AH. Normative data for rotational chair stratified by age. *Laryngoscope*. 2016;126(2):460-463. https://doi.org/10.1002/lary.25497
31. Maes L, Dhooge I, de Vel E, et al. Normative data and test-retest reliability of the sinusoidal harmonic acceleration test, pseudorandom rotation test and velocity step test. *J Vestib Res*. 2008;18(4):197-208.
32. Maes L, Dhooge I, D'haenens W, et al. The effect of age on the sinusoidal harmonic acceleration test, pseudorandom rotation test, velocity step test, caloric test, and vestibular-evoked myogenic potential test. *Ear Hear*. 2010;31(1):84-94. https://doi.org/10.1097/AUD.0b013e3181b9640e
33. Valmaggia C, Rütsche A, Baumann A, et al. Age related change of optokinetic nystagmus in healthy subjects: a study from infancy to senescence. *Br J Ophthalmol*. 2004;88(12):1577-1581. https://doi.org/10.1136/bjo.2004.044222
34. Kendall PC, Sheldrick RC. Normative data for normative comparisons. *J Consult Clin Psychol*. 2000;68(5):767-773.
35. Hoffer ME, Levin BE, Snapp H, Buskirk J, Balaban C. Acute findings in an acquired neurosensory dysfunction. *Laryngoscope Investig Otolaryngol*. 2019;4(1):124-131. https://doi.org/10.1002/lio2.231
36. Leigh RJ, Zee DS. *The Neurology of Eye Movement*. New York, NY: Oxford University Press; 2006.
37. Baloh RW, Sills AW, Kumley WE, Honrubia V. Quantitative measurement of saccade amplitude, duration, and velocity. *Neurology*. 1975;25(11):1065-1070. https://doi.org/10.1212/wnl.25.11.1065
38. Bahill AT, Clark M, Stark L. The main sequence, a tool for studying human eye movements. *Math Biosci*. 1975;24(3–4):191-204.
39. Horn PS, Pesce AJ. *Reference Intervals: A User's Guide*. Washington, DC: AACC Press; 2005.
40. Horowitz GL. Defining, establishing, and verifying reference intervals in the clinical laboratory, approved guideline; 2010.
41. Bin Zahid A, Hubbard ME, Lockyer J, et al. Eye tracking as a biomarker for concussion in children. *Clin J Sport Med*. 2018;30(5):433-443. https://doi.org/10.1097/JSM.0000000000000639
42. Ciuffreda KJ, Kapoor N, Rutner D, Suchoff IB, Han ME, Craig S. Occurrence of oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry*. 2007;78(4):155-161. https://doi.org/10.1016/j.optm.2006.11.011
43. Cochrane GD, Christy JB, Almutairi A, Busettini C, Swanson MW, Weise KK. Visuo-oculomotor function and reaction times in athletes with and without concussion. *Optom Vis Sci*. 2019;96(4):256-265. https://doi.org/10.1097/opx.0000000000001364
44. Danna-Dos-Santos A, Mohapatra S, Santos M, Degani AM. Long-term effects of mild traumatic brain injuries to oculomotor tracking performances and reaction times to simple environmental stimuli. *Sci Rep*. 2018;8(1):4583. https://doi.org/10.1038/s41598-018-22825-5
45. Heitger MH, Anderson TJ, Jones RD, Dalrymple-Alford JC, Frampton CM, Ardagh MW. Eye movement and visuomotor arm movement deficits following mild closed head injury. *Brain*. 2004;127(3):575-590. https://doi.org/10.1093/brain/awh066
46. Hardin AP, Hackell JM, Committee On P, Ambulatory M. Age limit of pediatrics. *Pediatrics*. 2017;140(3):e20172151. https://doi.org/10.1542/peds.2017-2151
47. Maruta J, Ghajar J. Detecting eye movement abnormalities from concussion. *Prog Neurol Surg*. 2014;28:226-233. https://doi.org/10.1159/000358786
48. Warden DL, Bleiberg J, Cameron KL, et al. Persistent prolongation of simple reaction time in sports concussion. *Neurology*. 2001;57(3):524-526.
49. King JE, Pape MM, Kodosky PN. Vestibular test patterns in the NICoE intensive outpatient program patient population. *Mil Med*. 2018;183(suppl_1):237–244. doi:https://doi.org/10.1093/milmed/usx170
50. Olsson JE. Neurotologic findings in basilar migraine. *Laryngoscope*. 1991;101(1 Pt 2 Suppl 52):1-41. https://doi.org/10.1002/lary.1991.101.s52.1
51. Engelken EJ, Stevens KW, Bell AF, Enderle JD. Linear systems analysis of the vestibulo-ocular reflex: clinical applications. *Biomed Sci Instrum*. 1993;29:319-326.
52. Maes L, Vinck BM, Wuyts F, et al. Clinical usefulness of the rotatory, caloric, and vestibular evoked myogenic potential test in unilateral peripheral vestibular pathologies. *Int J Audiol*. 2011;50(8):566-576. https://doi.org/10.3109/14992027.2011.576706
53. Fujiwara M, Ding C, Kaunitz L, Stout JC, Thyagarajan D, Tsuchiya N. Optokinetic nystagmus reflects perceptual directions in the onset binocular rivalry in Parkinson's disease. *PLoS One*. 2017;12(3):e0173707. https://doi.org/10.1371/journal.pone.0173707
54. Garbutt S, Riley DE, Kumar AN, Han Y, Harwood MR, Leigh RJ. Abnormalities of optokinetic nystagmus in progressive supranuclear palsy. *J Neurol Neurosurg Psychiatry*. 2004;75(10):1386-1394. https://doi.org/10.1136/jnnp.2003.027367
55. Shin YJ, Park KH, Hwang JM, Wee WR, Lee JH, Lee IB. Objective measurement of visual acuity by optokinetic response determination in patients with ocular diseases. *Am J Ophthalmol*. 2006;141(2):327-332. https://doi.org/10.1016/j.ajo.2005.09.025
56. Valmaggia C, Proudlock F, Gottlob I. Optokinetic nystagmus in strabismus: are asymmetries related to binocularity? *Invest Ophthalmol*

Vis Sci. 2003;44(12):5142-5150. https://doi.org/10.1167/iovs.03-0322
57. Peterka RJ, Black FO, Schoenhoff MB. Age-related changes in human vestibulo-ocular reflexes: sinusoidal rotation and caloric tests. *J Vestib Res*. 1990;1(1):49-59.
58. Wall C 3rd, Black FO, Hunt AE. Effects of age, sex and stimulus parameters upon vestibulo-ocular responses to sinusoidal rotation. *Acta Otolaryngol*. 1984;98(3–4):270-278. https://doi.org/10.3109/00016488409107563
59. Moller C, Odkvist L, White V, Cyr D. The plasticity of compensatory eye movements in rotatory tests. I. the effect of alertness and eye closure. *Acta Otolaryngol*. 1990;109(1–2):15-24. https://doi.org/10.3109/00016489009107410

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Kullmann A, Ashmore RC, Braverman A, et al. Normative data for ages 18-45 for ocular motor and vestibular testing using eye tracking. *Laryngoscope Investigative Otolaryngology*. 2021;6(5):1116-1127. https://doi.org/10.1002/lio2.632