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Original Article

Clinical Assessment of the Nystagmus Fixation Suppression Test: An Experimental Study

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BACKGROUND: Assessment of nystagmus fixation suppression can be used as an additional diagnostic tool for patients with an acute vestibular syndrome to distinguish between a central or peripheral cause. We investigated the ability of physicians to detect fixation suppression using a nystagmus simulation model.

METHODS: We used a nystagmus simulator to measure the accuracy of the nystagmus fixation suppression test. Fixation suppression was assessed randomly in 6170 trials by 20 otorhinolaryngologists and neurologists, segregated into 2 groups based on their neurootological experience, a beginner and an experienced group. The simulator presented random nystagmus slow velocity (SPV) reductions and presented 3 conditions with either changed nystagmus frequency, amplitude, or both.

RESULTS: The cutoff for the discernment of fixation suppression ranged from 1.2 to 14°/s nystagmus velocity difference. The more intense the baseline nystagmus was, the more difficult was the detection of fixation suppression. There was not significant difference ($P > .05$) in the cutoff values in the experts group compared to the novices for all 3 different conditions. Both, novices and experts, detected frequency changes easier than differences of the nystagmus amplitude. Test sensitivity was very low (19%-65%) for discernment of small nystagmus velocity differences of ≤2°/s by experts.

CONCLUSION: In our study, there was no difference between experts and novices in detection of nystagmus suppression by visual fixation. The examiners could only detect large suppression effects at low-intensity baseline nystagmus. Overall, the sensitivity and accuracy of a clinical fixation suppression test is low and the assistance with a video-oculography device is highly recommended.

KEYWORDS: Nystagmus suppression test, Frenzel glasses, Nystagmus

INTRODUCTION

The distinction between a central cause and acute unilateral vestibulopathy (AUVP) in patients presenting with an acute vestibular syndrome (AVS) remains a challenge despite major diagnostic advances and the development of standardized new guidelines in recent years. With the introduction of a 3-step bedside oculomotor examination "HINTS" (head impulse, nystagmus, test of skew) in 2009, the diagnostic accuracy to detect vestibular strokes in AVS patients has improved.[1] However, this HINTS examination does not have a 100% sensitivity to detect strokes, especially in paucisymptomatic patients with a falsely abnormal head impulse test. Additional clinical signs complementary to the "HINTS" examination at the bedside have already been discussed in previous publications.[2,3] In particular, the nystagmus suppression test[4] can increase the diagnostic accuracy, especially considering the limited significance of MRI or CT diagnostics within the first 24 hours after symptom onset.[5]

The influence of visual fixation on nystagmus has been widely studied,[6-10] and previous studies have repeatedly shown that visual fixation suppression of nystagmus may be impaired in central pathologies, especially in posterior fossa pathologies.[11-14] However, the sensitivity of the clinical assessment of fixation suppression is low, according to previously conducted studies.[15]

A recently published study suggested the use of video-oculography (VOG) to improve test accuracy and to distinguish between AUVP or vestibular stroke.[4] A nystagmus velocity reduction of less than 2°/s was considered as nystagmus fixation suppression

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failure.[4] Such small differences might be detectable by video goggles, but it remains questionable whether the human eye might be able to discern this.

Therefore, we sought to assess the ability of physicians to discern changes in nystagmus intensity and to assess whether there was any visible suppression effect using a nystagmus simulator and virtual Frenzel glasses.

MATERIAL AND METHODS

Nystagmus Simulator

To represent spontaneous nystagmus and for the assessment of fixation suppression, we developed a simplified 3D model of a human head including animated virtual eyes using "unity" software (Unity Technologies, San Francisco**,** USA) (Figure 1 and see Appendix, Video 1).[16] This simulator generated a virtual nystagmus with different degrees of nystagmus intensity in terms of velocity, which is the product of frequency and amplitude. The amplitude is therefore inversely proportional to the frequency. This means that the amplitude decreases when the frequency increases while the overall slow phase velocity remains stable.

There is high variability in nystagmus frequency and amplitude for a given nystagmus velocity within the subject's reason why we chose 3 different test conditions: (1) Frequency modulated velocity with constant nystagmus amplitude (4°, "'FRQ"' condition), (2) Amplitude modulated velocity at a constant nystagmus frequency (3°/s, "AMP" condition), and (3) a combined modulation of amplitude and frequency for a given velocity ("FRQ-AMP" condition). Our chosen nystagmus parameters were based on previously collected data from patients with an acute vestibular syndrome (AVS).[17,18] Nystagmus velocities in AVS patients ranged between 1 and 25°/s SPV reason why we chose 6 different baseline velocities for the simulated spontaneous nystagmus (1, 5, 10, 15, 20, or 25°/s).

The 6 possible test sequences were tested alternately to avoid order effect bias, due to the training or the decreasing concentration of the participants.

Nystagmus was presented on a laptop screen (HP Envy 360, 15", AMD Ryzen). We first presented nystagmus without fixation (Frenzel glasses on) for a duration of 2 seconds, followed by nystagmus with visual fixation (Frenzel glasses off). The participants had to rate whether nystagmus velocity remained unchanged (no nystagmus fixation suppression) or whether nystagmus was reduced after the removal of the Frenzel glasses (positive nystagmus fixation suppression). We used the right and left mouse keys for recording the participant's responses (binary variable). The assessment adopted a standard forced-choice procedure to decide whether there was nystagmus fixation suppression or not. The results could only be reviewed at the end of each cycle. It was not possible to repeat single simulations or correct an answer. Mistyped answers were corrected posthoc. The whole evaluation process for every participant took about 40 minutes. Each participant assessed 100 simulations of nystagmus per condition, that is, assessed fixation suppression in a total of 300 simulations. All test parameters, conditions, and the participant's decision (suppression yes/no) were recorded in a .csv file.

Participants and Statistical Analysis

Twenty physicians participated in this study, of which 10 were experienced (ENT experts with an ENT board license) and 10 were novices (ENT or Neurology novices in a tertiary referral center). The local ethics committee (KEK) decided that the study did not require approval because the project did not fall under the Human Research Act (IRB Decision No: BASEC Req-2020-01176). Informed consent was obtained from all participants.

We calculated ROC curves stratified by baseline SPV, condition, and experience (novices and experts). We compared ROC curves between experts and novices using the method of DeLong et al (1988). The cutoff points for the minimum perceived differences of SPV (Delta

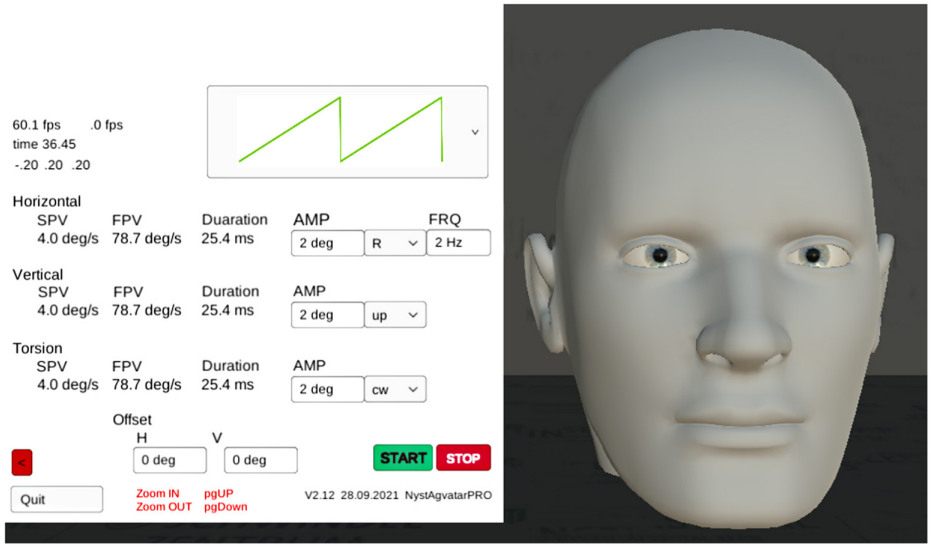

Figure 1. In the program, users can define horizontal, vertical, and torsional movements of nystagmus. The slow phase velocity is calculated by the entered parameters amplitude and frequency. Our test program, on the other hand, calculates the amplitude, frequency, or both depending on the mode, with a defined SPV as baseline and the reduction in SPV for the second nystagmus is randomized.

SPVmin) that could be discriminated by the participants were chosen based on Jouden's J. We performed a UNIVARIATE ANOVA to compare the calculated cutoffs between novices and experts. All analyses were performed in Statistical Package for the Social Sciences (SPSS, for Windows, version 25.0, IBM SPSS Corp.; Armonk, NY, USA) and $P < .05$ was considered significant.

RESULTS

We assessed fixation suppression using 6170 nystagmus simulations resulting in 10-28 simulations per participant, condition, and nystagmus baseline intensity. Of these 6170 simulations, there was no fixation suppression in 93 of them. Simulations with a low-intensity baseline nystagmus (1°/s) were not significant across conditions.

The cutoff for the discernment of fixation suppression increased proportionally with the baseline spontaneous nystagmus. The more intense the baseline nystagmus was, the more difficult the detection of fixation suppression was. There was no significant difference ($P > .05$) in the cutoff values in the experts group compared to the novices for all 3 different conditions. Both novices and experts detected frequency changes easier than differences in the nystagmus amplitude. For low-intensity nystagmus (1-10°/s), cutoffs were similar for both groups in all 3 different conditions (Figure 2).

Accuracy of the Clinical Nystagmus Suppression Test

There was no significant difference between experts and novices in the accuracy of the nystagmus suppression test (Table 1). The greatest difference in specificity comparing experts and novices was detected at a baseline nystagmus of 15°/s with frequency modulation. Experts were 20% better than the novices. Only at this condition and velocity do we see a significant difference in accuracy between experts and novices.

Both groups showed an increase in sensitivity and specificity with the increase in baseline SPV until 10°/s and then remained relatively stable regardless any further increase. The greatest difference in sensitivity between the 2 groups was at baseline SPV of 5°/s in the frequency modulated condition (experts performed 13% better than the novices).

Fixation Suppression and Stroke Prediction

Regarding stroke prediction, meaningful differences equal to or smaller than 2°/s have been reported,[4] which were only discernible with low intensity nystagmus at ≤5°/s. Test sensitivity was very low for discernment of small nystagmus velocity differences of ≤2°/s (10%-91.9% across conditions and for both experts and novices). Again, frequency modulated nystagmus was better detected (28.3%-91.9%) compared to amplitude modulated nystagmus (10%-55.8%) and combined frequency/amplitude (18.8%-64.8%). We found high sensitivity only for simulations at low intensity nystagmus (5°/s SPV) and frequency modulation of nystagmus in both groups of physicians (Table 2).

DISCUSSION

In this study, we investigated the ability of experts and novices to discern a decrease in nystagmus intensity through visual fixation. Our results support that experts are not superior in the assessment of the nystagmus suppression test compared to novices. Moreover, the discrimination of small velocity differences of 2°/s nystagmus, which would be necessary to diagnose a vestibular stroke using the spontaneous nystagmus suppression test,[4] could only be detected at low baseline nystagmus; however, sensitivity was low.

Background and Comparison with Other Studies

A recent study[19] looked at the ability of physicians to detect nystagmus differences during the supine roll test in patients with horizontal semicircular canal positional vertigo (HC-BPPV) in order to determine the affected side. Therefore, like our study, participants had to detect differences in nystagmus velocity.

In their study, 44 video recordings were made and assessed by 14 medical students, and 11 medical personnel trained in neurology or neuro-otology. The accuracy of bedside lateralization of HC-BPPV was 83.5% after the first presentation, and 86.0% after the second presentation, and there was no difference between the medical students and trained personnel after the second presentation. Our study also showed no differences across all conditions between experts and novices. It seems that evaluation of nystagmus suppression cannot be influenced by experience and it may have to do with

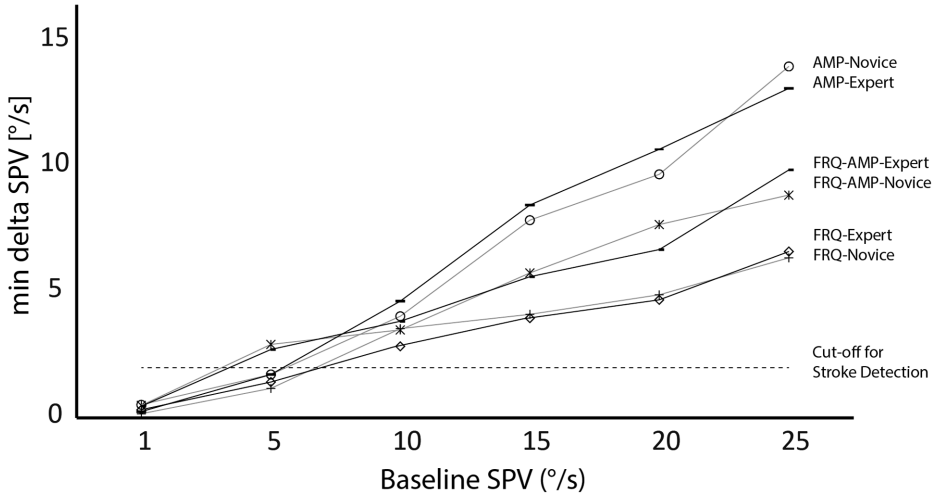

Figure 2. The cutoff for the discernment of fixation suppression increased proportionally with the baseline spontaneous nystagmus. Both novices (gray lines) and experts (black lines) detected frequency changes (FRQ) easier than differences in the nystagmus amplitude (AMP). The dotted line illustrates the cutoff for stroke detection (2°/s delta SPV).

Table 1. Sensitivity, Specificity, and Accuracy of the 3 Different Test Conditions and Groups and *P*-Value Comparing Experts' and Novices' Performance

Condi-tion	Baseline Nystagmus (°/s Slow Phase)	Sensitivity [%]		Specificity [%]		Accuracy [%]		*P* Expert vs. Novice
		Experts	Novices	Experts	Novices	Experts	Novices	
FRQ/AMP	1	65	55	91	66	81	63	
	5	82	78	70	66	80	73	.028
	10	78	69	80	86	84	82	.855
	15	80	83	79	73	84	83	.247
	20	77	79	88	79	87	82	.368
	25	84	83	84	85	89	89	.215
AMP	1	25	49	88	38	47	48	
	5	50	45	95	86	74	61	.1636
	10	65	72	83	93	78	79	.6881
	15	74	75	88	82	84	79	.8677
	20	86	77	89	94	90	86	.2766
	25	78	79	86	76	87	82	.9598
FRQ	1	68	45	42	69	54	55	
	5	77	64	64	81	73	77	.47
	10	73	85	81	60	83	77	.255
	15	75	77	94	74	91	79	.0035
	20	63	68	96	89	87	86	.766
	25	76	75	86	83	87	86	.818

a limited ability of the human eye to detect slight changes in nystagmus velocities. The better accuracy results in this study can most likely be explained by the higher velocities in BPPV than in an acute vestibular syndrome. The velocity of the faster nystagmus in this study was about 20°/s and the average difference of the nystagmus velocities was about 14°/s.

Table 2. Sensitivity of Nystagmus Suppression Detection for Potential Stroke Prediction

Condition	Baseline SPV (°/s)	Sensitivity [%] *	
		Experts	Novices
FRQ/AMP	1		
	5	64.8	60.3
	10	52.1	41.9
	15	43.6	37.5
	20	18.8	25.0
	25	32.6	30.0
AMP	1		
	5	55.8	51.0
	10	25	39.4
	15	23	20.7
	20	22	19.4
	25	10	11.6
FRQ	1		
	5	91.9	90.4
	10	53.6	57.3
	15	39.6	46.0
	20	30.4	30.8
	25	28.3	35.8

*For cutoff 2°/s delta SPV.

In another study conducted with random dot patterns, it was shown that just noticeable velocity differences are minimal at velocities between 4 and 64°/s and show a U-shaped discrimination curve as a function of stimulus velocity.[20] According to this study, humans can distinguish 5%-10% of velocity changes for the dots moving horizontally at a speed of 4-64°/s. When the dots move very slowly (<4°/s) or rather fast (>64°/s), humans can only detect the difference of more than 10%-20% of the initial velocity. However, the duration exposed to the stimulus, and the shape, size, and contrast of the stimulus may affect the results. In our study, participants were only able to detect velocity differences of ~23.5%-58.5%, however, our task was more complex since the eye movements were modulated at 3 various conditions in terms of velocity, frequency, and amplitude. In addition, we used computer screens providing only two dimensions instead of 3 dimensions at the bedside when using Frenzel glasses. Real-life bedside examinations might increase the physician's performance. It could be shown, for example, that the lipreading performance of deaf participants was better under live conditions than over TV screens.[21] Although our results cannot be generalized, most of the expert physicians use more sensitive video Frenzel's (2D condition) rather than Frenzel glasses. It could be shown that the sensitivity in detecting nystagmus was better with video Frenzel's due to the complete removal of visual fixation (examination in darkness).[10,22] In a further study, a smartphone bedside test was developed to objectify the fixation suppression of the vestibulo-ocular reflex in patients with a cerebellar syndrome and healthy subjects.[23] They compared the collected smartphone data with video-oculography during a sinusoidal stimulation on a rotatory chair. The sensitivity of the video

ratings to detect an impaired fixation suppression-VOR was 99%, its specificity 92%. This study with per-rotatory nystagmus showed high baseline velocities and a large reduction of SPV from 38.5 ± 12.2°/s to 2.7 ± 3.3°/s in the healthy controls compared with the patients with cerebellar syndrome from 50.3 ± 9.5°/s to 31.3±20.3. These high velocities and large differences may explain the better results compared with our study with a lower intensity of nystagmus.

We found a slightly statistically significant difference between novices and experts only in the condition with frequency modulated nystagmus with a 15°/s baseline nystagmus velocity. The reason for that is that frequency differences were easier to assess than amplitude. Contrary to a previous study assessing the expert performance of clinical head impulse tests, where the amplitude of a corrective saccade was easier to discern than its velocity or latency.[24]

Strengths and Limitations

This is the first study to test the ability of physicians to detect spontaneous nystagmus suppression in various conditions and to investigate the role of experience.

In order to create standardized conditions, we decided to use a computer simulation to collect the data instead of video recordings from real patients. This approach did not only offer a standardized assessment but also covered also all kinds of different conditions affecting the detection of nystagmus. There are inconsistent test conditions when testing patients with Frenzel glasses in dim light.[25] Our simulations, however, are only a simplified approximation to a real examination of the visual fixation suppression test in patients with spontaneous nystagmus. For example, we presented a purely horizontal eye movement without any torsional component. We observed a large variability of nystagmus frequency and amplitude in patients[26] reason why we took arbitrary values of frequency and amplitude for our simulations. It is still unknown whether there is a predominant change in the frequency or amplitude of nystagmus during the suppression test. Older studies examining the various nystagmus parameters of evoked nystagmus found an increase in frequency with fixation.[6,27,28] In recent studies that investigated the change in nystagmus parameters under different visual fixation conditions, a slight decrease in frequency was found with fixation.[10,21] Our simulations, however, allowed the assessment of isolated nystagmus parameters, which would not have been possible with real-world data. Testing the nystagmus suppression in patients with an acute vestibular syndrome would be more challenging since dizzy patients may close their eyes or blink.

Potential Implications

Our study showed a relatively poor accuracy of the nystagmus suppression tests in simulations with low nystagmus velocity (see Table 1). This finding is important because this test is used for the discrimination between peripheral and central nystagmus, and an accurate test is crucial for the avoidance of any misdiagnosis. Thus, especially in the case of central nystagmus where a slow spontaneous nystagmus <13°/s is more likely to be evident,[14] a statement about fixation suppression without a video-oculography recording is most probably too inaccurate. At higher nystagmus velocities, as it occurs more often with AUVP (0-22.5°/s), an assessment without VOG would be more accurate. However, the sensitivity for detecting small velocity differences of 2°/s with high nystagmus intensities is low, as indicated in Table 2.

Diagnosing vertigo in patients remains a complex task that requires a comprehensive approach, including a detailed medical history and thorough neurological and neuro-otological examinations. It is crucial to consider these assessments as an interconnected whole rather than individual examinations, such as the nystagmus fixation suppression test, and the accuracy highly relies on the clinician's experience.

In our study, there was no difference between experts and novices in the detection of simulated nystagmus suppression by visual fixation. The examiners could only detect large suppression effects at low-intensity baseline nystagmus. Overall, the sensitivity and accuracy of a clinical fixation suppression test are low, and the assistance with a video-oculography device is highly recommended.

Ethics Committee Approval: This study did not require approval because the project did not fall under the Human Research Act in Switzerland (IRB Decision No: BASEC Req-2020-01176).

Informed Consent: Informed consent was obtained from the participants who agreed to take part in the study.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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Appendix: Video of the virtual nystagmus simulation with representation of 4 different conditions: Examples 1 and 2 show no nystagmus suppression under visual fixation but different baseline nystagmus, while examples 3 and 4 show a nystagmus suppression under visual fixation. Here is the link of the video: https://vimeo.com/935454489/f570b34acf?share=copy