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Relation Between Horizontal Saccade Test and Anti-Compensatory Saccade in the Suppression Head Impulse Test Paradigm

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억제두부충동검사에서의 반보상적 단속운동과 수평단속안구운동검사와의 관련성

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Background and Objectives There is limited study reported on the relationship between horizontal saccades and anti-compensatory saccades (ACS) in the suppression head impulse paradigm (SHIMP). We investigated the relationship between horizontal saccades and ACS in SHIMP in individuals with normal vestibular function and determined the correlation between the associated factors.
Subjects and Method Medical records of 79 patients with normal vestibular function and brain magnetic resonance images were retrospectively reviewed.
Results ACS and horizontal saccades results were strongly correlated with velocity (R=0.345, p<0.001) and latency (R=0.547, p<0.001). The latency of ACS was significantly shorter (p<0.001) than that of horizontal saccades. The velocity of ACS was negatively correlated with the latencies of ACS (R=-0.318, p<0.001) and horizontal saccades (R=-0.322, p<0.001). Bilateral ACS latency (R=0.384 and 0.471 in right and left, p<0.001 in both side) and left side ACS velocity (R=-0.263, p=0.019) were significantly affected by age.
Conclusion ACS in the SHIMP was strongly correlated with horizontal saccades. However, the latency of ACS was shorter than that of horizontal saccades. Therefore, patient age and results of the horizontal saccades tests should be considered while interpreting the ACS velocity, which reflects vestibulo-ocular reflex function in patients with vestibulopathy.
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Keywords Head impulse test; Saccade; Vestibulo-ocular reflex.

Introduction

The video head impulse test (vHIT) is a commonly used clinical tool for assessing vestibulo-ocular reflex (VOR). Currently, two protocols, the head impulse paradigm (HIMP) and suppression head impulse paradigm (SHIMP), are available for vHIT. The fundamental physiology is similar between HIMP and SHIMP, and both tests evaluate the VOR gain during rapid head rotation. Furthermore, the results of the HIMP and SHIMP tests are highly consistent and complementary in assessing VOR function.[1-3)]

HIMP and SHIMP protocols differ in the presence of catch-up saccades, which are considered normal in SHIMP, but abnormal in HIMP. The catch-up saccade in SHIMP, also known as an "anti-compensatory saccade (ACS)", is a rapid eye movement that adjusts the compensatory eye movement caused by VOR during head rotation. Furthermore, the velocity of the ACS reflects the function of the VOR.[1,3,4] Numerous studies have investigated the results of HIMP tests in healthy individuals and those with various pathological conditions. In comparison, studies on the properties of the SHIMP tests are relatively scarce, as the SHIMP test was developed more recently.[4] Notably, the mechanism of eye movement in ACS is essentially similar to that in the ipsilaterally-directed visually guided saccade test. The retinal slip of the target initiates both saccades, transmits signals along the saccade pathway, and eventually results in the contraction or release of the external orbital muscles. However, few studies have investigated the relationship between the saccade test and SHIMP. We hypothesized that horizontal saccade test and ACS in lateral semicircular canal are strongly correlated.

Therefore, we investigated the relationship between saccades test and SHIMP test in individuals with normal vestibular function. Furthermore, we explored the factors to be considered while interpreting ACS.

Subjects and Methods

Enrollment

Medical records of patients aged >15 years who underwent vestibular function tests (caloric test, video nystagmogram, random saccade test, and SHIMP) and brain MRI between January 01, 2021, to January 01, 2023, were searched. We identified 150 patients that met the criteria. Patients were excluded if they had 1) MRI indicating abnormal lesions in the brain, 2) bilateral vestibulopathy according to the criteria from the Barany Society, 3) caloric canal paresis >25%, 4) vHIT gain of the lateral semicircular canal <0.8 in at least one ear, 5) nystagmus observed on video nystagmogram, and 6) final accuracy of saccades <80%. Finally, 79 participants were enrolled in this study. The study protocol was approved by the Institutional Review Board of Gangnam Severance Hospital (project number 3-2023-0105). The informed consent was waived due to the retrospective design of this study.

Vestibular function tests

The bithermal caloric test (SLVNG; SLMED, Seoul, Korea), saccades test using video nystagmogram system (NOTC-S; Neuro Kinetics, Pittsburgh, PA, USA), and vHIT (ICS Impulse; Otometrics, Taastrup, Denmark) were conducted on all patients. A conventional bithermal caloric test was performed with open-loop water irrigators at 30°C and 44°C for 30 s and a video nystagmography system. The SHIMP and HIMP tests were conducted 20 times in random directions for each of the six semicircular canals, with a peak velocity of 200–250°/s, a rotation amplitude of 15°, and a duration of 150–200 ms. The VOR gain was automatically calculated. The properties (velocity and latency) of the ACS in SHIMP were adopted from an automated algorithm provided by the manufacturer. As the vHIT was applied only to the right eye, the velocity and latency of the horizontal saccades were also adopted to the same eye. The horizontal saccades latency was defined as the mean latency of all saccades to random degrees. The saccade velocity was calculated by determining the area under the curve of the degree (x-axis) and velocity (y-axis). The latency and velocity of the horizontal saccades were automatically calculated using software provided by the manufacturer. SHIMP results of the lateral semicircular canal and ipsilateral horizontal saccades were matched for analysis. For instance, right-side ACS that is induced by the right lateral semicircular canal SHIMP was compared to the horizontal saccade directed to the right side. In the random saccade test, patients request to gaze a visual target (dot) that randomly appears in the range of 6 to 32 degrees (horizontal) from the center for 45 seconds.

Statistical analysis

Statistical analyses were conducted using SPSS software ver. 23 (IBM Corp., Armonk, NY, USA). The PRISM software (version 8.0; GraphPad Software, San Diego, CA, USA) was used for visualization. Pearson's correlation analysis was used to evaluate the relationships between the variables. Partial correlation analysis was used to control the age effect. The paired t-test was used to compare the values between the right and left sides. Values are presented as mean±standard deviation. Statistical significance was set at $p<0.05$ significance.

Results

Random saccade latency correlated to the SHIMP parameters

Our cohort included 79 individuals with normal vestibular function tests; the mean age was 54.7±17.7 years old, and 33 were male (Table 1). The interaural differences in SHIMP parameters and horizontal saccades latency were analyzed using a pairwise test. The right-side SHIMP gain was significantly higher at 0.038 ($p<0.001$) than that on the left side.

Table 1. Information on the enrolled participants

Factor	Mean±standard deviation	*p*-value
Age, years	54.7±17.7	N/A
Male:Female	33:46	N/A
Horizontal saccade velocity, AUC		0.986
Toward Rt side	9776.0±1353.5	
Toward Lt side	9774.5±1291.5	
Horizontal saccade latency, ms		0.138
Toward Rt side	229.7±60.8	
Toward Lt side	224.1±49.7	
SHIMP gain		<0.001*
Toward Rt side	0.990±0.104	
Toward Lt side	0.952±0.095	
SHIMP ACS latency, ms		0.517
Toward Rt side	214.5±51.0	
Toward Lt side	212.3±48.4	
SHIMP ACS peak velocity, deg/s		0.313
Toward Rt side	304.9±45.3	
Toward Lt side	309.6±57.6	

*$p<0.05$. ACS, anti-compensatory saccade; N/A, not applicable; Rt, right; Lt, left; AUC, area under the curve

Other parameters, including horizontal saccades latency, ACS latency, and ACS velocity, did not significantly differ between the right and left sides.

Correlation analysis (Table 2) revealed that age significantly affected horizontal saccades latency, ACS latency, and ACS (left side) velocity. After adjusting for age (Fig. 1), we observed a bilateral positive correlation between horizontal saccades and ACS velocities (R=0.333 and 0.365, p=0.003 and 0.001, in right and left, respectively) and between horizontal saccades and ACS latencies (R=0.408 and 0.536 for right and left, respectively, p<0.001 for both). Furthermore, we observed a negative correlation between horizontal saccades latency and ACS velocity (R=-0.235 and -0.290, p=0.038 and 0.010, on right and left, respectively), as well as between ACS latency and ACS velocity (R=-0.204 and -0.285, p=0.074 and 0.011, in right and left, respectively). To validate this result, we analyzed the conjugated data from the right and left sides (Fig. 2). The results indicated a consistent correlation with a high correlation coefficient.

Table 2. Correlation matrix of factors

	Age	Saccade Vel	Saccade Lat	SHM gain	ACS Lat	ACS Vel
Toward right						
Age						
Saccade Vel	R=-0.059					
	p=0.607					
Saccade Lat	R=0.395***	R=-0.247*				
	p<0.001	p=0.028				
SHM gain	R=-0.098	R=0.040	R=-0.160			
	p=0.392	p=0.724	p=0.160			
ACS Lat	R=0.384***	R=-0.153	R=0.498***	R=-0.113		
	p<0.001	p=0.179	p<0.001	p=0.320		
ACS Vel	R=-0.220	R=0.337**	R=-0.298**	R=0.008	R=-0.268*	
	p=0.052	p=0.002	p=0.008	p=0.941	p=0.017	
Toward left						
Age						
Saccade Vel	R=-0.008					
	p=0.943					
Saccade Lat	R=0.370**	R=-0.282*				
	p=0.001	p=0.012				
SHM gain	R=0.044	R=-0.016	R=-0.061			
	p=0.703	p=0.888	p=0.593			
ACS Lat	R=0.471***	R=-0.168	R=0.614***	R=-0.004		
	p<0.001	p=0.140	p<0.001	p=0.970		
ACS Vel	R=-0.263*	R=0.354**	R=-0.358**	R=0.074	R=-0.367**	
	p=0.019	p=0.001	p=0.001	p=0.519	p=0.001	

*$p<0.05$; **$p<0.01$; ***$p<0.001$. Vel, velocity; Lat, latency; SHM, suppression head impulse paradigm; ACS, anti compensatory saccade; R, correlation coefficient

ACS latency is significantly shorter than horizontal saccades latency

We compared ACS and horizontal saccades latencies observed in the correlation analysis using pairwise analysis owing to the significantly positive correlation between them. Saccade latency is unaffected by amplitude; therefore, the horizontal saccades and ACS latencies were directly compared in each individual. Other related factors, such as ACS and horizontal saccades velocities, were not analyzed because they were not measured in the same units. The difference between the two latencies was significant ($p<0.001$), with the ACS latency being shorter than the horizontal saccades latency. The mean difference was 14.28 ms, with a standard deviation of 48.7 ms.

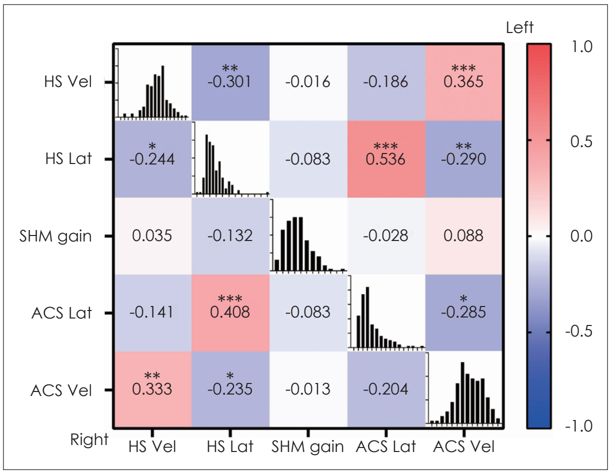

Fig. 1. Correlation matrix after controlling age. Numbers in the cells indicate the correlation coefficient. Cells in the left-lower are results toward the right side, and cells in the right-upper are results toward the left side. The histogram of conjugated data (right and left) is presented in the midline. *$p<0.05$; **$p<0.01$; ***$p<0.001$. HS, horizontal saccade test; Vel, velocity; Lat, latency; SHM, suppression head impulse paradigm; ACS, anti-compensatory saccade.

Discussion

Our findings suggested that ACS and horizontal saccades were strongly correlated with velocity (R=0.345, $p<0.001$) and latency (R=0.547, $p<0.001$). Furthermore, the latency of the ACS was significantly shorter ($p<0.001$) than that of the horizontal saccades. The velocity of the ACS was negatively correlated with the latencies of the ACS (R=-0.318, $p<0.001$) and the horizontal saccades (R=-0.322, $p<0.001$). However,

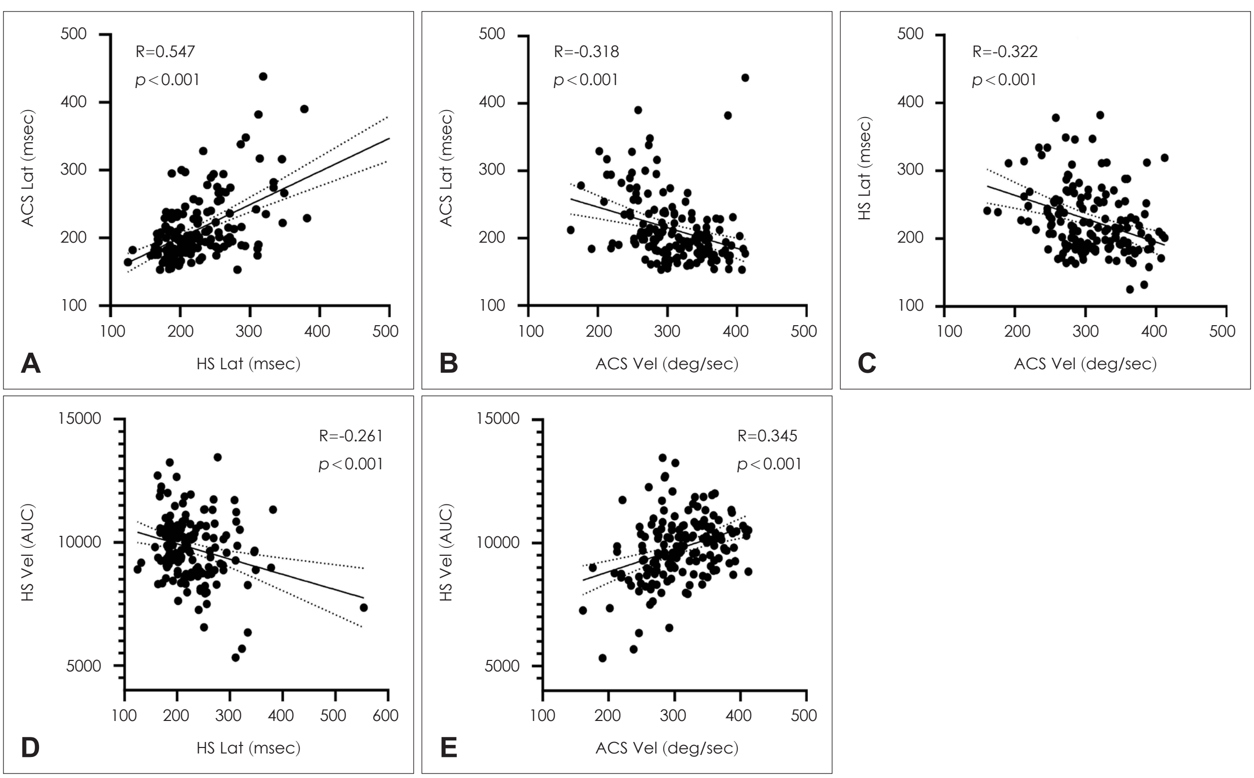

Fig. 2. Correlation plots of each factor. ACS latency vs. horizontal saccades latency (A), ACS latency vs. ACS velocity (B), horizontal saccades latency vs. ACS velocity (C), horizontal saccades velocity vs. horizontal saccades latency (D), and horizontal saccades velocity vs. ACS velocity (E). Pearson correlation analysis was conducted using the data from both the right and left sides. Solid lines indicate the correlation coefficient, and dashed lines indicate a 95% confidence interval. Each dot indicates an individual result. ACS, anti-compensatory saccade; HS, horizontal saccade test; R, correlation coefficient; Lat, latency; Vel, velocity; AUC, area under the curve.

the SHIMP gain did not significantly correlate with age, horizontal saccades velocity, horizontal saccades latency, ACS latency, or ACS velocity. In addition, an interaural difference was observed only in the SHIMP gain.

The interaural differences observed in the SHIMP gain were consistent with those in previous studies and the results obtained using the HIMP protocol.[1,5] This interaural difference in the vHIT gain can be attributed to the asymmetric properties of the medial and lateral rectus muscles and their excitatory and inhibitory pathways.[6,7] The vHIT gain is evaluated in the right eye; therefore, the gain of the right-sided head impulse can be higher owing to the more robust action of adduction compared with abduction. Similarly, in the visually guided saccade test, higher velocity and lower latency were observed in adduction than in abduction.[8] However, we observed no interaural differences in ACS or horizontal saccades. The horizontal saccades results may have been affected by the different target distances (amplitude) between each saccade and the difference in the starting position of each saccade. The saccade direction and final eye position of the ACS were similar to those of the inward-impulse HIMP, in which the final eye position was the midline of the head. However, the inward-impulse HIMP test showed an interaural difference in gain in a previous study.[5] The absence of interaural differences in ACS may result from the fundamental difference between the VOR and ACS, although they share a distal neural pathway.[9,10]

ACS velocity likely reflects remnant VOR function in patients with vestibulopathy.[1,3,4] However, considering the results of this study, this does not apply to healthy vestibules. ACS is strongly correlated with horizontal saccades factors rather than VOR gain. In addition to the strong correlation between velocity and latency, the negative correlation between velocity and latency in the ACS was similar to that in the horizontal saccades. The negative correlation between saccade latency and saccade velocity is possibly owing to age, which affects both latency and velocity, as reported in previous studies.[8,11] Therefore, ACS latency and velocity should be interpreted according to age and horizontal saccades results. In the future, these factors should be more deeply considered when analyzing the ACS data.

Saccade latency was shorter in the ACS than in the horizontal saccades. Several factors reportedly reduce the saccade latency. First, predictability may affect the latency. Rey-Martinez, et al.[12] reported that ACS latency was negatively correlated with the predictability of the protocol. Given that our SHIMP protocol was randomly directed, this may be a minor cause. Second, the cervico-ocular reflex, which possibly triggers the generation of covert saccades in the HIMP, may shorten ACS latency.[13] Lastly, VOR may shorten the latency of ACS than horizontal saccade that exclusively depends on visual stimulation. Since the neural pathway of ACS has not yet been established, further research is needed to elucidate the cause of this phenomenon.

The retrospective design of this study was a limitation. To compensate for this, we excluded patients with abnormal values in other vestibular function tests, including the bithermal caloric test and video nystagmography. Patients with poor final horizontal saccades accuracy were also excluded from the study. However, the enrolled patients may not be entirely healthy since we only excluded patients who were 'objectively' abnormal.

In conclusion, ACS in SHIMP was strongly correlated with horizontal saccades. However, they are not identical because the latency of the ACS is shorter than that of the horizontal saccades. The velocity of the ACS, which reflects VOR function in patients with vestibulopathy, should be interpreted while considering patient age and the results of the horizontal saccades test.

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Author Contribution

Conceptualization: Seong Hoon Bae. Data curation: Han Cheol Lee, Seungjoon Yang. Formal analysis: Han Cheol Lee. Funding: Sung Huhn Kim. Methodology: Seong Hoon Bae. Project administration: Seungjoon Yang. Supervise: Sung Huhn Kim. Visualization: Han Cheol Lee. Writing—original draft: Seong Hoon Bae, Han Cheol Lee. Writing—review & editing: Seong Hoon Bae.

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