Functional and Anatomical Correlates of Impaired Velocity Storage

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Abstract

Velocity storage (VS), a brainstem function, extends the low-frequency response of the vestibular system. To better understand VS mechanisms and characteristics in humans, we analyzed retrospectively functional measures of gait, electrophysiological measures of vestibular function, and imaging studies in an attempt to determine clinical, electrophysiological, and anatomical correlates of abnormalities in VS.

Two cohorts of patients referred to our Risk of Falls Assessment Clinic participated in this investigation. Group 1 (control) patients demonstrated normal caloric and rotary chair tests. Group 2 patients with impaired velocity storage (experimentals) differed clinically from Group 1 only by demonstrating abnormal multifrequency vestibulocular reflex phase measures on rotational testing.

Results showed that Group 2 patients had greater impairments in postural stability and gait than Group 1 patients. Additionally, 80% of patients in Group 2 and none in Group 1 showed pontine hyperintense lesions on MRI.

Key Words: Electronystagmography, rotational testing, velocity storage, vestibular

Abbreviations: CDP = computerized dynamic posturography; ENG = electronystagmography; MRI = magnetic resonance imaging; SOT = sensory organization test; T2WI = T2 weighted image; TE = echo time; TR = repetition time; VOR = vestibulo-ocular reflex; VS = velocity storage

Sumario

La velocidad de almacenamiento (VS), una función del tallo cerebral, Amplía la respuesta a bajas frecuencias del sistema vestibular. Para entender mejor los mecanismos y características de la VS en humanos, analizamos retrospectivamente medidas funcionales de la marcha, medidas electrofisiológicas de función vestibular, y estudios de imágenes, en un intento de determinar correlaciones clínicas, electrofisiológicas y anatómicas en las anormalidades de la VS.

Dos cohortes de pacientes referidos a nuestra Clínica de Evaluación de Riesgo de Caídas participaron en esta investigación. Los pacientes del Grupo 1 (control) demostraron normalidad en las pruebas calóricas y de silla rotatoria. Los

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pacientes del Grupo 2 con velocidad de almacenamiento alterada (experimentales) fueron diferentes de aquellos del Grupo 1 sólo por demostrar medidas anormales en la fase de reflejo vestíbulo-ocular multifrecuencial, en pruebas de rotación.

Los resultados mostraron que los pacientes del Grupo 2 tenían mayor alteración en la estabilidad postural y la marcha, que los pacientes del Grupo 1. Además, el 80% de los pacientes en el Grupo 2 y ninguno del Grupo 1, mostraron lesiones pontinas hiperintensas en la RMN

Palabras Clave: Electronistagmografía, pruebas rotacionales, velocidad de almacenamiento, vestibular

Abreviaturas: CDP = Posturografía Dinámica Computarizada; ENG = Electronistagmografía; MRI = Imágenes por Resonancia Magnética; SOT = Prueba de organización sensorial; T2WI = Imagen ponderada T2; TE = Tiempo de Eco; TR = tiempo de repetición; VOR = Reflejo Vestíbulo Ocular; VS = Almacenamiento de Velocidad

The vestibular system, like the auditory system, responds to sensory inputs across a range of frequencies. In this regard, the peripheral vestibular system is capable of transducing head accelerations for frequencies between approximately 0.01 Hz (e.g., slow postural sway when standing still) and 5 Hz (e.g., active head turns and during ambulation; Leigh, 1996). Rapid acceleration of the head moves the endolymph and mechanically deflects the cupula. However, the mechanical properties of the cupula make the system less sensitive for frequencies below 0.8 Hz and above 5 Hz (Dickman and Correia, 1989; Baloh and Honrubia, 1990; Wall, 1990). On the other hand, slow postural sways of 0.01 Hz are more likely detected by the central and not the peripheral vestibular system (Raphan et al, 1979).

Constant velocity earth-axis rotation causes an initial deflection of the horizontal semicircular canal cupula with a subsequent burst of activity from vestibular afferents. As the cupula returns to its neutral position, vestibular afferent discharges decrease (Goldberg and Fernandez, 1971). The intensity of the vestibular nystagmus generated by the vestibulocular reflex-VOR (i.e., the compensatory eye movement generated in response to stimulation of, in this example, the horizontal semicircular canals) in response to the neural input has an initial rise in intensity and then decreases in a similar manner. However, the difference in the time course of the activity between the vestibular afferent activity and the VOR is significantly different. The time constant of vestibular nerve fibers innervating the horizontal semicircular canal is approximately six seconds, and VIIIth nerve discharges disappear completely after 15–20 seconds. On the other hand, the time constant of the VOR is approximately 16 seconds. Thus, the eye response to sustained rotation persists two to three times longer than the actual peripheral vestibular "drive," suggesting the presence of a neural integrator in the central vestibular system that extends the low-frequency response of the VOR by one order of magnitude (Cohen et al, 1977; Raphan et al, 1979; Cohen et al, 1981). This process of extending low-frequency sensitivity in the vestibular system is now known as *velocity storage* (Raphan et al, 1979).

Central pathways of VS, which remain to be fully elucidated, include "direct" and "indirect" pathways that drive the VOR. The "direct" pathway consists of first order neurons from the VIIIth nerve, second order neurons that leave the vestibular nuclei and terminate on the nuclei of the extraocular muscles, and third order efferents that extend from those nuclei to the extraocular muscles. The "direct" pathway can change its burst activity levels quickly and alters eye position with a short latency (i.e., 16 msec latency; Galiana et al, 1984).

The "indirect" VS pathway receives input from the periphery as does the "direct" pathway. Unlike the "direct" pathway, however, output from the "indirect" pathway persists for a longer period of time than the input it receives from the periphery (Galiana et al, 1984), which means that it has slow charge and discharge time constants (Raphan et al,

1979; Waespe et al, 1983; Raphan and Cohen, 1996).

Activity from the "direct" and "indirect" VS pathways is integrated centrally to drive the VOR (Raphan et al, 1979). A commissural network for both systems originates in the brainstem and provides positive feedback to the vestibular nuclei. The "direct" pathway commissural fibers are more rostrally located in the pons than are the "indirect" pathway commissural fibers. Commisural fibers for the "indirect" pathway reside in the lateral crescents of the rostral medial vestibular nucleus (Holstein et al, 1999). Ablation of the dorsal parts of the central medial vestibular nucleus, caudal to the abducens nucleus, causes bilateral loss of VS (Yokota et al, 1996). Midline lesions in rostro-dorsal medulla, caudal to the abducens nucleus, also abolish VS but leave the "direct" vestibular and optokinetic pathways intact (Wearne et al, 1996).

The cerebellum plays an important modulatory role in VS function. Olivo-cerebellar projections (i.e., from the rostral medulla to the nodulus and uvula) serve to convey afferent vestibular input to regions of the cerebellum that are topographically distinct but close to those regions receiving input from the "direct" pathway (Wearne et al, 1996; Horn et al, 1999). Efferent fibers from these areas project back to regions of the superior and medial vestibular nuclei. Complete lesioning in regions of the nodulus and uvula, which receive horizontal canal afferents, causes an *increase* in the time constant of the VOR and periodic alternating nystagmus (Wearne et al, 1996).

Finally, the afferent drive routed from the vestibular nerves to the medial vestibular nucleus provides the VS mechanism with its "store" of neural activity. Several studies have suggested that removal of the peripheral sensory input effectively disables VS mechanisms thereby affecting the sensitivity of the vestibular system to low-frequency stimuli (Wearne et al, 1996; Cohen et al, 1983).

In summary, VS is dependent on the integrity of (1) an electrical drive from the periphery (end organ and VIIIth nerve fibers), (2) vestibular nuclei, (3) commissural fibers in the "indirect" pathway, and (4) connections between the vestibular nuclei and the cerebellum.

In order to better understand VS mechanisms and characteristics in humans, we analyzed retrospectively data on patients who were evaluated from February 2001 to September 2002. Electrophysiological and imaging studies were reviewed in an attempt to determine clinical, electrophysiological, and anatomical correlates of abnormalities in VS.

METHODS

Patient Populations

Two cohorts were identified in the Risk of Falls Assessment Clinic (Jacobson, 2002). These patients were referred to the clinic either because they had fallen in the past and the cause was unknown, or because their caregivers and/or physician felt they were at risk for falling and wanted their concerns validated. Group 1 consisted of patients who demonstrated normal caloric examinations and normal phase, gain, and symmetry measures on rotational testing. Group 2 included patients who demonstrated clinically normal caloric examinations and, additionally, demonstrated normal gain and symmetry measures on rotational testing but who showed multifrequency abnormally large phase leads on rotational testing. Both abnormalities in VOR gain and phase have been described previously in patients with impaired VS (Barin and Durrant, 2000).

Investigation 1: Analysis of Differences between Groups on Functional Measures

Patients underwent, at a minimum, electronystagmography (ENG), rotary chair testing, and computerized dynamic posturography (CDP), and completed a Dizziness Handicap Inventory (DHI; Jacobson and Newman, 1990; Newman and Jacobson, 1993).

The ENG consisted of a conventional test battery that included tests of ocular motility, positional and positioning (e.g., Hallpike maneuver) nystagmus, and either a monothermal warm caloric test (Jacobson and Means, 1985; Jacobson et al, 1995) or an alternate binaural bithermal caloric test (Jacobson and Newman, 1993a, 1993b).

Rotary chair testing included frequencies of 0.01 Hz–0.32 Hz (Jacobson and Newman, 1991). Rotational testing was conducted with a Neuro Kinetics, Inc. (Pittsburgh, PA) Model

1010 rotary chair system. Bitemporal ENG recordings were conducted while each patient was rotated at 0.01 Hz, 0.02 Hz, 0.04 Hz, 0.08 Hz, 0.16 Hz, and 0.32 Hz (i.e., maximum velocity, 50 degrees/sec, maximum acceleration, 3 degrees/sec^2, 6 degrees/sec^2, 13 degrees/sec^2, 25 degrees/sec^2, 50 degrees/sec^2, and 101 degrees/sec^2 for frequencies 0.01 Hz, 0.02 Hz, 0.04 Hz, 0.08 Hz, 0.16 Hz, and 0.32 Hz, respectively). VOR gain, phase, and symmetry were quantified. To calculate the magnitude of VOR cancellation, the slow phase gain recorded at 0.16 Hz in darkness was divided into the gain obtained when the patient was rotated in light while fixating on a stationary target that rotated with the chair.

EquiTest® CDP testing (NeuroCom, Clakamas, OR) consisted of the sensory organization subtest (SOT). The SOT consisted of six differing conditions of increasing difficulty. Each condition had three trials, each lasting 20 seconds. For each trial, patients were asked to remain as stable as possible. In Condition 1, patients were asked to stand, face forward, and stare at a horizon painted on a cloth visual surround. Condition 2 was the same as the first with the exception that patients were asked to close their eyes (i.e., conventional Romberg). Under such conditions, patients were deprived of visual input and relied on somesthetic and vestibular inputs to remain upright. In Condition 3, patients faced forward with eyes open; however, if they swayed forward or backward the visual surround swayed with them. In this "vision sway-referenced" condition, patients were presented with conflicting visual information if they swayed (e.g., they were swaying, yet the visual sense was providing conflicting information to the central nervous system that they were standing upright). In Condition 4, patients were asked to face forward with eyes open; however, if they swayed forward or backward the platform swayed with them. Under this "support sway-referenced" condition, patients were presented with inaccurate somesthetic information that they had to suppress. In Condition 5, patients were asked to close their eyes, and the support surface was sway-referenced. Patients had to rely solely on accurate vestibular system input to remain upright in this condition. Finally, in Condition 6, with eyes open, both vision and support information were sway-referenced so that patients had to suppress

inaccurate visual and somesthetic information in order to remain upright. The variable that was quantified by the EquiTest® protocol was the maximum peak-to-peak sway (measured in degrees). The limits of sway in normal subjects is approximately 12 degrees. The results of each subtest of the SOT were plotted on a scale from 0 to 100 percent with 100 percent representing complete stability and 0 percent representing the limits of stability (i.e., a fall). In addition to stability scores for each individual condition, the SOT provided a composite score (i.e., from a minimum score of 0 to a maximum score of 100) representing average performance on the six conditions.

Additionally, patients completed a Timed "Up and Go" Test (Podsiadlo and Richardson, 1991) in the context of the Risk of Falls Assessment. Several other evaluations were conducted in the context of the Risk of Falls Assessment. The Timed "Up and Go" Test is a measure of the elapsed time required for the patient to rise to standing from an armchair, walk 3 meters, turn, walk back to the chair, and sit down.

Investigation 2: Analysis of Group Differences on Anatomical Measures

Magnetic resonance imaging studies were reviewed for a subset of patients in Groups 1 and 2. Conventional T1- and T2-weighted images, and, in some cases, diffusion-weighted sequences were interpreted by a neuroradiologist (SP) and a clinical neurologist (NMR), who were unblinded to the clinical data.

Data Analysis

Group paired comparisons were conducted with a Student's t-test. Bonferroni adjusted probabilities are reported where multiple comparisons were made.

The study was approved by the Institutional Review Board (IRB) of the Henry Ford Health System.

RESULTS

Investigation 1: Analysis of Differences between Groups on Functional Measures

Demographics

Subjects were 25 patients seen in the Risk of Falls Assessment clinic at our facility. The mean age of the entire sample was 73 years (sd 11 years), and there were 18 females (72%). These patients were divided into two groups. Group 1 consisted of 11 patients (mean age 69 years, sd 10 years, seven female) who demonstrated normal caloric test results, and normal VOR phase, gain, and symmetry measures on rotary chair testing. Group 2 consisted of 14 patients (mean age 77 years, sd 10 years, 11 female) who also demonstrated normal caloric test results and normal VOR gain and symmetry

measures on rotary chair testing. However, unlike patients in Group 1 the patients in Group 2 showed abnormal measures of VOR phase at a minimum of three adjacent octave frequencies beginning at 0.01 Hz.

The mean data for Groups 1 and 2 are summarized in Tables 1–3. A Student's t-test showed that the group differences in age were not statistically significant (p = 0.07). A Student's t-test also was conducted to determine whether there existed group differences in self-perceived dizziness handicap. Although the patients in Group 2 tended to demonstrate higher total DHI scores than Group 1, these differences were not statistically significant (p = 0.07).

Vestibular Function Studies

Group differences in physiological measures of balance function were evaluated with a Student's t-test. When appropriate, Bonferroni adjusted probabilities are reported for multiple comparisons. The entire patient

Table 1. Mean (sd) DHI, Caloric, and Gait Data Collected for Groups 1 and 2 in Investigation 1

Variable	DHI (points)	Total Warm SPV (degree/sec)**	Timed "Up and Go" (sec)*
Group 1	34.36 (19.41)	67.11 (33.79)	10.36 (2.79)
Group 2	49.21 (19.45)	36.93 (16.24)	15.14 (6.31)

*p ≤ 0.05; **p ≤ 0.01

Table 2. Mean (sd) Rotary Chair Gain Data (i.e., range = 0–1) Collected in Investigation 1

Variable	Gain .01 Hz **	Gain .02 Hz	Gain .04 Hz	Gain .08 Hz	Gain .16 Hz	Gain 32 Hz	Fixation ratio
Group 1	0.32 (0.13)	0.46 (0.07)	0.50 (0.15)	0.62 (0.09)	0.62 (0.17)	0.66 (0.09)	9.87 (6.64)
Group 2	0.19 (0.04)	0.34 (0.09)	0.45 (0.10)	0.58 (0.09)	0.71 (0.14)	0.65 (0.16)	11.50 (5.58)

**p ≤ 0.01

Table 3. Mean (sd) Rotary Chair Phase Data (i.e., phase lead = +deg, phase lag = -deg) Collected in Investigation 1

Variable	Phase .01 Hz (degree)***	Phase .02 Hz (degree)*	Phase .04 Hz (degree)***	Phase .08 Hz (degree)***	Phase .16 Hz (degree)	Phase .32 (degree)
Group 1	41.45 (8.39)	28.00 (3.24)	12.30 (4.42)	5.50 (3.15)	1.56 (3.05)	-1.25 (6.20)
Group 2	65.57 (12.01)	46.64 (13.02)	27.43 (7.80)	14.50 (4.22)	6.14 (4.72)	-1.43 (4.86)

*p ≤ 0.05; *** p ≤ 0.001

Table 4. Mean (sd) Rotary Chair Symmetry (%) Data Collected in Investigation 1

Variable	Symmetry .01 Hz	Symmetry .02 Hz	Symmetry .04 Hz	Symmetry .08 Hz	Symmetry .16 Hz	Symmetry .32 Hz
Group 1	9.89 (8.47)	11.40 (12.60)	6.22 (11.92)	-.43 (7.87)	-5.22 (6.24)	5.00 (7.91)
Group 2	-1.64 (10.89)	2.07 (12.67)	0.29 (7.31)	2.14 (9.83)	-1.42 (6.61)	-1.14 (7.45)

Table 5. Mean (sd) Computerized Dynamic Posturography (Sensory Organization Test) Data Collected in Investigation 1 for Groups 1 and 2

Variable	Condition 1 (points)	Condition 2 (points)	Condition 3 (points)	Condition 4 (points)	Condition 5 (points)	Condition 6 (points)***	Composite (points)**
Group 1	92.00 (4.34)	90.00 (4.38)	88.18 (4.75)	78.27 (8.55)	45.64 (32.58)	53.18 (30.15)	66.09 (14.43)
Group 2	88.33 (6.41)	80.50 (11.59)	77.17 (20.87)	47.75 (33.25)	13.75 (20.39)	3.67 (12.70)	42.50 (12.87)

$**p \leq 0.01$; $***$ $p \leq 0.001$

sample did not receive an alternate binaural bithermal caloric test. However, at a minimum, the entire patient sample did receive a warm monothermal caloric test. The group difference in the total warm caloric response (i.e., the sum of left and right warm caloric maximum slow phase eye velocities) was significant ($t = 2.92$, df = 22, $p = 0.008$). Group 2 showed significantly smaller total warm caloric responses. Only group differences in VOR gain at 0.01 Hz were statistically significant (i.e., 0.01 Hz - $t = 3.48$, df = 23, $p = .01$). Patients in Group 2 showed lower, but clinically normal, gain values than did patients in Group 1 (see Table 2). A gain value of 0.25 at 0.01 Hz separated well Groups 1 and 2. That is, 27% of subjects in Group 1 and 86% of subjects in Group 2 showed a VOR gain that was ≤0.25 for the 0.01 Hz rotational frequency. There were statistically significant group differences in VOR phase (i.e., reflecting increased phase leads) at 0.01 Hz–0.16 Hz frequencies (0.01 Hz - $t = 5.65$, df = 23, $p = < 0.001$; 0.02 Hz, $t = 3.11$, df = 17, $p = 0.006$; 0.04 Hz - $t = 5.51$, df = 22, $p < 0.001$, 0.08 Hz - $t = 4.67$, df = 18, $p = 0.001$). The group mean phase data are shown in Table 3. Group 2 showed significantly larger phase leads. There were no significant group differences in symmetry measures (see Table 4). Finally, group differences in VOR suppression were not statistically significant.

Balance and Gait Studies

There were significant group differences in the composite score on sensory organiza-

tion testing of CDP (Composite score; $t = 4.14$, df = 21, $p < 0.003$). The significant difference in the composite score occurred as a function of the overall lower stability scores across conditions that were significantly different only on Condition 6 (eyes open, surround and platform, sway-referenced; $t = 5.21$, df = 21, $p < 0.001$; see Table 5). Finally, performance on the Timed "Up and Go" Test differed between groups ($t = 2.33$, df = 23, $p = 0.03$). Patients in Group 2 required an additional 4.78 seconds on average to complete the task (see Table 1).

### Investigation 2: Analysis of Group Differences on Anatomical Measures

Demographics

Of the 11 patients in Group 1, five patients (mean age 65 years, sd = 10 years, three female) were found to have undergone magnetic resonance imaging within six months of the Risk of Falls Assessment. For Group 2, 10 of 14 patients (mean age 80 years, sd = 7 years, seven female) were found to have undergone MRI scanning within six months of the Risk of Falls Assessment.

MRI Findings

The results of these analyses are shown in Figures 1 and 2 and are summarized in Table 6. Evidence of ischemic brainstem disease (i.e., chronic or acute) affecting the rostral medulla and/or pons was observed for
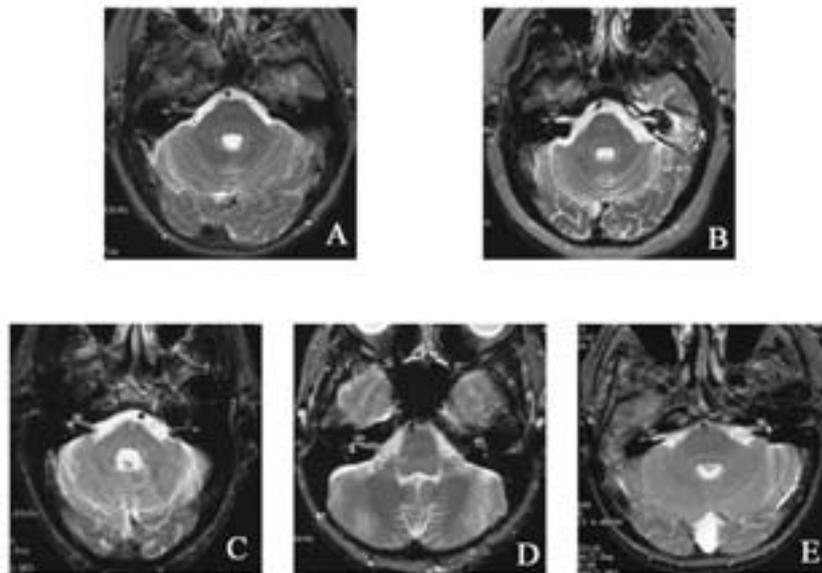
Figure 1. *A–E:* Axial T2WI of the brainstem for the five falls risk patients from Group 1 (i.e., normal caloric and rotary chair test results). Note in all cases the absence of intra-axial lesions.

none of the patients in Group 1 (Figure 1) but for 80% of patients in Group 2 (Figure 2).

DISCUSSION

The results of the present investigation showed that the two patient groups differed in several respects. On physiological (i.e., functional) measures, patients in Group 2 demonstrated reduced, but clinically normal, total warm slow phase velocity, and, reduced, but clinically normal, VOR gain at 0.01 Hz on rotational testing compared to

Group 1. These results confirm previous observations of a close relationship between the results of caloric testing and low-frequency rotational testing (Hamid et al, 1987).

It has been asserted that the reductions in gain and increases in phase of the VOR to low-frequency rotation in elderly patients may have little functional significance (Grossman et al, 1988, 1989; Baloh et al, 1993). However, it has been our empirical observation that postural stability is poorer in patients with low-frequency gain and phase abnormalities on rotational testing than for
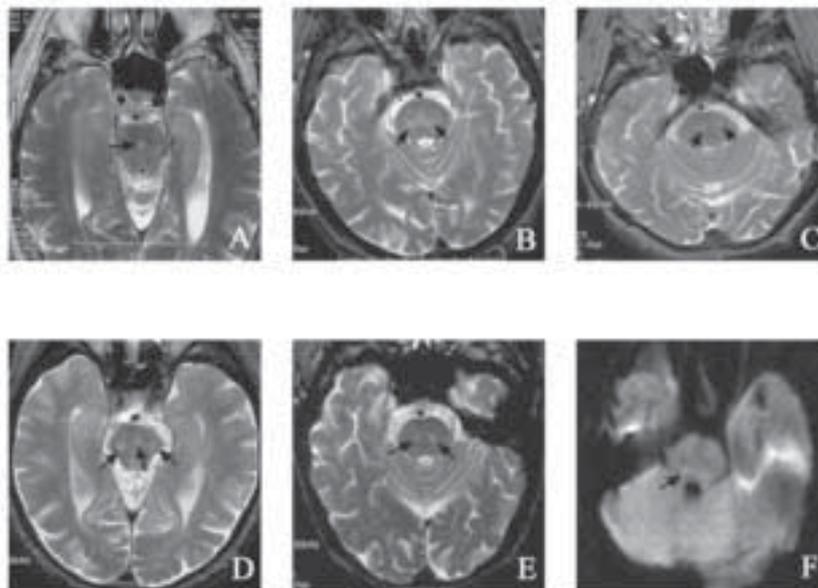
Figure 2. Axial T2WI (*A–E*) and diffusion weighted image of the brainstem (*F*) obtained for six representative patients in Group 2 who showed normal caloric test results and normal gain and symmetry but abnormal phase measures on rotary chair testing. *A*: Axial T2WI (Fast Spin Echo TR 3000/TE 102) showing midline pontine ischemic lesion. *B*: Axial T2WI (TR 2450/TE 90) through the pons demonstrating a relatively large central/paracentral hyperintense lesion in the midpontine region (arrows). *C*: Axial T2WI (TR 2600/TE 90) through the pons demonstrating multiple punctate hyperintense lesions (arrows). *D*: Axial T2WI (TR 2450/ TE 90) through the pons demonstrating multiple hyperintense lesions (arrows). *E*: Axial T2WI (TR 2450/TE 90) through the pons demonstrating multiple punctate and confluent hyperintense lesions (arrows). *F*: Axial diffusion weighted image (single shot EPI TR 9999/TE 88.5) through the brainstem demonstrating a right, acute, pontine, ischemic lesion (arrow).

Table 6. Summarized MRI Results for Groups 1 and 2

Patient Number	Age/Sex	Group Assignment	MRI Result
1N	71/M	Group 1	Normal—No focal intra-axial lesion
2N	60/F	Group 1	Normal—No focal intra-axial lesion. Slight dolichoectasia of the basilar artery
3N	62/F	Group 1	Normal—No focal intra-axial lesion
4N	80/M	Group 1	Normal—No focal intra-axial lesion
5N	54/F	Group 1	Normal—No focal intra-axial lesion
1A	90/F	Group 2	Abnormal—Bilateral symmetrical hyperintense lesions in the pons
2A	87/F	Group 2	Normal—No focal intra-axial lesion
3A	67/F	Group 2	Abnormal—Right, acute, pontine ischemic lesion
4A	74/M	Group 2	Abnormal—Large central/paracentral hyperintense lesion in the midpontine region
5A	79/M	Group 2	Abnormal—Multiple, hyperintense, pontine lesions
6A	86/F	Group 2	Abnormal—Multiple punctate hyperintense, pontine lesions
7A	82/F	Group 2	Normal—No focal intra-axial lesion
8A	82/F	Group 2	Abnormal—Multiple punctate and confluent hyperintense lesions
9A	81/F	Group 2	Abnormal—Midline pontine lesion
10A	71/F	Group 2	Abnormal—Old 5 mm ischemic infarct at the floor of fourth ventricle

Note: Of the samples, 0% of the patients in Group 1 and 80% of the patients in Group 2 demonstrated ischemic brainstem lesions.

patients whose performance is normal. That is, in fact, what we observed in the present investigation. Patients with evidence of impaired VS (e.g., multifrequency phase leads in the face of clinically normal VOR gain) have impaired postural stability. In particular, CDP results showed that these patients had poor postural instability overall but especially when forced to rely on distorted visual and proprioceptive information to remain upright. Additionally, these patients demonstrated poor performance on a functional measure of gait (i.e., Timed "Up and Go" Test). These findings were not surprising since we have observed impairments in somesthetic pathway function (i.e., supported by abnormal tibial nerve somatosensory evoked potential test results) in 75% of patients referred to our Risk of Falls Assessment Clinic (Jacobson, 2002). In most cases we have been able to localize these abnormalities to impairments in peripheral nerve function.

The results of this investigation may suggest that age-related decrements in the supporting senses of vision and somesthe-sia make intact vestibular system function more important for helping patients maintain postural stability. This contention is supported by existing published evidence. Age-related (i.e., >70 years of age) degeneration of the somesthetic system, and specifically peripheral nerve function in the lower extremities, has been well documented (O'Sullivan and Swallow, 1966; Ochoa and Mair, 1969; Behse and Buchthal, 1971; Dorfman and Bosley, 1979). Age-related decrements in visual functions (e.g., depth perception, contrast sensitivity) also are known to occur with advancing age (Nevitt et al, 1989; Lord et al, 1991; Lord et al, 1992). Additionally, investigations utilizing CDP in young and elderly subjects have shown significant group differences in postural stability when both vision and somesthetic inputs are distorted. In these investigations, when the force platform was sway-referenced to distort somesthetic input but vision was undistorted (or when the visual surround was sway-referenced to distort vision but the platform was fixed), there were small differences in performance between

the elderly and younger individuals (Wolfson et al, 1992; Shepard et al, 1993). However, when visual and somesthetic information was distorted, postural stability was significantly poorer for the elderly subjects (Wolfson et al, 1992; Shepard et al, 1993). These findings, identical to our own in the present investigation, suggest that elderly subjects who have lost VS and are confronted with inaccurate information conveyed by distorted supporting senses of vision and/or somesthesia (e.g., Conditions 5 and 6 on the SOT) are far less capable of remaining stable than their cohorts for whom VS is intact. We now are investigating this constellation of findings (i.e., normal caloric examination, normal gain and symmetry measures with multifrequency abnormal VOR phase leads observed on rotational testing) as a potential independent predictor of falls in the elderly.

Our data indicated that 80% of the patients in Group 2 with electrophysiological evidence of impaired VS demonstrated ischemic brainstem lesions. None of the patients in Group 1 with normal VOR gain, phase, and symmetry measures on rotational testing demonstrated ischemic brainstem lesions. It was not possible to determine whether the ischemic lesions directly involved specific locations felt to be critical for the generation of VS, but we consider the MRI data to represent sentinel evidence. In other words, we postulate that ischemic disease in the brainstem greatly increases the likelihood of VS impairment. It is our assertion that the present data suggest that elderly patients with clinically normal caloric test data who demonstrate normal gain and symmetry measures on rotary chair testing but who demonstrate multiple frequency phase leads should be considered at risk for having ischemic brainstem lesions.

It is worth noting we would have interpreted the vestibulometric examination as normal had the ENG examination been conducted in isolation. That is, had caloric testing been our only index of vestibular system function, we would have been left with an unsteady, falls-prone patient with no explanation for their behavior. This fact argues strongly for the multifrequency assessment of vestibular system function to augment the information obtained from the conventional ENG examination.

Finally, there were potential weaknesses with the present investigation that we would

like to acknowledge. This was a retrospective investigation where the sample sizes for both Investigations 1 and 2 were small. It is possible that the samples sizes were not large enough to permit generalization of our findings to the general clinical population. Patients (i.e., experimentals) in Group 2 were compared to a second sample of patients in Group 1 (i.e., who showed normal balance function test results). Both patient groups had been referred to our clinic for an assessment of risk of falling. Accordingly, the control group did not constitute an age- and gender-matched sample of normal neurologically intact elderly. Additionally, interpretation of the MRI scans was conducted in an unblinded, and potentially biased, manner. Despite these potential shortcomings, we feel that the results support our interpretation of the data. This represents the first report of the relationship between electrodiagnostic and imaging findings in a cohort of patients with evidence of impaired VS of central nervous system origin. The next step will be to conduct a prospective investigation to determine the diagnostic efficiency of the ENG and rotary chair test results for the identification of patients with ischemic brainstem lesions.

REFERENCES

Baloh R, Honrubia V. (1990) *Clinical Neurophysiology of the Vestibular System*. Philadelphia: F.A. Davis.

Baloh RW, Jacobson KM, Socotch TM. (1993) The effect of aging on visual-vestibulocular responses. *Exp Brain Res* 95:509–516.

Barin K, Durrant JD. (2000) Applied physiology of the vestibular system. In: Canalis RF, Lambert PR, eds. *The Ear: Comprehensive Otology*. Philadelphia: Williams and Wilkins, 113–140.

Behse F, Buchthal F. (1971) Normal sensory conduction in the nerves of the leg in man. *J Neurol Neurosurg Psychiatry* 34:404–414.

Cohen B, Henn V, Raphan T, Dennett D. (1981) Velocity storage, nystagmus, and visual-vestibular interactions in humans. *Ann N Y Acad Sci* 374:421–433.

Cohen B, Matsuo V, Raphan T. (1977) Quantitative analysis of the velocity characteristics of optokinetic nystagmus and optokinetic afternystagmus. *J Physiol* 270:321–344.

Cohen B, Suzuki J, Raphan T. (1983) Role of the otolith organs in generation of horizontal nystagmus: effect of selective labyrinthine lesions. *Brain Res* 276:159–164.

Dickman JD, Correia MJ. (1989) Responses of pigeon horizontal semicircular canal afferent fibers. II. High-

frequency mechanical stimulation. *J Neurophysiol* 62:1102–1112.

Dorfman LJ, Bosley TM. (1979) Age related changes in peripheral central nerve conduction in man. *Neurology* 29:38–44.

Galiana HL, Flohr H, Jones GM. (1984) A reevaluation of intervestibular nuclear coupling. *J Neurophysiol* 51:242–259.

Goldberg JM, Fernandez C. (1971) Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. I. Resting discharge and response to constant angular accelerations. *J Neurophysiol* 34:635–660.

Grossman GE, Leigh RJ, Abel LA, Lanska DJ, Thurston SE. (1988) Frequency and velocity of rotational head perturbations during locomotion. *Exp Brain Res* 70:470–476.

Grossman GE, Leigh RJ, Bruce EM, Huebman WP, Lanska DJ. (1989) Performance of the human vestibulo-ocular reflex during locomotion. *Neurophysiology* 62:264–272.

Hamid MA, Hughes GB, Kinney SE. (1987) Criteria for diagnosing bilateral vestibular dysfunction. In: Graham MD, Kemink JL, eds. *The Vestibular System: Neurophysiological and Clinical Research.* New York: Raven Press, 115–118.

Holstein GR, Martinelli GP, Wearne S, Cohen B. (1999) Ultrastructure of vestibular commissural neurons related to velocity storage in the monkey. *Neuroscience* 93:155–170.

Horn AKE, Buttner U, Buttner-Ennever JA. (1999) Brainstem and cerebellar structures for eye movement generation. In: Buttner U, ed. *Vestibular Dysfunction and Its Therapy.* Basel: Karger, 1–25.

Jacobson GP. (2002) Development of a clinic for the assessment of risk of falls in elderly patients. *Semin Hear* 23:161–178.

Jacobson GP, Means ED. (1985) Efficacy of a monothermal warm water caloric screening test. *Ann Otol Rhinol Laryngol* 94:377–381.

Jacobson GP, Newman CW. (1990) The development of the Dizziness Handicap Inventory (DHI). *Arch Otolaryngol Head Neck Surg* 116:424–427.

Jacobson GP, Newman CW. (1991) Rotational Testing. *Semin Hear* 12:199–225.

Jacobson GP, Newman CW. (1993a) Background and technique of caloric testing. In: Jacobson GP, Newman CW, Kartush J, eds. *Handbook of Balance Function Testing.* Chicago: Mosby-Yearbook, 156–192.

Jacobson GP, Newman CW. (1993b) Interpretation and usefulness of caloric testing. In: Jacobson GP, Newman CW, Kartush J, eds. *Handbook of Balance Function Testing.* Chicago: Mosby-Yearbook, 193–234.

Jacobson GP, Rupp K, English S, Newman CW. (1995) A reappraisal of the monothermal warm caloric screening test. *Ann Otol Rhinol Laryngol* 104:942–945.

Leigh RJ. (1996) What is the vestibulo-ocular reflex and why do we need it? In: Baloh RW, Curthoys GM, eds. *Disorders of the Vestibular System.* New York: Oxford University Press, 12–19.

Lord SR, Clark RD, Webster IW. (1991) Visual acuity and contrast sensitivity in relation to falls in an elderly population. *Age Ageing* 2:175–181.

Lord SR, Mclean D, Strathers G. (1992) Physiological factors associated with injurious falls in older people living in the community. *Gerontology* 38:338–346.

Nevitt MC, Cummings SR, Kidd S, Black D. (1989) Risk factors for recurrent nonsyncopal falls. A prospective study. *JAMA* 261:2663–2668.

Newman CW, Jacobson GP. (1993) Balance handicap assessment. In: Jacobson GP, Newman CW, Kartush J, eds. *Handbook of Balance Function Testing.* Chicago: Mosby-Yearbook, 380–391.

Ochoa J, Mair WGP. (1969) The normal sural nerve in man: II Changes in the axons and Schwann cells due to aging. *Acta Neuropathol* 13:217–239.

O'Sullivan DJ, Swallow M. (1966) The fiber size and content of the radial and sural nerves. *J Neurol Neurosurg Psychiatry* 29:205–213.

Podsiadlo D, Richardson S. (1991) The timed "up and go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 39:142–148.

Raphan T, Cohen B. (1996) How does the vestibulo-ocular reflex work? In: Baloh RW, Halmagyi GM, eds. *Disorders of the Vestibular System.* New York: Oxford University Press, 20–47.

Raphan T, Matsuo V, Cohen B. (1979) Velocity storage in the vestibulo-ocular reflex arc (VOR). *Exp Brain Res* 35:229–248.

Shepard NT, Schultz A, Alexander NB, Gu MJ, Boismier T. (1993) Postural control in young and elderly adults when stance is challenged: clinical versus laboratory measurements. *Ann Otol Rhinol Laryngol* 102:508–517.

Waespe W, Cohen B, Raphan T. (1983) Role of the flocculus and paraflocculus in optokinetic nystagmus and visual-vestibular interaction: effects of lesions. *Exp Brain Res* 50:9–33.

Wall C. (1990) The sinusoidal harmonic acceleration rotary chair test. Theoretical and clinical basis. *Neurol Clin* 8:269–285.

Wearne S, Raphan T, Cohen B. (1996) Nodulo-uvular control of central vestibular dynamics determines spatial orientation of the angular vestibulo-ocular reflex. *Ann N Y Acad Sci* 781:364–384.

Wolfson L, Whipple R, Derby CA, Amerman P, Murphy T, Tobin JN, Nashner L. (1992) A dynamic posturography study of balance in healthy elderly. *Neurology* 42:2069–2075.

Yokota J-I, Reisine H, Raphan T, Cohen B. (1996) Effects of microinjection of muscimol in the vestibular nuclei on velocity storage and estimation of head velocity by the otolith organs. *Ann N Y Acad Sci* 781:718–723.