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Vestibular impairments on objective diagnostic tests in HIV+ women and control men and women

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Abstract

Objective: To describe the value of two vestibular test batteries across ages in healthy men and women for detecting vestibular disorders and to compare the occurrence of vestibular disorders in the healthy adult population and women with HIV disease.

Study Design: Two groups were tested on the battery of objective diagnostic tests of the vestibular system.

Setting: Two tertiary care centers

Subjects: Healthy controls (284 women, 105 men) and women (63) with HIV/AIDS (HIV+) who are being followed in a longitudinal study of HIV. They were tested on objective diagnostic tests of the vestibular system.

Results: In all age decades healthy controls had evidence of vestibular impairment, significantly more in older adults. HIV+ subjects, all females, did not differ from healthy control females.

Conclusion: These data suggest that at all ages people do have decreased vestibular function, even young, asymptomatic and apparently healthy adults. HIV disease, itself, does not cause an increased prevalence of peripheral vestibular disorders when HIV is controlled on antiretroviral medication.

Keywords

vestibular; aging; epidemiology; HIV; AIDS; public health; VNG; diagnostic testing

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Introduction

Vertigo and balance problems are symptoms of disorders of the vestibular system. They are common in the adult population, although the exact prevalence is unknown. In Sheldon's 1948 survey of seniors' health problems women reported vertigo more frequently than men, and sooner in old age.[1] This pattern holds true across a variety of surveys, reviews of insurance and medical reports, and countries.[2–13] Recent analyses of data from questions used in the Balance and Dizziness Supplement to three years of the National Health Interview Survey support those findings.[14] Few of those reports, however, are supported by evidence from either clinical examinations or data from objective diagnostic tests.

An exception is the work on seniors by Agrawal and her colleagues using vestibular evoked myogenic potentials (VEMP).[15] Despite the high variability and the lack of norms[16,17] VEMP is useful for indicating possible superior canal dehiscence and major unilateral weakness. Also, age-related decrements in the vestibulo-ocular reflex have been known for many years.[18]

At a minimum, objective diagnostic testing should include the gold-standard bi-thermal caloric test and Dix-Hallpike maneuvers,[19] or the side-lying test when the Dix-Hallpike maneuver cannot be performed,[20] and other positional tests.[21,22] The most comprehensive test batteries also include VEMP as well as low frequency sinusoidal tests of the vestibulo-ocular reflex in darkness and full-field tests of optokinetic nystagmus, all performed in a rotatory chair. Although the value of the rotatory chair and VEMP in diagnostic testing is well established[22–27] many clinical facilities do not have rotatory chairs and some facilities still do not use VEMP.

The literature on the occurrence of vestibular disorders in HIV/AIDS is mixed. In 1990 one study of HIV+ men compared to healthy controls found no abnormalities on bi-thermal caloric testing but 5 of 29 HIV+ subjects had abnormalities on positional testing or sinusoidal rotational testing, compared to none in the 33 healthy controls.[28] Hausler et al.[29] reported that 8 of 14 symptomatic HIV+ patients with AIDS had vestibular impairments but asymptomatic HIV+ patients had no vestibular impairments. These studies were performed prior to the use of modern highly active antiretroviral therapy (HAART). In another study of 60 HIV+ subjects with a range of disease severity, on bi-thermal caloric testing 6 subjects with mild disease, 8 subjects with moderate disease and 8 subjects with severe disease showed abnormal responses but none showed abnormalities on Dix-Hallpike testing; 4 healthy controls shows abnormalities, suggesting an effect of the disease.[30] The authors did not state the type of antiretroviral medication that patient-subjects used. Castellano et al.[31] found no evidence of vestibular impairment in 29 asymptomatic HIV+ adults compared to 20 healthy controls, although they did find evidence of impaired oculomotor control, suggesting central nervous system involvement.

More recently in a sample of 53 HIV+ adults with a range of level of disease 79% of HIV+ subjects were shown to have vestibular impairments compared to 18% of healthy controls.[32] A study of self-reported vertigo showed that 3 months after starting HAART subjects had a marked increase in vertigo but it abated by 6 months after starting HAART.[33]

This finding may be due to the effect of attention or, as the investigator suggested, the effect of prioritizing symptoms. A more recent paper reported more vestibular impairments in HIV+ subjects than healthy controls,[34] but that work may have been confounded by the use of video head impulse tests, which are unreliable.[35] The effects of HIV on the vestibular system in subjects whose disease is controlled on HAART remains unclear.

In the present study we tested two groups of subjects on the same standard comprehensive clinical battery of objective diagnostic tests. Using healthy controls we found the frequencies of vestibular impairments across age decades to learn if middle-aged and older subjects really do differ. Then, using a convenience sample of women with HIV/AIDS, we compared the frequencies of vestibular disorders in the two groups to learn if virologically controlled HIV+ women differ from healthy controls. Finally, we compared the complete battery to the use of the battery without cervical evoked myogenic potentials, which is not available in some labs, to learn if the frequencies of vestibular impairments, overall, differ with and without that test.

Methods

Subjects

Healthy controls were recruited from both of our laboratories. At Lab 1, they were recruited from the community in the metropolitan area and from staff and visitors at the institution. The cohort in Lab 1 included 262 females, aged 21.9 to 87.6 yrs, mean age 49.6 yrs, and 105 males aged 21.4 to 84.5 yrs, mean age 48.3 yrs. No HIV+ subjects were recruited from Lab 1.

At Lab 2, only females were recruited because all subjects were recruited from the Women's Interagency Health Study (WIHS), a longitudinal study of women with HIV/AIDS and healthy controls. The 22 control subjects were aged 36 to 48 years, mean 43 years. The 63 HIV+ subjects were aged 48 to 72 years, mean age 57.0 yrs.

All subjects were ambulatory without gait aids and had no known history of vestibular or other otologic disease other than routine age-related presbycusis, and no history of neurologic disorders. No subjects had disorders of ocular motility. No subjects took medication for anxiety, nausea or other medications with vestibular-suppressant effects. All subjects gave written informed consent prior to participation. This study was approved by the Institutional Review Board for Human Subjects Research for Baylor College of Medicine and Affiliated Hospitals and by the Georgetown University Institutional Review Board.

Testing

In both labs subjects were tested on cervical VEMP (cVEMP) using surface Ag/AgCl electrodes placed over the bulk of the sternocleidomastoid halfway between the mastoid tip and the sternal notch, with the reference electrode over the sternum and the ground electrode on the forehead. Testing was performed at 500 Hz, maximum 100 dB nHL, 200 msec interval testing (Lab 1) and 80 msec interval testing (Lab 2), with 50 (Lab 1) or 100

(Lab 2) sweeps per trial. Responses were considered abnormal if thresholds were < 70 dB or marked asymmetry ≥ 100%.

In both labs eye movements were recorded using infra-red video-oculography. All subjects were tested on Dix-Hallpike maneuvers, supine roll tests, and bi-thermal caloric tests with water at 30° C and either 43°C (Lab 1) or 44° (Lab 2). The cut-point for bi-thermal caloric testing was set at ≥20% unilateral weakness. Results of Dix-Hallpike maneuvers were considered abnormal if three or more beats of nystagmus were recorded. Subjects were also tested on saccades and pursuit. In both labs a subject was coded as abnormal for oculomotor tests if one or more abnormal scores were found.

The Standard Test Battery included all tests mentioned above. Because some clinical labs do not give cVEMP, when we did the statistical analyses we compared the use of the Standard Test Battery to a Reduced Test Battery without cVEMP results.

Statistical methods

The change in abnormal findings over age decades (20s to 80s) was assessed by a Cochran-Armitage test for trends. Within each age group, the difference in abnormal findings between the two test batteries was assessed by the McNemar test. Other group comparisons were performed by Chi-square/ Fisher exact tests. $P < 0.05$ was considered significant. Statistical analyses were performed using SAS statistical software (version 9.4; Cary, NC).

Results

Healthy controls

No subjects had impairments on saccades, pursuit or positional tests other than Dix-Hallpike maneuvers. If subjects were scored as abnormal, they had at least one abnormal response on Dix-Hallpike testing or other components of the Standard Test Battery, and the Reduced Test Battery. All decades showed at least some subjects with vestibular impairments. The frequency of abnormalities differed depending on the test battery used. See Table 1.

For healthy controls overall, we found a significant increase in abnormal findings from age decades 20 to 80 on the Standard Test Battery ($p=0.003$, Chi-square test for trend) and approaching significant on the Reduced Test Battery ($p=0.056$). The increase in abnormal findings is pronounced starting at about age decade 70 for the Standard and Reduced Test Batteries ($p's<0.05$). Similar results were found between men and women although significant trends were only observed for women because of the smaller sample of men.

To determine if the two test batteries yielded statistically significantly different percentages of abnormal results we collapsed the age groups. We found differences between the test batteries, $p< 0.0001$. Then we did pairwise comparisons of test batteries by age decades. In the 20-year olds, results did not differ between the Standard and Reduced Test Batteries. In the 80-year olds, the differences between the Standard and Reduced Test Batteries approached significance, $p=0.08$. See Table 1.

The study had fewer males (n = 105) than females (n = 262). To determine the influence of gender on having an abnormality we compared men and women on each test battery. No significant differences were found between males and females in frequency of abnormal responses on any variations of the test battery. See Table 2.

To determine if the results on the Standard Test Batteries were comparable from the two institutions, we compared the percentages of abnormal findings per institution using only the female subjects from Institution 1. The comparison overall was significant, p=0.009. Lab 1 had 39% abnormalities; Lab 2 had 9% abnormalities, p=0.009. When that finding was broken down by specific tests, no differences were found in the percentage of abnormalities on bi-thermal caloric testing (p=0.48) and cVEMP (p=0.21).

On Dix-Hallpike testing the Chi-square test showed a significant difference between the two labs (p=0.006). In Lab 1, 28% of female subjects had abnormal Dix-Hallpike responses. In Lab 2 no abnormal Dix-Hallpike responses were found. The sample size from Lab 2 was smaller than the sample size from Lab 1 and the age range was narrower, so these results should be interpreted with caution. Due to this difference comparisons between HIV+ subjects and healthy controls were performed without the Dix-Hallpike tests.

HIV+ subjects compared to controls

When HIV+ subjects were compared to healthy controls matched on age (within 5 years) the groups did not differ significantly on either the Standard Test Battery (without Dix-Hallpike) (p=0.22) or just the Reduced Test Battery (without Dix-Hallpike) (p=0.25). In HIV+ subjects on the Standard Test Battery, 21% (11 of 63 subjects) had vestibular abnormalities compared to 14% of healthy controls (24 of 171 subjects). The values were similar for the Reduced Test Battery: 18% (11 of 63) HIV+ subjects compared to 12% (20 of 171) healthy controls.

Within HIV+ tests

Among HIV+ subjects, in the 40-year old group 29% of subjects (2 of 7) had abnormal results. In the 50-year age group, 19% of subjects (6 of 31) had abnormal results. In the 60-year age group 21% of subjects (5 of 24) had abnormal results. The single subject in the 70-year age group did not have an abnormal result. The sample sizes were small so these data should be interpreted with caution. The percentages of abnormal vestibular results on the Standard Test Battery did not differ across the 40-, 50-, and 60-year old age groups (Chi-square test, p=0.86).

HIV+ patients may differ by the level of viral load, or use of monotherapy prior to receiving modern highly active antiretroviral therapy (HAART), or ever having had a diagnosis of AIDS. Therefore the HIV+ group was tested for within-group differences on those variables. Data on viral load were unavailable for three subjects. The percentage of vestibular disorders did not differ between subjects who had detectable and undetectable levels of viral load, on both the Standard Test Battery (p=0.99) and Reduced Test Battery (p=0.99). Likewise, the percentage of vestibular disorders did not differ between subjects who had had monotherapy on the Standard Test Battery (p=0.49) and the Reduced Test Battery (p=0.71). Also, the percentage of subjects who had vestibular disorders did not differ between subjects who had ever been diagnosed with AIDS and subjects who had not, on the Standard Test Battery

(p=0.58) and the Reduced Test Battery (p=0.21). Thus, none of these variables influenced scores. See Table 3.

Discussion

The results in healthy controls support the idea that vestibular disorders are more prevalent in people over the age of 60 years, especially in the 70- and 80-year old groups. The oldest group seems to plateau, but that finding may be due to the small sample size. Unexpectedly, we found that even young and middle-aged adults have many abnormalities. This finding indicates that even young and middle-aged adults who do not seek care for symptoms may have vertigo and balance problems.

Physicians who care for adults of all ages should be prepared to deal with patients whose complaints are consistent with vestibular disorders, even if they are relatively young. These data support the need to improve education about vestibular disorders for primary care and some specialty health care providers in medicine, nursing and rehabilitation. The finding of significant deficits in the 70-year old group suggests that training for providers who care for seniors should include a good education about vestibular disorders.

The lack of differences between healthy controls and HIV+ subjects supports the idea that with good control of the virus HIV+ subjects have no greater chance of developing vestibular disorders than non-HIV-infected people. Thus, this finding is good news.

Limitations of the study

The findings from the 80-year-old control group should be interpreted with caution due to the small sample size. Recruiting a healthy cohort in that age group was challenging. Labs 1 and 2 had different frequencies of positive responses on Dix-Hallpike testing for women of the same age. This difference is easily explained. The sample sizes were different and that variable, alone, may account for the lack of positive findings in Lab 2. The HIV+ group included only females and was relatively small. A study with a larger sample of HIV+ subjects and male as well as HIV+ subjects, might have shown different results.

Conclusion

Compared to younger adults seniors have significantly more abnormalities on objective VNG testing even on the reduced battery but even younger subjects have more abnormalities on testing than was previously thought. Therefore, younger patients who complain of symptoms of vestibular disorders should be tested. Adults aged 40 to 70 years who have HIV but who are virologically well-controlled are at no greater risk for having abnormalities on objective vestibular testing than people in the same age group who do not have HIV. Therefore, infectious disease specialists and otolaryngologists need not be especially concerned for their risk of having vestibular disorders.

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Table 1.

Age group percentages of abnormal results on test batteries (sample size per age in parentheses). Within each age decade % abnormal with Standard and Reduced test battery is compared by McNemar test.

Test Battery % abnormal	**Age decades**							**Total (N=453)**
	> 20 (N=73)	**> 30 (N=71)**	**> 40 (N=73)**	**>50 (N=92)**	**> 60 (N=82)**	**>70 (N=50)**	**> 80 (N=12)**	
Standard Test Battery	35.6 %	36.6 %	28.8 %	38.0 %	39.0 %	56.0 %	58.3 %	38.6 %
Reduced Test Battery	32.9 %	29.6 %	23.3 %	28.3 %	31.7 %	48.0 %	33.3 %	31.4 %
p-value	0.16	0.03	0.04	0.003	0.01	0.04	0.08	<0.0001

Table 2.

Female/ male percentages of abnormal results on test batteries (sample sizes in parentheses). Male and female subjects were compared on each test battery (Standard and Reduced) by Chi-square test.

Test Battery % Abnormal	Group			p-value
	Females (N=347)	Males (N=106)	Total (N=453)	
Abnormal Standard Test Battery	38.6 %	38.7 %	38.6%	0.99
Abnormal Reduced Test Battery	31.7 %	30.2 %	31.4%	.77

Table 3.

Percentages of only HIV+ subjects who had abnormal findings on the Standard and Reduced Test batteries (sample size in parentheses) on detectable/ undetectable viral load; ever having had monotherapy (yes/no); and ever having been diagnosed with AIDS (yes/no). N=sample size. P-value is based on Chi-square or Fisher exact test.

Test battery % abnormal	Level of Viral Load			Ever Monotherapy			Ever AIDS		
	Detectable N=14	Undetect-able N=46	p-value	No N=47	Yes N=16	p-value	No N=12	Yes N=25	p-value
Standard Test Battery	21.4%	21.7%	0.99	23.4 %	12.5%	0.49	16.7%	8.0%	0.58
Reduced Test Battery	21.4 %	21.7%	0.99	19.2%	12.5%	0.71	16.7%	4%	0.21