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Age predicts the absence of caloric-induced vertigo

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Abstract

Introduction: The absence of vertigo during the caloric test, despite a robust response, has been suggested to represent a central vestibular system phenomenon. The purpose of this investigation was to determine the prevalence of absent caloric-induced vertigo perception in an unselected group of patients and to assess possible predicting variables.

Methods: Prospective investigation of 92 unselected patients who underwent caloric testing. Inclusion criteria were that each patient generate a maximum slow phase velocity (maxSPV) $\geq$ 15 deg/sec and a caloric asymmetry of $\leq$10%. Following the caloric, patients were asked, "Did you have any sensation of motion?"

Results: Results showed 75% of patients reported motion with a mean age of 56.51 years compared to a mean age of 66.55 in the 25% of patients reporting an absence of motion. A logistic regression was performed and the overall model was statistically significant accounting for 29% of the variance in caloric perception. The significant predictor variables were patient age and maxSPV of the caloric response. The effect size for both variables was small with an odds ratio of .9 for maxSPV and 1.06 for age.

Conclusions: The current investigation showed that both age and maxSPV of the caloric response were significant predictors of vertigo perception during the caloric exam. However, the association between age and caloric perception is not conclusive. Although there is evidence to suggest that these findings represent age-related changes in the central processing of vestibular system stimulation, there are additional unmeasured factors that influence the perception of caloric-induced vertigo.

keywords: Vestibular; Vertigo; Central processing; Caloric test; Aging

1. Introduction

Clinicians who evaluate vestibular function may be presented with a patient that perceives the cutaneous aspects of the caloric stimulus (i.e. the hot or cold water rushing in their ear), but reports having no sensation of motion or vertigo during the caloric exam. They may comment that they feel "nothing" or a mild sensation of "floating". These cases are most perplexing in patients whose peripheral vestibular system generates a robust response measured through the vestibulo-ocular reflex (VOR). Anecdotal evidence suggests that these patients usually are elderly. The underlying mechanism and clinical significance of the absent post-caloric self-motion perception in the presence of a clinically normal peripheral vestibular response is unknown. However, there is evidence to suggest this phenomenon may implicate the central vestibular system pathways and may produce postural instability.

Takeda et al., 1995, first reported this phenomenon in patients with known lesions involving the parieto-temporal lobe (i.e. analogous to the "vestibular cortex" in nonhuman mammals). The investigators described the patients as experiencing

Abbreviations: SPV, slow phase velocity; VNG, videonystagmography.

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"nystagmus-sensation dissociation", defined as "brisk caloric nystagmus without simultaneous sensation of vertigo" (Takeda et al., 1995). Takeda and colleagues later described this phenomenon in a small subset of healthy participants and reported that the degree of self-motion perception during the caloric test was correlated with the magnitude of cerebral blood flow in the parietal lobe, further implicating the central vestibular structures in the perception of caloric-induced vertigo (Takeda et al., 1996).

A more recent report from Chiarovano et al. (2016) described patients who demonstrated the absence of rotatory vertigo after caloric irrigation as having "vestibular neglect". They observed this finding in a small sample of older adults, and suggested that this blunted motion perception is both more pervasive in older adults and may place them at greater risk for falling (Chiarovano et al., 2016). Specifically, the investigators evaluated 20 subjects, ten of whom were older adults ($\geq$65 years) who were selected based on self-reported postural instability and an absence of perceived vertigo after warm caloric irrigations. The second group consisted of 10 age and sex-matched control subjects who did not report postural instability and did report a sensation of vertigo following warm caloric irrigation. For both groups the mean peak slow phase nystagmus velocity (maxSPV) was $\geq$15 deg/sec. The patient was shown as perceiving motion if, "… there was perception of body rotation whose direction (to the right or left) could be given clearly by the patient …" (p 3). The investigators reported no group differences in caloric velocities or degree of caloric asymmetry. Not surprisingly, although postural stability on the Equitest was normal for the control group, the test was abnormal for the experimental group and especially for conditions 5 and 6 that are most dependent on normal vestibular system function. The design of this investigation had some shortcomings. First, by virtue of the subject selection criteria there were significant differences in the balance function of the two groups (i.e. those with a history of postural instability were unstable on the Equitest protocol). Additionally, caloric-induced vertigo was absent by subject selection criterion. Thus, the two subject groups demonstrated abnormal performance from the start. It remains unclear how pervasive absence of post-caloric motion perception is in a consecutive sample of clinical patients who produce robust and symmetrical caloric responses. Further, it remains unclear if this phenomenon is exclusively observed in older patients who may be at greater risk for central vestibular impairments.

The purpose of this investigation was to determine the prevalence of absent caloric-induced vertigo perception in an unselected group of patients and to assess possible predicting variables for a lack of vertigo perception. Accordingly, the current investigation was conducted in an effort to determine whether an absent post-caloric motion perception occurs only in elderly patients.

2. Methods

The subjects were 92 patients (mean age 59.18 years, sd 18.2, 41male) who were referred to the Balance Function Laboratory at the Vanderbilt University Medical Center for an assessment of their dizziness. Each patient received a quantitative vestibular assessment by a licensed and certified audiologist. The assessment included a videonystagmography (VNG) examination that culminated in a monothermal warm caloric test (Jacobson et al., 1995; Jacobson and Means, 1985; Murnane et al., 2009) or a bithermal water caloric test.

Criteria for acceptance to this investigation was that each subject had to generate a mean maxSPV $\geq$15 deg/sec for both left and right warm caloric irrigations. Further, the monothermal warm caloric asymmetry could not exceed 10% (Murnane et al., 2009). The only protocol for this investigation was the patient's answer to the question, *"Did you have any sensations of motion after the water was placed in your ear?"* The response was recorded as a binary answer of "yes" or "no". For this investigation we scored as positive those responses that denoted self-motion including "shifting," "rocking," "sliding," "floating and spinning," and "rolling." We chose to include descriptions other than "spinning," or "rotating" due to the difficulty some patients had in describing their experience. The study protocol was approved by the local Institutional Review Board (IRB #171520).

2.1. Statistical analysis

Patients were grouped according to whether or not they perceived a sensation of movement during the caloric exam yielding two groups, *presence of vertigo* and *absence of vertigo*. Summary statistics, means, and standard deviations were reported to describe the continuous variables (i.e. age, maxSPV), and count and percent were used to describe categorical variables (e.g. gender). Differences between ears were examined using t-tests if the variable was continuous and Chi-squared tests if the variable was categorical. Associations between continuous variables were assessed using the Pearson correlation. In addition, logistic regression was used to assess the probability of perceiving vertigo during the caloric test and odds ratios were reported as an indication of effect size. Significance of variables was examined at alpha = .05. The analysis were completed in SPSS, version 24.0 (IBM SPSS Statistics for Windows, Armonk, NY).

3. Results

The total cohort included 92 consecutive patients who underwent caloric testing and whose results were both normal and robust with maxSPV >15 deg/sec. Patient demographics are shown in Table 1. Of the total cohort, the majority, 69/92 (75%), reported a perception of vertigo during the caloric test while 23/92 (25%) reported an absence of vertigo. Of those who reported an absence of vertigo, the mean age was 66.55 years compared to a mean age of 56.51 years in the group who did report the presence of vertigo. Although the mean age was greater in the absent group, approximately half of the patients in the absent group, 11/23 (48%), were under the age of 65.

There was no significant ear effect on vertigo perception ($\chi^2(1)$ = .113, p = .737) and no significant ear effect on

Table 1
Demographics of the two groups (Presence of vertigo, Absence of vertigo) including their gender distribution, mean age, and mean maxSPV.

Predictor variables	Group		Total cohort (n = 92)
	Presence of vertigo (n = 69)	Absence of vertigo (n = 23)	
Gender	38 females	13 females	51 females
	31 males	10 males	41 male
Age (SD)	56.51 (18.0)	66.55 (16.9)	59.18 (18.2)
maxSPV (SD)	34.25 (14.9)	26.22 (7.9)	32.24 (13.9)

maxSPV = maximum slow phase velocity, given in deg/sec.
SD = standard deviation.

maxSPV (t = .759, p = .449). Further analyses concerning the perception of caloric irrigations were based on the maxSPV from warm caloric irrigation in the left ear only.

A logistic regression was performed to predict the probability that a patient would report an absence of vertigo during the caloric test. The predictor variables were patient age, maxSPV of the caloric response, and patient gender. Results from the logistic regression model are shown in Table 2.

The overall model was statistically significant ($\chi^2(1) = 20.064$, $p < .001$), indicating that the predictors, as a set, reliably predict caloric perception. The model with all predictors (age, maxSPV, gender) accounted for 29% of the variance in caloric perception and correctly classified 79.3% of cases (see Table 3). As shown in Table 3, the correct prediction of perceiving vertigo was 94.2%. However, the correct prediction of the absence of caloric perception, a rarer event, was only 34.8%.

Table 2 shows that the significant predictors include age and maxSPV and non-significant coefficients were produced for gender. Thus, the gender of the patient did not significantly predict whether they perceived vertigo during the caloric test. The negative coefficient for maxSPV indicates that the finding of an absent caloric perception decreases as maxSPV increases. Further, the odds ratio for maxSPV is less than 1 (OR = .910, 95% CI = .856, .968) indicating that the absence of vertigo perception is less likely to occur as maxSPV increases. Specifically, for every 1 deg/sec increase in maxSPV, the likelihood of an absent percept of vertigo is .9 times as likely. In other words, the odds are decreased by ~10%.

In contrast, the absence of caloric perception increases as age increases. That is, the absence of vertigo perception is more likely to occur as age increases. Although age is a significant predictor, the odds ratio is very small. For every 1 year increase in age, the likelihood of an absence of vertigo perception during the caloric test increases by a factor of 1.06 (OR = 1.061, 95% CI = 1.024, 1.099). In other words, the odds are increased 6% per year.

Patient age and caloric maxSPV were positively and weakly correlated (r = .312, p = .002) and data are shown in Fig. 1.

Table 2
Logistic regression analysis of vertigo perception as a function of the predictor variables age, maxSPV, and gender. Odds ratios are given with 95% confidence intervals.

Predictor variables	*B*	S.E.	Wald χ^2	p	Odds ratio	95% Confidence interval for odds ratio	
						Lower	Upper
Age (years)	.059	.018	10.598	.001	1.061	1.024	1.099
maxSPV (deg/sec)	-.094	.031	9.045	.003	.910	.856	.968
Gender	.416	.563	.545	.461	1.515	.502	4.572
Constant	2.193	1.234	3.158	.076	.112		
Model χ^2	20.064			.000			
Nagelkerke R^2	.290						

B = coefficient in log-odds units.
S.E. = standard errors associated with the coefficients.
maxSPV = maximum slow phase velocity.

Table 3
Classification Table showing the observed and predicted values of the dependent variable (caloric perception) based on the full logistic regression model. The table shows how many cases were correctly predicted and how many cases were not correctly predicted. The table also shows the overall percent of cases that were correctly predicted by the model.

		Predicted vertigo		Percentage correct
		Yes	No	
Observed vertigo	Yes	65	4	94.2
	No	15	8	34.8
Overall percentage				79.3

4. Discussion

The current investigation demonstrated that both decreasing age and increasing maxSPV were associated with an increased likelihood of experiencing a sensation of movement during the caloric exam. However, not all patients who reported an absence of caloric perception were over the age of 65. Although much is known about the effects of age on the peripheral vestibular system (e.g. Ishiyama, 2009), the effects of age on the sensation of movement during vestibular stimulation (i.e. whether induced via the caloric test, physiologic movement, or secondary to a vestibular lesion) remains unclear.

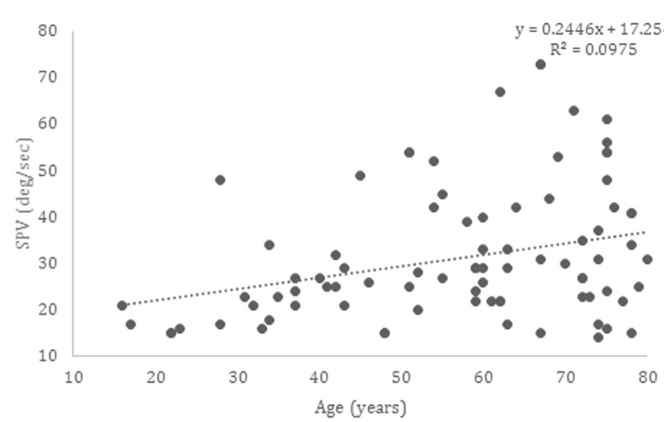

Fig. 1. Correlation between maxSPV (deg/sec) and age (years). Scatterplot showing maxSPV (deg/sec) as a function of age (years), including a best line of fit showing a linear regression. A weak, positive relationship is illustrated between caloric maxSPV and age. That is, as subject age increases so does maxSPV for the warm a caloric stimulus.

4.1. Self-report perception of vertigo

A lack of vertigo perception in elderly patients following provocation (e.g. following caloric irrigation or during a positive Dix-Hallpike maneuver) has been previously reported (Batuecas-Caletrio et al., 2013; Fernandez et al., 2015; Piker and Jacobson, 2014; Tuunainen et al., 2012). Batuecas-Caletrio conducted a retrospective review of 404 patients diagnosed with BPPV and assessed the clinical presentation, including self-report symptoms, in their patient cohort grouped by age (i.e. those ≥70 years of age and those younger than 70 years). Remarkably, 31.3% of BPPV patients over the age of 70 years reported unsteadiness as their primary symptom, not spinning vertigo. Only 10.6% of the younger group reported unsteadiness while 89.4% reported vertigo (Batuecas-Caletrio et al., 2013). Piker and Jacobson (2014) conducted a retrospective review of case histories from 233 consecutive dizzy patients and compared results between younger (ages 18−64 years) and older (65 years and older) patients. Perception of rotation or spinning was observed in 65% of the younger adults and only 32% of older adults. The odds of reporting true vertigo were 4 times greater in younger adults compared to adults over the age of 65. However, older patients were 3 times more likely to present with BPPV (Piker and Jacobson, 2014), a condition in which we typically expect perceptions of short-lasting but intense spinning vertigo.

4.2. Central integration and perception of self-motion

The absence of vertigo perception in older adults in scenarios where we expect vertigo to be perceived (i.e. during a caloric irrigation, BPPV) may represent an impairment of central transmission, reception, or integration of peripheral vestibular system information. Central integration of vestibular input is believed to contribute to our conscious awareness of self-motion (Brandt and Dieterich, 1999). Sensations of self-motion can be induced by electrical stimulation of the intraparietal sulcus and the posterior part of the superior temporal gyrus in humans (Penfield, 1957). These results implicate the parieto-temporal lobe in the perception of vertigo. Animal studies in nonhuman mammals have suggested this region in humans to be analogous to the "vestibular cortex" in monkeys (Brandt and Dieterich, 1999). Further, patients with known ischemic lesions involving the parieto-temporal lobe have been reported to experience an absence of vertigo during the caloric exam (Takeda et al., 1995) and the perception of vertigo correlates with cerebral blood flow in the parietal lobe (Takeda et al., 1996). Specifically, Takeda and colleagues examined the effects of caloric stimulation on the regional cerebral blood flow of both the temporal and parietal cortex in 10 healthy volunteers. Although there was no difference in maximum slow phase eye velocity between subjects (i.e. vestibular-ocular reflex [VOR] was intact), 4 subjects reported no sensation of vertigo, 4 subjects reported vertigo, and 2 subjects reported dizziness. In other words, the absence of caloric perception was observed in a subset of individuals with intact peripheral vestibular system function. Although the degree of self-motion perception induced by the caloric test was not associated with the magnitude of the VOR, it was correlated with the magnitude of cerebral blood flow in the parietal lobe (Takeda et al., 1996). Their findings suggest that the parietal lobe is involved in the perception of caloric-induced vertigo.

Both cross-sectional and longitudinal imaging studies in healthy older adults have shown extensive white matter damage and gray matter loss greater in the parietal and frontal lobar regions compared with temporal and occipital lobes (e.g. Courchesne et al., 2000; Resnick et al., 2003). These findings are observed even in very healthy older adults (Resnick et al., 2003). Tissue loss in these regions may account for changes in central integration of sensory input from peripheral vestibular organs, possibly manifesting as the absence of caloric-induced vertigo. Furthermore, the same white matter changes are associated with decreased performance in cognitive functioning and changes in postural stability (e.g. Baloh et al., 2003; Gunning-Dixon and Raz, 2000).

5. Study limitations and future studies

This was a relatively small sample (i.e. N = 92). It is possible that additional information could be obtained by increasing the sample size and determining whether the age differences we observed occurred only for patients who reported rotatory perceptions.

Although age was a significant predictor for an absence of motion perception during the caloric exam, the effect size was small (Chen et al., 2010). The closer the odds ratio is to 1, the smaller the effect and the odds ratio for age and maxSPV were 1.06 and .9, respectively. Furthermore, the total model only accounted for 29% of the variance. Thus, there are other factors that determine an individual's perception of motion during the caloric test. These factors may include random individual variation due to the subjective nature of vertigo perception, susceptibility to motion sensitivity/sickness, state anxiety levels, conditions that may result in heightened sensory awareness (e.g. migraine), and various unknown variables. Additionally, the caloric test does not constitute a true physiologic stimulus so it may be that these individuals simply did not perceive the effects from the caloric and this finding does not generalize to any other aspect of vestibular processing. Future studies examining the relationship between these many other factors and caloric perception may help to explain a greater percentage of the variance.

In order to further examine the premise of a central integration impairment, future studies should also focus on the association between the absence of caloric perception and functional consequences of not perceiving caloric perception. Specifically, the functional consequences we would expect to find in central vestibular lesions, namely changes in cognitive function and gait and balance function. These would include specific areas of cognition such as spatial navigation and spatial memory, as these are known to be directly affected by vestibular loss (e.g. Brandt et al., 2005; Kremmyda et al., 2016).

6. Summary

The current investigation showed that both age and maxSPV of the caloric response were significant predictors of vertigo perception during the caloric exam. However, the association between age and caloric perception is not definitive as approximately half of the patients reporting an absence of vertigo were under the age of 65 years. The association between age and vertigo perception is worth exploring further as there is evidence showing differences in self-report symptoms, specifically a lack of spinning sensations, in older patients with BPPV compared to younger patients and there is ample evidence suggesting that the lack of vertigo perception is a central processing issue.

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