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Vestibular perception and the vestibulo-ocular reflex in young and older adults

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INTRODUCTION

Imbalance affects more than 30% of the population over the age of 65 and over half of the elderly by age 90 (Colledge et al. 1994; Jonsson et al. 2004). About one-third of community-dwelling elderly persons and 60 percent of nursing home residents suffer falls related to imbalance each year (Fuller 2000). Ten percent of older persons who fall sustain serious injuries such as fractures, joint dislocations, or severe head injuries (Sterling et al. 2001). Falls are the leading cause of accidental death in people older than 65 years (CDC 2003). Loss of vestibular function is correlated with increased risk of falling in the elderly (Fife and Baloh 1993; Murray et al. 2005; Pothula et al. 2004).

Important and innovative tests have been developed recently for identifying vestibular lesions (Colebatch and Halmagyi 1992; Halmagyi and Curthoys 1988), but the most commonly used measures, such as rotational chair testing and caloric nystagmography, remain essentially the same as when they were developed a century ago (Bárány 1906). These common tests have wide ranges for normal responses and are strongly subject to variations in technique (Baloh et al. 1984; Gonçalves et al. 2008; Ward et al. 2008). They also correlate poorly with symptoms of imbalance in the elderly (Baloh et al. 2003). This suggests that development of improved or alternative measures vestibular function would be of broad value, including identifying older adults with a risk of falling and in improving our knowledge of the pathophysiology contributing to falls in the elderly.

One possible alternative test of vestibular function is the quantification of psychometric thresholds (Bourke et al. 2012; Guedry 1974). Psychometric thresholds have long been considered to be attractive methods for measuring vestibular function (Veits 1931), although interest in them has been eclipsed until recently by the ubiquitous use of reflexive vestibular

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responses such as the vestibulo-ocular reflex (VOR). One early method of quantification was to measure the time required during a constant rotational acceleration about the earth-vertical axis before a subject noted a sense of turning. This time, multiplied by the rotational acceleration, was termed “Mulder’s Product.” This value was found to be about 2 deg/sec across a range of normal subjects (Van Egmond et al. 1949). Another method was to stop the movement of a subject rotating at various velocities. The highest velocity at which the subject did not report the perception of an “after-rotation” was defined as the threshold (Van Egmond et al. 1949). Thresholds calculated using this technique were reported to be between 1 and 4 deg/sec, with an average of about 2.5 deg/sec. These values corresponded well to threshold expressed as Mulder’s product (Bourke et al. 2012). Later work using sinusoidal stimuli, analogous to those provided by a “torsion swing” or rotating Bárány chair for measuring the VOR, showed that thresholds to rotations about the vertical plane depended on the frequency of stimulation, with lower frequencies having higher thresholds (Benson et al. 1989; Valko et al. 2012).

We recently investigated psychophysical thresholds to vestibular stimuli by measuring *discrimination* between suprathreshold rotational velocities in addition to the threshold to *detection* of movement as had been done previously (Mallery et al. 2010). This was motivated by the observation that few natural head movement trajectories actually contain the onset of motion from a dead stop, meaning that discrimination thresholds might be a highly relevant metric for measuring vestibular function in realistic situations. This offers another possible method for gaining information from psychophysical techniques. Here, we compared the detection and discrimination perceptual thresholds of younger and older adults. We also compared these values to the phase and gain of their VOR to evaluate the relationship between psychometric and reflexive vestibular measurements.

MATERIALS AND METHODS

The Washington University School of Medicine Human Studies Committee approved this study. 19 younger (range 20–26 years, mean $\pm$ SD = 22 ± 2) and 16 older (range 63–84 years, mean $\pm$ SD = 73 ± 7) people took part in the study. Exclusion criteria were a history of otologic or neurologic disease or a history of falling. All older subjects passed the Short Blessed Test as a screen for intact cognition (Katzman et al. 1983). Pure tone average (500, 1000, and 2000 Hz) auditory thresholds of older subjects in the left ear were 27 ± 14 dB HL (mean $\pm$ SD) and in the right ear were 28 ± 12 dB HL. Pure tone averages (PTA) were collected from a subsample of six of the younger subjects. In five of the younger subjects, PTAs were 10 ± 3 in the left ear and 9 ± 3 in the right ear. A sixth young participant was unexpectedly found to have a bilaterally symmetric “cookie-bite” audiogram with thresholds of about 40 dB at 1 kHz. His data were excluded from statistical analysis with the rest of the younger group but are described separately. With his removal, the age range of the younger subjects was 20–25 years, mean $\pm$ SD = 22 ± 1 . All participants verified sound cues in the experiment to be easily audible.

The experimental apparatus consisted of a customized race car seat rotated about the earth-vertical axis by an electric motor (Kollmorgen Goldstar DDR D063M7, Danaher Motion, Radford, VA). Subjects were held in the chair using a four-point harness and were

surrounded by foam padding to reduce proprioceptive feedback. Headphones (FM Basic 26000, MSA Sordin, Värnamo, Sweden or MDR-7506, Sony, Japan) provided Gaussian noise generated by Matlab (MathWorks, Natick, MA) to prevent perception of external noise. Chair motion was generated by custom-written software in Matlab and sent to the chair controller via the Matlab Data Acquisition Toolbox in conjunction with a National Instruments Data Acquisition device (BNC-2090, Austin, TX). No subject reported being aware of motor noise or other possible motion cues during the experiment. Details of this method have been published previously, including control experiments by us and others to verify that vibratory or proprioceptive cues did not contribute to rotational thresholds over the range of stimulus intensities presented here (Mallery et al. 2010; Valko et al. 2012).

Two separate psychophysical experiments were performed. In each experiment, subjects were presented with sinusoidal rotations about the earth-vertical axis at a frequency of 0.5 Hz. Experiments consisted of a series of trials, each of which took the form of a two-alternative, two-interval forced-choice task consisting of a reference stimulus and a comparison stimulus. Subjects chose which of two sequential sinusoidal stimuli was “faster.” For detection thresholds, the reference stimulus was defined to be 0 deg/sec and for discrimination thresholds the reference stimulus was 60 deg/sec.

For the experiments here, we used a “three-down one-up” adaptive staircase paradigm (Levitt 1971). If the subjects correctly identified the comparison as being faster three consecutive times, the comparison stimulus was reduced (brought closer to the reference stimulus) to make the task harder. A single error increased the comparison stimulus. Eventually, this three-down, one-up paradigm stabilizes at a point where the subject is correct 79% of the time, which was defined here as the threshold.

The starting comparison velocities were determined based on several initial trials for each subject so that they always started well above threshold in a range where they were confident and correct in their answers. Starting comparison velocities for the detection experiment were 2, 1.5, or 1 deg/sec for younger subjects and 5 deg/sec for older subjects. For the discrimination experiment, starting comparison velocities were 70 or 75 deg/sec. The order of the two intervals was randomized, with the envelope of the sinusoidal stimulus modulated according to a raised cosine. The subjects were cued with an 800 Hz tone to indicate when each interval occurred (Fig. 1). Subjects were asked to identify which interval was “faster.” Step sizes were set to be 0.1 deg/sec for detection thresholds and 0.5 deg/sec for discrimination thresholds, with the threshold determined by averaging the last five reversals (Macmillan and Creelman 2005).

The VOR in response to harmonic sinusoidal rotations about the earth-vertical axis was determined in a convenience sample of 11 of the older subjects at frequencies of 0.025, 0.05, 0.25, and 0.5 Hz and peak velocity of 60 deg/sec using standard clinical equipment (System 2000, Micromedical Technologies, Chatham, IL).

RESULTS

A scatterplot of the detection thresholds is shown in Fig. 2A. The mean threshold ($\pm$ SD) of the younger population was 0.69 ± 0.29 deg/sec and of the older population was 0.81 ± 0.42 deg/sec. There was no statistical difference between the thresholds of the two groups (Mann-Whitney, $p = 0.45$). Discrimination thresholds are shown in Fig. 2B. The mean discrimination threshold of the younger population was 4.83 ± 1.80 deg/sec and of the older population was 4.33 ± 1.57 deg/sec. These discrimination thresholds were also not different between the younger and older subjects (Mann-Whitney test, $p = 0.41$).

The relationship between detection and discrimination thresholds for younger and older subjects is shown in Fig. 3. There was no correlation between detection and discrimination thresholds in either the younger (Spearman's $r = 0.10$, $p = 0.72$) or the older (Spearman's $r = 0.41$, $p = 0.12$) subjects.

The average gains and phase leads of the VOR in both the older and younger subjects are shown in Table 1. Two-way repeated-measures ANOVA of the VOR results indicated no significant difference in gain and phase lead between the two age groups across frequencies (between age-groups: Gain: $F(1, 42) = 0.23$, $p = 0.64$; Phase: $F(1, 42) = 2.55$, $p = 0.13$). The relationship of VOR gain and phase to psychophysical thresholds for older people is shown in Fig. 4. Across all frequencies, there was no significant relationship of thresholds to VOR gain or phase in younger or older subjects (Table 2).

Among the younger group whose audiometric thresholds were found to be normal, PTAs varied from 7 to 13 dB HL. There was no relationship between PTA and vestibular thresholds in this group (Spearman's r : detection threshold: $r = -0.10$, $p = 0.95$; discrimination threshold: $r = -0.80$, $p = 0.33$). We also tested one younger subject with abnormal audiometric thresholds (PTA = 43 dB HL). Despite his elevated audiometric threshold, his vestibular detection and discrimination thresholds were normal. Among the older group, PTAs varied from 10 to 48 dB HL. There was no relationship between PTA and vestibular thresholds among older people (Spearman's r : detection threshold: $r = 0.43$, $p = 0.069$; discrimination threshold: $r = -0.14$, $p = 0.58$).

DISCUSSION

A primary purpose of this work was to determine the effect of aging on psychophysical thresholds. We found no significant difference between the detection thresholds of younger and older subjects undergoing 0.5 Hz earth-vertical sinusoidal rotations determined using a two-alternative, two-interval forced choice paradigm. This confirms an earlier study of detection thresholds, which also found no relationship to age while using a somewhat different, single-interval paradigm consisting of solitary raised-cosine rotations at 0.5 Hz (Roditi and Crane 2012). Others have also failed to find a difference with age, with one study finding that thresholds to motion along a 0.5 Hz triangular velocity trajectory about the earth-vertical axis remained stable across a range of ages (Seemungal et al. 2004). Others, however, have found that other stimulus conditions did result in age-related changes in detection thresholds. Roditi and Crane (2012) found that detection thresholds to rotations

about the earth-vertical axis at higher stimulus frequencies than 0.5 Hz increased with age, and Kingma (2005) showed a similar age-related effect measuring linear accelerations along the nasal-occipital axis (Kingma 2005; Roditi and Crane 2012).

We extended the results of these previous studies to examine *discrimination* rather than just *detection* thresholds. This was motivated by previous work in other sensory systems demonstrating that discrimination thresholds provide additional information that detection thresholds do not. In the auditory system, the SISI (Short Increment Sensitivity Index), for example, quantifies audiometric discrimination thresholds, rather than detection thresholds, as a specific measure of cochlear damage in sensorineural hearing loss. A person may have good detection (i.e., normal thresholds on an audiogram) but poor SISI results (Buus et al. 1982a, 1982b). Speech recognition can also be considered a discrimination test of supra-threshold auditory performance as opposed to pure-tone average measurements, which represent a detection task. Discrimination performance is also important in the diagnosis of abnormalities in other sensory systems. In the visual system, loss of contrast sensitivity is a sensitive early marker of glaucoma (Hawkins et al. 2003).

By analogy, discrimination thresholds might also be expected to provide complementary information for vestibular measurements. First, the consequences of imbalance, such as falls, may occur more commonly when the head and body are already in motion (analogous to a discrimination task) rather than from a stationary position (which might be better measured using a detection task). Second, detection and discrimination thresholds may be influenced by anatomically and physiologically distinct parts of the peripheral system. Three different populations of vestibular afferents originate in the vestibular periphery, with each thought to be tuned to carry information about specific frequencies or velocities of head movements (Baird et al. 1988; Hullar et al. 2005; Sadeghi et al. 2007; Straka and Dieringer 2004). It seems reasonable to at least speculate that discrimination thresholds could depend on the function of afferent classes tuned to higher stimulus intensities, whereas detection thresholds might be better at representing the function of afferents that preferentially signal lower intensity head movements.

We found for the first time that discrimination thresholds did not change with aging in a population of normal subjects. This allowed us to examine further the findings of Roditi and Crane, who found that thresholds did not change with aging during an earth-vertical rotation task at 0.5 Hz but did at a higher frequency (Roditi and Crane 2012). It was uncertain based on their study whether the changes seen with aging were specific to the higher frequency or might have actually been more closely dependent on the higher accelerations also inherent in that higher stimulus. As our discrimination stimulus tested function at the same frequency but higher accelerations, and we found no elevation of thresholds with aging, it could be concluded that the effect seen by Roditi and Crane (2012) may have indeed been determined by frequency more than acceleration.

We chose to use a 0.5 Hz stimulus because it is within the frequency range over which the semicircular canals are believed to contribute meaningful information about head movements, because its relatively short duration limited the overall time required to complete the psychophysical task, and because it allowed us to compare our results to

previous work in our laboratory (Mallery et al. 2010). We have previously shown that discrimination thresholds in normal young people increase at higher reference stimulus amplitudes, exceeding the prediction provided by Weber's Law (Mallery et al. 2010). This suggests that discrimination thresholds, like detection thresholds, are highly stimulus dependent and using a different stimulus paradigm (such as other frequencies or comparison velocities) might uncover a relationship with aging that is not evident here (Benson et al. 1986; Grabherr et al. 2008; Haburcakova et al. 2012; Mallery et al. 2010). Making that observation would itself be revealing, as these differences would offer an additional avenue for clinical or basic-science applications of perceptual tasks.

The other major purpose of this study was to determine the relationship of psychophysical thresholds to conventional measures of vestibular reflexes in response to rotation. Several previous studies have shown that subjects with extreme levels of vestibular loss do have elevated thresholds. For example, we have previously reported psychophysical thresholds in a patient with congenital loss of vestibular function due to cytomegalovirus infection, resulting in no measurable VOR (Mallery et al. 2010). This patient had dramatically elevated detection thresholds for earth-vertical rotations at 0.5 Hz of 37 deg/sec and a discrimination threshold at reference velocity of 40 deg/sec of 28 deg/s, with these thresholds probably achieved with input from proprioceptive or vibratory inputs. A similar result was also seen in an experiment with a different design, where three bilaterally vestibular-deficient subjects demonstrated no perception of rotation when seated in a chair performing steps of increasing acceleration up to a maximum velocity of at least 82.5 deg/sec (Cutfield et al. 2011). That study also found that a group of 12 subjects with unilateral loss demonstrated elevation of both reflexive and nystagmic thresholds. In the otolith system, a similar correlation between psychophysical threshold and reflexive performance has been seen across a range of oVEMP responses (Agrawal et al. 2013). We therefore conclude that the thresholds reported here were very unlikely to have been influenced by somatosensory cues.

Whereas psychometric studies may not add extra information in subjects whose vestibular reflexive responses are decreased, here we attempted to determine the relationship between psychometric and reflexive responses in subjects with normal or near-normal angular VOR. We found no evidence of a strong relationship between gain or phase thresholds and detection or discrimination thresholds measured at 0.5 Hz, suggesting that psychometric results may indeed provide information not available from reflexive measurements alone. Recent data suggest, for example, that subjects with migraine have altered perceptual thresholds to tilt although they do not necessarily have different VOR responses than normal controls (Lewis et al. 2011; Sharon and Hullar 2013). The finding that there is no close correspondence between perceptual values and the VOR supports the concept that the two may indeed carry different information about peripheral vestibular function leading, likely dictated by higher-order processes (Merfeld et al. 2005a, 2005b). This difference might be exploited in the future to investigate conditions such as chronic imbalance, mal de debarquement, migraine-induced imbalance, or even a history of falling in the elderly whose source might be found in higher-level circuits than those governed exclusively by the VOR.

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Figure 1.

Stimulus trajectories. Black line represents chair velocity, where positive numbers indicate rightward yaw in the subject's frame of reference (clockwise when viewed from above). Gray bars represent the duration of the signal tone. Panel A: Detection paradigm. In the example trial illustrated here, the comparison interval had a peak velocity of 1.5 deg/sec and came after the reference interval, which for the detection paradigm had a peak velocity of 0 deg/sec by definition (stationary). Panel B: Discrimination paradigm. In this case, the comparison interval had a velocity of 65 deg/sec and came before the reference interval, which for the discrimination paradigm always had a peak velocity of 60 deg/sec.

Figure 2. Detection and discrimination thresholds as a function of age. Filled symbols, young subjects; open symbols, older subjects. Panel A: Detection thresholds. Panel B: Discrimination thresholds, with respect to a reference velocity of 60 deg/sec.

Figure 3.

Discrimination thresholds as a function of detection thresholds. Dark diamonds, young subjects; open diamonds, older subjects. Discrimination thresholds determined with respect to a reference velocity of 60 deg/sec.

Figure 4. Psychophysical thresholds as a function of VOR in older subjects. Left, gain; right, phase. Circles, detection; squares, discrimination.

Table 1

VOR	0.025 Hz		0.05 Hz		0.25 Hz		0.50 Hz	
	Subjects	Gain	Phase	Gain	Phase	Gain	Phase	Gain
Old		0.50 ± 0.05	23.82 ± 8.70	0.55 ± 0.08	14.55 ± 5.05	0.58 ± 0.13	3.45 ± 3.83	0.75 ± 0.13
Young		0.53 ± 0.12	17.00 ± 8.19	0.56 ± 0.06	10.20 ± 2.28	0.59 ± 0.04	2.20 ± 1.64	0.79 ± 0.10

Gain and phase lead (deg re velocity) of VOR (mean ± SD)

Table 2

Frequency	Gain		Phase	
	Detection	Discrimination	Detection	Discrimination
0.025	<i>0.56 (0.35)</i>	<i>-0.21 (0.92)</i>	<i>-0.60 (0.35)</i>	<i>0.00 (1.0)</i>
	0.27 (0.42)	-0.22 (0.52)	0.01 (0.97)	0.22 (0.51)
0.05	<i>0.21 (0.78)</i>	<i>0.74 (0.33)</i>	<i>-0.67 (0.23)</i>	<i>0.00 (1.0)</i>
	0.38 (0.24)	-0.04 (0.90)	0.42 (0.20)	0.40 (0.22)
0.1	<i>0.50 (0.45)</i>	<i>0.60 (0.42)</i>	<i>0.21 (0.78)</i>	<i>0.40 (0.75)</i>
	0.37 (0.26)	0.08 (0.81)	0.04 (0.91)	0.41 (0.21)
0.5	<i>0.50 (0.45)</i>	<i>-1.00 (0.08)</i>	<i>0.41 (0.52)</i>	<i>0.60 (0.42)</i>
	0.16 (0.63)	0.18 (0.60)	-0.46 (0.15)	-0.51 (0.11)

Relationship of VOR to psychophysical thresholds (Spearman's rho; p-value in parentheses).

Younger subjects italicized, older subjects bolded.