Aging and the peripheral vestibular system

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ABSTRACT

Whereas much has been learned about age-related auditory changes in the inner ear, relatively little is known about the aging effects on the vestibular part of the inner ear—the peripheral vestibular system. Here we review relevant literature with regard to the prevalence of vestibular dysfunction, vestibular functional and structural changes in the elderly. The prevalence of vestibular dysfunction increases with age. Functionally, as age increases, VEMP amplitudes decrease, VEMP thresholds increase, VOR gain of HIT decreases. Due to the complexity of the vestibular system, variations in subject age and measurement techniques, findings in VEMP latency and caloric tests are conflicting. To address this, a direct measure of the peripheral vestibular system should be applied. Structurally, age-related loss in vestibular ganglion and otocochlea have been noted; hair cell changes are not well defined; while subcellular changes remain to be explored. Defining how the onset of vestibular dysfunction correlates with structural degeneration will offer insights into the mechanisms underlying vestibular aging.

The inner ear consists of the cochlea and vestibular organs. The two are similar but different. They have same receptors (hair cells) and same internal environment (endolymph). The cochlea detects sound, while the vestibular organs detect head motion. Aging of the cochlea has been extensively studied, but we know relatively little about age related effects on the peripheral vestibular system. Our aim is to review the prevalence of vestibular dysfunction, and functional and structural changes of the peripheral vestibular system in the elderly.

1. Prevalence of vestibular dysfunction in the elderly

In the US, vestibular dysfunction affects 18% of adults aged 40 to 49, 49% of adults aged 60 to 69 and more than 80% of people aged over 80 years (Agrawal et al., 2009). In Connecticut, 24% (261 of 1087) of citizens aged over 72 years reported dizziness (Tinetti et al., 2000); while in North Carolina, more than 30% of the elderly reported dizziness (Sloane et al., 2001). These results suggest that the prevalence of vestibular dysfunction increases with age, and that some elderly with vestibular dysfunction may not report dizziness.

Benign paroxysmal positional vertigo (BPPV) is the most frequent form of peripheral vestibular dysfunction (Neuhausser et al., 2005). It accounts for 8% of dizziness/vertigo in the general population (von Brevern et al., 2007), 34% of dizziness in persons aged 50 years and older (Davis, 1994), and 39% of dizziness in persons 70 years and older (Katsarkas, 1994). The prevalence of BPPV increases with age such that it is seven times higher in those aged 65 years and over relative to those aged 15–40 years (Liu et al., 2017; von Brevern et al., 2007).

Vestibular dysfunction significantly contributes to falls in the elderly (Liston et al., 2014). Falls and related injuries (e.g. fractures, joint dislocations, and head injury) are the sixth highest cause of death (Dunn et al., 1992; Sterling et al., 2001).

2. Functional aging of peripheral vestibular system

Vestibular organs consist of the utricle, saccule and three semicircular canals. Otolith organs (utricle and saccule) detect linear accelerations of head. The horizontal, anterior and posterior semicircular canals detect head rotations around a vertical axis, in the sagittal plane and frontal plane, respectively. Here we investigate changes in four measurements of these vestibular organs: c-VEMP, o-VEMP, caloric test and head impulse test (HIT).

Cervical vestibular evoked myogenic potentials (cVEMP) is recorded from sternocleidomastoid muscle (SCM) and is a manifestation of the vestibulo-spinal reflex and saccular function. cVEMP response rate, threshold and amplitude remain steady until up to 50–60 years of age.
(Li et al., 2015a; Singh et al., 2014; Su et al., 2004). Then threshold increases, amplitude and response rate decline (Agrawal et al., 2012; Akin et al., 2011; Brantberg et al., 2007; Layman et al., 2015; Li et al., 2015a; Maes et al., 2010; Maleki et al., 2014; Nguyen et al., 2010; Singh et al., 2014; Su et al., 2004). Among those changes, age-related decreases in cVEMP amplitude have been observed in all the studies which indicates that cVEMP amplitude is a sensitive indicator of vestibular aging. Most investigators find age-related latency increases (Brantberg et al., 2007; Li et al., 2015a; Maleki et al., 2014; Singh et al., 2014; Su et al., 2004), while few fail to find any change in p1 latency or n1 latency (Layman et al., 2015; Nguyen et al., 2010; Su et al., 2004). Different stimulations (tone burst or click) and sex ratio may account for the inconsistency.

Ocular VEMP (oVEMP) is recorded from the extraocular muscles and is a manifestation of the vestibulo-ocular reflex and utricular function. oVEMP response rate remains steady until up to 60–80 years of age and then decreases (Li et al., 2015a; Tseng et al., 2010). oVEMP shows age-related amplitude decreases, whether it’s stimulated by vibrations, clicks or tone bursts (Agrawal et al., 2012; Chang et al., 2012; Iwasaki et al., 2008; Layman et al., 2015; Li et al., 2015a; Nguyen et al., 2010; Rosengren et al., 2011; Tseng et al., 2010). Amplitude is reported to decrease by 2.9 μV/decade (Li et al., 2015a). As to the latency, all studies find age-related increases (Chang et al., 2012; Iwasaki et al., 2008; Layman et al., 2015; Rosengren et al., 2011; Tseng et al., 2010), although one does not (Nguyen et al., 2010). Women may be less likely to show this latency change than men (Layman et al., 2015).

In caloric test, warm and cool water or air in the ear canal stimulates the horizontal semicircular canal and cause nystagmus. Although increased slow-phase velocity has been noted in adults aged over 66 in one study (Maes et al., 2010), other studies fail to find any age-related changes in caloric testing (Mallinson and Longridge, 2004; Zapala et al., 2008).

Head impulse testing (HIT) can be used to test the function of the three semicircular canals. VOR gain-ratio of eye rotation to head rotation is usually close to 1 and decreases as the head velocity increases (Matiño-Soler et al., 2015; McGarvie et al., 2015). Age-related VOR changes also correlate with head impulse velocity. Linear VOR gain remains stable until age 70 years for head impulses at 180–200° per second, until age 79 years for impulses at 160–180° per second and until age 90 years for head impulses less than 160° per second (Agrawal et al., 2012; Li et al., 2015b; Matiño-Soler et al., 2015; McGarvie et al., 2015). Thereafter, linear VOR gain declines by 0.012 per year (Li et al., 2015b; Mossman et al., 2015). Moreover, the amplitude of compensatory saccade increases with age in that adults aged around 76 years made larger compensatory saccades compared with adults aged 45 (Anson et al., 2016). Vertical VOR gain remains stable until 89 years of age (McGarvie et al., 2015).

As we noted, c- and o-VEMP decline after 50–60 years of age; VOR of HIT decline after 70–90 years of age. It could be that the otolith organs degenerate earlier than the semicircular canals. Or perhaps the VOR is compensated by central gain (Karmali et al., 2018). The conflicting findings could be due to the complexity of the vestibular system, variation in subject age, and variation in measurement techniques.

cVEMP, oVEMP, caloric test and HIT are indirect measurements of the peripheral vestibular function. cVEMP depends on vestibular-spinal reflex; oVEMP, caloric test and HIT depend on VOR. Both reflexes involve the vestibular nerve, vestibular nucleus, accessory nucleus (e.g. abducens nucleus) and muscles (e.g. extraocular muscles). This means that the tests may be affected by components other than the vestibular part of the reflex. Direct measures of vestibular function combined with measures of VOR can provide a more complete analysis of peripheral vestibular function. To directly measure peripheral vestibular function, we test vestibular sensory evoked potential (VsEP) in animal models. This compound action potential is generated by the vestibular nerve in response to linear head acceleration and relayed to the brain through the vestibular pathway. We should explore application of VsEP in human subjects and compare with existing methods.

3. Structural aging of the vestibular system

Two types of hair cells (Type I and Type II) are located in the five vestibular organs. Type I and Type II hair cells differ in morphology. Most studies found a decline in type I, type II and total hair cell density and number in the five organs in subjects with a mean age of 84 years and 94 years (Lopez et al., 2005; Merchant et al., 2000; S. D. Rauch et al., 2001; Walther and Westhöfen, 2007). Type I hair cells decline at a greater rate in the cristae than in utricle and saccule; type II hair cells decline at the same rate in the five vestibular end organs (Merchant et al., 2000; Rauch et al., 2001). However a study based on unbiased stereological analysis finds no age-related loss of hair cells in utricles of subjects with a mean age of 82 years (Gopen et al., 2003). The two types of hair cells are organized in two clearly distinguishable zones (central/striolar zone and peripheral/extrastriolar zone) of the vestibular sensory epithelia. These two zones differ in spike timing, cell organization and afferent innervation. For now, we do not have a clear understanding about the effect of aging on the two zones.

The vestibular ganglion (Scarpa’s ganglion) innervates hair cells through synaptic contact. The number of ganglion cells decline after 30 years of age by 57 cells per year (Park et al., 2001; Velázquez-Villasenor et al., 2000). Although the vestibular nerve fiber shows no change in number during aging, amylod bodies (pathologic proteinaceous fibrous aggregates) in the nerve show an increase in the transverse area (Fuji i et al., 1990).

Otoconia are bio-crystals in the saccule and utricle which sense linear acceleration and gravity through displacement of otoconia. Otoconia show a decrease in numbers, volume, and changes in shape during aging, both in the saccule and utricle (Igarashi et al., 1993; Walther et al., 2014; Walther and Westhöfen, 2007). And otoconia in the saccule degenerate at a greater rate than those in utricle (Igarashi et al., 1993).

As we know, vestibular hair cell synapses release neurotransmitter in response to head movement, onto the post synaptic afferent. Synapses in auditory hair cells are more susceptible to noise and aging than hair cell itself (Kujawa and Liberman, 2009; Makary et al., 2011). Whether this is true for synapses in vestibular hair cells remains to be explored.

4. Conclusion

In summary, the prevalence of vestibular dysfunction goes up with age. Functionally, as age increases, VEMP amplitudes decrease, VEMP thresholds increase, VOR gain of HIT decrease. Due to the complexity of the vestibular system, variations in subject age and measurement techniques, findings in VEMP latency and caloric test are conflicting. To address this, we should apply a direct measure of the peripheral vestibular system. Structurally, age-related loss in vestibular ganglion and otoconia have been noted; hair cell changes are not well defined; subcellular changes remain to be explored. Defining how the onset of vestibular dysfunction correlate with structural degeneration will offer insights into mechanisms underlying vestibular aging.

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