Why dizziness is likely to increase the risk of cognitive dysfunction and dementia in elderly adults

Paul F Smith

ABSTRACT
Dementia is recognised to be one of the most challenging diseases facing society, both now and in the future, with its prevalence estimated to increase substantially by 2050. The potential contributions of age-related sensory deficits have attracted little attention until recently, when a landmark study suggested that hearing loss could be a greater risk factor for dementia than hypertension, obesity, smoking, depression, physical inactivity or social isolation. Over the last decade, evidence has been gradually accumulating to suggest that the other part of the inner ear, the balance organs or ‘vestibular system’, might also be important in the development of cognitive dysfunction and dementia. Increasing evidence suggests that dizziness associated with vestibular dysfunction, a common reason for patients consulting their GPs, increases the risk of cognitive dysfunction, including dementia, and our understanding of the basic neurobiology of this sensory system supports this view. This paper aims to review and critically evaluate the relevant evidence.
‘otoconia’ (calcium carbonate crystals) that generate an inertial force on the hair cells during head movement, causing a change in electrical potential (see Figure 2). In this respect, it is important to note that the most primitive form of the otoliths (‘statoliths’) are estimated to have evolved approximately 670 million years ago, and they exist in invertebrates such as jellyfish. This is their only means of detecting upright, which is necessary for survival. Therefore, given their evolutionary age, the otoliths might be expected to have developed major contributions to balance in humans. The vestibular system, through short-latency brainstem pathways, generates rapid eye movements that compensate for the unintentional movement of the head, eg, movement of the head due to the pulse beat (the vestibulo-ocular reflexes or VORs) and maintains the stability of the visual image of the world on the retina. The vestibular system also generates rapid vestibulo-spinal reflexes (VSRs) which adjust posture for unintentional movement, enabling us to keep our balance. Without a normal vestibular system, vision would become blurred (a condition known as ‘oscillopsia’) and balance and locomotion become disrupted.

Information about angular and linear head movement is also transmitted to higher centres of the brain, where it contributes to the conscious experience of moving through the environment and to cognitive processes such as memory. As we move through the environment, the vestibular hair cells in the semi-circular canals and otoliths detect every head movement, and transmit this information to areas of the brain such as the hippocampus, where it is assimilated and stored to provide a spatial map of our movements. This information is integrated with other sensory information, such as that from the visual, auditory, tactile, olfactory and proprioceptive systems, and formulated into mathematical maps of the spatial world, allowing us to navigate through it more effectively.

In the 1970s, specific neurons were discovered in the hippocampus that selectively discharged in response to specific areas of the environment. In 1944, the Nobel Prize in Medicine or Physiology was awarded to John O’Keefe, Edvard Moser and Britt-Mayer Moser for these discoveries, which have become known as the brain’s ‘global positioning system’.

In 2014, the Nobel Prize in Medicine or Physiology was awarded to John O’Keefe, Edvard Moser and Britt-Mayer Moser for these discoveries, which have become known as the brain’s ‘global positioning system’. Since then, both place cells and grid cells have been demonstrated to rely on vestibular information from the inner ear. Therefore, one reason why vestibular-related dizziness contributes to falls, is that not only does it impair fast vestibular reflexes such as the VORs and VSRs, but it impairs the ability of the brain to integrate self-motion information and to navigate through the spatial environment and form spatial memories. Information from the vestibular system is distributed widely throughout the central nervous system and is involved in higher cognitive function. There is increasing evidence that the otoliths may be important for cognitive processing independently of the semi-circular canals; this is one reason why the evolutionary age of the otoliths is of interest.

In recent years, a substantial amount of epidemiological evidence has been published to support the idea that age-related hearing loss is a risk factor for dementia. For example, in a seminal study published in the *Lancet*, it was reported that the contribution of hearing loss to the incidence of dementia was greater than hypertension, obesity, smoking, depression, physical inactivity and social isolation. This result seemed surprising, because sensory systems had never been considered particularly important to dementia, except perhaps for olfactory function as a potential biomarker.

It is important to note that the Livingstone et al study was based on data from high-income countries and the evidence from low-to-middle income countries is less convincing in this respect. Over the last several years, further evidence in support of the importance of hearing loss for the development of dementia has been published, although it is not entirely consistent.

Less attention has been given to the other part of the inner ear, the vestibular system (see Figure 1); however, evidence is mounting that age-related vestibular disorders could also be a significant risk factor for the development of cognitive dysfunction and dementia, along with
hearing loss. The vestibular system is known to degenerate with age, as with other sensory systems, with decreases in hair cells in the semi-circular canals and otoliths, a reduction in the number of neurons in the vestibular nerve and brainstem vestibular nucleus, and a deterioration of vestibular reflex responses. As shown in the Iceberg model in Figure 3, clinical presentation of age-related vestibular symptoms usually includes ‘presbystasis’ (the imbalance of disequilibrium) or ‘presbyvertigo’ (vertigo), or both, possibly with a decrease in vestibular perception; however, it is possible for age-related vestibular symptoms to be sub-clinical and therefore harder to detect. Animal studies supporting the role of the vestibular system in cognitive function

The literature relating the vestibular system to cognitive function, especially spatial memory, dates back to the 1960’s. Numerous studies have reported evidence

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vestibular disease</td>
<td>20–50%</td>
<td>Benign paroxysmal positional vertigo (BPPV), labyrinthitis, vestibular neuritis</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>10–30%</td>
<td>Arrhythmia, congestive heart failure, vasovagal conditions (eg, carotid sinus hypersensitivity)</td>
</tr>
<tr>
<td>Systemic infection</td>
<td>10–20%</td>
<td>Systemic viral and bacterial infections</td>
</tr>
<tr>
<td>Psychiatric conditions</td>
<td>5–15%</td>
<td>Depression, anxiety, hyperventilation</td>
</tr>
<tr>
<td>Metabolic disturbances</td>
<td>5–10%</td>
<td>Hypoglycemia, hyperglycemia, electrolyte disturbances, thyrotoxicosis, anemia</td>
</tr>
<tr>
<td>Medications</td>
<td>5–10%</td>
<td>Anti-hypertensives, psychotropic drugs</td>
</tr>
</tbody>
</table>

Table 1: Common causes of dizziness in primary care practice. From Agrawal et al with permission.
Figure 2: (A) Schematic representation of the plates of the otolithic receptors (the utricular and saccular maculae). The arrows show the preferred polarization of the hair cell receptors across the maculae. The dashed lines are lines of polarity reversal (lpr). The striola refers to a band of receptors on either side of the lpr. Schematics of type I (B,D) and type II receptors (C,E) show how linear acceleration acts on the otoliths and so deflects the hair bundles of individual receptors. From Curthoys et al’ with permission.
that unilateral or bilateral lesions of the peripheral vestibular system impair spatial memory in various maze and foraging tasks.\textsuperscript{14,29–31} In some cases, these have been conducted even 14 months after bilateral vestibular lesions (BVL) in rats, and the spatial memory deficits remain.\textsuperscript{32} A variety of potentially confounding factors have been controlled for, including vision, degree of motor activity, anxiety and auditory function, and the results have been consistent.\textsuperscript{29–32} BVL has been demonstrated to impair the function of neurons in the hippocampus that encode places in the environment (‘hippocampal place cells’),\textsuperscript{11,12} EEG activity in the theta frequency range,\textsuperscript{33–35} which is thought to regulate place cell function, and theta EEG activity among grid cells of the entorhinal cortex.\textsuperscript{13} Neurons in the thalamus which encode head direction (‘head direction cells’), are also dysfunctional following BVL.\textsuperscript{36} Together, these abnormalities in the function of place cells, grid cells and head direction cells, are likely to underlie the spatial memory deficits observed in animals.\textsuperscript{14,15} Furthermore, transgenic mice without otoconia and therefore without otolith function (‘otolith deficient tilted mice’), but with normal semi-circular canal function, have been shown to have aberrant hippocampal place cell and head direction cell activity.\textsuperscript{36,37} In addition, a variety of neurochemical changes have been documented in the hippocampus following BVL, including changes in the N-methyl-D-aspartate (NMDA) subtype of glutamate receptor and muscarinic acetylcholine (ACh) receptors,\textsuperscript{38–40} both of which are implicated in hippocampal learning and memory processes.
Taken together, the data from animal studies strongly indicate an important role for the vestibular system in spatial cognition. Although the specific pathways through which vestibular information reaches areas of the brain such as the hippocampus, are yet to be fully elucidated, projections from the vestibular nucleus and cerebellum are likely to transmit information via multiple routes, particularly the thalamus (see Figure 4). It is speculated that there is a ‘theta pathway’, which involves projections from the brainstem vestibular nucleus complex (VNC) to the pedunculopontine tegmental nucleus (PPTg), then via various nuclei to the medial septum, which releases ACh into the hippocampus; a ‘head direction pathway’, from the VNC via head direction cells of the anterodorsal nucleus of the thalamus (ADN) to the medial entorhinal cortex (MEC), to the hippocampus; a major thalamic pathway which transmits vestibular information to the parietal cortex and then on to the MEC and hippocampus; and a transcerebellar pathway. The detailed pathways are depicted in Figure 4.

Figure 4: ADN, anterodorsal nucleus of the thalamus; DTN, dorsal tegmental nucleus; Interpositus N, anterior and posterior interpositus nuclei; LMN, lateral mammillary nuclei; MEC, medial entorhinal cortex; MG, medial geniculate nucleus; NPH, nucleus prepositus hypoglossi; Parietal C, Parietal cortex; PaS, parasubiculum; Perirhinal, Perirhinal cortex; PoS, posterior subiculum (i.e dorsal part of the pre-subiculum); Post HT, posterior hypothalamus; Postrhinal, postrhinal cortex; PPTg, pedunculopontine tegmental nucleus of Gudden; Pulv, pulvinar; RPO, reticularis pontis oralis; SUM, supramammillary nucleus; ViM, ventralis intermedius nuclei of the thalamus; VLN, ventral lateral nucleus of the thalamus; VNC, vestibular nucleus complex; VPI, ventral posterior inferior nucleus of the thalamus; VPL, ventral posterior lateral nucleus of the thalamus; VPM, ventral posterior medial nuclei of the thalamus. From Hitler et al. with permission.
Vestibular contributions to cognitive function in humans

Consistent with the studies in animals, many studies conducted over the last two decades have demonstrated that vestibular disorders are associated with the impairment of cognitive function in otherwise normal healthy adults. The studies reviewed were identified using a Pubmed search between 1989 and 2020, using ‘vestibular’ and ‘cognition’ as key words. All of the studies were included; they consisted of two main types: survey and epidemiological studies; and clinical experimental studies (Table 2). Among the symptoms that have been reported are difficulty concentrating, deficits in attention and spatial memory, verbal fluency, mental rotation, and dyscalculia and other forms of numerical cognition (see Table 2). Although some 51 such studies have been published since 1989, only a subset of them (21) have controlled for hearing loss, either by excluding patients with hearing loss or by controlling for it statistically in the analysis of the data. Table 2 provides a summary of the studies that have controlled for hearing loss and therefore where the deficits can be considered to be mainly vestibular in origin. Dobbels et al have argued that few of the studies reporting cognitive deficits in humans with vestibular disorders, have controlled for hearing loss. However, a careful review of the literature suggests that is not the case. Of course, there are cases in which vestibular and auditory symptoms present together, for example, in Meniere’s disease, in which case they are both likely to contribute to cognitive deficits. Beyond controlling for hearing loss, the major weaknesses of the epidemiological studies are that they often include ‘heterogeneous vestibular disorders’ (bilateral vestibular loss, unilateral vestibular loss, vestibular neuritis, benign paroxysmal positional vertigo (BPPV), etc.) and do not include the same controls as the experimental studies (see Table 2). The available experimental studies are based on samples of patients with different vestibular disorders, but each one of them includes a sample of patients which is compared to a control group without vestibular dysfunction (see Table 2).

Studies in humans which have combined structural and functional neuro-imaging with behavioural assays, have also provided compelling evidence that vestibular sensory inputs are important for human spatial cognition. In a seminal study of patients with neurofibromatosis type 2 (NF2) who underwent bilateral vestibular nerve section, it was observed that the NF2 patients exhibited significantly poorer spatial navigation skills, measured using a virtual Morris Water Maze Task, which required no movement other than that of a mouse to control a cursor on a computer screen. These spatial cognitive deficits were correlated with reduced hippocampal volumes (approximately 17%) compared to age- and sex-matched controls. Only one of these patients exhibited total hearing loss post-operatively and all of them were 8–10 years post-BVL. Subsequent studies have provided further evidence of impaired spatial memory and hippocampal atrophy in patients with other vestibular disorders such as Meniere’s disease. A recent study of over 100 healthy adults reported that poorer vestibular function was correlated with significantly reduced hippocampal volume.

In our most recent study, we have found that age is statistically related to a bilateral decrease in the volume of the hippocampus and the left entorhinal cortex.

Vestibular dysfunction as a risk factor for dementia

As a result of the animal and human studies demonstrating that peripheral vestibular lesions caused spatial memory deficits, Previc suggested that loss of vestibular function might be implicated in the development of dementia, including Alzheimer’s disease (AD). His argument was based partly on the limitations of the β-amyloid (Aβ) hypothesis of AD, but the idea can be considered independently of that hypothesis. The central vestibular system, including the brainstem VNC, contributes to major cholinergic inputs to the hippocampus, which is damaged in AD. Bilateral vestibular loss in rats also results in a decrease in acetylcholine (ACh) receptors in the hippocampus.

There have been only a few studies that have directly investigated the relationship between vestibular function and AD, all of them conducted by the same group. The first studies investigated the statistical relationship between vestibular dysfunction and
Table 2: Studies conducted in humans that have reported cognitive deficits associated with different types of vestibular dysfunction, in which hearing loss has been controlled for in some way, either by excluding subjects with hearing loss or by controlling for it statistically in a multiple logistic regression model. Where 'No ( )' occurs, the first number in the brackets indicates the number of subjects without hearing loss and the second, the total sample size.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Diagnosis</th>
<th>Cognitive impairment</th>
<th>Hearing loss?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epidemiological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sang et al (2006)54</td>
<td>Heterogeneous vestibular disorders</td>
<td>Difficulty concentrating, thoughts seem blurred</td>
<td>No (33/50)</td>
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<tr>
<td>Jauregui-Renaud et al (2008)55</td>
<td>Heterogeneous vestibular disorders</td>
<td>Difficulty concentrating, thoughts seem blurred</td>
<td>No (37/50)</td>
</tr>
<tr>
<td>Jauregui-Renaud et al (2008)56</td>
<td>Heterogeneous vestibular disorders</td>
<td>Difficulty concentrating, thoughts seem blurred</td>
<td>No</td>
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<tr>
<td>Semenov et al (2016)46</td>
<td>Vestibular dysfunction</td>
<td>Digit symbol substitution test</td>
<td>No</td>
</tr>
<tr>
<td>Bigelow et al (2016)44</td>
<td>Vestibular vertigo</td>
<td>Cognitive impairment</td>
<td>No</td>
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<tr>
<td>Bigelow et al (2020)57</td>
<td>Vertigo</td>
<td>Attention, learning</td>
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<tr>
<td><strong>Clinical experimental</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Risey and Briner (1990/1991)54</td>
<td>Vertigo</td>
<td>Dyscalculia</td>
<td>No</td>
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<tr>
<td>Redfern et al (2004)59</td>
<td>Unilateral vestibular section</td>
<td>Increased RT for complex tasks</td>
<td>No</td>
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<tr>
<td>Brandt et al (2005)53</td>
<td>Bilateral vestibular section</td>
<td>Impaired spatial memory</td>
<td>No</td>
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<tr>
<td>Talkowski et al (2005)49</td>
<td>Vestibular dysfunction</td>
<td>Impaired spatial orientation, difficulty concentrating</td>
<td>No</td>
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<tr>
<td>Gomez-Alvarez (2011)51</td>
<td>Unilateral vestibular loss</td>
<td>Impaired spatial orientation, difficulty concentrating</td>
<td>No</td>
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<tr>
<td>Caixeta et al (2012)52</td>
<td>Chronic vestibular dysfunction</td>
<td>Verbal fluency</td>
<td>No</td>
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<td>Candidi et al (2013)53</td>
<td>BPPV, vestibular neuritis</td>
<td>Mental rotation</td>
<td>No</td>
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<tr>
<td>Bigelow et al (2015)45</td>
<td>Vestibular dysfunction</td>
<td>Spatial cognition</td>
<td>No</td>
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<tr>
<td>Kremmyda et al (2016)52</td>
<td>Bilateral vestibular section</td>
<td>Impaired spatial memory</td>
<td>No (13/15)</td>
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<td>Moser et al (2017a)44</td>
<td>Vestibular neuritis</td>
<td>Impaired numerical cognition</td>
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<tr>
<td>Moser et al (2017b)45</td>
<td>Vestibular neuritis</td>
<td>Increased redundancy, impaired generation of random numbers</td>
<td>No</td>
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<td>Lofti et al (2017)56</td>
<td>Vestibular defects, ADHD</td>
<td>Choice reaction time</td>
<td>No</td>
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<tr>
<td>Sugaya et al (2018)57</td>
<td>Dizziness</td>
<td>Trail-making test</td>
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<td>Deroualle et al (2019)58</td>
<td>Vestibular neuritis</td>
<td>Embodied spatial cognition</td>
<td>No</td>
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<tr>
<td>Dobbels et al (2019)70</td>
<td>Bilateral vestibular loss</td>
<td>Attention</td>
<td>No</td>
</tr>
<tr>
<td>Pineault et al (2020)59</td>
<td>Various type of vestibular loss</td>
<td>Benton visual retention test, Trail making test</td>
<td>No</td>
</tr>
</tbody>
</table>

Abbreviations: UVL, unilateral vestibular loss; BPPV, benign paroxysmal positional vertigo; UVN, unilateral vestibular neurectomy; ADHD, attention deficit hyperactivity disorder; RT, reaction time.
clinical syndromes of cognitive impairment, such as mild cognitive impairment (MCI) and AD. Harun et al.\(^7\) investigated the prevalence of vestibular dysfunction in 32 patients with AD and 15 with MCI, compared to 94 controls, and estimated that patients with bilaterally absent cervical vestibular-evoked myogenic potentials (cVEMPs, a measure of saccular function), had a greater than three-fold increased odds of AD (OR 3.42, 95% CI 1.32–8.91, \(P=0.011\)). Furthermore, a 1 \(\mu\)V increase in cVEMP amplitude was associated with a decreased odds of AD (OR 0.28, 95% CI 0.09–0.93, \(P=0.038\)). Higher ocular VEMP (oVEMP, indicative of utricular function) amplitude was associated with a decreased odds of AD (OR 0.92, 95% CI 0.85–0.99, \(P=0.036\)). However, there was no significant difference between the MCI group and the controls. Importantly, there was no significant association between VOR function and AD, indicating that semi-circular canal function was not implicated, only the otoliths, the most primitive part of the vestibular system.

In a follow-up study, Wei et al.\(^8\) examined vestibular function in 51 patients with AD, 26 with MCI and 295 matched controls. The cVEMP, the oVEMP and the VOR were all tested. Compared to controls, they found that people with cVEMP impairment had a 3–4 fold increase in the odds of being in the MCI group (OR 3.0, 95% CI 1.1–8.5, \(P=0.04\)) and those with oVEMP impairment had an almost four-fold increased odds of being in the MCI group (OR 3.9, 95% CI 1.4–11.3, \(P=0.01\)). Compared to controls, they found that people with impaired cVEMPs had a five-fold increased odds of being in the AD group (OR 5.0, 95% CI 2.0–12.3, \(P=0.001\)) and those with abnormal oVEMPs had a greater than four-fold increased odds of being in the AD group (OR 4.2, 95% CI 1.9–9.1, \(P=0.001\)). Importantly, VOR gain (the ratio of head velocity to eye velocity) was not significantly related to group membership.

There are a number of limitations of these studies which must be noted, however. First, hearing loss was not controlled for in these studies of AD and MCI, so it is possible that it may have been a contributing factor. Second, the sample sizes of AD patients were relatively small, \(n=32\) and 51, and therefore the studies need to be replicated.\(^7\)\(^8\) Third, the studies were cross-sectional, and the samples may not have been representative of a broader population.\(^9\) In particular, patients with both vestibular and cognitive impairment may have been more likely to present than those with either condition alone, resulting in a potential overestimation of the proportion of vestibular dysfunction in AD (‘Berksonian bias’).\(^10\) Fourth, it is conceivable that the poor performance by AD patients on the cVEMP and oVEMP testing could have been due to their inability to understand and follow instructions; however, the authors reported that this was not the case.\(^7\)\(^8\) Finally, the relationship between cVEMP/oVEMP function and AD was a statistical one involving logistic regression and does not necessarily indicate a causal relationship.\(^7\)\(^8\) For example, aside from the possibility that vestibular dysfunction contributed to the development of AD, it is possible that AD pathology might have caused vestibular dysfunction.

One potential explanation for the relationship between vestibular dysfunction and AD might be that AD pathology (eg, \(\beta\)-amyloid (A\(\beta\))) extends into the central vestibular pathways from the vestibular nucleus to the thalamus and beyond, thereby impairing vestibular function. Although there have been no specific studies of A\(\beta\) deposition in ‘vestibular-related areas’ of the brain, vestibular information is distributed widely,\(^4\) (see Figure 4), therefore it is likely that AD pathology extends to many brain regions receiving vestibular input. However, in a recent study of vestibular function in 98 participants aged 77.3 (±8.26) from the BLSA, A\(\beta\) deposition was measured using amyloid C-11 Pittsburgh Compound B (\(^{11}\)C-PB).\(^8\) The authors found that 22.4% of the sample were positive for PiB; however, there was no statistically significant relationship between the extent of A\(\beta\) deposition and any measure of vestibular function. This study was designed to investigate preclinical AD, but no such study has been performed in patients diagnosed with AD. Another possible explanation is that vestibular impairment directly contributes to medial temporal lobe neurodegeneration and AD, possibly as a result of reduced vestibular sensory input to areas of the brain such as the hippocampus, as occurs for auditory input.\(^8\)
Further studies have concentrated on whether vestibular loss is associated with specific phenotypes of AD, especially those with spatial cognitive deficits. Some AD phenotypes are characterised by predominantly amnestic symptoms compared to others which are characterised by more motoric and spatial impairment. In a study of 50 patients with MCI or AD, Wei et al observed that patients with vestibular loss were significantly more likely to exhibit impairment in neurocognitive tests of spatial skills, for example the Money Road Map test (MRMT). When patients were divided into ‘spatially normal’ and ‘spatially impaired’ groups based on their performance in the MRMT, only 25% of the spatially normal patients were found to have vestibular dysfunction compared to 96% of the spatially impaired patients. In a further study of 60 patients with MCI or AD, patients with vestibular dysfunction were significantly more likely to have difficulty driving, an activity closely linked to spatial cognitive ability. It is possible, therefore, that vestibular dysfunction contributes to the development of a ‘spatial’ subtype of AD, increasing the probability of symptoms such as spatial disorientation, wandering, and an increased risk of falling. However, these two studies have similar limitations to the original one by Harun et al: there were no controls for hearing loss, the sample sizes were relatively small, the studies were cross-sectional and in Wei et al, the postural measurements were not specific to vestibular function. Finally, the statistical association reported does not indicate causality.

The only available study that provides any evidence that vestibular loss might be causally involved in the development of cognitive impairment and dementia is by Liao et al. They investigated prior medical conditions that were associated with late-onset Alzheimer’s disease dementia (LOAD) using a population-based matched case control study based on the National Health Insurance Research database of Taiwan and the Catastrophic Illness Certificate database, between the years 1997 and 2013. The definitions of prior diseases were based on the first three digits of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). The total case group consisted of 4,600 patients who were newly diagnosed with LOAD between 2007 and 2013, who were then matched to 4,600 controls by both age and sex. Using multivariate logistic regression and path analysis, the authors reported that the incidence of LOAD was positively correlated with prior anxiety (ICD code 300), functional digestive disorder (ICD code 564), psychopathology-specific symptoms (ICD code 307), disorders of the vestibular system (ICD code 386), concussion (ICD code 850), disorders of the urethra and urinary tract (ICD code 599), disorders of refraction and accommodation (ICD code 367) and hearing loss (ICD code 389). While the authors conclude that these data suggest that vestibular dysfunction may therefore be a risk factor for LOAD, the limitations of the study include limited information regarding other confounding factors such as body mass index, blood pressure, diet, smoking, diabetic therapy etc.; and the specific nature of the diagnosis may have varied according to factors affecting access to a neurologist. At present, there are no comparable data available on potential vestibular contributions to dementia associated with Parkinson’s disease or fronto-temporal dementia.

One of the intriguing aspects of the studies in cognitively-normal and vestibular-impaired adults is the demonstration of a link between saccular function and cognition. We have recently reported that saccular function is a statistically significant predictor of the decrease in hippocampal volume that occurs with age. Saccular stimulation has been demonstrated to activate the multisensory vestibular cortex involved in spatial information processing. In guinea pigs and rats, selective electrical stimulation of the utricle and saccule has been shown to cause widespread activation of the hippocampus. There is increasing evidence that the otoliths, the saccule in particular, have a critical role in spatial
memory due to their importance in the perception of gravitational vertical. We have recently reported that mice lacking otolithic function from birth, exhibit major developmental delays by post-natal day 9, including spatial memory deficits. Interestingly, considerable electrophysiological evidence suggests that the neurons in the VNC that subserve the VOR are separate from those involved in the VSR pathways and the pathways to the limbic system and neocortex. This means that it is possible for the vestibular pathways that give rise to the conscious perception of self-movement and contribute to spatial memory, to be compromised, without VOR deficits necessarily being exhibited, and that only VSRs such as VEMPs would indicate a vestibular deficit. Figure 5 summarises the hypothesis that saccular dysfunction, in particular, might contribute to the development of cognitive dysfunction that preferentially includes spatial cognitive deficits.

Conclusions

The available evidence suggests that vestibular dysfunction, including that associated with age-related vestibular loss, has a significant negative impact on cognitive function. Vestibular impairment may therefore be a risk factor for the development of dementia, including AD. Previc has recently suggested that, given the increased prevalence of vestibular disorders in females, vestibular dysfunction may contribute to their increased incidence of AD. However, the majority of the evidence to date is correlational; therefore, caution must be exercised in interpreting these findings. The potential combined effects of both hearing loss and vestibular loss are unknown but could be expected to be much greater. Of course, it is important to note that some otological disorders involve both auditory and vestibular symptoms (e.g., Meniere's disease). Understanding the

Figure 5: Conceptual model of impact of aging on vestibular function (notably saccular function), which contributes to neurodegeneration of neural circuits involved in vestibular processing and deterioration, specifically in spatial cognitive ability. From Agrawal et al with permission.
full implications of vestibular dysfunction for cognitive decline is potentially of great importance for the health of the elderly, since effective therapies are available to treat vestibular disorders.95 One of the principal treatments for vestibular impairment is vestibular rehabilitation, a suite of physical therapy-based exercises in which head movements are used to stimulate the vestibular system and gradually encourage the brain to adapt to the loss of normal vestibular function.96 Several studies have reported that vestibular rehabilitation can improve cognitive function in healthy adults and in patients with intractable dizziness.67,97 However, at present, studies from the US indicate that only a small number of people with AD are referred for vestibular rehabilitation.98 Since vestibular impairment may be a modifiable risk factor for dementia, the impact of vestibular loss on cognition should be considered along with hearing loss as a critical area for research.

Competing interests:
Nil.

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URL:

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