Influence of BPPV and Meniere's Disease on cognitive abilities:

A Questionnaire-Based Study

Rohit Bhattacharyya

20AUD026

This Dissertation is submitted as part of fulfilment for the Degree of

Master of Science in Audiology

University of Mysore, Mysuru

All India Institute of Speech and Hearing

Manasagangotri, Mysuru- 570006

August 2022

Certificate

This is to certify that this dissertation entitled **"Influence of BPPV and Meniere's Disease on cognitive abilities: A Questionnaire-Based Study"** is the bonafide work submitted as part of fulfilment for the Degree of Master of Science in Audiology of the student with Registration No. 20AUD026. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other Universities for the award of any other diploma or degree.

Mysuru

August 2022

Prof. M. Pushpavathi

Director,

All India Institute of Speech and Hearing

Mysuru- 57006

Certificate

This is to certify that this dissertation entitled **"Influence of BPPV and Meniere's Disease on cognitive abilities: A Questionnaire-Based Study"** is the bonafide work submitted as part of fulfilment for the Degree of Master of Science in Audiology of the student with Registration No. 20AUD026. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other Universities for the award of any other diploma or degree.

Mysuru

August 2022

Guide

Dr. Animesh Barman

Professor in Audiology

Department of Audiology

All India Institute of Speech and Hearing

Mysuru- 57006

Co- guide

Mr Freddy Antony

Assistant Professor in Clinical Psychology

Department of Clinical Psychology

All India Institute of Speech and Hearing

Mysuru- 57006

Declaration

This dissertation entitled **"Influence of BPPV and Meniere's Disease on cognitive abilities: A Questionnaire-Based Study"** is the result of my own study under the guidance of Dr Animesh Barman, Professor in Audiology and co- guidance of Mr Freddy Antony, Assistant Professor in Clinical Psychology, All India Institute of Speech and Hearing and has not been submitted earlier to any other Universities for the award of any other diploma or degree.

Mysuru **Register Number:** 20AUD026

August 2022

Acknowledgements

This dissertation has been a great learning experience throughout its course. At the very outset of this report, as I stand to complete this work, I would like to extend my heartfelt obligation to all the personages who have helped me in this endeavour. Without their active guidance, support, help, cooperation and encouragement, I would not have made headway in this study.

I am extremely thankful to my faculty guide Dr Animesh Barman for his guidance and for his valuable guidance and support in accomplishing this study. The little things you have taught me regarding reviewing an article, writing, presentation and the overall approach are impeccable. Thank you for trusting, believing in me and playing a significant role in moulding me into the student researcher I am today. Sir, you are also a sporting legend in AIISH, and I find you to be a true inspiration in how you balance your commitment to sports with your demanding schedule; I hope to be able to do the same in the future.

Mr Freddy Antony, Sir, you have been a guiding source throughout my dissertation journey. Thank you for your constant encouragement and kind

suggestions, which have helped me accomplish my work more efficiently and under less stress. Thank you for believing in me and playing a significant role in moulding me into the student researcher I am today.

I'd also want to express my gratitude to our beloved director, Dr M. Pushpavathi, for allowing me to undertake this research.

I also acknowledge, with a deep sense of reverence, my gratitude towards Ma and Deauta (Dr.B. N Bhattacharyya & Ms Arunima Bhattacharyya), my sister Isha, my koka and aaita (Late D.N Bhattacharyya and Ms Geetanjali Bhattacharyya) and Chunchun who has always supported me morally and inspired me in different ways to be a better person every day.

A special mention to Dr Sandeep Maruthy, Dr Prashanth Prabhu, Dr Abhishek BP, and Dr Nisha KV for introducing me to the research world and mentoring me throughout my undergraduate and post-graduate studies years at AIISH.

Special to mention to Dr Ajith Kumar, Dr Prawin Kumar, Dr Niraj Singh, Dr Sujeet Sinha, Dr Sreeraj, Dr Chandni Jain, Dr Devi, Dr Geetha, Dr P Manjula, Dr Jayshree Shanbal, Dr K Yashoda, Dr Rajasudhakar, Dr Brajesh

Priyadarshi for your guidance and support throughout. Special mention to my clinical mentors Dr Sharath K, Dr Vikas M, Dr Antony J, Dr Jithin Raj and Mr Baba.

A huge thank you to all the participants who were such a sport and volunteered with consent for my dissertation.

I am very grateful to Dr Vasanthlakhmi and Dr Srinivas for the statistical help. I would also express my gratitude to the Department of ENT for helping me with the case selections

Ritwik, Shashish, Sandeep, Amar, Adya and a special mention to Sushmitha; you have been my powerhouses and survival kits at AIISH. Thank you for all those fun, work, and countless conversations and discussions. Thank you for being my extended family.

To my Bodhi boys, Delvin, Bahis, Ashiq, Rajkumar, Bikram, Sahil, Amit, Akshay, Ranjit and Ashish, thanks for the countless crazy memories and for making my hostel life the best.

Hrishi, Deepika, Tanu, Vibhuti, Neha, Naina, Jeslin, Supriya, Varsha, Sahana, Vibha, Sanjay, Sajna, Prakruti, Nikhilesh, Akash, Banu and the rest

of Class Artifacts and Masters Artifacts gang for all the memories in AIISH and beyond.

Thanks to my friends Parigyan, Bhishak, Raju, Madhu, Manis, Manash, Rahul, Manab, Nafisa, Jishnu thank you for being great friends throughout and all the support .

Thanks to Mangal Sir, Anup Sir, Sreeki Sir, Shiva Sir, Raghav Sir, Kishore Sir and all the seniors for all the help and countless memories. Special mention to Shashank Sir for all the interactions and for helping me settle into college life.

Sunny Sir, Akshit Sir, Aman Sir, Jeevan Sir, Prateek Sir, Anshuman Sir, Ankit Sir, Mridul Sir, Bandhan Sir Anima Ma'am, Kenie Ma'am, Architha Ma'am thank you for being good friends and seniors throughout.

Thanks to Anirban, Deepshikha, Nishanth, Debendu, Sahil, Devraj, Abra, Rajilis, Manthan, Jeeva, Anuprarthana, Zaifer, Mayank, Ritik, and Raunak. It was fun in my college life to have such amazing juniors.

To the players of AIISH FC, members of Papa's Kitchen, members of the Skit and Fashion Show teams and all the badminton and volleyball players, I had a beautiful time with all of you guys.

Last but not least, gratitude goes to all my friends, faculty, juniors and seniors who directly or indirectly helped me complete the study.

Any omission in this brief acknowledgement does not mean a lack of gratitude.

And, dear readers, this research's value lies in how you see it. I trust you, and thank you for the proper use in advance.

Table of Contents

List of Tables

L i s t o f

List of Figures

ABSTRACT

The vestibular system comprises peripheral and central connections that travel from the inner ear to the midbrain and subsequently to the subcortical structures. Any structural abnormality could lead to problems related to cognition. Recent clinical reports suggest that vertigo patients also frequently complain of associated cognitive symptoms, including attention, memory, spatial perception, navigation, mental rotation and mental representation of three-dimensional space, which are not necessarily related to any particular episode of vertigo (Guidetti et al., 2020). Meniere's Disease (MD) and Benign paroxysmal positional vertigo (BPPV) are the two most common causes of vestibular vertigo (Neuhauser, 2016). Although there is an increasing research interest in vestibular disorders and cognition, the relationship between specific vestibular disorders and cognition has been less explored. Thus, the study aimed to find if there is any cognitive problem associated with patients diagnosed with BPPV and MD and find a relation between them.

A non-experimental standard group comparison research design was employed. A total of 107 subjects participated in the survey, out of which, Group-I had 29 subjects (Mean age = 53.96 years) who were clinically normal, Group II had 38 (Mean age = 50.71 years) subjects diagnosed with BPPV and Group III had 40 (Mean age = 54.55 years) subjects diagnosed with Meniere's disease. The study was conducted in an online/tele-mode, where a google form was sent to the subjects via email/WhatsApp. A total of 10 questions related to cognition, primarily selected from the Neurobehavioral Cognitive Status Examination (NCSE), were present, along with demographic details,

which the participants had to fill. For each response, the score of 0 for "Yes," 1 for "Sometimes," and 2 for "No" were assigned for the analysis. The overall score for each subject for all the ten questions was calculated with a maximum score of 20 and a minimum of 0. Shapiro-Wilk's test was done, and the data was found to be non-normally distributed. Kruskal-Wallis H test was conducted, and it was found that there was a significant difference in scores between Group I and Group II ($p<0.05$) and Group I and Group III ($p<0.05$). Chi-square tests were done for the ten cognition-related questions with respect to the overall scores assigned. It revealed that responses were dependent on the groups, i.e., for Group I number of people with cognitive problems was less (i.e., the overall scores were less), for Group II, it was more (i.e., overall scores were more). Mann-Whitney U test was conducted to check if the associated problems like hypertension, diabetes and hearing loss significantly affected the responses within the groups, and it revealed no significant difference ($p>0.05$).

From the current study, it can be inferred that there is a significant relationship between cognitive problems in participants who have BPPV and MD. However, no association between cognitive problems between BPPV and MD was found. This agrees with the findings reported in studies on the vestibular system's contribution to cognitive function, which suggests vestibular disorder may lead to spatial memory deficits, attention problems, dyscalculia and other cognition-related difficulties (Gurvich et al., 2013a). By establishing a relationship between cognition and vestibular disorder, we can provide a better holistic diagnosis and rehabilitation services to improve the patients quality of life.

Chapter 1

INTRODUCTION

Vertigo is usually defined as a feeling of an individual that things are spinning or moving around (Bhattacharyya et al., 2017). However, in the general population, this term is frequently associated with symptoms of dizziness (feeling of being light-headed or 'swimmy'). The three semi-circular canals and two otolith organs that make up the vestibular apparatus are essential for maintaining balance and gaze stabilization. However, an expanding amount of literature acknowledges that the vestibular system's function extends far beyond these rudimentary reflexes.

Vestibular networks within subcortical structures travel through the midbrain and subsequently into the inner ear, compromising a complicated network of varied paths. Due to these diffused connections, different points along the routes are expected to affect vestibular function. Furthermore, it is made up of white matter and nerves, especially the vestibulocochlear nerve, a composite sensory nerve that makes it susceptible to various injuries and weakens cell signalling (Gurvich et al., 2013a). Thus, damage to the vestibular system could lead to functional damage and cause vertigo/dizziness. Recent clinical reports suggest that vertigo patients also frequently complain of associated cognitive symptoms, including attention, memory, spatial perception, navigation, mental rotation and mental representation of three-dimensional space, which are not necessarily related to any particular episode of vertigo or dizziness (Guidetti et al., 2020). Numerous animal research conducted over the past few decades have consistently shown that mice

with vestibular injuries have deficiencies in spatial cognition (Wallace et al., 2002; Zheng et al., 2012).

The prevalence of vestibular disorders and comorbid conditions increases with age (Agrawal et al., 2013). Studies focusing on the epidemiology of vertigo and dizziness have reported a lifetime prevalence between 20% to 35% (Teggi et al., 2016). The vestibular disorders substantially have a negative impact on quality of life. Thus, this reduces the capacity of individuals to carry out regular activities effectively (Smith, 2017a).

Cognitive functions like spatial memory, navigation etc., are common impairments seen in the elderly population, especially with dementia. As with ageing, vestibular cells or neurons could be lost, leading to vestibular pathologies. Thus vestibular dysfunction may be one of the risk factors that cause such cognitive disorders, especially in the elderly (Jun et al., 2020).

Several animal studies have been conducted to find a link between cognitive ability and vestibular systems. It has been found that bilateral vestibular dysfunction has generated aberrant place cell responses and theta rhythm in the hippocampus (Hitier et al., 2014) and, more recently, in the entorhinal cortex (Jacob et al., 2014). Previous studies reveal that individuals with bilateral vestibular loss who underwent surgery had bilateral atrophy of the hippocampus of around 17%, which coincided with spatial memory deficiencies (Brandt et al., 2005a). Recent investigations found that individuals with even partial bilateral vestibular loss had a bilateral drop in grey matter volume in the brain (Hüfner et al., 2007).

It has been well established that long-standing, untreated hearing loss causes cognitive impairment; however, the relation between vestibular problems and cognition is less explored. Studies have shown that minimal hearing loss is linked to worse results on memory and executive function tests (Lin et al., 2011). Early treatment of age-related HL, such as hearing aids, may lessen the adverse functional effects on grey matter atrophy, leading to cognitive issues (Slade et al., 2022). Thus, a question arises if the long-standing hearing loss would cause sensory deprivation to the brain over time, leading to cognitive problems; similarly, could untreated and long-standing vestibular symptoms show the same?

Benign paroxysmal positional vertigo (BPPV) and Meniere's disease (MD) are the most common causes of vestibular vertigo, accounting for a maximum number of cases in specialized dizziness clinics (Neuhauser, 2016). Although the relation between BPPV and cognition has been less explored, there is some evidence of vestibular and cognitive symptoms in the case of Meniere's disease. Meniere's disease (MD) frequently reports abnormal emotional processing and vertigo symptoms. In Meniere's disease, uncertainty intolerance is most likely linked to anxiety and other emotional distress (Kirby & Yardley, 2009). Studies to assess the quality of life for patients suffering from vertigo have been conducted, and there are several questionnaires for it. One of the most common is the Dizziness Handicap Inventory (DHI). The DHI serves as a widely used clinical tool for quantifying the effect of vertigo on quality of life (QOL) in the functional, emotional, and physical domains. However, the DHI and other questionnaires such as the Dizzy Factor Inventory, Vertigo Symptom Scale, and Vertigo-Dizziness-

Imbalance Questionnaire focus on physical handicaps and the emotional impacts (i.e., anxiety and depression) on QOL and contain very few questions addressing specifically to cognitive dysfunction as a result of dizziness (Lacroix et al., 2016; Liu et al., 2019).

Studying the association between vestibular problems and cognition could also help better rehabilitate and manage the particular disorder causing the vestibular issues if a correlation is found. Cognitive-behavioural therapy (CBT) is a psychotherapeutic treatment that helps people learn how to identify and change destructive or disturbing thought patterns that negatively influence behaviour and emotions. Studies revealed that CBT and Vestibular rehabilitation therapy (VRT) could be coupled in treating dizziness-specific handicaps and discomfort, and CBT practitioners may be able to broaden their practice (Wan et al., 2018a). While the findings are preliminary, it can be recommended to the audiologist to consider CBT as a rehabilitation option and a supplement in treating dizzy patients along with VRT.

1.1 Need for the study

Thus, it is evident that vertigo patients frequently complain of associated problems such as emotional disturbances, anxiety, fear, and cognitive issues. Studies have found more difficulty in performing cognitive-based activities than mobility-based ones. Although tools are available to assess the other parameters, there is a narrow focus on evaluating the cognitive problems faced by patients suffering from vertigo. Several studies have shown that vestibular problems could also lead to cognitive problems (Brandt et al., 2005c; Smith & Zheng, 2013; Dobbels et al., 2019; Bigelow et al., 2020a).

Thus, finding from this study could be used for appropriate rehabilitation and recommendations for a better quality of life. Thus, a suitable questionnaire could be used to identify cognitive problems in BPPV and Meniere's disease.

1.2 Aim of the study

The present study aims to explore if there is a cognitive problem associated with patients diagnosed with BPPV and Meniere's disease.

1.3 Objectives of the study

- To describe the nature of cognitive problems associated with BPPV.
- To describe the nature of cognitive problems associated with MD.
- To compare cognitive problems faced by patients diagnosed with BPPV and MD.
- To compare the cognitive abilities in clinical groups (patients diagnosed with BPPV & MD) with a control group (clinically normal individuals).

Chapter 2

REVIEW OF LITERATURE

This review will discuss recent clinical studies into cognitive impairment in the context of various vestibular disorders, recent epidemiological/survey studies linking vestibular dysfunction with cognitive impairment, cognitive issues caused by auditory vs vestibular disorders in various animal and human studies, recent evidence linking vestibular impairment to hippocampal atrophy, and finally cognitive management options for vestibular disorders.

2.1 Prevalence of vertigo

Murphy et al. in 2021 stated that between May 2017 and August 2019, 215 patients out of 901 (24%) were referred to an otologist with dizziness as a presenting complaint. Anxiety, sadness, migraine/headaches, and heart illness were all relevant comorbidities. This research showed that many patients sent to an otologist from general care have dizziness and vertigo, highlighting the necessity for multidisciplinary vestibular/balance centres to address and manage these patients. According to a neurotologic assessment by Neuhauser in 2007, it was found that vertigo had a prevalence of 4.9 %, migrainous vertigo at 0.89 percent, and benign paroxysmal positional vertigo at 1.6 %.

Vertigo, dizziness, and unsteadiness (VDU) are typical symptoms that have traditionally been associated with several types of vestibular and non-vestibular dysfunctions. A population-based study in north-eastern France looked at the

epidemiology of each symptom. It was revealed that vertigo had a prevalence of 48.3 percent, unsteadiness had a prevalence of 39.1 percent, and dizziness had a prevalence of 35.6 %. The three symptoms were linked, they happened more frequently (69.4%) in groups rather than alone, occurred less than once per month, and 90 %of episodes lasted less than two minutes (Bisdorff et al., 2013).

According to Langhagen et al., 2015, dizziness and vertigo appeared to be equally common in elementary school pupils as adults.

The prevalence of balance problems (vertigo, dizziness, and disequilibrium) was investigated in an epidemiological study of aged persons, the longitudinal and cross-sectional gerontological and geriatric population survey from Göteborg, Sweden (H70). The researchers looked at different age groups. Balance problems were found in 36 % of women and 29 % of men over 70. Women had more balance issues than men, and their problems worsened with age. At the age of 88–90 years, the corresponding results were 51–45%. The most common symptom (11–41 %) was poor balance or unsteadiness. 2–17 % of patients said they had rotating symptoms. On the other hand, other indications and symptoms were much less common (Jönsson et al., 2004).

In a nationally representative survey of US children aged 3-17 years, the 1-year prevalence of vertigo was 1.56 %. After controlling for demographic and confounding health variables (otitis media and headaches/migraines), children with vertigo had significantly higher odds of attention deficit disorder, learning disability, intellectual disability, and special education services. Children with vertigo were also more likely to

have emotional, concentration, or behavioural difficulties and a short attention span. In children in the United States, vertigo is linked to an elevated risk of cognitive and mental comorbidity. These findings support the theory that the vestibular system is critical for children's everyday cognitive and mental development (Bigelow et al., 2020b).

BPPV was shown to have a lifetime prevalence of 2.4 %, a one-year prevalence of 1.6 %, and a one-year incidence of 0.6 %. An episode lasted an average of two weeks. BPPV caused medical consultation, stoppage of daily activities, or sick leave in 86 % of infected people. Only 8% of those who were afflicted received effective treatment in total. Age, migraine, hypertension, hyperlipidemia, and stroke were all independently linked with BPPV in multivariate analysis (Von Brevern et al., 2007). BPPV's prevalence was 9% in younger adults, according to Kerrigan et al., 2013.

Diabetes may impact the vestibular system via a mediating mechanism of hypertension (D'Silva et al., 2015). BPPV was seen in 46 % of people with type 2 diabetes (DM) compared to 37 % without diabetes. Hypertension mediated 42% of the link between type 2 DM and BPPV, indicating that hypertension is a full mediator in the interaction between type 2 DM and BPPV.

2.2 Hearing loss and its association with cognitive problems

Dementia and cognitive impairment are marked by a gradual and tragic loss of most cognitive ability, functional independence, and social interactions. Dementia has a significant cost impact on society, equivalent to the economic effects of heart disease and cancer. Cognitive impairment can be clinically silent for years due to its insidious start;

as a result, diagnosis happens late in the illness process, and treatment becomes essentially worthless. A better knowledge of the relationship between hearing loss and cognition could have significant consequences for detecting and diagnosing cognitive decline in older adults with hearing loss. The discovery of dementia predictors may aid in discovering the disease's pathophysiological causes, creating more effective medical diagnosis and treatment and early intervention. Hearing loss has an association with language comprehension in those with less cognitive impairment (normal/predementia group), and as cognitive impairment increases (moderate or severe dementia group), the contributing effect of hearing loss as a cognitive ability-impairing factor also increases, according to a review of the literature (Peracino & Pecorelli, 2016).

Dementia is a severe disease and a significant public health concern that affects people all over the world. A rising body of evidence suggests an independent link between age-related hearing loss (ARHL) and dementia, making ARHL a viable target for dementia prevention methods. However, before formulating clear clinical guidelines and therapeutic recommendations addressing ARHL as a modifiable risk factor, a causative link between ARHL and dementia must be established. The importance of addressing this result, as well as standard processes (e.g., microvascular illness) and causative mechanisms (e.g., depletion of cognitive reserve and social isolation,) may explain the nature of this link (Hubbard et al., 2018; Chern & Golub, 2019). It was also found that the higher the hearing loss is, the poorer the cognitive test scores are for memory and executive function (Lin, Ferrucci, et al., 2011). Lin et al. in 2011 and Wayne

& Johnsrude in 2015 also supported the finding that hearing loss is linked to an increased risk of all-cause dementia.

Alzheimer's disease and hearing loss are both common among the elderly. The co-occurrence of the two illnesses adds to the complexity of an individual's care and management plan. Ray et al., 2019 studied dementia and hearing loss in the care-home setting because most residents have one or both conditions. He concluded that hearing loss and dementia might be linked through various pathways, but the data on how they work together is currently lacking. While it is believed that early detection and treatment of hearing impairments would assist in preventing the development of cognitive impairment in the future, data to support this is insufficient.

Granick et al., 1976 investigated the effect of moderate hearing loss on cognitive performance. One Group consisted of 47 individuals with an average age of 71.5 years chosen for their exceptional health. The second Group comprised 38 females, all of whom had significant physical pathology and were 75.9 years old on average. Hearing loss at various frequency ranges (ranging from 125 to 8000 Hz) was linked to performance on cognitive tests like the WAIS, with age effects partially removed. For both samples, the results show a strong link between hearing loss and the scores earned on the cognitive tests. Verbal-type tests reveal these connections in far greater detail than performance testing. The findings suggest that older people may be more cognitively adept than their test results, and hearing is a crucial factor to consider when evaluating their cognitive abilities. Similar results related to age, hearing loss and cognitive impairment were found by Gurgel et al., 2014 whom he stated that older adults with HL

have a higher risk of dementia and experience a faster drop in Modified Mini-Mental Status Exam (3MS-R) scores than their non-hearing-impaired counterparts. According to the data, hearing loss may be a sign of cognitive deterioration in persons aged 65 and up. Auditory perceptual skills and working memory were also found to be affected due to hearing loss, as reported by Lentz et al. in 2022.

Studies were conducted on how hearing loss and cognitive capacity affected the cognitive processing burden when listening to speech in noisy environments. Pupillometry (i.e., the assessment of pupil dilation) and subjective ratings were used to determine cognitive load. With diminishing speech intelligibility, the pupil response progressively increased. Regarding improving speech intelligibility in noise, ageing and hearing loss were linked to reduced effort release. These characteristics may cause cognitive fatigue early in difficult listening situations or be related to shallow speech processing in difficult listening situations. More research is needed to understand the mechanisms that underpin these findings fully. Across all speech intelligibility levels, better TRTs and a more expansive word repertoire were linked to more mental processing burden. This suggests that using linguistic skills to better voice perception is connected to a higher level of listening load (Zekveld et al., 2011).

2.3 Physiological basis of the vestibular system and its relationship with cognitive abilities

The vestibular system's vestigial nature makes our central nervous system closely related. Vestibular beginnings within subcortical structures travel through the midbrain

and subsequently into the inner ear, compromising a complicated network of varied paths. Due to the diffuse connection, different points along the routes are expected to affect vestibular function. Furthermore, it is made up of white matter and nerves, especially the vestibulocochlear nerve, a composite sensory nerve that makes it susceptible to various injuries and weakens cell signalling (Gurvich et al., 2013a).

A potential neurological explanation for the coexistence of vestibular and psychiatric symptoms is provided by the numerous well-established connections between the vestibular system and brain regions involved in cognitive and emotion processing, despite the lack of direct evidence to support direct pathology of the vestibular apparatus in psychiatric disorders (Balaban & Jacob, 2001).

2.3.1 Involvement of the brainstem

The raphe nuclei and locus coeruleus are two brainstem regions linked to several psychiatric disorders and share connections with the vestibular nuclei. The raphe nuclei receive projections from the vestibular nuclei and send serotonergic and non-serotonergic projections to the vestibular nuclei (Cuccurazzu & Halberstadt, 2008) and send axon collaterals to the central amygdaloid nucleus.

Both vestibular function and the processing of emotions depend on the limbic system. The vestibular system and brain networks involved in emotional processing are directly connected through the parabrachial nucleus (PBN) network. According to (Balaban & Thayer, 2001), the PBN has reciprocal connections with the vestibular nuclei and the amygdala, hypothalamus, locus coeruleus, and prefrontal cortex.

2.3.2 Cortical connections to the vestibular system

Uncertainty persists regarding the precise locations and roles of the brain areas that process vestibular input (Zu Eulenburg et al., 2012). It has been hypothesized that because the anterior cingulate cortex is thought to be a component of the human vestibular cortex (López-Larson et al., 2002), it may act as a link between the vestibular sensorimotor areas and the prefrontal affect divisions that control motivational states.

2.4 Animal studies related to the vestibular system and cognition

Early research on spatial navigation in animals suggested that animals employed external allocentric cues and non-visual idiothetic signals like vestibular and proprioceptive information to recall their way around a familiar environment (Ossenkopp et al., 1990).

Using a foraging task in which rats had to recall their way back to a home base two weeks after surgery, (Wallace et al., 2002) presented the first detailed assessment of spatial memory following bilateral vestibular injuries. This well-controlled study used intratympanic sodium arsanilate chemical lesions of the vestibular labyrinth and used an electronic tracking device to measure the behaviours of the rats. In the absence of visual cues, they discovered that rats with bilateral vestibular deafferentation (BVD) had severe spatial memory problems.

According to a study by (Baek et al., 2010), rats who were 14 months post-BVD were more significantly affected in a spatial memory foraging task in the dark than those

5 months post-op, which used the most prolonged postoperative time interval used to date.

Rats with induced Bilateral vestibular damage were shown to have poor spatial memory even in bright light. Rats with BVD at 6 weeks post-op performed considerably worse in a radial arm maze challenge than sham controls (Ferrè & Harris, 2017).

It's unclear whether animals experience spatial memory impairment due to brain vestibular dysfunction. There have also been reports of attentional and non-spatial object recognition memory problems in some animal investigations using surgical BVD (Zheng, Goddard, et al., 2009).

2.5 Human studies based on vestibular disorders & cognition

2.5.1 Memory related

The most important takeaway from recent research is that vestibular dysfunction can lead to cognitive impairment, especially in the elderly. Patients with vestibular abnormalities must be treated for symptoms like these (Smith, 2017b).

Perceptual and memory abnormalities in patients with perilymph fistula syndrome by Grimm et al., 2009. From a total of 102 patients, more than 95 percent experienced long-term "disorientation" in any scenario where visual and vestibular information conflicted, such as when the visual field moved without the patient moving. More than 85% of the patients claimed to have some form of memory loss—performance in the impaired range for digit symbol, block design, and picture organization.

2.5.2 Related to Spatial perception

Yardley et al., 2001 assessed the postural stability on a moving platform of individuals with a different vestibular disorder as they were asked to perform various non-spatial and spatial tasks. They discovered that as the balancing activity got harder, the students' reaction times slowed, and they performed less accurately on tasks requiring spatial and non-spatial thinking. The authors hypothesized that the act of monitoring direction could place heavy demands on cognition in a patient with vestibular dysfunction, which may result in subpar performance on a cognitive task.

During dual tasks, those with vestibular disorders have a slower gait speed, more imbalance, and veering than healthy people. However, the cerebral mechanisms remain unknown. (Hoppes et al., 2020) investigated if those who experience visual vertigo (VV) have different cerebral activation during dual-task walking than people who don't have VV. There were no variations in cognitive performance across the groups. When walking on uneven terrain or doing a dual task, both groups slowed down; participants in the VV group walked slower than those who didn't have the problem under all scenarios. In all situations, patients with VV demonstrated lower brain activation in the bilateral prefrontal areas than CON subjects. During dual-task walking, VV participants showed lower prefrontal brain activation than CON participants. Lower cortical activity in VV patients could be related to a shift in attention away from the cognitive task to favour dynamic balance preservation.

Research on the impact on cognition in patients with vertigo due to spatial disorientation was conducted by (Gresty & Golding, 2009). Numerous activities were employed to assess cognitive performance in various situations, such as visual-vestibular mismatch, vection, spinning, Coriolis, balance, and flight manoeuvres. The authors concluded that significant individual differences in handling disorientation and errors on cognitive tasks were observed, and protection against disorientation is provided by familiarity with and practice on a test.

2.5.3 Related to Anxiety and depression

Ataxia and oscillopsia are the symptoms of impaired vestibular function that are most noticeable. The syndrome of vestibular dysfunction, however, is more complex and includes concentration and memory problems, anxiety disorders, and reflex deficiencies (Smith et al., 2010).

It is significantly more challenging to distinguish poor performance on cognitive assessments in humans from emotional problems. In humans, vestibular dysfunction is frequently linked to depressive and anxiety disorders, such as panic attacks and phobias (Persoons et al., 2003; Furman, et al.,2006; Best et al., 2006; Gurvich et al., 2013).

It has been suggested that anxiety disorders can cause vestibular-related dizziness in addition to being a direct result of vestibular dysfunction and selective serotonin uptake (Asmundson et al., 1998; Tecer et al., 2004; Best et al., 2006). Cognitive deficiency may lead to emotional issues incidentally. However, according to Halberstadt & Balaban, 2006,serotonin-releasing neurons in the dorsal raphe nucleus also extend into

the amygdala and brainstem vestibular nucleus. This result raises the possibility that variations in emotional tone have direct effects on the vestibular system.

2.6 Auditory vs vestibular involvement in cognitive abilities

Studies have repeatedly discovered that rats without vestibular lesions but with the tympanic membrane removed considerably outperform animals with vestibular lesions in cognitive activities (Zheng et al., 2012). This finding is in line with research on individuals with vestibular dysfunction. Hearing loss may not be the primary factor causing spatial memory problems in animals with BVD (Brandt et al., 2005b).

Additionally, animal research has demonstrated that lesions to the auditory and vestibular systems have distinct effects on learning and memory. These experiments used various aminoglycosides, such as streptomycin and neomycin, with varying toxicity for the auditory and vestibular hair cells (Schaeppi et al., 1991). It is unclear if the cognitive losses linked to vestibular dysfunction in animals are only related to a decline in spatial memory. According to specific animal experiments employing surgical BVD, there are also abnormalities in attention and non-spatial object recognition memory (Zheng, Balabhadrapatruni, et al., 2009).

The documented cognitive abnormalities with vestibular lesions likely have much to do with the relationship between vestibular dysfunction and anxiety and depression (Balaban & Thayer, 2001; Staab, 2006).

2.7 Assessment of cognitive problems and vestibular disorders

Several investigations have revealed a link between cognitive failure and vestibular dysfunction. However, the Patient-Reported Outcome Measures questionnaires that address the chief vestibular complaint in this patient cohort fail to indicate this dysfunction domain. The findings show that cognitive impairment is common in chronic vestibular diseases, including peripheral disorders like MD. Age may play a more negligible effect on cognitive dysfunction than the length of vestibular symptoms before diagnosis (and care) and specific etiologies. This is not effectively addressed in Patient-Reported Outcome Measures surveys, and it could be neglected during diagnosis. Appropriate identification may aid in tailoring treatment, particularly rehabilitation programs, to the needs of specific patients (Rizk et al., 2020).

Patient-reported outcome surveys for dizzy patients provide minimal insight into the cognitive dysfunction that patients frequently experience.

Lacroix et al. in 2016, proposed an internet-based Neuropsychological Vertigo Inventory (NVI; French) that assesses attention, memory, emotion, spatial perception, time perception, vision, and motor abilities. The NVI was created to evaluate dizziness and/or vertigo patients' self-reported cognitive impairments. The NVI has 28 items and 7 subscales in its original French language edition. The data analysis revealed that a 22-item NVI with four domains was supported: affective mood, temporal memory, spatial memory, and visual-spatial cognition. The NVI is a technique for determining which cognitive constructs are affected by vestibular deficits. The cognitive impairment of

patients with vertigo was measured using the English version of the neuropsychological vertigo inventory (NVI). It was found that cognitive dysfunction is similar in vestibular migraine patients to Meniere's disease patients, although it is higher in BPPV patients. The Dizziness Handicap Inventory's (DHI) inability to assess the cognitive domain is shown in the absence of difference in scores among these patients (Liu et al., 2019a). However, additional investigations of reliability and convergent validity are required before the NVI can be used in therapeutic settings (Jacobson et al., 2020).

The World Health Organization Quality of Life-BREF questionnaire, which is a standardized questionnaire, was used to assess the quality of life of patients with vertigo, and the authors concluded that when compared to healthy controls, vertigo patients had a significant rise in negative feelings and a significant drop in cognitive indices and quality of life.

Patients with vestibular disorders may experience cognitive problems, although there is no consensus on the type or severity of these issues. Cognitive dysfunction in a well-defined group of neuro-otology patients, controlling for any confounding factors with demographic data and scores from the depression, anxiety, and stress scale, was considered. Even though evaluations of cognitive dysfunction were linked to emotional distress, they were much higher in patients who were not suffering from depression, anxiety, or stress. Thus, it was concluded that patients suffering from dizziness and vertigo have significant cognitive impairment, affecting their attention and perception of space and time. (Xie et al., 2022).

2.8 Specific disorders related to vestibular problems and cognition.

The raphe nuclei, locus coreuleus, hippocampus, amygdala, insular cortex, anterior cingulate cortex, putamen, prefrontal cortex, parietal lobe, occipital lobe, and cerebellum were chosen as the 12 vestibular-related brain regions known to be associated with mental illnesses. Parkinson's disease (PD), major depressive disorder (MDD), bipolar disorder (BPD), schizophrenia (SCZ), post-traumatic stress disorder (PTSD), body dysmorphic disorder (BDD) or obsessive-compulsive disorder (OCD), and attention deficit hyperactivity disorder were among the psychiatric conditions that were present (ADHD) (Gurvich et al., 2013a).

A longitudinal study was conducted to find cognitive problems linked to anxiety and maintenance in persons with Meniere's disease. Baseline anxiety was found to be associated with intolerance of uncertainty, fear-avoidance of physical activity, the assumption that dizziness will develop into a severe attack of vertigo, and various sickness perception subscales when symptom severity was adjusted for (emotional representations, consequences, psychological causes, and perceived treatment effectiveness). These correlations were discovered in individuals who received and did not receive self-help booklets. Thus the study's findings imply that in Meniere's disease, intolerance of uncertainty is linked to anxiety (Kirby & Yardley, 2009).

Wang et al. 2016, conducted a study to see how migraine-associated vertigo (MV) affects patients' cognitive state and quality of life. Cognitive test scores in MV patients were considerably lower than in the simple migraine group (MMSE, tracing, memory,

and VFT scores). The MV group had the highest TMT-A and TMT-B scores, followed by the simple migraine group. The MV group had a higher rate of deep brain, peripheral lateral ventricle, and total white matter lesions than the simple migraine group. Finally, the MV group had significantly greater deep lesion and peripheral lateral ventricle ratings than the simple migraine group. The MV group had considerably poorer physical, social, mental, and total health scores than the simple migraine group. It was concluded from the study that Patients with MV have more severe cognitive impairment than patients with a simple migraine or healthy volunteers, have a higher rate of brain white matter lesions, and have a lower quality of life.

A study was conducted on patients with the clinical diagnosis of frontotemporal dementia (FTD) to see if vestibular problems have a role in the clinical symptoms of FTD. During vestibular suppression (VS) tests, caloric nystagmus was not always inhibited in the FTD syndrome group. Furthermore, VS was shown to be considerably decreased in people with FTD syndrome who had gait disturbances compared to those who did not. This investigation found that, regardless of the neuropathological background, VS dysfunction in patients with FTD leads to an inability to regulate vestibular function through visual perception. In patients with FTD syndrome, this could be linked to gait disturbance (Nakamagoe et al., 2016).

2.9.1 Unilateral vs Bilateral vestibular disorders

Study using standardized cognitive tests, bilateral vestibular loss (BVL) patients' memory performance ranged from normal to superior, but they performed poorly in the

virtual maze scenario. In addition, the patients' bilateral hippocampal volume was smaller than that of sex- and age-matched controls, who were also comparable to the patients in terms of years of education and prior navigating experience. As a result, BVL patients performed worse than controls in hippocampus-dependent spatial learning in a computer-based virtual test without the need for vestibular cues (Brandt et al., 2005b).

Patients with bilateral vestibular loss performed worse on the test when they had to recall a navigation route to a previously visible target but not while the target was visual, indicating that the effect was memory-related (Schautzer et al., 2003). Brandt et al. in 2005 used the Weschler memory test to demonstrate that the patients' non-spatial memory ability was normal or above normal. Additionally, the patients' hippocampal volume was much lower than the controls. There was only a substantial rise in the cerebrospinal fluid volume; there was no significant loss in the volume of the total brain, the volume of grey matter, or the white matter. This effect was bilateral and localized to the hippocampus. Notably, just one BVD patient experienced complete postoperative hearing loss.

Zu Eulenburg et al. (2010) showed that individuals who had recovered from unilateral vestibular neuritis, regardless of the laterality of the vestibular neuritis, displayed a significant decrease in the volume of the left posterior hippocampus. These results suggest that three different sensory systems appear to be involved in VN's central compensatory processes. As a direct result of increased internuclear vestibular crosstalk between the medial vestibular nuclei, the vestibular system first demonstrated increased white matter in the commissural fibres. Second, due to increased processing of

proprioceptive information in the right gracile nucleus, a shift to the somatosensory system was made to re-establish postural stability. Third, in VN patients with persistent peripheral vestibular hypofunction, there was a bilateral increase of grey matter in the middle temporal (MT)/V5 bilaterally.

2.10 Reading and writing difficulties due to vestibular problem

Risey & Briner 1990 described a link between central vertigo and dyscalculia. They reported that 20% of patients with vertigo had robust errors in backward counting. The specific error noted by the authors involved the skipping of a decade when counting backwards by twos, as, for example, in the sequence ". . . 84, 82, 70, 78, 76, 74, 72, 60, 68, 66, . . .". Usually, these subjects did not even recognize the error when they were shown their responses in written form. Patients who have the disorder generally struggle to perform mental calculations. Longer counting times were evident; when the inaccuracy was delivered to the patients visually, they could not spot it.

2.11 Management options for patients with vertigo and cognitive problems

A study conducted on recurrent BPPV patients reported that some patients complained of residual symptoms even after a successful canalith repositioning procedure. High-dose betahistine was more effective in alleviating residual dizziness than low-dose betahistine. Wan et al., 2018 conducted a study to see if adding cognitive behavioural therapy (CBT) to low-dose betahistine would make the treatment of recurrent BPPV patients more effective than only high-dose betahistine. The 25-item Dizziness Handicap Inventory (DHI), Hamilton Anxiety Rating Scale (HARS), and Hamilton

Depression Rating Scale (HDRS) were used to record and examine the duration of residual dizziness. These findings showed that by combining low-dose betahistine with CBT, low-dose betahistine might treat residual dizziness as effectively as high-dose betahistine. Furthermore, low-dose betahistine combined with CBT had some advantages over high-dose betahistine in reducing depression and anxiety symptoms, which could be investigated further.

The efficiency of a comprehensive psychological approach to vestibular rehabilitation was tested in a study. A total of 18 patients experiencing vertigo because of a brain injury were included in the study. Patients with vestibular disorders were evaluated and referred to the therapy program. The treatment comprised of a behavioural exposure program to movements and activities that caused vertigo and anxiety to aid compensation for vestibular impairment and physical anxiety symptoms. Self-rating questionnaires and a sway monitor were used to assess vertigo and balance, emotional discomfort, vertigo handicap, and coping techniques. The 18 patients benefited greatly from this vestibular rehabilitation program, as their scores on measures of vertigo symptoms, handicap, mental distress, physical flexibility, and postural stability increased dramatically after therapy, compared to no change during a waiting list period (Gurr & Moffat, 2001).

Ferrari et al., 2014 compared psychiatric-psychosomatic comorbidities, such as anxiety, sadness, somatization symptoms, and alexithymia in a group of BPPV patients to healthy controls and assessed gender differences. Affective symptomatology, such as depression, demoralization, phobia and anxiety, and somatization, were shown to be

considerably more common in BPPV patients, suggesting that the female gender may be a risk factor

This study aimed to see how successful vestibular rehabilitation combined with cognitive behavioural therapy was at treating dizziness. Improvements in walking time and better coping with dizziness-provoking movements in the Dizziness Handicap Inventory showed statistically significant improvement. However, there were no effects on domains related to anxiety or sadness. Thus the authors concluded that in elderly persons, cognitive behavioural therapy paired with vestibular rehabilitation reduces dizziness and, therefore that cognitive behavioural therapy and vestibular rehabilitation can be used together to treat dizziness (Johansson et al., 2001).

Diagnostics and management of concussions (mTBI) for children, adolescents, and adults are among the most often addressed topics in the healthcare setting. There is currently no "gold standard" for assessing and managing concussion patients. However, research has been conducted on the subject. A case report of a 70-year-old man with a cortical and labyrinthine concussion was taken for the study. The American Institute of Balance – Vestibular Cognitive Integration (AIB-VCI) used the protocol for examining and caring for the cortical and labyrinthine elements of the patient's concussion. The patient could perform at his desired vestibular and cognitive levels promptly after the concussion, which was a huge success. A wealth of material is available in the literature on patients with comparable symptoms who do not respond to treatment. This was a huge success, as the patient could promptly return to his pre-concussion vestibular and cognitive levels. There is a wealth of literature on patients with comparable symptoms

who do not recover as quickly or have lost vestibular and cognitive ability (McCrory et al., 2012). This shows that the AIB-VCI could be an excellent way to assess and manage patients with vestibular and labyrinthine concussions (Gans RE & Kurtzer DA, 2017).

The first study to show that caloric vestibular stimulation (CVS) can enhance verbal and spatial memory in humans was conducted by (Bächtold et al., 2001), and the impact was more substantial for proper ear stimulation. However, CVS stimulates vestibular reflexes, making it challenging to distinguish those effects from those on cognitive function. A study by (Falconer & Mast, 2012) suggests that CVS can improve performance on an egocentric transformation challenge. There is currently very little information available about how noisy GVS impacts memory. It is unclear whether the result has any connection to vestibular lesions' effects on spatial memory. One theory is that any positive impact of GVS is simply a product of the fact that vestibular information reaches numerous areas of the neocortex and will likely alter how sensory information is integrated (Wilkinson et al., 2008).

Therefore, the study's purpose was to assess whether there were any cognitive concerns associated to the BPPV and MD and hence it is clear from the literature review that there may be a strong correlation between cognitive problems and vestibular impairment.

Chapter 3

METHODS

The research aimed to study any cognitive problems associated with patients diagnosed with BPPV and MD using a standardized questionnaire. A non-experimental standard group comparison research design was employed to analyze the cognitive issues and to compare the different parameters associated with cognition within and across the groups. The study was conducted in an online/tele-mode.

3.1 Participants

A total of 107 subjects participated in the study. Out of the 107, Group-I had 29 subjects clinically normal, Group II had 38 subjects diagnosed with BPPV and Group III had 40 subjects diagnosed with Meniere's disease. The clinical groups were diagnosed by ENT specialists and RCI-certified audiologists (staff and faculty of AIISH).

Group I – Normal subjects with no history of vertigo or associated problems that could impact balance and equilibrium were taken for the study.

Group II – Patients diagnosed with BPPV with no other otological problem or associated problems like ear discharge, ear pain, history of surgery and unilateral BPPV were taken for the study.

Group III – Patients diagnosed with Meniere's disease. Unilateral MD cases were taken for the study. Patients with no other otological or associated problems like ear discharge, ear pain, or history of surgery were taken for the study.

Hearing loss was not regarded as an exclusion factor because it was anticipated that most of the participants in the institute's database would have hearing loss.

Subjects' consent and willingness to participate in the study were considered. The consent form had information regarding the study's title, a brief description of the research topic and the approximate amount of time it'll take to complete the questionnaire. The details were also explained verbally to the subjects. The Google form's initial section was the consent form, which included the alternatives "Yes" and "No" for subjects to select from. If the subjects voluntarily decided to participate in the study, they had to choose 'Yes', and further questions were followed. Other questions did not follow if the subjects responded with "No."

3.2 Sample selection

Group, I was clinically normal subjects with no history of any otological problems, and their participation was requested via phone call, WhatsApp or in-person interactions. 30 potential subjects were contacted, who was regarded as a clinically normal group, out of which 29 subjects responded and gave their consent to participate in the study. The clinical groups, i.e., Group-II and Group-III, were selected from the AIISH clinical database after a detailed analysis of the case files.

Selection of case files - With permission from the concerned authority, the data from the AIISH Client Database Management Software (CDMS) was utilized for selecting the cases. Information was collected for patients diagnosed with "Meniere's disease" and "BPPV." The cases were later confirmed from the clinical records

maintained at the department of ENT. A total of 131 case files were screened from January 2017 to May 2022, out of which 10 subjects were rejected as they didn't fall into the inclusion criteria, which included bilateral BPPV cases, recurrent BPPV cases, MD with other comorbid conditions etc., and 12 subjects did not respond to the phone call/email. Thus, the study was conducted on a total of 78 clinical subjects. The 29 non-clinical subjects were randomly selected from known contacts. However, they underwent a quick GHQ-5 questionnaire (Shamasunder et al., 1986) for general health screening.

3.3 Procedure

The procedure involved three phases. Phase I involved the selection of standard questionnaires. Phase II Involved administration of questioners through online or tele-mode. Phase III involved analysis of the information gathered.

3.3.1 Phase I: Selection of the questionnaire

In the preliminary phase, following a literature search on the questionnaires that evaluate a person's cognitive symptoms, 3 standardized questionnaires were selected and were given to 3 RCI certified experienced Audiologists. The 3 standardized questionnaires were Symptom Checklist-90-Revised, WHODAS 2.0 and The Neurobehavioral Cognitive Status Examination (NCSE). The audiologists' recommended that questions related to cognition from the Neurobehavioral Cognitive Status Examination (NCSE) were most appropriate for this study. The NCSE is a screening examination that assesses cognition in a brief but quantitative fashion and uses independent tests to evaluate functioning within five major cognitive ability areas:

language, constructions, memory, calculations, and reasoning (Kiernan et al., 1987). The NCSE has 93 questions in total, out of which 10 questions are related to cognition. These 10 questions were considered for the current study.

An e-questionnaire, i.e., a Google Form, which included the below-mentioned details, was prepared:

The questionnaire had 2 sections: (a) Demographic Details and (b) Cognitive related questions selected from NCSE

Part a)

- Questions on demographic details about the participants' names, ages, gender, and diagnosis were asked.
- Questions related to the history of BP, diabetes, tinnitus, and if they were under any medication were asked.

Part b)

- 10 questions from the selected standardized questionnaire were asked.

The questionnaire is attached as Annexure I.

3.3.2 Phase II: *Administration of the questionnaire*

The researcher interviewed participants online (google meet) or over the telephone. The interview began with disclosing information pertinent to the study and vouching for informed consent. After detailed instructions were provided to the participants, the questionnaire was sent via mail/WhatsApp. The instructions were in English in the consent form and the

questionnaire; however, the details were also instructed in Hindi and Kannada as and when required. The instructions involved regarding the procedure of the questionnaire to be administered. The subjects were asked if they were comfortable filling the questionnaire on their own, which was sent via WhatsApp or email. If not, the questions were verbally read out along with the response options by the researcher and the subject's responses were collected. The questionnaire, demographic details, and consent form are attached as Annexure I.

Group I, i.e., the non-clinical population, was screened through a self-administered General Health Questionnaire five (GHQ), designed by Goldberg (1972), an effective first-stage screening tool for the detection of non-psychotic psychiatric illnesses. It is simple, easy to administer, acceptable and has high validity (Shamasunder et al.,1986). The responses were recorded on a Likert Scale rating from 1 (Not at all) to 3 (Much more than usual). A score of 2 and above is considered psychiatrically ill per the guidelines of GHQ-5. Participants from Group, I were also asked about their otological history and if they had any hearing-related problems.

Group II and Group III were contacted via telephone, and the questionnaire was sent. The subjects who were capable and willing to fill the questionnaire independently were asked to fill it themselves; for the rest, the researcher filled the form by verbally asking the questions via phone.

3.3.3 Phase III: *Analysis of the information gathered*

For each response in the questionnaire related to cognition, a score of 0 for "Yes," 1 for "Sometimes," and 2 for "No" were given during the analysis and an 'overall score' for the cognitive abilities of each subject for all the 10 questions was calculated. The maximum possible score was 20, and the minimum possible score was 0. The higher scores would indicate that the subject had less cognitive-related problems, and lower scores would suggest that the subjects had more cognitive problems.

3.4 Statistical analysis

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 25. Descriptive analysis was carried out for the socio-demographic variables, including frequency, percentage, mean age, gender, and associated conditions (hearing loss, diabetes, BP). The obtained data regarding the cognitive scores were compared across the three groups using inferential statistical analysis. The influence of associated conditions on the three groups was also analyzed. Shapiro Wilk's test of normality was conducted to check whether the data obtained were normally distributed or not. The test revealed that the data were non-normally distributed. Thus, a non-parametric Kruskal Wallis -H test was administered to compare the cognitive-related problems between the 3 groups. The effect size was calculated between the groups using Cohen’s d equation (Lakens, 2013) to understand how significant the differences were. For each of the ten cognitive-based questions, a Chi-square test was done to determine whether the responses varied depending on the groups. Item analysis was conducted to assess the test's overall effectiveness as well as the effectiveness of the test's individual items (questions). Mann Whitney U test was carried out to compare the subjects

with hearing loss vs normal hearing. Analysis was also carried out for the subjects within the groups with a history of hypertension and diabetes vs subjects who didn't have any associative problems.

Chapter 4

RESULTS

The collected data were tabulated and statistically analyzed using SPSS version 25.0 (Frey, 2017). Appropriate descriptive and inferential statistical analyses were conducted to compare between and within the groups.

4.1 Demographic details

The total subjects taken for the study were 107 (N=107), out of which 29 were in Group I, i.e., in the control group or the clinically normal Group; 38 subjects diagnosed with Benign Paroxysmal Positional Vertigo (BPPV) were categorized as Group II, and 40 subjects diagnosed with Meniere's disease (MD) were categorized as Group III. Of the 107 subjects, 60 were male, and 47 were female as shown in Figure 1. The age ranged from 49 to 60 years for Group I, from 31 to 66 years for Group II and 34 to 79 years for Group III. The mean age was 53.96 (SD = 3.39), 50.71(SD = 8.77) and 54.55 (SD = 9.82) years for the three groups, respectively as shown in Figure 2. All the 107 subjects had given their consent to participate in the study and answered all the questions in the questionnaire.

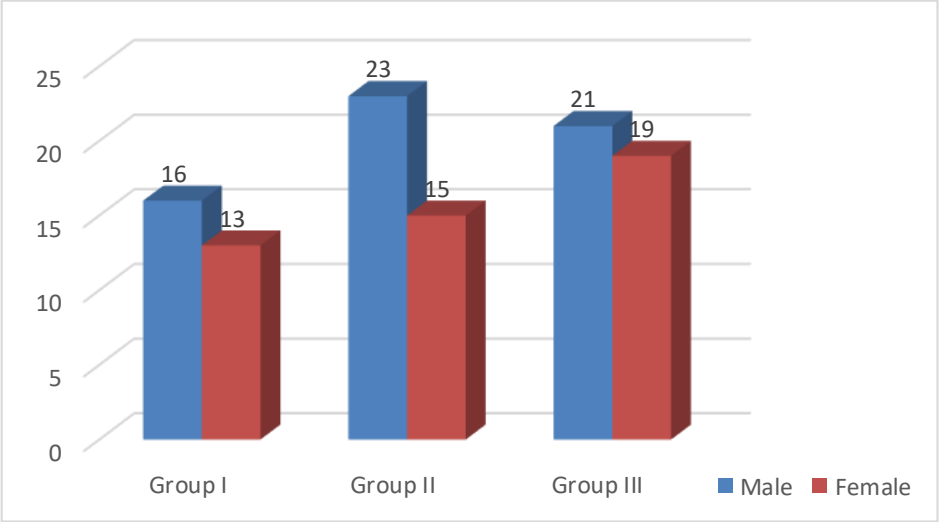


Figure 1: *Distribution of gender across the group*

Figure 2: *Distribution of the number of subjects across age (in years)*

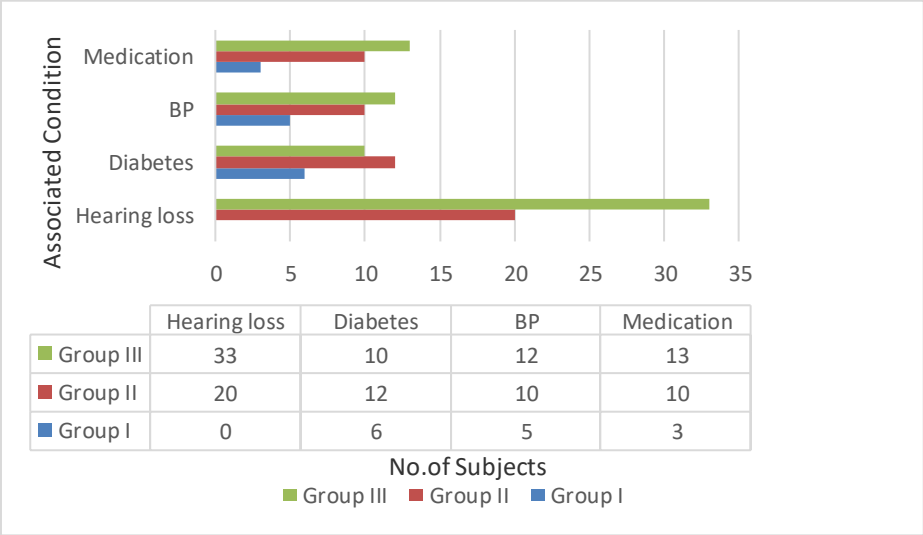
4.2 Associated condition

Group, I had 6 subjects with diabetes and 5 subjects with BP, with 3 under medication for the same. Group II had 12 participants with diabetes and 10 subjects with BP, with 10 under medication. Group III had 10 subjects with diabetes and 12 subjects with BP, with 13 under medication, as shown in Figure 1.3. Subjects with any other medical history like the history of surgery or trauma were excluded from the study.

4.3 Otological complaints

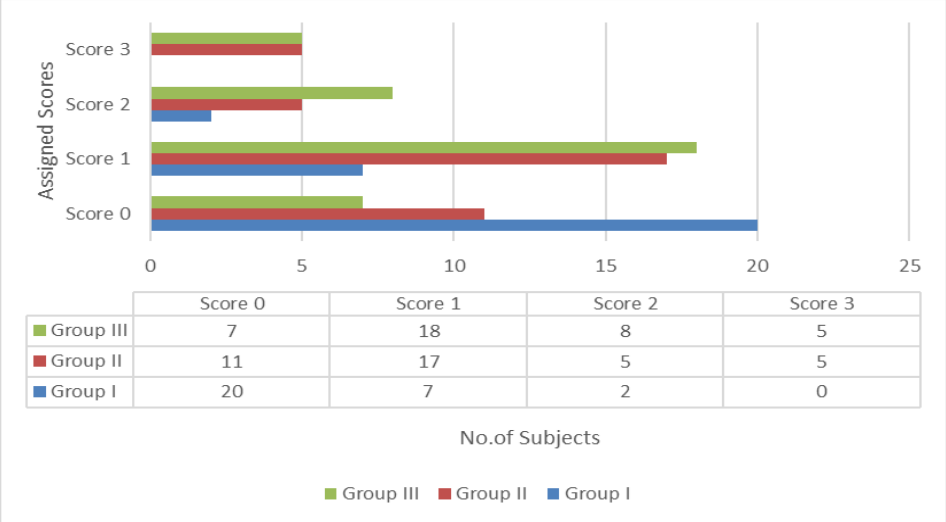
None of the subjects in the control group, i.e., Group I, had a history of hearing loss. 15 out of 38 individuals in Group II and 33 out of 40 individuals in Group III had been diagnosed with hearing loss, as shown in Figure 3. Other than subjects with reduced hearing sensitivity, subjects with other otological complaints like otalgia, otorrhea, itching sensation or blockage were excluded from the study.

Figure 4 depicts the groups with associated factors (i.e., hearing loss, diabetes, or BP). A score of '0' was assigned for the subjects who reported none of these associated conditions. A score of '1' was given if the subjects had any of the associated conditions, '2' if they reported any two associated conditions or '3' if the subjects reported all the three associated conditions. Thus an 'Overall associated score' was later used to compare cognitive abilities and non-specific associated conditions.



	Hearing loss	Diabetes	BP	Medication
Group III	33	10	12	13
Group II	20	12	10	10
Group I	0	6	5	3

Figure 3: *Distribution of subjects with associated conditions (*BP- Blood Pressure)*



	Score 0	Score 1	Score 2	Score 3
Group III	7	18	8	5
Group II	11	17	5	5
Group I	20	7	2	0

Figure 4: *Distribution of scores across groups for non-specific associated conditions*

4.4 GHQ Screening test results

All the subjects in Group I passed the GHQ-5 screening tests (scored less than 2 on all the questions) and were considered for the study.

4.5 Comparison between the groups

One of the study's objectives was to check if BPPV and Meniere's disease have any cognitive symptoms. Thus, for each response, scores were assigned during the analysis, i.e., 0 – for 'Yes', 1 – for 'Sometimes' and 2 -for 'No'. The overall score for each subject for all the 10 questions was calculated. Thus, higher scores would indicate that the subject had a less cognitive problem, and lesser scores would suggest that the subject had significant cognitive issues. Therefore, the 'Overall score' for the subject will determine their cognitive ability. It was observed that subjects diagnosed with BPPV and Meniere's disease had mean overall scores of 6.76 and 7.67, respectively, significantly less than the control population, which had a mean score of 19.58. It has been tabulated in Table 1.

Table 1

Mean, Standard deviation (SD), median and Interquartile deviation (IQR) of cognitive scores across the groups

	Mean	**SD**	**Median**	**IQR**	**Minimum**	**Maximum**
Group I	19.58	0.62	20.00	1.00	18	20
Group II	6.76	5.13	7.50	7.25	0	20
Group III		5.87	7.00	7.00	0	20

4.6 Test of normality

The Shapiro-Wilk normality test was carried out to check if the data for overall scores followed a normal distribution. The data was found to be non-normal ($p > 0.05$) except for Group II, as shown in Table 2.

Table 1

Shapiro-Wilk's test of normality results across groups

	Test Statistics	**Degrees of Freedom**	***p* value**
Group I	0.66	29	0.001
Group II	0.94	28	0.19
Group III	0.90	27	0.01

Kruskal-Wallis H test was carried out to check if there was a significant difference between the groups. Figure 5 shows a significant difference between the groups ($p < 0.01$). Thus, the Dunn-Bonferroni posthoc test was done for pairwise comparison between the three groups. The test revealed a significant difference between Group I, Group II, and Group I and Group III, but no significant difference between Group II and Group III, as shown in Table 3. The effect size was calculated between the groups using Cohen's d equation (Lakens, 2013), and it was found that there was no effect between Groups II and III. A medium effect between Groups I and II and Groups I and III was seen as the values were close to 0.5, as shown in Table 3.

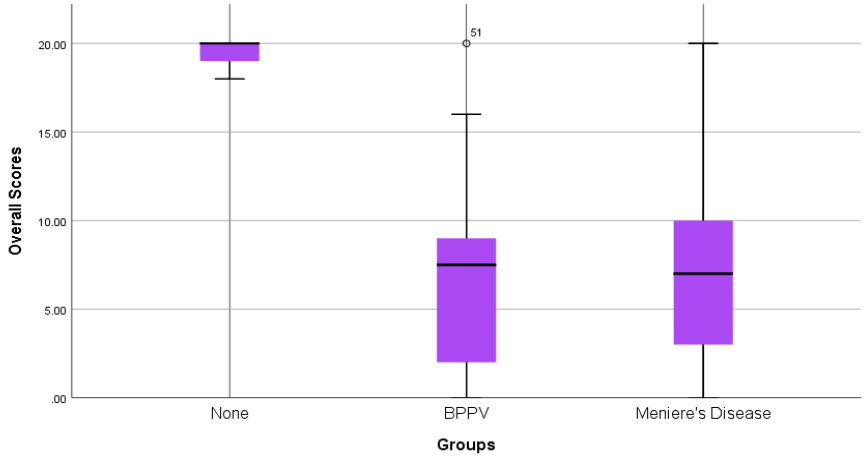


Figure 5: *Kruskal-Wallis test for between-group comparison*

Table 2

Scores of the Dunn-Bonferroni posthoc test for pairwise comparison between the groups

	H- value	***p*-value**	***Effect Size*(η_H^2)**
Group II-III	3.69	0.59	-0.01
Group II-I	51.70	**0.01**	0.45
Group III-I	48.01	**0.01**	0.42

Chi-square tests were done for the descriptive analysis of all the 10 questions, as depicted in Table 4. The Chi-square test revealed a significant association ($p < 0.05$) between the cognitive abilities and the groups, i.e., the responses to the cognitive-based questions changed according to the group. For Group I, the number of people with cognitive problems was less; for Group II and III, the number of people with cognitive problems was more, as seen in Table 4.

Table 3

Chi-square test scores with respect to the cognitive-based questions across groups

Questions	Group I	Group II	Group III	Chi-square (significance)
1. Does it seem that you can't think as quickly as before (i.e. before the diagnosis)?	Yes = 0 (0%) Sometimes = 5 (17.2%) **No = 24 (82.8%)**	**Yes =23 (60.5%)** Sometimes =10 (26.3%) No =5 (14.3%)	**Yes = 23 (57.5%)** Sometimes = 8 (20.0%) No = 9 (22.5%)	$p < 0.01$
2. Does it seem that you find it hard to think clearly?	Yes = 0 (0%) Sometimes =0 (0%) **No = 29 (100%)**	**Yes = 22 (57.9%)** Sometimes = 12 (31.6%) No = 4 (10.5%)	**Yes =21 (52.5%)** Sometimes = 12 (30.0%) No = 7 (17.4%)	$p < 0.01$
3. Does it seem that you are easily more distracted?	Yes = 0 (0%) Sometimes =0 (0%) **No = 29 (100%)**	**Yes =24 (63.2%)** Sometimes = 8 (21.1%) No =6 (15.8%)	**Yes =21 (52.5%)** Sometimes =12 (30.0%) No =7 (17.5%)	$p < 0.01$
4. Does it seem that you can't concentrate?	Yes =0 (0 %) Sometimes =0 (33.3%) **No =29 (14.8%)**	**Yes =21 (55.3%)** Sometimes =10 (26.3%) No = 7 (18.4%)	**Yes = 21 (52.5%)** Sometimes =12 (30.0%) No =7 (17.5%)	$p < 0.01$
5. Do you have trouble remembering the right words when talking?	Yes =0 (0%) Sometimes= 2 (6.9%) **No = 27 (93.1%)**	**Yes =20 (52.6%)** Sometimes= 11 (28.9%) No =7 (18.4%)	**Yes =18 (45.0%)** Sometimes =15 (37.5%) No =7 (17.5%)	$p < 0.01$
6. Do you have trouble understanding others?	Yes= 0 (0%) Sometimes =1 (3.4%) **No = 28 (96.6%)**	**Yes =20 (52.6%)** Sometimes =11 (28.9%) No =7(18.4%)	**Yes =13 (45.0%)** Sometimes =11 (37.5%) No = 3 (17.5%)	$p < 0.01$
7. Do you have trouble following conversations?	Yes = 0 (0%) Sometimes = 2 (6.9%) **No = 27 (93.1%)**	**Yes =19 (50.0%)** Sometimes =16 (42.1%) No = 3 (7.9%)	**Yes =21 (52.5%)** Sometimes =11 (27.5%) No =8 (20%)	$p < 0.01$

8. Do you have trouble with your speech?	Yes = 0 (0%) Sometimes = 0 (0%) **No= 29 (100%)**	Yes =13 (34.2%) **Sometimes= 20 (52.6%)** No=5 (13.2%)	**Yes=14 (35.0%)** **Sometimes=14 (35.0%)** No=12 (30.0%)	$p < 0.01$
9. Do you have trouble with reading?	Yes = 0 (0%) Sometimes =0 (0%) **No = 29 (100%)**	Yes=13 (34.2%) **Sometimes =18 (47.4%)** No =7 (18.4%)	Yes= 13 (32.5%) **Sometimes =14 (35.0%)** No =13 (32.5%)	$p < 0.01$
10. Do you have trouble with writing?	Yes = 0 (0%) Sometimes =2 (6.9%) **No = 27 (93.1%)**	Yes = 11 (28.9%) **Sometimes =15 (39.5%)** No = 12 (31.6%)	Yes =13 (32.5%) **Sometimes =14 (35.0%)** No= 13 (32.5%)	$p < 0.01$

Table 4 shows that patients with BPPV and MD significantly declined their cognitive abilities in the questions regarding quick thinking and decision-making (i.e., questions 1 and 2). Over 55% of patients with BPPV and over 50% of patients with MD reported having a problem, and roughly 20% to 30% of these patients responded to having the problem "sometimes". Similarly, over 55% of patients with BPPV and over 50% of patients with MD were often easily distracted and had trouble concentrating due to their problems (questions 3 and 4). In comparison, about 20-30% of the patients only occasionally experienced difficulties. However, the normal group displayed no issues in these cognitive domains. Nearly 45 to 50 % of patients with BPPV and MD also struggled with memory. They had trouble keeping up with conversations, remembering the appropriate words to use during a conversation, and understanding others (questions

5, 6 and 7). More than 90% of the patients in the normal group said they had no problems in this domain. Over 50% of patients with BPPV had occasionally encountered speech-related issues, and about 34% of patients had speech-related difficulties frequently. MD patients—approximately 35 percent—suffered from speech-related problems either frequently or occasionally. In contrast to BPPV and MD patients, none of the subjects in the normal group displayed any speech-related issues (question 8).

In contrast, only 13 percent of BPPV patients and 30 percent of MD patients had no speech-related difficulties. Patients with BPPV and MD occasionally reported reading and writing problems, with rates of 47 percent and 35 percent for reading and 39 percent and 35 percent for writing, respectively (question 9 and 10). However, fewer cognitive issues were overall seen in the reading and writing domain, and more participants chose to answer "No" to the questions than did the other subjects. Thus, the results show that cognitively relevant tasks like memory and concentration were more adversely impacted than other domains in Group II and Group III.

Item analysis was conducted to evaluate the effectiveness of the test's individual items (questions) and the test. All 10 questions had a good internal consistency and high item correlation as the Cronbach's alpha value (α) was around 0.7 to 0.8 (Ursachi et al., 2015).

Table 4

Item analysis of the cognitive-based questions

Questions	**Cronbach's alpha value (α)**
1. Does it seem that you can't think as quickly as before (i.e. before the diagnosis)?	0.74
2. Does it seem that you find it hard to think clearly?	0.81
3. Does it seem that you are easily more distracted?	0.82
4. Does it seem that you can't concentrate?	0.71
5. Do you have trouble remembering the right words when talking?	0.84
6. Do you have trouble understanding others?	0.85
7. Do you have trouble following conversations?	0.83
8. Do you have trouble with your speech?	0.85
9. Do you have trouble with reading?	0.82
10. Do you have trouble with writing?	0.73

4.7 Associated factors and their influence on cognition

Mann-Whitney U test was carried out to check if the confounding variables significantly affected the groups' responses as shown in Table 6.

Table 5

Mann-Whitney U test for subjects with Diabetes, BP, and Hearing loss within groups

	Diabetes		**BP**		**Hearing Loss**	
	|Z|	*p value*	|Z|	*p value*	|Z|	*p value*
Group I	0.99	0.41	1.07	0.38	-	-
Group II	1.26	0.20	2.25	**0.02**	0.38	0.71
Group III	1.07	0.56	1.14	0.26	0.76	0.46

From Table 6, it can be inferred that positive history of diabetes had no significant effect ($p > 0.05$) on the cognitive scores for all three groups. Similarly, there was no significant effect ($p > 0.05$) on cognitive scores for subjects with a history of hearing loss for Group II and Group III. Group I had no subjects with a history of hearing loss. For subjects with a history of hypertension (BP) in Group II, a significant effect was observed ($p = 0.02$), i.e. subjects with a positive history of BP had significantly poorer cognitive abilities. However, no significant effect of any associated conditions was observed in the subjects in Groups I and III.

4.8 Comparison of cognitive abilities (Overall Score) vs non-specific associated condition (Overall associated scores)

To analyze whether the presence or absence of any of the associated conditions (hearing loss, diabetes, hypertension) influenced the results, a score of '0', '1', '2'or '3' was assigned when a subject had no history of any of the associated condition, had any one of the associated condition, had any two of the associated condition or had all of the three associated condition, respectively and 'overall associated score' was obtained for each subject. The 'overall associated score' was compared to the cognitive scores of the subjects, as depicted in Figure 6. From Figure 6, it can be inferred that although cognitive problems were widely spread across the subjects in the 3 groups, the problem was more in subjects having more associated conditions. Chi-square test results showed a significant association (p=0.04) between the cognitive problems and associated conditions, i.e. subjects with all three associated conditions (diabetes, high blood pressure, and hearing loss) coupled with a diagnosis of BPPV or MD exhibited more

cognitive problems than subjects in the same group who only had one or two associated conditions. Similarly, subjects with 2 associated conditions exhibited more cognitive problems than subjects with 1 or fewer associated conditions. The last group of subjects exhibited more cognitive problems than those with no associated conditions, even if only one condition existed. Therefore, the presence of a cognitive issue increases with comorbidity.

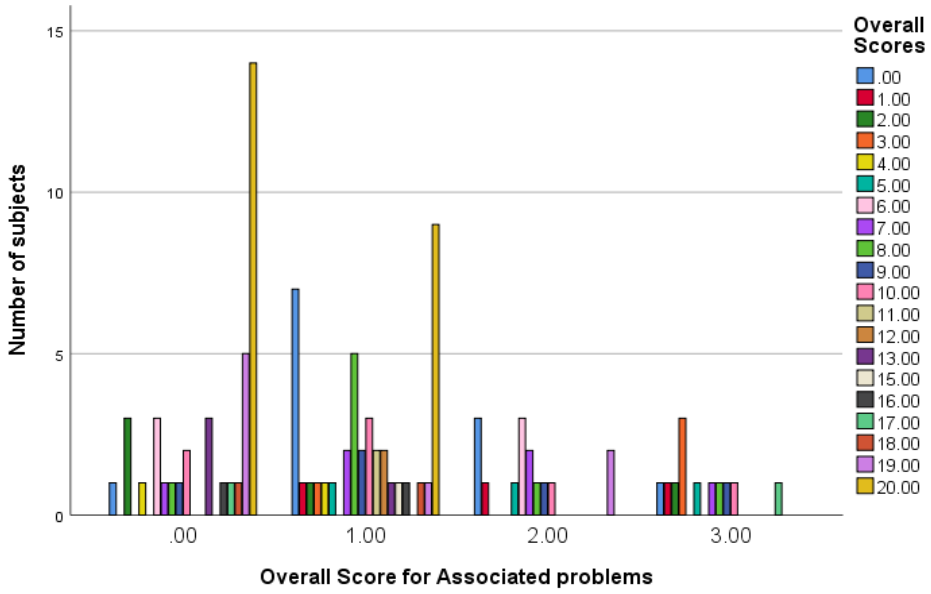


Figure 6: *Overall scores of cognitive abilities and non-specific associated conditions*

4.9 Summary of the results

The results of the present study revealed a significant difference in the cognitive scores between Group I and Group II and Group I and Group III, indicating that subjects with BPPV and MD had cognitive-related issues. There was no significant difference in the cognitive scores between Group II and III. Effect size was calculated, and a medium effect was found between Group I and II and Group I and III. Cognitive-related questions about thinking skills, memory and distractibility were most affected, whereas reading and writing skills were least involved in the groups. Item analysis was conducted and a good item correlation was found for all the 10 questions. No significant association was found between associated conditions like diabetes and hearing loss, and cognitive abilities for all three groups. However, cognitive scores were found to be significantly poorer for subjects with BPPV and the comorbid condition of BP. The results also revealed a significant association between comorbidity and cognitive abilities, i.e. the cognitive scores were poorer when more comorbid factors were present.

Chapter 5

DISCUSSION

In recent years, substantial evidence has suggested a link between loss of vestibular function and cognitive issues. The current study reveals interesting finding with respect to vestibular problems and cognitive symptoms. The results showed significant differences in cognitive abilities between subjects with vertigo and subjects without vertigo. These results could hold immense clinical importance in better assessment and management.

5.1 BPPV and Cognition

The study's first objective was to determine if there is any cognitive-related problem in patients with BPPV. The BPPV group was compared to the normal group after administering the questionnaire. The results revealed a significant difference in cognitive scores between the BPPV and the normal groups. The BPPV group gave more "Yes" responses to the items pertaining to cognition, indicating that their disorder was causing them cognitive difficulties as compared to normal.

The results of the present study corroborate those of several studies on BPPV and cognitive issues. Kim et al. (2021) used a population cohort to evaluate the risk of dementia in patients with BPPV. The BPPV group had a greater risk of dementia than the matching control group. Male sex, high income, living in a rural area, having a history of hypertension, diabetes, or dyslipidaemia, as well as not having a history of ischemic heart disease, stroke, Meniere's disease, or head trauma, were all linked to an increased risk of

dementia among BPPV patients. However, most of those factors were not considered in the current study. BPPV could be the first sign of degenerative alterations to the neurological system, and the possible explanation could be the otoconial separation resulting from macular and vestibular degeneration. Investigations have shown that BPPV patients have saccular macula neuronal degeneration (Yang et al., 2008). Patients with BPPV have been observed to have saccular ganglion cell loss and loss of ganglion cells in the superior or inferior vestibular nerve, affecting roughly 50% and 30% of the temporal bone, respectively (Gacek, 2003). In dementia patients, neuronal degeneration is known to impact the phylogenetically older neurons (Nandi & Luxon, 2009). Because the vestibular system is the phylogenetically first sensory system (Lyness et al., 2003), its degradation might be a prodromal or early stage of dementia. BPPV tends to be identified earlier than full-blown dementia because the symptoms of spinning-type vertigo are more noticeable than those linked to cognitive impairment. Thus, the current study also showed that BPPV was associated with an increased risk of cognitive issues and could be due to similar physiological reasons. The fear and anxiety that is associated with massive attacks of vertigo could also be a cause for distractibility and lack of concentration, however further evidences are required to arrive at a conclusion.

5.2 Meniere's disease and cognition

A similar trend was observed for the study's second objective, where patients diagnosed with MD were compared with the normal group. A significant difference was observed between them, i.e., compared to the normal group, the MD group responded to

questions about cognition with more "Yes" responses, indicating that their disorder was causing them to have problems with their cognitive abilities.

Chari et al. (2021) examined Dizziness Handicap Inventory (DHI) Performance and Subjective Cognitive Symptoms in individuals with Meniere's Disease and vestibular migraine. They concluded that patients with vestibular disorders like MD had a significant prevalence of cognitive impairment. Using a statewide cohort sample of data from the South Korean National Health Insurance Service, another study looked into the relationship between MD and the risk of dementia (Lee et al., 2022). The findings showed that people with Meniere's disease experienced higher rates of vascular dementia, Alzheimer's disease, and all-cause dementia than those in the comparison group. The hippocampus is well known for being involved in memory, learning, and emotion. As a result, the hippocampus has been the subject of investigations on neurodegenerative illnesses. According to a study by Brandt et al. (2005), patients with bilateral vestibular loss had a considerably atrophying hippocampus compared to controls (16 percent decreased relative to controls). According to other research, the hippocampus volume of patients with Meniere's disease was considerably lower than that of controls (Van Cruijsen et al., 2009; Seo et al., 2016). The hippocampus is an area in the brain responsible for learning and memory; any structural or functional damage to it could be a reason for cognitive deficits in MD.

Additionally, Meniere's disease causes mental stress due to limits in everyday activities brought on by chronic dizziness and associated ear problems. Atrophic alterations in the hippocampus could come from the stress's activation of the

hypothalamus-pituitary-adrenal axis, which increases cortisol output (Lupien et al., 1998; Dickerson et al., 2004). In patients with psychotic illnesses, increased emotional stress is also linked to a lower hippocampus volume (Collip et al., 2013). It suggests that the later onset of Meniere's disease may be connected to the emergence of dementia-related symptoms.

Patients from Meniere's disease also suffer from a condition called brain fog, a form of fluctuating cognitive impairment that many people with vestibular problems experience. The brain needs to work significantly more challenging to maintain equilibrium when the vestibular system is damaged, and this continuous effort has an adverse effect on cognitive performance. As a result, there could be a clouding of consciousness and a loss of mental energy, which can impede executive function, memory, recall, decision-making, and recall of words. Many patients struggle to remember people's names and the precise things they need to perform. As stated by Glenn Schweitzer (2020) in a case study, he reported difficulty in speech as words tend to slip off the tongue, and he lost track of why he entered rooms when Meniere's disease symptoms worsened, and brain fog made an appearance. Brain fog can severely interfere with the capacity to be productive in daily life, even if individuals aren't actively experiencing balance issues like vertigo or dizziness.

5.3 Comparison between BPPV and Meniere's disease and cognitive abilities

The third objective of the study was to compare the cognitive abilities between BPPV and MD. The findings from the study revealed that the two clinical groups had a

problem with cognitive abilities compared to the normal group. However, there was no significant difference between these two clinical groups regarding cognitive abilities. Using the Neuropsychological Vertigo Inventory (NVI), Liu et al. (2019) researched the quantification of cognitive dysfunction in patients with BPPV, MD and vestibular migraine (VM). Despite being substantially younger than BPPV patients, the study discovered that VM patients had significantly more cognitive issues.

Contrary to the current study's findings, MD patients also had higher cognitive impairment than BPPV patients. VM and MD did not significantly differ from one another, demonstrating that even peripheral vestibular disorders like MD can result in cognitive dysfunction comparable to central vestibular disorders like VM, which could be due to MD causing a reduction in hippocampus volume (Van Cruijsen et al., 2009; Seo et al., 2016). The results may have been influenced by the fact that MD and VM had lower mean ages than BPPV. Because younger patients could have greater demands in everyday life, such as those related to childcare and work performance, they may be more affected by cognitive impairment than older patients. Given that age is an essential factor in determining cognitive function (Harada et al., 2013) thus, in the current study, the mean ages of the two groups were almost similar and older compared to the study by Liu et al., 2019. Hence, similar cognitive scores were obtained for the two groups.

5.4 Cognitive problems in patients with BPPV and MD based on the questionnaire

Table 4 shows that patients with BPPV and MD significantly declined their cognitive abilities. Questions related to thinking skills, memory and distractibility were maximally affected. In BPPV, it could be due to the neural degeneration in the ganglion

cells due to otoconia loss, as stated by Yang et al. (2008), which may affect the input travelling to the cerebral cortex for higher cognitive tasks like thinking, reasoning and memory. Research shows that otolithic functioning and cognition could have a link. Few studies have discovered a connection between saccular function and cognition (Bigelow & Agrawal, 2015; Xie et al., 2017; Wei et al., 2018).

Contrary to Bigelow and colleagues' research, Dobbels et al. (2019) study did not find a statistically significant link between saccular function and cognition. The variations in the study methodologies for the two studies could mitigate this. A dearth of literature discusses the saccule's role in cognitive function (Dobbels et al., 2019). In MD, cognitive functioning may be affected because of Brain fog. Due to this condition, executive function, memory, recall, decision-making, and verbal recall can all be affected by a possible clouding of consciousness and a lack of mental energy, which is also seen in the current study.

Studies have also shown that MD leads to hippocampal loss. The hippocampus is a crucial component of the limbic system of the brain. Learning, empathetic reactions, memory development, and storage are all significantly influenced by hippocampal function. Trouble in following conversation and speech were seen as less affected, and reading and writing problems were least affected in patients with BPPV and MD. The part responsible for speech in the brain is the frontal lobe (Broca's area). There is a lack of evidence that vestibular problem damages this part of the brain. It is also less likely to be affected as no significant vestibular network is innervating this brain area. The occasional trouble in speech and conversation could be due to the condition of Brain fog

which leads to difficulty in word recall and cause words to get stuck in the mouth, as Glenn Schweitzer (2020), in MD patients. For BPPV patients, problems in speech and conversation could be due to neural degeneration due to otoconial loss, which may affect the firing rate of the nerve. The patients could miss out on input messages from other speakers. However, further investigation is required to come to a precise conclusion.

There are reports that vestibular problems could lead to dyscalculia. In 1990, Risey and Briner identified a connection between central vertigo and dyscalculia. Dyscalculia has been linked to thalamic lesions (Basso1 et al., 1987). It is also established that there are multiple connections between the thalamus and the vestibular, auditory, and association cortices (Streitfeld, 1980; Luethke et al., 1988). It is conceivable that an anatomical or physiological abnormality at the level of the thalamus or, more likely, the temporoparietal cortex is the cause of dyscalculia observed in individuals with central vertigo.

Furthermore, vestibular system disorders have been linked to learning disabilities in children (Bundy et al., 1987). A similar reason could cause reading and writing problems for the patients in the current study. However, the present study was conducted on an adult population. Thus, further research is required to conclude. Thus, the cognitive domains in the questionnaire pertaining to memory, thinking, concentration, speech, reading and writing abilities would help determine if patients with BPPV or MD also suffer from these cognitive issues.

5.5 Influence of Associated conditions on cognition

In the current study, several subjects in the 3 groups of clinically normal, BPPV and MD, with associated conditions of diabetes, hypertension (BP) or hearing loss, as depicted in Figures 3 and 4. The present research attempted to check whether any of these conditions affected cognitive abilities as there was evidence that diabetes, BP or hearing loss significantly affected cognitive performance.

It is clear from the current study that having a history of diabetes did not affect the cognitive scores for any of the three groups. There was no discernible impact on cognitive performance for patients with BPPV and MD with a history of hearing loss. A substantial effect was seen in BPPV patients with a history of hypertension (BP), i.e., subjects with a positive history of BP had a significantly worse cognitive performance. However, none of the accompanying conditions had a noticeable impact on the patients with MD.

Studies reported that individuals with diabetes might also suffer a cognitive decline over time (Gispen & Biessels, 2000; Biessels et al., 2008; Kumar et al., 2009; Ruis et al., 2009; Creavin et al., 2012). However, in the current study, the influence of diabetes on cognitive abilities was found to be insignificant in the groups. Studies also show that persons with hypertension may eventually decline their cognitive function (Skoog, 2003; Birns & Kalra, 2008; Knecht et al., 2009; Hajjar et al., 2011; Power et al., 2013). Similar findings have been evident in the current study, where subjects diagnosed with BPPV and associated conditions of BP reported significantly more cognitive problems than those without BP. However, a significant difference was not observed for

the group with MD. This could be due to the difference in the severity and duration of the associated condition of BP, which was not accounted for in this study. Further analysis could be carried out to check for the association of BP in BPPV and MD with respect to the duration and severity of the problem.

A dearth of evidence explains how ailments like diabetes and high blood pressure are linked to cognitive issues in vestibular disorders.

There is ample evidence that hearing loss leads to dementia and other cognitive problems (Granick et al., 1976; Lin, 2011; Peracino, 2014; Dawes et al., 2015; Lawrence et al., 2018). Thus, in the current study, a within-group comparison was conducted to check whether hearing loss affected the cognitive problem. The results revealed no significant difference, i.e. hearing abilities had no influential role in patients who had BPPV and MD and were suffering from cognitive-related issues. Hence the cognitive problem in the subjects with BPPV and MD could be due to the vestibular problem or a combination of both. This result supports various studies where similar findings were reported. In an animal study conducted by Smith & Zheng, 2013, the middle ear structures (tympanic membrane and the ossicles) were removed to partially achieve auditory control (partial sound transmission to the cochlea). They found that animals without vestibular lesions but with the tympanic membrane removed outperform animals with vestibular abnormalities in cognitive activities. Another supporting study claims that spatial memory issues in animals with BVD are not primarily caused by hearing loss and could be due to vestibular deficits (Brandt et al., 2005a).

Additionally, animal research has demonstrated that lesions to the auditory and vestibular systems have distinct effects on learning and memory (Schaeppi et al., 1991). Thus, from the current study, it can be concluded that hearing loss may not be influential in developing cognitive problems in patients with vestibular deficits. However, to arrive at a precise conclusion, further analysis needs to be conducted considering the type, degree, duration and mode of rehabilitation (HA, CI), etc. and compare the vestibular and hearing problem.

An attempt was also made to check whether more comorbid conditions influenced cognitive difficulties in the current study. Figure 5 demonstrated a significant relationship between cognitive problems and associated conditions. The subjects with all three associated conditions (diabetes, high blood pressure, and hearing loss) and a diagnosis of BPPV or MD exhibited more cognitive problems than subjects in the same group who only had one or two associated conditions.

Studies regarding diabetes, hypertension and hearing loss is linked to cognitive abilities independently have been well established (Biessels et al., 2008; Kumar et al., 2009; Ruis et al., 2009; Birns & Kalra, 2008; Knecht et al., 2009; Hajjar et al., 2011; Power et al., 2013; Lin, 2011; Peracino, 2014; Dawes et al., 2015; Lawrence et al., 2018). Studies regarding cognitive impairment and comorbidities have been conducted. These studies reveal that people with cognitive impairment have more serious medical comorbidities than those without cognitive impairment (Doraiswamy et al., 2002; Lyketsos et al., 2005; Rise et al., 2016). Thus the progression of the cognitive problems may be impacted by the comorbidity in the current study. It may be possible to enhance

cognition with the optimal management of medical comorbidities. The role of medical comorbidity in vestibular disorders and the development or evolution of the cognitive disorder, as well as the mechanisms behind its neuropathologic consequences, could be the subject of future research.

Chapter 6

SUMMARY AND CONCLUSION

The current research aimed to assess if BPPV and MD patients have any cognitive problems. A non-experimental standard group comparison research design was used, and 107 subjects (29 normal, 38 BPPV & 40 MD) participated in the survey via online/tele-mode. The clinically normal subjects had no history of vertigo. Unilateral cases of MD and BPPV with no other otological complaints like ear discharge, ear pain or any history of ear surgery, were taken for the study. 10 out of 93 questions which are related to the cognitive domain were selected from a standardized questionnaire i.e., the Neurobehavioral Cognitive Status Examination (NCSE), and was used to compare the cognitive scores of individuals with BPPV and MD and the data obtained from clinically normal subjects. The study revealed a significant increase in cognitive problems in BPPV patients compared to the normal group, which could be due to the neural and vestibular degeneration because of the macular otoconial loss in patients with BPPV as there are networks from the otoliths to the cortical structures in the brain that are responsible for the cognitive functioning. The fear and anxiety could also be a factor due to the severe attacks of vertigo that the patients may experience. Similarly, the results showed poorer cognitive abilities for the MD group compared to the normal group, which could be due to hippocampal loss and brain fog in MD. However, there was no significant difference in cognitive scores in BPPV and MD groups due to the similar age groups taken in the study. Based on the questionnaire, cognitive domains like memory, thinking abilities and distractibility were severely affected as compared to domains like reading and writing

skills, which could be due to the fact that the affected areas in the brain due to vestibular problems like BPPV and MD are the areas responsible for the former domains rather than the latter. Associated factors like BP, diabetes and HL were also assessed to check if they had any influence on the results, and it was found that their diabetes and HL had no significant effect on the cognitive performance of all the groups; however, subjects with BPPV who also had BP, had a slightly poorer cognitive performance as compared to those who don't. The study also revealed that the more comorbid conditions along with the disorder, the more will be the cognitive problem for all the groups.

Thus to conclude, the current study reveals that there could be cognitive issues present in patients with BPPV and MD which may include memory difficulties , thinking difficulties , lack of concentration , speech and conversation problems and also reading and writing difficulties. The cognitive issues were found to more affected with comorbid conditions. Thus, the present study acknowledges this multi-faceted nature of vertigo, which might also involve cognitive-related issues along with balance issues. Therefore, it is crucial for individuals with a vestibular problem to activate neuropsychological compensation, get over avoidance, and build confidence and independence. Psychological aspects (mood, cognition, and behaviour) are also impacted and must be addressed simultaneously while managing vestibular disorders.

6.1 Clinical Implications

The current study's findings suggest that patients with BPPV and MD are likely to have cognitive issues as both the groups' cognitive abilities are significantly lower than the normal groups.

The results also suggest that every patient with BPPV or MD should at least be screened for their cognitive abilities, if a complete diagnostic test battery is not possible.

The outcome of the current study highlights that patients with BPPV and MD might require training to improve their cognitive abilities and counselling to deal with their problems effectively. Cognitive behavioural therapy (CBT) along with Vestibular Rehabilitation Therapy (VRT) could be provided for holistic management and better quality of life for these patients. Thus, the study also emphasizes the importance of a team approach in managing vestibular disorders.

The study's results also add information to the existing literature regarding the association of cognitive problems in patients with vestibular disorders.

6.2 Limitations of the study

Purposive, non-random sampling was conducted in the study, subjected to researcher and sampling biases. Amidst the pandemic, performance-based cognitive tests couldn't be done. The data collection was done online, which might have affected the responses. The influence of tinnitus on Meniere's disease was not studied in the current research. The vestibular disorder's severity and effect on cognitive abilities were not

considered. Duration and severity of the comorbid factors were not considered. The influence of management of HL (untreated or treated) was not considered in the study. The study did not consider the impact of factors like age, gender, socio-economic status, or education level. Due to these limitations, further research is still necessary to validate and corroborate the conclusion of the current study.

6.3 Future research

The study can be done on a larger population. Research on different vestibular disorders and how they relate to cognitive issues could be explored. Along with questionnaires, performance-based tests related to cognition could be done along with the questionnaire. The vestibular disorder's severity and effect on cognitive abilities can be studied. Duration and severity of the comorbid factors and their association with cognitive problems could be studied. Factors like age, gender, socio-economic status and education level and their influence on the cognitive abilities of patients with vestibular disorders can be studied.

REFERENCES

Agrawal, Y., Ward, B. K., & Minor, L. B. (2013). Vestibular dysfunction: Prevalence, impact and need for targeted treatment. *Journal of Vestibular Research : Equilibrium & Orientation*, *23*(3), 113. https://doi.org/10.3233/VES-130498

Asmundson, G. J. G., Larsen, D. K., & Stein, M. B. (1998). Panic disorder and vestibular disturbance: an overview of empirical findings and clinical implications. *Journal of Psychosomatic Research*, *44*(1), 107–120. https://doi.org/10.1016/S0022-3999(97)00132-3

Bächtold, D., Baumann, T., Saándor, P. S., Kritos, M., Regard, M., & Brugger, P. (2001). Spatial- and verbal-memory improvement by cold-water caloric stimulation in healthy subjects. *Experimental Brain Research*, *136*(1), 128–132. https://doi.org/10.1007/S002210000588

Baek, J. H., Zheng, Y., Darlington, C. L., & Smith, P. F. (2010). Evidence that spatial memory deficits following bilateral vestibular deafferentation in rats are probably permanent. *Neurobiology of Learning and Memory*, *94*(3), 402–413. https://doi.org/10.1016/J.NLM.2010.08.007

Balaban, C. D., & Jacob, R. G. (2001). Background and history of the interface between anxiety and vertigo. *Journal of Anxiety Disorders*, *15*(1–2), 27–51. https://doi.org/10.1016/S0887-6185(00)00041-4

Balaban, C. D., & Thayer, J. F. (2001). Neurological bases for balance-anxiety links.

Journal of Anxiety Disorders, *15*(1–2), 53–79. https://doi.org/10.1016/S0887-6185(00)00042-6

Best, C., Eckhardt-Herrn, A., Diener, G., Bense, S., Breuer, P., & Dieterich, M. (2006). Interaction of somatoform and vestibular disorders. *Journal of Neurology, Neurosurgery, and Psychiatry*, *77*(5), 658. https://doi.org/10.1136/JNNP.2005.072934

Biessels, G. J., Deary, I. J., & Ryan, C. M. (2008). Cognition and diabetes: a lifespan perspective. *The Lancet Neurology*, *7*(2), 184–190. https://doi.org/10.1016/S1474-4422(08)70021-8

Bigelow, R. T., & Agrawal, Y. (2015). Vestibular involvement in cognition: Visuospatial ability, attention, executive function, and memory. *Journal of Vestibular Research : Equilibrium & Orientation*, *25*(2), 73–89. https://doi.org/10.3233/VES-150544

Bigelow, R. T., Semenov, Y. R., Hoffman, H. J., & Agrawal, Y. (2020a). Association between vertigo, cognitive and psychiatric conditions in US children: 2012 National Health Interview Survey. *International Journal of Pediatric Otorhinolaryngology*, *130*. https://doi.org/10.1016/J.IJPORL.2019.109802

Bigelow, R. T., Semenov, Y. R., Hoffman, H. J., & Agrawal, Y. (2020b). Association between vertigo, cognitive and psychiatric conditions in US children: 2012 National Health Interview Survey. *International Journal of Pediatric Otorhinolaryngology*, *130*. https://doi.org/10.1016/J.IJPORL.2019.109802

Birns, J., & Kalra, L. (2008). Cognitive function and hypertension. *Journal of Human Hypertension 2009 23:2*, *23*(2), 86–96. https://doi.org/10.1038/jhh.2008.80

Bisdorff, A., Bosser, G., Gueguen, R., & Perrin, P. (2013). The epidemiology of vertigo, dizziness, and unsteadiness and its links to co-morbidities. *Frontiers in Neurology*, *4 MAR*, 29. https://doi.org/10.3389/FNEUR.2013.00029/BIBTEX

Brandt, T., Schautzer, F., Hamilton, D. A., Brüning, R., Markowitsch, H. J., Kalla, R., Darlington, C., Smith, P., & Strupp, M. (2005a). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. *Brain : A Journal of Neurology*, *128*(Pt 11), 2732–2741. https://doi.org/10.1093/BRAIN/AWH617

Brandt, T., Schautzer, F., Hamilton, D. A., Brüning, R., Markowitsch, H. J., Kalla, R., Darlington, C., Smith, P., & Strupp, M. (2005b). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. *Brain : A Journal of Neurology*, *128*(Pt 11), 2732–2741. https://doi.org/10.1093/BRAIN/AWH617

Brandt, T., Schautzer, F., Hamilton, D. A., Brüning, R., Markowitsch, H. J., Kalla, R., Darlington, C., Smith, P., & Strupp, M. (2005c). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. *Brain*, *128*(11), 2732–2741. https://doi.org/10.1093/BRAIN/AWH617

Brandt, T., Schautzer, F., Hamilton, D. A., Brüning, R., Markowitsch, H. J., Kalla, R., Darlington, C., Smith, P., & Strupp, M. (2005d). Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. *Brain*, *128*(11), 2732–2741. https://doi.org/10.1093/BRAIN/AWH617

Bundy, A. C., Fisher, A. G., Freeman, M., Lieberg, G. K., & Izraelevitz, T. E. (1987). Concurrent validity of equilibrium tests in boys with learning disabilities with and without vestibular dysfunction. *The American Journal of Occupational Therapy : Official Publication of the American Occupational Therapy Association*, *41*(1), 28–34. https://doi.org/10.5014/AJOT.41.1.28

Chari, D. A., Liu, Y. H., Chung, J. J., & Rauch, S. D. (2021). Subjective Cognitive Symptoms and Dizziness Handicap Inventory (DHI) Performance in Patients With Vestibular Migraine and Menière's Disease. *Otology & Neurotology : Official Publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, *42*(6), 883–889. https://doi.org/10.1097/MAO.0000000000003081

Chern, A., & Golub, J. S. (2019). Age-related hearing loss and dementia. *Alzheimer Disease and Associated Disorders*, *33*(3), 285. https://doi.org/10.1097/WAD.0000000000000325

Collip, D., Habets, P., Marcelis, M., Gronenschild, E., Lataster, T., Lardinois, M., Nicolson, N. A., & Myin-Germeys, I. (2013). Hippocampal volume as marker of daily life stress sensitivity in psychosis. *Psychological Medicine*, *43*(7), 1377–1387. https://doi.org/10.1017/S003329171200219X

Creavin, S. T., Gallacher, J., Bayer, A., Fish, M., Ebrahim, S., & Ben-Shlomo, Y. (2012). Metabolic Syndrome, Diabetes, Poor Cognition, and Dementia in the Caerphilly Prospective Study. *Journal of Alzheimer's Disease*, *28*(4), 931–939.

https://doi.org/10.3233/JAD-2011-111550

Cuccurazzu, B., & Halberstadt, A. L. (2008). Projections from the vestibular nuclei and nucleus prepositus hypoglossi to dorsal raphe nucleus in rats. *Neuroscience Letters, 439*(1), 70–74. https://doi.org/10.1016/J.NEULET.2008.04.094

D'Silva, L. J., Staecker, H., Lin, J., Sykes, K. J., Phadnis, M. A., McMahon, T. M., Connolly, D., Sabus, C. H., Whitney, S. L., & Kludinga, P. M. (2015). Retrospective data suggests that the higher prevalence of benign paroxysmal positional vertigo in individuals with type 2 diabetes is mediated by hypertension. *Journal of Vestibular Research*, *25*(5–6), 233–239. https://doi.org/10.3233/VES-150563

Dawes, P., Emsley, R., Cruickshanks, K. J., Moore, D. R., Fortnum, H., Edmondson-Jones, M., McCormack, A., & Munro, K. J. (2015). Hearing Loss and Cognition: The Role of Hearing Aids, Social Isolation and Depression. *PLOS ONE*, *10*(3), e0119616. https://doi.org/10.1371/JOURNAL.PONE.0119616

Dickerson, S. S., Gruenewald, T. L., & Kemeny, M. E. (2004). When the Social Self Is Threatened: Shame, Physiology, and Health. *Journal of Personality*, *72*(6), 1191–1216. https://doi.org/10.1111/J.1467-6494.2004.00295.X

Dobbels, B., Mertens, G., Gilles, A., Claes, A., Moyaert, J., Van De Berg, R., Van De Heyning, P., Vanderveken, O., & Van Rompaey, V. (2019). Cognitive Function in Acquired Bilateral Vestibulopathy: A Cross-Sectional Study on Cognition, Hearing, and Vestibular Loss. *Frontiers in Neuroscience*, *13*(APR). https://doi.org/10.3389/FNINS.2019.00340

Doraiswamy, P. M., Leon, J., Cummings, J. L., Marin, D., & Neumann, P. J. (2002). Prevalence and Impact of Medical Comorbidity in Alzheimer's Disease. *The Journals of Gerontology: Series A*, *57*(3), M173–M177. https://doi.org/10.1093/GERONA/57.3.M173

Falconer, C. J., & Mast, F. W. (2012). Balancing the mind: Vestibular induced facilitation of egocentric mental transformations. *Experimental Psychology*, *59*(6), 332–339. https://doi.org/10.1027/1618-3169/A000161

Ferrari, S., Monzani, D., Baraldi, S., Simoni, E., Prati, G., Forghieri, M., Rigatelli, M., Genovese, E., & Pingani, L. (2014). Vertigo "in the pink": The impact of female gender on psychiatric-psychosomatic comorbidity in benign paroxysmal positional vertigo patients. *Psychosomatics*, *55*(3), 280–288. https://doi.org/10.1016/J.PSYM.2013.02.005

Ferrè, E. R., & Harris, L. R. (2017). The Effects of Complete Vestibular Deafferentation on Spatial Memory and the Hippocampus in the Rat: The Dunedin Experience. *Vestibular Cognition*, 107–131. https://doi.org/10.1163/9789004342248_008

Frey, F. (2017). SPSS (Software). *The International Encyclopedia of Communication Research Methods*, 1–2. https://doi.org/10.1002/9781118901731.IECRM0237

Gacek, R. R. (2003). Pathology of benign paroxysmal positional vertigo revisited. *Annals of Otology, Rhinology and Laryngology*, *112*(7), 574–582. https://doi.org/10.1177/000348940311200702

Gispen, W. H., & Biessels, G. J. (2000). Cognition and synaptic plasticity in diabetes mellitus. *Trends in Neurosciences*, *23*(11), 542–549. https://doi.org/10.1016/S0166-2236(00)01656-8

Granick, S., Kleban, M. H., & Weiss, A. D. (1976). Relationships between hearing loss and cognition in normally hearing aged persons. *Journal of Gerontology*, *31*(4), 434–440. https://doi.org/10.1093/GERONJ/31.4.434

Gresty, M. A., & Golding, J. F. (2009). Impact of vertigo and spatial disorientation on concurrent cognitive tasks. *Annals of the New York Academy of Sciences*, *1164*, 263–267. https://doi.org/10.1111/J.1749-6632.2008.03744.X

Grimm, R. J., Hemenway, W. G., Lebray, P. R., & Black, F. O. (2009). The Perilymph Fistula Syndrome Defined in Mild Head Trauma. *Http://Dx.Doi.Org/10.3109/00016488909138632*, *108*(S464), 1–40. https://doi.org/10.3109/00016488909138632

Guidetti, G., Guidetti, R., Manfredi, M., & Manfredi, M. (2020). Vestibular pathology and spatial working memory. *Acta Otorhinolaryngologica Italica*, *40*(1), 72. https://doi.org/10.14639/0392-100X-2189

Gurr, B., & Moffat, N. (2001). Psychological consequences of vertigo and the effectiveness of vestibular rehabilitation for brain injury patients. *Brain Injury*, *15*(5), 387–400. https://doi.org/10.1080/02699050010005904

Gurvich, C., Maller, J. J., Lithgow, B., Haghgooie, S., & Kulkarni, J. (2013a). Vestibular

insights into cognition and psychiatry. *Brain Research*, *1537*, 244–259. https://doi.org/10.1016/J.BRAINRES.2013.08.058

Gurvich, C., Maller, J. J., Lithgow, B., Haghgooie, S., & Kulkarni, J. (2013b). Vestibular insights into cognition and psychiatry. *Brain Research*, *1537*, 244–259. https://doi.org/10.1016/J.BRAINRES.2013.08.058

Hajjar, I., Quach, L., Yang, F., Chaves, P. H. M., Newman, A. B., Mukamal, K., Longstreth, W., Inzitari, M., & Lipsitz, L. A. (2011). Hypertension, white matter hyperintensities, and concurrent impairments in mobility, cognition, and mood: The cardiovascular health study. *Circulation*, *123*(8), 858–865. https://doi.org/10.1161/CIRCULATIONAHA.110.978114/DC1

Halberstadt, A. L., & Balaban, C. D. (2006). Serotonergic and nonserotonergic neurons in the dorsal raphe nucleus send collateralized projections to both the vestibular nuclei and the central amygdaloid nucleus. *Neuroscience*, *140*(3), 1067–1077. https://doi.org/10.1016/J.NEUROSCIENCE.2006.02.053

Harada, C. N., Natelson Love, M. C., & Triebel, K. L. (2013). Normal cognitive aging. *Clinics in Geriatric Medicine*, *29*(4), 737–752. https://doi.org/10.1016/J.CGER.2013.07.002

Hitier, M., Besnard, S., & Smith, P. F. (2014). Vestibular pathways involved in cognition. *Frontiers in Integrative Neuroscience*, *8*(JUL), 59. https://doi.org/10.3389/FNINT.2014.00059/BIBTEX

Hoppes, C. W., Huppert, T. J., Whitney, S. L., Dunlap, P. M., Disalvio, N. L., Alshebber, K. M., Furman, J. M., Kwon, Y. H., & Rosso, A. L. (2020). Changes in Cortical Activation During Dual-Task Walking in Individuals With and Without Visual Vertigo. *Journal of Neurologic Physical Therapy : JNPT*, *44*(2), 156–163. https://doi.org/10.1097/NPT.0000000000000310

Hubbard, H. I., Mamo, S. K., & Hopper, T. (2018). Dementia and Hearing Loss: Interrelationships and Treatment Considerations. *Seminars in Speech and Language*, *39*(3), 197–210. https://doi.org/10.1055/S-0038-1660779/ID/BR00682-41

Hüfner, K., Hamilton, D. A., Kalla, R., Stephan, T., Glasauer, S., Ma, J., Brüning, R., Markowitsch, H. J., Labudda, K., Schichor, C., Strupp, M., & Brandt, T. (2007). Spatial memory and hippocampal volume in humans with unilateral vestibular deafferentation. *Hippocampus*, *17*(6), 471–485. https://doi.org/10.1002/hipo.20283

Jacob, P. Y., Poucet, B., Liberge, M., Save, E., & Sargolini, F. (2014). Vestibular control of entorhinal cortex activity in spatial navigation. *Frontiers in Integrative Neuroscience*, *8*(JUNE), 38. https://doi.org/10.3389/FNINT.2014.00038/BIBTEX

Jacobson, G. P., Piker, E. G., Hatton, K., & Roberts, R. A. (2020). A factor analytic assessment of the English translation of the neuropsychological vertigo inventory (NVI). *Journal of Otology*, *15*(2), 45–49. https://doi.org/10.1016/J.JOTO.2019.09.005

Johansson, M., Åkerlund, D., Larsen, H. C., & Andersson, G. (2001). Randomized controlled trial of vestibular rehabilitation combined with cognitive-behavioral

therapy for dizziness in older people. *Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, *125*(3), 151–156. https://doi.org/10.1067/MHN.2001.118127

Jönsson, R., Sixt, E., Landahl, S., & Rosenhall, U. (2004). Prevalence of dizziness and vertigo in an urban elderly population. *Journal of Vestibular Research*, *14*(1), 47–52. https://doi.org/10.3233/VES-2004-14105

Jun, H., Bramian, A., Soma, S., Saito, T., Saido, T. C., & Igarashi, K. M. (2020). Disrupted Place Cell Remapping and Impaired Grid Cells in a Knockin Model of Alzheimer's Disease. *Neuron*, *107*(6), 1095-1112.e6. https://doi.org/10.1016/J.NEURON.2020.06.023

Kiernan, R. J., Mueller, J., Langston, J. W., & Van Dyke, C. (1987). The Neurobehavioral Cognitive Status Examination: a brief but quantitative approach to cognitive assessment. *Annals of Internal Medicine*, *107*(4), 481–485. https://doi.org/10.7326/0003-4819-107-4-481

Kim, S. Y., Yoo, D. M., Min, C., & Choi, H. G. (2021). Increased Risk of Neurodegenerative Dementia after Benign Paroxysmal Positional Vertigo. *International Journal of Environmental Research and Public Health*, *18*(19), 10553. https://doi.org/10.3390/IJERPH181910553

Kirby, S. E., & Yardley, L. (2009). Cognitions associated with anxiety in Ménière's disease. *Journal of Psychosomatic Research*, *66*(2), 111–118. https://doi.org/10.1016/J.JPSYCHORES.2008.05.027

Knecht, S., Wersching, H., Lohmann, H., Berger, K., & Ringelstein, E. B. (2009). How much does hypertension affect cognition?: Explained variance in cross-sectional analysis of non-demented community-dwelling individuals in the SEARCH study. *Journal of the Neurological Sciences*, *283*(1–2), 149–152. https://doi.org/10.1016/J.JNS.2009.02.362

Lacroix, E., Deggouj, N., Salvaggio, S., Wiener, V., Debue, M., & Edwards, M. G. (2016). The development of a new questionnaire for cognitive complaints in vertigo: the Neuropsychological Vertigo Inventory (NVI). *European Archives of Oto-Rhino-Laryngology : Official Journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : Affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery*, *273*(12), 4241–4249. https://doi.org/10.1007/S00405-016-4135-X

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for t-tests and ANOVAs. *Frontiers in Psychology*, *4*(NOV). https://doi.org/10.3389/FPSYG.2013.00863/ABSTRACT

Langhagen, T., Albers, L., Heinen, F., Straube, A., Filippopulos, F., Landgraf, M. N., Gerstl, L., Jahn, K., & Von Kries, R. (2015). Period Prevalence of Dizziness and Vertigo in Adolescents. *PLOS ONE*, *10*(9), e0136512. https://doi.org/10.1371/JOURNAL.PONE.0136512

Lee, I. H., Yu, H., Ha, S. S., Son, G. M., Park, K. J., Lee, J. J., & Kim, D. K. (2022). Association between Late-Onset Ménière's Disease and the Risk of Incident All-

Cause Dementia. *Journal of Personalized Medicine*, *12*(1), 19. https://doi.org/10.3390/JPM12010019

Lentz, J. J., Humes, L. E., & Kidd, G. R. (2022). Differences in Auditory Perception Between Young and Older Adults When Controlling for Differences in Hearing Loss and Cognition. *Trends in Hearing*, *26*. https://doi.org/10.1177/23312165211066180

Lin, F. R. (2011). Hearing Loss and Cognition Among Older Adults in the United States. *The Journals of Gerontology: Series A*, *66A*(10), 1131–1136. https://doi.org/10.1093/GERONA/GLR115

Lin, F. R., Ferrucci, L., Metter, E. J., An, Y., Zonderman, A. B., & Resnick, S. M. (2011). Hearing Loss and Cognition in the Baltimore Longitudinal Study of Aging. *Neuropsychology*, *25*(6), 763. https://doi.org/10.1037/A0024238

Lin, F. R., Metter, E. J., O'Brien, R. J., Resnick, S. M., Zonderman, A. B., & Ferrucci, L. (2011). Hearing Loss and Incident Dementia. *Archives of Neurology*, *68*(2), 214–220. https://doi.org/10.1001/ARCHNEUROL.2010.362

Liu, Y. F., Locklear, T. D., Sharon, J. D., Lacroix, E., Nguyen, S. A., & Rizk, H. G. (2019a). Quantification of Cognitive Dysfunction in Dizzy Patients Using the Neuropsychological Vertigo Inventory. *Otology & Neurotology : Official Publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*, *40*(7), E723–E731. https://doi.org/10.1097/MAO.0000000000002311

Liu, Y. F., Locklear, T. D., Sharon, J. D., Lacroix, E., Nguyen, S. A., & Rizk, H. G. (2019b). Quantification of Cognitive Dysfunction in Dizzy Patients Using the Neuropsychological Vertigo Inventory. *Otology and Neurotology*, *40*(7), E723–E731. https://doi.org/10.1097/MAO.0000000000002311

López-Larson, M. P., DelBello, M. P., Zimmerman, M. E., Schwiers, M. L., & Strakowski, S. M. (2002). Regional prefrontal gray and white matter abnormalities in bipolar disorder. *Biological Psychiatry*, *52*(2), 93–100. https://doi.org/10.1016/S0006-3223(02)01350-1

Luethke, L. E., Krubitzer, L. A., & Kaas, J. H. (1988). Cortical connections of electrophysiologically and architectonically defined subdivisions of auditory cortex in squirrels. *The Journal of Comparative Neurology*, *268*(2), 181–203. https://doi.org/10.1002/CNE.902680205

Lupien, S. J., De Leon, M., De Santi, S., Convit, A., Tarshish, C., Nair, N. P. V., Thakur, M., McEwen, B. S., Hauger, R. L., & Meaney, M. J. (1998). Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nature Neuroscience 1998 1:1*, *1*(1), 69–73. https://doi.org/10.1038/271

Lyketsos, C. G., Toone, L., Tschanz, J. A., Rabins, P. V., Steinberg, M., Onyike, C. U., Corcoran, C., Norton, M., Zandi, P., Breitner, J. C. S., & Welsh-Bohmer, K. (2005). Population-Based Study of Medical Comorbidity in Early Dementia and "Cognitive Impairment, No Dementia (CIND)": Association With Functional and Cognitive Impairment: The Cache County Study. *The American Journal of Geriatric*

Psychiatry, *13*(8), 656–664. https://doi.org/10.1097/00019442-200508000-00004

Lyness, S. A., Zarow, C., & Chui, H. C. (2003). Neuron loss in key cholinergic and aminergic nuclei in Alzheimer disease: a meta-analysis. *Neurobiology of Aging*, *24*(1), 1–23. https://doi.org/10.1016/S0197-4580(02)00057-X

Moss, F., Ward, L. M., & Sannita, W. G. (2004). Stochastic resonance and sensory information processing: a tutorial and review of application. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *115*(2), 267–281. https://doi.org/10.1016/J.CLINPH.2003.09.014

Murphy, C., Reinhardt, C., Linehan, D., Katiri, R., & O'Connor, A. (2021). A review of primary care referrals for patients with dizziness and vertigo: prevalence and demographics. *Irish Journal of Medical Science (1971 -) 2021 191:1*, *191*(1), 385–389. https://doi.org/10.1007/S11845-021-02575-6

Nakamagoe, K., Kadono, K., Koganezawa, T., Takiguchi, M., Terada, M., Yamamoto, F., Moriyama, T., Yanagiha, K., Nohara, S., Tozaka, N., Miyake, Z., Aizawa, S., Furusho, K., & Tamaoka, A. (2016). Vestibular Impairment in Frontotemporal Dementia Syndrome. *Dementia and Geriatric Cognitive Disorders Extra*, *6*(2), 194–204. https://doi.org/10.1159/000445870

Nandi, R., & Luxon, L. M. (2009). Development and assessment of the vestibular system. *Https://Doi.Org/10.1080/14992020802324540*, *47*(9), 566–577. https://doi.org/10.1080/14992020802324540

Ossenkopp, K. P., Prkacin, A., & Hargreaves, E. L. (1990). Sodium arsanilate-induced vestibular dysfunction in rats: effects on open-field behavior and spontaneous activity in the automated digiscan monitoring system. *Pharmacology, Biochemistry, and Behavior*, *36*(4), 875–881. https://doi.org/10.1016/0091-3057(90)90093-W

Peracino, A. (2014). Hearing loss and dementia in the aging population. *Audiology & Neuro-Otology*, *19 Suppl 1*, 6–9. https://doi.org/10.1159/000371595

Peracino, A., & Pecorelli, S. (2016). The Epidemiology of Cognitive Impairment in the Aging Population: Implications for Hearing Loss. *Audiology & Neuro-Otology*, *21 Suppl 1*(1), 3–9. https://doi.org/10.1159/000448346

Persoons, P., Luyckx, K., Desloovere, C., Vandenberghe, J., & Fischler, B. (2003). Anxiety and mood disorders in otorhinolaryngology outpatients presenting with dizziness: validation of the self-administered PRIME-MD Patient Health Questionnaire and epidemiology. *General Hospital Psychiatry*, *25*(5), 316–323. https://doi.org/10.1016/S0163-8343(03)00072-0

Power, M. C., Tchetgen, E. J. T., Sparrow, D., Schwartz, J., & Weisskopf, M. G. (2013). Blood pressure and cognition:Factors that may account for theirinconsistent association. *Epidemiology (Cambridge, Mass.)*, *24*(6), 886–893. https://doi.org/10.1097/EDE.0B013E3182A7121C

Ray, M., Dening, T., & Crosbie, B. (2019). Dementia and hearing loss: A narrative review. *Maturitas*, *128*, 64–69. https://doi.org/10.1016/J.MATURITAS.2019.08.001

Rise, I. V., Haro, J. M., & Gjervan, B. (2016). Clinical features, comorbidity, and cognitive impairment in elderly bipolar patients. *Neuropsychiatric Disease and Treatment*, *12*, 1203. https://doi.org/10.2147/NDT.S100843

Rizk, H. G., Sharon, J. D., Lee, J. A., Thomas, C., Nguyen, S. A., & Meyer, T. A. (2020). Cross-Sectional Analysis of Cognitive Dysfunction in Patients With Vestibular Disorders. *Ear and Hearing*, *41*(4), 1020–1027. https://doi.org/10.1097/AUD.0000000000000825

Ruis, C., Biessels, G. J., Gorter, K. J., Van Den Donk, M., Kappelle, L. J., & Rutten, G. E. H. M. (2009). Cognition in the Early Stage of Type 2 Diabetes. *Diabetes Care*, *32*(7), 1261–1265. https://doi.org/10.2337/DC08-2143

Schaeppi, U., Krinke, G., FitzGerald, R. E., & Classen, W. (1991). Impaired tunnel-maze behavior in rats with sensory lesions: vestibular and auditory systems. *Neurotoxicology*, *12*(3), 445–454. https://europepmc.org/article/med/1745435

Schautzer, F., Hamilton, D., Kalla, R., Strupp, M., & Brandt, T. (2003). Spatial memory deficits in patients with chronic bilateral vestibular failure. *Annals of the New York Academy of Sciences*, *1004*, 316–324. https://doi.org/10.1196/ANNALS.1303.029

Seo, Y. J., Kim, J., & Kim, S. H. (2016). The change of hippocampal volume and its relevance with inner ear function in Meniere's disease patients. *Auris Nasus Larynx*, *43*(6), 620–625. https://doi.org/10.1016/J.ANL.2016.01.006

Shamasunder, C., Sriram, T. G., Raj, S. G. M., & Shanmugham, V. (1986). VALIDITY

OF A SHORT 5-ITEM VERSION OF THE GENERAL HEALTH QUESTIONNAIRE (G.H.Q). *Indian Journal of Psychiatry*, *28*(3), 217. /pmc/articles/PMC3172533/?report=abstract

Skoog, I. (2003). Hypertension and Cognition. *International Psychogeriatrics*, *15*(S1), 139–146. https://doi.org/10.1017/S1041610203009104

Smith, P. F. (2017a). The vestibular system and cognition. *Current Opinion in Neurology*, *30*(1), 84–89. https://doi.org/10.1097/WCO.0000000000000403

Smith, P. F. (2017b). The vestibular system and cognition. *Current Opinion in Neurology*, *30*(1), 84–89. https://doi.org/10.1097/WCO.0000000000000403

Smith, P. F., Darlington, C. L., & Zheng, Y. (2010). Move it or lose it--is stimulation of the vestibular system necessary for normal spatial memory? *Hippocampus*, *20*(1), 36–43. https://doi.org/10.1002/HIPO.20588

Smith, P. F., & Zheng, Y. (2013a). From ear to uncertainty: vestibular contributions to cognitive function. *Frontiers in Integrative Neuroscience*, *7*(NOV). https://doi.org/10.3389/FNINT.2013.00084

Smith, P. F., & Zheng, Y. (2013b). From ear to uncertainty: Vestibular contributions to cognitive function. *Frontiers in Integrative Neuroscience*, *7*(NOV), 84. https://doi.org/10.3389/FNINT.2013.00084/BIBTEX

Staab, J. P. (2006). Chronic dizziness: the interface between psychiatry and neuro-otology. *Current Opinion in Neurology*, *19*(1), 41–48.

https://doi.org/10.1097/01.WCO.0000198102.95294.1F

Streitfeld, B. D. (1980). The fiber connections of the temporal lobe with emphasis on the rhesus monkey. *The International Journal of Neuroscience*, *11*(1), 51–71. https://doi.org/10.3109/00207458009147579

Tecer, A., Tükel, R., Erdamar, B., & Sunay, T. (2004). Audiovestibular functioning in patients with panic disorder. *Journal of Psychosomatic Research*, *57*(2), 177–182. https://doi.org/10.1016/S0022-3999(03)00568-3

Teggi, R., Manfrin, M., Balzanelli, C., Gatti, O., Mura, F., Quaglieri, S., Pilolli, F., Redaelli de Zinis, L. O., Benazzo, M., & Bussi, M. (2016). Point prevalence of vertigo and dizziness in a sample of 2672 subjects and correlation with headaches. *Acta Otorhinolaryngologica Italica : Organo Ufficiale Della Societa Italiana Di Otorinolaringologia e Chirurgia Cervico-Facciale*, *36*(3), 215–219. https://doi.org/10.14639/0392-100X-847

Ursachi, G., Horodnic, I. A., & Zait, A. (2015). *How reliable are measurement scales? External factors with indirect influence on reliability estimators*. https://doi.org/10.1016/S2212-5671(15)00123-9

Van Cruijsen, N., Hiemstra, W. M., Meiners, L. C., Wit, H. P., & Albers, F. W. J. (2009). Hippocampal volume measurement in patients with Ménière's disease: a pilot study. *Http://Dx.Doi.Org/10.1080/00016480601127000*, *127*(10), 1018–1023. https://doi.org/10.1080/00016480601127000

Von Brevern, M., Radtke, A., Lezius, F., Feldmann, M., Ziese, T., Lempert, T., & Neuhauser, H. (2007). Epidemiology of benign paroxysmal positional vertigo: a population based study. *Journal of Neurology, Neurosurgery & Psychiatry*, *78*(7), 710–715. https://doi.org/10.1136/JNNP.2006.100420

Wallace, D. G., Hines, D. J., Pellis, S. M., & Whishaw, I. Q. (2002). Vestibular information is required for dead reckoning in the rat. *Journal of Neuroscience*, *22*(22), 10009–10017. https://doi.org/10.1523/JNEUROSCI.22-22-10009.2002

Wan, T. J., Yu, Y. C., Zhao, X. G., Tang, P., & Gong, Y. S. (2018a). Efficacy of betahistine plus cognitive behavioral therapy on residual dizziness after successful canalith repositioning procedure for benign paroxysmal positional vertigo. *Neuropsychiatric Disease and Treatment*, *14*, 2965. https://doi.org/10.2147/NDT.S182809

Wan, T. J., Yu, Y. C., Zhao, X. G., Tang, P., & Gong, Y. S. (2018b). Efficacy of betahistine plus cognitive behavioral therapy on residual dizziness after successful canalith repositioning procedure for benign paroxysmal positional vertigo. *Neuropsychiatric Disease and Treatment*, *14*, 2965–2971. https://doi.org/10.2147/NDT.S182809

Wayne, R. V., & Johnsrude, I. S. (2015). A review of causal mechanisms underlying the link between age-related hearing loss and cognitive decline. *Ageing Research Reviews*, *23*, 154–166. https://doi.org/10.1016/J.ARR.2015.06.002

Wei, E. X., Oh, E. S., Harun, A., Ehrenburg, M., & Agrawal, Y. (2018). Vestibular Loss

Predicts Poorer Spatial Cognition in Patients with Alzheimer's Disease. *Journal of Alzheimer's Disease*, *61*(3), 995–1003. https://doi.org/10.3233/JAD-170751

Wilkinson, D., Nicholls, S., Pattenden, C., Kilduff, P., & Milberg, W. (2008). Galvanic vestibular stimulation speeds visual memory recall. *Experimental Brain Research*, *189*(2), 243–248. https://doi.org/10.1007/S00221-008-1463-0

Xie, D., Welgampola, M. S., Miller, L. A., Young, A. S., D'Souza, M., Breen, N., & Rosengren, S. M. (2022). Subjective Cognitive Dysfunction in Patients with Dizziness and Vertigo. *Audiology and Neurotology*, *27*(2), 122–132. https://doi.org/10.1159/000518188

Xie, Y., Bigelow, R. T., Frankenthaler, S. F., Studenski, S. A., Moffat, S. D., & Agrawal, Y. (2017). Vestibular loss in older adults is associated with impaired spatial navigation: Data from the triangle completion task. *Frontiers in Neurology*, *8*(APR), 173. https://doi.org/10.3389/FNEUR.2017.00173/BIBTEX

Yang, W. S., Kim, S. H., Lee, J. D., & Lee, W. S. (2008). Clinical significance of vestibular evoked myogenic potentials in benign paroxysmal positional vertigo. *Otology and Neurotology*, *29*(8), 1162–1166. https://doi.org/10.1097/MAO.0B013E31818A0881

Yardley, L., Gardner, M., Bronstein, A., Davies, R., Buckwell, D., & Luxon, L. (2001). Interference between postural control and mental task performance in patients with vestibular disorder and healthy controls. *Journal of Neurology, Neurosurgery & Psychiatry*, *71*(1), 48–52. https://doi.org/10.1136/JNNP.71.1.48

Zekveld, A. A., Kramer, S. E., & Festen, J. M. (2011). Cognitive load during speech perception in noise: the influence of age, hearing loss, and cognition on the pupil response. *Ear and Hearing*, *32*(4), 498–510. https://doi.org/10.1097/AUD.0B013E31820512BB

Zheng, Y., Balabhadrapatruni, S., Masumura, C., Munro, O., Darlington, C. L., & Smith, P. F. (2009). Bilateral vestibular deafferentation causes deficits in a 5-choice serial reaction time task in rats. *Behavioural Brain Research*, *203*(1), 113–117. https://doi.org/10.1016/J.BBR.2009.04.027

Zheng, Y., Cheung, I., & Smith, P. F. (2012). Performance in anxiety and spatial memory tests following bilateral vestibular loss in the rat and effects of anxiolytic and anxiogenic drugs. *Behavioural Brain Research*, *235*(1), 21–29. https://doi.org/10.1016/J.BBR.2012.07.025

Zheng, Y., Goddard, M., Darlington, C. L., & Smith, P. F. (2009). Long-Term deficits on a foraging task after bilateral vestibular deafferentation in rats. *Hippocampus*, *19*(5), 480–486. https://doi.org/10.1002/HIPO.20533

Zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *NeuroImage*, *60*(1), 162–169. https://doi.org/10.1016/J.NEUROIMAGE.2011.12.032

Zu Eulenburg, Peter, Stoeter, P., & Dieterich, M. (2010). Voxel-based morphometry depicts central compensation after vestibular neuritis. *Annals of Neurology*, *68*(2), 241–249. https://doi.org/10.1002/ANA.22063

APPENDIX

Annexure I – Google Form

Influence of BPPV and Meniere's Disease on cognitive abilities: A Questionnaire-Based Study

You are invited to the research study titled 'Influence of BPPV and Meniere's Disease in cognitive abilities: A Questionnaire Based Study '. The questionnaire will take less than 5 minutes to fill. Your participation in this study will be voluntary. The information you share with us will be confidential to the full extent of the law. We would be very thankful if you could complete the survey.

Section 1

I understand the nature of the research project, and I consent to participate in this research project.	Yes	No

Section 2

Socio-demographic Details

Name:

Previously/Currently diagnosed as BPPV/Meniere's disease/None

Age (in years):

Gender:

1. Do you have any history of diabetes?	Yes	No
2. Do you have any history of blood pressure (BP)?	Yes	No
3. Are you under any medication for diabetes/BP?	Yes	No
4. Do you have a history of tinnitus (ringing sensation in the ears)?	Yes	No

Section 3

Questions related to cognitive abilities (Taken from the NCSE questionnaire)

Instructions: Please answer the following questions based on your experience during the course of your disorder or in your current condition.

1. Does it seem that you can't think as quickly as before (i.e., before the diagnosis)?	Yes	Sometimes	No
2. Does it seem that you find it hard to think clearly?	Yes	Sometimes	No
3. Does it seem that you are easily more distracted?	Yes	Sometimes	No
4. Does it seem that you can't concentrate?	Yes	Sometimes	No
5. Do you have trouble remembering the right words when talking?	Yes	Sometimes	No
6. Do you have trouble understanding others?	Yes	Sometimes	No
7. Do you have trouble following conversations?	Yes	Sometimes	No
8. Do you have trouble with your speech?	Yes	Sometimes	No
9. Do you have trouble with reading?	Yes	Sometimes	No
10. Do you have trouble with writing?	Yes	Sometimes	No

----------x----------