VESTIBULAR TEST FINDINGS IN AUDITORY NEUROPATHY SPECTRUM DISORDERS: A SYSTEMATIC REVIEW

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CERTIFICATE

This is to certify that this dissertation entitled "**Vestibular Test findings in Auditory Neuropathy Spectrum Disorders: A Systematic Review**" is a bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student with Registration Number 20AUD032. This has been carried out under the guidance of the faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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This is to certify that this dissertation entitled "**Vestibular Test findings in Auditory Neuropathy Spectrum Disorders: A Systematic Review**" has been prepared under my supervision and guidance. It is also certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is to certify that this dissertation entitled "**Vestibular Test findings in Auditory Neuropathy Spectrum Disorders: A Systematic Review**" is the result of my own study under the guidance of Dr. Sujeet Kumar Sinha, Associate Professor, Department of Audiology, All India Institute of Speech and Hearing, Mysuru, and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru **Registration No: 20AUD032**

August, 2022

Dedicated to

My Family

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ABSTRACT

Introduction: Auditory neuropathy (ANSD) is a hearing condition defined by an absence of Auditory Brainstem Response (ABR), presence of Otoacoustic Emissions (OAE) and cochlear microphonics (CM). cVEMP, oVEMP, vHIT and Caloric tests can be used to diagnose the neuropathy of the vestibular branch of the eighth cranial nerves in patients with ANSD. It is rare to have isolated auditory neuropathy or vestibular neuropathy; instead, the most frequent condition is "audio-vestibular neuropathy" which affects both branches of the eighth cranial nerve.

Aim: To conduct a systematic review of articles on vestibular test findings in people with ANSD.

Method: The articles were searched in various databases. For the purpose of this systematic review, 17 papers in total fulfilled the inclusion and exclusion criteria. The QUADAS-2 risk of bias assessment tool was used to ensure the quality and possible risk of bias for each article in this study.

Results: Most studies indicate that more than 90 percent of people with ANSD do not exhibit cVEMP and oVEMP responses. A few studies have also shown that people with ANSD may have higher VEMP thresholds, prolonged peak and interpeak latencies, and lower amplitudes. The vHIT test showed reduced VOR gain in all semicircular canals as well as the occurrence of both covert and overt saccades in ANSD individuals. Furthermore, Caloric test revealed hypoactive responses among individuals with ANSD.

Conclusion: The majority of these findings pointed to a vestibular impairment in people with auditory neuropathy spectrum disorders. These articles also found that individuals

with ANSD have no vestibular signs or symptoms. The results of these many tests assist to understand the vestibular pathways affected in ANSD individuals, from which a treatment plan may be developed to rehabilitate these patients and enhance their quality of life.

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Chapter 1

INTRODUCTION

Auditory neuropathy (ANSD) is a hearing condition defined by an absence of Auditory Brainstem Response (ABR), presence of cochlear microphonics (CM) and Otoacoustic Emissions (OAE). Clinically, ANSD is defined as (1) hearing loss of any degree, (2) normal outer hair cell function as evidenced by the presence of OAEs and/or CM, (3) abnormal evoked potentials beginning with a wave I of the ABR, (4) poor speech perception, and (5) absence of acoustic reflexes to ipsilateral and contralateral tones (Starr et al., 1996). The lesion in ANSD in confined to the auditory nerve or the synapse between the inner hair cell and the auditory nerve. The vestibular nerve could also be impacted by a neuropathic disorder affecting the cochlear nerve (Sinha et al., 2013a).

The prevalence of vestibular neuropathies in ANSD patients is unknown. They are typically not seen as the best candidates for vestibular examinations. Such an assumption could be supported by the subtleties of their symptoms. Only one out of every five people with ANSD have at least one vestibular symptom (Prabhu & Jamuar, 2017). Additionally, the subjective and objective vestibular system tests performed on these people did not provide any significant information on the vestibular signs and symptoms that is present in individuals with ANSD (Sinha et al., 2013a).

Isolated auditory or vestibular neuropathy is uncommon, with "audio-vestibular neuropathy" involving both eighth cranial nerve branches being the most prevalent disease (Sazgar et al., 2010). A number of investigations in individuals with ANSD have used caloric tests to assess the superior vestibular nerve. Starr et al., (1996) discovered

vestibulopathy in five out of 10 patients with ANSD. Sheykholeslami et al., (2000) found vestibulopathy in all three ANSD individuals they examined.

In addition, the function of inferior and superior vestibular nerve have been studied in ANSD individuals. Previous research has found that the superior vestibular nerve and saccule have greater likelihood of impairment in ANSD individuals than the inferior vestibular nerve (Singh et al., 2016). The poor cervical vestibular evoked myogenic potential results reflect a sacculo-collicpathway dysfunction impacting the inferior vestibular nerve (Kumar et al., 2007). Furthermore, ocular vestibular evoked myogenic potential is altered, indicating abnormal superior vestibular nerve activity (Sinha et al., 2013b).

A caloric test can be utilized to assess the functioning of the horizontal semicircular canal and it afferent pathways i.e., the physiology of the superior vestibular nerves. This test mainly assesses the functioning of the low-frequency functioning of the Horizontal (Lateral) semicircular canal reflex function. Hu et al., (2020) found that caloric test findings were abnormal in 70 percent of the individuals diagnosed with ANSD.

1.1 Aim of the study

The study aimed to systematically review all the articles related to vestibular test findings in individuals with ANSD.

1.2 Review Question

Whether individuals with ANSD have vestibular issues along with auditory issues?

Chapter 2

METHOD

2.1 Searches

The articles related to the topic were searched in the following databases: Google Scholars, Pub Med, Web of Science, Scopus, Ovid Medline, and Cochrane Library. The search terms utilized to search the articles were Auditory neuropathy, auditory neuropathy spectrum disorders, vestibular issues in ANSD, vestibular disorders in ANSD, video head impulse test in auditory neuropathy, caloric test in auditory neuropathy, vestibular evoked myogenic potentials in auditory neuropathy and Vestibular and ANSD. Boolean operators such as AND, OR, AND/OR were used while searching the databases. The searches were restricted to studies that had full-text availability, were published in English, and included human beings as participants. To discover additional studies for inclusion, a search of the publications was conducted right before the final analysis. The publication dates were not restricted. To find further research on vestibular disorders in people with ANSD, a search was conducted until right before the analysis. All the articles that defined any vestibular issues in ANSD were considered for the initial search.

2.2 Types of the study included

The articles for the systematic review included original research data for the study, i.e., case series, retrospective or prospective studies, and cross-sectional studies. Articles with participants less than three subjects, review articles, any systematic review, and case studies were excluded from the analyses. Studies that have described vestibular issues in ANSD associated with other disorders such as Friedrich's ataxia, Hereditary

Sensory-motor neuropathy, etc. were excluded from the study. Also, the studies that reported vestibular issues in ANSD children aged less than ten years were excluded.

2.3 Condition or domain being used:

The predominant domain studied for the systematic review were as follows:

1. Presence or absence of vestibular evoked myogenic potentials in auditory neuropathy spectrum disorders
2. Latency and amplitude of vestibular evoked myogenic potentials in auditory neuropathy spectrum disorders
3. Caloric test findings in auditory neuropathy spectrum disorders
4. VOR gain using video head impulse test in auditory neuropathy spectrum disorders
5. Presence/absence of refixation saccades in auditory neuropathy spectrum disorders
6. Vestibular signs and symptoms in auditory neuropathy spectrum disorders
7. Correlation between different test findings in auditory neuropathy spectrum disorders.

2.4 Participants/Population

Studies that defined vestibular issues in individuals with ANSD of age range between 10 years to 50 years were considered for this systematic review. Also, studies that defined the absence or presence of vestibular signs and symptoms in ANSD were included. Studies which had individuals with other disorders such as Friedrich's ataxia, Hereditary Sensory-motor neuropathy, etc. were excluded from the study.

2.5 Analysis

2.5.1 Data Extraction (selection and coding):

All the titles and /or abstracts that were retrieved from the databases that are acceptable according to the study's inclusion and exclusion criteria were independently reviewed by two reviewers. Any discrepancy between the two reviewers findings was settled through discussion or, if needed, by the third reviewer's opinion. Similarly, the independent reviewers were involved in the full-text screening of the studies' articles, which followed the same process. Also, the justifications for exclusion were documented and checked in agreement with PRISMA criteria. The risk of bias was examined independently, and two independent authors extracted all data. One researcher created the data extraction forms, piloted and updated by two others. The following data items were of concern but were not limited to latency, amplitude, and asymmetry ratio of C-VEMP, O-VEMP, VOR gain of VHIT, saccades, and hypo and hyper functioning in Caloric Tests.

2.5.2 RISK OF BIAS (QUALITY) ASSESSMENT

At each screening stage, two reviewers were involved to overcome the reviewer bias where conflicts were resolved via discussions. In 2011, Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) was developed. A recent version of the tool was used in this study to assess the risk of bias and usefulness of each diagnostic study for the systematic review. QUADAS-2 comprises 4 domains, including patient selection, index test(s), reference standards and flow & timing (Whiting et al., 2011). There is a total of 11 questions which covers a set of signaling questions under each domain. It was categorized as having a low risk of bias if the domain has more 'yes' responses, and if it

has maximum 'no' responses, it was considered to have a high risk of bias. Applicability concerns of the primary diagnostic accuracy studies were assessed as low/high/unclear concerns. The domains and the set of signaling questions under each is listed below.

Domain 1: Patient selection

- Was a consecutive or random sample of patients enrolled?
- Was a case-control design avoided?
- Did the study avoid inappropriate exclusions?

Domain 2: Index test(s)

- Were the index test results interpreted without knowledge of the results of the reference standard?
- If a threshold was used, was it pre-specified?

Domain 3: Reference standard

- Is there reference standard likely to correctly classify the target condition?
- Were the reference standard results interpreted without knowledge of the results of the index test?

Domain 4: Flow and Timing

- Was there an appropriate interval between index test(s) and reference standard?
- Did all the patients receive a reference standard?
- Were all patients included in the analysis?

Out of the 11 questions, percentage of 'yes' were calculated for each study once the rating or each questions was obtained. Risk of bias assessment instructions provided by The Joanna Briggs Institute (Moola et al., 2015) was utilized to categorize the percentage of positive answers in the questions. According to their

guidelines, when only up to 49 percent of the answers were 'yes', it is considered as high risk of bias; moderate risk of bias when 50 percent– 69 percent of the answers were 'yes'; and low risk of bias when more than 70 percent of the answers were 'yes'.

2.5.3 Strategy for data synthesis

The data synthesis was carried out by analyzing the homogeneity of the data, and different analysis parameters such as VOR Gain, VOR Gain asymmetry ratio & presence and absence of refixation saccades, latency and amplitude of VEMPs, hyper functional/hypo functional caloric responses.

2.5.4 Analysis of subgroups or subtests: None

Chapter 3

RESULTS

This study aimed to systematically review articles concerning vestibular test findings in individuals with ANSD. This study's objective was to examine and summarize the findings of literature relating to vestibular test results in ANSD patients. The following parameters of the different vestibular test findings were considered.

1. Prevalence of VEMP, vHIT and Caloric test findings in individuals with ANSD

2.Threshold, Amplitude, Latency as well as asymmetry ratio of VEMP test results in individuals with ANSD

3. VOR gain and prevalence of saccades in vHIT test among individuals with ANSD

4. Hypo function and hyper function in Caloric test results in individuals with ANSD.

3.1 Studies selection

A total of 1291 research articles were retrieved from the different electronic databases. After removing 122 duplicate entries, 1169 articles were found in the domain of vestibular test results and ANSD. After the title and abstract screening of 1169 articles, 30 articles meeting the objectives of the article were selected. Of the remaining thirty articles, two manuscripts were not available in English. Seven articles had participants with ages below ten years and above fifty years. Four articles described participants associated with other neurological conditions. Full-text screening resulted in the removal of 13 manuscripts. Finally, 17 articles that met the inclusion criteria were taken into consideration for the systematic review. The selection of papers, screening procedure, and criteria for article exclusion were all done using the Preferred Reporting

Items for Systematic Reviews and Meta-analysis (PRISMA) flowchart, which is shown below.

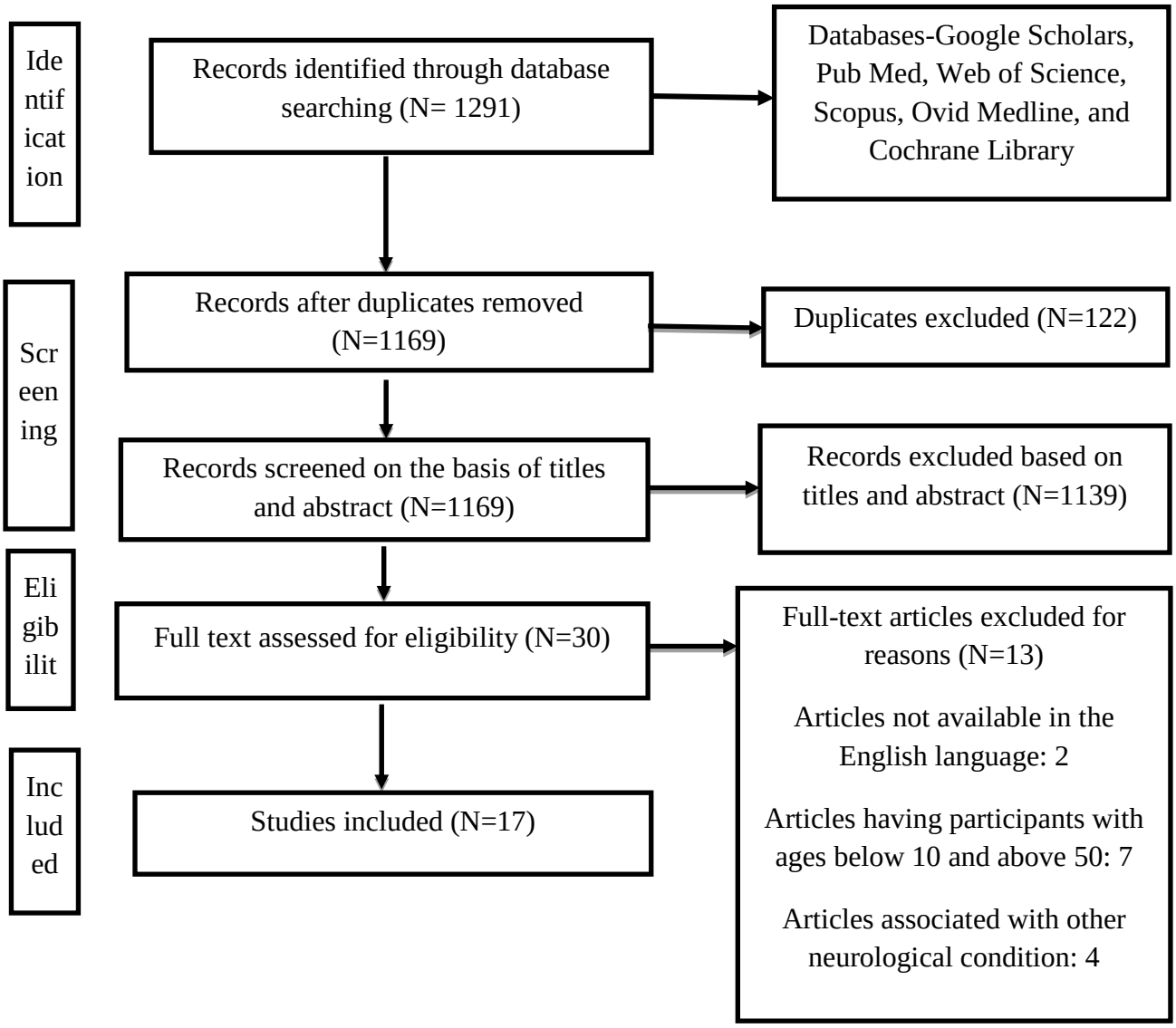

Figure 3.1: Preferred Reporting Items for Systematic Reviews and Meta-analysis(PRISMA) Flowchart for Selection of the articles

3.2 Risk of Bias Assessment

The quality of the selected studies was assessed using QUADAS-2, which resulted in the grading of 17 research based on the risk of bias involved in several domains such as patient selection, index tests, reference standard, and flow and timing. The biggest threat observed was in the area of patient selection. The risk of bias in the research's applicability also resulted in the articles that are characterized as having low, unclear and high risk of bias. In terms of applicability concern, all domains had no risk of bias. In the patient selection domain, seven research domain considered had unclear risk of bias. Articles with high risk of bias were reviewed with extra care. The risk of bias in the included article is shown in Table 3.1.

Table 3.1

Risk of Bias for different study included in the systematic review

		Risk of Bias				Applicability concern			
S.I. No.	Study	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference Standard	Percentage of "Yes"
1.	Starr (1996)								72.72%
2.	Fujikawa & Starr (2000)								63.63%
3.	Sheykholeslami et al., (2000)								81.81%
4.	Kumar et al., (2007)								72.72%
5.	Sazgar et al., (2010)								72.72%
6.	Sinha et al., (2013a)								81.81%
7.	Sinha et al., (2013b)								63.63%
8.	Jingmiao Wang et al., (2013)								54.54%
9.	Sujeet et al., (2014)								54.54%

10.	Ismail et al., (2014)								72.72%
11.	Emami & Farahani, (2015)								72.72%
12.	Singh et al., (2016)								72.72%
13.	Wang et al., (2017)								54.54%
14.	Sinha et al., (2019)								72.72%
15.	Sinha et al., (2020)								63.63%
16.	Hu et al., (2020)								36.36%
17.	Chen et al., (2021)								63.63%

Indicators:

Low risk of bias

Unclear risk of bias

High risk of bias

Table 3.2

Shows the research characteristics of the chosen articles, the tests conducted, and the results

S.N.	Title of article	Authors & Year	Methods	Results	Other test findings
1.	Auditory Neuropathy	Arnold Starr, Terence W. Picton, Yvonne Sininger, Linda J. Hood and Charles I. Berlin (1996)	Ten participants Age range- Children and young adults Tests done: Caloric test	Two patients showed abnormal caloric test results. Caloric vestibular function testing revealed normal horizontal nystagmus and vertigo in two individuals but failed to elicit this response in two other individuals. On lateral gazing, three patients had horizontal nystagmus. There were no additional testing done on these individuals to determine if the vestibular impairment was peripheral or central.	The audiogram patterns revealed a low-frequency loss (a rising slope) in five patients, three patients had a flat frequency loss, and two had a high frequency loss (a falling slope).

2.	Vestibular neuropathy accompanying auditory and peripheral neuropathies	Fujikawa S and Starr A (2000)	Total- 14 participants (7 Men and 7 Women) Age range- 10 to 75 years Tests done: Caloric Test	Out of 14 subjects, 5 had a normal response, 9 had an abnormal response in the caloric test (five patients had an absent caloric response and three had asymmetrical response).	
3.	Vestibular Function in Auditory Neuropathy	Kianoush Sheykholeslami, Kimitaka Kaga, Toshihira Murofushi, And Dominic W. Hughes (2000)	Total- Three patients (all female) Age range-57, 61 and 71 years old) Tests Done: c-VEMP and Caloric test	Absent cVEMP in all 3 ANSD individuals. Out of three individuals, only the right ear of one patient responded to caloric stimulation causing horizontal nystagmus without vertigo.	Reported abnormal findings in Romberg and Fukuda stepping test in eyes closed condition.

4.	Vestibular Evoked Myogenic Potential as a Tool to Identify Vestibular Involvement in Auditory Neuropathy	Kaushlendra Kumar, Sujeet Kumar Sinha,NirajKumar Singh, Ashutosh Kumar Bharti, Animesh Barman (2007)	Participants: Ten people (seven males and three females) age ranged 15 to 35 years old. Tests done: Vestibular evoked myogenic potentials (VEMPs)	Nine of the ten participants exhibited abnormal or absent VEMP responses. Only one of the subjects had normal VEMP results. Three of the nine patients were found to have abnormal VEMP findings whereas six patients had no VEMP response on both the sides. Sixteen of the twenty ears examined exhibited abnormal VEMP findings, and only one participant had bilaterally normal VEMP, showing that vestibular disorders affect 80 percent of the individuals diagnosed with Auditory Neuropathy.	Results suggested no correlation between abnormal VEMP findings and vestibular symptoms.

				VEMPs were lacking or delayed in latency, and their amplitude was lowered in 16 of the 20 ears,	
5.	Vestibular evoked myogenic potential (VEMP) in patients with auditory neuropathy: Auditory neuropathy or audiovestibular neuropathy?	Amir Arvin Sazgar, Nasrin Yazdani, Nima Rezazadeh & Alireza Karimi Yazdi **(**2010**)**	Participants: 8 patients diagnosed as ANSD in the age range-21 to 45 years mean age of 28.6 ± 8.1 years Tests Done: C-VEMP	Normal VEMP responses were seen in three ears (two on the left and one on the right), Atypical responses in four ears and No VEMPs in nine.	

6.	Involvement of peripheral vestibular nerve in individuals with auditory neuropathy	Sujeet Kumar Sinha, Animesh Barman, Niraj Kumar Singh, G. Rajeshwari, R. Sharanya (2013)	Total -3 subjects Age range of 19–21 years Tests done: c-VEMP Caloric testing	C- VEMP was absent in both ears Caloric- Hypo functional responses bilaterally Central vestibular test results were normal for all the participants	
7.	Cervical and ocular vestibular evoked myogenic potentials test results in individuals	Sujeet Kumar Sinha, Kruthika Shankar, Raja Sharanya (2013)	Total of 11 participants (4 males and 7 females, n=22 ears) Age Range- 15 to 28 years. Tests done: Ocular VEMP Cervical VEMP	O- VEMP- Absent in all participants (100percent) C- VEMP- Absent (90.90percent) Six (54.54 percent) of the 11 participants did not report any vestibular complaints, The remaining five (45.46 percent) had various forms of vestibular	

	with auditory neuropathy spectrum disorders			symptoms.	
8.	Influence On Vestibular Function By Auditory Neuropathy	Wang Jingmiao, Jiang Xinxia, Shan Chunguang (2013)	Total- 32 participants (18 females and 14 males) Age range-9years to 32 years (mean age-20) Tests done: Caloric test	6 patients had abnormal results in the caloric test of which, 5 individuals had bilateral horizontal semicircular canal reduction or paralysis whereas, one patient had unilateral horizontal semicircular canal reduction, an indication of an abnormal caloric test.	
9.	Cervical vestibular evoked myogenic	Kumar Sinha Sujeet, Kumar Singh Niraj, Barman Animesh,	Experimental Group-ANSD Total -26 individuals (10 males	96.15percent (50 ears) –absence of cVEMP responses. Normal- 1.9 percent (1 ear) of the study group.	No significant relationship between the audiometric configuration and the

	potentials and caloric test results in individuals with auditory neuropathy spectrum disorders	G. Rajeshwari, and R. Sharanya (2014)	and 16 females) in the age range of 13 to 42 years (mean = 21.8 yrs). Cervical vestibular-evoked myogenic potentials (cVEMPs) Caloric Testing	Abnormal n13-p23 amplitude combination -1.9 percent (1 ear). Hypo activity was the most common response, with 86.53 percent (45 ears) of the persons evaluated displaying it. A lower fraction of the population, 5.76 percent (3 ears), had reactions that were outside the recording range's maximum limit and were thus classed as hyperactive. 7.69 percent (4 ears) of the ANSD group exhibited responses that were well within the control group's normative range.	caloric response. No significant relationship between the audiometric configuration, and the cVEMP responses. No statistically significant association between the caloric response and the cVEMP response. There was no significant relationship between

					the severity of hearing loss and the cVEMP and caloric test results.
10.	Evaluation of 20ochlea-vestibular functions in patients with auditory neuropathy	Namea M. Ismail, Soha A. Makky, Amal E. Besher, Dalia H. Galhom (2014)	Total- 40 individuals Age Range- 15 to 55 years Tests done: VEMP test Caloric test	VEMP present bilaterally in 15 individuals (37.5percent), unilaterally in 10 patients (25percent), and absent in 15 patients (37.5 percent) unilateral weakness in caloric test in 10 individuals. These 10 individuals also had absent VEMP response on the same side of weakness in caloric test	

11.	Saccular dysfunction in children with sensorineural hearing loss and auditory neuropathy/auditory dyssynchrony	Seyede Faranak Emami, Farhad Farahani (2015)	Participants age range = 7 to11 years with mean age of 9 years, Total-Thirteen children (11 cases of unilateral ANSD + two cases of bilateral ANSD Test done: C- VEMP test	11 ears cVEMPs were abnormal [lower amplitudes and longer latencies (n = 11) and no response in 4ears	
12.	Assessment of otolith mediated neural reflexes through	Niraj Kumar Singh, Sujeet Kumar Sinha &Animesh Barman (2016)	Total -31 individuals (14 Males and 17 Females) Age range- 14 to 45 years (Mean age 21.58±6.98 years)	C- VEMP absent in 51 ears Normal in 3 individuals bilaterally and 5 individuals unilaterally Mean p1 latency- no significant difference between control group and clinical	There was no significant relationship between the onset of the disease and the

	cervical and ocular vestibular evoked myogenic potentials in individuals with auditory neuropathy spectrum disorders		Tests done: C- VEMP and oVEMP	group Mean n1 latency longer in clinical group then control group interpeak latency interval- longer in clinical group than control group Control group's mean peak-to-peak amplitudes were bigger, and the asymmetry ratio was lower than the clinical group. O-VEMP Absent in 56 ears. Normal in 2 individuals bilaterally and 2 individuals unilaterally Mean n1 latency- normal between control and experimental groups	occurrence of vestibular symptoms. The timeframe since starting was not substantially related to cVEMP response absence or oVEMP response absence. The findings demonstrated no statistically significant relationship between

				Mean p1 latency- delayed in clinical group Interpeak latency difference- prolonged in the clinical group Mean asymmetry ratio- larger in clinical group Peak to peak amplitude- lower in clinical group.	the presence of symptoms and the lack of cVEMP. There was also no statistically significant relationship between the presence of symptoms and the lack of oVEMP. There was no significant relationship between the severity of

					hearing loss and the lack of oVEMP as well as cVEMP.
13.	Clinical relationship between auditory neuropathy and nervous system diseases	Jingbo Wang, LanlanJin, Jun Chen, Xiaobi Fang, Zhisu Liao (2017)	The average age of 30 normal individuals- is 22.0 ±6.73 years The average age of 10 individuals with abnormal caloric test findings- is 20.3 ± 7.97 years Caloric test	In the Caloric Test 30 individuals (75percent) had a bilaterally normal caloric test. Nine individuals (22.5percent) had bilateral Semi-circular canal paresis One individual (2.5percent) had left side semi-circular canal paresis	There was no clear relationship between age and vestibular impairment.
14.	Agreement/dis	Sujeet Kumar	Total- 3 individuals (2	VHIT Test	

	agreement between caloric and video head impulse tests: does it reveal something? Report from three individuals with auditory neuropathy spectrum disorder	Sinha, Shalini Bansal &Anuj Kumar Neupane (2019)	Males and 1 Female) Tests done: Video Head Impulse Test Caloric Test	Two individuals had reduced VOR gain and presence of refixation saccades One individual had normal VOR gain and absent refixation saccades All 3 participants had Hypo functional caloric responses.	

15.	Importance of Vestibulo-ocular Reflex Gain and Refixation Saccade Analysis in Individuals with Auditory Neuropathy Spectrum Disorder	Sujeet Kumar Sinha, Anuj Kumar Neupane, Krithika Gururaj (2020)	Total-50 participants (36 males and 14 females) 25 individuals (7 females and 18 males) had normal hearing(control group) and other 25 individuals (7 females and 18 males) (experimental group) age range of 16 to 40 years (Mean-29.20; SD-7.8)	Reduced VOR gain (lesser than 0.8) in at least 1 of the semi-circular canals. Only 1 participant had appropriate VOR gain in all Semi-circular canal Corrective refixation saccades are present in all ANSD groups.	There was no substantial relationship between VOR gain scores and the duration of the diseases. There is no association between pure tone thresholds and VOR gain levels for the left and right canals (except for the LP canal) The right canal VOR gain scores were

					correlated with right ear pure tone thresholds, while the left canal VOR gain scores were correlated with left ear pure tone thresholds. There was no link between VOR gain and the absence or presence of saccades in any of the semicircular canals.

16.	Vestibular dysfunction in patients with auditory neuropathy detected by vestibular evoked myogenic potentials	Juan Hu, Zichen Chen, YuzhongZhang , Yong Xu, Weijun Ma, Yan Zhang , Junli Wang, Yanfei Chen, Min Xu , Hui Yang , Qing Zhang (2020)	ANSD- 22 participants (44 ears) Gender-seven males and 15 females, Age Range- 5 to 47 years (27.3 ± 9.4 years) Out of 22 patients All (22) underwent O-VEMP and C-VEMP	Absent responses in 73 percent in oVEMP and 84 percent of cVEMP. Aberrant oVEMP response was seen in six cases (14percent). Abnormal cVEMP response- Three individuals (7 percent). Normal response- (14 percent in oVEMP and 9 percent in cVEMP) The caloric test had a 70percent abnormal rate overall. vHIT- VOR gains In the lateral semicircular canals-one patient had abnormal VOR gains on both sides.	

			20 individuals underwent the caloric test. 10 were assessed with vHIT test, 9 of these assessed with SHIMP test.	Anterior semicircular canals- Abnormal VOR gains in two individuals. Posterior Semicircular Canal-One patient had aberrant VOR gains on both sides. SHIMP- 8 had normal gains and one had abnormal gains	
17.	Retro-labyrinthine Lesion Site Detected by Galvanic Vestibular Stimulation	Zi-chen CHEN, Yu-zhong ZHANG, Huan-di ZHAO, Xinyu WEI, Toshihisa Murofushi, Juan HU, Ying CHENG,	Total- 14 participants (3 Males and 11 Females) Age range- 16- 38 years (Mean- 30.6 ± 6.4) Tests cVEMP	Total- 28 ears Absent rates ACS- cVEMP- 92.9percent (26/28 ears) GVS- cVEMP-67.9percent (19/28 ears) ACS-oVEMP- 85.7percent (24/28	

	Elicited Vestibular-evoked Myogenic Potentials in Patients with Auditory Neuropathy	Fei-yunCHEN, Xin-da XU, Min XU, Qing ZHANG **(**2021**)**	GCVEMP oVEMP GOVEMP Caloric test-(1 participant didn't go for the caloric test)	ears) GVS- oVEMP- 53.6percent (15/28 ears) Caloric test- 61.5percent (8/13).	

3.3 Vestibular Signs and Symptoms in individuals with ANSD

Starr et al., (1996) first reported vestibular sign and symptoms in individuals with auditory neuropathy spectrum disorders (ANSD). These authors reported that even though two out of ten individuals with ANSD had vestibular dysfunction, they did not have any clinical indications or symptoms of vestibular dysfunction.

Kumar et al., (2007) assessed ten individuals diagnosed with ANSD for vestibular dysfunction. Only three participants with ANSD had a history of dizziness. Six out of nine subjects did not report of dizziness at any time. The authors suggested no one-to-one relationship between impaired or lacking VEMP and vestibular symptoms.

Sinha et al., (2013a) carried out c-VEMP test on 3 individuals in the age range of 19–21 years diagnosed with ANSD. These authors found that two of the three individuals identified with ANSD did not have any substantial complaints about vestibular symptoms; however the third person did have vestibular symptoms that persisting over six months.

Sinha et al., (2013a) also reported a correlation between the disorder duration and the presence/absence of vestibular symptoms in ANSD patients. Sinha et al., (2013b) stated lack of any vestibular symptoms in six (54.54 percent) participants whereas, the symptoms were present in remaining five (45.46 percent) patients with ANSD.

Singh et al., (2016) reported absence of vestibular symptoms in patients with ANSD. Also, the findings demonstrated no statistically significant relationship between the absence/presence of vertigo symptoms and the absence/presence of cVEMP or oVEMP.

3.4 Clinical test results in individuals with ANSD

Limited studies have performed the clinical tests of imbalance to check the diagnostic efficacy in individuals with ANSD. Sinha et al., (2013a) performed Romberg test and Fukuda Stepping test and reported that two of the three subjects with ANSD showed rightward deviation. Sinha et al., (2013a) also found a correlation between the audiometric thresholds and the side of the deviation; i.e. individuals with ANSD always deviated towards the side which had poor audiometric thresholds. Sheykholeslami et al., (2000) performed Romberg and Fukuda stepping test(in eyes closed and eyes open condition) in 3 individuals with ANSD. The authors reported abnormal findings in Romberg and Fukuda stepping test in eyes closed condition.

3.5 VEMP Test

3.5.1 Prevalence and incidence of VEMP findings in individuals with ANSD

Sheykholeslami et al., (2000) recorded cVEMP using click stimulus in three individuals with ANSD. These authors observed absent cVEMP responses in all the 3 ANSD individuals.

Kumar et al., (2007) recorded VEMP using 250 click stimuli with band pass filter of 30 Hz to 1500 Hz at an intensity of 99 dBnHL for 120 ms duration in ten individuals diagnosed with ANSD. The authors reported abnormal cVEMP in nine out of ten subjects. Among these nine individuals three patients exhibited reduced amplitude of VEMP, six had absence of cVEMP response on both sides

Sazgar et al., (2010) performed cVEMP using 500Hz Tone Burst stimuli with band pass filter of 10 Hz–1.2 kHz at an intensity of 95 dBnHL for 100 ms duration on 8 individuals with ANSD (16 ears). The age range of the participants was between the ages

of 21 and 45, with a mean of 28.6 ± 8.1 years. These authors reported absent cVEMP response in 9 ears, abnormal cVEMP response in 4 ears.

Sinha et al., (2013a) carried out c-VEMP test on 3 individuals in the age range of 19–21 years diagnosed with ANSD. These authors recorded C-VEMP using 500Hz Tone Burst stimuli with band pass filter of 30 Hz–1500 kHz at an intensity of 95 dBnHL for 50 ms duration. The authors found that none of the ANSD individuals had a cVEMP response in both ears.

Sinha et al., (2013b) recorded cVEMP using 500Hz Tone Burst stimuli at 95dBnHL for 50 ms post stimuli with 10 ms pre-stimulus time duration in 11 individuals with ANSD. The results of the study suggests absent cVEMPs in 20 out of 22 ears. Similarly, these authors also recorded oVEMP using 500Hz Tone Bursts at the rate of 5.1/s at 95dBnHL intensity. The results revealed that oVEMPs were lacking in all 22 ears (100 percent) of people with auditory neuropathy spectrum diseases.

Sujeet et al., (2014) performed cVEMP on 26 individuals (52 ears) diagnosed with ANSD. The authors suggested absence of cVEMP response in 96.15 percent. Ismail et al., (2014) performed cVEMP in 40 individuals with ANSD. The recording for cVEMP was done using broad band click at 95dBnHL with filter setting of 30-1500Hz. .The authors were able to observe the presence of bilateral cVEMP in 15 individuals (37.5 percent), unilaterally in 10 individuals (25 percent), and absent in 15 individuals (37.5 percent).

Singh et al., (2016) performed cVEMP and oVEMP on 31 individuals diagnosed with ANSD and on 31 healthy individuals who were considered as a control group. The findings of this study revealed absent cVEMP in 51 ears, normal in 3 individuals

bilaterally and 5 individuals unilaterally accounting for 11 ears (17.74 percent). The findings of this study also revealed, absent oVEMP in 56 ears, normal in 2 individuals bilaterally and 2 individuals unilaterally accounting for 6 ears (9.67 percent).

Hu et al., (2020) performed cVEMP & oVEMP in 22 individuals diagnosed with ANSD. All 22 individuals with ANSD (44 ears) underwent the cVEMP and oVEMP tests. These authors could observe majority of the individuals in the study group had absent cVEMP response in 84 percent of the individuals and an absent oVEMP response in 73 percent of the individuals. Also, abnormal cVEMP response was found in 7 percent (3 individuals) and abnormal oVEMP response was seen in 14 percent (6 individuals) in the study group. On the other hand, the authors could observe normal cVEMP response in 9 percent of the individuals and normal oVEMP response in 14percent of the individuals diagnosed with ANSD.

Chen et al., (2021) performed air-conducted sound (ACS) VEMP and Galvanic vestibular stimuli (GVS) VEMP on 14 individuals (28 ears) diagnosed with ANSD. The authors recorded cVEMP and oVEMP using acoustic and galvanic stimulus. The results of this study revealed absence of tone burst evoked cVEMP in 92.9 percent (26/28 ears), absence of galvanic cVEMP in 67.9 percent (19/28 ears), absence of tone burst evoked oVEMP in 85.7 percent (24/28 ears), absence of galvanic oVEMP in 53.6 percent (15/28 ears) of the individuals with ANSD.

Emami & Farahani, (2015) performed cVEMP on thirteen children (15 ears), eleven of whom had unilateral ANSD and two of whom had bilateral ANSD. In the experimental group of this study, the authors observed absent cVEMP response in 4 ears

and abnormal cVEMP (longer latency and lower amplitude) in 11 ears diagnosed with ANSD.

3.5.2 Threshold of VEMP in ANSD

Hu et al., (2020) recorded cVEMP and oVEMP using 500Hz Tone Burst stimulus at a level of 131 dBSPL in 22 individuals with ANSD. Concerning cVEMP response in this study, the authors reported a higher threshold (123.1 ± 6.4 dB SPL) in ANSD when compared to the control group (118.2 ± 6.2 dB SPL, $p<0.05$). Similarly, for oVEMP ANSD group's threshold was 124.5 ± 6.3 dB SPL, which was higher than compared to the control group's threshold (119.0 ± 4.9 dB SPL, $p< 0.01$).

Chen et al., (2021) performed air-conducted sound (ACS) VEMP and Galvanic vestibular stimuli (GVS) VEMP on 14 individuals (28 ears) diagnosed with ANSD. The results indicated that, in the GVS-cVEMP, the control group had threshold of 3.0 mA whereas the ANSD group had 4.0mA. Similarly, for GVS-oVEMP the control group had threshold of 2.0 mA whereas the ANSD group had 4.0 mA respectively.

3.5.3 Latency of VEMP in ANSD

Emami & Farahani, (2015) performed cVEMP on thirteen children (15 ears), eleven of them had unilateral ANSD and two of them had bilateral ANSD. The latency of p13 and N23 peaks of cVEMP for the control group was 13.1 ± 1.0 ms, and 23.1 ± 1.6 msec respectively. In individuals with ANSD p13 latency was 17.2 ± 1.4 msec, and n23 latency was 28.5 ± 2.2 ms; results suggested increased latency of cVEMP in ANSD.

Singh et al., (2016) performed cVEMP and oVEMP on 31 individuals diagnosed with ANSD and 31 healthy individuals were considered as a control group. The study's findings indicated no statistically significant change in mean latency of p13 and n23

peaks between individuals with ANSD and healthy controls. Also, there wasn't any statistically significant difference in mean latencies of oVEMP peaks between ANSD and healthy individuals.

Hu et al., (2020) reported p1 and n2 latency of cVEMP to be 17.3 ± 2.3 ms and 23.0 ± 2.2 msec in ANSD, which was identical to the control group. But for oVEMP n1 peak latency was 11.1 ± 1.1 ms and p1 latency was 15.6 ± 0.7 ms for ANSD, which was significantly longer than those seen in the control group (p1=10.3 ± 0.7 ms and n1=14.7 ± 1.3 ms, $p < 0.01$). Chen et al., (2021) found prolongation of ACS-oVEMP n1 latency in ANSD, GVS-oVEMP n1 and p1 latency prolongation in ANSD.

3.5.4 Amplitude of VEMP in ANSD

Sujeet et al., (2014) reported a mean amplitude of p13-n23 complex (μV) – 44.10 ± 18.71 (Range – 19.73-88.60), and mean p13-n23 complex inter-ear amplitude asymmetry (percent) – 15.06 ± 9.23 (Range – 3.41-34.60) in healthy individuals. Among ANSD individuals 96 percent of them had absence of cVEMP response. In remaining 4 percent of the individuals one individual with ANSD had normal VEMP amplitude whereas, the other one had abnormal VEMP amplitude. Emami & Farahani, (2015) reported cVEMP reduced peak to peak amplitude in ANSD individuals(14.1 ± 5.7μV) compared to healthy individuals (45.9 ± 3.8μV).

Singh et al., (2016) reported reduced peak to peak amplitude (1.84 ± 0.36μV) in individuals with ANSD compared to the healthy controls. Among the individuals with ANSD with the presence of oVEMP (n=6 ears), the peak to peak amplitude was 2.88 ± 1.36μV which was again smaller compared to the healthy individuals.

Hu et al., (2020) reported cVEMP amplitude to be 75.4± 5 35.93 μV in ANSD, which was substantially lower than the control group's (235.1 ± 142.2μV). Similarly, for oVEMP, the amplitude was 3.0 ± 1.1 μV in ANSD, which was lower than the normal group's (6.9 ± 4.3 μV, $p < 0.01$). Chen et al., (2021) reported that for GVS-oVEMP the amplitude was 5.6 μV in ANSD group whereas, the amplitude was 15.0 μV in the control group. With reference to this finding the authors concluded that GVS-oVEMP amplitude was lowered among individuals with ANSD.

3.6 Video head impulse test results (vHIT results)

3.6.1 VOR gain and Saccades in ANSD

Sinha et al., (2019) performed vHIT on 3 individuals diagnosed with ANSD. The lateral canal was assessed using vHIT. The average of 20 trials was used to compute VOR gain. The result of this study revealed reduced VOR gain in 2 individuals whereas, normal VOR gain in 1 individual diagnosed with ANSD.

Sinha et al., (2020) investigated vHIT on 50 participants where the participants were divided into 2 groups. Among the total 50 participants, 25 participants (7 females and 18 males) who had normal hearing sensitivity were considered as control group whereas, the other 25 participants (7 females and 18 males) with the age range between 16-40 years ($\bar{x}$=29.20; σ =7.8) were diagnosed with ANSD and considered as the experimental group. All individuals received head impulses in the lateral plane, the left anterior right posterior (LARP) plane and in the right anterior left posterior (RALP) plane. The authors reported reduced VOR gain (lesser than 0.8) in at least 1 of the semi-circular canals in individuals with ANSD. However, only 1 participant had normal VOR in all Semi-circular canals.

Hu et al., (2020) performed HIMP on 10 ANSD individuals and SHIMP on 9 individuals diagnosed with ANSD. VOR gains along with the presence or absence of corrective saccades were analyzed. The results of this study revealed reduced VOR gain on both sides in 1 individual for lateral semi-circular canal, reduced VOR gain in 2 individuals for anterior semi-circular canal, and reduced VOR gain on both sides in 1 individual for posterior semi-circular canal. 9 of these individuals also went for the SHIMP test, where 8 individuals had normal VOR gain and only 1 individual had abnormal VOR gain.

Sinha et al., (2019) reported presence of refixation saccades in 2 individuals whereas, absence of refixation saccades in 1 individual diagnosed with ANSD. Sinha et al., (2020) reported presence of both i.e. covert and overt types of refixation saccades in individuals with ANSD. However, these corrective saccades were absent in healthy controls. Hu et al., (2020) absence of overt corrective saccades and acceptable anti-compensatory saccades in the SHIMP test in ANSD. In the vHIT test, three ANSD patients had overt corrective saccades, detected on both sides of the lateral canal. One patient had significant saccades in both vertical canals (posterior and anterior canals). The SHIMP test revealed that most patients had normal anti-compensatory saccades, except one patient, who had no SHIMP saccades on either side.

3.7 Caloric test results in ANSD

Starr et al., (1996) performed caloric test on ten patients consisting as either children or young adults of both genders. The results of this study revealed abnormal vestibular caloric tests in two patients. Also, caloric vestibular function testing revealed

normal horizontal nystagmus and vertigo in two individuals but failed to elicit this response in two other individuals.

Fujikawa & Starr, (2000) performed caloric test on 14 individuals diagnosed with ANSD (7 Men and 7 Women) with the age range of 10 to 75 years for their study. In the caloric test the caloric stimulation was induced using the closed-loop system where the water irrigation was done with the help of the balloons inserted in the External Auditory Canal. Bi-thermal stimulation was performed at 30^0C and 44^0C. The results revealed that, out of 14 subjects, 5 subjects had normal response whereas; the remaining 9 subjects had abnormal response in the caloric test. The results also revealed among 9subjects with abnormal findings in the caloric test, 5 had absent caloric results and 3 had asymmetrical responses.

Sheykholeslami et al., (2000) performed caloric testing on three individuals. Ice water (20 cm^3) was utilized to irrigate the external auditory meatus which would help to create a temperature gradient across the lateral semicircular canal. Out of three individuals in the study, only the right ear of one patient responded to caloric stimulation with 20 cm^3 cold water causing horizontal nystagmus without vertigo, whereas, neither vertigo or horizontal nystagmus was observed in the other ear. In summary, Caloric stimulation with ice water failed to induce nystagmus or dizziness.

Sujeet et al., (2014) performed caloric testing on 26 ANSD individuals (10 male sand 16 females) in the age ranging from of 13 to 42 years (mean = 21.8 yrs) for the study. There were other 26 individuals who were considered as the control group for this study. However, the most prevalent result among 26 individuals (52 ears) with ANSD was hypo activity, which was detected in 86.53 percent (45 ears), whereas hyperactivity

was found in 5.76 percent (3 ears) and even normal caloric responses were attained in 7.69 percent (4 ears).

Wang et al., (2013) performed caloric tests on 32 individuals with ANSD. The results showed that out of 32 individuals, 6 had abnormal results in the caloric test of which 5 individuals had bilateral horizontal semicircular canal reduction or paralysis whereas 1 patient had unilateral horizontal semicircular canal reduction; an indication of an abnormal caloric test.

Ismail et al., (2014) performed the caloric test using bithermal stimuli with the use of open loop system for water irrigation, which was lasted for 30 seconds at 30^0C and 44^0C temperature. The authors reported unilateral weakness in caloric test in 10 ANSD individuals.

Wang et al., (2017) investigated caloric test on 40 individuals diagnosed with ANSD. These authors found 30 individuals (75 percent) had a bilaterally normal caloric test, 9 individuals (22.5 percent) had bilateral canal paresis and 1 individual (2.5 percent) had left side semi-circular canal paresis.

Sinha et al., (2019) performed caloric test in three individuals diagnosed with ANSD. The authors used open loop system for water irrigation to stimulate lateral semicircular canals. Bi-thermal water irrigation at 30^0C and 44^0C were used for a time duration of 30 second for each irrigation..The results of this study revealed hypo functional caloric response in all the 3 individuals diagnosed with ANSD.

Hu et al., (2020) performed caloric tests using bi-thermal stimuli in 22 individuals (44 ears) diagnosed with ANSD. The results of the study suggest an abnormal caloric response in 70 percent of the individuals with ANSD. 8 of the 20 individuals with ANSD

had unilateral semi-circular canal weakness and six had bilateral semi-circular canal weakness.

Chen et al., (2021) performed caloric test on 13 ANSD individuals (26 ears) in the age range between 16 to 38 years (Mean- 30.6 ± 6.4). Results revealed absent caloric response in 61.5 percent (8/13) individuals diagnosed with ANSD.

Chapter 4

DISCUSSION

Considering the various test results of vestibular test in individuals with Auditory Neuropathy Spectrum Disorder (ANSD) the results suggests that most of the individuals have either absent or abnormal responses in different vestibular test findings. The results of the studies also suggest that vestibular test findings were abnormal despite no presence of any vestibular signs and symptoms. The results of all the studies are suggestive of auditory as well as vestibular problems among individuals with ANSD. The findings of these vestibular tests not only help audiologists to know about the disorder but also a treatment line to be used to rehabilitate these individuals and hence achieving a quality of life.

4.1 VEMP test

The majority of the studies suggest absence of cVEMP and oVEMP responses in more than 90 percent of the individuals with ANSD.

Absence of VEMP responses in individuals with ANSD is suggestive of lesion of sacculocolloic pathway of utriculoocular pathway dysfunction (Sinha et al., 2013a; Singh et al., 2016; Emami & Farahani, 2015). However, an OAE/CM test finding in ANSD individuals is suggestive of a normal inner ear function. Hence it is unlikely that there is a lesion of saccule or utricle in individuals with ANSD. The lesions in ANSD could be confined to the vestibular nerve. There are evidences to suggest the demyelination or axonal diseases in ANSD individuals. It is likely that along with the demyelination of the auditory nerve there could be an demyelination of the vestibular branch of the nerve also. Such demyelination of the nerve or axonal diseases in the nerve could lead to an absence

of VEMP responses in ANSD individuals. Further oVEMP has been found to be more absent compared to the cVEMP in ANSD. Singh et al., (2016) hypothesized that the length of the superior vestibular nerve is more compared to the inferior vestibular nerve. The nerves with longer length are more susceptible for lesion compared to lesion with shorter length. Hence the oVEMPs are likely to be absent in more number on individuals with ANSD compared to cVEMPs.

Further few studies have also suggested increase in VEMP threshold in individuals with ANSD as compared to the healthy individuals.

Hu et al., (2020) obtained cVEMP and oVEMP responses, where the authors could observe a higher threshold in both the types of VEMPs. Based on these findings these authors attributed these impairment due to lesions beyond the labyrinth and impairment of vestibular spinal cord instead of otolith organs. Similar findings were observed by Chen et al., (2021) where these authors found increased thresholds in GVS-cVEMP and GVS-oVEMP and reported that retro-labyrinthine sites are involved in AN patients, particularly impairment of both the inferior and superior vestibular nerves in the VCR and VOR pathways.

Further, the studies also report an increase in latency of the peaks and interpeak latency in individuals with ANSD.

Emami & Farahani, (2015) reported of increased latency in the experimental group was due to impairment in the inferior vestibular nerve. Singh et al., (2016) reported that the prolonged inter-peak latency difference and N1 latency in the presence of normal-like p1 latencies are caused by the gradual slowdown of neural conduction throughout the inferior vestibular nerve. For oVEMP, these authors reported mean p1

latency was prolonged in the clinical group; interpeak latency difference was prolonged in the clinical group. These authors explained this findings by how neuropathy gradually gets worse as the neural impulse moves through the nerve, as was mentioned in the prior section on cVEMP.

Hu et al., (2020) observed normal interpeak latency for cVEMP but an increase in interpeak latency in ANSD participants. Based on these findings these authors attributed these impairment due to lesions beyond the labyrinth and impairment of vestibular spinal cord instead of otolith organs.

Chen et al., (2021) found prolonged ACS-oVEMP and GVS-oVEMP responses. These authors reported that retro-labyrinthine sites are involved in ANSD patients, particularly impairment of both the inferior and superior vestibular nerves in the VCR and VOR pathways. These authors also explained the evoked responses with aberrant values and lacking results may show that vestibular system participation might vary from proper functioning to total vestibular areflexia; moreover, the deviant parameters reflect a gradual progression in the different phases of vestibular system participation in such patients.

Further the studies also have reported a decrease in amplitude in individuals with ANSD.

Sujeet et al., (2014) reported the aberrant n13-p23 amplitude could be a sign of a problem with the sacculus, and/or inferior vestibular nerve. Emami & Farahani (2015) found lower amplitudes and longer latencies were due to impairment in the inferior vestibular nerve (Saccular anomaly).

Singh et al., (2016) reported decreased amplitude for cVEMP was due to weaker performance of the sacculocolic pathway. Some people with ANSD may have reduced or absent waveforms due to dys-synchrony or asynchrony of neuronal firing in the inferior vestibular nerve, which is comparable to the findings for the cochlear branch of the VIIIth cranial nerve, which has been linked to substantially reduced or absent auditory evoked brainstem responses. Similarly, for oVEMP some people with ANSD may have reduced or absent waveforms due to dys-synchrony or asynchrony of neuronal firing in the superior vestibular nerve.

Hu et al., (2020) revealed cVEMP and oVEMP amplitude was lower than control group and attributed these impairment due to lesions beyond the labyrinth and impairment of vestibular spinal cord instead of otolith organs. Chen et al., (2021) concluded that GVS-oVEMP amplitude was lowered; reported that retro-labyrinthine sites are involved in AN patients, particularly impairment of vestibular nerves.

4.2 Video head impulse test results (vHIT results)

There are total three articles, out of which two articles revealed reduced VOR gain whereas, one of these articles showed majority of ANSD patients had adequate VOR gains. However, one article showed normal VOR gains in vHIT test where the authors described this unusual vestibular pattern is unique.

Sinha et al., (2019) revealed reduced VOR gain and justified due to impairment in the neurons, which are responsible to excite and fire irregularly neurons once transient stimuli is provided for excitation. Sinha et al., (2020) observed that VOR gain was reduced (lesser than 0.8) in at least 1 of the semi-circular canals in individuals with ANSD. The authors explained these findings due to incapability of neural pathway,

which includes the inferior and superior vestibular nerves, is unable to produce the requisite number of action potentials for the VOR reflex pathway to function properly, which results in a decreased VOR gain. Hu et al., (2020) showed majority of ANSD patients had adequate VOR gains in the vHIT and SHIMP tests and described this type of unusual vestibular pattern is unique.

There are three articles which discussed about the refixation saccades: two revealed the presence of refixation saccades whereas one article revealed absence of refixation saccades in ANSD subjects.

Sinha et al., (2019) revealed presence of refixation saccades are caused by differences in excitation between two canals in the same orthogonal direction, which causes the VOR to produce a compensating eye movement to maintain the stability of the gaze even while the head is moving.

Sinha et al., (2020) revealed that refixation saccades were estimated and shown to be present in individuals with ANSD. These authors explained these findings as the refixation that is compensatory saccades are a sign of weaker semicircular canals because they are unable to stabilize the gaze with eye movements that are equally rapid and counterclockwise to head rotation. The occurrence of this finding is a result of differences in excitation across two canals that are in the same orthogonal direction, which causes the VOR to produce a compensating eye movement to ensure the stability of the gaze even though the head is rotating.

Hu et al., (2020) performed the vHIT test; where only few individuals displayed abnormalities pertaining to overt corrective saccades. This occurrence could be the outcome of the semicircular canals' functional recovery during the course of the disease.

4.3 Caloric test

There are eleven articles which discussed about the prevalence of vestibular dysfunction in caloric test and found that majority of these individuals had abnormal caloric test findings.

Starr et al., (1996) showed abnormal vestibular caloric tests due to either of demyelinating neuropathy and/or axonal neuropathy. Fujikawa & Starr, (2000) revealed abnormal findings in the caloric test, due to peripheral neuropathies which occurs due to either of axonal neuropathy and/or demyelinating neuropathy.

Sheykholeslami et al., (2000) reported abnormal caloric stimulation was due to the vestibular branching of the VIIIth cranial nerve as well as the regions it innervates can also be damaged in those with auditory neuropathy (isolated condition).

Sinha et al., (2013a) showed bilateral hypo functional responses and suggests that the superior vestibular nerve and/or the lateral semicircular canal are not functioning properly. Wang et al., (2013) preformed caloric testing and revealed a decrease in functioning or paralysis of the lateral semicircular canal, suggesting that vestibular abnormalities were present and that vestibular dysfunction may be a contributing factor to the pathological impairment.

Sujeet et al., (2014) revealed the most prevalent result was hypo activity whereas very few had hyperactivity. Since the superior vestibular nerve and/or the posterior SCC may have been involved, these people were classified as having auditory-vestibular neuropathy. This corresponds to the neurological system, represented by the superior and inferior vestibular nerves, being unable to produce the requisite number of potentials for cVEMPand/or caloric responses.

Ismail et al., (2014) unilateral weakness in caloric test likewise, these individuals also had absent VEMP responses on the same side of weakness in the caloric test. Thus, inferior vestibular neuropathy, superior vestibular neuropathy and superior/inferior vestibular neuropathy might be used to categorize the vestibular neuropathy.

Wang et al., (2017) found semi-circular canal paresis; revealed that the primary structure and vestibular branching of the auditory nerve were also affected. However, because vestibular neuropathy progresses slowly, people with auditory neurosis may be able to use a variety of compensatory mechanisms to offset their vestibular impairment, which typically appears as asymptomatic for vestibular dysfunction.

Sinha et al., (2019) observed hypo functional caloric response. In a caloric testing, the stimulation is likely to excite neuron having regular firing if a low-frequency stimulus is applied to the vestibular system. This is because the nerve fibers controlling the VOR gain function have regular neural spike timing. Thus, the caloric testing that it uses to encode the frequency may be selectively impaired.

Hu et al., (2020) revealed semi-circular canal weakness due to abnormality in semicircular canal functioning particularly for the neurons that encodes the low frequency to generate a reflex.

Chen et al., (2021) explained the evoked responses with abnormal values and lacking results may show that vestibular system participation might vary from proper functioning to total vestibular areflexia; moreover, the deviant parameters reflect a gradual progression in the different phases of vestibular system participation in such patients.

Chapter 5

SUMMARY and CONCLUSION

The systematic review summarizes the findings of different vestibular tests in individuals with auditory neuropathy spectrum disorders. Most of these studies suggest a vestibular deficit on in individuals with auditory neuropathy spectrum disorders.

Vestibular Signs and Symptoms in individuals with ANSD

Most of the studies indicated absence of vestibular sign and symptoms in individuals with ANSD. Further, some studies showed lack of relationship between the presence/absence of vertigo symptoms and the presence/absence of cVEMP or oVEMP.

Clinical test results in individuals with ANSD

There in no one to one correlation between different vestibular tests findings in individuals with ANSD. Some studies found a correlation between the audiometric thresholds and the side of the deviation; i.e. individuals with ANSD always deviated towards the side which had poor audiometric thresholds.

Here is the summary of all the tests findings in ANSD.

VEMP Test

The results of all the studies indicate an absence of VEMP waveform in more than 90 percent of the individuals with ANSD. The ANSD individuals in whom there is a presence of response, the amplitude of cVEMPs and oVEMPs are abnormally reduced. As the amplitude of various peaks are reduce the threshold of VEMPS are higher in ANSD participants. The latency of the P1, NI peak of cVEMP and N1, P1 peak of oVEMP are abnormally prolonged compared to the healthy individuals.

vHIT Test Results

There are only three studies that have characterized the VOR gain in ANSD participants. These studies indicate a reduced VOR gain for all the six semicircular canals in individuals with ANSD. In addition, there is a presence of both the overt and covert saccades in all the individuals with ANSD.

Caloric Test Results

The results of the caloric test indicate presence of hypoactive responses in caloric test in all the individuals with auditory neuropathy spectrum disorders.

CONCLUSION

Results of the various test indicate a presence of vestibular dysfunction in individuals with ANSD. However, most of the times a vestibular evaluation is not done on ANSD subjects as they do not present with any vestibular sign and symptoms. The absence of vestibular sign and symptoms in ANSD subject is because of the bilateral distribution of the disorder and central compensation occurring in these individuals.

RESEARCH GAP

Although, the results indicate vestibular Hypo function in majority of the individuals with ANSD, there are some lacunae in these reports. First, majority of the studies have reported peripheral vestibular test findings in ANSD individuals. The central vestibular test findings have not been reported in detail. Also, the presence or absence of a neurological disorder in ANSD has not been mentioned. Most of the study also did not perform a complete vestibular test battery in ANSD participants. None of the articles have mentioned the progression of the disorder and their findings in the follow up testing.

None of the articles had mentioned about the auditory and vestibular rehabilitation that could be incorporated in ANSD individuals.

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