MULTIFREQUENCY NARROWBAND CHIRP EVOKED MASSETER VESTIBULAR-EVOKED MYOGENIC POTENTIAL IN HEALTHY YOUNG ADULTS

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Register No: P01II21S0066

This dissertation is submitted as part of fulfilment for

the Degree of Master of Science in Audiology

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SEPTEMBER-2023

CERTIFICATE

This is to certify that this dissertation entitled **"Multifrequency Narrowband Chirp Evoked Masseter Vestibular-evoked myogenic Potential in healthy young adults"** is a bonafide work submitted as a part of fulfilment for the degree of Master of Science (Audiology) of the student with Registration Number: P01II21S0066. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other university for the award of any other Diploma or Degree.

Mysuru,

September 2023

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Mysuru,

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DECLARATION

This is to certify that this dissertation entitled **"Multifrequency Narrowband Chirp Evoked Masseter Vestibular-evoked myogenic Potential in healthy young adults"** is the result of my own study under the guidance of Dr. Sujeet Kumar Sinha, 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:** P01II21S0066

September 2023

Acknowledgement

Firstly, I would like to express gratitude to myself for the commitment I displayed throughout the completion of this dissertation. Engaging in research, analyzing data, and crafting this document has truly been an experience to behold.

All this experience would not have been possible without the unwavering support of my guide, Dr. Sujeet Kumar Sinha. Your expertise, dedication and commitment have significantly enriched the quality of this dissertation. Your insightful feedback and encouragement have made this research journey more pleasant. I have gained an immense amount of knowledge from you. Beyond your clinical and research expertise, your life perspectives and thought-provoking insights on various subjects have enriched my understanding. Thank you wholeheartedly sir, for being an exceptional mentor.

I would like to render my thanks to the director of AIISH, Dr. M Pushpavathi, for permitting me to carry out this study.

I would also like to thank the HOD, Dept. of Audiology, Dr. N Devi, for permitting me to use the instruments and the facilities available for this study.

I would like to thank my family for being all. Amma, Whatever I am today is because of you. Nobody can go through what you have been through. You have dedicated all your life to me and Keerthi. I have realized what true love is from you. I can’t thank you enough for all the sacrifices you have made for us. Appa, you will forever remain my first and most important teacher. You've shared a lot of wisdom and knowledge with me throughout my life. I am deeply thankful for your unwavering support and for carrying us through all the way to this day. Keerthi, I'm not sure if any other sister could have brought as much beauty into my life as you have. You are more than just a sister; you've always cared for me, even *during our disagreements, and looked out for me in every possible way. You've been a friend, family, and caretaker all rolled into one. Thank you for all the things.*

My sincere thanks to Vinayagar sir for serving as an unofficial co-guide throughout the course of this dissertation. You have generously assisted and instructed me in numerous aspects, from data collection to completing the writing. Without your guidance, this dissertation would not have been as manageable as it has been. I extend my heartfelt thanks for your support throughout this journey.

My special thanks to Kalaiyarasan sir for helping me with my data collection on so many occasions. Opening FAAR and waiting for my data collection would have been a tiring help, but you were there helping me on so many days. Thank you sir.

I would also like to thank Adithya mam, Rajesh sir, Krithi mam and Aishwarya mam for helping me during this dissertation.

I extend my thanks to all the participants of this study for taking your time and being part of my data collection.

I want to express my gratitude to all the staff members of both my undergraduate and postgraduate programs for their support in numerous ways throughout my college journey. Your contributions have been invaluable to my growth and development.

I would like to thank Nirmala for being a constant support from my UG college days to the present. From being a stranger in school and becoming the best friend I can get, our journey has been remarkable. Always, I will be indebted to your care and friendship.

I want to thank Yamini for making my days better during these years. There is so much joy a person can feel from your presence and I am glad to have that. You have made *my life during my postgraduate years all the more eventful. You have shown me different perspectives on life. Thank you for all.*

I would like to thank Shimola for all the wonderful memories we have created in these two years of postgraduate. I will cherish all the moments of our little trips and talks. Thank you, dissertation partner.

I extend my heartfelt thanks to Ashok, Chinna, and Udhai for the countless cherished memories we've created together. From late-night outings to moments of endless laughter, from last-minute exam preparations to the invaluable life advice you've provided, there are so many experiences that words cannot fully capture. I couldn't have asked for a better group of friends than you guys. Over the years, starting from day one of college, I've been able to rely on your support in numerous situations. Thank you for everything.

I thank Guru Anna and Bala for making my stay in the hostel so much more vibrant and memorable. The moments we shared will remain cherished in my heart for years to come.

I would like to offer special thanks to my fellow posting mates, Gagan, Nimisha, Nutan, and Thejashwini, for making my hours at the clinics enjoyable. Your presence certainly brightened my days.

I thank Nishanth for the support he has been during these two years of PG.

I thank all my UG and PG classmates, Seniors and Juniors for making my college journey pleasant and enjoyable.

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Abstract

Introduction:

The masseter vestibular evoked myogenic potential (mVEMP) is a relatively new assessment tool utilized to examine the vestibulo-masseteric reflex. Recently, studies have been increasing to understand the significance of mVEMP better. However, there is still little information available on the normative of mVEMP.

Aim of the study:

The study aimed to characterize the latency of p11 and n21 peaks, and the amplitude of the p11-n21 peak complex of narrow band chirp evoked masseter VEMP in healthy young adults.

Method:

The study involved a group of 30 individuals whose ages ranged between 18 and 30 years. Each participant underwent masseter VEMP testing using narrowband chirp stimuli of 500, 1000, 2000, and 4000 Hz at 125 dB SPL.

Results:

The results showed that the response rate was higher for 500 and 1000 Hz with a 100% response rate, whereas the response rate was reduced for 2000 Hz (95%) and 4000 Hz (80%) narrow band chirp stimuli. There were significant differences in the p11 and n21 latencies of the responses across frequencies. The latency of the p11 and the n21 peaks were shortest for the 500 Hz stimulus, followed by the 1000 Hz, 2000 Hz and 4000 Hz stimuli. This indicates that as the frequency of the stimulus increases, the latency of the response also increases. The amplitude measures of the p11-n21 peak complex showed significant differences across frequencies except between the 500 and 1000 Hz responses. The 500 Hz response had the largest amplitude, followed by the 1000 Hz, 2000 Hz and 4000 Hz. This

indicates that as the frequency of the stimulus increases, the amplitude of the p11-n21 peak complex decreases.

Conclusion:

This study suggests that when narrowband chirp stimuli of different frequencies, such as 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz are used, different normative should be used for analyzing the response of each frequency. The study's results indicate that 500 Hz and 1000 Hz chirps are the best stimuli for recoding mVEMP.

Chapter I

Introduction

The inner ear has two different sensory organs for hearing and balance. The cochlea is an organ of hearing, whereas the vestibular organs are responsible for balance functions. The body's balance function is mainly maintained by the proprioceptive, the visual and the vestibular systems. The combined activity of these three systems helps stabilize and maintain the body's balance during various activities. The peripheral part of the vestibular system includes sensory organs such as the otoliths (saccule and utricle), semicircular canals (lateral, anterior, and posterior) and the vestibular nerve. The central part of the vestibular system includes the brainstem, cerebellum, and cortex. The saccule and utricle react to linear head motion and static head tilt about the gravitational axis. The semicircular canals respond to rotational movements of the head. Three reflexes are mainly involved in the vestibular system: Vestibulo-ocular, vestibulospinal, and vestibulo-collic. The vestibulo-ocular reflex helps to maintain stable vision during head motion; the vestibulospinal reflex helps to stabilize the body, and the vestibulo-collic reflex acts on neck muscles to stabilize the head.

Vestibular-evoked myogenic potentials are short-latency potentials elicited by presenting high-intensity sound to the ear, and the responses are recorded using surface electrodes. These potentials are used to evaluate the function of the otolith organs and the related pathways. There are two main variants of vestibular evoked myogenic potentials: Cervical vestibular evoked myogenic potentials (cVEMP) and Ocular vestibular evoked myogenic potentials (oVEMP). The cervical vestibular evoked myogenic potential is an inhibitory response and assesses the sacculocolloic reflex pathway. In contrast, the ocular vestibular evoked myogenic potential is an excitatory response and assesses the vestibular-ocular reflex pathway. The masseter vestibular evoked myogenic potential (mVEMP) is a relatively new assessment tool utilized to examine the vestibulo-masseteric reflex. Intense acoustic stimulation triggers activation of the masseter muscles via the intricate vestibular-trigeminal pathway. The masseter muscles exhibit short-latency inhibitory responses recorded by placing surface electrodes over the masseter muscles. mVEMP has mainly been evaluated in individuals using either a click or a 500 Hz tone burst stimulus (Thirusangu & Sinha, 2023).

Chirp is an acoustic stimulus developed originally to compensate for the travelling wave delay in the cochlea, thereby increasing neural synchrony. After its development, it has been used extensively in electrophysiological measurements like ABR and ASSR. It has been shown to be effective in eliciting VEMPs. In recent years, the mVEMP has been explored more to identify its usefulness in assessing the vestibular and related systems.

1.1 Need of the study

1.1.1 Need for mVEMP

The masseter muscles support the jaw against gravity. The intricate vestibular-trigeminal system allows for the activation of the masseter muscles in response to auditory stimuli. At first, it was illustrated as a bilateral and symmetrical p11/n15 biphasic waveform following unilateral or bilateral transmastoid electrical stimulation. This response has subsequently been termed the vestibulo-masseteric reflex (VMR) and, more recently, recognized as the masseteric VEMP (mVEMP) (de Natale et al., 2019) . Masseter VEMP has been employed to evaluate brainstem lesions in conditions such as idiopathic rapid eye movement disorder (de Natale et al., 2018), multiple sclerosis (Magnano et al., 2014, 2016), Parkinson's disease (de Natale et al., 2015a, 2015b). Patients with idiopathic rapid eye movement disorder exhibit significantly prolonged p1 latencies and reduced amplitudes in mVEMP responses (de Natale et al., 2018). Masseter VEMPs are more sensitive in identifying the brainstem lesion than the cVEMP and oVEMP (Puligheddu et al., 2019).

This highlights the involvement of the brainstem in idiopathic rapid eye movement disorder and underscores the significance of mVEMP in understanding brainstem degeneration. The rapid and brief vestibular effects with short durations and latencies might not play a significant role in postural control. Still, they could contribute to precise adjustment of voluntary motor output in the masseter muscles. This is achieved by promptly delivering vestibular inputs that offer swift control over the jaw muscles (Deriu et al., 2005).

There has been an increase in studies recently to understand the significance of mVEMP. However, there is still little information available on the normative of mVEMP. Therefore, it is necessary to investigate recording the masseter VEMPs in healthy persons.

1.1.2 Need for mVEMP with Chirp stimulus

Click and Tone burst stimulus has been used to record masseter VEMP (Deriu et al., 2005; Thirusangu & Sinha, 2022; Vignesh et al., 2021). Research has indicated that the amplitude of mVEMP evoked by tone bursts is greater than the response elicited by click stimuli (Thirusangu & Sinha, 2023). Chirp is another stimulus that has been utilized to record cervical and ocular VEMP (Cebulla & Walther, 2019; Ozgur et al., 2015). A chirp stimulus is an auditory stimulus whose frequency changes over time and either rises (up-chirp) or falls (down-chirp). Chirp stimuli compensate for the time delay in the auditory periphery, increasing the temporal synchronization between the neural components. The primary characteristic of the CE-chirp is that the frequency of the stimulus signal progressively increases over time (Wang et al., 2013). Chirp stimuli with frequencies centered at 500, 1000, 2000, and 4000 Hz improve neural synchrony and deliver frequency-specific information (Elberling & Don, 2010). It has been reported that the amplitude of VEMPs is generally higher, and the latency of VEMP peaks is shorter for chirp stimulus compared to the click and tone burst stimulus (Aydin et al., 2022; Wang et al., 2013). Ozgur et al. (2015) recorded cVEMP using a chirp stimulus and reported that the chirp-evoked cervical VEMP had shorter latencies but smaller amplitudes than other stimuli. Sequential or quasi-simultaneous chirp has also been used to elicit VEMPs and has been shown to be better at recording cVEMP and oVEMP than the other stimuli (Cebulla & Walther, 2019).

Thus, there are equivocal findings regarding the efficacy of chirp stimulus in recording the cervical and ocular VEMPs. No studies have seen the chirp stimulus's efficacy in recording the masseter VEMPs in normal, healthy young individuals. So, there is a need to study the effect of chirp stimulus in mVEMP.

1.2 Aim of the study

The present study aimed to characterize the latency and amplitude of Chirp evoked masseter VEMP in healthy young adults.

1.3 Objectives of the study

The study's objectives were to characterize the latency of p11 and n21 peaks and the amplitude of the p11-n21 complex for chirp-evoked masseter VEMP in young, healthy adults.

Chapter II

Review of Literature

Vestibular Evoked Myogenic Potentials (VEMPs) are responses from the otolith organs recorded using sound, vibration, or galvanic stimulation (Rosengren et al., 2019). The cervical vestibular-evoked myogenic potential (cVEMP) and the ocular vestibular-evoked myogenic potential (oVEMP) are the two most used VEMPs. These potentials are used to measure the sacculocollic and otolithic ocular reflexes, respectively. Electromyographic (EMG) responses from the sternocleidomastoid muscle can be recorded in cervical VEMP (Colebatch & Halmagyi, 1992; Rosengren et al., 2019), whereas in ocular VEMP (oVEMP), responses are recorded from ocular muscles (inferior oblique muscle) through surface electrodes (Todd et al., 2007). Vestibular-evoked myogenic potentials can also be recorded in other body muscles such as the gastrocnemius muscle (Rudisill & Hain, 2008), the triceps muscle (Cherchi et al., 2009), the trapezius muscle (Ferber-Viart et al., 1998), and the masseter muscle (Deriu et al., 2005).

Masseter VEMP

The vestibular system regulates many brainstem and postural motor functions (Lacour & Borel, 1993). Among the muscles supplied by the vestibular inputs, the masseter muscles are significant because they help maintain the jaw's position away from its resting position in dynamic and static situations and assist in chewing and speech (Lund & Olsson, 1983; Miralles et al., 1988). Masseter vestibular evoked myogenic potentials (mVEMP) are inhibitory reflex responses with brief latencies measured from the masseter muscles. This vestibulomasseteric reflex might offer rapid vestibular signal access to control the jaw muscles, allowing for accurate modulation of voluntary motor output to the masseter muscles (Deriu et al., 2003).

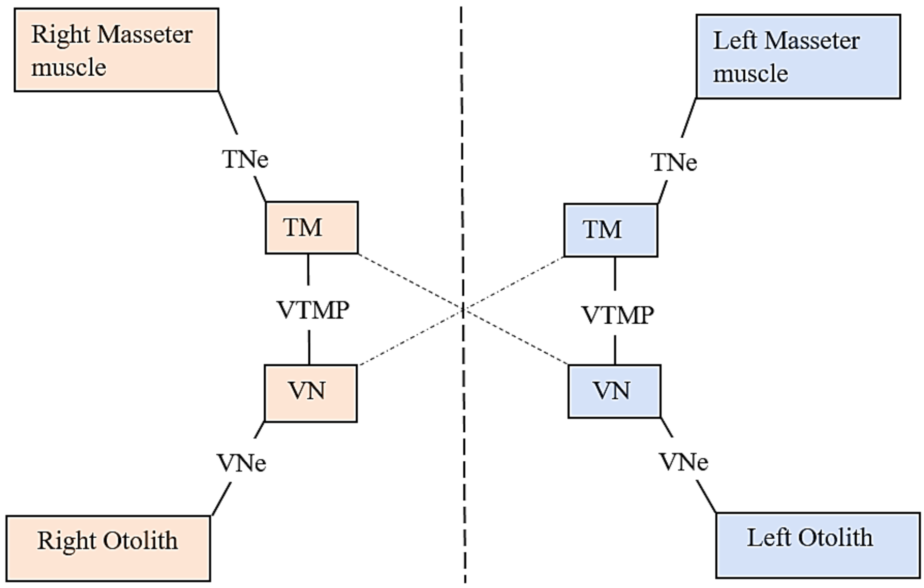
The vestibulomasseteric reflex's natural response to an abrupt head tilt upwards or downwards may be its primary purpose. For example, inhibiting the masseters may be helpful if the head is rapidly lowered and vice versa if the head is suddenly thrown upward. Beyond the effects of soft-tissue viscoelasticity and stretch reflexes, the vestibular system's impact on the masseter muscles could play a role in stabilizing the jaw while in motion (Miles et al., 2004a, 2004b). This influence may also assist in maintaining even pressures on both sides of the jaw during chewing, even when the head is tilted to one side (Deriu et al., 2007).

Masseter VEMP pathway

a. Vestibulomassetric reflex pathway

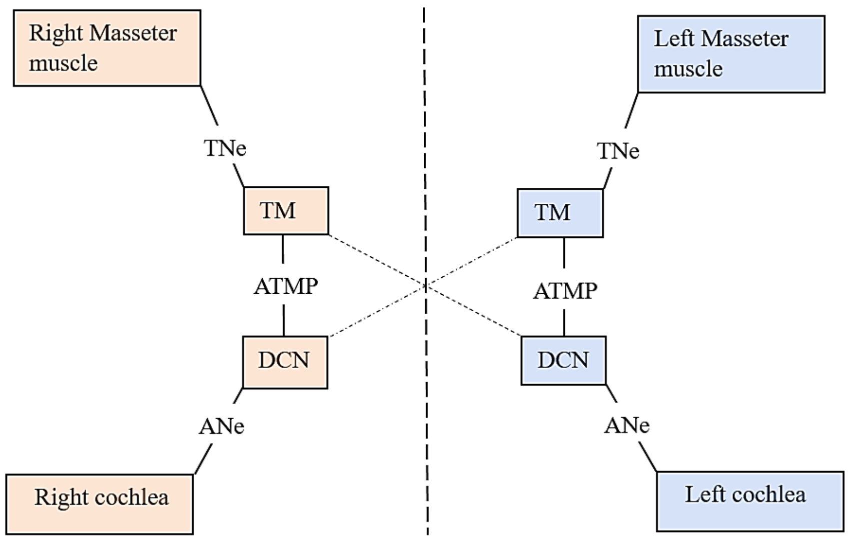
The reflex pathways for cVEMP and oVEMP are ipsilateral and contralateral, respectively. The pathway for masseter VEMP is bilateral. There may be a more intricate neuronal mechanism mediating the vestibulomasseteric reflex. It has been suggested that its structure resembles a pair of contrasting pathways: an excitatory tonic control, which is bilateral and asymmetric, operating through polysynaptic pathways, and an inhibitory phasic control, which is bilateral and symmetric, functioning via oligosynaptic pathways (Deriu et al., 2007). There are two pathways. These are known as vestibulomassetric reflex pathways and acoustic–massetric reflex pathways. The schematic diagram of the vestibulo masseteric and acoustic-masseteric reflex pathways is given below in Figures 2.1 and 2.2, respectively.

Figure 2.1. *Vestibulo masseteric reflex pathway*



Note: TNe - Trigeminal nerve, TMN - Trigeminal Motor Nucleus, VTMP - Vestibulo Trigeminal Monosynaptic Pathway, VN – Vestibular Nucleus, VNe – Vestibular Nerve.

Figure 2.2 *Acoustic-masseteric reflex pathway*

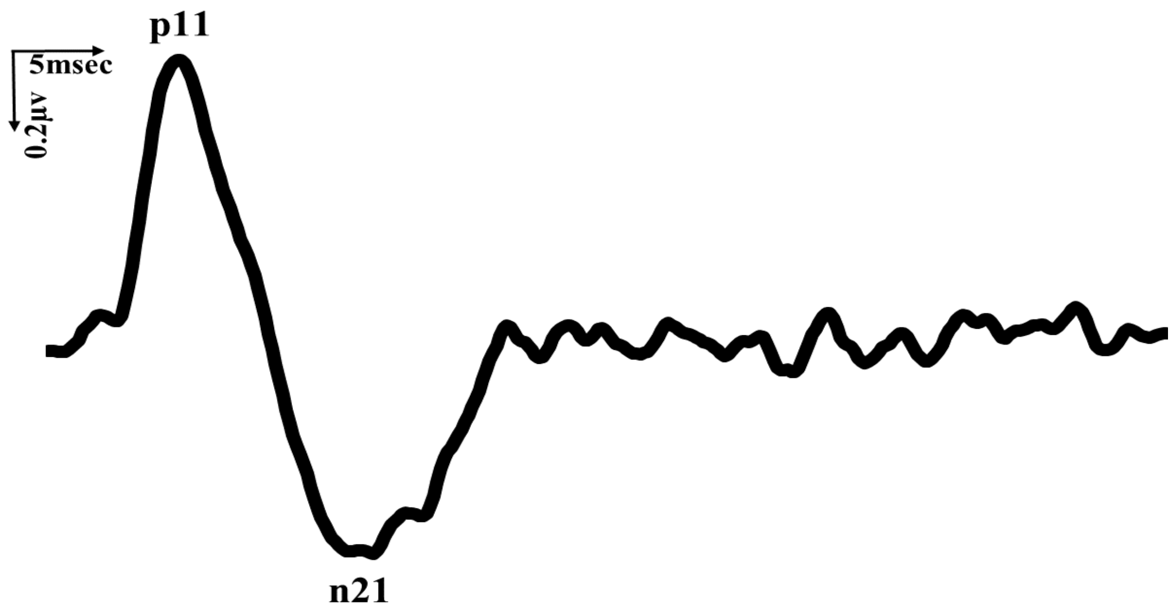


Note: TNe - Trigeminal nerve, TMN - Trigeminal Motor Nucleus, ATMP -Acoustic Trigeminal Monosynaptic Pathway, DCN – Dorsal cochlear Nucleus, ANe –Auditory Nerve.

Characteristics of Masseter VEMP (mVEMP)

Masseter VEMP is an inhibitory reflex response recorded by unilateral or bilateral stimulation from the masseter muscles. The mVEMP response consists of two short latency partially overlapping reflexes: the p11/n15 vestibulo-masseteric reflex (VMR), which is of vestibular origin, and the p16/n21 acoustic-masseteric reflex (AMR), which is a jaw-acoustic reflex. The p11/n15 response of vestibular origin has a higher threshold, whereas the p16/n21 acoustic response has a lower threshold (de Natale et al., 2019; Deriu et al., 2005). A representative waveform of the masseter VEMP has been given below in Figure 2.3

Figure 2.3



Representative mVEMP waveform showing the p11 and n21 peaks

Latency of mVEMP in Normal Population

Deriu et al. (2003) recorded masseter VEMP using electrical stimulation. Using electrical stimulation, Deriu et al. (2003) reported the mean peak latency of p11 and n15 to be 11.3 ms and 14.8 msec. Deriu et al. (2005) reported that the p11 peak latency ranged from 10.8 to 13.8 ms in their study of 18 healthy volunteers. The mean p11 peak latency for a 100 dB nHL clicks stimulus was shown to be 11.9 ms for unilateral stimulation, whereas, for bilateral stimulation, the mean latency was reported to be 12.1 ms. The mean p11 and p16 peak latency in another study with nine subjects were reported to be 11.9 ms and 16.6 ms, respectively (Deriu et al., 2007). Ginatempo et al. (2013) studied normative mVEMP in 60 healthy adults using click stimulus and reported the mean p11 and n16 latency as 11.2 ms and 15.37 ms.

de Natale et al. (2019) recorded mVEMP in 82 healthy adults using the click stimulus. In this study, the mean p11 peak latency was 11.17 ms, and the mean n21 peak latency was 19.68 ms. Loi et al. (2020) found the mean latency of the p11 peak as 12 ms and the n21 peak latency as 20.4 ms. The reliability was found to be good to excellent for the mVEMP testing. Vignesh et al. (2021) recorded mVEMP in 44 healthy adults using 500 Hz tone burst stimulus and reported the mean peak latency of p11 and n21 to be 13.2 ms and 21.4 ms. Thirusangu & Sinha (2022) explored the different montage effects on mVEMP responses, and the latency of p11 and n21 peaks for the combined data was 13.51 ms and 19.30 ms for zygomatic montage and 13.72 ms and 20.09 ms for mandibular montage.

Romero et al. (2022), in their study to assess the effect of different EMG target levels in mVEMP evaluation, obtained the mean p11 and n21 latency of 14.8 ms and 23.4 ms for a target EMG of 50 µv. Neupane et al. (2023) explored the effects of different stimulus types in mVEMP evaluation. The reported mean p11 latency measures of the right ear were 11.76 ms,14.31 ms and 11.3 ms for clicks, 500 Hz tone burst and 500 Hz Narrow band CE chirp, respectively. The mean latency of the p11 peak for the left ear was 12.57 ms for clicks, 15.11 ms for 500 tone burst and 11.48 ms for 500 narrow band CE chirp. In the same way, the mean n21 latency for the right and left ears was 19.96 ms and 19.73 ms for clicks, 23.47 ms and 24 ms for 500 Hz tone burst and 19.85 ms and 19.56 ms for 500 Hz narrowband chirp.

The amplitude of mVEMP in Normal Population

Deriu et al. (2003) studied mVEMP responses using electrical vestibular stimulation, and reported the mean amplitude of the p11-n15 peak complex to be around 0.83 µv during unilateral cathodal stimulation. Deriu et al. (2005), in their investigation of mVEMP responses using unilateral and bilateral 100 dB nHL click stimulation, found the average amplitude for unilateral stimulation to be 0.42 µv and for bilateral stimulation 0.71 µv. The amplitude of the response was significantly larger for bilateral stimulation in comparison to that of unilateral stimulation. The amplitude response to clicks at 90 dB nHL was approximately 40% smaller compared to the response to clicks at 100 dB nHL. Ginatempo et al. (2013) analyzed normative mVEMP data in 60 healthy adults and observed the amplitude of the Vestibulo-Masseteric Reflex and Acoustic-masseteric reflex to be 0.64 µv and 0.51 µv, respectively.

de Natale et al. (2019) found the amplitude of the p11-n21 peak complex to be 0.72 µv and 1µv for unilateral and bilateral stimulation, respectively. In Loi et al. (2020) study, the mean amplitude of the mVEMP p11-n21 peak complex obtained using zygomatic montage was 0.83 µv for unilateral stimulation and 1.15 µv for bilateral stimulation. Vignesh et al. (2021) conducted mVEMP recordings using tone bursts and stated that the average amplitude of the p11-n21 peak complex was 0.86 µv. Thirusangu & Sinha (2022), in their study of mVEMP responses using different montages, have found the mean p11-n21 peak complex as 0.48 µv for ipsilateral responses. Romero et al. (2022) evaluated mVEMP and obtained a mean p11-n21 peak amplitude of 0.7 µv with a target EMG of 50 µv. Neupane et al. (2023), in their study using different stimuli, found the mean p11-n21 amplitude for the right and left ears as 0.54 µv and 0.49 µv with clicks, 0.74 µv and 0.75 µv with 500 Hz tone burst and 0.75 µv and 0.74 µv with 500 Hz narrow band CE chirp stimulus.

Threshold of mVEMP in Normal Population

Deriu et al. (2005) observed that although the p11 wave threshold intensity varied between patients, it was consistently greater than 80-90 dB. In their study with 18 individuals, the p11 wave threshold was 80 dB in 9 subjects, 90 dB in 7 subjects, and more than 90 dB in 2 subjects for click stimulus. de Natale et al. (2019) demonstrated that at stimulation levels between 98-113 dB, the vestibulo-masseteric reflex (p11 wave) was not present; only the acoustic-masseteric reflex (p16/n21 wave) was discernible. The p11 wave of the VMR, on the other hand, was noticeable in all participants at intensities ranging from 128-138 dB. Due to the overlap of these reflexes, the n15 component either could not be identified or appeared as a minor deflection within the p11/n21 mixed potential involving both vestibular and cochlear aspects. Differentiating between these two reflexes was not feasible within the intensity range of 113-123 dB.

Acquisition parameters of mVEMP:

Filters setting

Various filter settings have been employed to record mVEMP responses. Some authors have used a 0.3–2000 Hz filter setting to record mVEMP (Deriu et al., 2003, 2005, 2007; Vignesh et al., 2021). Several authors have recorded the mVEMP responses using filter settings of 5–5000 Hz (de Natale et al., 2015a, 2015b, 2018, 2019; Loi et al., 2020; Magnano et al., 2014, 2016; Puligheddu et al., 2019). Romero et al. (2022) used 5-1500 Hz filter settings to record the masseter VEMP. Thirusangu & Sinha (2022) obtained the mVEMP responses using 0.1-3000 Hz filter settings. 0.3-1500 Hz as the high and low pass filter setting was used by (Neupane et al., 2023).

Time window:

Early studies used a time window of 100 ms after stimulus delivery with a 50 ms prestimulus window (Deriu et al., 2003, 2005, 2007; Vignesh et al., 2021). Several studies used a time window with 50 ms prestimulus and 150 ms post-stimulus, totalling 200 msec (de Natale et al., 2015a, 2015b, 2018, 2019; Loi et al., 2020; Magnano et al., 2014, 2016; Puligheddu et al., 2019). Romero et al. (2022) used a 100 msec epoch with a 20 ms prestimulus interval and 80 ms post-stimulus interval. A time window having 70 ms post-stimulus and 20 ms prestimulus acquisition was used by (Thirusangu & Sinha, 2022). Neupane et al. (2023), used an analysis time window of 80 ms, which included a prestimulus duration of 20 ms.

Amplification

Most studies have amplified the obtained mVEMP response by a factor of 5000 (de Natale et al., 2015a, 2015b, 2019; Deriu et al., 2003, 2005, 2007; Loi et al., 2020; Magnano et al., 2014, 2016; Neupane et al., 2023; Puligheddu et al., 2019; Thirusangu & Sinha, 2022; Vignesh et al., 2021). A different amplification factor of 3000 was used by de Natale et al. (2018) in their mVEMP acquisition in individuals with idiopathic REM sleep behaviour disorder. Romero et al. (2022) obtained the mVEMP responses using a 2000 amplification factor.

Electrode montage

Throughout the mVEMP experiments, primarily, two different electrode montages have been used. In the mandibular montage, the ground electrode is placed on the forehead, the active electrode is placed on the masseter muscle belly, and the reference electrode is positioned along the lower border of the mandible. In the zygomatic montage, the ground electrode is positioned on the forehead, the reference electrode is placed in the middle of the zygomatic arch, and the active electrode is placed in the lower third of the masseter muscle.

Some studies utilized mandibular montage with reference electrodes over the mandibular angle (de Natale et al., 2015a, 2015b, 2018; Deriu et al., 2003, 2005, 2007;

Magnano et al., 2014, 2016; Puligheddu et al., 2019). Both mandibular and zygomatic montages were compared and used in the mVEMP analysis by various authors. These studies have found no significant difference in the response characteristics but a better response elicitation rate with zygomatic montage (de Natale et al., 2019; Ginatempo et al., 2013; Loi et al., 2020; Thirusangu & Sinha, 2022). In recent studies, zygomatic montage has been used in acquiring mVEMP responses (Neupane et al., 2023; Romero et al., 2022; Vignesh et al., 2021).

Muscle contraction

The amount of target EMG muscle contraction utilized to elicit reliable mVEMP responses ranges from 30-50% (de Natale et al., 2015a, 2015b; Deriu et al., 2007; Loi et al., 2020; Magnano et al., 2014, 2016; Neupane et al., 2023; Puligheddu et al., 2019; Thirusangu & Sinha, 2022; Vignesh et al., 2021). In a preliminary investigation by Deriu et al. (2003), the individuals were instructed to achieve an electromyography (EMG) target of 30% of their maximum voluntary contraction. In their study, Deriu et al. (2005) instructed the participants to maintain a steady target level of 50% of their maximal voluntary contraction during the data collection. Romero et al. (2022) examined the influence of different target EMG levels by employing five specific levels of muscle contraction as targets (namely, no contraction [rest], 30, 50, 100, and 150 µV). They found no significant difference in the latency parameters with an increase in EMG levels, but the peak-to-peak amplitude increased with an increase in the EMG activation.

Table 2.1

Summary of Acquisition Parameters of Different mVEMP Studies

S.No	Authors	Filters (Hz)	Time window (ms)	Amplification	Electrode montage	Muscle contraction
1	Deriu et al. (2003)	0.3–2000	Prestimulus - 50 Post-stimulus-100	×5000	Mandibular	30%
2	Deriu et al. (2005)	0.3–2000	Prestimulus - 50 Post-stimulus-100	×5000	Mandibular	50%
3	Deriu et al. (2007)	0.3–2000	Prestimulus - 50 Post-stimulus-100	×5000	Mandibular	30-50%
4	Ginatempo et al. (2013)				Mandibular and Zygomatic	30-50%
5	Magnano et al. (2014,2016)	5–5000	Pre-stimulus - 50 Post-stimulus-150	×5000	Mandibular	30-50%
6	de Natale et al. (2015a,2015b)	5–5000	Pre-stimulus - 50 Post-stimulus-150	×5000	Mandibular	30-50%
7	de Natale et al. (2018)	5–5000	Pre-stimulus - 50 Post-stimulus-150	×3000	Mandibular	30-50%
8	de Natale et al. (2019)	5–5000	Prestimulus - 50 Post-stimulus-150	×5000	Mandibular and Zygomatic	30-50%
9	Puligheddu et al. (2019)	5–5000	Prestimulus - 50 Post-stimulus-150	×5000	Mandibular	30-50%

10	Loi et al. (2021)	5–5000	Pre-stimulus - 50 Post-stimulus-150	×5000	Mandibular and Zygomatic	30-50%
11	Vignesh et al. (2021)	0.3–2000 Hz	Prestimulus - 50 Post-stimulus-100	×5000	Zygomatic	30-50%
12	Thirusangu and Sinha, (2022)	0.1-3000	Prestimulus - 20 Post-stimulus -70	×5000	Mandibular and Zygomatic	30-50%
13	Romero et al. (2022)	5-1500	Pre-stimulus - 20 Post-stimulus - 80	×2000	Zygomatic	0,30,50,100 and 150 µV
14	Neupane et al. (2023)	0.3-1500	Prestimulus - 20 Post-stimulus - 80	×5000	Zygomatic	30-50%

Stimulus parameter of mVEMP

Stimulus type

In the early study of mVEMP by Deriu et al. (2003), they used Electrical vestibular stimulation to record mVEMP responses by presenting electrical stimuli of 2 ms duration. Clicks stimulus of 0.1 ms has been used predominantly in studies (de Natale et al., 2015a, 2015b, 2018, 2019; Deriu et al., 2005, 2007; Loi et al., 2020; Magnano et al., 2014, 2016; Puligheddu et al., 2019). Later, Vignesh et al. (2021) evaluated the effect of tone burst 500 Hz (2-0-2 cycle) stimulus in mVEMP responses and reported the tone burst evoked responses to be more prominent in amplitude and delayed in latency in comparison to that of the clicks evoked mVEMP. Romero et al. (2022) also utilized a 500 Hz tone burst stimulus of 4 ms duration in their study.

Thirusangu & Sinha (2022), in their study examining the montage effect, used Toneburst 500 Hz (2-1-2 cycle) as the stimulus and reported this tone burst stimulus as an efficient stimulus in recording mVEMP responses. Neupane et al. (2023) conducted a comparison of mVEMP responses generated using various stimuli, including a 100 µs click, a 500-Hz tone burst with rise, plateau, and fall times of 2–0–2, and a 500-Hz narrowband CE chirp (360–720 Hz) lasting 4.5 milliseconds. They found that the 500 Hz NB CE chirp and click-evoked mVEMP exhibited shorter latency responses than those mVEMP evoked by the 500 Hz tone burst. Additionally, the click-evoked response demonstrated the smallest peak-to-peak amplitude, while the amplitude of responses evoked by the tone burst and chirp stimuli was larger.

Intensity

Deriu et al. (2003) recorded mVEMP using electrical stimulation with a 5mA intensity. In the investigations of recording mVEMP, stimulation intensities ranged from 70 to 100 dB NHL (Deriu et al., 2005, 2007). Ginatempo et al. (2013) used different intensities from 143– 108 dB-SPL in acquiring mVEMP responses. Click stimuli with varying intensities of 143 dB SPL and 108 dB SPL were used to record the VMR and AMR responses (Magnano et al., 2014, 2016). de Natale et al. (2015a, 2015b) presented the stimulus at an intensity of 140 dB SPL. Some authors have recorded mVEMP responses at 138 dB SPL (de Natale et al., 2018; Puligheddu et al., 2019).

The impact of stimulation intensity was assessed in a group of 10 subjects by administering stimuli ranging from 98 dB SPL to 138 dB SPL. (de Natale et al., 2019). Tone burst stimulus with an intensity of 125 dB pe SPL has been used in studies (Romero et al., 2022; Thirusangu & Sinha, 2022; Vignesh et al., 2021). Neupane et al. (2023), while examining mVEMP responses with different stimuli, presented stimulus with the intensity of 95 dB NHL, which corresponds to the peak sound pressure levels (peSPLs) of 120 dB peSPL for the 500-Hz NB CE-Chirp, 130 dB peSPL for the click, and 119 dB peSPL for the 500-Hz tone burst.

Stimulus Rate

The stimulus for mVEMP recording was presented with a 3 Hz repetition rate (Deriu et al., 2003, 2005, 2007). A 5 Hz repetition rate was used in their study by many authors (de Natale et al., 2015a, 2015b, 2018, 2019; Ginatempo et al., 2013; Loi et al., 2020; Magnano et al., 2014, 2016; Puligheddu et al., 2019). A 5.1 Hz repetition rate was used for stimulus presentation in studies by (Neupane et al., 2023; Thirusangu & Sinha, 2022; Vignesh et al., 2021). Romero et al. (2022) recorded the mVEMP responses using 5.4 Hz stimulus repetition rate.

Number of sweeps

The number of sweeps utilized in mVEMP recording ranged from 300 –500 (de Natale et al., 2015a, 2015b, 2018, 2019; Deriu et al., 2005, 2007; Loi et al., 2020; Magnano et al., 2014, 2016). Puligheddu et al. (2019) used 250-400 sweeps to obtain a reliable mVEMP response. Some authors have used 300 sweeps for mVEMP recording (Thirusangu & Sinha, 2022; Vignesh et al., 2021). Romero et al. (2022) used a minimum of 128 sweeps to obtain replicable responses. Neupane et al. (2023) maintained 200 sweeps per recording for the three stimuli they used in their mVEMP study.

Table 2.2

Summary of Stimulus parameters of different mVEMP studies

S.no	Authors	Stimulus type	Intensity	Stimulus rate	Number of sweeps
1	Deriu et al. (2003)	Electrical stimulus	5mA	3 Hz	

2	Deriu et al. (2005)	Click	70 to 100 dB NHL	3 Hz	300 –500
3	Deriu et al. (2007)	Click	70 to 100 dB NHL	3 Hz	300 –500
4	Ginatempo et al. (2013)	Click	143 to 108 dB-SPL	5 Hz	
5	Magnano et al. (2014,2016)	Click	143 dB SPL and 108 dB SPL	5 Hz	300 –500
6	de Natale et al. (2015a, 2015b)	Click	140 dB SPL	5 Hz	300 –500
7	de Natale et al. (2018)	Click	138 dB SPL	5 Hz	300 –500
8	de Natale et al. (2019)	Click	138 dB SPL and 108 dB SPL	5 Hz	300 –500
9	Puligheddu et al. (2019)	Click	138 dB SPL	5 Hz	250-400
10	Loi et al. (2021)	Click	138 dB SPL and 108 dB SPL	5 Hz	300 –500
11	Vignesh et al. (2021)	500 Hz Tone burst (2-0-2 cycle)	125 dB pe SPL	5.1 Hz	300
12	Thirusangu and Sinha, (2022)	500 Hz tone burst (2-1-2 cycle)	125 dB pe SPL	5.1 Hz	300

13	Romero et al. (2022)	500 Hz tone burst (2-0-2 cycle)	125 dB pe SPL	5.4 Hz	128
14	Neupane et al. (2023)	Click, 500 Hz tone burst and 500 Hz NB CE chirp	95 dB NHL	5.1 Hz	200

Clinical Applications of mVEMP:

Parkinson's disease:

In recent years mVEMP has been a reliable tool in identifying various pathologies. de Natale et al., (2015a) studied brainstem abnormalities in individuals with early and later stages of Parkinson's disease (PD) using vestibular evoked myogenic potentials. A total of 14 patients with early Parkinson's disease (PD) (with a mean disease duration of 1.42 ± 0.7 years), 19 patients with advanced PD (with a mean disease duration of 7.26 ± 2.9 years), and 27 age-matched control individuals participated in the study. They underwent cervical, masseter, and ocular vestibular evoked myogenic potentials (VEMPs) assessments. Abnormalities in cervical VEMP (cVEMP) were observed in 3.7% of controls, 35.7% of early PD cases, and 47.4% of late PD cases. For masseter VEMP (mVEMP), abnormalities were present in 7.4% of controls, 42.8% of early PD cases, and 63.2% of late PD cases.

In terms of ocular VEMP (oVEMP), abnormalities were found in 3.7% of controls, 50% of early PD patients, and 47.4% of late PD patients. The rate of VEMP changes was comparable across PD groups but significantly greater in PD than in controls. However, there was a difference between early and advanced Parkinson's disease in the abnormality pattern. In the late Parkinson's disease (PD) group, the most prevalent alteration was the lack of response, succeeded by reduced amplitude and delayed latency. Similarly, in the early PD group, absent responses were frequently observed, followed by latency delay and decreased amplitude. The researchers proposed that impairment across the VEMP battery could signify an issue spanning the entire brainstem. This suggests that degeneration in such structures might influence nearby regions linked to vestibular nuclei through direct pathways and/or indirect interneuronal circuits.

In a different study by de Natale et al. (2015b), the rate of abnormality for cVEMP and oVEMP was found to be 41.7% and 45.8%, respectively. In contrast, the abnormality for mVEMP was found to be 66.7% in a group of patients with Parkinson's disease. The amplitude of the mVEMP was significantly smaller in the Parkinson's group when compared to the control group. In contrast, the latency parameters did not show any significant variations in any of the three VEMPs.

Multiple sclerosis

Magnano et al. (2014) examined the vestibulo-masseteric (VMR), acoustic-masseteric (AMR), vestibulo-collic (VCR), and trigemino-collic (TCR) reflexes in 60 Multiple sclerosis patients and discovered that the reflexes were abnormal in 62.1%, 55.1%, 25.9%, and 58.6% of cases, respectively. The p11 peak latency of vestibulo-masseteric (VMR) and the p16 peak latency of the acoustic-masseteric (AMR) reflexes were significantly delayed in the multiple sclerosis group. The mean p11 peak latency was 11.4 ms and 12.6 ms in the normal and the multiple sclerosis group, respectively. The mean p16 peak latency was 15.7 ms in the normal group and 16.6 ms in the multiple sclerosis group. The amplitude measures did not show any significant differences in the vestibulo-masseteric (VMR) or acoustic-masseteric (AMR) reflexes. In 86.9% of instances, the four-BSR (Brainstem Reflex) battery was identified as a highly sensitive marker for detecting brainstem abnormalities. This four-BSR battery notably enhances the effectiveness of traditional Evoked Potentials (EPs) in promptly detecting brainstem impairment that might remain unnoticed through clinical evaluation and neuroimaging techniques.

Magnano et al. (2016), in their follow-up study with 45 multiple sclerosis patients after 15 months of baseline evaluation, showed an increase in the proportion of altered brainstem reflexes. The vestibulo-masseteric reflex (VMR) showed a significant increase in the abnormality pattern after 15 months of baseline evaluation. During baseline evaluation, the abnormality percentage of VMR was 57.8%, which increased to 71.1% after 15 months duration. The other brainstem reflexes, acoustic-masseteric (AMR), vestibulo-collic (VCR), and trigemino-collic (TCR) reflexes, also showed an increase in the abnormality pattern even though there was no significant difference. The authors found that the combined Evoked potentials and Brainstem reflexes battery are more sensitive in identifying the brainstem abnormalities in multiple sclerosis patients than the clinical/MRI assessment during both baseline and follow-up assessments.

Sangu Srinivasan et al. (2022) evaluated the mVEMP, oVEMP and cVEMP in 45 multiple sclerosis patients and reported 82.22% response abnormality in mVEMP. mVEMP had a higher percentage of abnormality than the cVEMP and oVEMP. The major abnormality noted in mVEMP was the absence of responses in 45.6%, followed by delayed latency in 13.35% and reduced corrected amplitude in 6.7% of multiple sclerosis individuals. The mean p11 latency of the right and left ears was 14.61 ms and 14.32 ms, whereas the mean n21 latency of the right and left ears was 22.58 ms and 22.09 ms. The corrected p11-n21 amplitude was 0.71 µv in the right ear and 0.83 µv in the left ear. The latency measures in the multiple sclerosis group differed significantly from the control group, and the amplitude did not show a significant difference between multiple sclerosis and the control group of healthy participants.

Rapid Eye movement disorder

In an investigation of idiopathic REM (Rapid eye movement) sleep Behavior Disorder (iRBD) patients, the VEMP test battery, including cervical, ocular and masseter VEMPs, showed 75% abnormality. cVEMP and oVEMP were abnormal in 45% and 50% of the patients with REM sleep disorder, and mVEMP was abnormal in 65% of the patients with REM sleep disorder. The amplitude of the responses was significantly delayed in the experimental group compared to the control group in all three VEMPs. The p11 peak latency in mVEMP and n10 peak latency in oVEMP showed a significant delay in the experimental group. The authors proposed that VEMPs could be well-suited for investigating brainstem conditions in neurological disorders, including the initial phases of diseases when apparent symptoms or structural abnormalities have not yet manifested (de Natale et al., 2018).

Puligheddu et al. (2019), in their study with isolated REM sleep behaviour disorder patients, evaluated cVEMP, oVEMP and mVEMP. Each examined VEMPs showed a greater alteration rate among iRBD patients than controls. iRBD patients showed decreased amplitudes in cVEMP and oVEMP compared to controls when each VEMP's morphology was examined. Patients with iRBD had substantially prolonged mVEMP peak latency of the p11 peak. The authors said that using VEMPs to detect changes in brainstem physiology appears to be helpful for locating putative neurological substrates of RBD. These findings demonstrate that VEMPs can detect even subtle changes in the physiology of the brainstem and can be helpful in the early diagnosis of neuronal malfunction.

To summarise the review, the masseter VEMP has been recorded by several researchers using different parameters. There are limited studies that also reported clinical usefulness of the masseter VEMP.

Chapter III

Methods

The present study aimed to characterize the masseter VEMP latency and amplitude for chirp stimuli at different frequencies. To meet the aim of the study, 30 young, healthy participants (15 males and 15 females) in the age range of 18-30 years were included for the study. The masseter VEMP was recorded ipsilaterally from both the ears of the participants.

Participant selection criteria

All the participants of this study had normal hearing sensitivity for both the air conduction and bone conduction audiometry. Tympanometry and Reflexometry results ruled out the presence of any middle ear disorders. Additionally, the participants did not report any vestibular signs and symptoms. They also did not report any other otological problems. They did not have any oromandibular dysfunction.

Instrumentation

- A calibrated audiometer, the Inventis Piano, equipped with TDH-39 headphones and enclosed in MX-41/AR ear cushions from Telephonics (Farmingdale, NY, USA), was used to measure the pure tone thresholds of all participants. The threshold for bone conduction was determined using a Radio ear B71 bone transducer headset from KIMMETRICS (Smithsburg, Maryland, USA).
- The Gradson-Stadler Incorporated (GSI) Tympstar middle ear analyzer (GSI VIASYS Healthcare, WI, USA) was employed to assess various parameters for each participant, including auditory reflex threshold, equivalent ear canal volume, peak static admittance, and tympanometric peak pressure.

- Intelligent Hearing systems (IHS) with ER-3A insert ear transducers were utilized for recording the auditory brainstem responses to rule out retro cochlear pathology.
- mVEMP was tested using Neurosoft dual channel AEP equipment with ER-3A insert ear transducer.

Test environment

All the audiological tests were conducted in acoustically treated rooms, and noise levels were maintained within the permissible levels.

Procedure

Pure tone Audiometry

A modified version of the Hughson and Westlake procedure (Carhart & Jerger, 1959) was utilized to conduct pure tone audiometry. This was carried out at octave frequencies from 250 Hz to 8000 Hz for air conduction and from 250 Hz to 4000 Hz for bone conduction for all participants.

Immittance

Tympanograms were obtained using a 226 Hz probe tone in both ears, and acoustic reflex thresholds were determined for both ipsilateral and contralateral recording using stimuli at 500, 1000, 2000, and 4000 Hz frequencies.

Auditory Brainstem Response

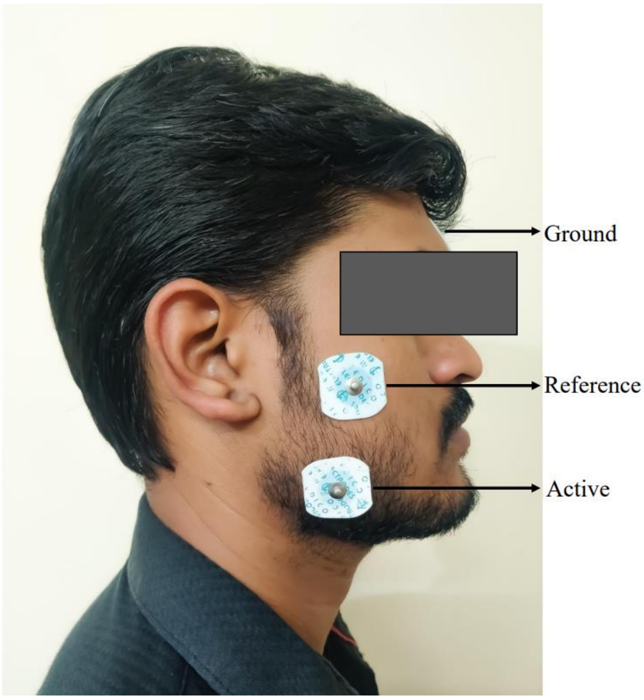
For ABR-siteof lesion testing, 90 dB nHL clicks were used. Electrodes were situated at Fz, M1, and M2 positions, with an electrode impedance of 5KΩ or less being accepted. ER-3A insert earphones were used to deliver the stimulus, with repetition rates of 11.1/s and 90.1/s. A bandpass filter ranging from 100 to 3000 Hz was applied to filter the responses. A total of 1500 sweeps of click stimulus were used to record ABR, and each recording was repeated to ensure the reproducibility of the responses.

<u>Masseter VEMP recording procedure</u>

All participants were positioned in an upright seated posture. The electrode sites were cleaned using NuPrep skin preparation abrasive gel. The silver chloride disc-type electrodes were used with the appropriate conduction gel. The electrodes were positioned according to the zygomatic montage approach. In this configuration, the active electrode (+) was situated on the lower third of the masseter muscle, the reference electrode (-) was placed at the midpoint of the zygomatic arch, and the ground electrode was positioned on the forehead. Surgical tapes were used to keep the electrodes in place without any movement during the testing. The absolute and inter-electrode impedance were maintained below 5KΩ and 2KΩ, respectively.

Figure 3.1

Zygomatic electrode montage of mVEMP



The participants were instructed to sit straight and to clench their teeth to activate the masseter muscle constantly during the recording. Real-time muscle monitoring feedback was provided during the recording, with 30 to 50% of the maximum contraction as the desired level. All the frequencies were recorded sequentially, and participants were provided two minutes of rest after each recording. Each recording was repeated twice to ensure the replication of responses.

The following parameters were used to do the mVEMP testing.

Table 3.1

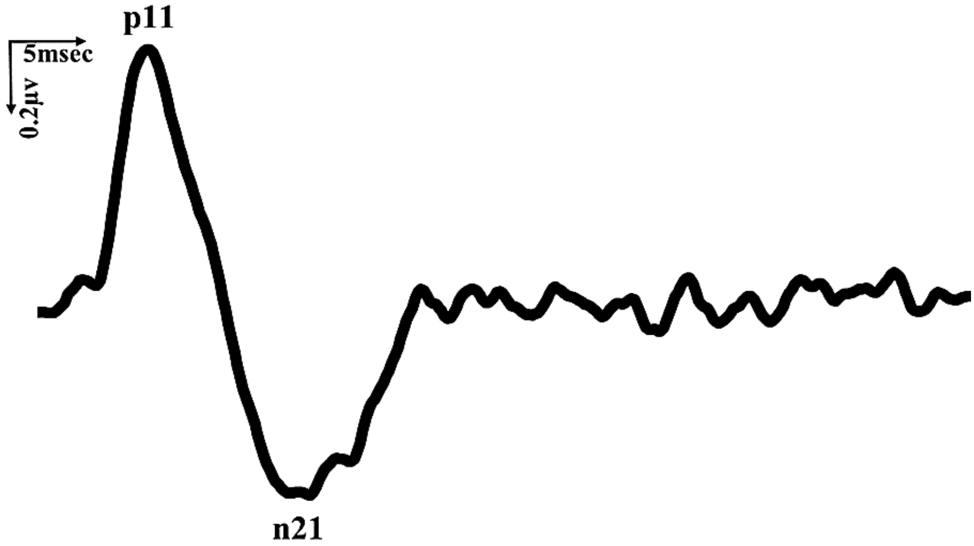
mVEMP recording parameters

Transducer	ER-3A insert ear transducer
Stimulus	Narrowband CE chirp stimuli centred at 500,1000,2000 and 4000 Hz
Intensity	125 dBpeSPL
Polarity	Alternating
Rate	5.1/s
Filter	10-2000Hz
Number of sweeps	200
Time window	60ms
Amplification	5000 X
Electrode montage	Zygomatic montage Active - Lower third of the masseter muscle Reference -Midpoint of the zygomatic arch Ground - Forehead
Presentation mode	Monaural
Recording mode	Ipsilateral

Data analysis:

Figure 3.2

Representative mVEMP waveform showing both p11 and n21 peaks



In all the recorded mVEMP responses using 500Hz, 1000Hz, 2000Hz and 4000Hz narrowband chirp stimulus, p11 and n21 peaks were marked. The absolute latency of the p11 peak and n21 peak and the peak-to-peak amplitude of the p11-n21 complex were measured. SPSS version 26 software was used for statistical analysis. The following statistical analyses were done.

1. Descriptive statistics was done to calculate the mean and standard deviation for the latency of the p11 peak and n21 peak at all frequencies.
2. Descriptive statistics was done to get the mean and standard deviation for the peak-to-peak amplitude of the p11-n21 complex for all the frequency responses.
3. Wilcoxon signed rank test was carried out to check the ear differences for all the frequencies.
4. Descriptive statistics were done again for the combined data of both the right and left ears for all the frequencies.

5. Friedman test was done to find out the significant main effect of different stimulus frequencies on p11 and n21 latency.
6. Wilcoxon signed rank test was done for pairwise comparison.
7. Friedman test was done to find out the significant main effect of different stimulus frequencies on the amplitude of the p11-n21 complex.
8. Wilcoxon signed rank test was done for the pairwise comparison.

Chapter – IV

Results

The current study aimed to characterize the Chirp evoked masseter VEMP at different stimulus frequencies in healthy young adults. In particular, the objectives of the study were to identify the latency of the p11 and n21 peaks and the amplitude of the p11-n21 peak complex for the narrowband chirp-evoked mVEMP responses at different frequencies.

The response rate of chirp evoked mVEMP at different frequencies:

A total of 30 young, healthy adults participated in the study. The response rate of the mVEMP for the 500Hz and 1000Hz chirp stimuli was 100% (30/30 ears) for both the right and left ears. The response rates for the right and left ears for the 2000Hz chirp stimulus were 93.33% (28/30 ears) and 96.66% (29/30 ears), and the response rates for the right and left ears for the 4000Hz chirp stimulus were 76.66% (23/30 ears) and 83.33% (25/23 ears), respectively.

The individual and grand averaged masseter VEMP waveforms for the right and left ear for all the frequencies are shown in Figure 4.1 and Figure 4.2, respectively.

Figure-4.1

Individual and grand averaged masseter VEMP waveforms at different chirp stimulus frequencies for the right ear

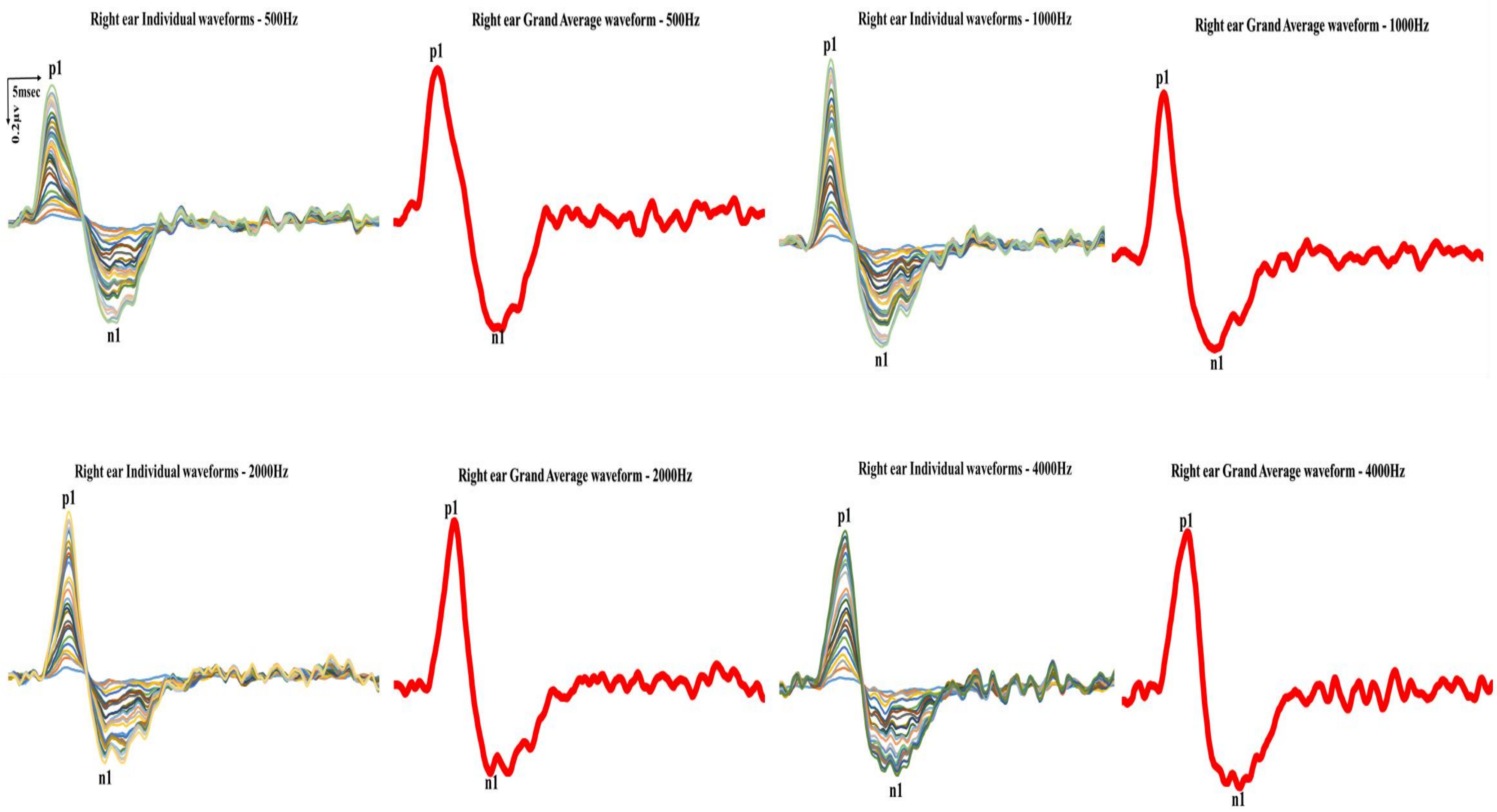
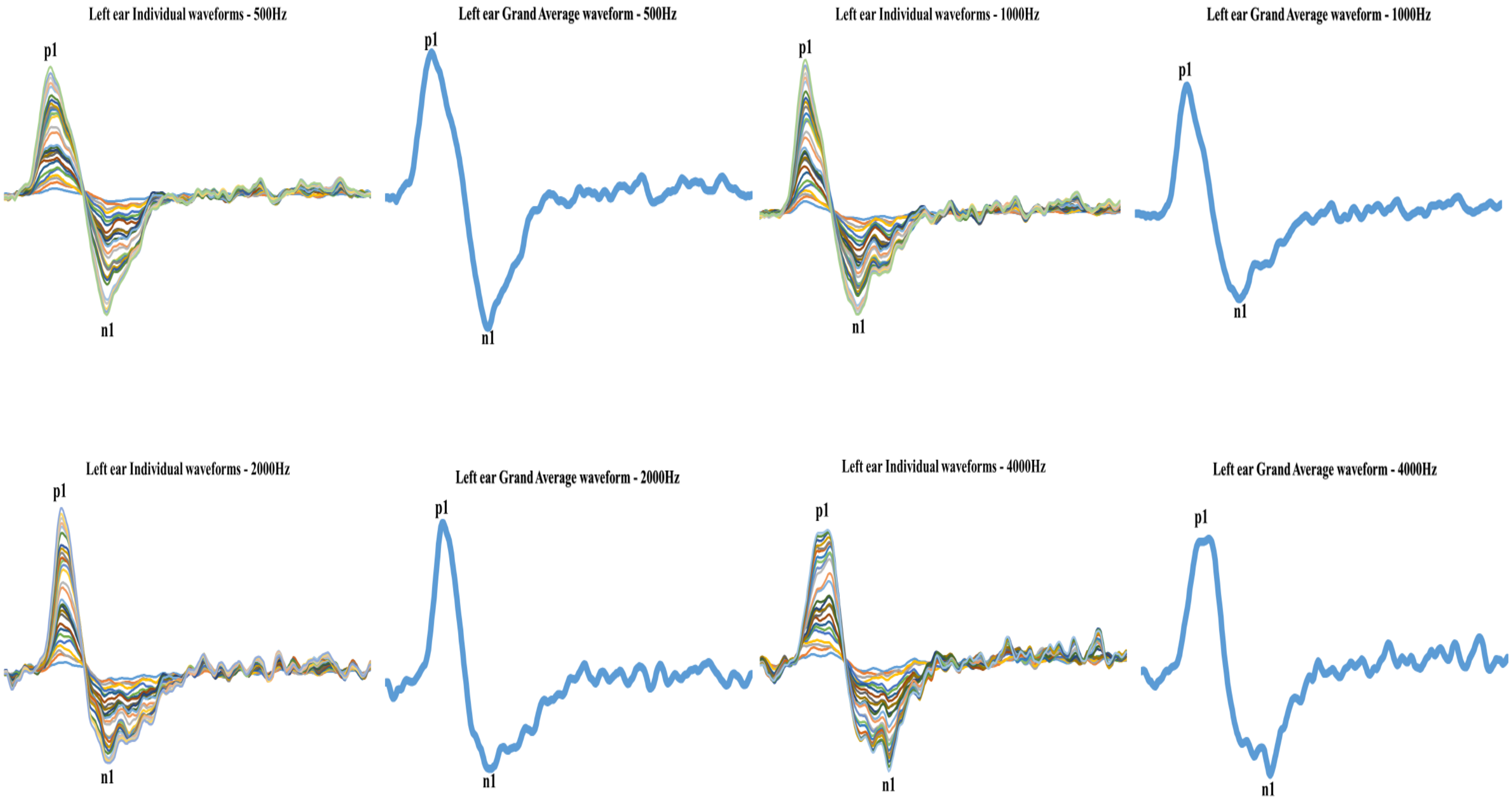


Figure-4.2

Individual and grand averaged masseter VEMP waveforms at different chirp stimulus frequencies for left ear



Latency of mVEMP:

The latencies of the p11 and n21 peaks were measured at all the narrowband chirp stimulus frequencies. The mean and the standard deviations for p11 and n21 latencies are given in Table 4.1

Table 4.1

Mean and standard deviation of the latencies of p11 and n21 peaks for all four frequencies of both ears

Stimulus Frequencies		p11 peak				n21 peak			
		Min	Max	Mean(ms)	SD	Min	Max	Mean(ms)	SD
500Hz	Right	5.70	10.70	7.66	1.154	14.80	23.90	18.22	1.97
	Left	5.70	10.70	8.05	1.35	15.10	22.80	18.51	1.75
1000Hz	Right	6.70	11.50	8.77	0.97	15.70	23.50	18.58	1.89
	Left	7.30	11.20	9.01	1.09	15.60	23.30	18.88	1.70
2000Hz	Right	7.70	11.50	10.06	0.95	16.40	23.20	19.37	1.76
	Left	8.70	12.30	10.13	0.85	16.30	23.40	19.32	1.77
4000Hz	Right	8.90	12.30	10.81	0.77	18.00	22.20	19.92	1.08
	Left	7.50	12.60	10.47	1.41	16.80	23.50	19.92	1.90

It can be seen from Table 4.1 that the latency of the p11 and n21 peaks are shorter for 500 Hz compared to other frequencies. There is a systematic increase in latency of p11 and n21 peak as the frequency of the stimulus increases from 500 Hz to 4000 Hz.

The ear differences were calculated using Wilcoxson Signed Rank test at all the chirp frequencies. The results of the Wilcoxon signed rank test for all four frequencies are given below in Table 4.2

Table 4.2

Wilcoxon signed rank test for all the frequencies

Stimulus Frequencies	p11 peak		n21 peak	
	Z	p	Z	p
500Hz	1.34	0.18*	1.28	0.19*
1000Hz	0.82	0.41*	1.31	0.18*
2000Hz	0.21	0.82*	0.36	0.71*
4000Hz	1.30	0.19*	0.41	0.67*

*Not significant

It can be seen from Table 4.2 that there is no significant difference in the p11 and n21 peak latencies of the right and left ears for the chirp stimulus at all frequencies. Hence, the right and left ears data were combined for all the frequencies, and the descriptive statistics were carried out again to obtain the mean and standard deviation of the combined data. The mean and standard deviation of the p11 and n21 latencies for the combined data are given in Table 4.3 below.

Table 4.3

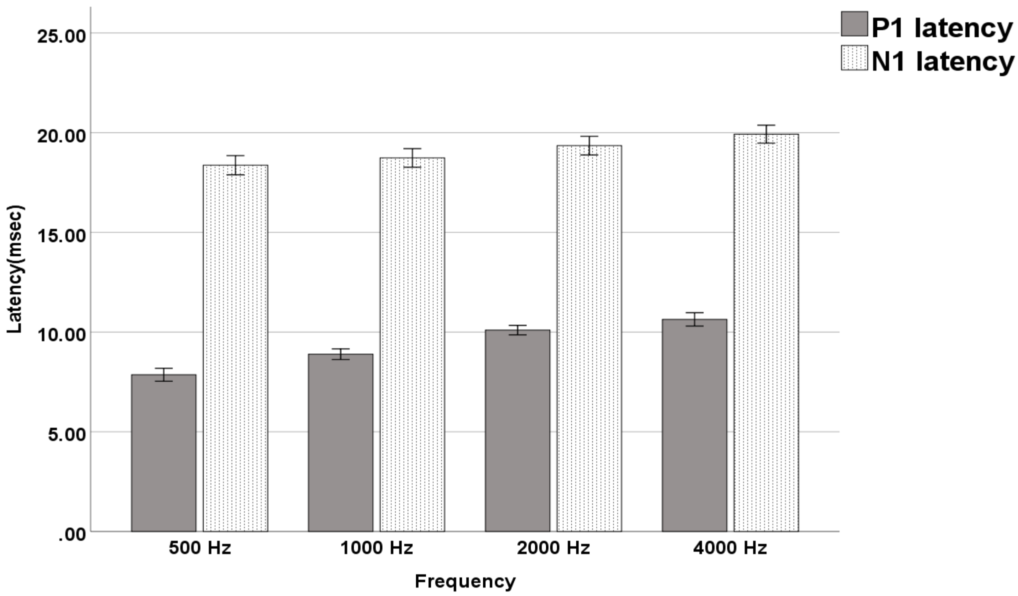
Mean and standard deviation of latency of p11 and n21 for all the frequencies combined ears

Stimulus Frequencies	N (no. of ears)	p11 peak Min	p11 peak Max	p11 peak Mean (ms)	p11 peak SD	n21 peak Min	n21 peak Max	n21 peak Mean (ms)	n21 peak SD
500Hz	60	5.70	10.70	7.85	1.26	14.80	23.90	18.36	1.85
1000Hz	60	6.70	11.50	8.89	1.03	15.60	23.50	18.73	1.79
2000Hz	57	7.70	12.30	10.09	0.89	16.30	23.40	19.34	1.75
4000Hz	48	7.50	12.60	10.63	1.15	16.80	23.50	19.92	1.55

It can be seen from Table 4.3 that the latency of the p11 and n21 peaks are shorter for 500 Hz, followed by 1000 Hz, 2000 Hz and 4000 Hz chirp stimulus. The same can be seen in the following Figure 4.3 below.

Figure 4.3

Mean latency of p11 and n21 peaks of mVEMP for 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz Narrowband chirp stimuli for the combined data



There were different amounts of data samples at different chirp frequencies, so a non-parametric test was carried out. Friedman test revealed a significant main effect in the mean latency of the p11 ($p<0.05$) and n21 ($p<0.05$) peaks of the mVEMP across the frequency responses of 500Hz, 1000Hz, 2000Hz, and 4000Hz. Wilcoxon signed rank test was done to understand the differences between different frequencies. The results of the Wilcoxon signed rank test of the p11 peak latencies are given in Table 4.4.

Table 4.4

Wilcoxon signed rank test for p11 peak latency

Frequency	500Hz	1000Hz	2000Hz	4000Hz
500Hz		P<0.05	P<0.05	P<0.05
1000Hz			P<0.05	P<0.05
2000Hz				P<0.05

Wilcoxson signed rank test revealed a significant difference for p11 peak latency between 500 Hz and 1000 Hz ($Z=5.659$, $P<0.05$), 500 Hz and 2000 Hz ($Z=6.429$, $P<0.05$), 500 Hz and 4000 Hz ($Z=5.863$, $P<0.05$). The p11 latency of 1000 Hz was also significantly different from 2000 Hz ($Z=5.964$, $P<0.05$) and 4000 Hz ($Z=5.639$, $P<0.05$). Similarly, the p11 latency of 2000 Hz significantly differed from 4000 Hz ($Z=3.250$, $P<0.05$).

The results of the Wilcoxon signed rank test of the n21 peak latencies are given in Table 4.5.

Table 4.5

Wilcoxon signed rank test for n21 peak latency

Frequency	500Hz	1000Hz	2000Hz	4000Hz
500Hz		P<0.05	P<0.05	P<0.05
1000Hz			P<0.05	P<0.05
2000Hz				P<0.05

Wilcoxson signed rank test revealed a significant difference in n21 peak latency between 500 Hz and 1000 Hz ($Z=2.413$, $P<0.05$), 500 Hz and 2000 Hz ($Z=3.474$, $P<0.05$) and 500 Hz and 4000 Hz ($Z=4.186$, $P<0.05$). The n21 latency of 1000 Hz was significantly different from 2000 Hz ($Z=2.261$, $P<0.05$) and 4000 Hz ($Z=3.334$, $P<0.05$). Similarly, the n21 latency of 2000 Hz significantly differed from 4000 Hz ($Z=2.132$, $P<0.05$).

Amplitude of mVEMP:

The amplitude measure of the p11-n21 peak complex was calculated for all the frequency responses. Table 4.6 below provides the findings of the descriptive statistics for all the measured frequencies.

Table 4.6

Mean and standard deviation of the amplitude of p11- n21 peak complex for all four frequencies of both ears

Stimulus		Amplitude of p11-n21 peak complex			
Frequencies		Min	Max	Mean(μv)	SD
500Hz	Right	0.60	1.70	1.01	0.30
	Left	0.40	2.00	1.01	0.43
1000Hz	Right	0.50	1.40	0.93	0.26
	Left	0.40	1.70	0.98	0.38
2000Hz	Right	0.30	1.50	0.82	0.29
	Left	0.40	1.80	0.87	0.31
4000Hz	Right	0.30	1.10	0.71	0.24
	Left	0.40	1.40	0.72	0.22

It can be seen from Table 4.6 that the amplitude of the p11-n21 peak complex is larger for 500 Hz compared to other frequencies. There is a systematic decrease in the amplitude of the p11-n21 peak complex as the frequency of the stimulus increases from 500 Hz to 4000 Hz.

The ear differences were calculated at all the chirp frequencies. The results of the Wilcoxon signed rank test of all four frequencies are given below in Table 4.7.

Table 4.7

Wilcoxon signed rank test for all the frequencies

Stimulus Frequencies	Amplitude of p11-n21 peak complex	
	Z	p
500Hz	0.07	0.95*
1000Hz	0.96	0.34*
2000Hz	0.79	0.43*
4000Hz	0.47	0.64*

*Not significant

It can be seen from Table 4.7 that there is no significant difference in the amplitude of the p11-n21 peak complex of the right and left ears for all the frequencies. Hence, the data of the right and left ears were combined for all the frequencies, and the descriptive statistics were carried out again to obtain the mean and standard deviation of the combined data. The mean and standard deviation of the p11- n21 peak complex for the combined data are given in Table 4.8.

Table 4.8

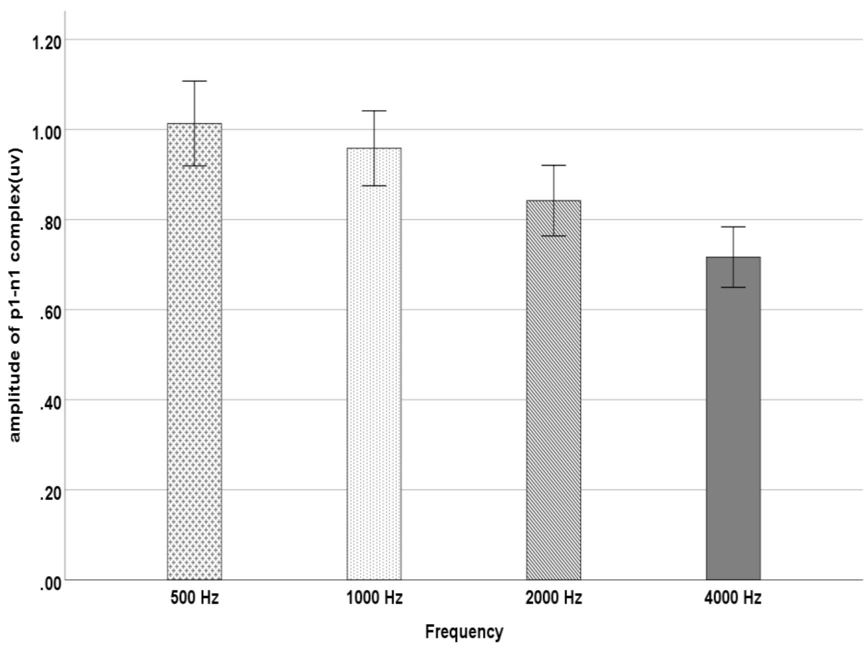
Mean and standard deviation of the amplitude of p11- n21 peak complex for all four frequencies of combined ears

Stimulus Frequencies	Amplitude of p11-n21 peak complex				
	N (no. of ears)	Min	Max	Mean(μv)	SD
500Hz	60	0.40	2.00	1.01	0.36
1000Hz	60	0.40	1.70	0.95	0.32
2000Hz	57	0.30	1.80	0.84	0.29
4000Hz	48	0.30	1.40	0.71	0.23

It can be seen from Table 4.8 that the amplitude of the p11-n21 peak complex is large for 500 Hz and reduced in the order of 1000 Hz, 2000 Hz and 4000 Hz chirp stimulus. The same can be seen in the following Figure 4.4

Figure 4.4

Mean amplitude of the p11-n21 peak complex of mVEMP for 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz Narrowband chirp stimuli



There were different amounts of data samples at different chirp frequencies, so a non-parametric test was carried out. Friedman test revealed a significant main effect in the mean amplitude of p11-n21 peak complex ($p<0.05$) of mVEMP across the frequency responses of 500Hz, 1000Hz, 2000Hz and 4000Hz. Wilcoxon signed rank test was done to understand the differences between different frequencies. The results of the Wilcoxon signed rank test of the amplitude of the p11-n21 peak complex are given in Table 4.9

Table 4.9

Wilcoxon signed rank test for the amplitude of p11-n21 peak complex

Frequency	500Hz	1000Hz	2000Hz	4000Hz
500Hz		P>0.05	P<0.05	P<0.05
1000Hz			P<0.05	P<0.05
2000Hz				P<0.05

Wilcoxson signed rank test revealed no significant difference in p11-n21 peak complex between 500 Hz and 1000 Hz response ($Z=1.70$, $P>0.05$). In contrast, it showed a significant difference in amplitude between 500 Hz and 2000 Hz ($Z=4.69$, $P<0.05$), 500 Hz and 4000 Hz ($Z=5.47$, $P<0.05$). The amplitude of the p11-n21 peak complex of 1000 Hz was also significantly different from the 2000 Hz ($Z=3.83$, $P<0.05$) and the 4000 Hz ($Z=5.28$, $P<0.05$) responses. The amplitude of the p11-n21 peak complex of 2000 Hz was significantly different from that of the 4000 Hz ($Z=4.24$, $P<0.05$).

To summarize the present study results, the response rate of the mVEMP of the combined ears is 100 % (60/60 ears) for the 500 Hz and the 1000 Hz Narrowband chirp stimuli, whereas the response rate is 95 % (57/60 ears) for the 2000 Hz and 80 % (48/60 ears) for the 4000 Hz Narrowband chirp stimuli. The latency of the p11 and the n21 peaks were shortest for the 500 Hz stimulus, followed by the 1000 Hz, 2000 Hz and 4000 Hz stimuli. This reveals that the latency of the response increases as the frequency of the stimulus increases. The amplitude measures of the p11-n21 peak complex showed that the 500 Hz response has the largest amplitude, followed by the 1000 Hz, 2000 Hz and 4000 Hz. This reveals that the amplitude of the p11-n21 peak complex decreases as the frequency of the stimulus increases.

Chapter V

Discussion

The present study aimed at characterizing the latency and amplitude of multifrequency narrowband chirp-evoked masseter VEMP in healthy young adults. The study's objectives were to characterize the latency of p11 and n21 peaks and the amplitude of the p11-n21 complex for narrowband Chirp evoked masseter VEMP in young, healthy adults. mVEMP testing was conducted in 30 individuals using four different frequency narrowband chirp stimuli of 500 Hz,1000 Hz, 2000 Hz, and 4000 Hz.

Latency of mVEMP with different chirp frequencies:

The p11 and n21 peak latencies significantly differed across the 500, 1000, 2000, and 4000 Hz stimulus frequencies. The p11 and n21 peak latencies increased systematically with the increase in the stimulus frequency of narrowband chirp. The 500 Hz response had the shortest latency, followed by the 1000 Hz, 2000 Hz and 4000 Hz. 4000 Hz chirp stimulus had the largest latency.

Previous mVEMP studies have used click and tone bursts as stimuli. They reported prolonged p11 and n21 latency for tone burst-evoked mVEMP responses than the click-evoked mVEMP (Thirusangu & Sinha, 2022; Vignesh et al., 2021). The latency of mVEMP peaks is shorter for chirp and click-evoked responses than for tone burst-evoked mVEMP responses. The 500 Hz chirp response latency value of the current study does not agree with the values obtained in this study. No study compared the latency of different mVEMP peaks across different chirp frequencies. However, in the literature, one of the studies by Lodha & Neupane (2022) compared the cVEMP latency across different chirp frequencies. Lodha & Neupane (2022) reported the shortest latency with a 4000 Hz stimulus compared to 500 Hz. However, in the present study, the latency for 500 Hz was the shortest, and 4000 Hz was the largest. Overall, the latency of mVEMP peaks are much earlier compared to the latency reported by (Neupane et al., 2023). The latency values obtained in this study are much shorter than those reported in any other mVEMP study.

ABR studies using narrowband CE chirps have also reported contradicting results regarding the latency parameter. Some studies have shown a decrease in latency with increasing the narrowband chirp frequency (Hamada et al., 2013; Kousht et al., 2019), whereas other studies have reported an increase in the latency with increasing the narrowband chirp frequencies (Megha et al., 2019; Rodrigues et al., 2013). This latency discrepancy across studies could be because of different types of chirp stimuli used across different studies. Lodha & Neupane (2022); and Neupane et al. (2023) used level-specific narrowband chirp stimulus to record cVEMP and mVEMP, whereas in the present study, level-specific chirps were not utilized.

One of the key variables determining VEMP latencies is the variation in stimulus rise time (Burgees et al., 2013; Kantner et al., 2014). As clicks have a significantly shorter rise time than tone bursts (TBs), their VEMP latencies also tend to be shorter. Shorter latencies obtained from narrowband CE-Chirps might be justified because the stimulus has a shorter rise time. The narrow band CE-chirps are subsets of the broadband CE chirp stimulus. They were developed by decomposing the broadband CE chirp stimulus. The narrow band CE-chirps were designed so that their temporal references (0 ms) coincided with the expected arrival time at the tympanic membrane of the 10,000 Hz component. As a result, the frequency components of the stimulus will arrive earlier, resulting in lower response latencies. Each narrowband CE-chirp has a determined timing to compensate for the cochlea travelling delay. The compensation times for 500, 1000, 2000 and 4000 Hz are 6.14, 4.54, 3.36, and 2.48 ms, respectively (Elberling & Don, 2010).

Many studies have also utilized a level-dependent chirp to record ABRs, cVEMPs, oVEMPs and mVEMPs. It has been shown previously that using level-independent narrowband CE chirps results in shorter response latencies at higher stimulation levels and longer response latencies at lower stimulation levels. The reason for this varied latency is that the delay compensation model of this level-independent chirp stimulus did not consider the upward spread of excitation at higher levels and an increased chance of the cochlear neural delay with frequency at lower levels. It considered only the cochlear travelling wave delay. A level-specific chirp stimulus was developed to overcome these discrepancies in the response (Elberling & Don, 2010). Finally, the response latency obtained in this study might be justified by the combined onset response properties of the mVEMP and the stimulus properties of the narrow band CE chirp stimulus. In the present study, a level-specific chirp stimulus was not utilized; hence, a difference in latency across different frequencies was observed.

Amplitude of mVEMP with different chirp frequencies

The amplitude of the p11-n21 peak complex showed a significant difference across the frequency response of 500, 1000, 2000, and 4000 Hz. The amplitude of the 500 Hz and 1000 Hz responses did not differ significantly. The amplitude of the p11-n21 peak complex decreased systematically with the increase in the stimulus frequency. The 500 Hz response had the largest amplitude, followed by the 1000 Hz, 2000 Hz and 4000 Hz.

The frequency tuning of the VEMPs (cVEMP and oVEMP) has been studied extensively. All the studies reporting frequency tuning have reported a better amplitude at 500 Hz tone burst frequency compared to other frequencies (Fu et al., 2021; Park et al., 2010; Taylor et al., 2012; Wei et al., 2013). Studies that have assessed the frequency tuning of cVEMP utilizing chirp stimulus have also reported a better amplitude of cVEMP at 500 Hz compared to other frequencies (Cebulla & Walther, 2019; Lodha & Neupane, 2022). In another investigation of oVEMP using narrowband CE chirps of 500 Hz and 1000 Hz, the results showed the largest amplitude with a 500 Hz chirp stimulus than the 1000 Hz chirp

(Mat et al., 2021). In the present study, the amplitude of mVEMP was higher for 500 Hz compared to other frequencies except for 1000 Hz. The results of the current study correlate well with the previous studies in terms of amplitude measures.

The tuning properties of vestibular evoked myogenic potentials are related to the physiological aspects of the otolith organs rather than the stimulus properties (Wei et al., 2013). The tuning properties of VEMP have been utilized to study the change in characteristics of the otolith organs in various pathologies. Todd et al. (2000) modelled the vestibular evoked myogenic potentials as a single mass-spring system and reported the resonance of the otolith organs around 300 Hz. However, some of the studies also showed the resonant frequency of otolith organs to be around 400 Hz to 800 Hz (Akin et al., 2003; Janky & Shepard, 2009; Murofushi et al., 1999; Rauch et al., 2004; Timmer et al., 2006; Todd et al., 2009). Wei et al. (2013) found that responses originating from the saccule exhibit two components: one displaying resonance around 300 Hz and the other at 1000 Hz. However, the low-frequency components contribute to over 75% of the overall response for tones below 500 Hz, while the high-frequency component accounts for over 75% of the response above 1000 Hz. Zhang et al. (2011) also reported two peaks; the first peak tuning was around 100 Hz, and the second peak had a tuning around 600 Hz. The 100 Hz peak is considered to have originated from the utricle, whereas the 600 Hz peak is considered to have originated from the saccule. The peripheral generators of the masseter VEMPs are also from the saccule; hence, a domination of the response might be seen at around 600 Hz. This could be a reason for the highest amplitude of the masseter VEMPs at 500 Hz in the present study.

Chapter VI

Summary and Conclusion

The vestibular system plays a crucial role in preserving our body's balance. It encompasses numerous reflex pathways connected to it. The three major reflexes of the vestibular system, such as Vestibulo-ocular, vestibulospinal, and vestibulo-collic reflexes, have been explored mostly. mVEMP (Masseter Vestibular-evoked myogenic potential) is a relatively new assessment tool for assessing the vestibulo-masseteric reflex pathway. The masseter muscles support the jaw against gravity. These muscles exhibit short-latency inhibitory responses for a high-intensity acoustic stimulus. Recording these responses helps us understand the integrity of the vestibulo-masseteric reflex pathway. Increasing research has been carried out in recent years to establish the normative for the mVEMP.

This study aimed at characterizing the mVEMP latency and amplitude for narrowband chirp stimuli of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz in healthy young individuals. To achieve the aim, 30 participants (15 males and 15 females) in the age range of 18-30 years were included in this study. A detailed case history was taken before including the participants in the study. The participants did not have any otological or vestibular-related complaints. A series of audiological tests were done to rule out any pathological conditions. The tests carried out include pure tone audiometry, immittance and auditory brainstem response.

The masseter VEMP testing was carried out using the narrow band chirp stimuli of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz. The stimulus was presented at 125 dB SPL with alternating polarity. Zygomatic electrode montage was used in which the active electrode was placed at the lower third of the masseter muscle and the reference electrode at the midpoint of the zygomatic arch with the ground electrode placed on the forehead. Two hundred sweeps were presented at the rate of 5.1/s for each recording. Monaural stimulation was used, and the responses were recorded ipsilaterally.

Analysis of the Masseter VEMP response

The absolute latency of the p11 peak and n21 peak and the peak-to-peak amplitude of the p11-n21 complex were measured. SPSS version 26 software was used for statistical analysis. The following statistical analyses were done.

- Descriptive statistics was done to calculate the mean and standard deviation for the latency of the p11 peak and n21 peak at all frequencies.
- Descriptive statistics was done to get the mean and standard deviation for the peak-to-peak amplitude of the p11-n21 complex for all the frequency responses.
- Wilcoxon signed rank test was carried out to check the ear differences for all the frequencies.
- Descriptive statistics were done again for the combined data of both the right and left ears for all the frequencies.
- Friedman test was done to find out the significant main effect of different stimulus frequencies on p11 and n21 latency.
- Wilcoxon signed rank test was done for pairwise comparison of the p11 and n21 latency.
- Friedman test was done to find out the significant main effect of different stimulus frequencies on the amplitude of the p11-n21 complex.
- Wilcoxon signed rank test was done for pairwise comparison of the amplitude of the p11-n21 complex.

The results of the study are as follows

- The response rate of the mVEMP of the combined ears is 100 % (60/60 ears) for 500 Hz and 1000 Hz Narrowband chirp stimuli, whereas the response rate is 95 %

(57/60 ears) for the 2000 Hz and 80 % (48/60 ears) for the 4000 Hz Narrowband chirp stimuli.

- ❖ The latency of the p11 and the n21 peaks were shortest for the 500 Hz stimulus, followed by the 1000 Hz, 2000 Hz and 4000 Hz stimuli. There were significant differences in the latency of the p11 and n21 peaks between all the frequencies. This study revealed that the response's latency increased as the stimulus frequency increased.
- ❖ The amplitude measures of the p11-n21 peak complex showed that the 500 Hz response has the largest amplitude, followed by the 1000 Hz, 2000 Hz and 4000 Hz. Expect the 500 and 1000 Hz, all other frequencies showed significant differences between them. This study revealed that the amplitude of the p11-n21 peak complex decreased as the frequency of the stimulus increased.

Conclusions

mVEMP is a non-invasive test for the assessment of the vestibulo-masseteric reflex pathway. From the results of the present study, it can be concluded that when using a narrowband chirp stimulus of different frequencies such as 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz, different normative should be used for analyzing the response of each frequency. The results of the study also indicate that 500 Hz chirp and 1000 Hz chirp is the best stimulus for recoding mVEMP. At other frequencies, the response rate is lesser, and the amplitude of mVEMP is less. The results of the study can be used in studying the frequency shift in various vestibular pathologies. The differences in the responses are not due to physiological reasons of the vestibular system but because of the differences in the stimulus characteristics.

Implications of the study

- The results of this study add information to the literature, providing the normative data of latency and amplitude for narrowband chirp-evoked mVEMP.
- This study emphasizes the importance of having stimulus-specific normative data for each diagnostic test.
- The results of the study can be utilized for studying the frequency tuning of the otolith system in various vestibular disorders.

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