EFFECT OF RISE/FALL AND PLATEAU TIME ON OCULAR VESTIBULAR EVOKED MYOGENIC POTENTIAL

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May, 2013.

CERTIFICATE

This is to certify that this dissertation entitled "**Effect of rise/fall and plateau time on ocular vestibular evoked myogenic potential**" is the bonafide work submitted in part fulfillment for the degree of Master of Science (Audiology) of the student with Registration No. 11AUD022). 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.

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CERTIFICATE

This is to certify that this dissertation entitled "**Effect of rise/fall and plateau time on ocular vestibular evoked myogenic potential**" has been prepared under my supervision and guidance. It is also certified that this has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This dissertation entitled "**Effect of rise/fall and plateau time on ocular vestibular evoked myogenic potential**" is the result of my own study under the guidance of Mr. Niraj Kumar Singh, Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore, and has not been submitted earlier in any other University for the award of any Diploma or Degree.

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Chapter 1

Introduction

Vestibular Evoked Myogenic Potential (VEMP) is muscle potential which has been shown to be elicited in response to acoustic (Colebatch & Halmagyi, 1994), mechanical (Halmagyi, & Colebatch, 1995) or galvanic (Welgampola & Colebatch, 2005) stimulation. VEMP has been successfully recorded from several muscles of the body which include Sternocleidomastoid muscle (Colebatch, Halmagyi, & Skuse, 1994), Triceps muscles (Rudisill & Hain, 2008), Trapezius muscle (Ferber-Viart, Duclaux , Colleaux & Dubreuil, 1997), and Splenius capitis (Wu, Young, & Murofushi., 1999) and extra-ocular muscles (Todd, Rosengren, Aw, & Colebatch, 2007). When recorded from extra-ocular muscles, mainly Inferior oblique muscle, it is referred to as ocular VEMP (Rosengren, Todd & Colebatch, 2005; Todd et al., 2007).

The ocular VEMP (oVEMP) response has been reported to be present in the 90-100% of young neurologically and otologically intact subjects (Chihara, Iwasaki, Ushio, & Murofushi, 2007; Piker, Jacobson, McCaslin, & Hood 2011). It is believed to evaluate the functioning of ascending vestibular pathway as crossed vestibulo-ocular reflex (Iwasaki, Smulders, Burgess, McGarvie, MacDougall, Halmagyi, & Curthoys, 2008) and is well accepted to be Utricular in origin (Curthoys, 2010; Halmagyi & Carey, 2010; Rosengren, Welgampola, & Colebatch 2010).

These short latency potentials have been reported to consist of a negativity around 10 ms, referred to as n1 and positivity at approximately 16 ms called p1 (Chihara et al., 2007; Walther, Rogowski, Hormann, Lohler, 2011; Piker, 2012). Elsewhere in literature, they are also termed as n10 and p17 (Todd, Rosengren, &

Colebatch, 2003) respectively based on their average latency at onset. The oVEMP thresholds have been found to vary between 80 and 90 dB nHL in response to 500 Hz air conduction tone-burst in healthy population (Park, Lee, Shin, Lee, & Park, 2010; Wang, Jaw, & Young 2009). Larger amplitudes of oVEMPs have been reported for contralateral stimulation than ipsilateral, as the Utriculo-ocular pathway has been found to be crossed in nature (Todd et al., 2007; Isu, Graf, Sato, Kushiro, Zakir, Imagawa, & Uchino, 2000). A fair to moderate test-retest reliability for amplitude and latency parameters of oVEMP response has also been reported (Singh, Sarda, Sinha, & Tamsekar, 2011). The oVEMP has been proved to be a valid and reliable test for vestibular assessment, especially the Utricle and the otolith-ocular pathway (Nguyen, Welgampola, & Carey, 2010). In a way, it has also been shown to complement cervical VEMP in the diagnosis of central as well as peripheral vestibular disorders (Piker, et al., 2011).

Need of the study

The literature on oVEMP is brimming with reports regarding the effect of various stimulus and acquisition parameters that affect oVEMP amplitudes and latencies. However, the findings across the studies show great variability. These may be related to the use of different stimulus parameters as there is still a lack of well accepted protocol for recording oVEMP. For example, the effect of age on the amplitude and latency parameters of oVEMP has been studied by Nyugen et al. (2010) as well as Tseng, Chou and Young (2010). The former used a 2 ms rise/fall time and 1 ms plateau time where as the later used 1 ms rise/fall and 0ms plateau time. The mean amplitude and latency values between the two studies varied widely. In case these values are to be considered normative for age matching, depending on the selection of the normative reference, the results of further studies might be affected (Nyugen et al., 2010 or Tseng et al., 2010). In order to determine the effect of various factors on oVEMP responses and to have lesser disagreement among different studies, there is need for a standard protocol. This can only be arrived at by evaluating the effect of each of the stimulus-related parameters on the response. This substantiates the need for evaluating the effects of each of these parameters on the oVEMP response. Rise/fall and plateau times are some of the most varied parameters across studies and thus there is a need to explore the impact of their variation on oVEMP response.

There is an apparent dearth of literature investigating the effects of rise/fall and plateau times on oVEMP. A study in this direction was carried out by Lee, Han, Ha, Jung, Kwak, Park and Shin (2008), who used three different plateau times (1, 2, and 3 ms) and rise/fall times (0.5, 1, and 2 ms) and evaluated the effects on response rates (incidence), amplitudes and latencies of the n1 and p2 peaks. The rise fall times of 0.5 ms and 1ms along with a plateau time of 2 ms were reported to produce best results. The rise/fall time of 2 ms and the plateau time of 3 ms were associated with lowest amplitudes. Further, the increase in rise/fall was reported to produce a subsequent prolongation in the individual peak latencies, though a likewise increase in plateau time did not correspond to change in latencies. Based on these findings, they concluded that the combination of 0.5 or 1 ms rise/fall time with 2 ms plateau time was best suited for oVEMP recording. The study made an attempt to explicitly check the effects of several rise/fall and plateau times on oVEMP response; however the conclusion based on only 13 subjects appears an inadequate sample size, considering a normative study. This might have contributed to higher variability observed in their study. A larger sample size may be able to reveal more reliable results.

Later, Cheng, Wu, and Lee (2012) also investigated the effect of different ramp (rise/fall time) and plateau times on response parameters of click as well as short tone burst evoked oVEMPs in healthy individuals. The stimuli used included 0.1-ms click, and 500-Hz short tone burst of rise-plateau-fall time of 0.5-2-0.5 ms, 0.5-4-0.5 ms, 2-2-2 ms, and 2-4-2 ms. Results revealed significantly smaller amplitude of n1-p1 peak and lower incidence rate with click stimuli when compared to short tone burst stimuli. There was no significant difference in amplitude measure of n1-p1 peak with different ramp and plateau times of short tone burst. But latency of n1 peak was prolonged by 1.4 ms with the change of ramp time from 0.5 ms to 2 ms for short tone burst stimuli. Also, there was lack of significant difference in latency of n1 with change in plateau time from 2 ms to 4 ms. However, the study was conducted using only two different rise/fall (0.5 & 2 ms) and plateau times (2 & 4 ms). The studies on cVEMP, a close cousin of oVEMP have shown changes in amplitude and latencies with increase in rise/fall (Cheng & Murofushi, 2001a) and plateau time (Cheng & Murofushi, 2001b). Hence, there is a need to include more number of rise/fall and plateau time combinations and study their effects oVEMP in a large sample.

Both the above studies (Lee et al., 2008 & Cheng et al., 2012) did not document the effects of variations in rise/fall & plateau times on later peaks of oVEMP (n2, p2 and n3) and the effect of change in the parameters on oVEMP thresholds. An additional pit-fall is non-consideration of 0 ms plateau (as in Blackman window), as many studies using a Blackman window (gating) might use this plateau time. Hence the effect of changing rise/fall and plateau time on the amplitude, latencies and the thresholds of these peaks also need to be explored.

Aim

The study investigated the effect of various rise/fall and plateau time combinations of short tone-bursts on different oVEMP parameters. The study also aimed at identifying optimal rise/fall and plateau time combinations of short tone-bursts for oVEMP recording.

Objectives

The specific objectives of the study were

1. To evaluate the effect of varying rise/fall and plateau times on response rate.
2. To evaluate the effect of varying rise/fall and plateau times on amplitude of various peaks of oVEMP.
3. To evaluate the effect of varying rise/fall and plateau times on latencies of various peaks of oVEMP.
4. To evaluate the effect of varying rise/fall and plateau times on threshold of oVEMP.

Hypothesis

The present study was taken up to test the Null hypothesis based on the above objectives. The null hypotheses were as follows:

1. There is no significant difference in response rates achieved by changing rise/fall and plateau times.
2. There is no significant difference in latencies obtained by changing rise/fall and plateau times of various peaks of oVEMP.
3. There is no significant change in rise/fall and plateau times on amplitudes of various peaks complexes of oVEMP.

4. There is no significant effect of changing rise/fall and plateau times on threshold of oVEMP.

Chapter 2

Review of literature

There have been many reports in the literature stating that sound evoked extra-ocular potentials are produced in response to bone-conduction stimuli. This led to the development of oVEMP, a decade after growth following cVEMP. Later, it was found that the oVEMP can be recorded in response to air-conducted clicks and tone bursts. oVEMP responses were absent in subjects with vestibular dysfunction, while those with normal vestibular function had normal responses. oVEMP responses have been known to be consistently obtained in healthy individuals, and studies have suggested that they are useful in evaluating patients with vestibular disorders (Iwasaki et al., 2008; Todd, Rosengren, Aw & Colebatch, 2007; Wang et al., 2009; Iwasaki, Chihara, Smulders, 2009).

There are several oVEMP studies that have investigated the effect of various subject as well as stimulus related parameters in normal subjects. A variation in these parameters can result into significant effect on the oVEMP results. Such different factors have been discussed as below:

Subject related factors

There are different subject related factors that have been studied in the literature. These factors include age, gender, ear of stimulation, body position, and electrode location. The findings pertaining to each of these have been described below:

Age.

Age related changes are not only evident in the auditory system but also seen in vestibular system. As age increases beyond 60 years, the vestibular system's responses have also been shown to undergo changes.There are various studies evaluating the effect of age on the parameters of oVEMP. While some studies shows an effect of advancing age on amplitude as well as latency measures, others reveal the effects only on amplitude of oVEMP.

Tseng et al. (2010) evaluated 70 subjects in the age range of 24 to 76 years who were divided into 6 groups by decade and obtained oVEMP for bone-conduction vibration mode of stimulation. Results showed 100% response rates in 20-59 age groups and lower for the age group above 60 years. The mean n1 and p1 latencies showed significant prolongation in those over 60 years, whereas the mean n1-p1 amplitude reduced significantly in subjects over 40 years. However, the asymmetry ratio of oVEMPs did not differ significantly among the age groups.

Nyugen et al. (2010) took 53 individuals ranging from 20-70 years of age and studied effect of age on oVEMP responses for three different stimuli, clicks, 500Hz tone-burst and bone-conduction vibration. The n1-p1 peak to peak amplitude were shown to reduce over 50 years of age whereas no significant effect of age on latencies and asymmetry ratio for all the three different types of stimuli were observed.

Piker et al. (2011) recorded oVEMP for 500 Hz tone-burst at 95 dB nHL using 2 channel recording, from ipsilateral and contralateral inferior oblique muscles. Age-related differences in oVEMP latencies, amplitudes, interaural amplitude asymmetries and thresholds were studied in 100 ears in the age range of 8-88 years. Subjects were divided into three groups - below 18 years, 18-49 years, and above 50 years. The amplitude of the responses significantly decreased and the threshold significantly increased with increasing age, with the greatest age effects occurring in subjects who were 50 years or older. Response rate was reported to be 100% in subjects less than 50 years of age while 77% for subjects who were above 50 years of age.

The effect of age on oVEMP parameters shows a general agreement regarding decrease in amplitude with increasing age whereas there are mixed findings considering the effect on latency measure of oVEMP. Nyugen et al. (2010) showed lack of effect of age on latency. In contrast to this, Tseng et al. (2010) found prolongation in latency above 60 years of age group. These differences in findings might have occured due to variations in method of recording, age range and also protocol used for recording of oVEMP.

Gender.

Gender differences have been shown to be present for a number of auditory evoked potentials. However, it has been sparingly explored for oVEMPs. Cheng, Sung and Young (2011) incorporated 10 males and 10 females using three different stimuli (air conduction, bone conduction and galvanic stimuli) and found larger n1-p1 amplitude in males than females for all three stimuli. However, latency of n1 and p1 did not reveal any gender difference. A major drawback of this study was a small sample size in each group especially for a normative study. Another group of researchers Xie, Xu, Bi, Jia, Zheng, and Zhang (2011) used a larger sample size as 30 males and 32 females and obtained similar results as those of Cheng et al., 2011 study.

While the finding of no gender differences for latencies by Piker et al. (2011) was similar to those discussed above, the findings regarding the effect of gender on amplitude was in contrast to the above mentioned predecessors. They reported a lack of difference in peak-to-peak amplitude between the genders. The numbers of individuals in gender groups across age were varied between the studies which might have contributed to contrastive findings.

Eye elevation.

In literature, it is agreed upon that upward gaze produces into maximum amplitude and lowest threshold when compared to the horizontal or downward gaze. The effect of gaze was studied by Iwasaki et al. (2008) in 5 individuals using bone-conduction vibration stimulation at forehead. Results revealed highest amplitude for n1 peak for upward gaze of 20- 25° and reduction in horizontal and no replicable peaks during downward gaze. Similar findings were reported by Welgampola, Migliaccio, Myrie, Minor and Carey (2009) who included 7 participants with superior canal dehiscence and 6 normals for 500 Hz pure tone stimuli.

Another study, demonstrated the effect of gaze on oVEMP responses for 500Hz tone burst (Rosengren, Govender & Colebatch, 2009) which included 10 healthy individua. The angle of vertical gaze was varied from maximal downward to upward gaze in 5-10° of increments. They concluded that increasing vertical gaze, increased oVEMP amplitude. Such effect was not observed for horizontal gaze.

Above mentioned studies have documented their findings mainly in terms of amplitude measure but not the latency of oVEMP responses. They have also used a very small sample size which is inadequate for normative study and varied protocol mainly in terms of type and duration of stimuli.

Murmane, Akin, Kelly, and Byrd (2011) recruited 17 participants to assess the effect of vertical gaze elevation, and obtained oVEMPS at gaze elevations of 0°, 15°, and 30°. The stimulus used for recording was 500 Hz tone-burst. oVEMP amplitude and response prevalence increased as gaze elevation increased from 0 to 30°, and the largest average n1-p1 amplitude was observed at a gaze elevation of 30°. Latency of n1 did not show significant effect with the change in angle of vertical gaze but absolute latency p1 prolonged with decreasing the angle of eye elevation. This finding regarding the effect on latency has been reported but not discussed. Authors of this study have evaluated the effect of gaze using optimal parameters but, at the same time, used limited gaze positions and small sample size in order to generalize the obtained results to the available population.

The above sets of studies have evaluated the effect of gaze elevation on latency and/or amplitude parameters of oVEMP. All of these studies have not discussed the effect on response rates. However, the effect of gaze elevation on amplitude appears to be in consensus across studies and the finding of enhancement in amplitude with increased gaze elevation appears universally acceptable.

Body position.

Govender et al. (2009) determined the effect of body position and head rotation in 10 healthy individuals and found truncal position to affect oVEMP amplitude. But there was no significant effect with the change in head rotation. The sample size was too small for the normative study to be generalized and used as standard position for recording of oVEMP.

The effect of body position was also studied by O'Neil (2010) in 30 participants (27females and 3 females) evaluating only one ear from every individual. oVEMP was recorded bilaterally in four positions which included upright with head level, supine with chin tilted 30º, and subject laid on the right and left side with chin tilted 30º toward the chest using 500 Hz tone-burst. Results revealed sitting upright to be the best position which caused lowest threshold when compared to other positions. He evaluated the effect of body position on threshold which was not documented in Govender et al. (2009) study. However, this study suffers a pit fall of not incorporating equal number of males and females and allowing gender differences to be affecting the results of the study. Further, the overall sample size of 30 ears was small for normative studies.

Stimulus related factors

A variation in stimulus related factors, like any other potential, could also affect oVEMP response parameters. There are numerous studies in the literature reporting the effect of such factors including intensity, type of stimuli, stimulus frequency, mode of stimulation, repetition rate and duration of stimulus and rise/fall and plateau times. The optimal stimulus parameters have to be derived from various investigations for oVEMP response recording. The effect of every factor has been discussed in the following sub-sections:

Intensity.

There is a general consensus regarding the effect of intensity on amplitude, latency, and response rate parameters. Most of the studies have shown an increase in n1-p1amplitude and response rate while reduction in threshold with increasing intensity (Akin, Murnane, & Proffitt, 2003; Rosengren et al., 2005; Chihara et al., 2007; Welgampola et al., 2009). However, no such effect was observed on latency measure of oVEMP responses.

The effects of stimulus level were determined for 34 ears at 500 Hz tone burst stimuli (Murmane et al., 2011). The stimuli were presented monaurally in 5 dB decrement from 125 to 100 dB peak SPL. The response amplitude and response prevalence increased as a function of stimulus level and the maximum response prevalence was obtained at the maximum level (125 dB peak SPL). On the other hand, mean absolute latency of both n1 and p1decreased as a function of stimulus level.

Though, there appears to be an unanimity regarding the effects of intensity on amplitude of oVEMP, the latencies seem to indicate towards the slight uncertainity.

While most studies have demonstrated a lack of change in latency with change in stimulus intensity (Rosengren et al., 2005; Chihara et al., 2007, Welgampola., 2009) others (Murmane et al., 2011) have reported a tendency for the absolute latencies to decrease as a function of increasing intensity. The differences between the two sets of studies appear difficult to ascertain and pinpoint to a particular factor. Use of variable stimulus parameters resulting in slight differences in morphology might be thought to be one of the reasons behind such a difference. Additionally, the above mentioned studies have not documented the effect of intensity on later peaks which are usually present in the oVEMP recordings of many studies but not described in the literature.

Repetition rate.

Most auditory evoked potentials have been shown to be affected by changes in stimulus presentation rates. oVEMP, being an auditory evoked potential, would appear to be also affected by such changes. The only study assessing the effect of different repetition rate (1, 5, 10, 20, 30, and 40Hz) was conducted by Chang, Cheng, Wang, & Young (2010). oVEMP was recorded on 25 individuals using bone-conduction mode of stimulation. They obtained highest amplitude for 20 Hz rate, 100% incidence rate and no difference on n1latency for varied rates. However, effect of the repetition rate was not documented on threshold and later peaks such as n2, p2 and n3. Additionally, this parameter has not been explored for an air-conduction evoked oVEMP.

Stimulus frequency.

It has been well documented in various studies that low frequency stimuli results into better oVEMP responses when compared to high frequency stimuli. Welgampola, Rosengren, Halmagyi, and Colebatch (2003) determined the optimum stimulus frequency, responses to 250, 500, 1000, and 2000 Hz bone conducted tone-bursts were measured in 10 subjects. They reported that oVEMP responses for 250 Hz had highest amplitude and lowest threshold. This study suffered a drawback of including only limited subjects for a normative study. The effect of change of stimulus frequency was not discussed with respect to latency of oVEMP peaks.

Chihara, Iwasaki, Fujimoto, Ushio, Yamasobaa and Murofushi (2009) reported frequency tunning properties in 12 healthy individuals using air-conduction and bone-conduction vibration of 250, 500, and 1000-Hz short tone- bursts (STB) (rise/fall time = 1 ms; plateau time = 2 ms). Results demonstrated that the best frequencies of the oVEMPs to air-conducted sound and bone-conducted vibration are 500 and 250 Hz, respectively in terms of threshold, prevalence rate and amplitude. The latencies of n1 decreased as the stimulus frequency increased for both mode of conduction. The conclusion made by authors of this study was based on small sample size and they also did not evaluate the effect of higher frequency on oVEMP parameters.

oVEMPs were obtained from one ear of each subject in 17 participants at 125dB peak SPL air-conduction tone- bursts of the octave frequencies from 250 to 4000 Hz (Murnane et al., 2011). The largest average n1-p1 amplitude and highest response prevalence were obtained at 500 Hz; both amplitude and response prevalence decreased at frequencies above and below 500 Hz. However, effect of stimulus frequency was not seen on the absolute latencies of p1 and n1 peaks. Authors varied the stimulus duration in terms of number of cycles across frequencies which could have resulted into differences observed. They also restricted number of subjects for a normative study which might indicate against the generalization of the results to the population.

Taylor, Bradshaw, Halmagyi, and Welgampolao (2012) studied oVEMPs in response to air-conducted tone-bursts (250–2000 Hz) in 14 patients with superior canal dehiscence (SCD) and 32 healthy controls. The most common optimal frequency for oVEMPs was 1000 Hz. Tone burst frequencies of 500 Hz and 1 kHz evoked significantly larger amplitudes than 250-Hz and 2-kHz stimuli. Though study incorporated effect of higher frequency (2000Hz) but did not investigate effect of stimulus frequency on latency measure of n1 and p1 peaks.

These results across various studies have shown broad frequency tuning with maximum amplitudes and response prevalence between 500 and 1000 Hz. This indicates that stimulus frequencies within this range are optimal for the clinical utility of the air-conduction oVEMP (Chihara et al., 2009; Todd et al., 2009; Park et al., 2010).

Mode of stimulation.

oVEMp can be recorded using different modes of stimulation like air-conduction, bone-conduction, mechanical and galvanic stimulation. There are many studies investigating air and bone conduction mode of stimulation. Wang et al. (2010) determined whether bone-conducted vibration (BCV) or air-conducted sound (ACS) is the optimal mode for eliciting oVEMPs. They included 12 healthy volunteers and found that BCV mode at Fz had a significantly higher response rate and larger n1-p1 amplitude of oVEMPs than that of the ACS mode. The mean latencies of n1 and p1 were longer for ACS mode when compared to BCV mode. Based on these findings, conclusion was made that BCV mode, Fz and inion may be the optimal sites for eliciting oVEMPs through BCV mode. This conclusion, however, might be erroneous owing to a very small sample size. The study also did not document effect of mode of stimulation on threshold of oVEMP responses.

Stimulus duration.

Stimulus duration is one of the stimulus related factors which has been found to vary across the studies. Usually, stimulus duration encompasses two important parameters, rise/fall time and plateau time. Most studies have indirectly explored the effect of stimulus duration on oVEMP through variations in these two parameters.

Lee et al. (2008) conducted a study on 13 subjects to investigate the effect of three different plateau times (1, 2 and 3 ms) and rise/fall times (0.5, 1 and 2ms) on prevalence rates, amplitudes and latencies of the n1 and p2 peaks. Their results indicated that 0.5 ms and 1 ms rise/fall time along with a plateau time of 2 ms produced the best results. On the other hand, a rise/fall time of 2 ms with a plateau time of 3 ms elicited the lowest amplitudes. Moreover, it was also seen that a further increase in rise/fall time resulted in subsequent prolongations in the individual peak latencies; however, a similar effect was not observed with increase in plateau time. Thus, it was concluded by the authors that the optimal combination for recording of oVEMP was using 0.5 ms or 1 ms rise/fall time along with 2 ms plateau time. Though the study has attempted to examine the effects of several rise/fall and plateau times on the amplitude of oVEMP, however their conclusion is based on a very small number of subjects which is inadequate to be considered as a normative study. Consequently, the high variability observed can be accounted for by the small sample size. More reliable results can be obtained if a study is undertaken using a larger sample size.

Subsequently, Cheng et al. (2012) administered oVEMP on 22 healthy individuals in the age range of 20-39 years using clicks as well as short tone burst stimuli. They aimed to investigate the effect of different ramp and plateau time on these stimuli. They used 0.1 ms click and 500 Hz tone burst having a rise-plateau-fall time of 0.5-2-0.5 ms, 0.5-4-0.5 ms, 2-2-2 ms, and 2-4-2 ms. It was found that click stimuli elicited significantly smaller amplitude of n1-p1 peak and lower incidence rate as compared to short tone burst stimuli. Further, no significant difference was found between the amplitude measure of n1-p1 peak with different ramp and plateau times of short tone burst. Moreover, authors found that the latency of n1 peak was prolonged by 1.4 ms with the change of ramp time from 0.5 to 2 ms for short tone burst stimuli. However, when the plateau time was increased from 2 to 4 ms, this effect was not evident. On the whole, this study used only two different rise/fall (0.5 & 2ms) and plateau times (2 & 4ms) and did not investigate the effects of further increase in rise/fall or plateau times. It has been found by studies on cVEMP that change in rise/fall (Cheng & Murofushi, 2001a) and plateau time (Cheng & Murofushi, 2001b) causes changes in amplitude.

Overall, both the studies by Lee et al. (2008) & Cheng et al. (2012) have neither documented the effect of changes in rise/fall time and plateau time on later peaks of oVEMP (n2, p2 and n3) nor have they investigated the effect of changes in these parameters would have on oVEMP thresholds of oVEMP. Another limitation observed is that none of the studies have considered a 0 ms plateau as in seen during Blackman gating. Therefore, further inquiry into the effects of rise/fall and plateau time on the amplitude, latencies and the thresholds of oVEMP is necessary.

Chapter 3

Method

Participants

Fifty ears of from the 50 participants (25 males & 25 females) recruited for the study in the age range of 18-25 years (Mean age = 21.5 years) were investigated using oVEMP. Only one ear of each individual was chosen owing to considerably long durations required for the evaluations. Out of the 50 participants, oVEMPs were recorded from right ear for 25 individuals and left ears of the remaining 25 individuals. A written consent was obtained from the participants before their recruitment to the study. Further, their participation in the study was on a non-payment basis, which was explicitly described in the informed consent form that they signed prior to their participation.

Inclusion criteria.

The participants included in the study had hearing sensitivity within normal limits as shown by their pure-tone thresholds of ≤ 15 dB HL at the octave frequencies from 250 Hz through 8000 Hz for air conduction and 250 Hz through 4000 Hz for bone-conduction. They also had speech recognition threshold within ±12 dB of the pure-tone average and speech identification scores in excess of 90%. Additionally, they had normal middle ear function which was indicated by ‘A’ type tympanogram and presence of acoustic reflex thresholds within normal limits.

Exclusion criteria.

Individuals having history of otological, vestibular or neurological disorders were not considered for the study. It was ensured through detailed structured case history. Their otological, vestibular and neurological intactness was further reinforced through the screening by an Otolaryngologist. Subjects with visual abnormalities such as squints, spontaneous nystagmus or other visual abnormalities were also excluded. Other exclusion criteria comprised of reduced uncomfortable level (<100 dB HL) for speech to ensure discomfort free testing at high stimulus levels which are used for recording of oVEMP.

Instrumentation

A calibrated two-channel diagnostic audiometer, Grason-Stadler Incorporated 61 (Eden Prairie, United States of America) with Telephonics TDH-50P supra-aural headphones housed in MX-41/AR ear-cushions, was used for obtaining air-conduction thresholds, speech recognition threshold (SRT), and speech identification scores (SIS). The same audiometer with Radioear B-71 bone-vibrator was used to obtain bone-conduction thresholds. A calibrated immittance meter, Grason-Stadler Incorporated Tympstar (Eden Prairie, United States of America) with default probe-assembly and contralateral insert earphones, was used to assess middle ear functioning. Bio-logic Navigator Pro (Natus Medical Incorporated, Illinois, United States of America) version 7.0.0, with impedance matched Etymotic ER- 3A insert earphones, was used to record and analyze oVEMP waveforms.

Test environment

All the tests were carried out in a well illuminated, air-conditioned, acoustically treated double room set up. The exceptions to this were immittance evaluation and oVEMP, both of which were administered in a single-room suite. The ambient noise levels in these rooms were within specified limits as per American National Standard Institute specifications (ANSI S3.1 1999).

Procedure

Pure-tone thresholds were obtained at octave frequencies from 250 Hz to 8000 Hz and 250 Hz to 4000 Hz for air- and bone-conduction respectively. Pure-tone thresholds were determined using the modified Hughson and Westlake procedure (Carhart & Jerger, 1959). Speech audiometry included determination of SRT, SIS and Uncomfortable loudness level (UCL).While obtaining SRT involved the presentation of spondees through use of Bracketing method to arrive at threshold (≥ 50 % criterion), the SIS was obtained by presenting the words from the phonemically balanced (PB) word list in the participants native language at affixed intensity of 40 dB HL above their SRT. Immittance evaluation incorporated tympanometry and reflexometry. Tympanometry was carried out with a probe-tone frequency of 226 Hz at 85 dB SPL by varying air pressure in the external ear canal from +200 daPa to -400 daPa. The same probe-tone frequency, along with reflex eliciting signal at octave frequencies from 500 Hz to 2000 Hz, were used to measure ipsilateral as well as contralateral acoustic reflex thresholds.

The subjects were seated comfortably in an upright posture for oVEMP acquisition. The electrode sites were scrubbed using an abrasive gel (Nuprep) to improve the skin impedance. Silver chloride disc-type electrodes were placed on the thus cleaned sites using conduction gel and secured in place using surgical plaster. An electrode montage reported appropriate by Chihara et al. (2007) was used to record the oVEMP responses. As per this montage, the non-inverting electrode was placed on the cheek approximately 1cm below the center of the lower eyelid, directly below the pupil when in forward center gaze, the inverting electrode was placed 2 cm below the non-inverting electrode while the ground electrode was placed on the forehead. A two-channel recording was achieved using the same electrode placement for the contralateral as well as the ipsilateral eye. Absolute and inter-electrode impedance was maintained below 2 kΩ and 5 kΩ respectively. Four different rise/fall times (2, 4, 6, & 8 ms) and plateau times (0, 2, 4, & 6 ms) were used in all possible combinations. The participants were instructed to maintain a supero-medial gaze position of 30° to 35° during the recording which has been reported to be appropriate for best recordings of oVEMP (Murmane et al., 2011). After every recording, a brief interval was given in order to avoid fatigue and eye irritation. The intensity was reduced in 10 dB SPL steps beginning with 125 dB SPL, in order to achieve threshold. The recorded activity was amplified by a factor of 30,000 and bandpass filtered between 1-1000 Hz (1dB/octave). Acoustic stimuli were presented at 125 dB SPL using 500 Hz short tone bursts with alternating polarity. The repetition rate was set to 5.1 Hz and analysis window to 64 ms including pre-stimulus baseline recording of 10 ms. A total of 150 sweeps were averaged for each run and an average of two replicated waveforms was considered the final oVEMP waveform for a particular rise/fall and plateau time combination.

Measures

The waveforms were analyzed to identify n1, p1, n2, p2 and n3 peaks. Thereafter, the absolute latencies and peak- to- peak amplitudes were measured at maximum intensity for every rise/fall and plateau time combination. The threshold was considered as the lowest intensity in dB SPL at which the responses were reliably recorded. A minimum of 20% of the waveforms were analyzed by another experienced Audiologist to counter the consequence of researcher's bias on the findings.

Statistical Analysis

A commercially available statistical tool, Statistical Package for Social Sciences (SPSS, version 16.0) was used for statistical analysis of obtained data. The analyzed data was subjected to Two-way Repeated measures of analysis of variance (Repeated measures ANOVA) to compare absolute latencies and peak-to-peak amplitudes and threshold for every rise/fall and plateau time combination. Separate Two-way repeated measures ANOVA were done for latency, amplitude, and threshold measures. In case of significant interaction between the variables, Repeated measures ANOVAs were done for each of the variables by keeping the other constant. This was followed by the Bonferroni adjusted multiple comparisons for pairwise comparisons of different rise/fall and plateau times.

In order to evaluate the extent of effect that rise/fall and plateau times had on the absolute latencies and peak-to-peak amplitude of various oVEMP peaks, a regression analysis was done for plateau time alone, rise/fall time alone and combination of rise/fall time and plateau time. Further, a regression equation was also generated for the same. Thus, the effect of rise/fall and plateau time on the oVEMP parameters were determined and best combination of rise/fall and plateau time was arrived at.

Chapter 4

Results

The present study used a total of 50 ears of 50 healthy individuals to record oVEMPs across sixteen rise/fall time and plateau time conditions. The response rate, absolute latencies, peak-to-peak amplitudes, and thresholds were calculated and the thus obtained data was subjected to statistical analysis. Additionally, the response prevalence (rate) was also calculated. Figure 1 shows the grand averaged waveforms for ipsilateral recordings. Figure 2 shows the same for contralateral recordings.

Response rate

The response rate was defined as the percentage of ears in which a particular response (peak) was present. Out of 50 ears, oVEMP responses were obtained in 47 ears thereby showing a response rate of 94% for the contralateral recordings. Similarly, the response rate for the ipsilateral recording was 58% by virtue of presence of ipsilateral responses in 29 ears. Thus, 94% and 58% of the participants had presence of at least one peak complex in their contralateral and ipsilateral recordings of oVEMP respectively. In addition, the response rates were also calculated separately for all five peaks (n1, p1, n2, p2, & n3) against the different rise/fall and plateau time combinations for ipsilateral as well as contralateral responses. The response rates for various peaks of contralateral as well ipsilateral responses have been depicted in Table1.

The response rates, as can be seen from the above table, revealed a tendency for reduction with increase in plateau times as well as rise/fall times. This was true for each of the peaks and for both ipsilateral as well as contralateral responses. The response prevalence was highest for peaks n1 and p1 and progressively declined for

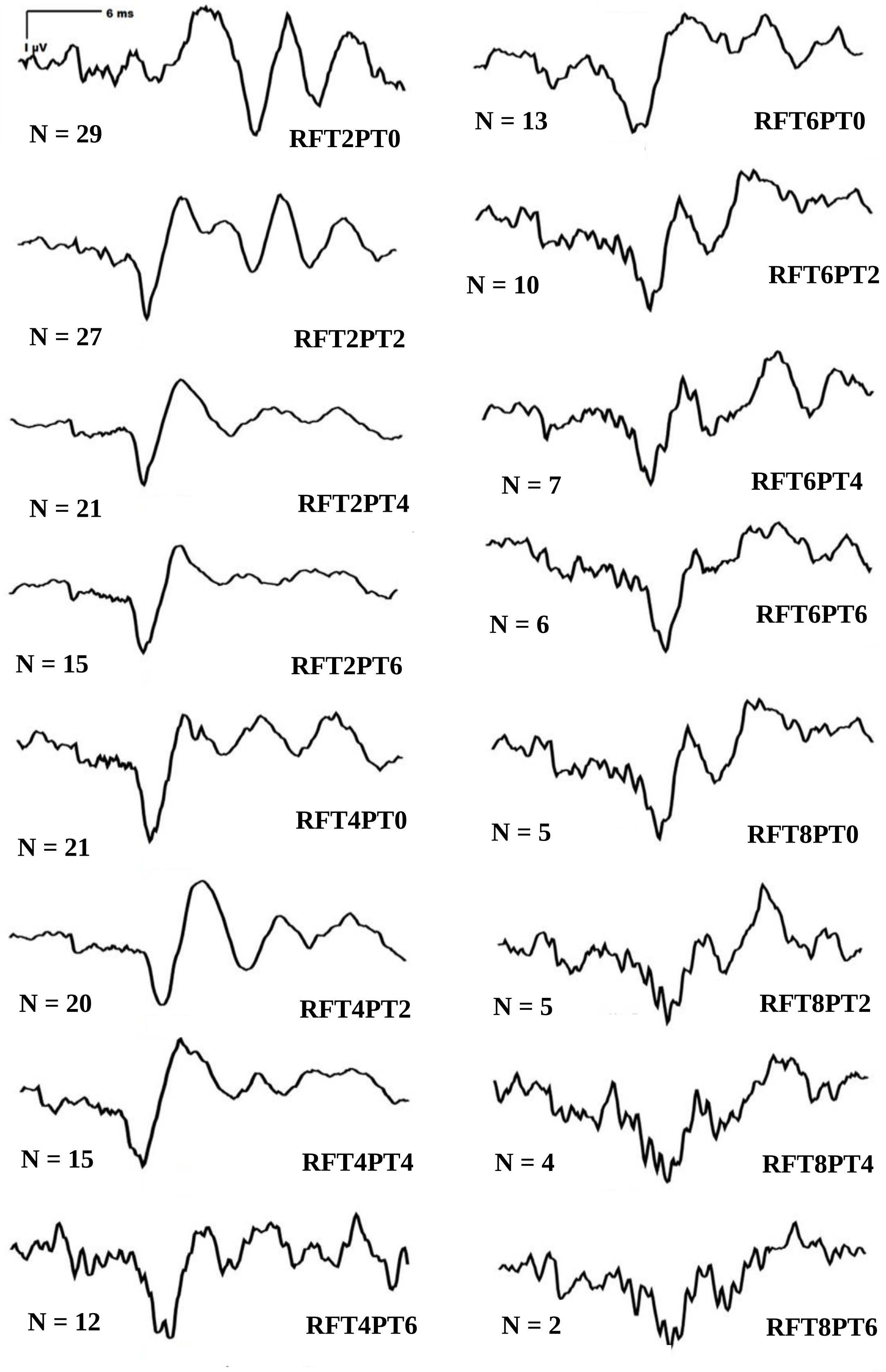

Figure 1. Grand averaged waveforms across various rise/fall and plateau times of ipsilateral recordings.

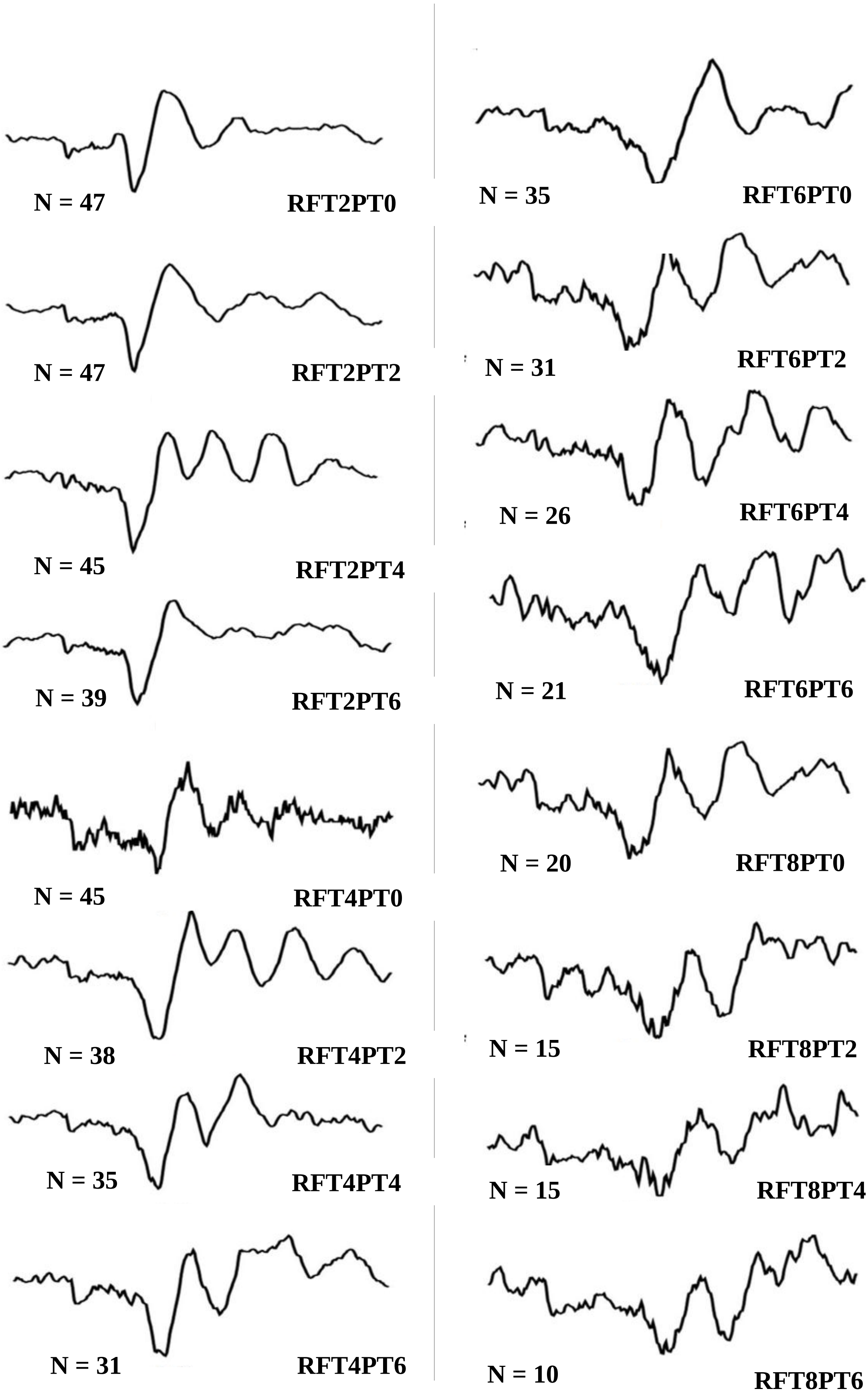

Figure 2. Grand averaged waveforms across various rise/fall and plateau times of contralateral recordings.

Table 1.

Response rates across different rise/fall and plateau time conditions for various peaks of contralateral and ipsilateral recordings.

Peaks	Rise/fall time	Contralateral response rate				Ipsilateral response rate			
		0 ms PT	2 ms PT	4 ms PT	6 ms PT	0 ms PT	2 ms PT	4 ms PT	6 ms PT
n1	2 ms	94%	94%	90%	78%	58%	54%	42%	30%
	4 ms	90%	76%	70%	62%	42%	40%	30%	24%
	6 ms	70%	62%	52%	42%	26%	20%	14%	12%
	8 ms	40%	30%	30%	20%	10%	10%	8%	4%
p1	2 ms	94%	94%	90%	78%	58%	54%	42%	30%
	4 ms	90%	76%	70%	62%	42%	40%	30%	24%
	6 ms	70%	62%	52%	42%	26%	20%	14%	12%
	8 ms	40%	30%	30%	20%	10%	10%	8%	4%
n2	2 ms	92%	92%	78%	70%	56%	40%	32%	28%
	4 ms	86%	62%	62%	60%	42%	32%	26%	20%
	6 ms	52%	58%	50%	36%	24%	18%	14%	6%
	8 ms	28%	26%	26%	22%	8%	8%	8%	6%
p2	2 ms	74%	70%	68%	42%	46%	38%	36%	26%
	4 ms	54%	50%	56%	28%	26%	24%	28%	18%
	6 ms	32%	40%	38%	12%	16%	18%	14%	8%
	8 ms	16%	24%	10%	2%	2%	6%	4%	0%
n3	2 ms	72%	66%	66%	32%	40%	34%	32%	18%
	4 ms	48%	48%	48%	24%	16%	18%	26%	18%
	6 ms	30%	40%	30%	8%	12%	16%	8%	8%
	8 ms	16%	20%	8%	4%	4%	0%	2%	0%

Note: ‘PT’: plateau time; ‘ms’: millisecond later occurring peaks. Additionally, the rise/fall times of 2 ms and 4 ms and the plateau times of 0 ms and 2 ms produced highest response rates irrespective of the response type (ipsilateral or contralateral) and peaks. The presence of at least one peak complex was considered for presence of a response and the overall rate was higher for contralateral responses when compared to ipsilateral responses across all the peaks. Further, in order to avoid loss of data during statistical comparisons, statistical analysis was done using only those rise/fall and plateau times where response rate was 70% or more for contralateral responses. This was fulfilled for rise/fall times of 2 ms and 4 ms and plateau times of 0 ms, 2 ms and 4 ms for the contralateral recording. Further, since the response rates were lower for ipsilateral recordings, the above criteria of 70% was modified to 30% for statistical analysis of ipsilateral recordings. This was also fulfilled by the same rise/fall and plateau times as those for contralateral recordings. Hence, only these rise/fall and plateau times were considered for further statistical analysis involving comparisons of rise/fall time and plateau time effect.

Latency

The effect of change in rise/fall times and plateau times on absolute latency of five peaks of oVEMP (n1, p1, n2, p2, & n3) was evaluated. The absolute latencies were observed to increase with increasing rise/fall time from 2 ms to 8 ms and plateau times from 0 ms to 6 ms for ipsilateral as well as contralateral recordings. Table 2 shows mean and standard deviation for latencies of n1, p1, n2, p2 and n3 peaks for contralateral as well as ipsilateral responses. The absence of standard deviation values at certain combinations of rise/fall and plateau times was due to presence of response in only one individual at that combination and blank cells represent the absence of that response among all the subjects.

Contralateral response latency.

The contralateral response latency was observed to prolong with increasing rise/fall time as well as plateau time. A Two-way repeated measures ANOVA was done to evaluate the significance of this trend of prolongation in latencies. The results of Two-way repeated measures ANOVA revealed a significant main effect of rise/fall time [$F(1,32) = 419.20$, $p<0.001$] on latency of n1. However, there was no significant main effect of plateau time [$F(2,64) = 1.62$, $p>0.05$] on the latency of n1. Further, there was also no interaction between the rise/fall times and plateau times for n1latency [$F(2,64) = 1.76$, $p>0.05$]. Since the main effect was observed only for rise/fall time and there were only two rise/fall times, Bonferroni adjusted multiple comparisons was not required. Figure 3 represents mean latency values and 95% confidence intervals across different rise/fall and plateau times for n1 peak.

In order to evaluate the extent of effect that rise/fall and plateau times had on the latency of n1, a regression analysis was done for plateau time alone, rise/fall time alone and combination of rise/fall time and plateau time. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.008 ($p<0.05$), 0.480 ($p<0.05$), and 0.495 ($p<0.05$) respectively. Further, a regression equation was generated for n1 latency which is as follows:

$$\text{n1 latency} = (0.271PT + 2.56RFT) - 8.497$$

where ‘PT’ stands for plateau time and ‘RFT’ for rise/fall time.

For the latency of p1, the results of Two-way repeated measures ANOVA revealed significant main effect of rise/fall time [$F(1,32) = 512.14$, $p<0.001$] as well

Table 2.

Mean and standard deviation for latency parameters of oVEMP for changes in rise/fall and plateau times for contralateral and ipsilateral responses.

Peaks	Rise/fall time	Contralateral response latency (mean ± SD)				Ipsilateral response latency (mean ± SD)			
		0 ms PT	2 ms PT	4 ms PT	6 ms PT	0 ms PT	2 ms PT	4 ms PT	6 ms PT
n1	2 ms	11.38 ± 1.30	11.47 ± 1.15	11.94 ± 1.64	12.29 ± 1.45	12.40 ± 2.40	11.83 ± 1.41	13.51 ± 2.37	14.09 ± 3.01
	4 ms	13.80 ± 0.94	14.38 ± 1.25	14.30 ± 1.48	14.50 ± 1.56	14.20 ± 1.16	14.90 ± 2.30	14.95 ± 1.53	14.61 ± 2.06
	6 ms	16.66 ± 1.57	16.78 ± 1.48	17.63 ± 2.86	16.62 ± 1.48	18.43 ± 3.14	18.45 ± 3.50	19.91 ± 2.99	18.03 ± 3.67
	8 ms	18.36 ± 1.25	18.91 ± 1.51	19.98 ± 3.08	19.42 ± 1.60	20.35 ± 4.06	21.00 ± 3.04	20.07 ± 1.58	22.32 ± 3.71
p1	2 ms	16.12 ± 1.88	16.92 ± 1.90	17.39 ± 2.30	17.55 ± 2.56	17.73 ± 2.50	17.31 ± 1.68	19.06 ± 2.46	19.08 ± 2.85
	4 ms	19.78 ± 1.60	19.79 ± 1.67	19.59 ± 1.77	19.36 ± 2.10	20.39 ± 1.52	20.73 ± 2.64	20.23 ± 1.94	21.46 ± 1.80
	6 ms	23.10 ± 1.67	22.90 ± 2.36	22.89 ± 2.51	22.20 ± 1.97	25.80 ± 2.84	24.15 ± 3.52	23.35 ± 3.45	23.75 ± 3.16
	8 ms	24.45 ± 1.90	25.40 ± 1.48	25.36 ± 2.42	25.16 ± 1.71	25.00 ± 3.63	26.55 ± 2.88	25.16 ± 2.01	27.61 ± 3.10
n2	2 ms	21.58 ± 2.67	22.31 ± 2.77	21.33 ± 2.57	22.22 ± 2.95	23.16 ± 3.00	23.01 ± 3.16	25.49 ± 3.41	25.55 ± 3.08
	4 ms	25.48 ± 2.47	24.90 ± 2.51	23.95 ± 2.63	24.57 ± 2.88	26.00 ± 2.55	25.74 ± 3.36	25.60 ± 2.04	27.00 ± 3.37
	6 ms	29.29 ± 2.00	27.51 ± 2.73	27.78 ± 2.70	26.7 ± 2.55	32.24 ±2.95	29.56 ± 3.67	28.62 ± 2.82	30.61 ± 3.79
	8 ms	29.03 ± 2.75	30.48 ± 1.48	30.61 ± 2.61	30.88 ± 1.71	29.70 ± 4.33	31.20 ± 2.62	30.63 ± 1.37	32.20 ± 3.75
p2	2 ms	26.09 ± 2.61	26.65 ± 3.36	26.61 ± 3.51	27.48 ± 3.49	27.59 ± 4.01	28.34 ± 3.90	28.99 ± 5.26	29.71 ± 2.88
	4 ms	30.03 ± 3.17	28.60 ± 2.99	29.39 ± 2.52	30.00 ± 3.14	31.12 ± 3.13	27.61 ± 5.56	30.36 ± 1.96	31.42 ± 2.10
	6 ms	33.49 ± 3.78	31.73 ± 4.78	33.20 ± 1.84	33.57 ± 3.66	36.10 ± 2.76	34.53 ± 3.85	34.70 ± 3.31	34.07 ± 4.97
	8 ms	33.98 ± 2.67	34.40 ± 3.43	36.65 ± 0.77	33.95	34.45	35.45 ± 2.88	32.70 ± 3.88	
n3	2 ms	30.45 ± 3.35	31.47 ± 4.52	30.53 ± 3.34	31.76 ± 4.09	32.20 ± 4.08	32.47 ± 3.51	33.15 ± 5.96	32.70 ± 2.88
	4 ms	34.56 ± 3.44	32.84 ± 3.96	34.14 ± 3.86	34.09 ± 4.50	35.26 ± 3.16	34.92 ± 4.04	35.55 ± 2.82	38.00 ± 2.63
	6 ms	38.96 ± 2.83	36.01 ± 5.38	38.01 ± 3.31	37.26 ± 4.46	40.40 ± 3.73	39.66 ± 3.79	40.02 ± 2.50	37.70 ± 5.83
	8 ms	38.29 ± 2.55	40.02 ± 2.22	39.07 ± 5.86	39.45 ± 2.12	35.07 ± 5.83		40.95	

Note: ‘PT’: plateau time; ‘ms’: milliseconds; ‘SD’: standard deviation.

as plateau time [$F(2,64) = 3.18$, $p<0.05$]. Additionally, a significant interactional effect of both the variables was evident on the latency of p1 [$F(2,62) = 7.72$, $p<0.01$].This brought about the need for conducting separate repeated measures ANOVA for rise/fall times of 2 ms and 4 ms at plateau times of 0 ms, 2 ms and 4 ms and also for plateau times of 0 ms, 2 ms and 4 ms at rise/fall times of 2 ms and 4 ms. For variation in rise/fall times from 2 ms to 4 ms, the repeated measures ANOVA revealed a significant main effect of rise/fall times on p1 latency at plateau times of 0 ms [$F(1,43) = 310.87$, $p<0.001$], 2 ms [$F(1,37) = 227.60$, $p<0.001$] and 4 ms [$F(1,32) = 95.65$, $p<0.001$]. Considering the use of only two rise/fall times for comparisons at each of the plateau times, the Bonferroni adjusted multiple comparisons was not necessitated. For changes in plateau times from 0 ms to 4 ms, there was also a significant main effect of plateau times on p1 latency at rise/fall time of 2 ms [$F(2,86) = 13.44$, $p<0.001$] but not at 4 ms [$F(2,62) = 1.18$, $p>0.05$]. Thus, the Bonferroni adjusted multiple comparisons between the plateau times was required only at the rise/fall time of 2 ms. At this rise/fall time, there was a significant difference between the plateau time of 0 ms and 2 ms ($p<0.01$) and also 0 ms and 4 ms ($p<0.001$) but not between 2 ms and 4 ms ($p>0.05$). Figure 3 represents mean latency values along with 95% confidence intervals across different rise/fall and plateau times for p1 peak.

Though both rise/fall times and plateau times were observed to affect the response, the extent of their impact on p1 latency required evaluation. Hence, a regression analysis was carried out for plateau time alone, rise/fall time alone and combination of rise/fall time and plateau time. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.005 ($p<0.05$), 0.370 ($p<0.05$), and 0.381($p<0.05$) respectively. Further, a regression equation was generated for the latency of p1 which is as follows:

p1 latency = (0.303PT + 2.952RFT) – 13.252

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

A Two-way repeated measures ANOVA was also done for n2 latency of contralateral recordings. The results demonstrated significant main effect of rise/fall times [F(1,27) = 161.463, $p<0.05$] as well as plateau times [F (2,54) = 4.319, $p<0.001$] on the latency of n2. Additionally, there was marginally significant interaction between rise/fall and plateau times [F(2,54) = 2.753, $p=0.073$]. Thus, separate repeated measures ANOVA were required for rise/fall times as well as plateau times by keeping the other constant. For variation in rise/fall times from 2 ms to 4 ms, the repeated measures ANOVA revealed a significant main effect of rise/fall times on n2 latency at plateau times of 0 ms [F(1,38) = 79.59, $p<0.001$], 2 ms [F(1,29) = 22.74, $p<0.001$] and 4 ms [F(1,29) = 32.15, $p<0.001$]. For changes in plateau times from 0 ms to 4 ms, there was also a significant main effect of plateau times on n2 latency at rise/fall time of 2 ms [F(2,74) = 3.36, $p<0.05$] and 4 ms [F(2,54) = 3.36, $p<0.05$]. The Bonferroni adjusted multiple comparisons was required only for plateau times and not for rise/fall times owing to the consideration of only two rise/fall times for statistical analysis. Results of Bonferroni adjusted multiple comparisons for pair-wise comparison revealed a significant difference between the plateau times of 2 ms and 4 ms ($p<0.05$) but not for other pairs ($p>0.05$). Figure 3 represents mean latency values and 95% confidence intervals across different rise/fall and plateau times for n2 peak.

The extent of effect of rise/fall time, plateau time and combination of both on n2 latency was evaluated using regression analysis. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.019 ($p<0.05$), 0.254 ($p<0.05$) and

0.267 ($p<0.05$) respectively. Further, a regression equation was generated for n2 latency which is as follows:

n2 latency = [(-0.416PT)+ (3.060RFT)] – 19.525

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

The results of Two-way repeated measures ANOVA for p2 latency revealed a significant main effect of rise/fall time [$F(1,13) = 14.46$, $p<0.01$] but not of plateau time [$F(2,26) = 1.10$, $p>0.05$]. Also, there was no significant interactional effect between rise/fall and plateau times [$F(2,26) = 1.17$, $p>0.05$] for p2 latency. The Bonferroni adjusted multiple comparisons for pair-wise comparisons of rise/fall times was not felt due to the use of only two rise/fall times in the final statistics owing to a low response rate for other rise/fall times. This was also not necessitated for plateau times due to a lack of significant main effect of plateau times on p2 latency. Figure 3 represents mean latency values and 95% confidence intervals across different rise/fall and plateau times for p2 peak.

A regression analysis was done to evaluate the extent of effect that rise/fall time, plateau time and combination of rise/fall and plateau times had on the latency of p2. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.001 ($p<0.05$), 0.183 ($p<0.05$) and 0.183 ($p<0.05$) respectively. Further, a regression equation was generated for p2 latency which is as follows:

p2 latency = (0.016PT + 2.913RFT) – 23.503

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

Results of statistical analysis using Two-way repeated measures ANOVA showed a significant main effect of rise/fall time [$F(1,12) = 52.85$, $p<0.001$] on n3 latency of contralateral response. On other hand, there was neither a significant main effect of plateau time [F(2,24) = 2.78, p>0.05] nor an interactional effect between rise/fall time and plateau time [F(2,24) = 1.10, p>0.05] on n3 latency. Thus, the need for Bonferroni adjusted multiple comparisons was not felt. Figure 3 represents mean latency values and 95% confidence intervals across different rise/fall and plateau times for n3 peak.

The r^2 values were generated for plateau time alone, rise/fall time alone and for the combination of two using regression analysis which were 0.001(p<0.05), 0.139 (p<0.05) and 0.139 (p<0.05) respectively. A regression equation was also generated for n3 latency which is as follows:

n3 latency = [(-0.052 PT) + (3.056 RFT)] – 27.852

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

Ipsilateral response latency.

A Two-way repeated measures ANOVA was also done for ipsilateral responses across rise/fall times of 2 ms and 4 ms and plateau times of 0 ms, 2 ms and 4 ms, though only for n1 and p1 peaks. Later peaks were not subjected to statistical analysis owing to the non-fulfillment of the criteria for 30% response rate between any of the rise/fall time and plateau time pairs for these peaks.

The results of Two-way repeated measure ANOVA showed a significant main effect of rise/fall times [F(1,7) = 156.18, p<0.001] on the latency of n1. However, there was no significant main effect of plateau times [F(2,14) = 2.83, p>0.05] as wellas interactional effect between rise/fall and plateau times [F(2,14) = 1.23,

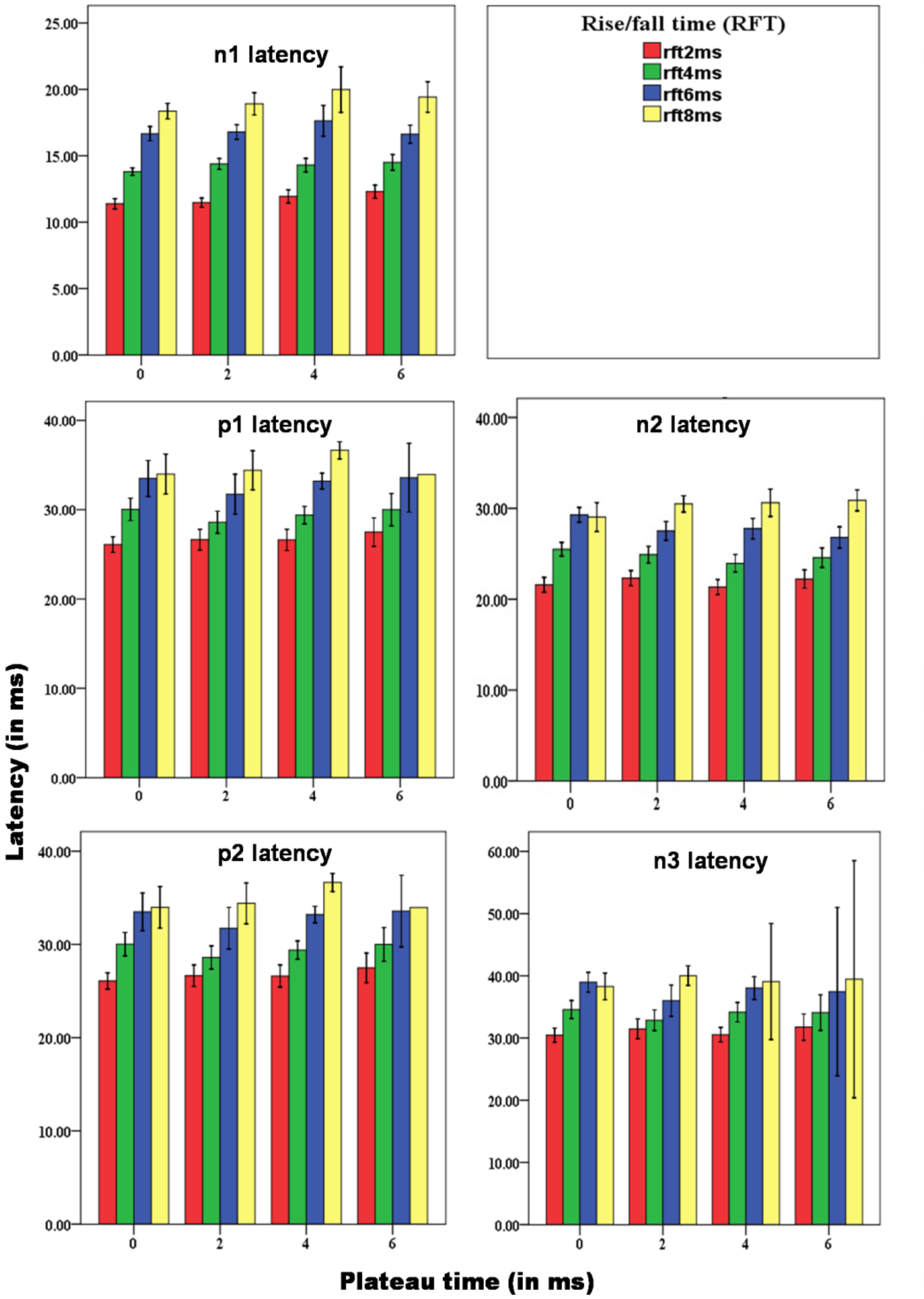

Figure 3. Mean and 95% confidence intervals across various rise/fall and plateau times for contralateral recording of oVEMP.

p>0.05] for n1 latency. Therefore, different rise/fall and plateau times pairs were not subjected to the Bonferroni adjusted multiple comparisons. Figure 4 represents mean latency values along with 95% confidence intervals across different rise/fall and plateau times for n1 peak.

The extent of contribution of effect of rise/fall time, plateau time and combination of rise/fall and plateau time was determined using regression analysis for latency of n1. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.043($p<0.05$), 0.207 ($p<0.05$) and 0.236 ($p<0.05$) respectively. Further, a regression equation was generated for n1 latency which is as follows:

n1 latency = (0.49PT + 2.058RFT) – 9.536

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

The p1 latency for ipsilateral recordings revealed no significant main effect of rise/fall times [$F(1,8) = 4.21$, $p>0.05$], plateau times[$F(2,16) = 0.14$, $p>0.05$] and also interactional effects between rise/fall and plateau times[$F(2,16) = 1.26$, $p>0.05$] on Two-way repeated measures of ANOVA. Hence, there was no need for further statistical analysis. Figure 4 represents mean latency values and 95% confidence intervals across different rise/fall and plateau times for p1 peak. Since, there was no main effect of any of the variables or interactional effects between variables, a regression analysis was not needed.

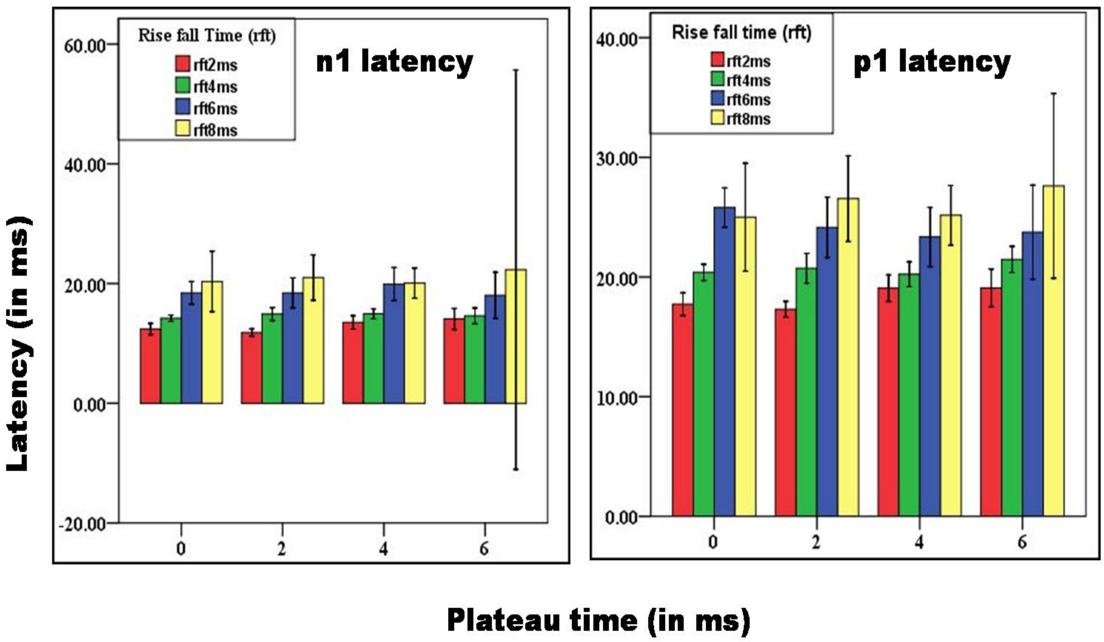

Figure 4. Mean and 95% confidence intervals across various rise/fall and plateau times for ipsilateral recording of oVEMP.

Amplitude

The effect of variation in rise/fall times and plateau times was explored and a trend towards reduction in amplitude with increase in rise/fall times and plateau times was observed for ipsilateral as well as contralateral responses. Table 3 shows mean and standard deviation for amplitude parameters across different rise/fall and plateau time combinations for contralateral as well as ipsilateral oVEMP responses. The absence of standard deviation values at certain combinations of rise/fall and plateau times was due to observation of response in only one individual at that combination and blank cells represent the absence of that peak complex response among all the subjects.

Table 3.
Mean and standard deviation for amplitude parameters of oVEMP for changes in rise/fall and plateau times for contralateral as well as ipsilateral responses.

Peak complexes	Rise/fall times	Contralateral response amplitude (mean ± SD)				Ipsilateral response amplitude (mean ± SD)			
		0 ms PT	2 ms PT	4ms PT	6 ms PT	0 ms PT	2 ms PT	4 ms PT	6 ms PT
n1-p1	2 ms	3.69 ± 2.93	3.46 ± 2.80	3.32 ± 2.99	2.81 ± 2.67	1.95 ± 0.92	2.04 ± 1.39	1.78 ± 0.71	1.64 ± 0.80
	4 ms	3.19 ± 2.89	2.40 ± 3.24	2.56 ± 2.46	2.50 ± 1.75	2.32 ± 1.17	1.83 ± 0.84	1.77 ± 0.96	1.68 ± 0.65
	6 ms	2.80 ± 2.05	2.66 ± 1.75	2.39 ± 1.31	2.29 ±1.50	2.62 ± 1.33	1.62 ± 0.76	2.05 ± 0.90	1.68 ± 0.23
	8 ms	2.17 ± 1.23	1.98 ± 0.83	1.95 ± 0.87	1.73 ± 0.46	1.80 ± 0.43	1.45 ± 0.40	2.12 ± 0.64	1.20 ± 0.40
p1-n2	2 ms	3.53 ± 2.30	2.86 ± 2.05	2.50 ± 1.55	2.61± 2.00	1.95 ± 1.01	1.80 ± 1.25	1.78 ± 1.04	1.50 ± 0.97
	4 ms	2.77 ± 2.60	2.30 ± 1.46	2.21 ± 1.72	2.45 ±1.63	1.91 ± 1.21	1.56 ± 0.80	1.55 ± 1.14	1.34 ± 0.62
	6 ms	2.58 ± 1.51	2.09 ± 1.19	2.15 ± 1.14	2.19 ± 0.96	2.07 ± 1.37	1.32 ± 1.25	2.19 ± 0.90	2.37 ± 0.46
	8 ms	1.41 ± 0.53	1.52 ± 0.68	1.54 ± 0.60	1.54 ± 0.49	1.15 ± 0.41	1.70 ± 0.41	1.57 ± 0.27	1.45 ± 0.36
n2- p2	2 ms	3.08 ± 2.09	2.33 ± 1.56	2.35 ± 1.83	2.45 ± 1.89	2.00 ± 1.46	2.18 ± 1.80	2.39 ± 1.72	2.47
	4 ms	2.67 ± 1.90	2.14 ± 1.57	2.66 ± 1.89	3.17 ± 1.51	1.76 ± 1.07	2.00 ± 2.03	2.39 ± 1.72	1.32 ± 1.83
	6 ms	2.63 ± 1.60	2.14 ± 0.83	2.79 ± 1.42	1.93 ± 1.98	2.58 ± 1.92	2.20 ± 0.84	2.12 ± 1.12	2.10 ± 1.15
	8 ms	1.46 ± 1.13	2.09 ± 0.55	2.34 ± 0.86	2.25 ± 1.17	2.45	2.24 ± 0.59	2.68 ± 1.73	2.85 ± 1.44
p2-n3	2 ms	2.53 ± 1.46	2.03 ± 1.19	2.34 ± 1.51	2.38 ± 1.39	2.25 ± 1.21	2.55 ± 2.11	1.89 ± 2.19	1.97 ± 1.26
	4 ms	2.36 ± 1.57	2.42 ± 1.80	2.90 ± 1.57	2.45 ± 1.57	1.97 ± 1.38	2.67 ±2.18	2.28 ± 1.65	2.16 ± 0.91
	6 ms	1.69 ± 1.37	1.99 ± 1.01	2.54 ± 1.95	2.19 ± 0.47	2.32 ± 1.83	2.04 ± 0.82	3.65 ± 2.60	1.66 ± 0.61
	8 ms	1.62 ± 0.91	1.65 ± 0.49	2.04 ± 0.50	2.02	1.87	1.46	2.04	

Note: ‘PT’: plateau time; ‘ms’: millisecond ; ‘SD’: standard deviation.

Contralateral response amplitude.

A Two-way repeated measures ANOVA was carried out to investigate the statistical significance of the trend towards reduction in amplitude with increasing rise/fall and plateau time for peak-to-peak amplitude. The results revealed a significant main effect of rise/fall times on n1-p1 peak-to-peak amplitude [$F(1,32) = 26.08$, $p<0.001$]. However, there was neither a significant main effect of plateau times [$F(2,64) = 1.12$, $p>0.05$] nor an interactional effect of plateau and rise/fall times [$F(2,64) = 0.695$, $p>0.05$] on n1-p1 contralateral peak-to-peak amplitude. Further, there was no need for Bonferroni adjusted multiple comparisons for different rise/fall times as only two rise/fall times were considered for statistical analysis. Additionally, this was also not needed for plateau times due to a lack of significant main effect of plateau times on the amplitude of n1-p1. Figure 5 represents mean amplitude and 95% confidence intervals across different rise/fall and plateau times for n1-p1 peak complex.

The extent of contribution of rise/fall times and plateau times had on the amplitude of n1-p1 was determined. A regression analysis was done for plateau time alone, rise/fall time alone and combination of rise/fall time and plateau time which yielded r^2 values of 0.004 ($p<0.05$), 0.019 ($p<0.05$) and 0.023 ($p<0.05$) respectively. Further, a regression equation was generated for n1-p1 amplitude which is as follows:

n1-p1 amplitude = (0.227 PT + 0.800 RFT) – 4.749

where ‘PT’ stands for plateau time and ‘RFT’ for rise/fall time.

The amplitude of p1-n2 showed a significant main effect of rise/fall times [$F(1,27) = 15.78$, $p<0.001$] and plateau times [$F(2,54) = 11.56$, $p<0.001$]. However, there was no significant interactional effect between rise/fall and plateau times [F(2,54) = 1.09, p>0.05] for the amplitude of p1-n2. The Bonferroni adjusted multiple comparisons for pair-wise comparison revealed significant difference between the plateau times of 0 ms and 2 ms ($p<0.05$) and also 0 ms and 4 ms ($p<0.001$) but not between 2 ms and 4 ms ($p>0.05$). As only two rise/fall times were taken for statistical analysis, Bonferroni adjusted multiple comparisons was not required for rise/fall times. Figure 5 represents mean amplitude and 95% confidence intervals across different rise/fall and plateau times for p1-n2 peak complex.

The r^2 values were calculated for rise/fall time alone, plateau time alone and combination of rise/fall and plateau time using regression analysis in order to evaluate the degree of effect of each these parameters on p1-n2 amplitude measure. The r^2 values for rise/fall time alone, plateau time alone and combination of rise/fall and plateau time were 0.027 ($p<0.05$), 0.024 ($p<0.05$), and 0.50 ($p<0.05$), respectively. A regression equation was generated for p1-n2 amplitude which is as follows:

p1-n2 amplitude = [(-0.352 PT) + (-0.617 RFT)] – 4.302

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

Results of Two-way repeated measures ANOVA also demonstrated no significant main effect of rise/fall times [$F(1,14) = 0.97$, $p>0.05$] and plateau times [$F(2,28) = 2.39$, $p>0.05$] on contralateral n2-p2 amplitude measure. But there was significant interactional effect of rise/fall and plateau times [$F(2,28) = 3.67$, $p<0.05$] on n2-p2 peak-to-peak amplitude. Hence, separate repeated measures ANOVA were done for rise/fall times of 2 ms and 4 ms at plateau times of 0 ms, 2 ms, and 4 ms and also for plateau times of 0 ms, 2 ms and 4 ms at rise/fall times of 2 ms and 4 ms. For variation in rise/fall times from 2 ms to 4 ms, the repeated measures ANOVA revealed no significant main effect of rise/fall times on n2-p2 peak-to- peak amplitude at plateau times of 0 ms [$F(1,26) = 3.14$, $p>0.05$] and 4 ms [$F(1,25) = 0.62$, $p>0.05$]. But there was a significant main effect of rise/fall times at plateau time of 2 ms [$F(1,19) = 6.33$, $p<0.05$] for n2-p2 peak-to-peak amplitude. For changes in plateau times from 0 ms to 4 ms, there was no significant main effect of plateau times on p1 latency at rise/fall time of 2 ms [$F(2,50) = 2.27$, $p>0.05$]. But there was marginally significant main effect of plateau times on rise/fall time of 4 ms [$F(2,34) = 3.14$, $p = 0.056$]. The Bonferroni adjusted multiple comparisons was not required for rise/fall times due to consideration of only two rise/fall and plateau times for comparison. Results of Bonferroni adjusted multiple comparisons for plateau times revealed marginally significant difference at rise/fall time of 2 ms ($p = 0.098$) and 4 ms ($p = 0.083$) between the plateau times pair of 0 ms and 2 ms. However, there was no significant difference for other pairs at rise/fall times of 2 ms and 4 ms. Figure 5 represents mean amplitude and 95% confidence intervals across different rise/fall and plateau times for n2-p2 peak complex.

A regression analysis was done for plateau time, rise/fall time and for combination of rise/fall time and plateau to determine the extent of effect of each of these parameters on n2-p2 amplitude. The r^2 values for plateau time alone, rise/fall time alone and combined condition were 0.007 ($p<0.05$), 0.002 ($p<0.05$) and 0.009 ($p<0.05$) respectively. Further, a regression equation was generated for n2-p2 amplitude which is as follows:

n2-p2 amplitude = (0.172 PT + 0.152 RFT) – 3.097

where ‘PT’ stands for plateau time and ‘RFT’ for rise/fall time.

For p2-n3 peak-to-peak amplitude, the results of statistical analysis using Two-way repeated measures ANOVA revealed no significant main effect of rise/fall time [$F(1,12) = 0.28$, $p>0.05$] and plateau time [$F(2,24) = 0.33$, $p>0.05$]. Further, there was also no significant interactional effect between rise/fall and plateau times [$F(2,24) = 1.16$, $p>0.05$]. Therefore, Bonferroni adjusted multiple comparisons for pair-wise comparison was not required. Since, there was no main effect of any of the variables or interactional effects between variables, a regression analysis was not needed. Figure 5 represents mean amplitude and 95% confidence intervals across different rise/fall and plateau times for p2-n3 peak complex.

Ipsilateral response amplitude.

A Two-way repeated measure ANOVA was carried out only for n1-p1 peak-to-peak amplitude as response rate was lower than the desirable criteria for other peak complexes. Results revealed a significant main effect of plateau times [$F(2,16) = 4.63$, $p<0.05$] on n1-p1 peak-to-peak amplitude. On other hand, there was no significant main effect of rise/fall times [$F(1,8) = 0.002$, $p>0.05$] and also no interactional effect between rise/fall times and plateau times [$F(2,16) = 2.29$, $p>0.05$] on n1-p1 peak-to-peak amplitude. Further, Bonferroni adjusted multiple comparisons revealed significant difference only between 4 ms and 0 ms plateau time pair ($p<0.05$). Figure 5 represents mean amplitude and 95% confidence intervals across different rise/fall and plateau times for n1-p1 peak complex.

With a view to determine the extent of effect that the rise/fall time, plateau time and the combination of both casted on n1-p1 amplitude, regression analysis was done. The r^2 values were obtained for rise time alone, plateau time alone and combined condition which were 0.007 ($p<0.05$), 0.001 ($p<0.05$) and 0.008 ($p<0.05$) respectively. A regression equation was also generated for n1-p1 amplitude which is as follows:

n1-p1 amplitude = (0.101 PT + 0.048 RFT) – 2.180

where 'PT' stands for plateau time and 'RFT' for rise/fall time.

Threshold

Threshold was measured across different rise/fall and plateau time combinations. It was defined as the lowest intensity level where n1-p1 complex was visually detected. For threshold measure, the later peaks were not considered due to lower response rate of these peaks in the present study. On observation of mean values, a trend towards elevation of threshold was noticed with increase in rise/fall and plateau times for ipsilateral as well as contralateral responses. The contralateral thresholds were observed to be lower (better) across different rise/fall and plateau times when compared to the ipsilateral thresholds. Table 4 show mean and standard deviation for threshold of oVEMP for changes in rise/fall and plateau times for contralateral as well as ipsilateral responses.

Table 4.
Mean and standard deviation for threshold of oVEMP for changes in rise/fall and plateau times for contralateral and ipsilateral responses.

Rise/fall time	Contralateral response threshold				Ipsilateral response threshold			
	0 ms PT	2 ms PT	4 ms PT	6 ms PT	0 ms PT	2 ms PT	4 ms PT	6 ms PT
2 ms	115.86 ± 6.26	116.95 ± 7.18	118.24 ± 6.68	120.29 ± 6.14	121.77 ± 4.75	121.42 ± 4.87	121.95 ± 5.58	122.00 ± 4.70
4 ms	118.55 ± 5.70	118.58 ± 7.06	120.16 ± 5.69	120.35 ± 6.37	120.71 ± 5.97	122.00 ± 4.70	123.12 ± 4.03	121.92 ± 4.80
6 ms	119.54 ± 6.16	118.54 ± 5.50	119.50 ± 5.10	121.87 ± 4.78	121.42 ± 4.97	123.46 ± 3.75	122.77 ± 4.40	123.33 ± 4.08
8 ms	121.81 ± 4.76	119.37 ± 5.12	122.69 ± 4.38	124.00 ± 3.16	123.00 ± 4.47	125.00	125.00	121.66 ± 5.77

Note: 'PT': plateau time; 'ms': milliseconds

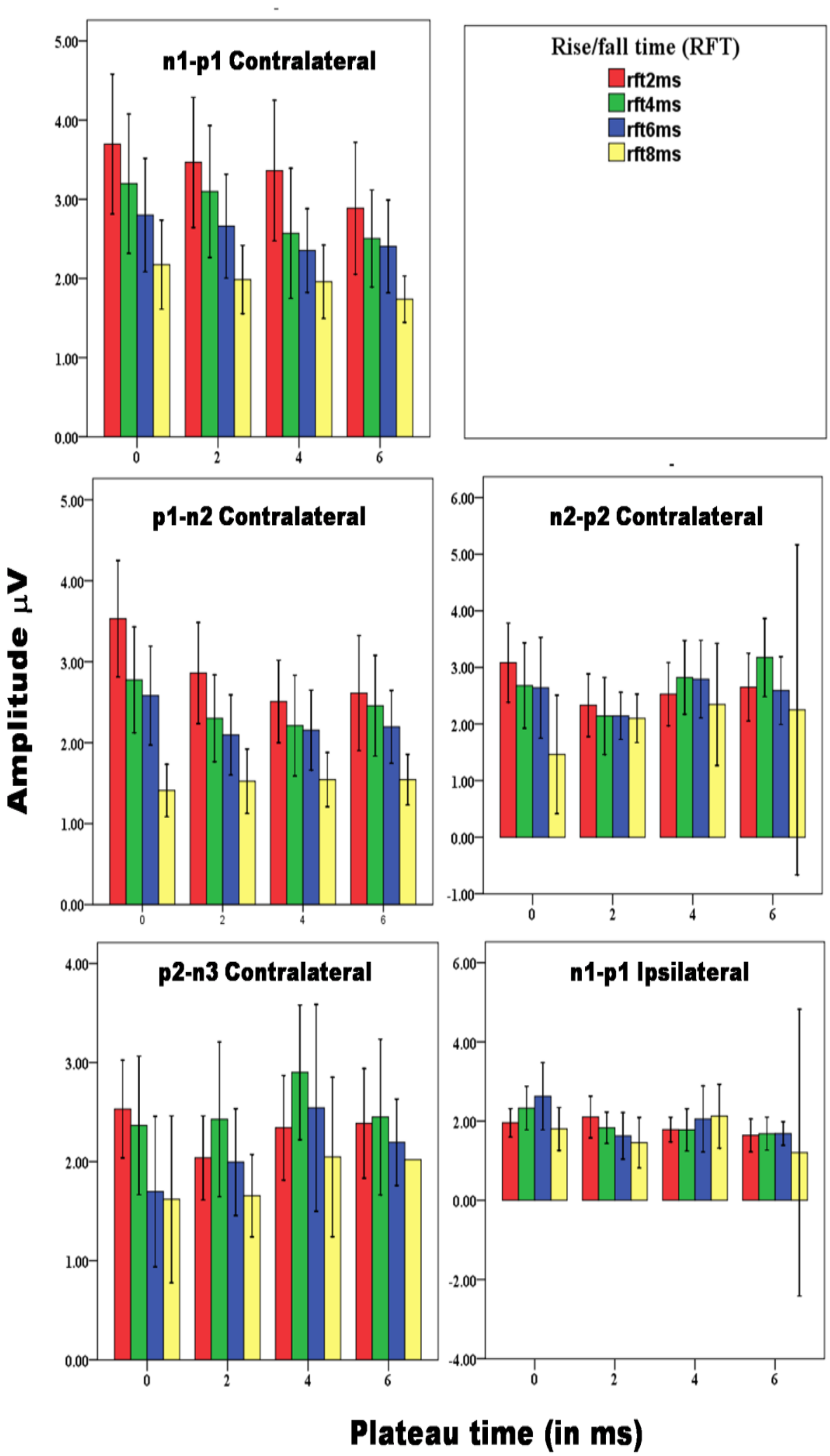

Figure 5. Mean and 95% confidence intervals across various rise/fall and plateau times of contralateral as well as ipsilateral recording.

Contralateral response threshold.

The results of statistical analysis using a Two-way repeated measures ANOVA for contralateral thresholds revealed a significant main effect of rise/fall times [F(1,28) = 8.19, $p<0.01$] as well as plateau times [F(2,56) = 3.54, $p<0.05$] on the threshold of oVEMP. Further, there was no significant interactional effect between rise/fall and plateau times [F(2,56) = 0.41, $p>0.05$] for contralateral thresholds. The Bonferroni adjusted multiple comparisons for pair-wise comparisons of rise/fall times were not felt due to the use of only two rise/fall times in the final statistics owing to a low response rate for other rise/fall times. However, this was necessitated for plateau times and the results showed significant difference only between 0 ms and 4 ms plateau times only ($p<0.05$). Figure 6 represents mean thresholds and 95% confidence intervals across different rise/fall and plateau times for contralateral recording.

The degree of impact of rise/fall time, plateau time and combination of rise/fall and plateau times on threshold was investigated. A regression analysis was done and r^2 values were obtained for rise/fall time alone, plateau time alone and combination of rise/fall and plateau time and these were 0.028 ($p<0.05$), 0.013 ($p<0.05$) and 0.040 ($p<0.05$) respectively. A regression equation was generated which is as follows:

Threshold = (0.927 PT + 2.192 RFT) – 112.957

where ‘PT’ stands for plateau time and ‘RFT’ for rise/fall time.

Ipsilateral response threshold.

Threshold measured for ipsilateral recordings showed no significant main effect of rise/fall times [$F(1,10) = 0.03$, $p>0.05$], plateau times [$F(2,20) = 2.32$, $p>0.05$] and also interactional effect between rise/fall and plateau times [$F(2,20) = 1.00$, $p>0.05$] when subjected to a Two-way repeated measures ANOVA. Thus, statistical analysis involving Bonferroni adjusted multiple comparisons was not required. Further, regression analysis was not carried out due to lack of significant main effect of rise/fall and plateau times on ipsilateral response threshold. Figure 6 represents mean thresholds and 95% confidence intervals across different rise/fall and plateau times for ipsilateral recording.

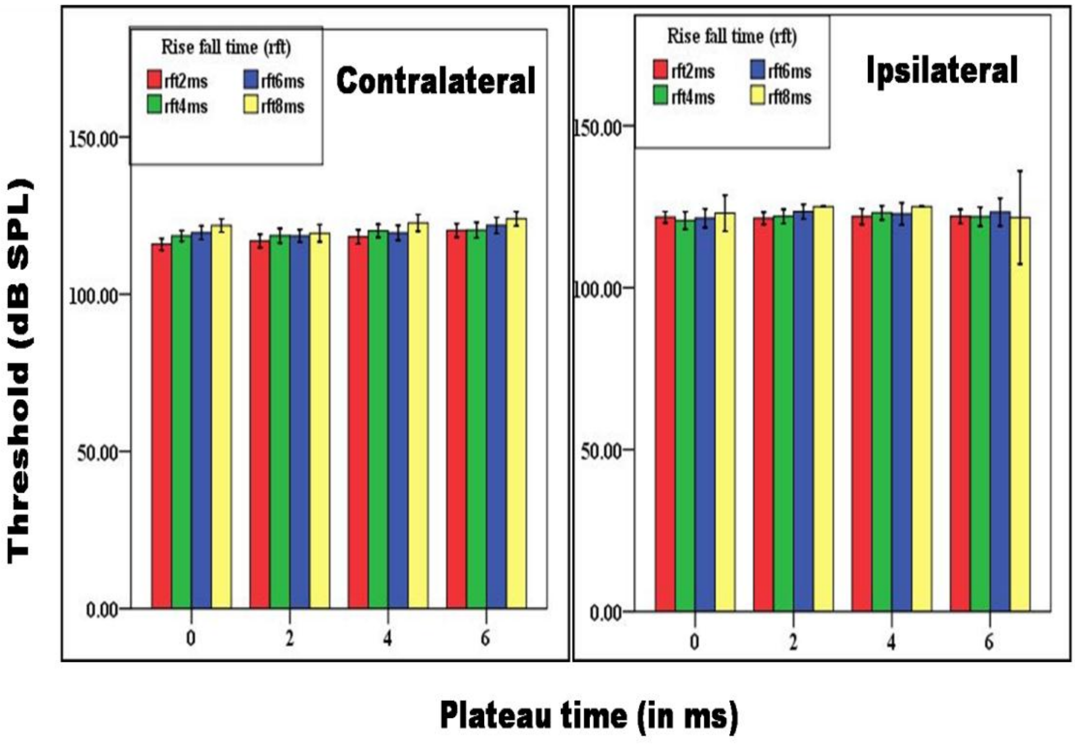

Figure 6. Mean and 95% confidence intervals across various rise/fall and plateau times of contralateral as well as ipsilateral recording.

In summary, varying rise/fall and plateau times had a noticeable effect on oVEMP parameters such as response rate, absolute latency and peak-to-peak amplitude for ipsilateral as well as contralateral recordings. In general, response rate decreased with increasing rise/fall and plateau times for ipsilateral as well as contralateral recordings, overall as well as for individual peaks. Latency of all the peaks (n1, p1, n2, p2 &n3) for contralateral recording increased with increasing rise/fall time from 2 ms to 8 ms whereas such effect was observed only for p1 and n2 peaks with increasing plateau times from 0 ms to 6 ms. For ipsilateral response latencies, only n1 peak latency increased with increasing rise/fall times whereas no such effect was observed for p1 latency. There was also no prolongation in latency with increasing plateau times for n1 and p1 peaks of ipsilateral recording. In addition, the extent of effect on latencies of all the peaks for ipsilateral as well as contralateral recording was greater for rise/fall times when compared to plateau times.

Amplitude of n1-p1, p1-n2 and n2-p2 peak complexes of contralateral responses reduced with increasing rise/fall times. On other hand, such effect was not for evidenced for p2-n3 peak complex. Also, with increasing plateau times, reduction in amplitude was evident only for p1-n2 and n2-p2 complex and not for n1-p1 and p2-n3 peak complexes during contralateral recordings. With respect to ipsilateral amplitude responses, n1-p1 amplitude reduced with increasing plateau times and had no effect of increasing rise/fall times. Further, the effect of rise/fall times was higher on amplitude of n1-p1, p1-n2, and p2-n3 of contralateral recording and also on amplitude of n1-p1 peak complex of ipsilateral recording. The plateau time had greater effect only for amplitude of n2-p2 complex.

In the present study, effect of varying rise/fall and plateau times on threshold parameter was also evaluated and it was found that contralateral threshold increased with increasing rise/fall and plateau times. Further, there was no effect of changing rise/fall and plateau times on threshold of ipsilateral recordings.

Chapter 5

Discussion

oVEMPs were recorded for various rise/fall times (2ms, 4ms, 6ms, & 8ms) and plateau times (0ms, 2ms, 4ms, & 6ms) from ipsilateral as well as contralateral inferior oblique muscles. The response rates, absolute latencies and peak-to-peak amplitudes were measured for five different peaks (n1, p1, n2, p2 & n3). Further, the thresholds, defined by the lowest level for presence of n1-p1 complex, were also evaluated.

The results showed overall response rate for contralateral recording to be 94% and ipsilateral recording to be 58%. A clear trend of decrease in response rate with increase in rise/fall times and plateau times was evident for overall response rate as well as individual peaks' prevalence. Evaluating the response rate of contralateral oVEMPs, Cheng et al. (2012) obtained response rates of 100% irrespective of changes in rise/fall times from 0.5 ms to 2 ms and plateau times from 2 ms to 4 ms. These findings were obtained for n1-p1 complex alone and appear comparable to 94% response rate of present study for contralateral recording of the same peak complex. However, the literature search from various search engines failed to reveal any relevant reports regarding the response rates of ipsilateral responses with the changes in rise/fall and plateau times. Hence, the findings of the present study may be considered the first in this context. Further, the present study also revealed higher response rates for contralateral responses compared to their ipsilateral counterparts at any given rise/fall and plateau times combination. This is in consonance with previously reported studies (Rosengren et al., 2005; Chihara et al., 2007; Todd et al., 2007; Govender et al., 2009; Wang et al., 2009; Murnane et al., 2011) who reported higher prevalence of the contralateral recording of oVEMP.

In the present study, the response rate was highest for n1 and p1 peaks and progressively reduced for later occurring peaks (n2, p2, & n3). These observations held good for both ipsilateral as well as contralateral recordings. However, there is a dearth of literature report regarding such observations.

Latency

The absolute latencies were measured for all five peaks for rise/fall times (2 ms to 8 ms) and plateau times (0 ms to 6 ms). The latencies of n1 and p1 peaks of contralateral recordings were found to prolong with increasing rise/fall times. The findings of the present study are in agreement with those reported previously (Lee et al., 2008; Cheng, Wu, & Lee, 2012). Both the set of studies reported prolongation of n1 as well as p1 latencies with increase in rise/fall time from 0.5 ms to 2 ms. Results of present study also showed a similar effect for later peaks (n2, p2 & n3) of contralateral response and for latency of n1 of ipsilateral recording with increasing rise/fall time. The effect of increasing rise/fall was on later peaks and ipsilateral responses have not been explored till date. Thus, there are no evidences for the same findings and the findings of the present study may be considered as the first in this regard.

The changes in rise/fall time and/or plateau time would correspond to changes in stimulus duration also. In this context, Welgampola and Colebatch (2001) investigated the effect of stimulus duration on the latency of oVEMP peaks by including stimulus durations from 1 ms through 20 ms. Results indicated towards reduction in latency of n1with increase in stimulus duration after 10 ms duration. However, p1 latency did not undergo any change after 5 ms. They attributed the finding of increase in the latencies to changes in stimulus duration. This finding however, cannot suffice the explanation of the results of the present study. The stimulus duration does not appear to be the sole reason behind prolongation of latencies. If it was so, the latencies for equal durations but different rise/fall and plateau times combinations should have been the same. But they were found to be very different in the present study. A 4 ms rise/fall time with 0 ms plateau time would be equal in duration to 2 ms rise/fall time with 4 ms plateau time (total stimulus duration of 8 ms). This notwithstanding, the mean latency of n1 for the former was found to be 13.80 ms while that for later was 11.94 ms. Thus, it does not appear that stimulus duration was the only factor. However, its contribution to the results cannot be completely neglected or irradicated. The possible explanation for the increase in latency with increasing rise/fall time could be hidden in the way the audio-vestibular nerve fibers respond to a stimulus. As the rise/fall time increases, the onset duration builds up and gradually increases for stimulus to attain its peak value (Cheng et al., 2012). This might cause slightly asynchronous firing of the onset fibers thereby resulting in prolongation of latencies of different peaks with increasing rise/fall times. The finding of no difference with changes in rise/fall time of the stimulus for some of the peaks of ipsilateral as well as contralateral origin might be attributed to inherent higher variability noticed for these peaks. A considerably lesser extent of impact of plateau time compared to rise/fall time further undermines the effect of duration to be the sole contributor for the observed effects.

The present study revealed no significant changes in the latency of n1 with variation in plateau times. But the differences were evident and significant when the latency of p1 for 0 ms plateau time was compared with the latency for plateau time of 2 ms. Likewise, the comparison between 0 ms and 4 ms plateau times for p1 latency also revealed significant difference. The findings of the present study appear to be in partial agreement with those reported previously in similar context (Lee et al., 2008; Cheng et al., 2012). While the present study revealed a significant effect of changing plateau time on p1 latency but not on n1 latency, the above mentioned studies reported a significant effect of neither. The differences in the findings between those reported previously and the present study might be attributed to a chance result as the effect of plateau time was significant only for p1 but not for most other peaks in the present study. The differences might also be brought about by the use of different plateau times between the studies. Lee et al. (2008) took into account the plateau times of 1 ms, 2 ms and 3ms which cannot form the pairs for which the differences were observed in the present study. Cheng et al. (2012) included 2 ms and 4 ms plateau time and observed no difference between these plateau times. In the present study also, there was no difference between these plateau times. However, Cheng et al. (2012) did not compare 0 ms plateau time with 2 ms or 4 ms plateau time. Had they compared, there might have been a likelihood of obtaining results similar to those of the present study. In the present study, a significant prolongation was also observed for n2 latency between the plateau times of 2 ms and 4 ms for contralateral response. In addition, there was no significant effect of changes in plateau time on n1 and p1 latency of ipsilateral responses. The effect of increasing plateau times on latencies of peaks of ipsilateral response needs to be explored to confirm the findings obtained in the present study. The lack of effect might be attributed to larger variability contributed by a considerably smaller number of participants (samples) in whom the ipsilateral responses were present.

Amplitude

The effect of changing rise/fall and plateau times was measured on peak-to-peak amplitude. Results showed a significant tendency for the peak-to-peak amplitudes of n1-p1 peak complex to reduce with increase in rise/fall times but no variation with changes in plateau times for contralateral recordings. This is in consonance with that reported previously in this context (Lee et al., 2008). They reported lowering of amplitude with increasing rise/fall time from 0.5 ms to 2 ms for n1-p1 complex. Though the rise/fall time and plateau times were different in the present study compared to those used by Lee et al. (2008), the trend appears to follow the same path of reduction in amplitude with increasing plateau times. The findings of the present study were also in agreement with those observed and reported by Cheng et al. (2012), who reported no effect of change in plateau times on n1-p1 peak-to-peak amplitude. Likewise, there was also reduction in amplitude of p1-n2 and n2-p2 complex with increase in rise/fall time but no significant effects for p2-n3 amplitude. Unfortunately, none of the other studies have evaluated effect of rise/fall time on peak-to-peak amplitude of these later peaks of oVEMP in the concurrent or past literature. They have neither been explored for ipsilateral responses nor for contralateral responses.

The findings of the present study of reduction in amplitude with increasing rise/fall times can be justified based on the concept of refractory period of audio-vestibular nerve. As vestibular nerve is a branch of vetibulocochlear nerve (8^{th} cranial nerve), same concept can be applied in this context. The vestibular nerve , like auditory nerve, has fibers with different spontaneous firing rates. The low spontaneous rate fibers fire in response to high intensity signal whereas high spontaneous rate fibers fire in response to low intensity signal (Winter, Robertson, & Yates, 1990). At lower rise/fall times, all types of spontaneous fiber are activated almost simultaneously due to shorter span between onset and attainment of full strength (intensity) and hence action potential amplitude is larger. On the contrary, the more gradual increase in stimulus intensity, consequent to larger rise/fall time, could cause a chain-like firing of the nerve fibers corresponding to different spontaneous rates and thus the amplitude of the corresponding action potential would be lower at any instant when compared to responses for shorter rise/fall times. With increase in rise/fall time, the onset duration builds up and increases and hence neural synchrony reduces due to fewer neurons firing simultaneously thereby resulting in smaller amplitude of the action potential at any given instance.

For the contralateral responses, there was no effect of plateau times on some peak-to-peak amplitudes. These findings are in agreement with those of Cheng et al. (2012) who also failed to show any effect of changes in plateau time on n1-p1 peak-to-peak amplitude. In contrast to above finding, Lee et al. (2008) reported reduction in peak-to-peak amplitude with increasing plateau time from 1 ms to 3 ms. This differences might have been result of difference in plateau times used. In the present study, 1ms and 3 ms plateau times were not included. Further, n1-p1 peak-to-peak amplitude of ipsilateral recording also did not show any change with increase in the plateau times. This is the only study which aimed at exploring the effect of changing plateau times on amplitude of different peak complexes other than n1-p1complex. Hence, the findings do not obtain substantial support from literature. However, the lack of difference for ipsilateral responses might be more due to a statistical phenomenon of larger variability due smaller sample size (response incidence in this case was lower for ipsilateral responses).

Threshold

There was a significant increase in contralateral threshold and lack of such effect on ipsilateral threshold with increasing rise/fall and plateau times. However, there are no investigations documenting effect of varying rise/fall and plateau times on oVEMP threshold. The present study can be considered as the first step in this direction. The threshold may be considered a variant of amplitude and thus might be expected to correlate with amplitude. In such a circumstance, the results for the effects of rise/fall and plateau time on amplitude might appear applicable for threshold. Hence, differences for contralateral recording but not for ipsilateral recording may be explained in the same vein. The use of slight asynchrony in onset related firing of nerve fibers, compounded by lower response rate resulting in more variability, can explain the existence of no difference for ipsilateral response.

Optimum combination

The results of the present study pointed towards an effect of rise/fall time as well as plateau time on oVEMP response parameters. However, effect of rise/fall time was considerably greater, as indicated by longer values of r^2 for each parameter, when compared to plateau times. At each of the plateau times, the rise/fall time of 2 ms was invariably associated with largest amplitudes and lowest thresholds for nearly all the peaks and this rise/fall time produced largest amplitudes and lowest thresholds, when used in conjunction with a plateau time of 0 ms. However, this is in contrast with those reported previously (Lee et al., 2008; Cheng et al; 2012). They found largest amplitudes for a combination of rise/fall times of 0.5 or 1 ms and the plateau time of 2 ms (Lee et al., 2008) and 0.5 ms of rise/fall time and 2 or 4 ms plateau time (Cheng et al., 2012). Nonetheless, the above studies arrived at the conclusion without the use of plateau time of 0 ms. Thus, 2 ms rise/fall time and 0 ms plateau time was associated with largest amplitudes and smallest thresholds along with comparable variability in all parameters to other rise/fall and plateau time combinations. This, when coupled with largest response prevalence (rate), points towards 2 ms rise/fall time and 0 ms plateau time as optimum combination for recording oVEMP and is hence recommended as optimum setting.

Chapter 6

Summary and Conclusion

oVEMP is a muscle potential recorded from Inferior oblique muscles of the eye. It is a biphasic potential representing the response of Utricle to intense acoustic, vibratory or galvanic stimulation. Like any other auditory evoked potential, oVEMPs are also likely to be affected by changes in stimulus related parameters. The variable use of stimulus related parameters may be the reason behind the differences shown in oVEMP findings in the concurrent literature, though evaluating the same aspect or population. One parameter that is constantly found to vary across studies is rise/fall and plateau time. The effect of rise/fall and plateau time on various response parameters has been investigated previously (Lee et al., 2008; Cheng et al., 2012), however not without disagreement in findings. In addition to the limited agreement between the two set of studies, these studies also used a restricted number of subjects. Further, they also did not consider 0 ms plateau time, a plateau time frequently used in studies when utilizing Blackman gating window. In addition to this, the effect of varying rise/fall and plateau time was also not explored on later peaks and threshold. Thus owing to the above discussed vagaries in literature, the present study aimed at evaluating the effect of rise/fall and plateau time on response rate, absolute latency, peak-to-peak amplitude and threshold parameters of oVEMP. An attempt was also made to overcome all the pitfalls of previously mentioned reports.

The study included rise/fall times of 2 ms, 4 ms, 6 ms and 8 ms and plateau times of 0 ms, 2 ms, 4 ms and 6 ms. oVEMPs were recorded from 50 ears of 50 participants (age range = 18-25 years) using two channel recording to obtain ipsilateral as well as contralateral responses. The acoustic stimuli were presented at

125 dB SPL and reduced in 10 dB steps to reach at the threshold. For recording of the responses, the stimuli used was of 500 Hz tone-burst presented at a repetition rate of 5.1 Hz. Keeping an analysis window of 64 ms, an averaged response for 150 sweeps was obtained. The response rates, absolute latencies, peak-to- peak amplitudes and thresholds for every rise/fall and plateau time combinations were measured. Further, these were subjected to statistical analysis using Two-way repeated measures ANOVA and Bonferroni adjusted multiple comparisons in order to determine the existence of significant difference for each parameter measured at various rise/fall and plateau times. Separate Repeated measures ANOVA were performed in case of the existence of significant interaction between the effects of rise/fall times and plateau times.

The results of the study indicated towards the existence of an effect of changing rise/fall and plateau time on various parameters of oVEMP. Response rate showed a trend towards a decline with increasing rise/fall and plateau times for ipsilateral as well as contralateral responses. The response rate was higher for contralateral responses when compared to the ipsilateral recordings. Among the peaks, the response rate was highest for n1 and p1 peaks irrespective of the response being ipsilateral or contralateral.

Latencies of oVEMP peaks revealed prolongation with increasing rise/fall times for all the peaks of contralateral recording but only n1 peak of ipsilateral recording. The latency of p1 of ipsilateral recording did not show any such effect with increasing rise/fall time. Unlike the rise/fall times, plateau times had an effect only on p1 and n2 peaks of contralateral recording. The possible reason for an increase of latency with increasing rise/fall and plateau is the building up of onset duration and gradual increase for stimulus intensity to attain its peak value, which might lead to asynchronous firing causing prolongation of latency.

The peak-to-peak amplitude also showed a trend towards lowering with advancing rise/fall and plateau times for n1-p1, p1-n2, and n2-p2 of contralateral recording. A similar effect was observed with increasing plateau times for p1-n2 and n2-p2 and not for n1-p1 and p2-n3 peak complex of contralateral recording. There was no effect of rise/fall time but a significant effect of plateau time on amplitude of n1-p1 peak for ipsilateral recording. This significant effect found can be explained on basis of asynchronous firing of nerve fibers, as a result of gradual increase in intensity, resulting in decrease in amplitude. This might be the effect of different spontaneous rate vestibular fibers responding sequentially rather than simultaneously.

The contralateral threshold showed a trend towards elevation with increase in rise/fall and plateau time but no such effect was found for ipsilateral recording. This can be justified based on findings of amplitude measure. With reduction in amplitude, there is a likelihood of increase in threshold which can be attributed to asynchronous firing of nerve fibers, as explained above for amplitude.

The findings of present study indicated towards largest amplitude and smallest threshold for a rise/fall time of 2 ms along with a plateau time of 0 ms for contralateral recording. The response rates were also highest for the above combination. In terms of the latencies, this combination revealed lowest variability. Thus, combination of 2 ms rise/fall time and 0 ms plateau time can be considered optimum for recording of 500 Hz acoustic tone-burst evoked oVEMPs. However, no specific trend could be observed for ipsilateral oVEMPs, probably due to larger variability and considerably lower response rates.

The present study investigated the effect of rise/fall and plateau time using rise/fall times of 2 ms, 4 ms, 6 ms and 8 ms and plateau times of 0 ms, 2 ms, 4 ms and 6 ms. The effect of in between rise/fall times (1 ms, 3 ms, 5ms & 7 ms) and plateau times (1 ms, 3 ms & 5 ms), which have been explored by one of the earlier studies, was not investigated in the present study. Therefore, future research can be carried out by considering the above mentioned rise/fall and plateau times. Also, more research may be required with regard to ipsilateral responses and extent of impact of varying rise/fall and plateau time on them may be further investigated.

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