Optimizing the response filter setting for acquisition of ocular vestibular evoked myogenic potential elicited by air-conduction tone bursts of 500 Hz

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Abstract

The clinical utility of ocular vestibular evoked myogenic potential (oVEMP) for identifying pathologies affecting the utricle is well established. However, a glance through the published reports has shown variable use of several stimulus and acquisition related parameters, especially the response filter setting. Although filter setting is a vital parameter for recording of any acoustically evoked potential, there is dearth of published reports regarding the optimum filter setting for the best recording of oVEMP. Therefore the present study aimed at evaluating the effects of changes in the response filter setting on parameters of oVEMP and identifying the optimum filter set for its reliable recording. For this, the contralateral oVEMP were obtained from 150 healthy individuals. The low-pass filters used were 500, 700, 1000, 1500, 2000, and 3000 Hz and the high-pass filters used were 0.1, 1, 10 and 30 Hz, in all possible combinations. The results revealed a significant reduction in n1 and p1 latencies with increase in high-pass and low-pass filters ($p < 0.05$) and a significant reduction in peak-to-peak amplitude of oVEMP with increasing the high-pass filter cut-off frequency ($p < 0.05$). Based on the findings, 0.1-1000 Hz appeared to be the optimum filter setting for recording oVEMP clinically.

Key words: Response filter set, air-conduction oVEMP, utricle

Introduction

Vestibular evoked myogenic potentials (VEMPs) are otolith initiated muscle responses elicited by acoustic (Colebatch & Halmagyi, 1992; Singh & Barman, 2013; Singh, Kumar, Aparna, & Barman 2014), vibratory (Halmagyi, Yavor, & Colebatch, 1995; Donnellan et al., 2010) or galvanic stimuli (Watson & Colebatch, 1998; Monobe & Murofushi, 2004; Welgampola & Colebatch, 2005; Iwasaki et al., 2011). These biphasic potentials can be recorded from several muscles of the body. These muscles include triceps muscles (Cherchi et al., 2009), soleus muscle (Cunha, Labanca, Tavares, & Goncalves, 2014), gastrocnemius muscle (Ruddissil & Hain, 2008), masseter muscles (Deriu et al., 2007), extensor muscles of the neck (Wu, Young, & Murofushi, 1999; Sakakura, Takahashi, Takayasu, Chikamatsu, & Furuya, 2005), sternocleidomastoid muscle (Colebatch & Halmagyi, 1992; Colebatch, Halmagyi, & Skuse, 1994) and inferior oblique muscle (Todd, Rosengren, & Colebatch, 2003; Rosengren, Todd, & Colebatch, 2005; Weber, Rosengren, Michels, Sturm, Straumann, & Landau, 2012).

Extra ocular muscles, especially the inferior oblique and the inferior rectus, are among several muscles of the human body that have been associated with the recording of VEMPs (Rosengren et al., 2005; Weber et al., 2012). When recorded from the extra-ocular muscles, the VEMP response has been found to show a negative peak with a latency of 10 ms (n1 or n10) and a positive peak with the latency of 15 ms (p1 or p15) (Todd et al., 2003). This biphasic potential is referred as ocular VEMP (oVEMP) (Rosengren et al., 2005; Chihara, Iwasaki, Ushio, & Murofushi, 2007; Todd, Rosengren, Aw, & Colebatch, 2007).

There has been a sudden surge in the studies on oVEMP ever since its first reports in early 2000s by Todd and colleagues (Todd et al., 2003; Rosengren et al., 2005). A large number of studies have been conducted on individuals with normal audio-vestibular system as well as those with different cochlear and vestibular pathologies and they have confirmed the otolithic, especially utricular, origin of the response (Halmagyi, Aw, Karlberg, Curthoys, & Todd, 2002; Minor, Carey, Cremer, Lustig, Streubel, & Ruckenstein, 2003; Zhou, & Cox, 2004; Modugno, Magnani, & Brandolini, 2006; Colebatch, 2010; Papathanasiou & Papacostas 2013). Subsequently the pathway for oVEMP has been reported to be similar to that of the transverse vestibulo-ocular reflex pathway, originating from the otolith organs and ending on the contralateral inferior oblique muscle of the eye, on the way crossing via the superior vestibular nerve, vestibular nuclei, and occulomotor nuclei (Jombik & Bahyl, 2005; Todd et al., 2007; Curthoys, Vulovic, Sokolic, Pogson, & Burgess, 2012).

During and even before the complete exploration of its pathway, oVEMP was being explored through clinical and basic research. The basic research, which later contributed to its clinical application in a big way, was mainly concentrated around its stimulus parameters. The effects of changes in several stimulus parameters like intensity (Murnane, Akin, Kelly, & Byrd, 2011), frequency (Chihara, Iwasaki, Fujimoto, Ushio, Yamasoba, & Murofushi, 2009; Singh & Barman, 2013, 2014), stimulus type (Todd et al., 2007; Curthoys, 2010), and repetition rate (Singh, Kadisonga, & Ashitha, 2014) on oVEMP responses were explored and as a result the optimum values of these parameters were suggested for the clinical recoding of oVEMP. Likewise, the response acquisition related parameters like electrode positioning (Murnane et al., 2011; Sandhu, George, & Rea, 2013) and degree of gaze elevation (Govender, Rosengren, & Colebatch, 2009; Murnane et al., 2011; Rosengren, Colebatch, Straumann, & Weber, 2013; Aisha & Singh, 2015) were explored and optimum values were recommended. The response filter setting (low-pass & high-pass filter) is one of the most important acquisition related parameters that affects all acoustically evoked potentials (Cacace, Shy, & Satya-Murti, 1980; Goodin, Aminoff, & Chequer, 1992) and oVEMP should be no different. However this aspect of oVEMP has largely gone unexplored.

Studies on oVEMP have used several different response filter settings. While most studies have used a low-pass filter of 1000 Hz and a high-pass filter of 1 Hz (Murnane et al., 2011; Piker, Jacobson, McCaslin, & Hood, 2011; Singh & Barman, 2013, 2014, 2015), some of the others have used band-pass filters of 5-500 Hz (Chihara et al., 2009; Seo, Saka, Ohta, & Sakagami, 2013), 0.5-500 Hz (Iwasaki et al., 2013), 10-750 Hz (Jerin, Berman, Krause, Ertl-Wagner, & Gurkov, 2014) and 20-2000 Hz (Nguyen, Welgampola, & Carey, 2010). This shows a lack of uniformity in the use of low-pass and high-pass filter in literature. Additionally, these studies have reported a wider range of mean values for the latencies (8 ms to 12 ms for n1 latency & 13 ms to 17 ms for p1 latency) and amplitude (3 µV to 10 µV) of oVEMP even among healthy individuals. This makes it difficult for the clinicians to use one of these values as normative for comparing against the pathological responses. The specific latencies and amplitudes of oVEMP found in each of the above mentioned studies are shown in Table 1. Although a large range of filter sets have been used, there is limited experimental evidence to support one of these as optimum or best filter set for eliciting air-conduction tone-burst evoked oVEMP.

Table 1.

Mean (and standard deviation) of latencies and amplitude of oVEMP found in studies using various band-pass filters

Band-pass filter used	Authors	n1 latency (in ms)	p1 latency (in ms)	Peak-to-peak amplitude (in µV)
1-1000 Hz	Murnane et al. (2011)	10.6 (1.0)	15.9 (1.0)	5.5 (4.4)
	Piker et al. (2011)	12.4 (1.0)	17.3 (1.3)	4.4 (3.1)
	Singh & Barman (2013)	NA	NA	11.2 (6.9)
	Singh & Barman (2014)	11.2 (0.9)	17.7 (1.1)	6.6 (1.2)
	Singh & Barman (2015)	11.2 (1.0)	16.3 (0.8)	11.4 (6.2)
5-500 Hz	Chihara et al. (2009)	11.0 (0.5)	16.0 (1.2)	7.2 (6.2)
	Seo et al. (2013)	10.4 (0.9)	16.4 (1.1)	NA
0.5-500 Hz	Iwasaki et al. (2013)	10.8 (0.7)	16.2 (1.3)	5.6 (4.7)
10-750 Hz	Jerin et al. (2014)	11.2 (0.2)	16.2 (0.2)	3.0 (0.4)
20-2000 Hz	Nguyen et al. (2010)	10.3 (0.5)	15.4 (0.8)	8.2 (6.2)

Note: ‘NA’- not mentioned in the study.

Recently Wang, Jaw and Young (2013) studied the effect of changing response filter on ocular vestibular-evoked myogenic potentials. In their study, oVEMP was recorded from 12 subjects with normal auditory and vestibular system using various high-pass (1 Hz, 10 Hz, & 100 Hz) and low-pass (500, 1000, & 2000 Hz) filters. Of these high-pass and low-pass filters, the low-pass filter of 1000 Hz was kept constant with all the high-pass filters to form band-pass filters of 1-1000 Hz, 10-1000 Hz and 100-1000 Hz. They found largest amplitude and 100% response rate for a band-pass filter of 1-1000 Hz. Further, the high-pass filter of 1 Hz was kept constant with all the low-pass filters to form band-pass filters of 1-500 Hz, 1-1000 Hz and 1-2000 Hz. For the variations in the low-pass filter, the authors reported no significant difference between the response filter conditions. Based on these results, the authors suggested that 1-1000 Hz was optimum for recording oVEMP. However, the conclusions drawn in the study are based on a very small sample size (N = 12). Further, the study did not compare the other frequently used filter sets in the literature. Hence the present study attempted to study the effects of response filter set on oVEMP elicited by air-conduction tone bursts of 500 Hz. The objectives of the present study were as follows:

1. To find the effect of changes in response filter setting on latency related parameters of oVEMP.
2. To find the effect of alterations in response filter setting on amplitude related parameters of oVEMP.
3. To find the effect of varying the response filter setting on signal-to-noise ratio of oVEMP waveforms.
4. To obtain the optimum filter setting for recording oVEMP based on the amplitude and signal-to-noise ratio.

Method

Participants

The study incorporated 150 (75 right & 75 left) ears of 150 individuals with normal auditory and vestibular systems in the age range of 18-35 years (mean = 22.7 years, standard deviation = 3.9 years) after obtaining the informed written consents. The normalcy of the auditory system was ensured through normal results on a battery of audiological tests including pure-tone audiometry, immittance evaluation, transient evoked oto-acoustic emissions and auditory brainstem response. The vestibular well-being of the participants was ensured through normal results on behavioural balance assessment using Fukuda stepping test, Romberg test, Tandem gait test and Past-pointing test. Additionally, a structured case history was obtained from the participants in order to ensure a lack of history of any otological, vestibular or neurological problems.

Procedure

Biologic Navigator Pro auditory evoked potential unit (version 7.2.1) was used to acquire oVEMP from all the participants. The testing was done in an acoustically treated room with ambient noise levels well within the acceptable levels for audiometric rooms (ANSI S3.1, 1991). The recording sites were cleaned with a commercially available abrasive gel to obtain absolute and inter-electrode impedance below 5 kΩ and 2 kΩ respectively. The electrodes were placed using adequate amount of commercially available conduction paste and secured in place with surgical plaster. The ground electrode was placed on the forehead, non-inverting electrode was placed 1 cm below the centre of the lower eye-lid and inverting 2 cm below the non-inverting. This electrode positioning used in the present study is similar to those used previously (Chihara et al., 2007; Singh & Barman, 2013, 2014, 2015).

The stimulus and acquisition parameters described by previous studies, except filter setting, were replicated for the acquisition of oVEMP (Chihara et al., 2007; Rosengren et al., 2009; Wang et al., 2009; Singh & Barman, 2013, 2014, 2015). Single-channel recording was done from the electrodes placed on the side contralateral to the stimulus ear as contralateral oVEMP was shown to be larger in amplitude than ipsilateral one (Singh, Valappil, & Mithlaj, 2015). The participants were instructed to elevate their gaze by 30^o in the mid-line in order to tense the inferior oblique muscle and increase its proximity to the surface during recording (Govender et al., 2009; Murnane et al., 2011; Rosengren et al., 2013). Alternating polarity 500 Hz tone-bursts, ramped using 1 ms rise/fall time and 2 ms plateau time, were delivered at an intensity of 125 dB peSPL through the standard insert earphones SINSER-012 of Biologic Navigator Pro evoked potential system. The repetition rate used was 5.1 Hz since this rate has been found to be most efficient in evoking oVEMP by virtue of producing largest signal-to-noise ratio, least amount of inter-individual variations and highest efficiency (Singh, Ashitha, & Kadisonga, 2014). Two hundred sweeps of electromyographic (EMG) activity was recorded using an epoch of 64 ms, which included a 10.5 ms pre-stimulus baseline recording. The responses were band-pass filtered using a number of different low-pass and high-pass cut-off frequencies. The low-pass cut-off frequencies used were 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz whereas the high-pass cut-off frequencies used were 0.1 Hz, 1 Hz, 10 Hz and 30 Hz, in all possible combinations to form band-pass filters. The slope of each of the filters was 12 dB/octave. These filter settings have been selected because these are the cut-offs that have most often been used in the studies on oVEMP in literature (Chihara et al., 2009; Iwasaki et al., 2009; Nguyen et al., 2010; Murnane et al., 2011; Piker et al., 2011; Seo et al., 2013; Wang et al., 2013; Jerin et al., 2014; Singh & Barman, 2013, 2014, 2015). The responses were multiplied by a factor of 30000, irrespective of the filter. The artifact rejection was switched-off in order to prevent unnecessary rejection of the inherently large amplitude myogenic potentials. The order of band-pass filter use was pseudo-random in order to avoid adulteration of the findings by the order of filter setting used. Adequate rest periods between recordings were given in order to avoid muscle strain and involuntary eye blinks.

Measures

The waveforms were analyzed by two independent experienced audiologists working in the area of vestibular assessment using VEMPs. An oVEMP was deemed present when the waveform was biphasic and it contained a negative going peak (n1) at about 10 ms (8-13 ms) followed by a positive going peak (p1) at about 15 ms (13-18 ms), as these are mean and range values reported for oVEMP peaks in the literature (Chihara et al., 2007; Cheng, Chen, Wang, & Young, 2009; Wang et al., 2009; Wegampola, Migliaccio, Myrie, Minor, & Carey, 2009; Nguyen et al., 2010; Park, Lee, Shin, Lee, & Park, 2010; Murnane et al., 2011; Piker, Jacobson, McCaslin, & Hood, 2011; Rosengren, Govender, & Colebatch, 2011; Winters, Campschroer, Grolman, & Klis, 2011; Taylor, Bradshaw, Halmagyi, & Welgampola, 2012a). The parameters analysed were n1 latency, p1 latency, and peak-to-peak amplitude. The SNR was calculated from each waveform using a MATLAB software using the following formula:

$\mathrm{SNR} = 20 \log(\mathrm{RMS}_{ep} / \mathrm{RMS}_{b})$

where 'SNR' is signal-to-noise ratio in dB, 'RMS_{ep}' is the root-mean-square of the oVEMP response in the time range of 8 to 20 ms and 'RMS_{b}' is the root-mean-square of the pre-stimulus baseline. The inter-judge reliability was high ($\alpha \geq 0.92$, Chronbach alpha test) for peak identification and the inter-judge agreement was also high for presence/absence of oVEMP ($K \geq 0.94$, Kappa coefficient).

Statistical analyses

The statistical analyses were performed using a commercially available software, Statistical Package for Social Science (SPSS, version 17.0). The comparison of each response parameter was achieved through separate two-way repeated measures ANOVA for low-pass filters and high-pass filters, separately for each response parameter. In case of a significant interaction between the variables, the use of focused tests of main effects through the techniques involving ANOVA have been recommended by several researchers (Kirk, 1982; Stevens, 1990; Rosnow & Rosenthal, 1989, 1991; Winer et al. 1991) and put to use by several studies of VEMP (Singh et al., 2014; Singh & Barman, 2015). Therefore in the present study, separate one-way repeated measures ANOVAs were done for all low-pass filters under each high-pass filter and all high-pass filters under each low-pass filter in case of significant interaction between the two kinds of filters. Bonferroni adjusted multiple comparisons were used for pair-wise comparison between different low-pass and high-pass filter pairs, in case a significant main effect was observed on the repeated measures ANOVA.

Results

Ocular VEMPs were recorded from randomly selected 75 right ears and 75 left ears (one ear of each participant) of 150 healthy individuals. The oVEMPs were present in 100% of the ears, irrespective of the band-pass filter. The individual averaged and grand averaged waveforms obtained for different high-pass and low-pass filters are shown in Figure 1.

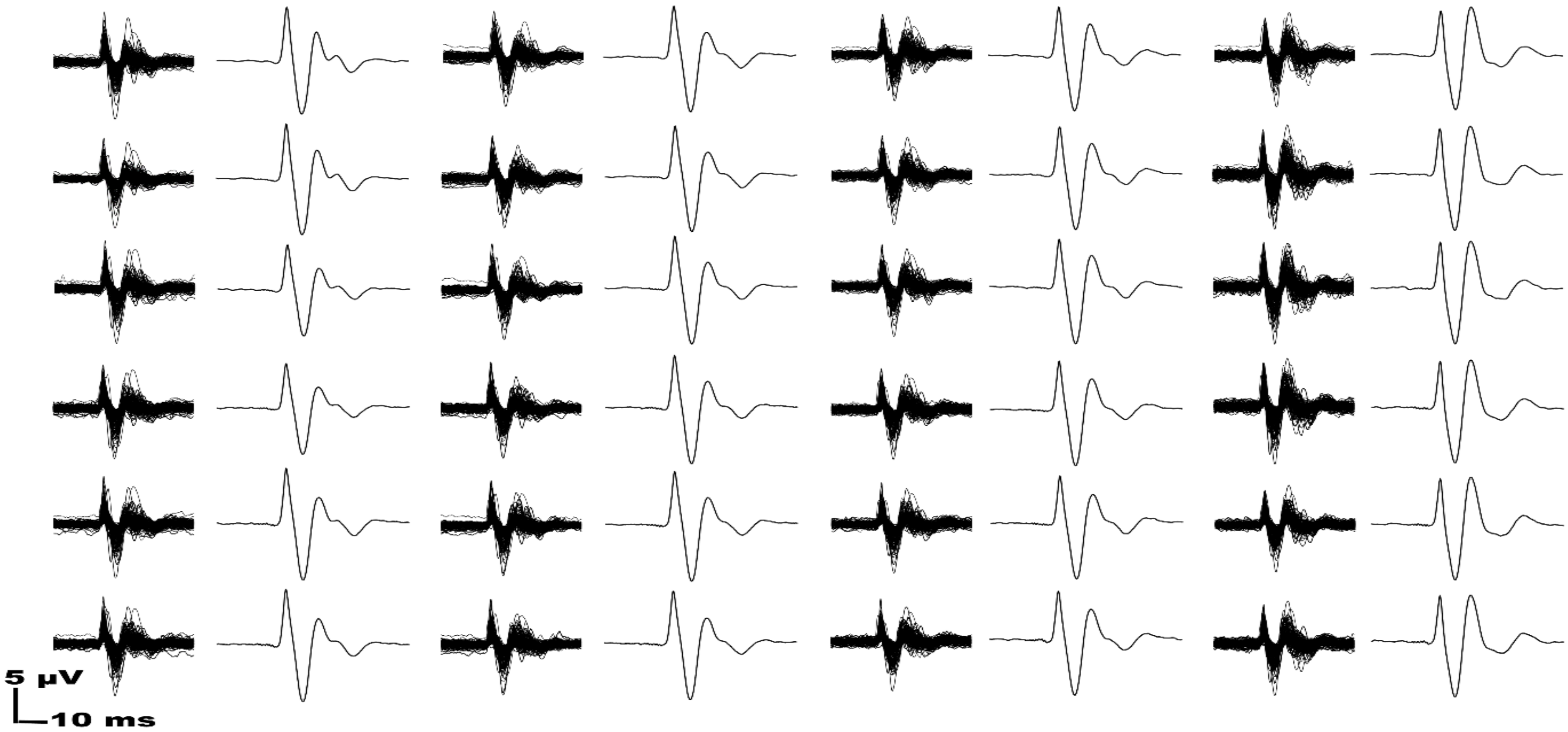


Figure 1: The individual averaged and grand averaged oVEMP waveforms acquired for various high-pass and low-pass filters from 150 healthy individuals. The high-pass filters of 0.1 Hz, 1 Hz, 10 Hz and 30 Hz are represented in columns (extreme left is for 0.1 Hz and extreme right for 30 Hz; progressively increasing from left to right) and low-pass filters of 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz are depicted in rows (topmost row is for 500 Hz and bottom most for 3000 Hz; progressively increasing from top to bottom direction).

The waveforms were analysed along three oVEMP parameters – latencies, amplitude and signal-to-noise ratio. The results for each of these parameters are discussed separately under specific headings in the subsequent sections that follow.

Effects of response filter setting on latencies of oVEMP

The latencies of n1 and p1 peaks were obtained and these were subjected to descriptive statistics for obtaining mean and standard deviation. Table 2 shows the mean and standard deviation of n1 and p1 latencies of oVEMP for various high-pass and low-pass filter combinations.

Table 2.

Mean and standard deviation of n1 and p1 latencies of oVEMP for various high-pass and low-pass filter combinations

Low-pass filters (in Hz)	High-pass filters (in Hz)							
	n1 latency (in ms)				p1 latency (in ms)			
	0.1	1	10	30	0.1	1	10	30
500	10.59 (0.50)	10.73 (0.57)	10.63 (0.53)	10.52 (0.56)	15.65 (0.92)	16.28 (0.85)	15.87 (0.86)	15.50 (0.90)
700	10.50 (0.57)	10.62 (0.61)	10.54 (0.57)	10.43 (0.62)	15.81 (0.87)	16.11 (0.81)	15.88 (0.79)	15.37 (0.73)
1000	10.47 (0.56)	10.50 (0.57)	10.47 (0.59)	10.31 (0.57)	15.90 (0.80)	16.15 (0.82)	15.90 (0.80)	15.37 (0.84)
1500	10.17 (0.92)	10.30 (0.60)	10.28 (0.65)	10.11 (0.72)	15.79 (0.83)	15.95 (0.83)	15.75 (0.83)	15.09 (0.81)
2000	10.31 (0.62)	10.35 (0.61)	10.29 (0.61)	10.14 (0.67)	15.87 (0.82)	15.92 (0.78)	15.79 (0.81)	15.16 (0.86)
3000	10.26 (0.63)	10.28 (0.68)	10.17 (0.61)	10.10 (0.82)	15.82 (0.82)	15.82 (0.86)	15.61 (0.78)	15.07 (1.00)

Note: Standard deviation values are mentioned within brackets for each band-pass filter.

The mean values from the table (Table 2) tend to suggest that increasing the low-pass or high-pass filter caused a subsequent shortening of n1 and p1 latencies. A two-way repeated measures ANOVA for high-pass and low-pass filters was done for n1 latency. The results revealed a significant main effect of high-pass filter [F(3,447) = 29.64, *p*< 0.001] and low-pass filter [F(5,745) = 118.76, *p*< 0.001] on n1 latency of oVEMP. There was no significant interaction between high-pass and low-pass filters [F (15, 2235) = 1.50, *p* > 0.05]. The Bonferroni adjusted multiple comparisons were done for pair-wise comparisons between different high-pass filters and also low-pass filters and the results revealed a significant reduction in n1 latencies with increase in high-pass as well as low-pass filters (*p* < 0.05), except a few pairs. Figure 2 shows the mean and 95% confidence intervals of n1 latencies across the low-pass and high-pass filters and the outcome of the Bonferroni adjusted multiple comparisons between various high-pass filters and low-pass filters.

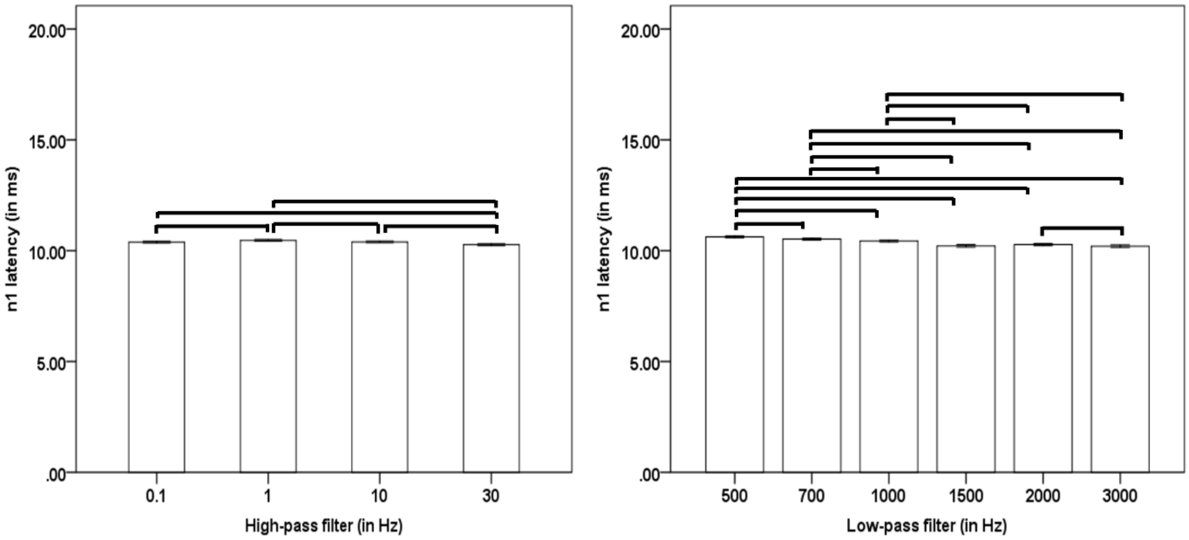


Figure 2: Mean and 95% confidence intervals of n1 latency of oVEMP and the outcome of Bonferroni adjusted multiple comparisons between various low-pass filters (right panel) and high-pass filters (left panel). The lines represent significantly different pairs on Bonferroni adjusted multiple comparisons (*p* < 0.05).

In terms of the p1 peak of oVEMP, there was a significant main effect of high-pass filter [F(3,447) = 233.09, *p* < 0.001] and low-pass filter [F(5,745) = 29.11, *p* < 0.001] on the latencies. Additionally there was a significant interaction between high-pass and low-pass filters [F(15,2235) = 11.47, $p < 0.001$]. In order to resolve the interaction, focussed tests of main effects involving separate one-way repeated measures ANOVAs for each high-pass as well as low-pass filters were taken up. There was a significant main effect of high-pass filters on p1 latency of oVEMP for low-pass filters of 500 Hz [F(3,447) = 76.04, $p < 0.001$], 700 Hz [F(3,447) = 82.82, $p < 0.001$], 1000 Hz [F(3,447) = 79.36, $p < 0.001$], 1500 Hz[F(3,447) = 115.13, $p < 0.001$], 2000 Hz [F(3,447) = 97.82, $p < 0.001$] and 3000 Hz [F(3,447) = 84.47, $p < 0.001$]. Bonferroni adjusted multiple comparisons at each of the low-pass filters revealed a significant difference in p1 latency between the high-pass filters ($p < 0.05$), except between some of high-pass filters at each low-pass filter. Figure 3 shows the mean and 95% confidence intervals of p1 latencies across the high-pass filters at each low-pass filter and the outcome of the Bonferroni adjusted multiple comparisons between various high-pass filters at each low-pass filter.

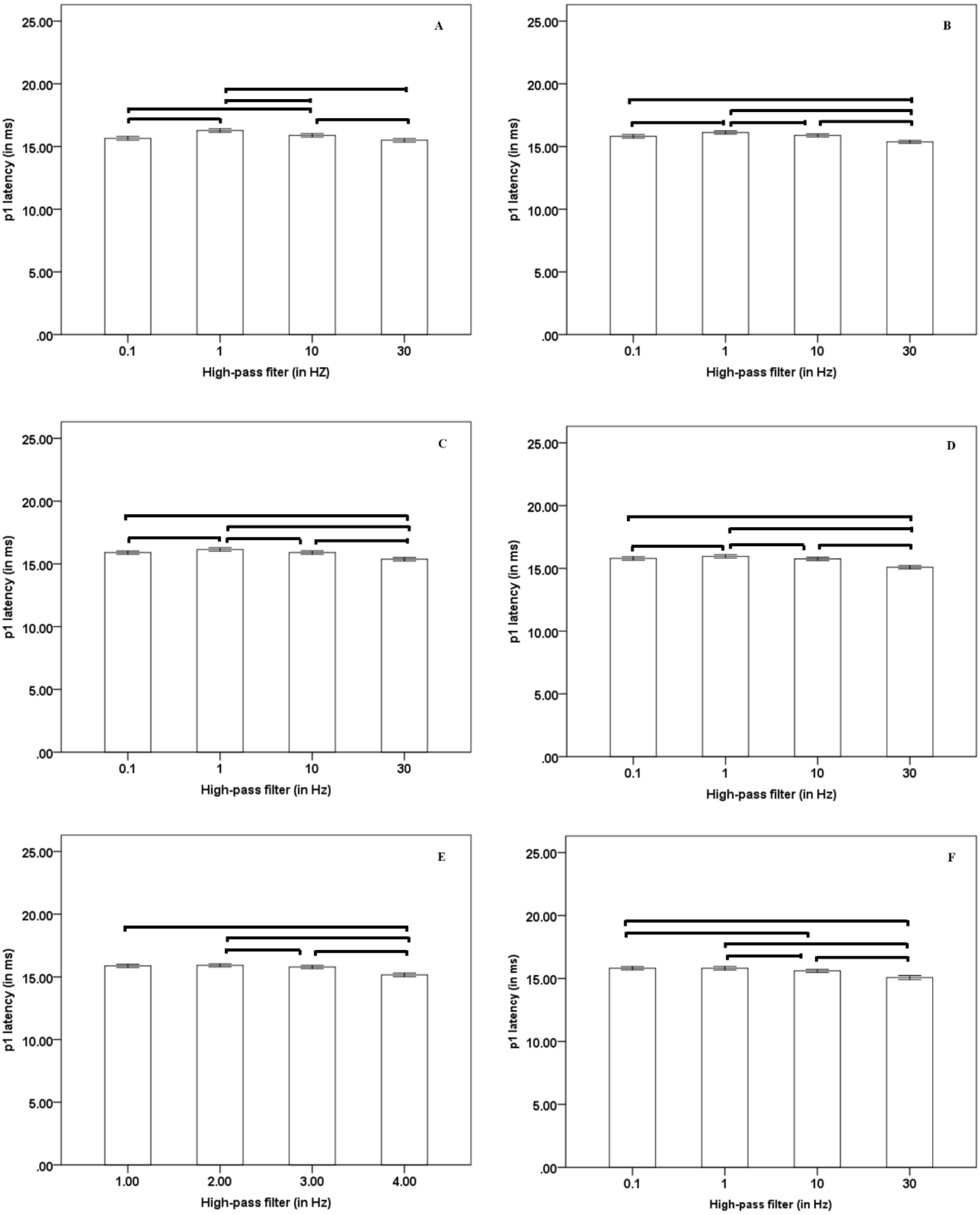


Figure 3: Mean and 95% confidence intervals of p1 latency of oVEMP and the outcomes of the Bonferroni adjusted multiple comparisons between various high-pass filters at each low-pass filter. Panels A, B, C, D, E and F represent the low-pass filters of 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz respectively.

Continuing with the focussed tests, one-way repeated measures ANOVA revealed a significant main effect of low-pass filters on p1 latency of oVEMP for high-pass filters of 0.1 Hz [F(5,745) = 7.69, $p < 0.001$], 1 Hz [F(5,745) = 26.30, $p < 0.001$], 10 Hz [F(5,745) = 11.83, $p < 0.001$] and 30 Hz [F(5,745) = 20.91, $p < 0.001$]. The Bonferroni adjusted multiple comparisons at each of the high-pass filter revealed a significant difference in p1 latency between the low-pass filters ($p < 0.05$), except between some of low-pass filters at each high-pass filter. Figure 4 shows the mean and 95% confidence intervals of p1 latencies across low-pass filters at each high-pass filters and the outcome of the Bonferroni adjusted multiple comparisons between various low-pass filters at each high-pass filter.

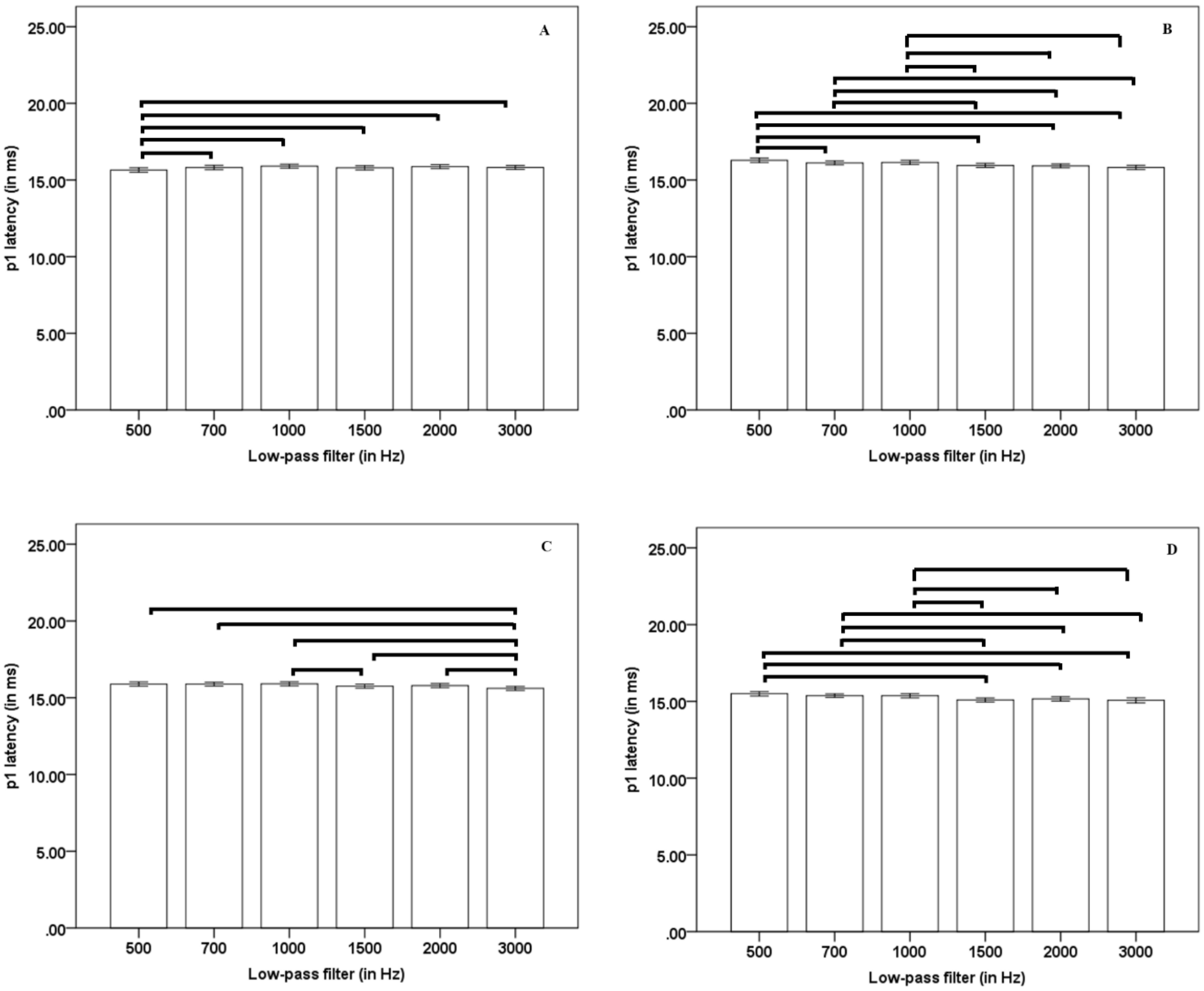


Figure 4: Mean and 95% confidence intervals of p1 latency of oVEMP and the outcomes of the Bonferroni adjusted multiple comparisons between various low-pass filters at each high-pass filter. Panels A, B, C and D represent the high-pass filters of 0.1 Hz, 1 Hz, 10 Hz and 30 Hz respectively.

Effects of response filter setting on amplitude of oVEMP

The peak-to-peak amplitudes were obtained from the response waveforms for each band-pass filter and subjected to descriptive statistics for obtaining mean and standard deviation. Table 3 shows the mean and standard deviation of peak-to-peak amplitude of oVEMP for various high-pass and low-pass filter combinations.

Table 3.

Mean and standard deviation of peak-to-peak amplitude and signal-to-noise ratio of oVEMP for various high-pass and low-pass filter combinations

Low-pass filters (in Hz)	High-pass filters (in Hz)							
	Peak-to-peak amplitude (in µV)				Signal-to-Noise ratio (in ms)			
	0.1	1	10	30	0.1	1	10	30
500	9.95	9.93	9.77	8.23	28.63	27.76	31.42	28.36
	(7.36)	(7.14)	(7.00)	(5.88)	(12.52)	(13.15)	(12.29)	(11.74)
700	10.27	9.79	9.62	8.34	29.70	27.59	30.34	29.73
	(7.83)	(6.92)	(6.73)	(5.77)	(11.97)	(12.23)	(11.92)	(12.10)
1000	10.62	9.94	9.67	8.32	30.25	28.43	30.28	28.89
	(7.67)	(7.06)	(6.69)	(5.87)	(13.17)	(12.18)	(11.74)	(11.01)
1500	10.59	10.08	9.76	8.41	31.39	27.12	29.32(1	29.21
	(7.62)	(7.34)	(6.97)	(5.89)	(13.50)	(12.30)	2.20)	(11.91)
2000	10.36	10.01	9.66	8.39	29.65	27.68	30.43	29.63
	(7.50)	(7.35)	(6.79)	(6.01)	(11.91)	(13.65)	(12.10)	(10.92)
3000	10.51	10.15	9.69	8.37	30.91	27.09	29.73	28.61
	(7.53)	(7.36)	(6.83)	(5.79)	(12.52)	(14.38)	(12.21)	(11.53)

Note: Standard deviation values are mentioned within brackets for each band-pass filter.

It can be observed from the mean values of peak-to-peak amplitude that increasing the high-pass filter appeared to result in reduction in the waveform amplitude whereas no such pattern seemed to be evident for changes in the low-pass filter setting. A two-way repeated measures ANOVA was done to evaluate the effect of different high-pass and low-pass filters on peak-to-peak amplitude of oVEMP. The results revealed a significant main effect of high-pass filter [F(3,447) = 72.77, $p < 0.001$] and low-pass filter [F(5,745) = 4.54, $p < 0.001$] on peak-to-peak amplitude of oVEMP. Further, there was significant interaction between high-pass and low-pass filters [F(15,2235) = 1.70, $p < 0.001$]. In order to resolve the interaction, focussed tests of main effects involving separate one-way repeated measures ANOVAs for high-pass as well as low-pass filters were undertaken. There was a significant main effect of high-pass filters on peak-to-peak amplitude of oVEMP for low-pass filters of 500 Hz [F(3,447) = 40.79, $p < 0.001$], 700 Hz [F(3,447) = 33.44, $p < 0.001$], 1000 Hz [F(3,447) = 49.80, $p < 0.001$], 1500 Hz [F(3,447) = 43.24, $p < 0.001$], 2000 Hz [F(3,447) = 41.02, $p < 0.001$] and 3000 Hz [F(3,447) = 47.02, $p < 0.001$]. The Bonferroni adjusted multiple comparisons at each of the low-pass filter revealed a significant difference in peak-to-peak amplitude between the high-pass filters ($p < 0.05$), except between some of the high-pass filters at each low-pass filter. Figure 5 shows the mean and 95% confidence intervals of peak-to-peak amplitudes across the high-pass filters at each low-pass filter and the outcome of the Bonferroni adjusted multiple comparisons between various high-pass filters at each low-pass filter.

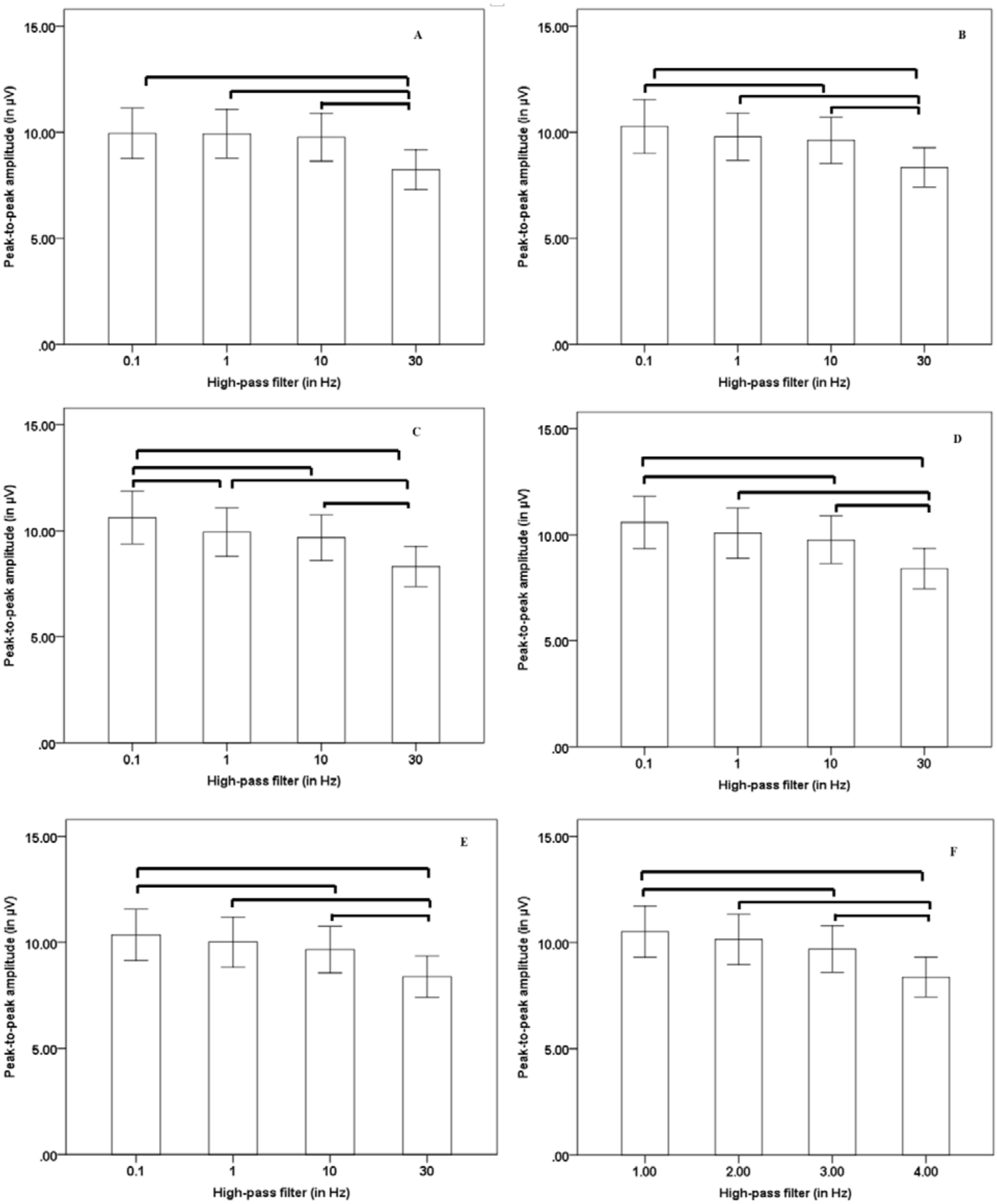


Figure 5: Mean and 95% confidence intervals of peak-to-peak amplitude of oVEMP and the outcome of Bonferroni adjusted multiple comparisons between various high-pass filters at each low-pass filter. Panels A, B, C, D, E and F represent the low-pass filters of 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz respectively.

Further, the focussed test of main effects involving one-way repeated measures ANOVA for low-pass filters under each high-pass filter revealed a significant main effect of low-pass filters on peak-to-peak amplitude of oVEMP for high-pass filters of 0.1 Hz [F(5,745) = 5.93, $p < 0.001$], 1 Hz [F(5,745) = 1.30, $p > 0.05$], 10 Hz [F(5,745) = 0.50, $p > 0.05$] and 30 Hz [F(5,745) = 0.53, $p > 0.05$]. The Bonferroni adjusted multiple comparisons at each of the high-pass filter revealed a significant difference in peak-to-peak amplitude between the low-pass filters ($p< 0.05$), except for some of low-pass filters at each high-pass filter. Figure 6 shows the mean and 95% confidence intervals of peak-to-peak amplitudes of oVEMP across the low-pass filters at each high-pass filter and the outcome of the Bonferroni adjusted multiple comparisons between various low-pass filters at each of the high-pass filters.

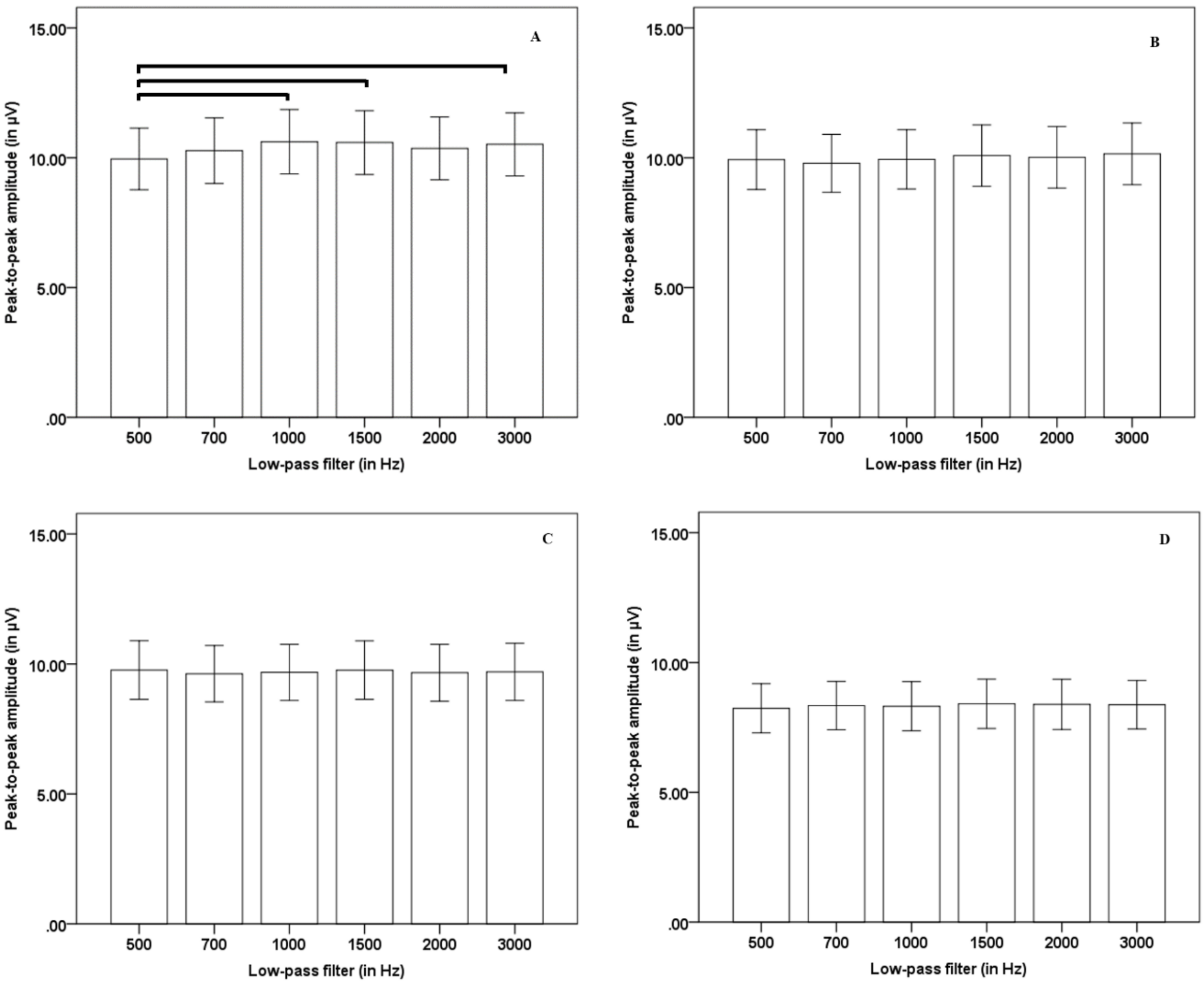


Figure 6: Mean and 95% confidence intervals of peak-to-peak amplitude of oVEMP and the outcome of Bonferroni adjusted multiple comparisons between various low-pass filters at each high-pass filter. Panels A, B, C and D represent the high-pass filters of 0.1 Hz, 1 Hz, 10 Hz and 30 Hz respectively.

Effects of response filter setting on signal-to-noise ratio of oVEMP waveforms

In terms of the signal-to-noise ratio of oVEMP, there was a significant main effect of high-pass filter [F(3,447) = 7.72, $p < 0.001$] but no significant main effect of low-pass filter [F(5,745) = 0.27, $p > 0.05$] on the signal-to-noise ratio. Further, there was significant interaction between high-pass and low-pass filters [F(15,2235) = 1.74, $p < 0.001$]. In order to resolve this interaction, focussed tests of main effects involving separate one-way repeated measures ANOVAs for each high-pass and low-pass filters were administered. There was a significant main effect of high-pass filters on SNR of oVEMP response waveforms for low-pass filters of 500 Hz [F(3,447) = 4.56, $p < 0.05$], 700 Hz [F(3,447) = 3.05, $p < 0.05$], 1000 Hz [F(3,447) = 1.94, $p > 0.05$], 1500 Hz [F(3,447) = 6.16, $p < 0.001$], 2000 Hz [F(3,447) = 2.64, $p < 0.05$] and 3000 Hz [F(3,447) = 5.75, $p < 0.05$]. The Bonferroni adjusted multiple comparisons at each of the low-pass filter revealed a significant difference in SNR between the high-pass filters ($p < 0.05$), except between some of the high-pass filters at each low-pass filter. Figure 7 shows the mean and 95% confidence intervals of signal-to-noise ratio of oVEMP response waveforms across the high-pass filters at each low-pass filter and the outcome of the Bonferroni adjusted multiple comparisons between various high-pass filters at each of the low-pass filters.

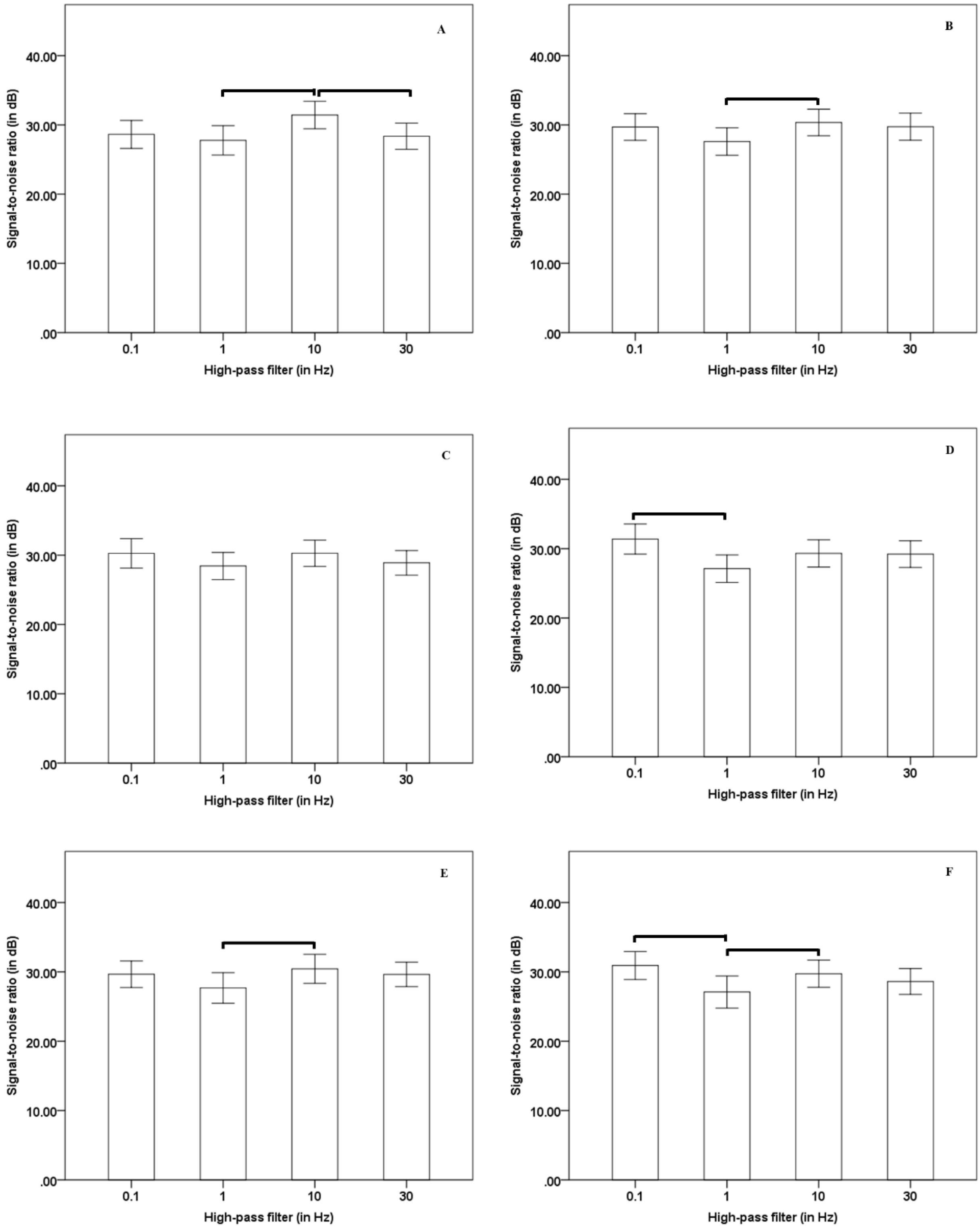


Figure 7: Mean and 95% confidence intervals of signal-to-noise ratio of oVEMP waveforms and the outcome of the Bonferroni adjusted multiple comparisons between various high-pass filters at each low-pass filter. Panels A, B, C, D, E and F represent the low-pass filters of 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz respectively.

Further, the focussed tests for evaluating the effects of low-pass filtering on the SNR of the oVEMP response waveforms demonstrated a significant main effect of low-pass filters on SNR for high-pass filter of 0.1 Hz [F(5,745) = 2.45, $p<0.05$] but not for 1 Hz [F(5,745) = 0.52, $p>0.05$], 10 Hz [F(5,745) = 1.58, $p>0.05$] and 30 Hz [F(5,745) = 1.00, $p>0.05$]. However, the Bonferroni adjusted multiple comparisons at each of the high-pass filter revealed no significant difference between the low-pass filters ($p > 0.05$). Figure 8 shows the mean and 95% confidence intervals of signal-to-noise ratio of oVEMP response waveforms across the low-pass filters at each of the high-pass filters.

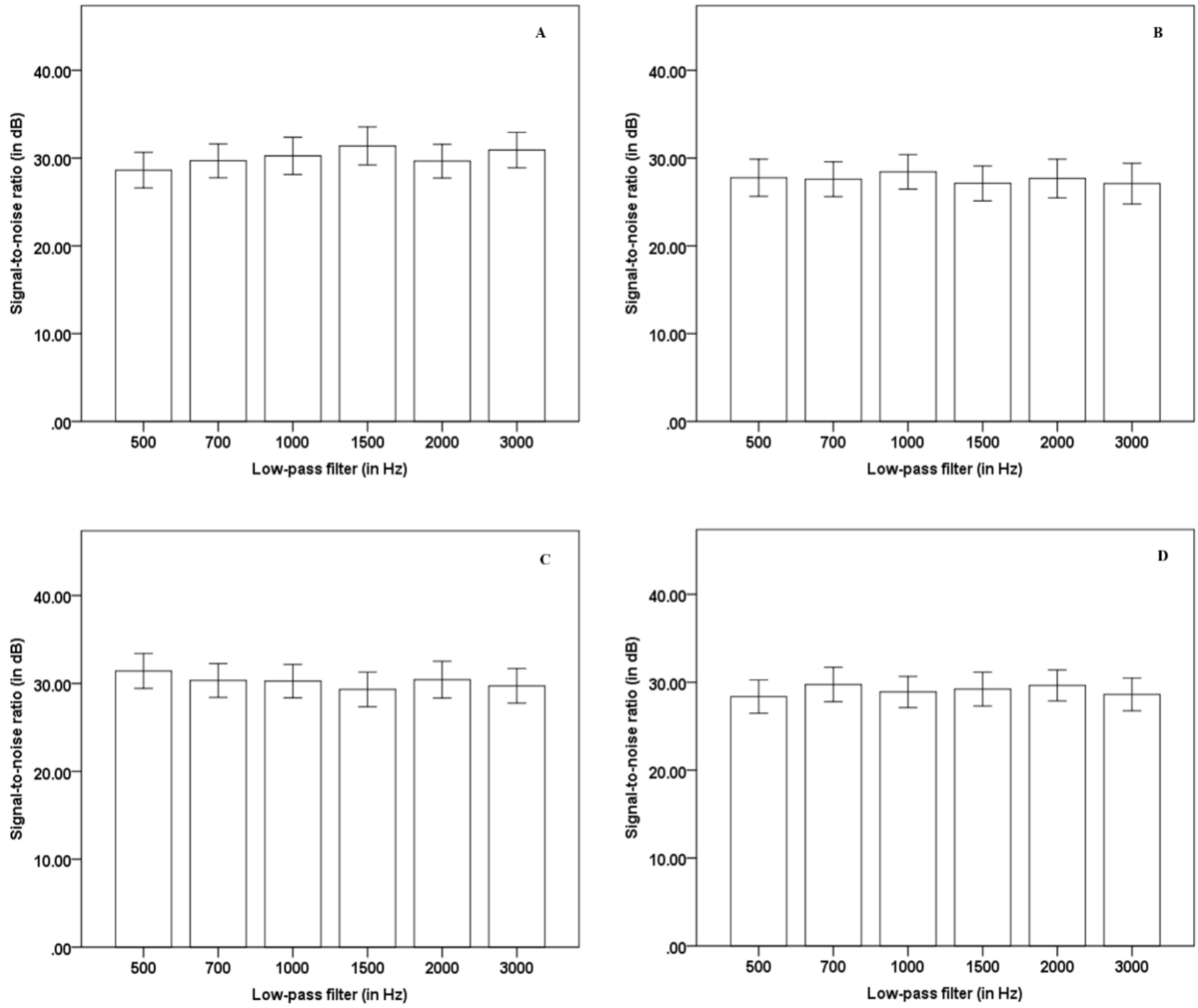
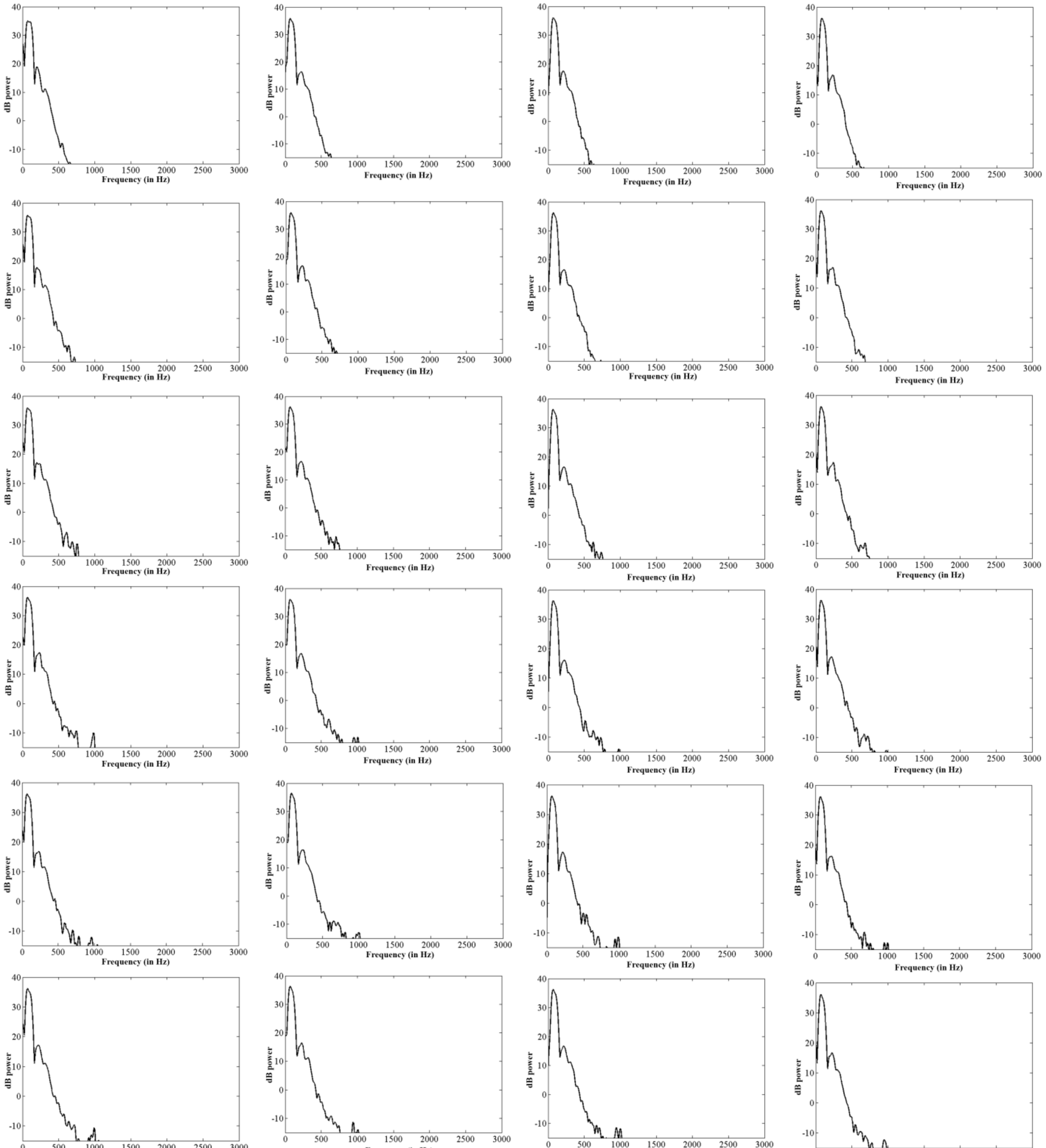


Figure 8: Mean and 95% confidence intervals of signal-to-noise ratio of oVEMP for various low-pass filters at each high-pass filter. Panels A, B, C and D represent the high-pass filter of 0.1 Hz, 1 Hz, 10 Hz and 30 Hz respectively.

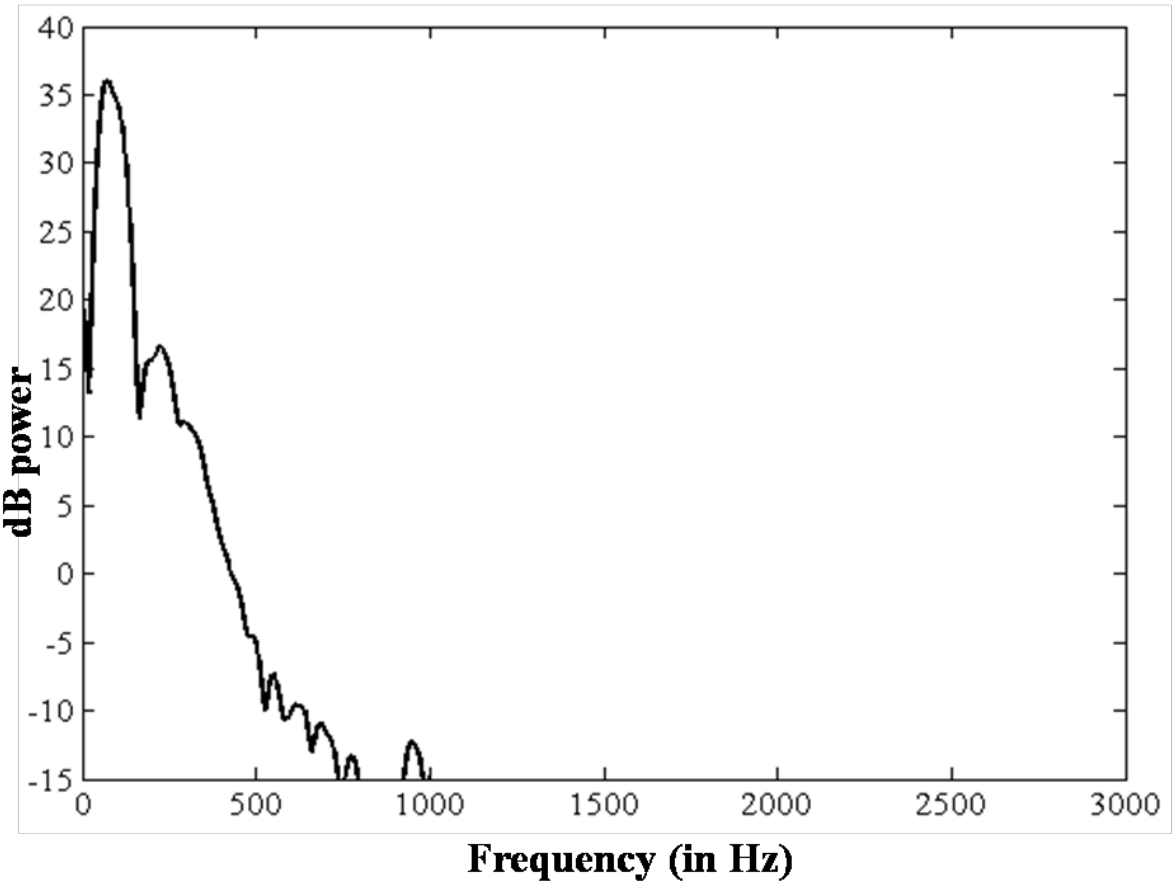
Ocular VEMPs were analysed for different band-pass filters. Overall it was found that the latencies reduced with increase in low-pass filter as well as high-pass filter. In terms of the peak-to-peak amplitude, there was significant reduction in amplitude with increase in high-pass filter but not in low-pass filter. There was no consistent pattern to the kind of effect that increasing the high-pass or low-pass filter had on the signal-to-noise ratio.

The power spectrum analysis

The power spectrum analysis was done to investigate the energy content in the oVEMP response waveform across the frequencies. For this, a MATLAB program was used. Power spectral density of the data was analyzed by using Welch modified periodogram method. Here the signal was divided into eight non overlapping windows with a hanning taper. The eight windows were then subjected to a 24576 point fast fourier transform and the spectral densities were averaged across the windows. This was the log transformed to obtain the power spectral densities in dB. The major energy was observed up to 500 Hz with the peak at around 100 Hz. There were no energy beyond 1000 Hz. Figure 9 shows the power spectrum of the response waveform of oVEMP of an individual.


dB power
40
30
20
10
0
-10
0
500
1000
1500
2000
2500
3000
Frequency (in Hz)

(A)



(B)

Figure 9: The power spectrum curves. (A): The power spectrum of oVEMP waveforms acquired for various high-pass and low-pass filters. The high-pass filters of 0.1 Hz, 1 Hz, 10 Hz and 30 Hz are represented in columns (extreme left is for 0.1 Hz & extreme right for 30 Hz; progressively increasing from left to right) and low-pass filters of 500 Hz, 700 Hz, 1000 Hz, 1500 Hz, 2000 Hz and 3000 Hz are depicted in rows (topmost row is for 500 Hz & bottom most for 3000 Hz; progressively increasing from top to bottom direction). (B): The power spectrum for the broadest band-pass filter (0.1-3000 Hz) used in the study has been zoomed to ensure ease of understanding of the components.

Discussion

The responses were obtained from 150 ears of 150 healthy individuals and they were found to be present in all the ears irrespective of the band-pass filter being used. This meant that the response rate of oVEMP was 100% for all the band-pass filters in the present study. This is in disagreement with the previous study in this regard which demonstrated significant reduction in response rate when the high-pass filter for recording oVEMP was changed from 1 Hz or 10 Hz to 100 Hz for the constant low-pass filter of 1000 Hz (Wang et al., 2013). Further, Wang et al (2013) did not observe a difference in response rate of oVEMP between the other band-pass filters (1-500, 1-1000, & 10-1000 Hz) which were similar to the findings of the present study. They suggested that the significant reduction in the response rate for this particular band-pass filter (100-1000 Hz) when compared to the other band-pass filters (1-1000 Hz & 10-1000 Hz) was because of the attenuation of significant amount of energy in the low frequency region as the peak energy was centred at about 100 Hz. Reduction in energy in these areas (below 100 Hz) would have caused much smaller waveforms and probably the absence of some of the already small amplitude waveforms in their study. In the present study also the major energy concentration was at around 100 Hz; however, the highest high-pass filter used was 30 Hz. This probably was not sufficient to completely eliminate the identification of responses in any individual, thereby causing a 100% response rate irrespective of the band-pass filter.

The results of the present study showed significant gradual shortening of latencies with increase high-pass as well as low-pass filter of the band-pass filter used for recording oVEMP. Although Wang et al (2013) observed a similar trend of reduction in latencies with increasing the low-pass and high-pass filters, the difference was significant only when the high-pass filter was increased from 1 to 100 Hz. Similar effects of changing the filter setting has been observed for other tone-burst evoked auditory evoked potentials like auditory brainstem responses (Hyde, 1985). The reason behind reduction in the latencies with increasing the low-pass and high-pass filter could be the phase distortion which is introduced by the high-pass and low-pass components of a band-pass filter (Hyde, 1985). The low-pass filter has been associated with the smoothening of the high-frequency components (Hyde, 1985). However, high-pass filter is believed to produce time lead components (negative delay) (Hyde, 1985). Furthermore, the high-pass filter effect was shown to be more pronounced compared to the low-pass filter. These factors in cohesion might have caused gradual shortening of the peak latencies in the present study.

In terms of the peak-to-peak amplitude, the results of the present study revealed significant progressive reduction in amplitude with increase in high-pass filter but not low-pass filter. This is again in cohesion with the findings of Wang et al (2013). These findings (no significant change in amplitude with changes in low-pass filter) could be attributed to the frequency composition of the oVEMP response which revealed only a small amount of energy between 500 Hz and 1000 Hz and almost no energy above 1000 Hz. Since the lowest low-pass filter in the present study was 500 Hz, changes in low-pass filter beyond 500 Hz did not significantly impact the amplitude as it possibly did not alter energy content within the response waveforms. Further, high-pass filter usually is associated depressing the amplitude of the given response and introducing an artificial succeeding peak of opposite polarity for the use of narrow filters (Hyde, 1985) like the one used in the present study. This might be one of the reasons behind the finding of reduction in the peak-to-peak amplitude of oVEMP with increase in the cut-off frequency of the high-pass filter. In addition, the major energy concentration in the power spectrum of the oVEMP waveforms (as revealed by the power spectrum analyses) is seen in the low frequency region with peak at about 100 Hz. This causes major changes in the response energy when the high-pass cut-off is progressively increased which in turn will yield responses with progressively smaller amplitudes.

The results of the present study showed significantly better signal-to-noise ratio for some of the high-pass filters; however there was no pattern to such differences. In fact most of the frequency pairs were significantly not different from each other. The differences might be attributed to the chance results. The lack of significant difference might be attributed to the attributes of a signal-to-noise ratio measurement. Signal-to-noise ratio is the difference between the signal level and the amplitude of the noise floor. Signal is a relatively stable factor in case of oVEMP as it describes the peak-to-peak amplitude which can be reliably recorded over several recordings (Nguyen et al., 2010; Tseng et al., 2010; Singh, Sarda, Sinha, & Tamsekar, 2011). However noise, which in case of electrophysiological tests like oVEMP would arise mainly from the physiological activities within the human body, is a random phenomenon (Dawson, 1950). This is likely to vary between epochs and also between individuals (Dawson, 1950). Therefore the difference between the response amplitude (signal), which is relatively constant, and noise would be less stable. This might have caused a lack of any pattern with variations in high-pass cut-off frequencies of the high-pass filter.

An optimum filter set should be capable of producing responses in all the individuals, should produce largest amplitude and relatively high signal-to-noise ratios. The results of the present study showed that increasing the low-pass filter cut-off to 1000 Hz will not only ensure acceptable frequency width that would accommodate all the possible signal (response) energy but also reduce the contamination from background noise, especially of high frequency. The use of high-pass filter of 0.1 Hz will ensure large amplitude which will ensure its detection even in older individuals with reduced muscle tone in whom the oVEMP amplitude is inherently small (Nguyen, Minor, Santina, & Carey, 2009). Therefore, the band pass filter of 0.1-1000 Hz appears to be the optimum filter setting for the clinical recording of oVEMP. This is in disagreement with the findings of Wang et al (2013) who found 1-1000 Hz as the optimum band-pass filter for recording of oVEMP. The differences between the studies could be attributed to the non-use of 0.1 Hz as a high-pass filter in the study by Wang et al (2013).

Conclusions

The findings of the present study revealed a significant trend towards shortening of the latencies with increase in the cut-off frequency of the low-pass and/or high-pass filter of a band-pass filter. Further, increasing the high-pass cut-off alone (and not low-pass) caused significant reduction in the peak-to-peak amplitude. The largest amplitudes were obtained for a band-pass filter of 0.1-1000 Hz. Although not significantly, this band-pass filter produced higher signal-to-noise ratio than most of the other band-pass filters. Therefore a combination of largest peak-to-peak amplitude and better signal-to-noise ratio for 0.1-1000 Hz band-pass filter makes this the optimum band-pass filter for clinical recordings oVEMP.

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