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Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults

by

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Abstract

Objective: The aim of this study was to compare cervical and ocular vestibular evoked myogenic potentials (cVEMP and oVEMP) in young gender- and age-matched black African and Caucasian male and female adults.

Design: A quasi-experimental between-subjects research design was utilised. This study was comparative in nature, thus data was collected in a cross-sectional manner from two age- and gender-matched racial groups, namely black African and Caucasian, and compared. Furthermore, interactions of gender and race were also examined in this research study.

Methods: Sixty healthy age- and gender-matched participants (30 black African, 30 Caucasian) between the ages of 18 – 25 years participated in this study. Fifteen males and fifteen females, within one year of the age of their racial participant counterparts, were included in each racial group. Latencies, peak-to-peak amplitudes and asymmetry ratios were analysed for both groups in these tests. Furthermore, auditory brainstem response (ABR) and electromyography (EMG) testing were conducted to investigate whether possible racial differences in VEMP tests could be attributed to differences in neural or muscular function.

Results: Black African participants demonstrated significantly shorter latencies of the n23 component of the cVEMP and the p15 component of the oVEMP, as well as larger peak-to-peak amplitude of the oVEMP response. Highly significant differences were found in all EMG measurements between the two racial groups, suggesting that these racial VEMP differences are primarily based on differences in muscular function between black Africans and Caucasians. Significant gender differences were observed in all tests conducted, with females predominantly displaying shorter latencies, while males had larger amplitudes.

Conclusions: Young black African adults demonstrated significant differences in both cVEMP and oVEMP responses, namely shorter latencies and larger amplitudes, in comparison to young Caucasian adults. Correlations with differences in EMG measurements suggest that these differences are primarily due to differences in muscular

function as opposed to neural function. Future research is required to confirm and expand on these findings.

Keywords

African
Auditory brainstem response (ABR)
Caucasian
Cervical vestibular evoked myogenic potentials (cVEMP)
Electromyography (EMG)
Race
Gender
Head diameter
Muscular characteristics
Ocular vestibular evoked myogenic potentials (oVEMP)

List of abbreviations

ABR	Auditory brainstem response
AC	Air conduction/air-conducted
ANOVA	Analysis of variance
BC	Bone conduction/bone-conducted
BPPV	Benign paroxysmal positional vertigo
cm	Centimetres
cVEMP	Cervical/collic vestibular evoked myogenic potential
dB HL	Decibels hearing level
dB nHL	Decibels normal hearing level
EMG	Electromyography/electromyographic
HSD	Honestly significant difference
M	Mean
mm	Millimetre
ms	Millisecond
µV	Microvolt
oVEMP	Ocular vestibular evoked myogenic potential
SCD	Superior semicircular canal dehiscence
p/s	Per second
SCM	Sternocleidomastoid
SD	Standard Deviation
VCR	Vestibulocollic reflex
VEMP	Vestibular evoked myogenic potential
VOR	Vestibulo-ocular reflex
VSR	Vestibulospinal reflex

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CHAPTER ONE

Introduction

1.1. Historical aspects and introduction to VEMPs

With increased understanding of vestibular pathophysiology and the ongoing development of new technology, techniques used to assess the vestibular system have developed extensively (Clarke, 2010). Vestibular evoked myogenic potentials (VEMPs) have a recent history, having only been described for the first time in the format known today in 1992 by Colebatch and Halmagyi and in 1994 by Colebatch, Halmagyi, and Skuse. However, their conclusions would not have been possible without the findings of prior studies.

Previous findings on myogenic (muscular) responses over the scalp and cervical muscles concluded that a vestibular response known as the “inion response” could be observed as a short-latency peak at 13 milliseconds (ms) (Bickford, Jacobson, & Cody, 1964; Cody, Jacobson, Walker, & Bickford, 1964; Bickford, Jacobson, & Galbraith, 1963). In more recent years, the inion response was re-examined by Colebatch and Halmagyi (1992) and Colebatch et al. (1994). Colebatch and colleagues (1994) recorded the inion response with alternative electrode placement, where electrodes were placed on the skin over the bulk of the sternocleidomastoid (SCM) muscle. Their findings confirmed the presence of a short latency response to loud acoustic stimulation and that the level of tonic muscle contraction influenced the response. An initial positive peak (known as p13 or P1) in the response, followed by a negative peak (known as n23 or N1) was reported. They also suggested that the p13-n23 peaks of the response were vestibular in origin and that the response was ipsilateral (Colebatch et al., 1994). This response became known as the cervical or collic vestibular evoked myogenic potential (cVEMP) and is regarded as a manifestation of the vestibulocollic reflex (VCR) (Welgampola & Colebatch, 2005). Although previously debated in literature, the origin of the cVEMP when using air-conducted (AC) stimuli is now accepted as being the saccule and inferior vestibular nerve, which innervates the saccule (Basta, Todt, & Ernst, 2005; Welgampola & Colebatch, 2005). Nowadays, cVEMPs may be evoked by brief bursts of AC sound, bone-conducted (BC) vibration or electrical stimulation (Rosengren, Welgampola, & Colebatch, 2010), and are commonly used in vestibular clinical practice for the assessment of saccular and inferior vestibular nerve function.

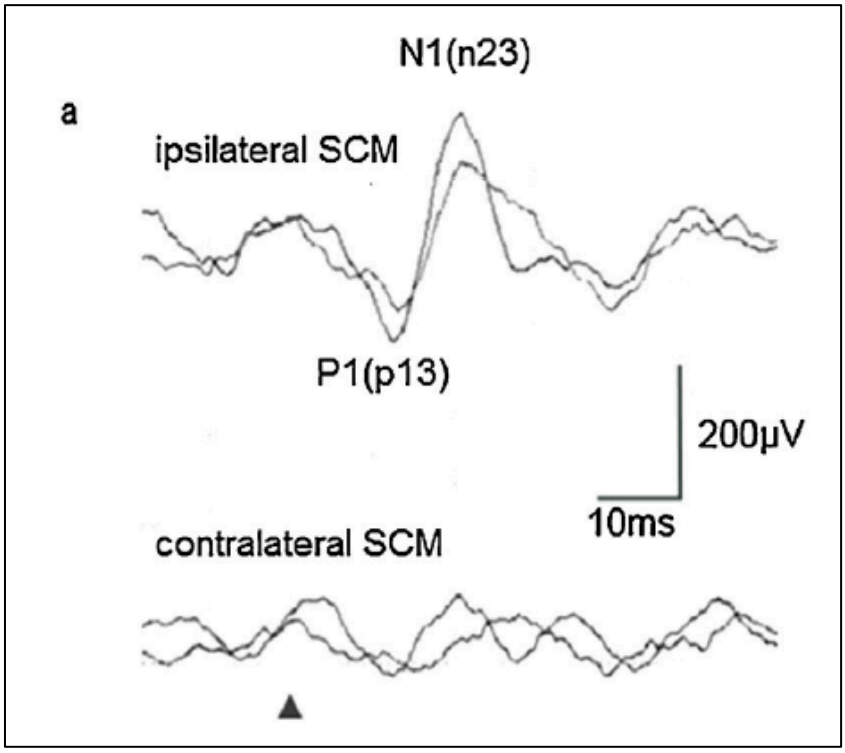

Figure 1: Normal cVEMP waveform to AC sound (from Murofushi, 2016)

In the last decade, the measurement of VEMPs has been extended to the extraocular muscles. Previous studies have reported short-latency vestibular evoked cortical potentials, which diffused towards the face and extraocular muscles, and were thought to be a representation of the vestibulo-ocular reflex (VOR) (Todd, Rosengren, & Colebatch, 2003; de Waele, Baudonnière, Lepecq, Tran Ba Huy, & Vidal, 2001; Sohmer, Elidan, Rodionov, & Plotnik, 1999). Rosengren, Todd, and Colebatch (2005) mapped these potentials to the sites that were closest to the eyes and found that the response was the largest when electrodes were placed below the eyes and the eyes were in a superomedial gaze, indicating that the responses originated from the extraocular muscles, specifically the inferior rectus muscle. These responses were shown to have a myogenic, rather than cortical, origin (Chihara et al., 2009; Welgampola, Migliaccio, Myrie, Minor, & Carey, 2009; Todd, Rosengren, Aw, & Colebatch, 2007). Nowadays, this type of VEMP is recorded from the inferior oblique muscle (Rosengren et al., 2010). This response became known as the ocular VEMP (oVEMP) and is regarded as a manifestation of the VOR (Rosengren et al., 2005; Todd et al., 2007). The oVEMP is characterised by a negative peak at approximately 10 ms, followed by a positive peak at approximately 15 ms (Castelein, Deggouj, Wuyts, & Gersdoff, 2008). The oVEMP can be elicited by AC stimuli and BC stimuli (Curthoys et al., 2014; Rosengren et al., 2010; Todd et al., 2007; Rosengren et al., 2005).

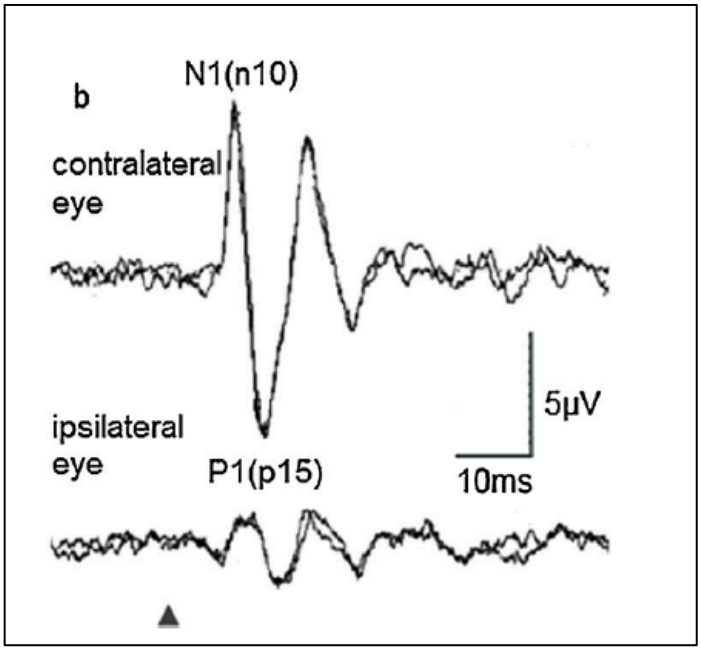

Figure 2: Normal oVEMP waveform to AC sound (from Murofushi, 2016)

The vestibular origin of the oVEMP has been heavily debated in literature until recently. Studies have confirmed the vestibular origin of the oVEMP, when using AC stimuli, as stemming from the utricle and superior vestibular nerve, which innervates the utricle (Papathanasiou, 2015; Curthoys et al., 2014). The saccular origin of the cVEMP response and utricular origin of the oVEMP response are differentiated by their different neuronal and motor projections (Govender, Dennis, & Colebatch, 2015; Curthoys et al., 2014; Uchino & Kushiro, 2011; Curthoys, 2010). In a study by Curthoys and colleagues (2014), it was found that although a utriculo-collic response can be detected, the response is very weak compared to the more robust and direct sacculocollic projections. Conversely, sacculo-ocular projections were found to be far weaker than the more robust utriculo-ocular projections. This suggests that the cVEMP (a manifestation of the VCR) reflects saccular function, while the oVEMP (a manifestation of the VOR) reflects utricular function. Another study by Govender and colleagues (2015) also supports the above findings on the cVEMP and oVEMP origin. They found that individuals with superior vestibular neuritis had impaired oVEMPs, but normal cVEMPs, whereas individuals with inferior vestibular neuritis had impaired cVEMPs, but normal oVEMPs. As the superior vestibular nerve innervates the utricle and impaired oVEMPs were seen, it could be concluded that the oVEMP is a measurement of superior vestibular nerve and utricular function. Similarly, as the inferior vestibular nerve innervates the saccule and impaired cVEMPs were seen, it could be concluded that the cVEMP is a measurement of inferior vestibular nerve and saccular

function. Ocular VEMPs have the potential to become a more integral component of the clinical vestibular test battery, however, due to the relatively new discovery of the oVEMP technique, it is not widely used in clinical practice.

1.2. Diagnostic value

Both cVEMPs and oVEMPs may be applied in the diagnosis of several peripheral vestibular disorders, and thus are valuable in determining the side and site of lesion of peripheral vestibular disorders. One of the peripheral vestibular disorders that may be identified with VEMPs is Ménière's Disease (Murofushi, 2016). Several studies have reported reduced or absent cVEMP responses in patients with Ménière's Disease (Katayama et al., 2010; de Waele, Huy, Diard, Freyss, & Vidal, 1999). However, a study by Egami, Ushio, Yamasoba, Yamaguchi, Murofushi, and Iwasaki (2013) indicated that the cVEMP response only has 50% sensitivity and 48.9% specificity for the detection of Ménière's Disease, which may mean that up to half of the Ménière's Disease patients would not have abnormal cVEMP responses. Another way of identifying endolymphatic hydrops, which is an underlying mechanism of Ménière's Disease, is using VEMP responses to observe whether the responses improve by dehydration (Murofushi, 2016). Approximately half of patients with Ménière's Disease demonstrate larger cVEMP amplitudes post-glycerol administration (Murofushi, Matsuzaki, & Takegoshi, 2001a). These variable findings highlight that these findings should be generalised with caution.

The VEMP responses may also be used to identify vestibular neuritis. Mixed findings have been reported for the cVEMP response in patients with vestibular neuritis (Murofushi, 2016; Govender et al., 2015). When using BC stimuli, an intact cVEMP response in the presence of an impaired oVEMP response is highly suggestive of superior vestibular neuritis (Govender et al., 2015). In other studies, cVEMPs were also reported abnormal using AC stimuli in approximately half of patients with inferior vestibular neuritis (Shin, Oh, Kim, Kim, Seo, Lee, & Park, 2012; Kim et al., 2008; Murofushi, Shimizu, Takegoshi, & Cheng, 2001b). In the oVEMP response, superior vestibular neuritis patients have been reported with absent or markedly reduced n10 components, decreased amplitudes and abnormally large asymmetry ratios on the affected side (Shin et al., 2012; Manzari, Tedesco, Burgess, & Curthoys, 2010). In the study by Govender and colleagues (2015), impaired oVEMPs and intact cVEMPs were also found to be highly suggestive of superior

vestibular neuritis and had a high sensitivity (~ 82%) in detecting this condition. Manzari et al. (2010) demonstrated that the oVEMP asymmetry ratio, when using BC stimuli, had a 94% diagnostic accuracy for the diagnosis of vestibular neuritis. The study by Govender and colleagues (2015) found 96% of patients with vestibular neuritis to reflect at least one abnormality in either cVEMPs or oVEMPs using AC and BC stimuli, which is indicative of a high sensitivity and specificity to the presence of vestibular neuritis. Although it is clear that both the cVEMP and oVEMP are useful in the diagnosis of vestibular neuritis, test results should always be interpreted within the context of a comprehensive vestibular test battery.

Both cVEMP and oVEMP responses may be applied in the diagnosis of superior semicircular canal dehiscence (SCD). Patients with SCD have been found to have significantly lower cVEMP thresholds, obtaining good wave morphologies down to levels of 75 decibels normalised hearing level (dB nHL), as well as larger amplitudes (Zuniga, Janky, Nguyen, Welgampola, & Carey, 2013; Yew, Zarinkhou, Spasic, Trang, Gopen, & Yang, 2012; Minor, 2005). The cVEMP response has been found to have a high sensitivity and specificity for the detection of SCD, with an 86% sensitivity and 90% specificity at intensities lower than or equal to 85 dB nHL reported by Zuniga et al. (2013) and 80% sensitivity and specificity reported in other studies (Govender, Fernando, Dennis, Welgampola, and Colebatch, 2016; Amoodi, Makki, McNeil, & Bance, 2011; Crane, Minor, & Carey, 2008). Similarly, oVEMP amplitude has also been shown to have a high sensitivity (87%) and specificity (93%) for the detection of SCD (Verrecchia, Westin, Duan, & Brantberg, 2016). These authors found patients with SCD to have larger oVEMP amplitudes. It is clear that the inclusion of cVEMP and oVEMP in the vestibular test battery is vitally important for the identification of SCD, as studies have shown that it is highly sensitive and specific for this condition.

Another condition that may be identified using cVEMPs and oVEMPs is vestibular migraine, also known as migraine-associated vertigo. Selected studies have shown that patients with vestibular migraine have reduced cVEMP amplitudes compared to adults with normal vestibular function (Mohamed, Amed, & Said, 2015; Murofushi, 2016). Patients with vestibular migraine have been found to demonstrate smaller cVEMP amplitudes, resulting in a smaller 500 – 1000 Hertz (Hz) cVEMP amplitude slope (Mohamed et al., 2015; Murofushi, Ozeki, Inoue, & Sakata, 2009). This 500 – 1000 Hz slope is calculated using the corrected cVEMP amplitude at each frequency. Furthermore, the preferred VEMP frequency tuning is unlikely to do so in vestibular migraine patients

(Murofushi et al., 2009). These authors also demonstrated that both 500 Hz and 1000 Hz toneburst cVEMPs have a 95 – 100% detection rate for vestibular migraine. Limited research has been conducted on the oVEMP response in patients with vestibular migraine, however existing research has reported oVEMPs that were absent, had delayed latencies or were of diminished amplitude in this population (Khalil, Hazzaa, & Nour, 2016; Zaleski et al., 2015). Although the diagnostic value of the cVEMP in this population has been established, further research is required to evaluate the sensitivity and specificity of the oVEMP for the detection of vestibular migraine.

Finally, research is limited in the field of VEMP findings in benign paroxysmal positional vertigo (BPPV); however, some studies have shown VEMPs to be affected in patients with BPPV. A study by Korres, Gkoritsa, Giannakakou-Razelou, Yiotakis, Riga, and Nikolpoulos (2011) showed abnormal cVEMP findings, namely predominantly delayed p13 latencies with a small percentage of patients having no recordable cVEMP, in 31.5% of posterior canal canalithiasis BPPV ears. Other studies have also found abnormal cVEMP responses in 30% of their posterior canal canalithiasis BPPV patients (Xu et al., 2016) and 25% of their posterior canal BPPV patients (BPPV variant not specified) (Nakahara, Yoshimura, Tsuda, and Murofushi, 2012). The previous research conducted on the cVEMP response in patients with BPPV confirms a trend of approximately one-third of posterior canal BPPV patients obtaining abnormal cVEMP responses, therefore data should be generalised with extreme caution. Limited research has been conducted on the oVEMP response in patients with BPPV. Nakahara et al. (2012) demonstrated abnormal oVEMPs in 66.7% of their patients with posterior canal BPPV, where oVEMP responses were predominantly absent. Similarly, Xu et al. (2016) found there to be abnormal oVEMP responses in 56% of their posterior canal canalithiasis BPPV patients. The VEMP responses carry more prognostic value than diagnostic value in detecting BPPV. The diagnosis of BPPV can still not be made without performing the Dix-Hallpike maneouvre and conducting a thorough case history interview.

1.3. Methodological aspects

Extensive research has been conducted on the most ideal stimulus and response parameters for both the cVEMP and oVEMP response. Typically, intensities of approximately 90 – 105 dB nHL are used to elicit the cVEMP response, however, testing at lower intensities may aid in the identification of SCD. A study by Wu and Murofushi

(1999) indicated that although a stimulus rate of 5 – 7 per second may be used, the optimal stimulation rate for clinical use is 5 p/s. A 0.1 ms click stimulus is the stimulus used most widely in cVEMP testing, however, Huang, Su, and Cheng (2005) found there to be only a 94% response rate when using the 0.1 ms click stimulus. These authors suggested a 0.5 ms click stimulus as the optimal stimulus for obtaining the cVEMP response. Frequency-specific tonebursts may also be used to elicit the cVEMP response, with a 500 Hz toneburst being the most widely used toneburst stimuli. Regarding the rise/plateau/fall time using toneburst stimuli, various suggestions have been made in literature. While certain authors prefer a 1 ms rise, with 2 ms plateau, other authors have suggested a two cycle rise and fall interval with no plateau (Wuyts, Furman, Vanspauwen, & Van de Heyning, 2007; Zapala, 2007; Young, 2006; Zhou & Clarke Cox, 2004). However, in studies by Cheng and Murofushi (2001a; 2001b), it was concluded that a 1 ms rise and fall intervals with 2 ms plateau time, would be the optimal rise/plateau/fall time to obtain 500 Hz cVEMP responses.

Concerning the response parameters of the cVEMP, various parameters have also been suggested in literature. The most widely used electrode montage for the cVEMP recording is with the active electrode over the upper third or half of the SCM muscle, the reference electrode is placed on the upper end of the sternum and the ground electrode placed on the forehead. This electrode montage has been adopted as the standard montage in several studies (Isaradisaikul, Navacharoen, Hanprasertpong, & Kangsanarak, 2012; Basta et al., 2005; Zhou & Clarke Cox, 2004; Cheng & Murofushi, 2001a; Cheng & Murofushi, 2001b; Welgampola & Colebatch, 2001). Zapala (2007) found that recordings with this cVEMP electrode montage will result in a clear P1 upward deflecting wave and N1 downward deflecting wave. The number of sweeps for cVEMP recordings may range between 64 and 256 (Welgampola & Colebatch, 2005; Zhou & Clarke Cox, 2004). As the cVEMP is a response that is largely influenced by degree of tonic muscle contraction (Rosengren, 2015; Lee, Kim, Son, Lim, Bang, & Kang, 2008), artifact rejection is switched off to avoid muscle responses being considered as artifacts. Filters are usually placed between 10 – 2000 Hz and the response is typically amplified 5000 times (Zapala, 2007; Welgampola & Colebatch, 2005).

Due to the relatively recent discovery of the oVEMP response, less research has been done on the most ideal stimulus and response parameters for the oVEMP. However, the stimulus and recording parameters for the oVEMP remain similar to those used for the

cVEMP (Rosengren et al., 2010). Intensities of 90 – 105 dB nHL, with stimulus repetition rate of 5 Hz, are also used in oVEMP recordings. Once again, both click and frequency-specific toneburst stimuli may also be used to elicit the oVEMP response. A recent study by Leyssens, Heinze, Vinck, Van Ombergen, Vanspauwen, Wuyts, and Maes (2016, under review) demonstrated that the highest reliability of the oVEMP response is using the longest rise/plateau/fall time of 1 – 4 – 1 ms, in combination with a newer electrode montage. Previously, the oVEMP electrode montage consisted of the active electrode on the orbital margin below the centre of the eye, the reference electrode on the cheek approximately 15 – 30 mm below the active electrode and the ground electrode placed nearby, on the chin, forehead or sternum (Rosengren et al., 2010). Recently, an alternative oVEMP electrode montage has been suggested (Leyssens et al., 2016; Vanspauwen, Wuyts, Krijger, & Maes, in press; Sandhu, George, & Rea, 2013), with the active electrode placed more laterally on the inferior oblique muscle, the reference electrode placed towards the medial canthus of the nose and the ground electrode on the chin or forehead. This alternative electrode positioning has been found to result in large oVEMP amplitudes and shorter n10 and p15 latencies (Leyssens et al., 2016). In order to reduce the impact of blinking on the oVEMP response, artifact rejection may be switched on. Filters may be placed from approximately 5 – 1000 Hz (Rosengren et al., 2010). As the oVEMP is a much smaller response compared to the cVEMP, the oVEMP may be amplified up to 50 000 – 100 000 times (Rosengren et al., 2010).

1.4. Influencing variables

Research has indicated that both the cVEMP and oVEMP response may be affected by a variety of factors, including aging (Maheu, Houde, Landry, & Champoux, 2015; Tseng, Chou, & Young, 2010; Basta, Todt, & Ernst, 2007; Ochi & Ohashi, 2003; Welgampola & Colebatch, 2001), presence of conductive pathology (Wang, Liu, Yu, Wu, & Lee, 2009; Wang & Lee, 2007), gender (Sung, Cheng, & Young, 2011; Xie, Xu, Bi, Jia, Zheng, & Zhang, 2011) and race (Li, Layman, Carey, & Agrawal, 2015). It is important that these factors are taken into consideration when using VEMPs in the clinical context.

It is a well-documented fact that the aging process has an effect on the amplitude and latencies of the cVEMP and oVEMP. Older adults display decreased amplitudes and prolonged latencies of P1 and N1 components in both the cVEMP and oVEMP responses and it has been found that the relationship between age and degradation of these

responses is linear (Kumar, Bhat, Sequeira, & Bhojwani, 2015; Li et al., 2015; Maleki, Jafari, Zarrinkoob, & Baghban, 2014; Tseng et al., 2010; Basta et al., 2007; Basta et al., 2005; Su, Huang, Young, & Cheng, 2004; Ochi & Ohashi, 2003). It is likely that this aging effect is due a decrease in vestibular hair cells, Scarpa's ganglion cells or cells of the vestibular brainstem (Basta et al., 2005). The literature on the aging effect on VEMPs highlights the need to consider the patient's age and its subsequent effect on the cVEMP and oVEMP responses in the clinical context.

The presence of middle ear pathology, such as otitis media, may also affect VEMPs (Wang et al., 2009; Wang & Lee, 2007; Yang & Young, 2003). In a study by Wang et al. (2009), it was found that patients with chronic otitis media had significantly prolonged cVEMP p13 latencies. Similar findings were previously reported in a study by Yang & Young (2003), who showed that only 59% of their participants with chronic otitis media had recordable cVEMP responses. Furthermore, patients with middle ear effusion have been shown to have prolonged cVEMP p13 and n23 latencies, as well as smaller amplitudes, than healthy individuals (Wang & Lee, 2007). These authors also demonstrated that a third of their participants had recordable VEMP responses following tympanic aspiration, indicating that the reduced or absent cVEMP prior to treatment could be attributed to the middle ear pathology. However, the effect of the middle ear pathology on the cVEMP response may be bypassed. Yang and Young (2003) demonstrated that by using a tapping method, they were able to obtain a 91% cVEMP response rate in patients with chronic otitis media, far higher than the 59% response rate obtained using AC stimuli. The effect of chronic otitis media on the oVEMP response has been investigated to a lesser extent. In a study by Chang, Cheng, and Young (2014), it was found that despite using BC stimuli, 62% of their participants with chronic otitis media had abnormal oVEMP responses. Unlike previous studies who found prolongation of latencies and smaller amplitudes in the cVEMP due to middle ear pathology, these authors reported completely absent oVEMPs in many of their participants who obtained abnormal responses.

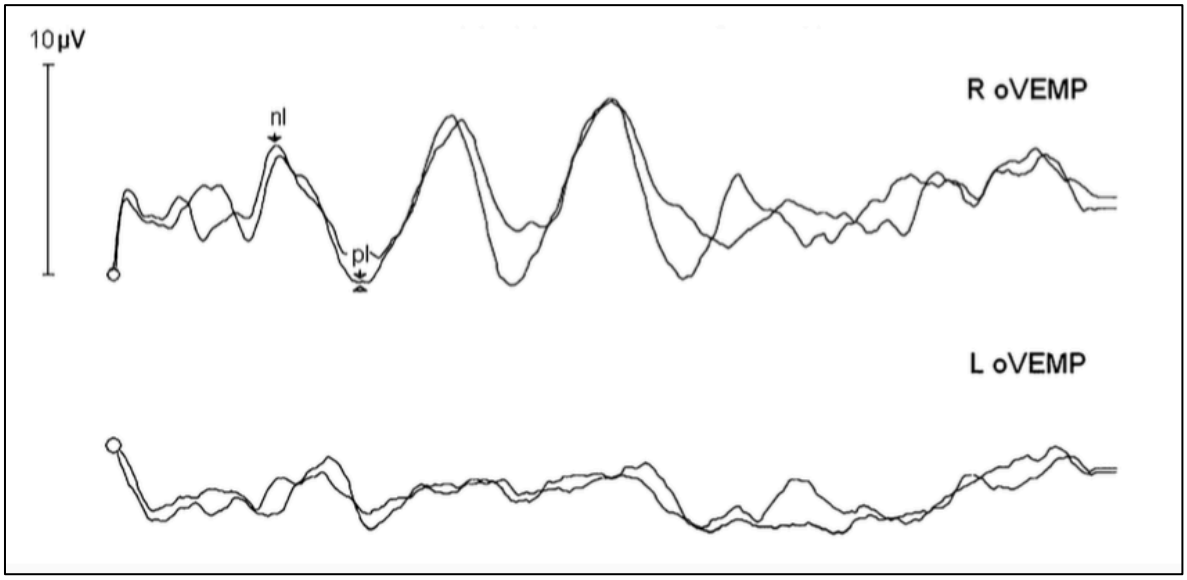

Figure 3: oVEMP response obtained from a patient with chronic otitis media in the left ear, compared to a healthy response in the right ear (taken from Chang et al., 2014)

Previous research has been conducted on the possibility of gender-based differences in cVEMP and oVEMP responses. Several studies have found there to be no differences by gender in the cVEMP p13 and n23 latencies, as well as the amplitude of this response (Carnaúba, Farias, Santos, De Oliveira, Rodrigues, & Menezes, 2011; Basta et al., 2007; Basta et al., 2005; Guillén, Garcia, Piñero, Del Ray, Pérez, & Garrigues, 2005; Ochi & Ohashi, 2003). However, mixed findings have been reported on the effect of gender on the oVEMP response parameters, namely latency and amplitude. Despite no oVEMP n10 or p15 latency differences being reported in literature, a gender-based amplitude difference has been reported in the oVEMP response by selected studies (Sung et al., 2011; Xie et al., 2011). It is reported that males obtain larger amplitudes than females (Sung et al., 2011; Xie et al., 2011), and it has been hypothesised that this difference may be attributed to a difference in muscle bulk between males and females (Sung et al., 2011). However, there are studies that contradict these findings, reporting no significant gender-based differences in oVEMP amplitude (Chou, Hsu, & Young, 2012; Versino et al., 2015). It is possible that this disparity in gender-based differences in oVEMP amplitude may be related to differing study population races and its subsequent effect on the muscle bulk seen in males. Previous studies have found there to be an race effect on muscle structure (Araujo et al., 2010; Gallagher et al., 1997).

A recent study by Li and colleagues (2015) has demonstrated that race may also be an influencing variable on the oVEMP response, but not the cVEMP response. These authors

compared black African and Caucasian older adults and found that black African participants presented with larger amplitudes and shorter n10 latencies for the oVEMP response. It was hypothesised by these authors that this racial difference may be due to a melanin difference in the two racial groups. Black African individuals have been found to have a higher presence of melanocytes in the vestibular organs than their Caucasian counterparts. These melanocytes are arranged closely to the vestibular dark cells, which are only found in the semicircular canals and utricle (Harada, 1983). This may explain why the study by Li et al. (2015) found a racial difference only in the oVEMPs, as they are a test of utricular function. As this is the only study to date that has reported on racial differences in VEMP responses, these results should be interpreted carefully, especially since the study population had an advanced mean age (72 years) and was neither age- or gender-matched.

1.5. Problem statement

Although extensive research has been conducted on certain factors that may affect the VEMP responses, such as aging (Kumar et al., 2015; Li et al., 2015; Maleki et al., 2014; Tseng et al., 2010; Basta et al., 2007; Basta et al., 2005; Su et al., 2004; Ochi & Ohashi, 2003) and presence of middle ear pathology (Wang et al., 2009; Wang & Lee, 2007; Yang & Young, 2003), contradictory findings have been seen in the effect of gender and race of the VEMP responses. This controversy in gender- and race-related differences in VEMP response parameters emphasises the importance of more prospective studies to confirm and expand on these findings. Therefore, the aim of the current study was to compare cVEMP and oVEMP responses in young gender- and age-matched black African and Caucasian male and female adults, thereby taking into consideration myoelectric activity and neck length. In order to determine if gender- or race-related differences are not solely related to muscle differences, the non-myogenic auditory brainstem response (ABR) was also determined in this study population.

CHAPTER TWO

Methodology

2.1. Aim

2.1.1. Main aim

The main aim of this research study was to compare VEMP response parameters, namely latency and amplitude, between young age- and gender-matched black African and Caucasian adults.

2.1.2. Sub-aims

The sub-aims of this research study were as follows:

- To compare the latency of the p13 and n23 peaks of the cVEMP response between age- and gender-matched young black African and Caucasian adults.
- To compare the peak-to-peak amplitude, rectified amplitude and asymmetry ratio of the cVEMP response between age- and gender-matched young black African and Caucasian adults.
- To compare the latency of the n10 and p15 peaks of the oVEMP response between age- and gender-matched young black African and Caucasian adults.
- To compare the peak-to-peak amplitude and asymmetry ratio of the oVEMP response between age- and gender-matched black African and Caucasian adults.
- To compare ABR wave I, III and V absolute latencies, waves I-III, III-V and I-V interpeak latencies, and wave I-V amplitude ratio between age- and gender-matched black African and Caucasian adults.
- To compare electromyography (EMG) amplitudes in relaxed and contracted muscle states between age- and gender-matched black African and Caucasian adults.

2.2. Research design

This research study was conducted using a quasi-experimental between-subjects research design (De Vos, Strydom, Fouche, & Delport, 2005). The study was comparative in nature, thus data was collected in a cross-sectional manner from two racial groups, namely black African and Caucasian, and compared. This research design was deemed appropriate for the current study, as various test responses were being compared between two participant groups and participant allocation was dependent on race. Both groups were age- and gender-matched. Furthermore, interactions of gender and race were also examined in this research study.

2.3. Ethical considerations

When conducting research, specifically research involving human participants, it is vitally important to ensure that the research complies with a variety of ethical principles. The ethical considerations of this research study complied with those set out by the South African National Health Act No. 61 (Republic of South Africa, 2003) and the Declaration of Helsinki (World Medical Association, 2013) and are as follows:

2.3.1. Permission from relevant authorities

Ethical clearance for this research study was obtained from the Research Ethics committee of the Faculty of Humanities, University of Pretoria, prior to the commencement of data collection (Appendix A). Permission was obtained from the Head of the Department of Speech-Language Pathology and Audiology at the University of Pretoria to conduct this research study (Appendix B). As the participants of this study comprised friends and acquaintances of the researcher, as well as students from the University of Pretoria who volunteered to participate in the study, permission was obtained from the Director of the Department of Student Affairs at the University of Pretoria to approach these students and request their participation (Appendix C).

2.3.2. Informed consent

All participants in this research study were given letters fully explaining the purpose and nature of the study and what actions were required of them, should they consent to participation in the study (Appendix D). All information was given to the participants using terminology that could be understood by laypersons. Participants were required to give written and verbal informed consent (Appendix D), therefore participation in this research study was entirely voluntary. If the participants had any queries relating to the research study before consenting to participation, opportunity was given for the participants to ask questions. Participants were allowed to discontinue their participation in this research study at any point. Where images of a participant were used, permission has been obtained to publish these images (Appendix E)

2.3.3. Referrals

Once data collection commenced, if a participant was identified as having a hearing loss or condition necessitating otologic management (e.g. otitis media), participants were given

the contact information of local audiologists and/or otorhinolaryngologists for further management of the condition. Participants requiring further management were given informational counselling on the importance of consulting these health professionals for the management of their condition.

2.3.4. Confidentiality and anonymity

The confidentiality and anonymity of all participants' identifying information and results was ensured in the current study. Each participant was given a research code, therefore the identity of each participant was kept confidential and was only known to the primary researcher. All information, medical or otherwise, provided by participants during the anamnesis (case history) interview was kept strictly confidential.

2.3.5. Honesty

No form of deception was used in this research study. All participants were given their test results, which were explained in lay terms to each participant. Participants were also verbally given the opportunity to request access to the final results of the research study. The research study was submitted to a scientific journal for publication, which was peer-reviewed prior to publication of the article in the journal. The research study was also presented as a Masters' dissertation, which was reviewed and supervised by three supervisors (Prof. Dr. Bart Vinck, Dr. Barbara Heinze and Prof. Dr. Leen Maes).

2.3.6. Plagiarism

The research study, scientific article and Masters' dissertation are the researchers' own original work. Where secondary material was cited in the study, this was acknowledged and referenced according to the APA 6th Edition referencing guidelines. This research study was conducted in accordance with the University of Pretoria policy on plagiarism. The originality of this study is declared in Appendix F.

2.3.7. Data storage

According to the policy of the University of Pretoria, data from this research study will be archived at the Department of Speech-Language Pathology and Audiology at the University of Pretoria in digital and hard copy for a period of 15 years. No identifying information for participants is included in these data files.

2.4. Research Participants

2.4.1. Study Population

Sixty normal hearing young adults, aged 18 – 25 years were included in this research study. Participants were recruited using purposive sampling. Data was collected from two age- and gender-matched racial groups, namely Caucasian and black African adults. All participants were required to be South African natives. Each racial participant group was equally gender-matched, with 15 males and 15 females in each group. Furthermore, participants selected for each racial group were similarly aged within a year of each other. The Caucasian group had a mean age of 21.7 years (standard deviation (SD) = 2.2), with ages ranging from 18.0 – 25.8 years. The black African group had a mean age of 21.0 years (SD = 2.1), with ages ranging from 18.0 – 24.9 years.

2.4.2. Selection Criteria

The participant inclusion criteria used in the research study is summarised in Table 1. All participants were required to meet these criteria, in order to qualify for participation in the study.

Table 1: Participant inclusion criteria

Selection Criteria	Required Result Criteria	Equipment Used
Participants should be aged between the ages of 18 – 25 years at the time of participation in the study.	The only previous study on racial differences in VEMP response parameters was conducted on a study population with advanced mean age (Li et al., 2015). Furthermore, advanced age has been shown to affect the VEMP response parameters (Maheu et al., 2015; Tseng et al., 2010; Basta et al., 2007).	Not applicable
Participants should have no history of vestibular disorders.	A history of previous or current vestibular dysfunction may affect the VEMP results negatively. A thorough vestibular anamnesis (case history) interview, using the SOSTONED tool (Wuyts, Van Rompaey, & Maes, 2016) was conducted. Participants were required to obtain normal results on the following vestibular assessments: • Head Impulse Test, • Fukuda Stepping Test, • Modified Clinical Test of Sensory Interaction of Balance (mCTSIB), • Absence of Spontaneous Nystagmus,	Frenzel goggles (Dix-Hallpike and observation of spontaneous nystagmus), foam mat (mCTSIB).

	• Dix-Hallpike Test.	
Participants should have normal middle ear functioning.	Middle ear pathology may significantly affect VEMPs (Wang & Lee, 2007; Wang, Liu, Yu, Wu, & Lee, 2009). Participants should present with type A tympanograms (Jerger, 1970) and normal ipsilateral stapedial reflexes.	Interacoustics AA222 Diagnostic Tympanometer (Interacoustics, USA)
Participants should have normal hearing sensitivity.	Participants should present with air-conduction pure tone hearing thresholds ≤ 15 decibels hearing level (dB HL) at octave intervals from 125 Hz to 8000 Hz (Northern & Downs, 2002). These thresholds were obtained using the modified Hughson-Westlake procedure (Carhart & Jerger, 1959).	GSI 61 Clinical Audiometer (Grason-Stadler, USA)

Furthermore, the current study had certain exclusion criteria. If the participants were found to have any of the following conditions during the screening process for inclusion in the study, they were prohibited from participating in the study:

- Current or previous peripheral or central vestibular disorders,
- Abnormal middle ear functioning (evidenced by obtaining Type A_S, A_D, B or C tympanograms and/or abnormal or absent stapedial reflexes),
- Conductive, mixed or sensorineural hearing loss with audiometric hearing thresholds > 15 dB HL,
- If the participant was not born in South Africa,
- If the participant was not between the ages of 18 – 25 years at the time of testing.

2.5. Data collection protocols and parameters

The test protocols and parameters for each test are detailed below. All testing took place at the Department of Speech-Language Pathology and Audiology at the University of Pretoria, and participants were only tested on one occasion. The cVEMP, oVEMP and ABR testing were all conducted using the Bio-Logic® Navigator-Pro® system (Natus Medical, USA) in a sound-treated room.

2.5.1. Screening tests

A variety of tests were conducted to screen participants for their candidacy to be included in the study (Table 1). The protocols and parameters use to screen participants for inclusion in the study has been described below in Table 2. A summary of the participants' test results for these screening tests can be found in Appendix G.

Table 2: **Protocols and parameters for screening tests**

Test	Protocol	Test Parameters/Equipment
Case History	A thorough vestibular anamnesis (case history) interview, using the SOSTONED tool (Wuyts et al., 2016) was conducted.	N/A
Otoscopy	Otoscopy was conducted by inserting a speculum attached to an otoscope in to the entrance of the ear canal to visualise the ear canal and tympanic membrane in each ear.	A Welch Allyn MacroView otoscope (Welch Allyn, USA) was used to conduct otoscopy.
Tympanometry	Tympanometry was performed by inserting a eartip into the ear canal and obtaining a complete seal of the ear canal.	A 226 Hz probe tone, and an Interacoustics AA222 diagnostic tympanometer (Interacoustics, USA) was used to conduct tympanometry.
Pure-tone audiometry	Audiometric thresholds were obtained using the modified Hughson-Westlake procedure (Carhart & Jerger, 1959).	Air-conduction pure tone hearing thresholds ≤ 15 dB HL at octave intervals from 125 Hz to 8000 Hz (Northern & Downs, 2002), using supra-aural headphones in a soundproof audiometric booth.
Head impulse Test	Participants' heads were turned approximately 30°, with their gaze fixated on a central point. The tester then guided their heads through a rapid turn to a central point.	N/A
Fukuda stepping test	Participants were instructed to take 50 steps on the spot, while their eyes were closed and their arms were extended horizontally in front of them.	N/A
Modified clinical test of sensory interaction of balance (mCTSIB)	Participants were instructed to stand on the floor or foam block with their arms crossed across their chest and their eyes open or closed.	Foam block
Spontaneous nystagmus	Participants were instructed to keep their eyes open with and without visual fixation, while wearing Frenzel goggles.	Frenzel goggles
Dix-Hallpike test	While wearing Frenzel goggles, participants were guided from a sitting position into a supine position with their heads turn 30° to either side. In the supine position, the participants' heads were also inclined 30° below the bed, to allow for the orientation of the horizontal semicircular canal.	Frenzel goggles Bed

2.5.2. Cervical VEMP (cVEMP) testing

During cVEMP testing, participants were required to lie in the supine position, with their heads turned to the contralateral side. Participants were instructed to lift their heads, maintaining the contralateral rotation and achieving a strong contraction of the SCM muscle, for the duration of the presentation of an acoustic stimulus. An AC 500 Hz toneburst was presented using insert earphones (3M EARTONE®, 3A), with an intensity of 95 dB nHL and a stimulus rate of 5.1 Hz. An alternating polarity and a rise/plateau/fall time of 2 – 0 – 2 (ms), with Blackman gating, was utilised for cVEMP testing. Filters were places at 10 Hz (high-pass) and 1500 Hz (low-pass). Self-adhesive electrodes (Ambu®, Bluesensor) were used, with the active electrode placed over the bulk of the SCM muscle, the reference electrode on the upper edge of the sternum and the ground electrode on the forehead (**Figure 4A**). Skin was prepared with alcohol swabs and Everi® conductive and abrasive paste prior to the positioning of the electrodes, to ensure that impedances were kept below 5 kΩ. Muscle tension was controlled for using a correction algorithm built into the Bio-Logic® Navigator-Pro® software for all amplitude measurements of the cVEMP, resulting in a rectified amplitude measure (Colebatch, 2009; Welgampola & Colebatch, 2005; Welgampola, Rosengren, Halmagyi, & Colebatch, 2003). The prestimulus rectification algorithm works as follows: after a raw waveform has been obtained and the researcher has marked points (p13 and n23) on the waveform, the prestimulus rectification function is calculated on the selected waveform. The absolute value of the prestimulus data is averaged during 20 ms and then divided into each of the 256 points along the cVEMP waveform that has been collected. New rectified waveforms are then calculated.

The cVEMP response consists of a large biphasic waveform made up of a large positive peak (P1 or p13) observed at approximately 13 ms, followed by a negative peak (N1 or n23) observed at approximately 23 ms (Castelein et al., 2008). In this research study, absolute latencies of p13 and n23, peak-to-peak raw and rectified amplitude and the asymmetry ratio (Welgampola & Colebatch, 2001) of rectified peak-to-peak amplitude were collected for the cVEMP response. The typical cVEMP response, raw and rectified, can be seen in **Figure 5 – 6** (Chapter 3)**.**

2.5.3. Electromyography (EMG) testing

In order to understand any possible race- or gender-related difference in cVEMP raw and rectified amplitude, it was important to obtain further information regarding each participant's muscle tension during contraction and relaxation, as well as their neck length.

The myoelectric values of the SCM muscles was measured by means of EMG testing during the contraction required for cVEMP procedures, as well as when the muscle was relaxed. The EMG recordings were conducted using a NeuroTrac™ ETS v1.0 device (Verity Medical LTD, United Kingdom). A single-channel recording with threshold of 18.5 µV/200.0 µV, with continuous sound feedback and a narrow filter was utilised. Self-adhesive electrodes (Lifecare®) were placed as follows: two electrodes on the bulk of the SCM muscle, approximately 2 centimetres (cm) apart and one electrode on the greater tubercle bony process of the humerus (**Figure 4C**).

The average EMG response (amplitude, measured in µV) of the SCM muscle in both contracted and relaxed states was calculated and recorded. This was taken as an indication of the average myoelectric signals during the contraction and relaxation of each SCM muscle. Participants were prepared in the same manner as cVEMP testing, however EMG and cVEMP testing was not conducted simultaneously. Participants were required to lift and relax their heads four times on each side, in response to a command given by the software, while EMG recordings were taken of the SCM muscle in a contracted and relaxed state. Contraction and relaxation cycles were five seconds long, with five trials in each test. Feedback was inhibited, as the purpose of the testing was not neuromuscular rehabilitation.

2.5.4. Neck length and sternocleidomastoid (SCM) width

The neck length on each side of the neck and width of each SCM muscle was recorded for every participant. The neck length of each participant was obtained by measuring the distance between two reference points on the neck, namely the mastoid bone tip and a point from the mastoid tip perpendicular to the clavicle, a measurement procedure previously used by Chang, Yang, Wang, & Young (2007). During this measurement, participants were required to turn their head to the contralateral side, however, they were not required to contract the SCM muscle by lifting their heads. The width of the SCM muscle was measured over the belly of the muscle, while the muscle was contracted. These measurements were taken using a flexible measuring tape and measured in centimetres (cm).

2.5.5. Ocular VEMP (oVEMP) testing

Participants were required to lie in the supine position and were instructed to maintain an upward gaze of 30° for the duration of testing. This was achieved by fixating their gaze on

a stationary marked sign adhered to the ceiling of the soundproof booth. For the oVEMP, a AC 500 Hz toneburst with intensity of 95 dB nHL, an alternating polarity, stimulus rate of 5.1 Hz and rise/plateau/fall times of 1 – 4 – 1 (ms) (with Blackman gating) were used. Self-adhesive electrodes (Ambu®, Bluesensor) were placed using an alternative 'nose' electrode position (Leyssens et al., 2016; Sandhu et al., 2013; Vanspauwen et al., in press), with the active electrode placed more laterally on the inferior oblique muscle, the reference electrode towards the medial canthus of the nose and the ground electrode on the forehead (**Figure 4B**). Skin was prepared in the same manner as cVEMP testing prior to the positioning of the electrodes.

The oVEMP response also consists of a biphasic waveform, with a negative peak (N1 or n10) observed at approximately 10 ms, followed by a positive peak (P1 or p15) observed at approximately 15 ms (Castelein et al., 2008). In the present research study, absolute latencies of n10 and p15, peak-to-peak amplitude and the asymmetry ratio (Welgampola & Colebatch, 2001) of peak-to-peak amplitude were collected for the oVEMP response. The typical oVEMP response can be seen in **Figure 7** (Chapter 3).

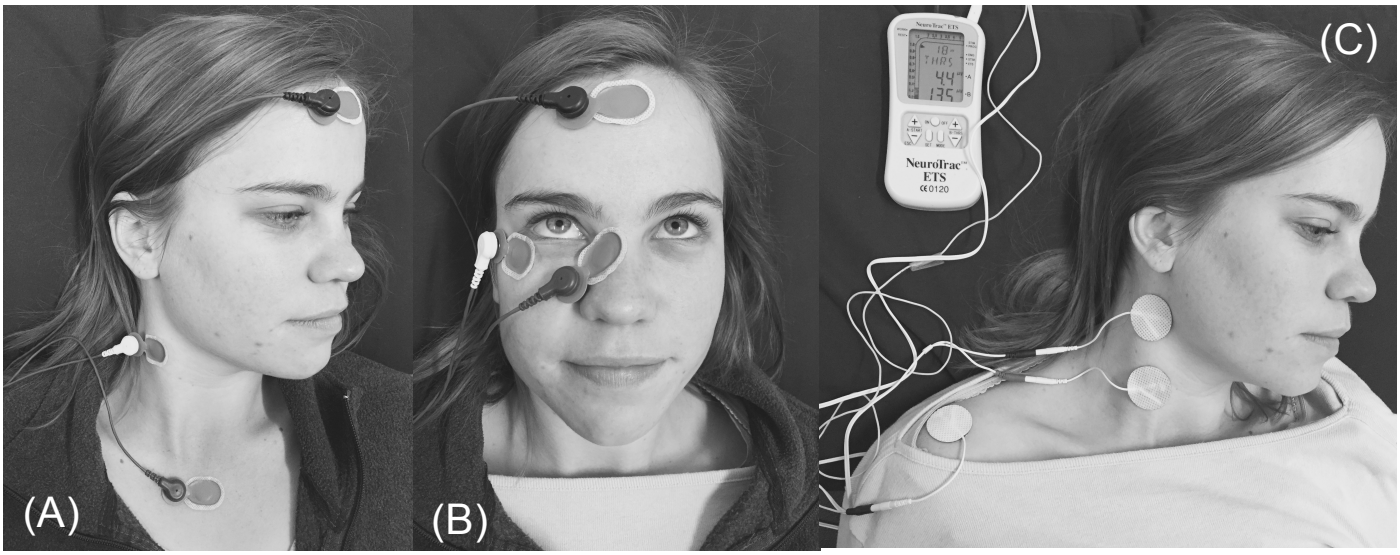

Figure 4: Electrode montages

Key: (A) Cervical vestibular evoked myogenic potential (cVEMP) electrode montage, (B) Ocular vestibular evoked myogenic potential (oVEMP) electrode montage, (C) Electromyography (EMG) electrode montage; permission was obtained from this participant to use images of her in this research study, which can be found in Appendix E.

2.5.6. Auditory brainstem response (ABR) testing

For the neurological ABR testing, participants were required to lie in the supine position without moving. AC stimuli with an intensity of 80 dB nHL and a stimulus rate of 13.3 Hz were presented using insert earphones (3M EARTONE®, 3A). Filters were placed at 3000 Hz (low-pass) and 30 Hz (high-pass) for ABR testing. Two traces of 2000 sweeps were conducted for both ears, in which both rarefaction and condensation polarities were used separately. Self-adhesive electrodes (Ambu®, Bluesensor) were placed as follows: the active electrode on the forehead, the reference electrode on the mastoid bone behind the test ear and the ground electrode on the mastoid bone behind the non-test ear. Skin was prepared in the same manner as cVEMP and oVEMP testing prior to the positioning of the electrodes.

The neurological ABR consists of a large waveform with five to seven peaks, occurring within 10 ms of the onset of a moderate intensity stimulus (Katz, Medwetsky, Burkard, & Hood, 2009). In this research study, the absolute latencies of waves I (~ 1.54 ms), III (~ 3.57 ms) and V (~ 5.52 ms), the interpeak latencies of waves I-III (~ 2.13 ms), III-V (~ 1.85 ms) and I-V (~ 3.98 ms), as well as the wave I-V amplitude ratio, were collected for the neurological ABR.

2.6. Reliability and validity

The reliability of a study refers to the stability and consistency of the measurements obtained from each participant (De Vos et al., 2005). All test measures in the current research study were repeated to ensure reliability and accuracy of all test results, as well as reduce possible participant variation. The same equipment was used with every participant and all equipment had been calibrated less than six months prior to data collection, to reduce possible instrument variation.

The validity of a study refers to the extent to which test measures used in the study reflect the function or concept it was intended to measure (De Vos et al., 2005). All test measures used in the current study were clinically validated by extensive previous research on the audiological test battery, VEMPs, ABR and EMG. The test order of cVEMP, oVEMP, ABR and EMG were randomised to avoid possible order bias and eliminate a fatigue effect in the participant.

2.7. Statistical analysis

Descriptive statistics, such as mean (M) and SD, were determined for the results of all response parameters of each test conducted as part of this study. Histograms, normal quantile plots and Shapiro-Wilk normality tests confirmed whether data was normally distributed. Significant differences in responses between the two racial groups, as well as gender, were evaluated by means of two-way analysis of variance (ANOVA) for normally distributed data. Non-normal variables that did not meet homogeneity of variances were first transformed with an appropriate transformation (natural log or square root). When transformations did not correct heteroskedasticity, the non-parametric two-way ANOVA alternative, the Scheirer-Ray-Hare test, was used. Significant interactions were further examined by means of one-way ANOVA and Tukey's honestly significant difference (HSD) tests. Data analysis was performed using STATA software (Version 12, StataCorp LP, Texas, USA). A p value of $<.05$ was used to indicate significance.

CHAPTER THREE

Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults

RESEARCH OUTPUT: JOURNAL ARTICLE

Comparing vestibular evoked myogenic potential response parameters in young black African[1] and Caucasian adults

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3.1. Abstract

Objective: The aim of this study was to compare cervical and ocular vestibular evoked myogenic potentials (cVEMP and oVEMP) in young gender- and age-matched black African and Caucasian male and female adults.

Methods: Sixty healthy participants (30 black African, 30 Caucasian) between the ages of 18 – 25 years participated in this study. VEMP latencies, peak-to-peak amplitudes and asymmetry ratios were analysed for both groups. Additionally, auditory brainstem response (ABR) and electromyography (EMG) testing were conducted to ascertain whether any observed difference in VEMP response parameters could be attributed to differences in neural or muscular function.

Results: Black African participants demonstrated significantly shorter latencies for the cVEMP n23 component and the oVEMP p15 component, as well as larger peak-to-peak raw amplitudes for both VEMP responses. Highly significant differences were found in all EMG measurements between the two race[2] groups. Significant gender differences were observed in all tests conducted, with females predominantly displaying shorter latencies, and males larger amplitudes.

[1] The term for the African participant group has been changed to 'black African' after the article was submitted to the journal for publication, as per the recommendation of the examiner.

[2] Where the article referred to ethnic or ethnicity, this has been changed to race/racial or race-related after the article was submitted to the journal for publication, as per the recommendation of the examiner.

Conclusions: Black African adults demonstrated significant differences in both cVEMP and oVEMP responses, namely shorter latencies and larger raw amplitudes, in comparison to Caucasian adults. Based on differences in EMG measurements, it is hypothesised that these differences are primarily due to differences in muscular function as opposed to neural function. Future research is required to confirm and expand on these findings.

Significance: These findings indicate that gender- and race-related normative data are needed for VEMP latency parameters, and especially for oVEMP amplitude parameters.

3.2. Introduction

Vestibular evoked myogenic potentials (VEMPs) have become a vital component of the vestibular test battery. The characteristics and origins of VEMPs were originally described by Colebatch and Halmagyi (1992), as well as Colebatch et al. (1994). These authors assessed the vestibulocollic reflex by measuring electromyographic (EMG) activity from surface electrodes adhered to the skin over the sternocleidomastoid (SCM) muscle, as a result of vestibular stimulation by sound (click) stimuli. Nowadays, VEMPs may be evoked by brief bursts of air-conducted sound, bone-conducted vibration or electrical stimulation (Rosengren et al., 2010). These are now referred to as 'collic' or 'cervical' VEMPs (cVEMPs), and are commonly used in vestibular clinical practice for assessment of saccular and inferior vestibular nerve function (Basta et al., 2005; Welgampola & Colebatch, 2005).

More recently, VEMPs have also been measured from extra-ocular muscles, specifically the inferior oblique muscle, in response to loud acoustic stimulation. These are known as 'ocular' VEMPs or oVEMPs, and are regarded to be a manifestation of the vestibulo-ocular reflex (Rosengren et al., 2005; Todd et al., 2007). Several stimuli can elicit the oVEMP, including air-conducted stimuli and bone-conducted stimuli (Curthoys et al., 2014; Rosengren et al., 2005; Rosengren et al., 2010; Todd et al., 2007). Recent studies have confirmed the origin of the oVEMP response, when using air-conducted stimuli, as stemming from the utricle and superior vestibular nerve (Curthoys et al., 2014; Papathanasiou, 2015). Due to the fact that both VEMP responses can be activated by air-

and bone-conducted stimuli, the origin of these responses cannot be differentiated by type of stimulus. Rather, the saccular origin of the cVEMP response and utricular origin of the oVEMP response are differentiated by their different neuronal and motor projections (Curthoys et al., 2014; Curthoys, 2010; Govender et al., 2015; Uchino & Kushiro, 2011). Curthoys et al. (2014) found that although an utriculo-collic response can be detected, it is very weak compared to the more robust and direct sacculocollic projections. Similarly, utriculo-ocular projections are far more robust than sacculo-ocular projections. Another study by Govender et al. (2015) also supports the above findings on the VEMP origin. They found that individuals with superior vestibular neuritis had impaired cVEMPs, but normal oVEMPs, whereas individuals with inferior vestibular neuritis had impaired oVEMPs, but normal cVEMPs. Ocular VEMPs have the potential to become a more integral component of the clinical vestibular test battery, as they can be applied in the diagnosis and differentiation of vestibular disorders, such as Ménière's disease and superior semicircular canal dehiscence (Kantner & Gürkov, 2012; Murofushi, 2016). However, due to the relatively new discovery of the oVEMP technique, it is not widely used in clinical practice.

There are a variety of factors that may affect cVEMPs and oVEMPs, including gender and race (Li et al., 2015; Sung et al., 2011). No significant differences by gender have been seen in the latencies of the p13 and n23 components, as well as the amplitude of the cVEMP response between males and females (Basta et al., 2007; Basta et al., 2005; Carnaúba et al., 2011; Guillén et al., 2005; Ochi & Ohashi, 2003). In contrast, more mixed findings are reported on the effect of gender on the oVEMP response. Whereas no significant n10 and p15 latency differences have been reported, oVEMP amplitudes have been found to be significantly larger for males compared to females (Sung et al., 2011; Xie et al., 2011). Sung et al. (2011) hypothesised that this difference in amplitude can be mainly attributed towards a difference in muscle bulk between males and females. However, later studies found no significant gender-based differences for any component of the oVEMP response, including amplitude (Chou et al., 2012; Versino et al., 2015).

A recent study by Li et al. (2015), demonstrated a significant effect of race on the oVEMP response parameters, with black African participants presenting with larger amplitudes and shorter latencies in oVEMPs, but not in cVEMPs. These authors suggested that this difference may be due to melanin differences in the two racial groups. Black African participants have a higher presence of melanocytes in the vestibular organs, with a close

arrangement to vestibular dark cells, which affects vestibular organ metabolism. These dark cells exist only in the semicircular canals and utricle (Harada, 1983), which may explain the significant effect of race on oVEMP response parameters, but not on cVEMP response parameters. Since this is the only study to date that has reported on racial differences in VEMP responses, these results should be interpreted carefully, especially since the study population had an advanced mean age (72 years) and was neither age- or gender-matched.

This controversy in gender- and race-related differences in VEMP response parameters emphasises the importance of more prospective studies to confirm and expand on these findings. Therefore, the aim of the current study was to compare cVEMP and oVEMP responses in young gender- and age-matched black African and Caucasian male and female adults, thereby taking into consideration myoelectric activity and neck length. In order to determine if gender- or race-related differences are not solely related to muscle differences, the non-myogenic auditory brainstem response (ABR) was also determined in this study population.

3.3. Method

3.3.1. Study population

Data was collected from two age- and gender-matched racial groups, namely, Caucasian and South African-born black African adults. Thirty participants in each racial group (fifteen males and fifteen females), aged between 18 – 25 years, were included in this study (Caucasian Mean (M) = 21.7 years, Standard Deviation (SD) = 2.2; African M = 21.0 years, SD = 2.1). To exclude participants with past or current vestibular disorders, a thorough vestibular anamnesis using the ‘SOSTONED’ tool (Wuyts et al., 2016), as well as a vestibular test battery (spontaneous nystagmus, head impulse test, Dix-Hallpike test, Fukuda stepping test, modified Clinical Test of Sensory Interaction of Balance) was performed. Normal middle ear functioning, as determined by type A tympanograms (Jerger, 1970), normal ipsilateral stapedial acoustic reflexes, as well as normal hearing sensitivity (evidenced by air-conduction pure-tone thresholds ≤ 15 dB HL at octave intervals from 0.125 kHz to 8 kHz) were also required**.** Pure-tone audiometry was conducted using a GSI 61 Clinical Audiometer (Grason-Stadler, USA), with supra-aural headphones. Audiometric thresholds were obtained using the modified Hughson-Westlake

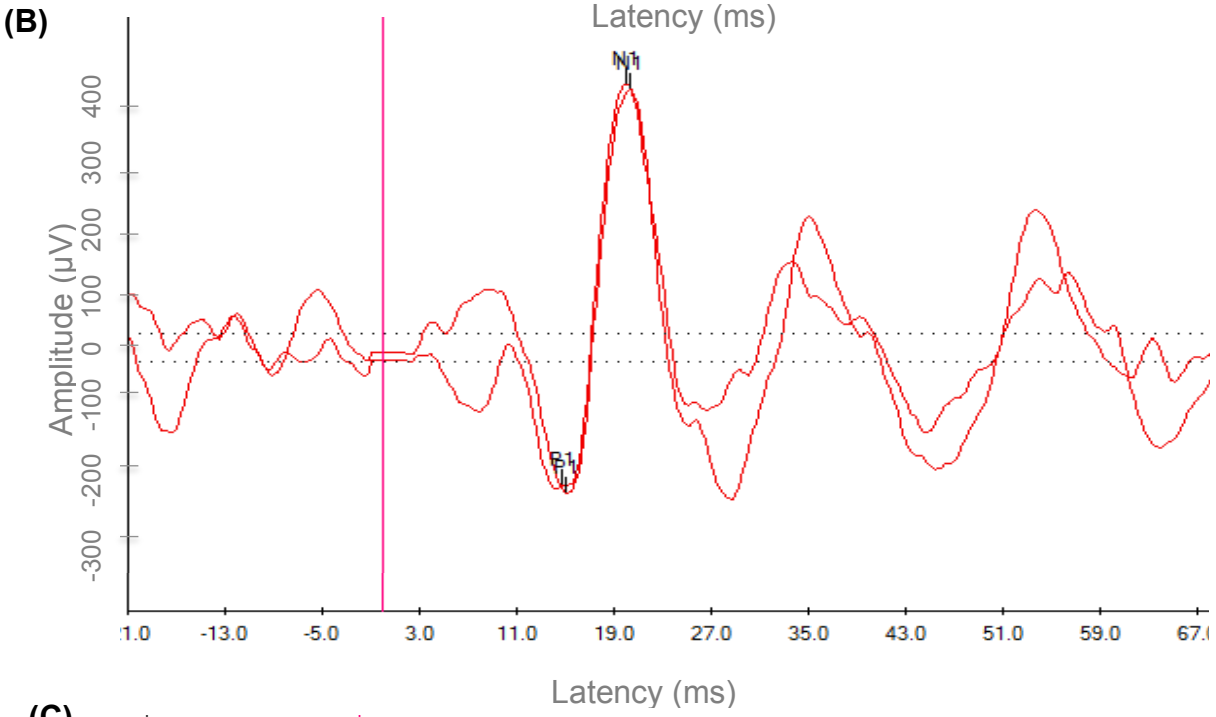
procedure (Carhart & Jerger, 1959). Acoustic immittance measurements were conducted using an Interacoustics AA222 Diagnostic Tympanometer (Interacoustics, USA). Tympanograms were obtained using an 85 dB SPL 226Hz probe tone. Ipsilateral stapedial reflexes were measured at 0.5, 1, 2 and 4 kHz. Ethical clearance for this study was obtained from the institutional ethics committee prior to the commencement of the study.

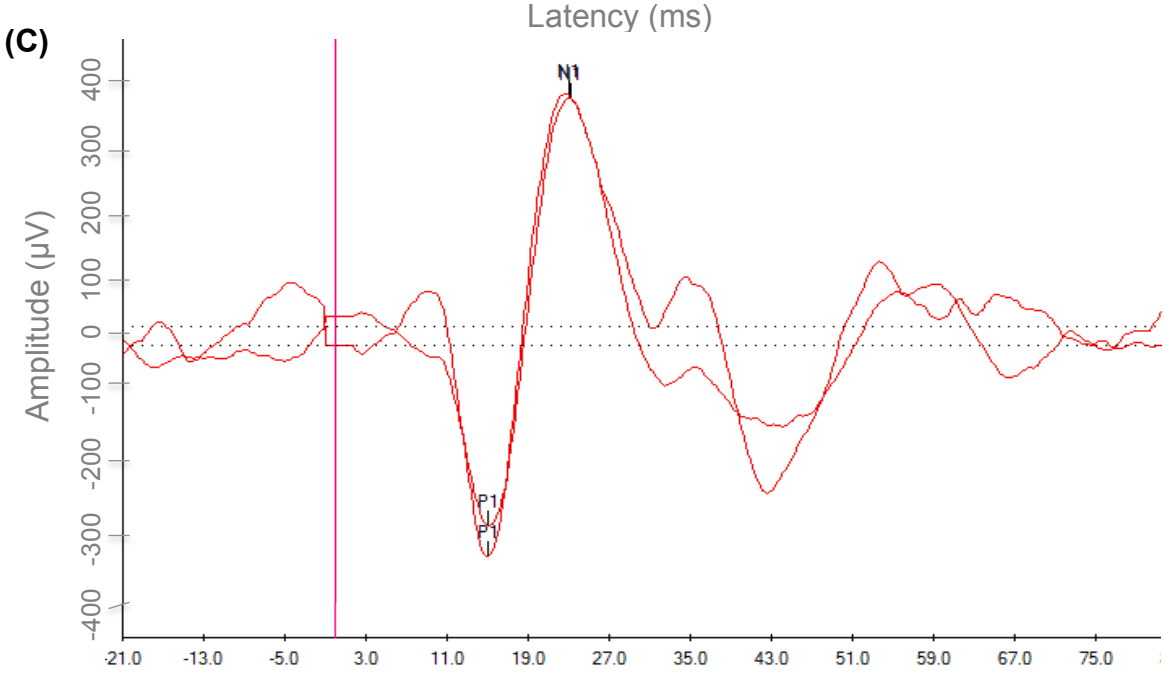
3.3.2. Research protocols and procedures

All measurements were conducted using the Bio-Logic® Navigator-Pro® system (Natus Medical, USA) in a sound treated room.

cVEMP testing

Participants were required to lie in the supine position and their heads were turned to the contralateral side. They were instructed to lift their heads and maintain a strong contraction of the SCM muscle for the duration of the presentation of an acoustic stimulus. An air-conducted 500 Hz tone burst was presented using insert earphones (3M EARTONE®, 3A), with an intensity of 95 dB nHL and a stimulus rate of 5.1 Hz, an alternating polarity and a rise/plateau/fall time of 2 – 0 – 2 (ms), with Blackman gating. Filters were placed at 10 Hz (high-pass) and 1500 Hz (low-pass). Self-adhesive electrodes (Ambu®, Bluesensor) were used, with the active electrode placed over the bulk of the SCM muscle, the reference electrode on the upper edge of the sternum and the ground electrode on the forehead **(Figure 4A**, Chapter 2**)**. Skin was prepared with alcohol swabs and Everi® conductive and abrasive paste prior to the positioning of the electrodes, to ensure that impedances were kept below 5 kΩ. Muscle tension was controlled for using a correction algorithm built into the software for all amplitude measurements of the cVEMP, resulting in a rectified amplitude measure (Colebatch, 2009; Welgampola & Colebatch, 2005; Welgampola et al., 2003). Absolute latencies of p13 and n23 (ms), peak-to-peak amplitude (raw and rectified) (μV) and the asymmetry ratio (Welgampola & Colebatch, 2001) of rectified peak-to-peak amplitude were collected. The typical cVEMP response, raw and rectified, can be seen below in **Figure 5 - 6.**





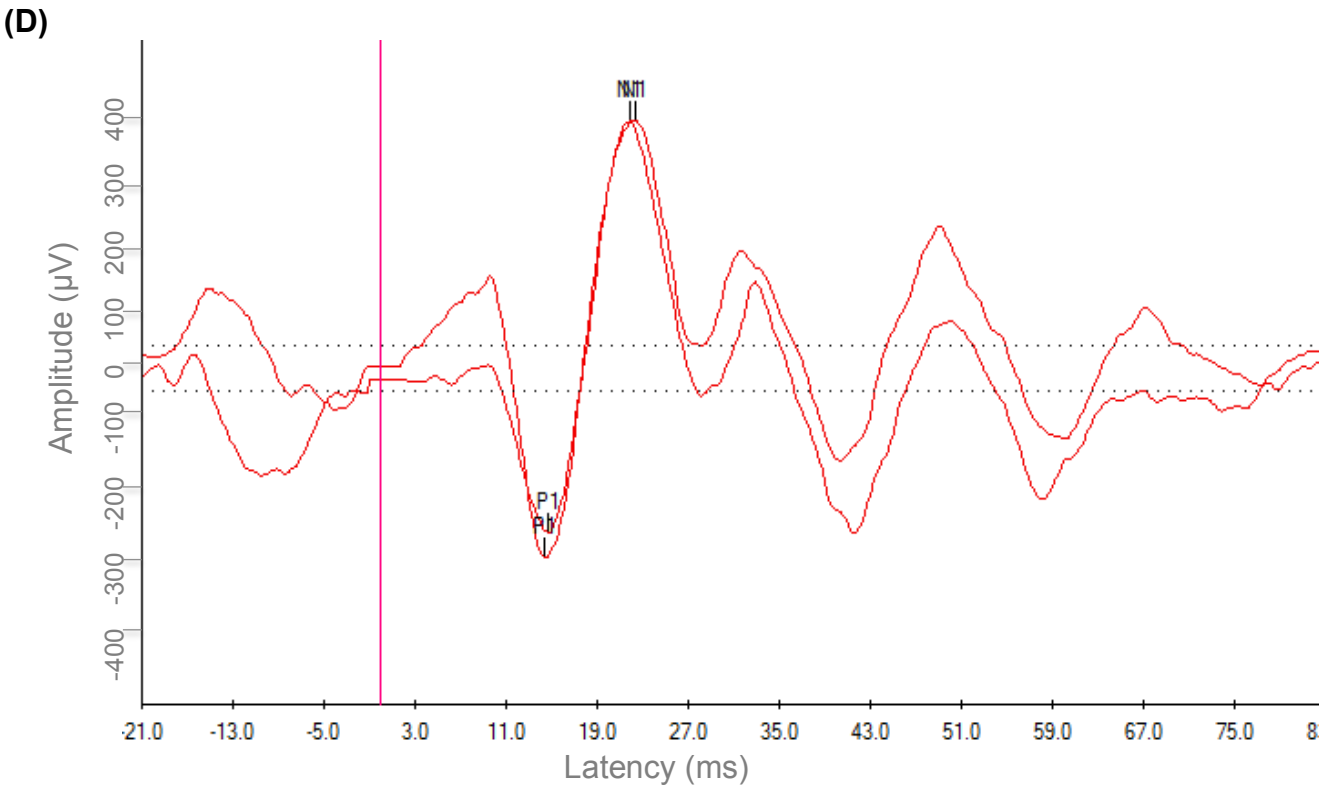
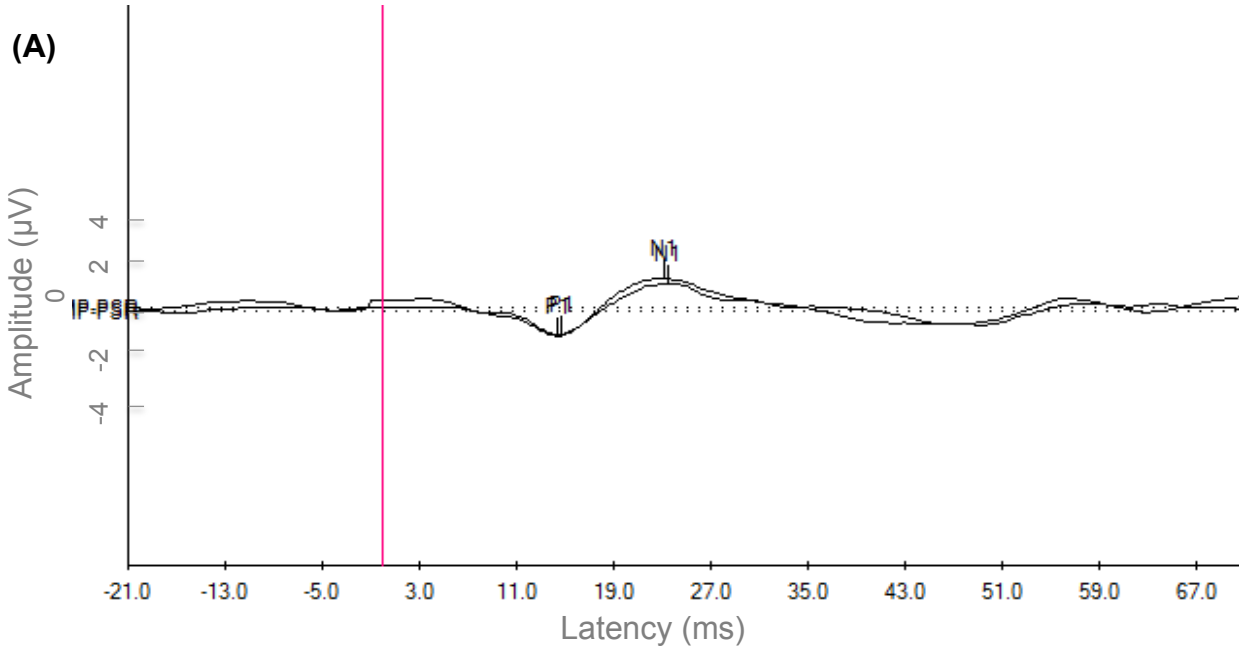


Figure 5: **Typical raw cVEMP response by race and gender**

(Key: (A) Caucasian female, (B) Black African female, (C) Caucasian male, (D), Black African male)



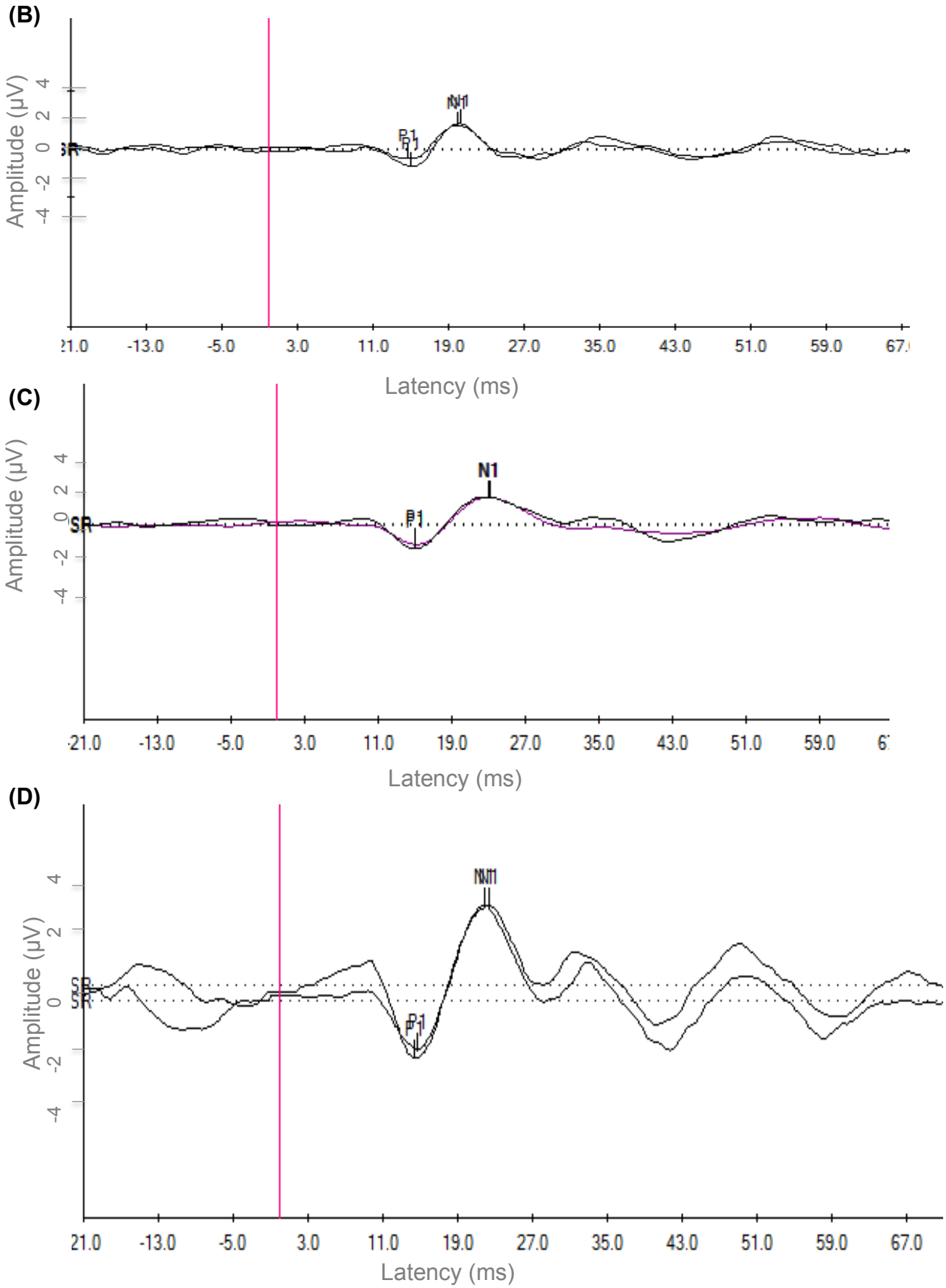


Figure 6: Typical rectified cVEMP response by race and gender

(Key: (A) Caucasian female, (B) Black African female, (C) Caucasian male, (D), Black African male)

EMG testing

In order to understand any possible difference in cVEMP amplitude between race and gender groups, it was important to obtain more information regarding each individual's muscle tension and neck length. The myoelectric values of the SCM muscles during the contraction required for cVEMP procedures were measured by means of EMG testing. Electromyographic recordings were conducted using a NeuroTrac^{TM} ETS v1.0 device (Verity Medical LTD, United Kingdom). A single-channel recording with threshold of 18.5 µV/200.0 µV, with continuous sound feedback and a narrow filter was utilised. Self-adhesive electrodes (Lifecare®) were placed as follows: two electrodes on the bulk of the SCM muscle, approximately 2cm apart and one electrode on the greater tubercle bony process of the humerus **(Figure 4C**, Chapter 2**)**. The average EMG response (µV) of each SCM muscle in a contracted and relaxed state was calculated and recorded. This was an indication of the average myoelectric signals during the contraction and relaxation of each SCM muscle. Participants were prepared in the same manner as for the cVEMP testing, however EMG and cVEMP testing were not conducted simultaneously. Participants were required to lift and relax their heads four times on each side, in response to a command given by the software, while EMG recordings were taken of the SCM muscle in a contracted and relaxed state. Feedback was inhibited, as the purpose of the testing was not neuromuscular rehabilitation. Furthermore, contraction and relaxation cycles were five seconds long, with five trials in each test.

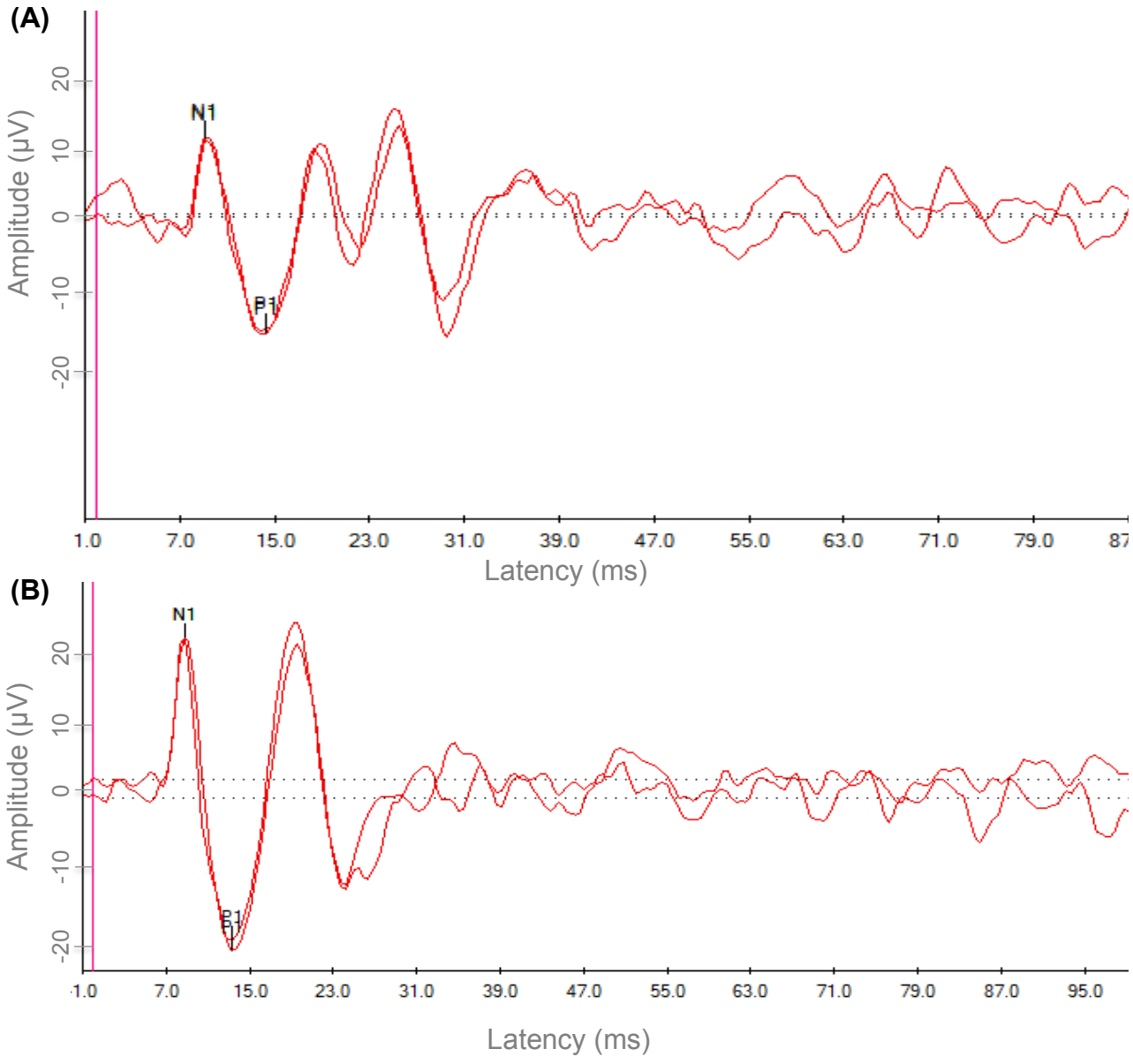
Measurement of neck length and SCM muscle width

The neck length of each participant was measured on each side by measuring the distance between two reference points on the neck, namely the mastoid bone tip and a point from the mastoid tip perpendicular to the clavicle, a measurement procedure previously used by Chang et al. (2007). The individual was required to turn the head to the contralateral side, but was not required to contract the SCM muscle for this measurement. The width of the SCM muscle was measured over the belly of the muscle, while the individual lifted the head while turned to contract the muscle. These measurements were taken using a flexible measuring tape and measured in centimetres (cm).

oVEMP testing

Participants were required to lie in the supine position and were instructed to maintain an upward gaze of 30° for the duration of testing, which was achieved by fixating their gaze on a stationary marked sign adhered to the ceiling of the booth. A 500 Hz toneburst with

intensity of 95 dB nHL, alternating polarity, a stimulus rate of 5.1 Hz and rise/plateau/fall times of 1 – 4 – 1 (ms), with Blackman gating was utilised. Filters were placed at 1 (12 dB/octave) (low-pass) and 500 Hz (high-pass). Self-adhesive electrodes were placed using an alternative oVEMP position (Leyssens et al., 2016; Sandhu et al., 2013; Vanspauwen et al., in press), with the active electrode placed more laterally on the inferior oblique muscle, the reference electrode towards the medial canthus of the nose and the ground electrode on the forehead **(Figure 4B**, Chapter 2**)**. Absolute latencies of n10 and p15 (ms), peak-to-peak amplitude (μV) and the asymmetry ratio (Welgampola & Colebatch, 2001) of peak-to-peak amplitude were collected. The authors decided not to perform EMG measurements of the inferior oblique muscle, due to the invasive nature of the measurement required for this muscle. A typical oVEMP response by race and gender can be seen in **Figure 7**.



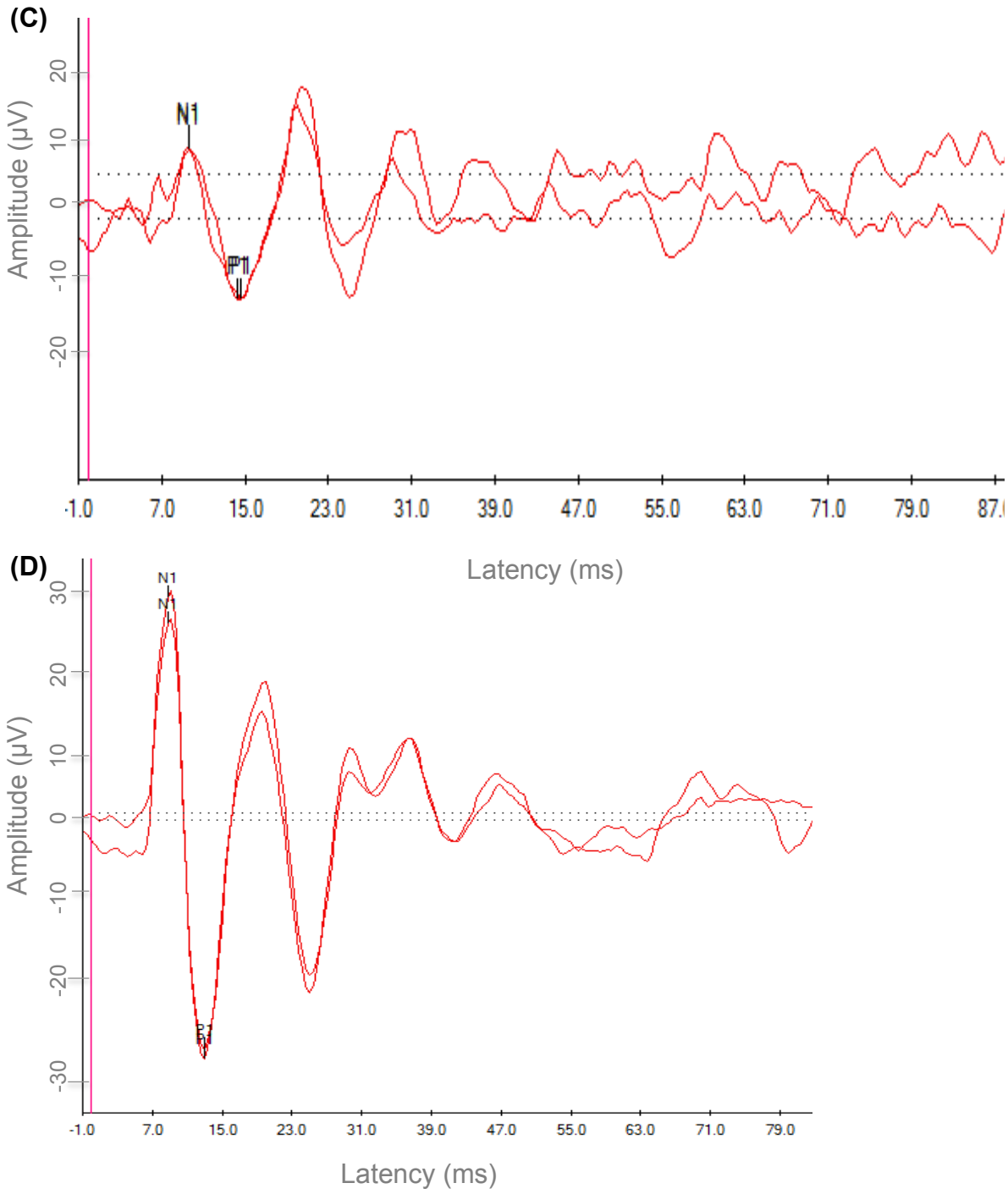


Figure 7: Typical oVEMP response by race and gender

(Key: (A) Caucasian female, (B) Black African female, (C) Caucasian male, (D), Black African male)

ABR testing

Participants were required to lie still and quiet in the supine position. Air-conducted click stimuli with an intensity of 80 dB nHL and a stimulus rate of 13.3/sec were presented using insert earphones (3M EARTONE®, 3A). ABR filter settings were between 3000 Hz (low-pass) and 30 Hz (high-pass). Two traces of 2000 sweeps were conducted for both ears, in which both rarefaction and condensation polarities were used separately. The following

electrode montage was used: the active electrode on the forehead, the ground electrode on the mastoid behind the non-test ear and the reference electrode on the mastoid behind the test ear. Absolute latencies of waves I, III and V, as well as the interpeak latency differences of waves I-III, III-V and I-V were recorded (ms). Furthermore, the Wave I-V amplitude ratio was calculated for all participants.

3.3.3. Data analysis

Descriptive statistics, such as mean and standard deviation were determined for the results of all response parameters of each test conducted as part of this study. Histograms, normal quantile plots and Shapiro-Wilk normality tests confirmed whether data was normally distributed. Significant differences in responses between the two ethnic groups, as well as gender, were evaluated by means of two-way analysis of variance (ANOVA) for normally distributed data. Non-normal variables that did not meet homogeneity of variances were first transformed with an appropriate transformation (natural log or square root). When transformations did not correct heteroskedasticity, the non-parametric two-way ANOVA alternative, the Scheirer-Ray-Hare test, was used. Significant interactions were further examined by means of one way ANOVA and Tukey's honestly significant difference (HSD) tests. Data analysis was performed using STATA software (Version 12, StataCorp LP, Texas, USA). A p value of <.05 was used to indicate significance.

3.4. Results

Two-way ANOVA confirmed that both black African and Caucasian groups were equally matched according to age and gender, with no significant difference in age across both gender (p = 0.368) and race (p = 0.211). Descriptive statistics are summarised in **Table 3**. Typical oVEMP and cVEMP responses by race and gender group are displayed in **Figures 5 - 7**.

A number of outliers were observed in the data and all analyses were run with and without the outliers. Only two variables were affected by the omission of outliers, namely cVEMP n23 latency on the right side and EMG contracted amplitude on the left side. Significant effects and interactions in all other variables were unchanged when outliers were excluded from analyses and only the results from analyses including all observations are reported.

Table 3: Descriptive statistics by race and gender

Parameter	Ear/ Side	CM (*n* = 15) Mean (SD)	CF (*n* = *15)* Mean (SD)	BAM (*n* = 15) Mean (SD)	BAF (*n* = 15) Mean (SD)
cVEMP					
p13 latency (ms)	Left	15.8 (1.1)	15.6 (1.5)	15.3 (1.0)	14.9 (1.3)
	Right	15.8 (1.3)	15.5 (1.6)	15.4 (1.4)	15.6 (1.9)
n23 latency (ms)	Left	23.4 (1.5)	22.6 (1.5)	22.2 (1.8)	21.7 (1.6)
	Right	23.8 (1.7)	22.7 (1.6)	22.1 (1.4)	21.8 (2.2)
Raw amplitude	Left	362.9 (211.9)	378.5 (189.0)	530.3 (223.6)	323.3 (216.3)
(µV)	Right	412.5 (309.6)	406.0 (193.9)	644.6 (341.1)	334.1 (259.7)
Rectified amplitude	Left	1.5 (0.7)	1.5 (0.5)	1.5 (0.6)	1.6 (0.6)
(µV)	Right	1.1 (0.5)	1.4 (0.7)	1.3 (0.7)	1.5 (0.9)
Asymmetry ratio (%)		26.8 (14.1)	13.7 (11.2)	21.9 (11.9)	20.2 (17.0)
oVEMP					
n10 latency (ms)	Left	9.6 (0.9)	9.1 (0.5)	9.6 (1.0)	9.1 (0.6)
	Right	9.5 (0.7)	9.2 (0.5)	9.7 (1.5)	8.9 (0.3)
p15 latency (ms)	Left	14.3 (1.0)	14.0 (0.8)	14.0 (1.6)	13.3 (0.8)
	Right	14.2 (1.2)	13.7 (0.7)	14.2 (2.0)	13.1 (0.6)
Amplitude (µV)	Left	11.6 (9.4)	14.8 (8.7)	17.0 (9.4)	22.5 (9.3)
	Right	10.8 (9.6)	15.9 (9.7)	17.8 (8.1)	18.3 (7.5)
Asymmetry ratio (%)		25.7 (24.7)	20.8 (20.0)	26.7 (22.8)	17.9 (16.5)
EMG					
Contracted	Left	58.1 (26.1)	80.8 (29.0)	116.7 (64.9)	91.6 (29.1)
amplitude (µV)	Right	76.3 (26.8)	73.4 (16.5)	150.4 (72.1)	106.2 (31.9)
Relaxed amplitude	Left	10.0 (5.0)	12.9 (6.5)	20.5 (10.3)	14.8 (5.4)
(µV)	Right	15.2 (10.9)	14.9 (8.1)	29.6 (13.1)	17.9 (7.5)
Neck length (cm)	Left	19.3 (1.7)	17.3 (1.9)	19.1 (1.4)	16.9 (1.3)
	Right	19.7 (1.9)	17.0 (1.8)	18.8 (1.3)	17.0 (1.7)
SCM muscle width	Left	6.8 (0.7)	6.4 (0.9)	6.9 (0.8)	6.4 (0.5)
(cm)	Right	6.5 (0.6)	5.8 (1.0)	6.7 (0.7)	6.2 (0.5)
ABR					
Wave I latency	Left	1.6 (0.1)	1.5 (0.1)	1.6 (0.2)	1.6 (0.1)
(ms)	Right	1.6 (0.2)	1.4 (0.2)	1.6 (0.1)	1.6 (0.2)
Wave III latency	Left	3.8 (0.2)	3.7 (0.1)	3.8 (0.2)	3.7 (0.1)
(ms)	Right	3.6 (0.2)	3.5 (0.2)	3.7 (0.2)	3.6 (0.1)
Wave V latency	Left	5.6 (0.2)	5.4 (0.2)	5.7 (0.2)	5.5 (0.1)
(ms)	Right	5.7 (0.2)	5.6 (0.3)	5.7 (0.2)	5.6 (0.2)
Wave I-III	Left	2.2 (0.1)	2.2 (0.2)	2.3 (0.2)	2.2 (0.2)
interpeak latency	Right	2.1 (0.2)	2.1 (0.2)	2.1 (0.3)	2.0 (0.2)
(ms)					
Wave III-V	Left	1.8 (0.2)	1.8 (0.1)	1.9 (0.2)	1.8 (0.1)
interpeak latency	Right	2.1 (0.2)	2.1 (0.2)	2.1 (0.2)	2.1 (0.2)
(ms)					
Wave I-V interpeak	Left	4.0 (0.1)	4.0 (0.2)	4.2 (0.2)	4.0 (0.2)
latency (ms)	Right	4.1 (0.3)	4.2 (0.3)	4.1 (0.2)	4.1 (0.3)
Wave I-V	Left	2.2 (1.6)	2.4 (1.9)	1.6 (1.3)	1.5 (0.7)
amplitude ratio	Right	1.6 (1.2)	1.6 (1.4)	2.1 (1.8)	2.4 (1.0)

(Key: CM = Caucasian male, CF = Caucasian female, BAM = black African male, BAF = black African female, SD = standard deviation, ms = millisecond, µV = microvolt)

3.4.1. cVEMP responses

All cVEMP response parameters were analysed statistically for gender and race effects by means of a two-way ANOVA. Two cVEMP response parameters demonstrated racial- or

gender-related differences. A significant main effect for race was observed for the n23 latency parameter, with black African participants displaying shorter latencies than their Caucasian counterparts (left F [1,56] = 6.98, *p* = 0.011; right F [1,56] = 8.12, *p* = 0.006) (**Figure 10A**). There was one extreme outlier in the n23 latency parameter on the right side, a black African female. Two-way ANOVA excluding this participant resulted in a significant main effect for gender (F [1,55] = 4.91, *p* = 0.031) in addition to the main race effect (F [1,55] = 13.55, *p* = 0.001). Furthermore, a significant interaction effect for gender and race was observed for the raw amplitude of the cVEMP response, with black African males obtaining larger raw amplitudes compared to black African females (left F [1,56] = 5.19, *p* = 0.023; right F [1,56] = 4.88, *p* = 0.031) (**Figure 8A**). No significant differences were noted for the p13 latency, rectified amplitude or the asymmetry ratio of the cVEMP.

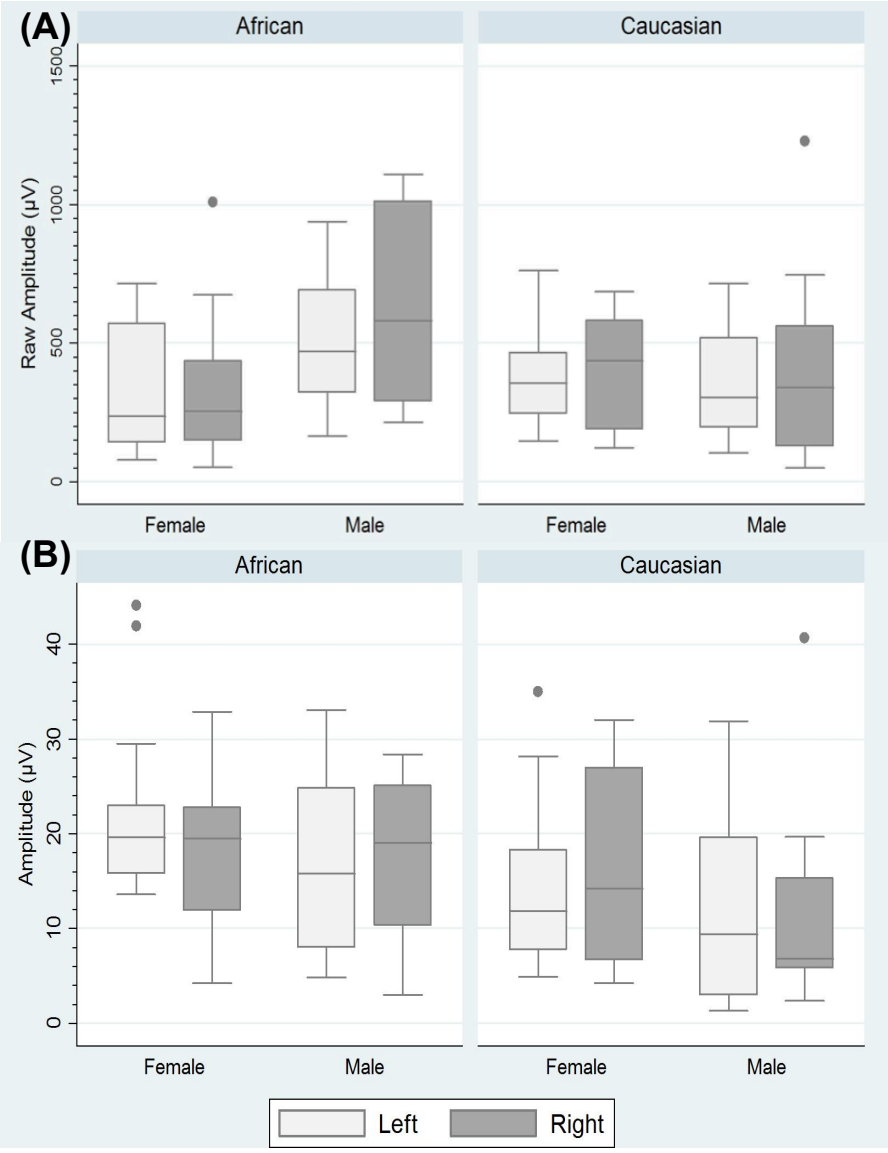


Figure 8: VEMP amplitude differences by race and gender

Key: (A) cVEMP raw amplitude differences, (B) oVEMP amplitude differences

3.4.2. EMG responses, neck length and SCM muscle width

The EMG response parameters were log-transformed and a two-way ANOVA tested the significance of main effects and interaction between gender and race. A significant interaction effect was observed for the contracted muscle state, where black African males obtained larger amplitudes in comparison to Caucasian males on the left side (left F [1,56] = 5.28, p = 0.025) (**Figure 9A**). However, there were two outliers (black African males) in the EMG contracted response on the left side and excluding these outliers from the ANOVA analysis rendered this interaction not significant (F [1,54] = 3.16, p = 0.081). A main effect for race was seen in the contracted muscle state on the right side (right F [1,56] = 26.77, p < 0.001), with black African participants obtaining larger amplitudes than Caucasian participants (**Figure 9A**). A similar trend was seen in the relaxed muscle state. A significant interaction of gender and race was noted for the relaxed muscle state on both sides (left F [1,56] = 4.88, p = 0.031; right F [1,56] = 4.37, p = 0.041), with black African males obtaining larger amplitudes compared to all three other participant groups (**Figure 9B**). For neck length and SCM muscle width, significantly shorter neck lengths and narrower muscles were measured for all female participants (length: left F [1,56] = 25.77, p < 0.001; right F [1,56] = 27.29, p < 0.001; width: left F [1,56] = 4.77, p = 0.033; right F [1,56] = 12.78, p = 0.001).

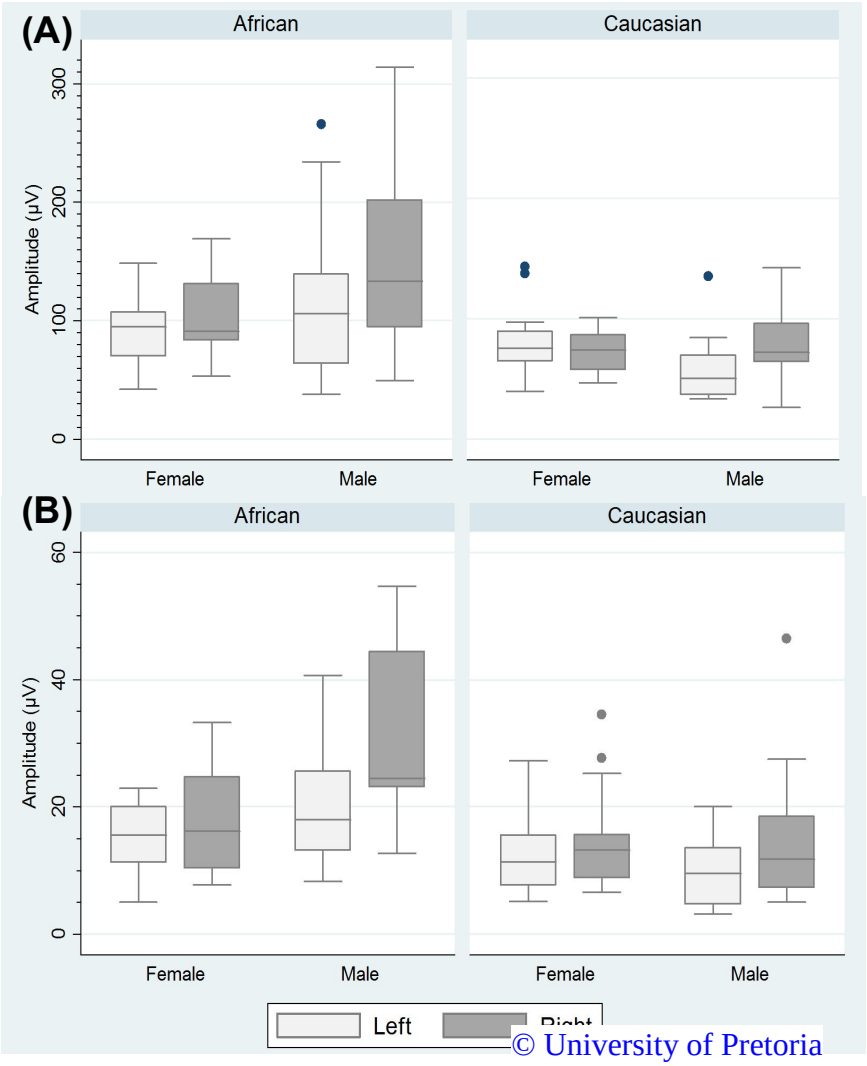


Figure 9: EMG Amplitude differences by race and gender

Key: (A) Contracted amplitude differences, (B) Relaxed amplitude differences

3.4.3. oVEMP responses

Two-way ANOVA indicated a significant main effect by gender for the n10 latency parameter on both sides (left F [1,56] = 6.62, p = 0.013; right F [1,56] = 4.62, p = 0.038), with females obtaining shorter latencies compared to males (**Figure 10B**). Furthermore, a significant main effect for race was observed for the p15 latency parameter on both sides (left F [1,56] = 6.33, p = 0.016; right F [1,56] = 4.57, p = 0.041), with black African participants obtaining shorter latencies than Caucasian participants (**Figure 10C**). For the amplitude parameter, a significant main effect was found in race for the oVEMP amplitude (left F [1,56] = 7.61, p = 0.008; right F [1,56] = 4.33, p = 0.042), with the black African group obtaining larger amplitudes compared to the Caucasian group (**Figure 8B**). The asymmetry ratio did not show any race- or gender-related differences.

3.4.4. ABR responses

The different ABR response parameters were analysed statistically in terms of gender and race by means of two-way ANOVA. An interaction of gender and race was seen in only the Wave I component in the right ear (right F [1,56] = 4.06, p = 0.048). A post hoc Tukey test showed that Caucasian females differed significantly from black African males and females, with Caucasian females obtaining shorter latencies of this component. Furthermore, the absolute latency of Wave V in the left ear displayed a main effect for race (left F [1,56] = 4.45, p = 0.039), with the Caucasian group obtaining a slightly shorter latency compared to the black African group. A main effect for gender was observed for the latencies of the Wave III component in both ears (left F [1,56] = 9.71, p = 0.003; right F [1,56] = 7.43, p = 0.009), the wave V component in the left ear (left F [1,56] = 16.46, p < 0.001) and the interpeak latency of Waves I-V in the left ear (left F [1,56] = 6.41, p = 0.014). Females obtained shorter latencies for the wave III and V components, as well as a shorter interpeak latency of Waves I-V in the left ear, compared to males.

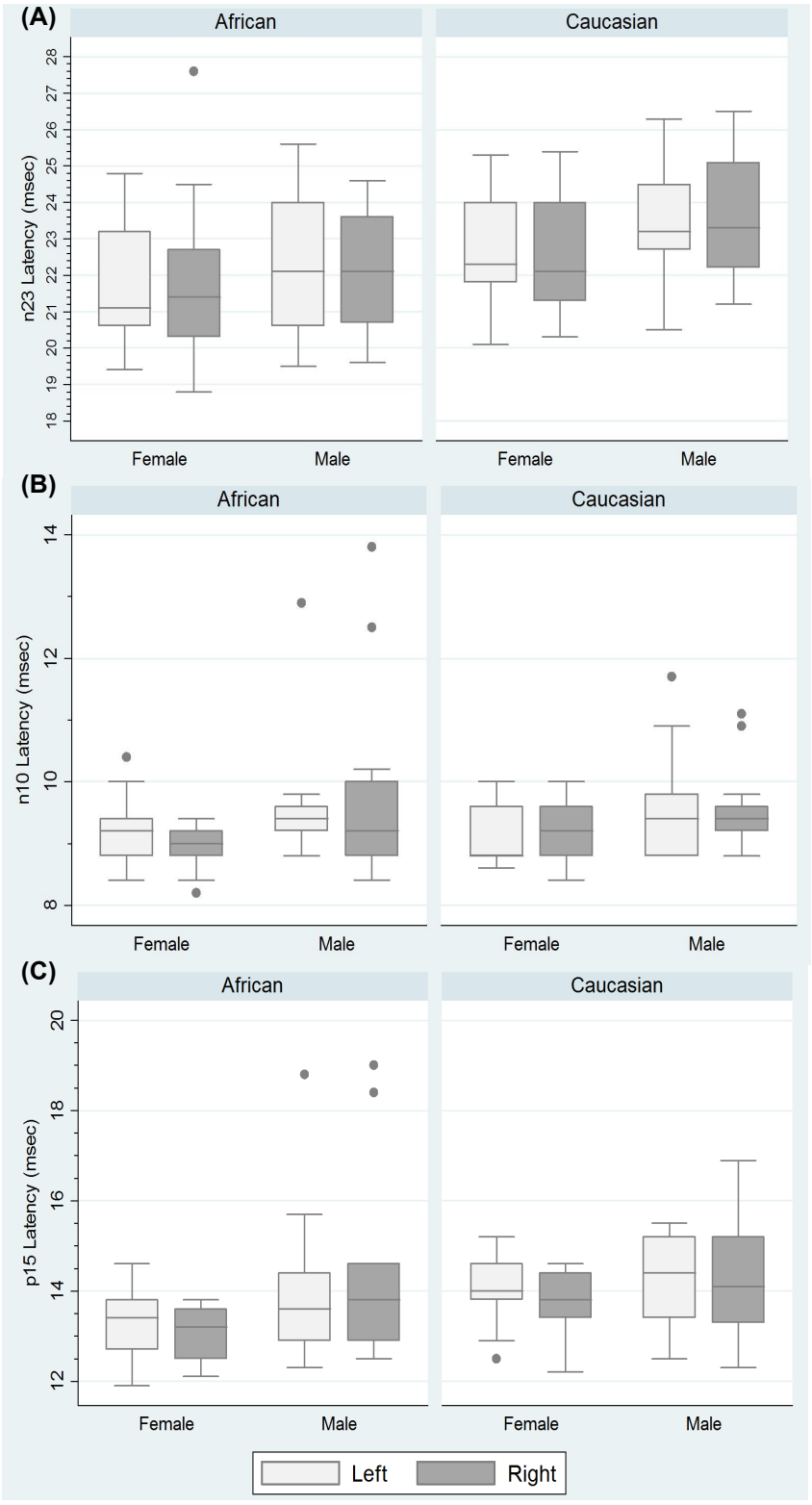


Figure 10: Latency differences by race and gender

Key: (A) cVEMP n23 latency differences, (B) oVEMP n10 latency differences, (C) oVEMP p15 latency differences

3.5. Discussion

Cervical VEMPs (cVEMPs) and ocular VEMPs (oVEMPs) are two clinical tests to examine saccular and utricular function, respectively (Curthoys et al., 2014; Weber & Rosengren, 2015; Welgampola & Colebatch, 2005; Xu et al., 2016). To date, there are still many controversies revolving around the most ideal stimulus and recording parameters for these tests, as well as possible confounding factors that could influence these parameters. This study has focused on the influence of race and gender on the VEMP response parameters, a topic with limited existing research.

3.5.1. Amplitude differences

The findings of the present study on the amplitude parameter of the cVEMP and oVEMP both agreed with and expanded on the findings of Li et al. (2015), indicating that racial and gender differences do indeed exist for this parameter. For the cVEMP, black African males obtained significantly larger raw amplitudes than black African females. The raw amplitude of the cVEMP response is directly related to the tonic contraction of the SCM muscle (Lee et al., 2008) and structural muscle differences may affect both latencies and the raw amplitude of the cVEMP response (Chang et al., 2007). Therefore, the cVEMP raw amplitude difference may be explained by differences in muscle bulk between males and females, since, males are known to have typically larger and stronger neck muscles than females (Kamibayashi & Richmond, 1998; Vasavada et al., 2008). This may allow males to achieve a larger contraction of the SCM muscle than females. It is necessary to consider why this cVEMP raw amplitude difference was seen in black African males and females, opposed to Caucasian males and females. Previous research has shown that black Africans have different muscle characteristics compared to Caucasians (Araujo et al., 2010; Gallagher et al., 1997). African-American adult males and females have larger skeletal muscle mass than Caucasians, evidenced by larger total body potassium (TBK) values (Gallagher et al., 1997). In another study, Araujo et al. (2010) found that although black African males (African M = 48 years) had higher lean muscle mass, they had lower levels of physical function, when compared to Caucasian males. This may indicate differences in specific muscle architecture by race, but this does not necessarily indicate higher levels of muscle function in these racial groups. This explanation for raw amplitude differences may be further corroborated by the EMG findings of the present study. Highly significant differences were noted in all EMG test conditions between the racial groups,

with black African males obtaining significantly larger amplitudes than the other three participant groups in both contracted and relaxed SCM muscle conditions. The EMG test is an effective test of muscle function and may give an indication of the myoelectric value of a muscle in different conditions (Konrad, 2006). This may indicate that young black African adults, specifically black African males, have different muscle characteristics compared to Caucasian males and females, which has also been evidenced in previous studies (Araujo et al., 2010; Gallagher et al., 1997).

As the raw amplitude of the cVEMP response is affected by tonic SCM muscle contraction (Lee et al., 2008), the interaction effect seen for the raw cVEMP amplitude may be attributed to differences in this tonic muscle contraction between the black African males and black African females, evidenced by higher amplitudes obtained by black African males in EMG measurements. Although statistically significant, this finding is clinically less significant. Raw cVEMP amplitudes are purely a reflection of tonic muscle contraction and are not an indication of saccular function. Rectified cVEMP amplitudes are used to control for muscle tension, thereby eliminating the effect of muscle differences between individuals and focusing on saccular function (Lee et al., 2008). When reviewing the rectified cVEMP amplitudes of all participant groups in the current study, no significant differences existed by gender or race. This indicates that differences seen for the cVEMP raw amplitude parameter between gender and race are purely based on muscle differences and not differences in saccular function. These results indicate that no separate gender- and race-related normative values are needed for cVEMP amplitude parameters, provided that rectified cVEMP amplitudes are used.

Significant differences were also seen for the oVEMP amplitude parameter, agreeing with the findings of Li et al. (2015). Black African individuals obtained larger amplitudes, compared to Caucasian individuals. This difference may be explained by a theory regarding the effect of melanin pigmentation on vestibular organ metabolism in the utricle suggested by Li et al. (2015). They hypothesised that the higher presence of melanocytes in the vestibular organs of black Africans and their close arrangement to vestibular dark cells may affect vestibular organ metabolism differently to that in Caucasians. These vestibular dark cells are present in the semicircular canals and utricle, but not in the saccule (Harada, 1983). This may explain how the utricular maculae are activated differently in a young adult black African population, as incoming vestibular stimulation may be metabolised and processed quicker. Another explanation for the racial oVEMP

amplitude difference may concern differences in facial morphology between black African and Caucasian adults. Talbert et al. (2014) found black African-American males to have a larger and more prominent periocular region than Caucasian-American males. The periocular region is the area where the active electrode of the oVEMP measurement is placed, and this means that the electrode may be placed more securely in a black African population compared to a Caucasian population. Furthermore, this may be an indication of a larger muscle area and mass in the black African population, which would affect the amplitude of the oVEMP. Additionally, this would also mean that the distance between the active electrode and reference electrode increases in this population, which has been shown to have a positive effect on the amplitude of the oVEMP response (Piker et al., 2011; Zuniga et al., 2014). However, further measurement of the inferior oblique muscle and periocular region is needed to confirm this theory. One other theory that may be suggested for the oVEMP amplitude difference is related to the findings of the current study on cVEMP raw amplitude. Black African adults exhibit muscle differences compared to Caucasian adults, as was seen with the EMG measurements and cVEMP raw amplitude. It is plausible to assume that these same differences may be seen in extraocular muscles, had the same EMG measurement been conducted on these muscles. Future research should measure racial extraocular muscle differences and their relation to oVEMP amplitude. Nevertheless, the findings of the current study indicate that separate race-related normative values are required for the oVEMP amplitude parameter.

3.5.2. Latency differences

Significant differences in the latency parameter were also observed in the present study. For the cVEMP, black African participants achieved significantly shorter n23 latencies in comparison to Caucasian participants. A previous study found no racial latency differences for the cVEMP response (Li et al., 2015); however, this study focused on the p13 latency parameter of the cVEMP and did not investigate any possible racial n23 latency difference. A possible explanation for the cVEMP latency difference found in the present study may be related to tonic muscle contraction of the SCM muscle. In a recent study by Rosengren (2015), it was found that p13 latency is affected by the degree of tonic muscle contraction, with weaker contractions resulting in prolonged latencies and stronger contractions resulting in earlier latencies. Furthermore, this study noted that weaker muscle contractions resulted in a poor or absent n23 component, but as the muscle contraction increased, the n23 component became more prominent. Thus, the latency of the n23 peak may very well be affected by the degree of muscle contraction. Since the EMG findings of

the present study indicated that black African individuals had larger raw amplitudes and thereby stronger muscle contraction than Caucasian individuals, this may explain the racial n23 latency difference of the present study. The ABR measurements that were performed in the present study to find possible gender and racial neural differences did not reveal similar latency trends when compared to the cVEMP results. A general main effect of shorter wave V latencies was observed for Caucasian participants and female participants. Therefore, the shorter n23 cVEMP latencies for black African participants is more likely to be caused by racial muscle differences. Although no significant main effect for race was noted for the cVEMP p13 latency, it was observed that both black African males and females obtained shorter latencies compared to their Caucasian counterparts. This may indicate that the p13 latency of this study was indeed affected by degree of muscle contraction, however, as exact degree of muscle contraction was not monitored during cVEMP testing, it is unknown whether all participants contracted maximally and what the subsequent effect on the p13 component was. If the focus of the present study had been to investigate racial differences in c- and oVEMP responses using varying degrees of contraction with real-time EMG monitoring, similar to the study by Rosengren (2015), a cVEMP p13 latency difference may have been observed at the maximal point of contraction for each participant group.

Similarly, black African participants also achieved significantly shorter p15 latencies for the oVEMP response, compared to Caucasian participants. These results are in contrast to the findings of Li et al. (2015), who found the shorter n10 latencies in African adults. However, it should be mentioned that they did not investigate p15 latency differences by race and gender. Furthermore, these authors hypothesised that the racial latency difference observed may also relate to genetics and environmental factors. The current study may not have observed a racial oVEMP n10 latency difference, as the participants were all South African-born black Africans and Caucasians, and may have a varied genetic make-up and environment compared to the black African- and Caucasian-American participants of the study by Li et al. (2015). The race-based p15 latency difference observed in the current study may also be explained by the mechanism relating to melanin pigmentation in the two racial groups, which has been explained above. Other theories that may affect the racial oVEMP p15 latency difference include those described for the differences seen in the oVEMP amplitude parameter. Talbert et al. (2014) found black African-American males to have larger periocular regions, which may also be an indication of larger extraocular muscles in this population. Although the EMG

measurements conducted as part of this study were not conducted on extraocular muscles, the racial differences seen in the EMG measurement of the SCM muscle may extend to the extraocular muscles. Racial differences in oVEMP p15 latency may be explained by differences in muscle contraction between black African and Caucasian adults, however, further research is warranted to confirm this theory.

For the oVEMP, a significant gender difference was also seen for the n10 latency parameter in the current study, with females obtaining shorter latencies. This contradicts previous research, which found no gender-based differences (Chou et al., 2012; Versino et al., 2015) or a difference only in amplitude of the oVEMP responses (Sung et al., 2011; Xie et al., 2011). One possible explanation for this n10 latency difference between males and females may be related to head diameter. Although no studies to date have investigated a correlation between head diameter and VEMPs, several studies have indicated a positive correlation in head diameter and ABR latencies (Dehan & Jerger, 1990; Nikiforidis, Koutsojannis, Varakis, & Goumas 1993; Trune, Mitchell, & Phillips, 1988). These studies indicated that a larger head diameter, typically seen in males, may cause later latencies of ABR peaks. A similar trend was also found in the current study, with longer ABR latencies for the male participants. The fact that the male participants of the current study also had significantly longer neck lengths, which was also found in a study by Vasavada et al. (2008), could also explain the longer cVEMP latencies for male participants. Another explanation for gender differences in ABR latencies suggested by Dehan & Jerger (1990) is the effect of hormones on the ABR response. They found that the ABR wave V latencies varied significantly during the changing hormonal environment of young females. Further research is required to link head diameter and neck length to gender differences in cVEMP latencies, as well as to investigate a possible effect of hormonal changes on the latency parameters.

It is noteworthy to mention that although the race- and gender-related VEMP latency findings of the current study may be statistically significant, these findings may not be clinically significant. The latencies obtained by the black African group were shorter, which is not considered to be a sign of vestibular pathology. Rather, prolongation of p13 and n23 cVEMP latency has been shown to indicate central pathologies affecting the vestibular system, such as vestibular schwannomas and demyelinating conditions (Brantberg, 2009). All latency measurements in the black African group were well within established normal

limits (Janky & Shepard, 2009). Nevertheless, they emphasise the importance for race- and gender-related normative values for the latency parameters.

3.5.3. Limitations and future research

Two main limitations of the present study should be mentioned. Firstly, using an objective measurement of neck length and other muscle properties of the SCM muscle, such as ultrasound or MRI scans, would have yielded more accurate results. Secondly, it is necessary to measure whether these observed differences in EMG of the SCM muscle also exist in the inferior oblique muscle and whether these results agree with the suggestion of the current study, that racial differences may be based on different muscle characteristics in racial groups.

3.6. Conclusion

Differences based on race and gender were found in both the cVEMP and oVEMP responses. Black African adults obtained shorter latencies and larger raw amplitudes than young Caucasian adults. Also, females obtained shorter latencies, males obtained larger amplitudes. Several theories may be suggested for these observed differences between racial and gender groups and emphasise the importance of gender- and race-related normative data for both cVEMP and oVEMP latency parameters, as well as oVEMP amplitude parameters.

CHAPTER FOUR

Discussion and Conclusion

4.1. Overview

Cervical VEMPs (cVEMP) and ocular VEMPs (oVEMP) are two clinical tests that are used to examine saccular and utricular function, respectively (Xu et al., 2016; Weber & Rosengren, 2015; Papathanasiou, 2015; Curthoys et al., 2014; Welgampola & Colebatch, 2005). To date, there are still many controversies revolving around the most ideal stimulus and recording parameters for these tests, as well as the different variables that may positively or negatively influence these parameters. The focus of this study has been to describe the influence of race and gender on the cVEMP and oVEMP response parameters, a topic with limited existing research. The findings of the present study have indicated that there are both race- and gender-related differences in these VEMP response parameters, which will be discussed below.

4.2. Amplitude differences

The findings of the present study on the amplitude parameter of the cVEMP and oVEMP both agreed with and expanded on the findings of previous research (Li et al., 2015) indicating that racial and gender differences do indeed exist for this parameter.

4.2.1. Combined race and gender differences in cVEMP amplitude

In the current study it was found that black African males obtained significantly larger raw amplitudes than black African females. Literature has indicated that the raw amplitude of the cVEMP response is directly related to the degree of tonic contraction of the SCM muscle (Rosengren, 2015; Lee et al., 2008; Akin, Murnane, Panus, Caruthers, Wilkinson, & Proffitt, 2004) and that structural muscle difference may affect both the latencies and the raw amplitude of the cVEMP response (Chang et al., 2007). Bearing this in mind, this cVEMP raw amplitude difference may be explained by both gender-related and race-related differences in muscle bulk. It is not surprising that the finding of the current study concerning the cVEMP raw amplitude was seen in males versus females, as males are known to have typically larger and stronger neck muscles than females (Vasavada et al., 2008; Kamibayashi & Richmond, 1998). As males have larger and stronger neck muscles, the black African males of the current study may have achieved stronger contractions of the SCM muscles than their black African female counterparts. Furthermore, it is necessary to consider why this cVEMP raw amplitude difference was seen between black

African males and females, as opposed to Caucasian males and females. Previous research has shown that black Africans have different muscle characteristics compared to Caucasians (Araujo et al., 2010; Gallagher et al., 1997). African-American adult males and females have larger skeletal muscle mass than Caucasians, evidenced by larger total body potassium (TBK) values (Gallagher et al., 1997). In another study, Araujo et al. (2010) found that although black African males (African M = 48 years) had higher lean muscle mass, they had lower levels of physical function when compared to Caucasian males. This may be an indication of differences in specific muscle architecture by race, but this does not necessarily indicate higher levels of muscle function in this racial group.

The suggestion of the current study, that cVEMP raw amplitude differences are based on differences in muscle structure and function, may also be corroborated by the EMG findings of the current study. Highly significant differences based on race were noted in all EMG test conditions, with black African participants obtaining significantly larger amplitudes than Caucasian participants in both contracted and relaxed SCM muscle conditions. Specifically, it was noted that black African males obtained larger amplitudes in both these muscle conditions than black African females, Caucasian males and Caucasian females. Electromyography (EMG) is an effective test of muscle function and may give an indication of the myoelectric value of a muscle in different conditions (Konrad, 2006). These findings may demonstrate that black African individuals, specifically black African males, have different muscle characteristics, which in turn influence the degree of muscle contraction compared to Caucasian individuals. This finding agrees with previous findings in literature (Araujo et al., 2010; Gallagher et al., 1997). As the raw amplitude of the cVEMP response is affected by tonic SCM muscle contraction (Rosengren, 2015; Lee et al., 2008; Akin et al., 2004), the interaction effect seen for the raw cVEMP amplitude may be attributed to differences in this tonic muscle contraction between the black African males and black African females, evidenced by higher amplitudes obtained by black African males in EMG measurements.

Although this finding in cVEMP raw amplitude is statistically significant, it may be clinically less significant. Raw cVEMP amplitudes are only a reflection of tonic SCM muscle contraction and do not indicate saccular or inferior vestibular nerve function. In order to control for muscle tension and contraction, cVEMP amplitudes are rectified or corrected. These rectified cVEMP amplitudes are then a more reliable indication of saccular function, as the effect of muscle tension on the cVEMP response has been eliminated (Lee et al.,

2008). When reviewing the rectified cVEMP amplitudes of all participant groups in the current study, no significant differences existed by gender or race. This indicates that differences seen for the cVEMP raw amplitude parameter between gender and race are purely based on muscle differences and not differences in saccular function.

4.2.2. Pure race or gender differences in cVEMP amplitude

No main effect of race or gender only was seen in the cVEMP raw or rectified amplitude in the current study.

4.2.3. Race differences in oVEMP amplitude

Significant differences were also seen for the oVEMP amplitude parameters, agreeing with the findings described in previous research (Li et al., 2015). In the current study, black African individuals obtained significantly larger oVEMP amplitudes compared to their Caucasian counterparts. This racial difference in oVEMP may be explained by several theories. In the study by Li et al. (2015), they hypothesised that this amplitude difference may be attributed to racial differences in melanin pigmentation and its subsequent effect on vestibular organ metabolism in the utricle. Black African individuals have been found to have a higher presence of melanocytes in the vestibular organs, and the close arrangement of these melanocytes to the vestibular dark cells, may affect vestibular organ metabolism differently to that in Caucasians. These vestibular dark cells are only found in the utricle and semicircular canals (Harada, 1983), which would explain why Li et al. (2015) did not see an amplitude difference in the cVEMP response. This may explain how the utricular maculae are activated differently in a young adult in a black African population, as incoming vestibular stimulation may be metabolised and processed quicker.

Another theory that may serve as an explanation for the racial oVEMP amplitude difference involves differences in facial morphology between black African and Caucasian adults. In a study by Talbert et al., (2014) African-American males were found to have larger and more prominent periocular regions than Caucasian-American males. The periocular region is where the oVEMP active electrode is placed. As this region is larger in black African males, the electrodes could be placed more securely in the black African participants of the current study. Furthermore, a larger periocular region may also be an indication of larger muscle area and mass in the black African population, which may affect the contraction of the inferior oblique muscle and thereby increase oVEMP amplitude. Additionally, this would also mean that the distance between the active

electrode and reference electrode increases in this population, which has been shown to have a positive effect on the amplitude of the oVEMP response (Piker et al., 2011; Zuniga et al., 2014). However, further research and measurement of this periocular region in black African individuals and its link to oVEMP amplitude is necessary.

Lastly, another theory that may be suggested for the oVEMP amplitude difference is related to the findings of the current study on cVEMP raw amplitude. Black African adults demonstrate different levels of muscle contraction compared to Caucasian adults, as was seen in the EMG measurements of the SCM muscle and cVEMP raw amplitude. It may be plausible to assume that these same racial muscle differences may extend to the extraocular muscles, had EMG measurements of the inferior oblique muscle been included in the current study. Further research should investigate the possibility racial extraocular muscle differences and their relation to oVEMP amplitude.

4.2.4. Gender differences in oVEMP amplitude

No main effect of gender, or an interaction effect of race and gender, was seen in the oVEMP amplitude in the current study.

4.3. Latency differences

The findings of the present study on the latency parameter of the cVEMP and oVEMP both contradicted, agreed with and expanded on the findings of previous research (Li et al., 2015) indicating that racial and gender differences do indeed exist for this parameter.

4.3.1. Race differences in cVEMP latencies

For the cVEMP, black African participants achieved significantly shorter n23 latencies in comparison to Caucasian participants. This finding contradicts findings in literature, which found no race-related latency differences for the cVEMP response (Li et al., 2015). However, the study by Li et al. (2015) did not investigate possible n23 latency differences and focused on possible racial differences related only to the p13 latency, of which they found none. This n23 latency difference may be explained by differences in tonic SCM muscle contraction. A recent study by Rosengren (2015) demonstrated that p13 latency is affected by the degree of tonic muscle contraction, with weaker contractions resulting in prolonged latencies and stronger contractions resulting in earlier latencies. Furthermore, it was noted by Rosengren (2015) that weaker muscle contractions resulted in a poor or

absent n23 component, but as the muscle contraction increased, the n23 component became more prominent. Therefore, the latency of the n23 component may very well be affected by tonic SCM muscle contraction; however further research is necessary to confirm this. As the EMG findings of the current study indicated that black African individuals had larger amplitudes and thereby stronger muscle contraction than Caucasian individuals, this may substantiate the theory that black African individuals obtained shorter n23 latencies due to stronger SCM muscle contraction. The ABR measurements that were performed in the present study to find possible gender and race-related neural differences did not reveal similar latency trends when compared to the cVEMP results. A general main effect of shorter wave V latencies was observed for Caucasian participants and female participants, which contradicts the findings for the cVEMP response. Although no significant main effect for race was noted for the cVEMP p13 latency, it was observed that both black African males and females obtained shorter latencies compared to their Caucasian counterparts. This may indicate that the p13 latency of this study was indeed affected by degree of muscle contraction, however, as exact degree of muscle contraction was not monitored during cVEMP testing, it is unknown whether all participants contracted maximally and what the subsequent effect on the p13 component was. If the focus of the present study had been to investigate racial differences in cVEMP and oVEMP responses using varying degrees of contraction with real-time EMG monitoring, similar to the study by Rosengren (2015), a cVEMP p13 latency difference may have been observed at the maximal point of contraction for each participant group.

4.3.2. Gender differences in cVEMP latencies

No main effect of gender, or interaction effect of race and gender, was seen for the cVEMP p13 or n23 latencies in the current study.

4.3.3. Race differences in oVEMP latencies

Similarly, black African participants also achieved significantly shorter p15 latencies for the oVEMP response, compared to Caucasian participants. This finding contradicts the findings regarding racial differences in oVEMP latency outlined in previous literature (Li et al., 2015). The study by Li et al. (2015) found there to be a race-related n10 latency difference, however these authors did not investigate the possibility of a race-related p15 latency difference. Furthermore, these authors hypothesised that the racial latency difference observed may also relate to genetics and environmental factors. The current study may not have observed a racial oVEMP n10 latency difference, as the participants

were all native South African black Africans and Caucasians, and may have a varied genetic make-up and environment compared to the black African- and Caucasian-American participants of the study by Li et al. (2015). This oVEMP p15 latency difference may be explained by the same theories suggested for the racial differences seen in the oVEMP amplitude parameter. These theories include the mechanism relating to melanin pigmentation in the two racial groups, the benefits of a larger periocular region in black African individuals and stronger tonic muscle contraction of the extraocular muscles, which have all been explained above. Further research is required to confirm the theories relating to a larger periocular region and the stronger tonic muscle contraction and its subsequent effect on oVEMP p15 latency.

4.3.4. Gender differences in oVEMP latencies

The oVEMP response was the only response to demonstrate a pure main effect of gender. A significant gender difference was seen for the oVEMP n10 latency parameter in the current study, with females obtaining shorter latencies than males. This finding contradicts the findings in literature, that no gender-based differences (Chou et al., 2012; Versino et al., 2015) or differences only in amplitude of the oVEMP responses (Sung et al., 2011; Xie et al., 2011) exist. One possible explanation for this n10 latency difference between males and females may be related to head diameter. Although no studies to date have investigated a correlation between head diameter and VEMPs, several studies have indicated a positive correlation in head diameter and ABR latencies (Dehan & Jerger, 1990; Nikiforidis et al.§, 1993; Trune et al., 1988). These studies indicated that a larger head diameter, typically seen in males, might cause later latencies of ABR peaks. A similar trend was also found in the current study, with longer ABR latencies for the male participants. The fact that the male participants of the current study also had significantly longer neck lengths, which was also found in a study by Vasavada et al. (2008), could also explain the longer cVEMP latencies for male participants. Another explanation for gender differences in ABR latencies suggested by Dehan and Jerger (1990) is the effect of hormones on the ABR response. They found that the ABR wave V latencies varied significantly during the changing hormonal environment of young females. Further research is required to link head diameter and neck length to gender differences in oVEMP latencies, as well as to investigate a possible effect of hormonal changes on the latency parameters.

It is noteworthy to mention that although the race- and gender-related VEMP latency findings of the current study may be statistically significant, these findings may not be clinically significant. The latencies obtained by the African group were shorter, and were well within established normal limits (Janky & Shepard, 2009), which is not considered to be a sign of vestibular dysfunction. Rather, prolongation of p13 and n23 cVEMP latencies has been shown to have a higher probability of indicating vestibular dysfunction (Brantberg, 2009).

4.4. Clinical relevance

Cervical VEMPs and ocular VEMPs may be applied in the diagnosis of several peripheral vestibular disorders (Murofushi, 2016), and as such, form a vital component of the vestibular test battery. However, research has shown that both the cVEMP and oVEMP may be influenced by a variety of factors, such as age (Kumar et al., 2015; Li et al., 2015; Maleki et al., 2014; Tseng et al., 2010; Basta et al., 2007; Basta et al., 2005; Su et al., 2004; Ochi & Ohashi, 2003), presence of middle ear pathology (Wang et al., 2009; Wang & Lee, 2007; Yang & Young, 2003), gender (Sung et al., 2011; Xie et al., 2011) and race (Li et al., 2015).

The current study demonstrated that cVEMP and oVEMP response parameters are influenced by both gender and race. Although the findings for cVEMP raw amplitude, n23 latency, oVEMP n10 and p15 latency and oVEMP amplitude are statistically significant, but clinically less significant, gender- and race-specific normative values may not be necessary. However, these findings emphasise that factors such as gender and race and their subsequent effect on the VEMP responses should still be considered in the clinical context.

4.5. Critical evaluation: strengths and limitations of the study

The current study was only the second study to describe the presence of possible race-related differences in the cVEMP and oVEMP responses (previously investigated by Li et al., 2015), and expanded on the limited research available on the effect of gender on these responses. However, this study was the first to investigate the combined effect of gender and race on both the cVEMP and oVEMP responses.

The size and distribution of the study population lends strength to the current study. This study population consisted of sixty healthy young adults that were gender- and age-matched. The previous study by Li et al., 2015, not only had an older population (mean age 72 years), but a population that was skewed in proportion of gender and race. There were no significant differences in age or gender in this study, and a younger population was specifically chosen to prevent the known effect of age on VEMPs influencing the findings of this study.

Furthermore, all measurements in this study were repeated to increase reliability and good wave morphologies were obtained in the cVEMP, oVEMP and ABR responses. This lends strength to the reliability of the findings in this study. Additionally, the order of cVEMP, oVEMP and ABR testing was randomised for each participant in the current study, to avoid the possibility of order bias on the results.

This study had three main limitations. Firstly, the method used to measure neck length and SCM muscle width was relatively subjective, and more accurate measurements of these components could be obtained with objective imaging equipment. Furthermore, investigating racial muscle properties using objective imaging equipment, such as ultrasound or MRI scans, should ideally substantiate the EMG findings of SCM muscle contraction in this study. Studies on similar muscle characteristics of other muscles have been previously been conducted using ultrasound or MRI scans (Hodges, Pengel, Herbert, & Gandevia, 2003; Dupont, Sauerbrei, Fenton, Shragge, Loeb, & Richmond, 2001). Secondly, the EMG measurement of myoelectric value should have been extended to the extraocular muscles, to confirm whether the racial muscle differences seen in the EMG measurement of the SCM muscle exist in the extraocular muscles too. The EMG measurements of extraocular muscles were not included in the current study, as they are measured using needle electrodes, which is very invasive and possibly painful. Thirdly, it may have been useful to also take note of the black African participants' ethnicities and included this variable in the data analysis of the study. This may have given the researchers more information on whether specific black African ethnicities are more positively correlated with racial differences in VEMP response parameters.

4.6. Future research

4.6.1. Cervical VEMP (cVEMP) latency parameters

Future research into racial differences seen in the cVEMP latency parameters should be focused on the effect of real-time monitoring of muscle contraction on the latencies of both p13 and n23 components; and whether racial p13 latency differences are seen if each participant contracts the SCM muscle maximally.

4.6.2. Ocular VEMP (oVEMP) amplitude and latency parameters

Future research into racial differences seen in the oVEMP amplitude and latency parameters should be focused on the following aspects:

- A study should focus on the impact of a higher presence of melanocytes closely arranged to the vestibular dark cells in the utricle and semicircular canals and its subsequent impact on vestibular organ metabolism.
- A study should focus on confirming that black African individuals have larger periocular regions and investigate possible racial differences in extraocular muscle structure and function, as well as the subsequent effect on oVEMP amplitude and latency.
- A study should investigate a possible correlation between smaller head diameter and hormonal involvement on shorter oVEMP n10 latencies in females.

4.6.3. Cervical VEMP (cVEMP) and ocular VEMP (oVEMP) response parameters

Future research into racial differences in both cVEMP and oVEMP response parameters should include black African participants' ethnicities, so that whether specific black African ethnicities are more positively correlated with racial differences in VEMP response parameters.

4.7. Conclusion

Differences based on race and gender were found in both the cVEMP and oVEMP responses. Concerning racial differences, black African adults obtained shorter latencies and larger raw amplitudes than young Caucasian adults in the cVEMP and oVEMP responses. When looking at gender differences, females obtained shorter latencies in the oVEMP response, while males tended to obtain larger amplitudes. Several theories, such

as differences in muscle contraction, varied vestibular organ metabolism and hormonal involvement, may be suggested for these observed differences between racial and gender groups. This study was limited in its method of neck length and SCM muscle measurement, as well as the fact that EMG measurements were not extended to the extraocular muscles. Despite the significant race- and gender-related findings of the current study, separate race- and gender-based normative values for VEMP responses are not required; however, this study still emphasises that factors such as gender and race and their subsequent effect on the VEMP responses should still be considered in the clinical context.

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Appendices

Appendix A: Faculty of Humanities research ethics committee approval letter

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Research Ethics Committee

2 June 2016

Dear Prof Vinck

Project:	**Comparing vestibular evoked myogenic potential response parameters in young African and caucasian adults**
Researcher:	**R Olinger**
Supervisor:	**Prof B Vinck**
Department:	**Speech-Language Pathology and Audiology**
Reference Number:	**12075427 (GW20160524HS)**

I am pleased to be able to inform you that the above application was **approved** by the **Research Ethics Committee** on 31 May 2016 and by the Dean of Humanities and the Registrar on 2 June 2016. Data collection may therefore commence.

Please note that this approval is based on the assumption that the research will be carried out along the lines laid out in the proposal. Should the actual research depart significantly from the proposed research, it will be necessary to apply for a new research approval and ethical clearance.

We wish you success with the project.

Sincerely

Prof MME Schoeman
Deputy Dean: Postgraduate Studies and Ethics
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail:tracey.andrew@up.ac.za

Kindly note that your original signed approval certificate will be sent to your supervisor via the Head of Department. Please liaise with your supervisor.

Research Ethics Committee Members: **Prof MME Schoeman (Deputy Dean);** Prof KL Harris; Dr L Blokland; Dr R Fasselt; Ms KT Govinder; Dr E Johnson; Dr C Panebianco; Dr C Puttergill; Dr D Reyburn; Prof GM Spies; Prof E Taljard; Ms B Taute; Dr E van der Klashorst; Mr V Sithole

Appendix B: Permission from Head of Department to conduct study

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA
Faculty of Humanities
Department of Speech-Language Pathology and Audiology

March 2016

Attention: Prof. Bart Vinck
HEAD: Department of Speech-Language Pathology & Audiology
University of Pretoria

Dear Prof. Vinck,

PERMISSION TO CONDUCT A RESEARCH STUDY

I, Renate Olinger, am a MA (Audiology) student at the Department of Speech-Language Pathology and Audiology at the University of Pretoria. It is a requirement of the MA (Audiology) degree to conduct a research project. I hereby request permission to conduct the research study detailed below.

Title: *Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults*

Student Researcher: Renate Olinger
Research Supervisors: Prof. Bart Vinck, Dr. Barbara Heinze and Dr. Leen Maes (University of Ghent, Belgium)

Design and Procedure
A quasi-experimental between-subjects research design will be used and data will be collected in a cross-sectional manner (data will only be collected from participants on one occasion and they will not be required to attend more than one session). This research project aims to investigate whether there is a difference in response parameters, namely latency and amplitude, of vestibular evoked myogenic potentials (VEMPs) in a young black African and Caucasian adult population.

Sixty male and female participants (30 black African, 30 Caucasian) between the ages of 18 and 25 years will be selected. A comprehensive case history will be taken and hearing tests will be conducted to confirm that all participants have normal hearing and middle ear functioning. Furthermore, the Fukuda Stepping test, Head Impulse test, modified Clinical Test of Sensory Integration of Balance, Dix-Hallpike and Roll test will be conducted to confirm that all participants have normal peripheral vestibular (balance) function.

Participants will be required to undergo four tests, namely cervical VEMPs (cVEMPs), ocular VEMPs (oVEMPs), auditory brainstem response (ABR) and electromyography (EMG) testing. The cVEMP and oVEMP tests are tests of vestibular (balance) function, while the ABR is a test of auditory neural function and the EMG test assesses the average electrical activity in muscles. The ABR and EMG tests will be conducted in order to ascertain whether any difference found is due to superior neural or muscular function.

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During the cVEMP test, electrodes will be placed in the middle of the sternocleidomastoid muscle in the neck (active electrode), on the sternum (reference electrode) and in the middle of the forehead (ground electrode). Participants will be lying down. They will be required to turn and lift their heads while an acoustic stimulus is presented through an earphone in one ear. In the oVEMP test, electrodes will be placed just below the eye (active electrode), on the bridge of the nose (reference electrode) and on the chin (ground electrode). Participants will also be lying down for this test. They will be required to look up at a marked spot on the ceiling, while an acoustic stimulus is presented through an earphone in one ear.

During the ABR test, electrodes will be placed on the mastoid bone behind each ear (reference and ground electrodes), as well as on the middle of the forehead (active electrode). Insert earphones will be inserted into each ear and the participants will be required to lie still with their eyes closed. No further action will be required from the participants. During the EMG test, electrodes will be places approximately two centimetres apart on the sternocleidomastoid muscle in the neck (two active electrodes) and on the bony process of the shoulder (ground electrode). Participants will be required to turn and lift their heads for a short duration of time, while lying in the supine position. They will be required to do this four times on each side.

Ethical Considerations: All participants will be given a letter fully explaining the nature of the research project and what will be required of them. Participants will have to give their consent for participation, therefore participation will be completely voluntary. All participants will be given a research code, therefore the identity and all particulars of patients will be kept anonymous and confidential, with the identity of the participants only known to the researcher. All results from the project will be archived at the University of Pretoria for fifteen years and a summary of the results will be made available to participants, should it be requested.

Risks and Benefits: There are no risks in participating in this research project and no harm will come to participants. Participants will not receive compensation for participating in this research project.

I believe that this research project will aid in the scientific advancement of knowledge in the field of vestibular audiology. This research may provide motivation for the establishment of different normative values for different ethnic groups in these specific vestibular tests.

Please contact us should require any further information.

Kind Regards,

Renate Olinger
Student Researcher
Tel: 074 996 9692
Email: renateiolinger@gmail.com

Prof. Bart Vinck
Supervisor
HEAD: Dept. of Speech-Language Pathology & Audiology

Dr. Barbara Heinze
Co-Supervisor
Senior Lecturer

PERMISSION FOR TO CONDUCT A RESEARCH STUDY

Herewith, I, **Prof. Bart Vinck**, Head of the Department of the Speech-Language Pathology & Audiology at the University of Pretoria, give permission for the research study titled: *Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults* to be conducted.

Signed: _____

Date: 7/4/2016

Appendix C: Director of Student Affairs' permission to use students from the University of Pretoria as voluntary participants

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

March 2016

Attention: Dr. Matete Madiba
DIRECTOR: Department of Student Affairs

Dear Dr. Madiba,

PERMISSION TO CONDUCT A RESEARCH STUDY WITH STUDENTS FROM THE UNIVERSITY OF PRETORIA

I, Renate Olinger, am currently a full-time MA (Audiology) student at the Department of Speech-Language Pathology and Audiology at the University of Pretoria. It is a requirement of the MA (Audiology) degree to conduct a research project. For my research project, young Black African and Caucasian adults between the ages of 18 – 25 years with normal hearing will be required. I hereby request permission to approach students from the University of Pretoria and request their voluntary participation in my research project.

Title: *Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults*

Student Researcher: Renate Olinger
Research Supervisors: Prof. Bart Vinck, Dr. Barbara Heinze and Dr. Leen Maes (University of Ghent, Belgium)

Design and Procedure
A quasi-experimental between-subjects research design will be used and data will be collected in a cross-sectional manner (data will only be collected from participants on one occasion and they will not be required to attend more than one session). This research project aims to investigate whether there is a difference in response parameters, namely latency and amplitude, of vestibular evoked myogenic potentials (VEMPs) in a young black African and Caucasian adult population.

Sixty male and female participants (30 black African, 30 Caucasian) between the ages of 18 and 25 years will be selected. A comprehensive case history will be taken and hearing tests will be conducted to confirm that all participants have normal hearing and middle ear functioning. Furthermore, the Fukuda Stepping test, Head Impulse test, modified Clinical Test of Sensory Integration of Balance, Dix-Hallpike and Roll test will be conducted to confirm that all participants have normal peripheral vestibular (balance) function.

Participants will be required to undergo four tests, namely cervical VEMPs (cVEMPs), ocular VEMPs (oVEMPs), auditory brainstem response (ABR) and electromyography (EMG) testing. The cVEMP and oVEMP tests are tests of vestibular (balance) function, while the ABR is a test of auditory neural function and the EMG test assesses the average electrical activity in muscles. The

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ABR and EMG tests will be conducted in order to ascertain whether any difference found is due to superior neural or muscular function.

During the cVEMP test, electrodes will be placed in the middle of the sternocleidomastoid muscle in the neck (active electrode), on the sternum (reference electrode) and in the middle of the forehead (ground electrode). Participants will be lying down. They will be required to turn and lift their heads while an acoustic stimulus is presented through an earphone in one ear. In the oVEMP test, electrodes will be placed just below the eye (active electrode), on the bridge of the nose (reference electrode) and on the chin (ground electrode). Participants will also be lying down for this test. They will be required to look up at a marked spot on the ceiling, while an acoustic stimulus is presented through an earphone in one ear.

During the ABR test, electrodes will be placed on the mastoid bone behind each ear (reference and ground electrodes), as well as on the middle of the forehead (active electrode). Insert earphones will be inserted into each ear and the participants will be required to lie still with their eyes closed. No further action will be required from the participants. During the EMG test, electrodes will be places approximately two centimetres apart on the sternocleidomastoid muscle in the neck (two active electrodes) and on the bony process of the shoulder (ground electrode). Participants will be required to turn and lift their heads for a short duration of time, while lying in the supine position. They will be required to do this four times on each side.

Ethical Considerations: All participants will be given a letter fully explaining the nature of the research project and what will be required of them. Participants will have to give their consent for participation, therefore participation will be completely voluntary. All participants will be given a research code, therefore the identity and all particulars of patients will be kept anonymous and confidential, with the identity of the participants only known to the researcher. All results from the project will be archived at the University of Pretoria for fifteen years and a summary of the results will be made available to participants, should it be requested.

Risks and Benefits: There are no risks in participating in this research project and no harm will come to participants. Participants will not receive compensation for participating in this research project.

I believe that this research project will aid in the scientific advancement of knowledge in the field of vestibular audiology. This research may provide motivation for the establishment of different normative values for different ethnic groups in these specific vestibular tests.

Please contact us should require any further information.

Kind Regards,

Renate Olinger
Student Researcher
Tel: 074 996 9692
Email: renateiolinger@gmail.com

Prof. Bart Vinck
Supervisor
HEAD: Dept. of Speech-Language Pathology & Audiology

Dr. Barbara Heinze
Co-Supervisor
Senior Lecturer

PERMISSION FOR THE USE OF STUDENTS FROM THE UNIVERSITY OF PRETORIA IN A RESEARCH PROJECT

Herewith, I, **Dr. Matete Madiba**, Director of Student Affairs at the University of Pretoria, give permission for students from the University of Pretoria to be used as voluntary research participants in the research project titled: *Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults*. This permission is given subject to the approval of this research project by the University of Pretoria Ethics Committee.

Signed: _____

Date: 7/4/16

Appendix D: Participant information letter and informed consent form

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

March 2016

Dear Participant,

INVITATION TO PARTICIPATE IN A RESEARCH STUDY

We would like to kindly invite you to participate in a research study from the Department of Speech-Language Pathology and Audiology at the University of Pretoria.

Information about the research study
The purpose of the study is to compare different aspects of two vestibular (balance) tests in black African and Caucasian young adults. The balance tests measure myogenic (muscular) responses at the level of the neck (known as cVEMPs) or beneath the eye (known as oVEMPs). These two balance tests test the functioning of four different parts of the balance system. Furthermore, an auditory brainstem response (ABR), which is a test of auditory neural function, and electromyography (EMG) testing, a measurement of average muscular activity, will be conducted in order to ascertain if any differences found the in VEMP results are due to a neural or muscular difference in the two groups.

Participant candidacy
For this study, normal hearing black African and Caucasian young adults between the ages of 18 – 25 years are required. Your hearing will be assessed by the means of the following audiological procedures:

- **Visual inspection of the ear canal and eardrum** using an otoscope,
- **Tympanometry and acoustic reflex measurement** to evaluate middle ear functioning. Participants in this study should present with normal middle ear functioning, which is reflected by a Type A tympanogram. The tests are conducted by placing an eartip in the ear and you will not be required to respond any further.
- **Pure-tone audiometry** will be used to determine if hearing thresholds are within normal limits. You will be required to indicate if sounds presented have been heard.

Furthermore, participants are required to have normal peripheral vestibular (balance) function, which will be assessed by means of a detailed case history interview, the Fukuda Stepping test Head Impulse test, the modified Clinical Test of Sensory Interaction and Balance (mCTSIB), the Dix-Hallpike and Roll test and the observation of spontaneous nystagmus.

Requirements from participants

The requirement from participants in this research study have been summarised below in Table 1.

Table 1: Summary of Requirements from Participants

	Test Name	Requirements	Sound
Procedures	Otoscopy	*See "Participant Candidacy" above.*	NS
	Tympanometry & Acoustic Reflexes		Sound presented
	Pure-Tone Audiometry		
	Fukuda Stepping Test	Walk on the spot with your eyes closed.	No sound presented through an earphone (NS).
	Head Impulse Test	Look at one spot while your head is rapidly turned.	
	mCTSIB Test	Stand on the floor/foam block with eyes open & closed.	
	Dix-Hallpike Test	Lie down from a sitting position with your head turned.	
	Roll Test	Turn your head while in a lying position.	
	Spontaneous Nystagmus	Observe movements of the eyes while you are sitting still.	
	cVEMPs	Your head will be turned to one side while you are lying down and you will be required to lift your head with three electrodes attached to your skin on your neck.	Sound presented through an earphone
	oVEMPs	You will need to look up while lying down, with three electrodes around your eyes.	
	ABR	You will need to lie still with your eyes closed, with three electrodes placed behind your ears and on your forehead.	
	EMG	You will need to lift your head while it is turned, with three electrodes attached to your neck.	NS

Test duration and venue
You will only need to come for testing once and testing will taking approximately 1.5 hours. All testing will be conducted at the Department of Speech-Language Pathology and Audiology at the University of Pretoria.

Possible risks and benefits associated with this study
Participants will not be exposed to any risk or experience any discomfort during this research study. There are no direct benefits of participating in this study and no reimbursements will be given to participants. However, information obtained from this study may assist in establishing new racial-specific normative data.

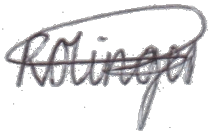
Confidentiality and anonymity
All your results will be recorded under an anonymous research code, therefore all your identifying information and results will be kept confidential. Only the researcher and the supervisors will have access to your information. The results of the research study will be stored at the Department of Speech-Language Pathology and Audiology for 15 years.

Sharing of results
The results obtained from this research study will be reported in the form of a scientific article and dissertation, which will be available to professionals in the field of audiology. The results from this research may be used by future researchers. If you would like a

summary of the findings of this research study, a copy can be made available to you when the project is complete.

Refusal or withdrawal from the research
Participation in this research is entirely voluntary, therefore you may withdraw from the study at any point, should you wish to do so.

Contact
Should you have any questions or concerns regarding any aspect of this study, please feel free to contact Ms. Olinger.



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UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA
Faculty of Humanities
Department of Speech-Language Pathology and Audiology

INFORMED CONSENT FORM

Comparing vestibular evoked myogenic potential response parameters in young black African and Caucasian adults

Surname: _____

First Name: _____

Date of Birth: _____

I hereby give consent to participate in the aforementioned research project and acknowledge that the data may be used in current and future research. I confirm that I understand what is required of me in this research project. I am aware that I may withdraw from this project, at any time, should I wish to do so.

_____ _____

Signature **Date**

Appendix E: Permission to use images of participant

PERMISSION TO PUBLISH PHOTOGRAPHS IN AN ARTICLE

I, **Nicole Kostlin**, hereby give my permission for photographs taken of me for the article entitled: *Comparing vestibular evoked myogenic potential response parameters in young African and Caucasian adults*, to be used in the publication of this article in a journal. I confirm that I am aware of the inclusion of these photographs in the article and have approved these photographs.

Signed: Nkost

Date: 11 August 2016

Appendix F: Anti-plagiarism declaration

UNIVERSITY OF PRETORIA

FACULTY OF HUMANITIES

RESEARCH PROPOSAL & ETHICS COMMITTEE

DECLARATION

Full name : **Renate Ilse Olinger**

Student Number : **12075427**

Degree/Qualification: **MA (Audiology)**

Title of ~~thesis~~/**dissertation**/~~mini-dissertation~~:

Comparing vestibular evoked myogenic potential response parameters in young African and Caucasian adults

I declare that this thesis / dissertation / mini-dissertation is my own original work. Where secondary material is used, this has been carefully acknowledged and referenced in accordance with university requirements.

I understand what plagiarism is and am aware of university policy and implications in this regard.

SIGNATURE

16 September 2016
DATE

ResPEthics Documentation NE 46/04 05/2004

Appendix G: Screening test results

The following summarised test results were seen for participants in the screening tests used for inclusion in the study:

Table 4: Screening test results

Test	Summarised Test Result
Case History	The SOSTONED tool (Wuyts, Van Rompaey, & Maes, 2016) was used as a case history interview tool, supplemented with questions regarding the participants' hearing and ear health. • All participants reported no history of or current diagnosed vestibular disorders. • Where participants had experienced a feeling of vertigo or dizziness, it could be attributed to extenuating conditions, such as low blood sugar or rotatory motion (such as on carnival rides). • Many participants reported a history of otitis media as a child and several participants had had grommets inserted at that time. • No participants reported abnormal hearing abilities.
Otoscopy	The majority of the ears examined showed healthy ear canals and tympanic membranes. An abnormal otoscopic examination was observed in 7.5% (9 of 120 ears) of the participants' ears, and included the following: • Excessive cerumen in the ear canal, • White plaque on the tympanic membrane, • Retracted tympanic membrane, • Reddened ear canal.
Tympanometry	All participants presented with Type A tympanograms and at least one stapedial reflex. The stapedial reflex intensity levels varied from 75 – 105 dB HL.
Pure-tone audiometry	All participants presented with a pure tone average (a combined average of the audiometric thresholds at 500, 1000 and 2000 Hz) ≤ 15 dB HL. The pure tone averages obtained ranged from 0 – 15 dB HL.
Head impulse Test	All participants presented with a negative result for the head impulse test, meaning that no saccadic eye movements were noted following a rapid head turn.
Fukuda stepping test	Although many participants moved forward and showed a slight rotation, the degree of rotation was not abnormal in any participant.
Modified clinical test of sensory interaction of balance (mCTSIB)	Although many participants showed minimal sway in the eyes-closed-unstable condition, no participants displayed abnormal sway or fell in any condition.
Spontaneous nystagmus	All participants had no spontaneous nystagmus, whether their gaze was fixated or not.
Dix-Hallpike test	All participants displayed no nystagmus at any stage of the Dix-Hallpike test, indicating the absence of BPPV.