An investigation of the Auditory P300 Event Related Potential across gender.

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Caskets of jewels and coffers of gold
Richer than I you can never be; I had a mother who read to me.'
- Stricland Gillilan –

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Abstract:

The P300 serves as a valuable tool in examining higher auditory functions such as auditory attention and discrimination. Exploration of the P300 could be of value in a multi-lingual South Africa where auditory processing evaluations still rely heavily on inappropriate linguistically dependent tests. The P300 could potentially provide an objective, non-linguistically dependent evaluation of auditory processing. The present study aimed to investigate the influences of gender on the Auditory P300 Event Related Potential (AERP) and to contribute to establishing a clinic-specific normative database. One hundred subjects (n=100) (50% male) with normal hearing and no history of psychiatric illness were evaluated using the “odd-ball” paradigm. The averages and ranges of the findings on latencies and amplitudes were reported. The average latency values for the P300 were calculated at 314.7ms with a standard deviation of 37.2 ms. The average amplitude values were calculated at 7.1 µV with a standard deviation of 6.1 µV. No significant gender effect was found. In conclusion further research is recommended to explore the clinical utility of the P300 in different age and gender groups, using different protocols.

Opsomming:

Die doel van die huidige studie was ‘n ondersoek na die invloed van geslag op die ouditiewe P300 en om ‘n bydrae te lewer in die samestelling van ‘n kliniek-spesifieke normatiewe databasis. Hierdie metings is van belang aangesien dit ’n waardevolle instrument is vir die evaluering van hoër ouditiewe funksies soos ouditiewe aandag en diskriminasie. Verdere ondersoeke in die P300 kan van kliniese waarde wees in ‘n multi-linguistiese Suid-Afrika waar evaluasies van ouditiewe prosessering steeds sterk leun op toetse wat linguisties afhanklik is en dus ontoepaslik is. Die ouditiewe P300 kan ‘n objektiewe, nie-linguistiese metode bied om ouditiewe prosessering te evalueer. Die studie het beoog om die effek van geslag op die latentheid en amplitude van die betrokke potensiale te ondersoek. ’n Honderd proefpersone (n=100)(50% manlik) met normale gehoor en geen geskiedenis van psigiatriese patologie nie, is geëvalueer met behulp van die “odd-ball” paradigma. Die gemiddelde en totale reikwydte van die latentheid en amplitude van elke potensiaal is opgeteken. Die gemiddelde latentheid en amplitude was bereken as 314.7ms en 7.1µV onderskeidelik. Die standaard afwyking vir die latenheid en amplitude was bereken as 37.2 ms en 6.1 µV. Geen betekenisvolle verskille tussen mans en vrouens is waargeneem nie. Die gevolgtrekking van die studie was dat verdere navorsing nodig is om die kliniese waarde van die P300 ten opsigte van verskillende ouderdoms- en geslagsgroepe te ondersoek, met behulp van verskeie toetsprotokolle.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

Glossary and abbreviations

ABR: Auditory brainstem response. An evoked potential that occurs between 1ms and approximately 10ms post-stimulus. It is usually defined as having five to seven prominent waves (peaks) labelled I through VII. Wave V is the most robust and commonly used wave in the series (McPherson, 1996).

Active Electrode: Any signal occurring at this electrode will have a phase inversion of 180°. In EP recording from the scalp, the term *active* may be misleading because all the electrodes across the scalp are considered active. The preferred term would be *inverting electrode* (McPherson, 1996).

ADHD: Attention deficit and hyperactivity disorder (Bellis, 2003).

AEP: Auditory evoked potentials. A general term used to refer to any evoked potential (EP) that is elicited using an auditory stimulus (McPherson, 1996).

Artefact: Any unwanted signal embedded in a recording that is not attributed to the desired neural response (McPherson, 1996).

Attend condition: The observer is attending to the target stimulus and is usually required to count or make some response (McPherson, 1996).

Behavioural response: Usually a verbal or motor response made by an individual in response to a stimulus. An example would be locating a sound in space or some other behaviour that is not a measurement of the biological measure (McPherson, 1996).

CAPD: Central auditory processing disorder (Bellis, 2003)

Cognition: The process whereby an individual internalises some external object or event (McPherson, 1996).

Common electrode: The relationship of one electrode to a second electrode; usually refers to the *non-inverting electrode* (McPherson, 1996).

Common: This has two meanings in EP: (1) The relationship of one electrode to a second electrode; usually refers to the *non-inverting electrode*; and (2) in

ERP is a signal that occurs with a large probability than a target signal and is generally to be ignored (McPherson, 1996).

Decay time: The amount of time it takes a gated signal to reach its minimum (McPherson, 1996).

Emitted P300: A P300 response by the absence of a second stimulus in paired stimulus paradigm when the subject has been instructed to 'guess' the presence or absence of the second stimulus prior to the trial (McPherson, 1996).

Endogenous: Refers to the ERP generated by an internal response to the external event and is usually due to perception or cognition. The nature of the response changes according to the internalisation of the event, not the dimension of the external event (McPherson, 1996).

EP: Evoked Potential. A series of electrical changes occurring in the peripheral and central nervous system following stimulation of an endogenous or peripheral nerve (McPherson, 1996).

ERP: Event-related potentials. An evoked potential elicited by an endogenous stimulus representing higher level processing (i.e. cognition) (McPherson, 1996).

Event-related potential: see ERP.

Evoked Potential: see EP.

Exogenous: Refers to an EP generated by an external stimulus. The nature of the response changes according to the dimensions of the external event (McPherson, 1996).

Far-field: A far-field recording occurs when the recording electrode is situated distally from the source (McPherson, 1996).

Microvolt: 10^{-6} volts. Abbreviated µV where 0.000001 volt equal 1µV (McPherson, 1996).

Montage: The electrode positions used to record an EP. Usually referred to the 10-20 international standard (Jasper, 1958).

Morphology: The qualitative features of an evoked potential. It usually takes into consideration the noisiness of the recording, the 'smoothness' of the recording and how the recording appears relative to a textbook example, or at least the ideal recording (McPherson, 1996).

Muscle artefact: Muscle potential that occurs to sensory stimulation or random movement and in a time frame that overlaps the desired recorded EP (see artefact)(McPherson, 1996).

N1: The first negative peak following the middle latency auditory evoked potentials occurring between 80-150ms in adults (McPherson, 1996).

N100: See N1.

Non-inverting electrode: See *Common electrode*

P1: The first positive peak following the middle latency auditory evoked potentials occurring between 55-80 ms in adults (also known as the P60) (McPherson, 1996).

P2: The second positive peak following the middle latency auditory evoked potentials or the first positive peak following the N100 and occurring between 145-180 ms in adults (also known as the P160) (McPherson, 1996).

P3: An endogenous event-related potential occurring between 220-380 ms in adults (also known as P300). The P3 may have two subcomponents: (1) P3a and (2) P3b (McPherson, 1996).

P300: See P3.

Perception: The process whereby an individual gathers information about objects or events (McPherson, 1996).

Plateau time: The time a signal remains on its maximum intensity (McPherson, 1996).

Rare signal: A target signal that occurs with a lesser probability than a second signal. The subject is usually asked to respond when the signal occurs (McPherson, 1996).

Reference electrode: The relationship of one electrode to a second usually refers to a common electrode (McPherson, 1996).

Sensation level: This is the intensity of a sound above or below an individual's own threshold. In some instances, the abbreviation has been inappropriately used for a sound level referring to SPL (McPherson, 1996).

Sound pressure level: SPL. An absolute value measured in dB representing the physical intensity of a sound (McPherson, 1996).

SPL: See *sound pressure level*.

Tone burst: Signals having a rise time, plateau time, and decay time of sufficient duration to be perceived as having tonal information. In this instance, tone would refer to a sinusoid or combination of sinusoids (McPherson, 1996).

µV: See *microvolt*.

10-20 international system: A systematic standard for electrode location (Jasper, 1958).

1. Background and rationale of the study.

The aim of this chapter is to introduce the auditory P300 Event Related Potential (AERP) and the problem that this study confronts, by providing the rationale thereof, describing the terminology used and presenting an overview of the content and organisation of the study.

1.1. Introduction

'*The greater the doubt the greater the awakening, the smaller the doubt the smaller the awakening. No doubt, no awakening*' (Chang, 2003)

The P300 event related potential (ERP) has been shown to be a useful tool of measurement both in the theoretical field of cognitive distance and clinically, as a measure of central nervous system functioning (McPherson, 1996). However, it has been shown to be easily influenced by both subject and stimulus factors. If this is to become a recognised clinical tool, these effects need to be quantified. The ERP is a relatively new tool in the advanced audiological test battery, since its first classification in 1965 (Hall, 1992). It is a differentially averaged, electrophysiological recorded signal which represents the neurological produced electrical potentials, which occurs as the subject mentally operates on a stimulus.

By definition, audiology is the science of hearing (Stach, 1998). Over the last decades audiology has been evolving as an academic field of study, as well as a clinical profession. The science of audiology includes the identification and diagnosis of any hearing impairment and equally important, the prevention and management of the disabilities caused by hearing impairments. According to Katz (2001), the primary goal of a diagnostic procedure is the successful rehabilitation of auditory impairment.

Pure tone threshold audiometry is the standard behavioural procedure for describing auditory sensitivity. The comparison of air- and bone-conduction thresholds provides a fundamental index of auditory function for otological diagnosis. Pure tone thresholds can thus be described as the cornerstone for diagnostic procedures and rehabilitative planning (Yantis, 1994).

Throughout the advancement of audiology, a great deal of effort has been invested in methods of determining hearing thresholds (the level at which tones are perceived as barely audible) (Martin, 1997). To this day the pure tone audiogram has served as the gold standard for various populations, but despite its widely accepted value, it has some limitations. Assessment of hearing by utilising pure tones provides valuable information regarding sensitivity, but only limited information concerning receptive auditory communication ability (Penrod, 1994). Auditory perception or speech perception as we experience it daily occurs, for example, on a conversational level. This phenomenon occurs on a supra-threshold level and not the threshold levels determined by the pure tone audiogram (Penrod, 1994). The pure tone audiogram provides valuable information with regard to the type, degree and configuration of a hearing loss, but the standard audiogram is insufficient for providing comprehensive diagnostic information regarding supra-threshold processes such as auditory perception and attention (Moncrieff & Jerger, 2000).

The need for supra-threshold evaluation procedures in the field of audiology has caused an emphasis shift towards test procedures that can reach beyond the peripheral hearing system to include processes such as auditory perception (Jirsa, 2002). Despite many test procedures used to evaluate auditory processing, there is still a great need for reliable procedures that could objectively evaluate some of the conscious processes involved in hearing (Bellis, 2003; Kraus, Burton Kock, McGee, Nicol & Cunningham, 1999; McFarland & Cacace, 1995; Hall, 1992).

1.2. Orientation

Researchers from a number of disciplines have used electrophysiological measures for years to evaluate aspects of the central nervous system (Hall, 1992). Until recently, audiologists have used electrophysiological measures primarily for the evaluation of the peripheral auditory system. The diagnostic usefulness of both the auditory brainstem response (ABR) and the middle latency response (MLR) has been thoroughly documented (Goldstein & Aldrich, 1999; Musiek, Baran & Pinheiro, 1994; Hall, 1992). In the last decade, more audiologists have started to direct their efforts towards using electrophysiological measures for to investigating and enhancing the understanding of audition in the central nervous system (Jirsa, 2001; Jerger, 1998). Substantial evidence is accumulating pertaining to the clinical relevance of a number of electrophysiological measures, including the P300 event-related potential (ERP) (Jirsa, 1992; Polich, 1998; Salamat & McPherson, 1999; Kiehl, Laurens, Duty, Forster & Liddle, 2001; Yordanova, Kolev & Polich, 2001).

The P300 is a far-field, differentially averaged electrophysiological recording of the electrical activity of the cortex in response to the internalisation of an auditory stimulus (Hall, 1992). It is an endogenous, or event related potential, as the response is dependent on an internal cognitive “event” that is relatively independent of stimulus features and subject characteristics (McPherson, 1996). The P300 auditory event-related potential (AERP) occurs between 300 to 700 ms (Jirsa & Clontz, 1990; Squires & Hecox, 1983), is a non-obligatory waveform that is elicited using the “odd-ball” paradigm. This means one stimulus is ‘common’ (frequent) and the other is odd (or infrequent). Generally the “odd-ball” stimulus will be randomly present for 20% of the time. As the P300 response is endogenous and dependent on the perceived difference between two stimuli, the extent of the difference between the two types of stimuli (i.e., frequent versus infrequent) will change the amplitude, latency and morphology of the response (McPherson, 1996). It is also called the P300b to separate it from an earlier occurring non-attentive waveform, often labelled the

P300a (Kiehl et al., 2001) (see Appendix C: Graphic illustration of ALLR and AERP).

The P300 matures later than the earlier waveforms such as the auditory brainstem response (ABR). Several studies show a decrease in latency and an increase in amplitude from the age of five through to the age of 16. This is followed by a progressive decrease in amplitude and an increase in latency throughout adulthood (Courchesne, 1978; Pfefferbaum, Ford, Roth & Kopell, 1980; Polich, Howard & Starr, 1985). The neural generator site for the P300 still raises great controversy because of the diffuse and complex nature of the structures involved. Accumulative evidence suggests involvement of the thalamus, inferior parietal lobe, temporal lobe, dorsolateral pre-frontal cortex, cingulated cortex, amygdale and the hippocampus (Jirsa, 2002).

The P300 is not elicited passively, but requires the active participation of the subject attending to specific stimuli in an on going train of standard stimuli (Salamat & McPherson, 1999; McPherson, 1996). As active listener participation is required to generate the P300 response it is widely accepted as a physiological measure of cognitive processing (Hall, 1992). The P300 reflects processes related to attention, decision-making and memory updating (McPherson, 1996). The P300 latency appears to be a function of stimulus evaluation time which relates to the recognition and categorisation of a stimulus (Alho, Sainio, Reinikainen & Naatanen, 1990), the speed of information processing (Courchesne, 1978) and short-term working memory processes (Yordanova et al, 2001). The P300 amplitude is related to the subjective probability of the stimulus, stimulus meaning and information processing (Johnson, 1986). It has been extensively used to evaluate various aspects of psychophysiology, psychopathology and ageing (Pfefferbaum et al., 1980; Polich et al., 1985; Ford, White & Csernansky, 1994). In general, results have shown an increase in latency and a decrease in amplitude in the clinical population (Jirsa, 2002). The P300 has also been used to investigate various learning and developmental processes in children, as well as adults,

including hyperactivity (Satterfield, Schell, Backs & Hidaka, 1984) and language and motor speech disorders (Mason & Mellor, 1984).

The P300 response has also been investigated in children with Central auditory processing disorders (CAPD). A significant relationship between P300 results (amplitude and latencies) and deficits in selective attention, short-term memory and auditory discrimination ability has been found in children with confirmed CAPD (Jirsa & Clontz, 1990). The P300 has also proved to be sensitive to behavioural changes resulting from therapeutic programmes, and may be most useful in monitoring therapy progress (Jirsa, 1992).

Despite the continued success of the P300 AERP, the interpretation of its waveforms remains debatable. Unlike the early auditory evoked potentials, latency and amplitude values for the P300 are variable, even within a normal population (Theunissen, 2002; McPherson, 1996; Hall, 1992). The P300 is more diffuse than other long latency auditory evoked potentials, because of the co-existing activity within the nervous system (McPherson, 1996). This inherent variability makes the clinical application of P300 results in the time domain difficult, even in experienced hands (Hall, 1992).

Due to its sensitivity to a great number of variables, including short-term memory and attention (Polich, Howard, Starr, 1983; Hall and Mueller 1997), the P300 has even less relevance for standard threshold seeking audiological procedures as deficits in these areas will influence the results (Hall, 1992). The science of audiology, however, encompasses substantially more than the clinical estimation of hearing thresholds. The value of auditory late latency responses exceeds the estimation of hearing thresholds (Kraus & McGee, 1994). What might present as a disadvantage in estimating hearing thresholds therefore yields great possibilities for utilisation as a tool for assessing processes that not only comprise an essential part of the hearing process, but

also plays a vital role in normal cognitive function (Polich et al 1985; Jirsa, 2002).

1.3. Rationale

The use of event-related potentials (ERP's) to identify pathological conditions of the auditory system is complex. Developments in the field of ERP have highlighted a more objective means of measuring a multitude of processes involved in the complete hearing process (Hall & Mueller, 1997).The P300 offers great promise as a clinical tool in the identification of disorders in cognitive functioning and auditory processing (Jirsa, 2002). However, it is limited by the inherent variability of the response, even in normal subjects (Hall and Mueller, 1992). Therefore it is of utmost importance to investigate the variability of its characteristics in normal subjects, in order to identify an abnormality accurately.

Unlike peripheral auditory evoked potentials such as the auditory brainstem response which is very stable and has clearly specified parameters (Hall, 1992), the auditory event-related potentials are subject to significant variations from both extrinsic and intrinsic factors. As a result of these variations, establishing a normative database requires precise specifications of the stimuli. These include recording conditions and environment, subject state (including age, gender, various biological and psycho-physiological factors) and response tasks (McPherson, 1996). Normative data has to be established on each variable, whether on the subject (e.g. gender, age) or the environment (e.g. stimulus, amplification).

In the auditory system, anatomic differences between males and females have been found in the planum temporal, a supratemporal region of the auditory association cortex (Kulynch, Vladar, Jones & Weinberger, 1994). Both behavioural (Cohen, Levy & McShane, 1989; McGuinness & Pribram,

1979; Rosenthal, Archer, Dimatteo, Koivumaki & Rogers, 1974) and physiological auditory pathway asymmetries are known to exist between gender in humans and animals (Ehret, 1987; Fitch, Brown, O'Conner & Tallal, 1993; King, Nicol, McGee & Krause, 1999). Hall (1992) does not consider gender such a significant factor as age in P300 measurements. In 1986, John Polich conducted a study showing no significant effect of gender on latencies or amplitude (Polich, 1986). However other studies found larger P300 amplitude in adult females compared to adult males (Niwa & Hayashida, 1993). More recent studies have also shown that P300 latencies vary as a function of age and gender (Ehlers, Wall, Garcia-Andrade & Phillips, 2001; Gölgeli, Süer, Ozesmi, Dolu, Ascioglu & Sahin, 1999; Bahramali, Gordon, Lagopoulos, Lim, Li, Leslie & Wright, 1999). It is thus important to establish a normative data base that encompasses the normal deviations of the P300.

The clinical definition of abnormality is based on the deviation from a mean population value of two to three standard deviations (McPherson & Starr, 1993). Therefore, an understanding of P300 variations is important to determine the limits of normal variations (Polich et al., 1985). Consequently, it is not only essential to determine the average values and the characteristics of the wave, but also the range and variability of these values within a normal group of subjects pertaining to gender.

If audiologists are to be involved in the investigation and management of hearing processes that reach beyond the peripheral hearing mechanism, but nevertheless have a significant influence on an individuals' auditory functioning, it is unavoidable that they are informed about the nature of these processes. As scientists we have an obligation towards research in this area.

1.4. Problem statement

In an attempt to determine the validity of any diagnostic procedure, it is necessary to establish the procedures' ability to perform as intended (Roeser, Valente & Hosford-Dunn, 2000). In the case of a P300 evoked response, it is important to establish if P300 latencies and amplitudes vary as a function of gender.

Preliminary studies (Theunissen, 2002; Ehlers et al., 2001; Gölgeli et al, 1999; Bahramali, et al., 1999; Niwa & Hayashida, 1993) have shown significant differences in latencies and amplitude values of the P300 response between genders. The current research study aims to establish a gender-matched normative database for the P300 auditory event-related potential. A recent study conducted at the University of Pretoria, South Africa, found a great need for further exploration on the effect of gender on the amplitude, and especially on the latency of the P300 auditory event-related potential (Theunissen, 2002). It is clear that there is a need for clinic-specific norms for gender.

The problem statement can therefore be formulated as follows:

What is the gender matched norms for the P300 auditory event-related potential at the Electrophysiology clinic at the Department of Communication Pathology, University of Pretoria?

2. Research Methodology

The research question underlying the current study has been discussed extensively in Chapter 1. This chapter aims to describe the operational method employed in this study. It is an attempt to validate the findings of the current study and to encourage further research on the use of auditory P300 evoked responses, to assess neural processing of speech in individuals with communication disorders.

2.1. Introduction

Although the word *research* strikes fear into the hearts of many audiologists and speech-language therapists, it should be recognised that what many of us do on a daily basis is, in essence, research (Bellis, 2003). According to Silverman (1977) there should be no difference in the way we answer clinically relevant questions, or test clinically relevant hypotheses for clinical or research purposes.

Scientific research is distinguished from other research by the systematic process of inquiry based on combined empirical and theoretical principles (Graziano, 1993). Leedy (1997) refers to the research methodology simply as an operational framework. Previous studies (Theunissen, 2002; Ehlers et al,. 2001; Gölgeli et al,. 1999; Bahramali et al., 1999; Niwa & Hayashida, 1993; Martin et al., 1988) have shown significant gender differences in the latency and amplitude values of the P300 auditory evoked potentials. In other studies, no significant differences between values for different genders regarding the P300 auditory evoked potentials were found (Polich, 1986; Hall, 1992; McPherson, 1996). The need arises to determine if significant gender differences exist, and to establish a normative data base, which can be used to interpret P300 auditory evoked potential recordings. These findings should also be validated as accurate and reliable.

2.2. Aims of Research

The aims of the research project were the following:

2.2.1. Main Aim

The aim of this study was to determine the range of latency and amplitude values for male and female subjects for the auditory P300 event- related potential in a group of young adults in order to establish a gender specific normative database.

The following sub-aims were formulated in order to realise the main aim of the study:

2.2.2. Sub-aims

- To determine the central tendencies (mean/average) of the latencies and amplitudes of the auditory P300 event-related potential.
- To determine the normal variation (standard deviation) of the auditory P300 event-related potential (latency and amplitude).
- To establish whether there are any significant differences in male and female subjects for the auditory P300 event-related potential (latency and amplitude)
- To determine whether using a subtraction protocol (subtracting the common/frequent wave from the rare/infrequent wave to obtain a 'derived' P300) to mark the P300 results in a statistical difference from marking the P300 on the rare/infrequent trace.

2.3. Research Design

A descriptive, quantitative normative research design was selected (Thomas & Nelson, 2001). Quantitative researchers seek to validate certain hypotheses and generalise their findings to apply their new knowledge to other people and situations (Leedy & Ormrod, 2001). This method generally applies objective measurements and data is usually converted into numerical values and statistics.

This method is the most applicable to the type of data required in this study. Objective measurements were taken and the results were given in numerical form (microvolt and milliseconds). The advantage of this method compared to the qualitative method is that it is more focused, with known variables and established guidelines, using deductive analysis, numbers and statistics (Leedy & Ormrod, 2001). Electrophysiological measurements of the auditory P300 event-related potential were used as the objective measurement (no response required from the subject). This study specifically focused on the morphological characteristics of the P300 wave, using the standard oddball paradigm in a specific age group and the results are given in the numerical values of these characteristics.

Controlled variables were identified as:

- Age
- Gender
- Hearing level
- Medication
- Cognitive abilities
- Cultural and logistical factors
- Psychological disease
- Subject's state of wakefulness

The measured variables are the values of the P300 latencies and amplitudes for each subject.

2.4. Subjects

For this study 50 subjects (n=100) between the ages of 18 and 30 were selected. All subjects were randomly selected.

2.4.1. Selection Criteria

Subjects were selected according to the following criteria:
(See Appendix B for Medical/Audiological History Questionnaire)

- **Age**

All subjects were between the ages of 18 and 30. According to the literature, this age group is described as having the shortest P300 latencies (optimal latencies) (Barajas, 1990). The latencies of the P300 decrease systematically throughout childhood, reaching asymptote after puberty (Polich et al., 1985) and waveforms generally do not reach adult values until the age of 17 (Buchwald, 1990).

- **Gender**

An equal distribution of gender was attempted (25 males and 25 females) so results could be compared statistically. The participants were divided into two groups according to gender.

- **Hearing**

Theoretically, there should be no direct effect of peripheral hearing loss on the P300 (Musiek & Geurkink, 1981). However, P300 latency can be indirectly affected by peripheral hearing loss, as N1 and P2 waves are often shifted in latency (causing a shift in P300 latency) in the presence of a hearing loss (Musiek &Lee, 1999). More recent studies have shown marked differences in event-related potentials in conditions associated with poor speech perception such as simulated hearing loss (Martin, Kurtzberg & Stapells, 1999; Martin, Sigal, Kurtzberg &Stapells, 1997) and sensorineural hearing loss (Oates,

Kurtzberg & Stapelles, 2002). For these reasons all subjects were required to have normal hearing levels at 500, 1000 and 2000Hz as the frequent stimuli are at 500Hz, and the infrequent stimuli at 2000Hz. Normal hearing in this case was defined as pure tone air conduction thresholds between 0 and 15 dB (Hall & Mueller, 1997).

- **Medication**

No subjects on any medication, such as central nervous system or psychotherapeutic drugs, which could have an effect on the P300 (Thomas, Lacono, Bonanni, D'Andreamatteo & Onofrj, 2001; Polich & Kok, 1997), were included in the study.

- **Cognitive Abilities**

The study required that all subjects, regardless of their age, should have normal cognitive functioning, since the P300 is affected by general cognitive functioning (McPherson, 1996). All the subjects were students or graduates from a tertiary institution, and it was therefore presumed that they have normal cognitive function.

- **Other factors known to influence the P300**

The test sample excluded subjects diagnosed with or suffering from the following conditions known to affect P300 values:

- Psychiatric disorders, such as depression and schizophrenia (Vandoolaeghe, Van Hunsel, Nuyten & Maes, 1998; Wagner, Roeschke, Fell & Frank, 1997),
- Patients with organic mental disorders, such as epilepsy, head injuries (Packard & Ham, 1996), dementia or stroke (Korpelainen, Kauhanen, Tolonen, Brusin, Mononen, Hiltunin, Sotaniemi, Suominen & Myllyla, 2000; Yanai, Fujikawa, Osada & Yamawaki, 1997) and

- Subjects who suffer from alcoholism (Hada, Porjesz, Chorlian, Begleiter & Polich, 2001).

2.4.2. Selection procedures

Non-probability sampling (Neuman, 1997) was used in the selection of research subjects. These subjects were selected based on certain selection criteria as well as availability (Time constraints of the research subjects).

Subjects had to comply with the selection criteria as stated in section 2.4.1. The following procedures were used:

- Subjects were approached personally, or by telephone, to determine if they were available for testing.
- Informed consent: All research subjects were briefed on the non-invasive nature of the procedure, the time involved in the execution of the procedure, confidentiality as well as the objective of the study. Furthermore, should they wish, all research subjects can request a copy of the test results obtained. A letter of consent was completed by each subject (See Appendix A).
- Relevant audiological and medical information was collected using an audiological case history form (Appendix B).
- An otoscopic examination of the external meatus and tympanic membrane was conducted to identify any possible pathology that could cause conductive hearing loss. In order to pass the otoscopic examination all subjects were required to have an identifiable light reflex, while the position, colour and transparency of the tympanic membrane were also taken into consideration (Hall & Mueller, 1997).
- Pure tone air conduction audiometry was performed to determine hearing thresholds at 500, 1000 and 2000 Hz for each subject. All thresholds were required to fall within the normal range of hearing

(0-15dB HL). A descending threshold-seeking procedure was used. Testing was conducted in a soundproof room at the University of Pretoria, which is routinely used for audiometric evaluations (Hall & Mueller, 1997).

2.4.3. Description of subjects

Using the selection criteria and procedures as described above, 50 subjects (50% male and 50% female) (n=100) were selected. All subjects were between the ages of 18 and 30.

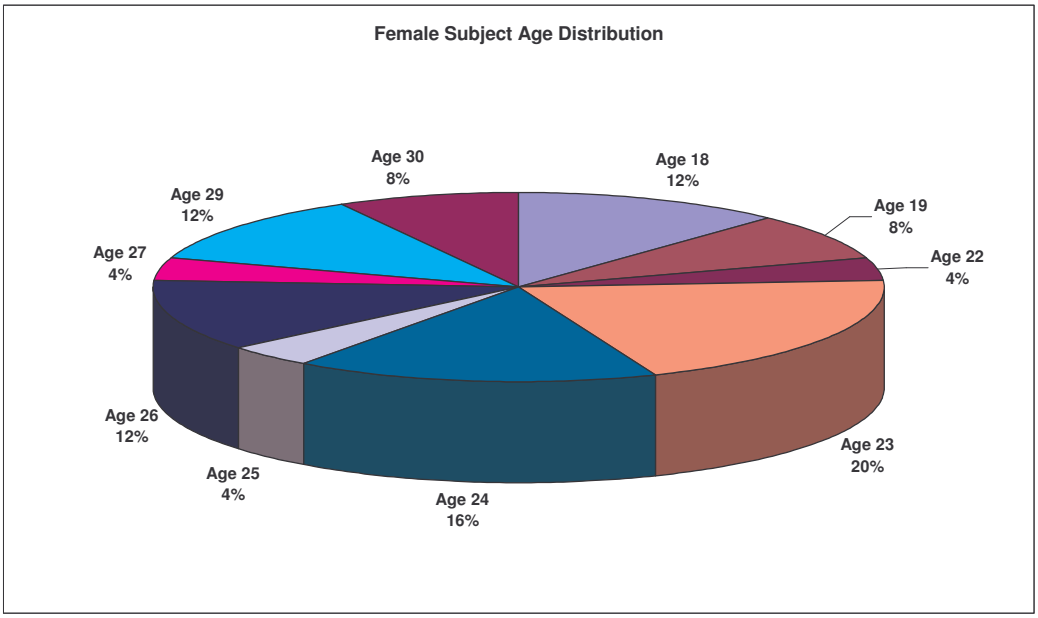


Figure 2.1: Female subject age distribution.

The mean age values for both male and female subjects were 24 years. Figure 2.1 and 2.2 depicts the age distribution per gender.

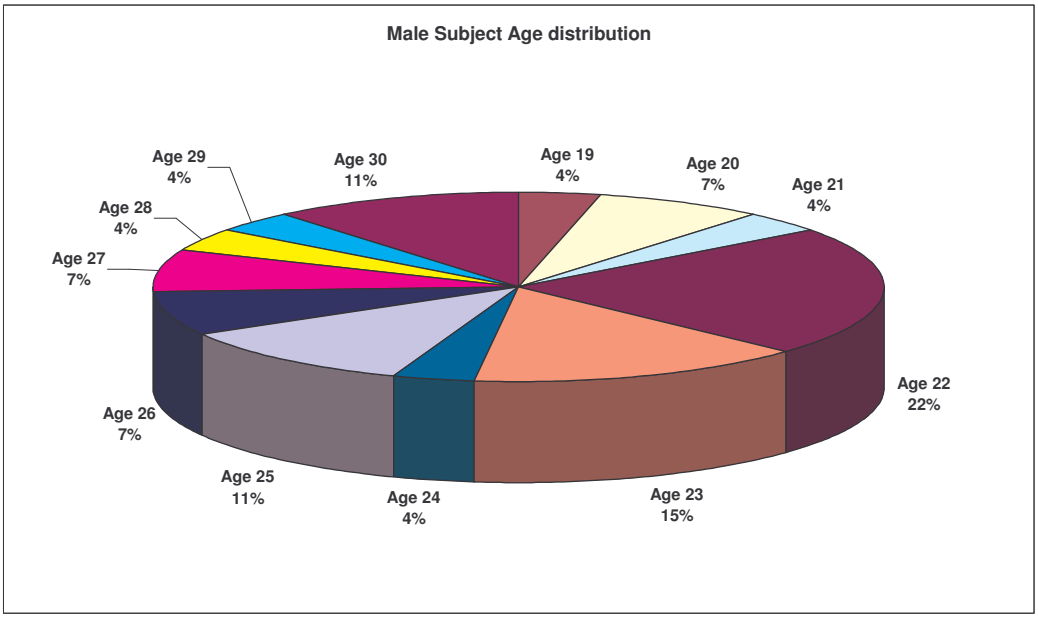


Figure 2.2: Male subject age distribution.

All subjects were required to have hearing sensitivity within the normal range (0-15 dB HL). The subjects were randomly selected with the notion to control the extraneous variables through randomisation (Silverman, 1977).

2.5. Material and apparatus

2.5.1. Subject selection material and apparatus

- Medical/audiological history questionnaire: This was initially employed in the selection of participants for the study. The questionnaire consisted of questions regarding previous hearing history (hearing problems, noise exposure, and ototoxic drugs), balance, tinnitus, current medication, psychiatric problems, organic mental disorders and alcoholism. These questions were based on

the subject selection criteria as stated earlier. An example of the questionnaire used may be viewed in Appendix B.

- Otoscopy: A Welch-Allyn otoscope was used for otoscopy.
- Pure-tone Audiometry: Pure-tone thresholds at 500, 1000 and 2000 Hz were measured using the GSI-61 audiometer (calibrated on 10 February 2004 according to SABS requirements as stated in SABS 0154-1999). *Telephonics* TDH-49P earphones with MX 41/JR cushioning were used. Testing was conducted in a single walled soundproof booth.

2.5.2. Data collection material and apparatus

- The auditory event-related potentials were recorded using a *Bio-logic Navigator 'E' Version 5.63 module 317 computer.*
- Testing was conducted in a single-walled soundproof booth in a sound-treated room.
- *Abrasive Skin Prepping Gel* was used to clean the areas where electrodes were placed in order to keep impedance values below 5kΩ as this could affect results (Ferraro & Durrant, 1994).
- *EEG Conductive Electrode Gel* was used for application of electrodes.
- Disc electrodes with a silver chloride surface connected to a *Bio-Logic* pre-amplifier were used for recordings.
- Electrodes were attached to the specific areas using *3M Medipore* tape.
- *Etymotic Research ER-3A* insert earphones with *Earlink Eartips* were used to present the stimulus in the ear of the subject.

2.6. Procedure

One set of data was collected from each subject namely, auditory P300 event-related potentials. Data was collected at the Department of Communication Pathology of the University of Pretoria.

2.6.1. Data collection

- Testing was conducted in a soundproof room at the University of Pretoria routinely used for electrophysiological evaluations.
- The skin of the subjects was cleaned using *Abrasive Skin Prepping Gel* on the areas where the electrodes were placed.
- *EEG Conductive Electrode Gel* was applied to each electrode before attaching them to the specified sites (see Table 2.1 for recording parameters).
- After the electrodes were attached, subjects were instructed to lie down comfortably in the supine position, but awake, as sleep affects the amplitude of the P300 waveforms (Hall, 1992). Subjects were instructed to lie as quietly as possible with their eyes closed to minimise interference.
- Subsequently, the subjects were instructed to count the infrequent stimuli while lifting their forefingers slightly every time they heard the infrequent stimulus. This ensured a recording of the P300 in the active or attend state (Musiek & Lee, 1999; Mertens & Polich, 1997; Lew & Polich, 1993).
- After instructions were given, impedance testing was conducted to determine whether the impedance values were below 5kΩ (Ferraro & Durrant, 1994). If impedance values were too high, electrode sites were cleaned again and electrodes reattached. This procedure was repeated until the correct impedance values were reached.
- Following the impedance testing, the insert earphones were placed in the subjects' ears, after which the door to the soundproof room was closed.
- The recording of the P300 waveforms subsequently commenced. Stimuli were presented through the insert earphones (See Table

2.2 for stimulus parameters). This resulted in two traces per recording, an ALLR (Auditory late latency response) from the common stimuli and the auditory P300 from the rare stimuli. Responses were averaged until a minimum of 25 infrequent stimuli and 100 frequent stimuli were presented to limit testing time and obtain a repeatable P300 waveform.

- After the recording, results were printed.

2.6.2. Stimulus parameters

The stimulus parameters utilised to evoke the Auditory P300 can be viewed in Table 2.1.

Table 2.1: Stimulus parameters for recording of Auditory P300.

Stimulus parameters		*Rational*	*References*
Stimulus type	Tone burst	Facilitates use of frequency-specific stimuli.	Musiek, Baran & Pinheiro, 1994; Hall, 1992; Hall & Mueller, 1997; Nourse,2000; Tremblay et al., 2003
Stimulus frequency	Frequent (85%):500Hz Infrequent (15%):2000Hz	Facilitates frequency discrimination task commonly used for oddball paradigms. May be varied as indicated.	Hall & Mueller, 1997; Musiek et al., 1994; Hall, 1992;
Stimulus intensity	70 dB nHL	High above threshold, as low intensity stimuli may result in smaller P3 amplitudes and longer latencies.	Musiek et al., 1994; Vesco et al., 1993
Rise and fall time	10 ms	Optimal ALLR recordings require rise and fall times of 10 ms or greater.	Onishi & Davis, 1968; Hall & Mueller, 1997; Tremblay et al., 2003
Plateau time	20 ms	Optimal ALLR recordings require rise and fall times of 10 ms or greater.	Onishi & Davis, 1968; Hall & Mueller, 1997; Tremblay et al., 2003
Stimulus rate	1 tone every 0.8 sec		Musiek et al., 1994; Hall & Mueller, 1997; Tremblay et al., 2003

2.6.3. Recording parameters

The parameters utilised in the recording of the Auditory P300 can be viewed in Table 2.2.

Table 2.2: Recording parameters for recording of the Auditory P300.

Recording parameters		Rationale	References
Montage	Active electrodes: Fz Referenced at: M1, M2 Ground Electrode: FpZ	P300 reliably recorded over frontal scalp area, maximum amplitude vertex.	Musiek & Lee, 1999; Hall, 1992; Hall & Mueller, 1997; Wall et al., 1991; Jasper, 1958
Channels	Two	Facilitated by available equipment.	Wall et al., 1991
Recording strategy	Oddball paradigm	Provides a variety of potentials (N1, P2 7 P300) without additional time.	Chermak & Musiek, 1997; Salamat & McPherson, 1999
Gain/Amplification	75 000	Response bigger than ABR therefore less amplification is needed.	Hall & Mueller, 1997; Tremblay et al., 2003
Filters	High filter: 100 Hz Low filter: 1 Hz	Sufficient to record low frequency responses and narrow enough to help reduce interference generated by muscle & eye movements.	Harris & Hall, 1990; Hall & Mueller, 1997; Tremblay et al., 2003
Analysis time	800ms	Sufficient time to accommodate P300 responses.	Musiek, Baran & Pinheiro, 1994; Hall & Mueller, 1997 Tremblay et al., 2003

2.6.4. Data analysis

Descriptive statistics were obtained for each component of the P300 auditory event-related potential. After the waveform was repeated, the P300 could be identified as the largest positive peak. The P300 followed the N2 between 250 ms and 380 ms (Wilson, 2000) in the waveform resulting from the infrequent stimulus. The P300 wave was marked in consultation with the research

supervisor. If the wave was bifurcated the largest peak was marked as the P300. If the wave appeared as a plateau, the point with the highest amplitude was marked as the P300 (see Appendix D) (McPherson, 1996).

A 'derived' P300 was obtained by subtracting the common/frequent wave from the rare/infrequent wave. On this derived trace the P300 was marked in the usual manner as discussed above. The marked waveforms were printed for further analysis.

Subsequently, the relevant information gathered from the printed data was tabulated using *Microsoft Excel* spreadsheets. Relevant information consisted of the latency (ms) and amplitude (μV) of each marked P300 waveform.

2.6.5. Data processing

To realise the sub-aims of the study*, Microsoft Excel* software was used to obtain descriptive statistics of the data. All procedures were done using the latency and amplitude values for the P300 recordings.

A univariate procedure was performed on every variable to determine:

- the mean of each variable,
- the standard deviation of each variable,
- the minimum and maximum of each variable and
- the percentiles of each variable.

The mean value of the amplitude and latencies was further analysed by utilising a non-parametric test, the *Wilcoxon Rank Sum Test*, to establish whether statistical differences existed between genders for the P300 AERP.

2.7. Ethical considerations

The explosion of biomedical and behavioural research in the last half of the twentieth century has bought about scrutiny of the ethical principles by which investigators should be guided. The Belmont Report of the National Commission for the Protection of Human Subjects Of Biomedical and Behavioural research, released in 1979, describes three basic ethical principles that should guide researchers. The first of principle is *respect* for persons, this signifies that the choice of autonomous persons must be respected and those with diminished autonomy should be protected. The Second principle is that of *beneficence* which implies an obligation to secure the well being of persons by not harming them and by maximizing the benefit-to-risk ratio. The third principle is *justice* meaning equality in the sharing of the risks and benefits. Many academic institutions cite the Belmont Report as the ethical standard to be applied before approving research under their jurisdiction. Internationally the Declaration of Helsinki is often the standard by which human subjects research is judged, although it is specific to medical as opposed to behavioural, research (Sininger, Chair, Marsh, Walden & Wilber, 2003).

Ethical clearance for this research study was obtained from the Ethics Committee of the University of Pretoria. Informed consent was obtained from each subject. Subjects were fully informed about the test procedures. They were made aware of their right to ask and have questions answered as well as their right to withdraw consent at any time. Participants were informed that data gathered during this study will be used for research purposes only (Letter of Consent: Appendix A).

3. Results and Discussion

The aim of this study was to determine the range of latency and amplitude values for male and female subjects for the auditory P300 event- related potential in a group of young adults and consequently to establish a gender specific normative database.

The results obtained will be discussed in the following section according to the sub-aims formulated in paragraph 2.2 of the methodology.

3.1. Average latencies and amplitudes of the auditory P300 event-related potential

The first sub-aim was to determine the central tendencies (average) of the latencies and amplitudes of the auditory P300 event-related potential.

The mean or average (sum of the measurements divided by the total number of measurements) (Ott & Mendenhall, 1994) of the latencies and amplitude of each data point is depicted in Table 3.1. The complete set of results with the latency and amplitude of the P300 as determined for each subject is represented in Appendix E. The average value of each variable is included in the results as this value is intended to represent “the best guess as to what is most characteristic of the total population” (Leedy & Ormond, 2001:268) and therefore comprises an essential part of the normative database.

Table 3.1 Mean/Average values of the latencies and amplitudes of ALLRs & P300.

Variable		*Mean*	*Standard deviation*
P100	Latency (in ms)	89.9	29.5
	Amplitude (in µV)	1.6	1.3
N100	Latency (in ms)	121.9	38.3
	Amplitude (in µV)	-3.0	3.8
P200	Latency (in ms)	188.3	34.02
	Amplitude (in µV)	3.5	5.7
P300	Latency (in ms)	314.7	37.2
	Amplitude (in µV)	7.1	6.1
P300	Latency (in ms)	309.9	34.6
(Subtracted)	Amplitude (in µV)	6.9	6.5

The average or mean P300 latency was established at 314.7 ms and 309.9 ms for the P300 subtracted wave. The amplitude measurements resulted in an average of 7.1 µV for the P300 wave and 6.1 µV for the P300 subtracted wave.

One disadvantage of using the mean is that it is sensitive to extreme values (Keller & Warrack, 2000). The median is a measure of central location which is not sensitive to extreme values. The median (50^{th} percentile) (Table 3.2) latency values for the P300 and the P300 subtracted wave were 311.7ms and 305.5ms respectively. The median (50^{th} percentile) amplitude values were calculated as 5.93µV and 4.85µV for the P300 and P300 subtracted respectively.

Table 3.2: Percentiles of the latencies and amplitudes of the P300 & P300 (subtracted).

Variable		*25th Percentile*	*Median*	*75th Percentile*	*IQR (inter quartile range)*
P300	Latency (in ms)	287.48	311.7	342.17	54.69
	Amplitude (in µV)	2.28	4.54	9.69	7.42
P300	Latency (in ms)	286.7	305.45	331.33	44.63
Subtracted	Amplitude (in µV)	2.6	4.85	9.41	6.81

The P300 peak was generally less precise in its repeatability than N100 and P200 and often required more than two recordings to obtain sufficient repetition. According to Wilson (2000) and Hall (1992), the ALLR and P300 show much greater variability than the ABR and the rules of repeatability do not strictly apply. Considering this statement, the reliability of the results is not significantly affected by the reduced repeatability.

Substantial research on the clinical value of the P300 in various fields has accumulated extensive literature on the expected values for P300 latencies and amplitudes. These fields include: Electrophysiological evaluation of auditory processing (Hall & Mueller, 1997), studies of various cognitive processes (Yamaguchi & Knight, 1991; McPherson, 1996), ageing (Goodin et al., 1978; Barajas, 1990; Coyle et al., 1991; Garcia de la Cadena et al., 1996; Kuegler, 1997) and a variety of different mental illnesses (Hada et al., 2001; Vandoolaeghe et al., 1998).

The findings in the current research can be related to a number of studies found in the literature. Differences in test protocols were apparent when comparing the studies, for instance:

- Electrode placements were different in virtually every study, depending on the facilities available and the preferences of the examiner. Nourse (2000), for example, used a one-channel recording with a single active electrode at Fz (high forehead), while Michalewski et al. (1982) recorded the P300 from three different active electrodes (mounted at Fz, Cz, and Pz). Anderer, Heibert and Semlitsch (1996) similarly reported separate findings for Fz, Cz and Pz. Bourtros et al. (1997) recorded P300s from Pz. Polich, Howard and Starr (1985) recorded responses from the vertex (Cz) site only and Picton et al. (1984) recorded from temporal, parietal, frontal and vertex sites. Salamat and McPherson (1999) recorded responses three times from 22 electrode sites. Wall et al. (1991) and Theunissen (2002) recorded the P300 response with active electrodes at Cz and Fz, similar to the present study.

- Stimulus parameters, such as stimulus intensity and interstimulus intervals varied greatly. Nourse (2000) experimented with three different protocols by altering the intensity values of the infrequent stimuli (using 25, 22 and 21 dBSL respectively). Michalewski et al. (1982) presented stimuli at 60 dBSL (similar to the present study), while Anderer et al. (1996) used a higher intensity of 90 dB SPL, identical to that of Picton et al. (1984) and similar to that of Boutros et al. (1997) who presented tones at 95 dB SPL. Salamat and McPherson (1999) recorded the P300 using three different interstimulus intervals. Wall et al. (1991) presented stimuli at an intensity of 85 dB nHL.

- Separate studies also showed differences in performance tasks required from subjects. Nourse (2000) and Polich, Howard and Starr (1985) used a frequency discrimination task (Oddball Paradigm, matching that of the present study), as did Picton et al. (1984), Boutros et al. (1997) and Theunissen (2002). Anderer et al. (1996) required an intensity discrimination task, while Michalewski et al (1982) instructed subjects to count omitted clicks (in other words discriminate between presence and absence of stimuli). Salamat and McPherson (1999) used a continuous performance task which required the subjects to

respond to frequent stimuli and refrain from responding to the infrequent stimuli.

- Selection criteria differed across studies, for instance in terms of age, a variable that has been established as a significantly influential factor (Hall, 1992). The different age groups of the different studies are depicted in Figure 3.1.

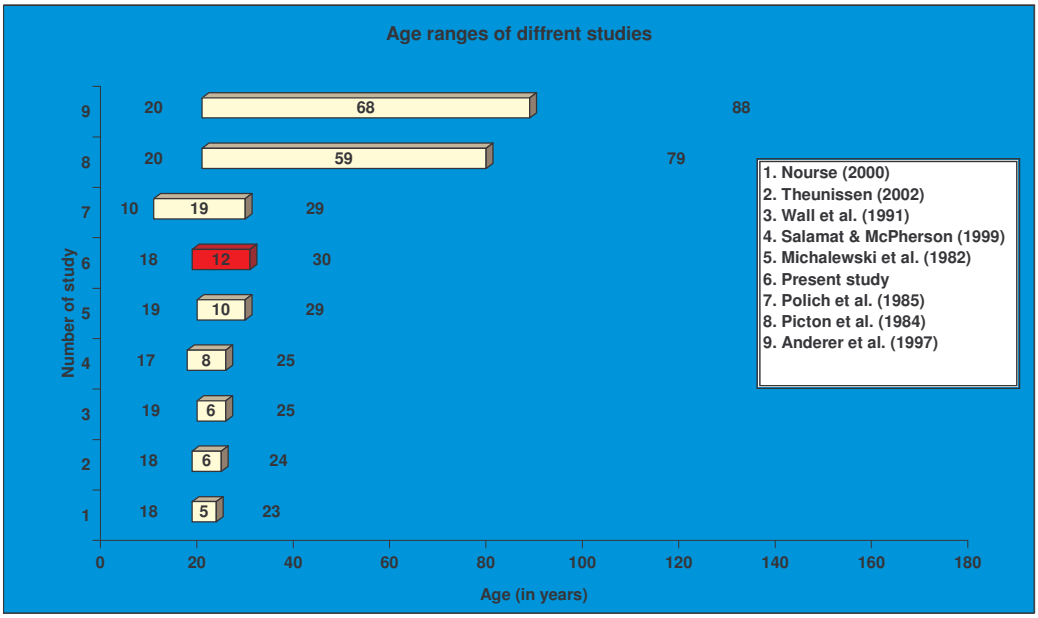


Figure 3.1: Age range of the different studies.

An additional study will be referred to (Boutros et al., 1997), which only reported the average age of the subjects (29.8 years). Although Anderer et al. (1996) used subjects from the greatest range of ages, they separately reported on findings in different age groups (e.g. 10-19 years; 20-29 years etc.). When referring to this study, the findings for the age group 20-29 years will be used. The results of the relevant studies are indicated in Table 3.3.

Table 3.3: Mean P300 latencies and amplitudes reported by different studies.

STUDY		*N*	*Age Range*	*Mean Latency*	*Mean Amplitude*
Present	**P300**	100	18-30	314.7 ms	7.1 µV
	P300 Subtracted	100	18-30	309.9 ms	6.9 µV
Theunissen (2002)		24	18-24	317.79 ms	9.58 µV
Nourse (2000)		20	18-23	303.1 ms 332.2 ms 319.1 ms	Absolute values not reported
Michalewski et al. (1982)		5	19-26	412.3 ms (Fz) 407.8 ms (Cz) 439.8 ms (Pz)	Absolute values not reported
Anderer et al. (1997)		58	20-29	353 ms (Fz) 355 ms (Cz) 361 ms (Pz)	8.8 µV (Fz) 15.9 µV (Cz) 19.5 µV (Pz)
Boutros et al. (1997)		40	Mean age: 29.8	328 ms	6.7 µV
Picton et al. (1984)		72	20-79	350 ms 366 ms 377 ms	11.8 µV 8.2 µV 8.5 µV
		18	20-29	287 ms	
		18	20-29	287 ms	
Salamat & McPherson (1999)		20	17-25	353.5 ms 372 ms 387.6 ms	17.9 µV 16.1 µV 15.68 µV
Wall et al, 1991		17	19-25	289 ms	13.2 µV

The latencies reported by Theunissen (2002), Nourse (2000) and Boutros et al. (1997) were all within 20 ms or closer to the present study's latencies for the P300 and the P300 subtracted wave. The latencies reported by Polich et al. (1985) for subjects between 10 and 19 years also showed a close resemblance, probably due to the proximity of the age group.

The latency values reported by Anderer et al. (1997), Picton et al. (1984) and Salamat and McPherson (1999) were relatively close to 360 ms (ranging from 350 ms to 387 ms). These values are about 40 ms above those reported in the present study, but are still within the normal range as defined by Wilson (2000). The latency values noted by Wall et al. (1991) were about 30 ms smaller than those generated by the present study but still within the normal range (Wilson, 2000).

The latency values reported by Michalewski et al. (1982) were approximately 100 ms higher than those of the present study and four other studies (Nourse, 2000; Boutros et al., 1997; Polich et al., 1985). None of the values reported by Michalewski et al. (1982) fell within the normal range for evoked responses as defined by Musiek et al. (1994) and Wilson (2000). The large differences in results may be explained in terms of the test protocol. Michalewski and colleagues (1982) used a test protocol with significant differences to the other studies. Their aim was to measure emitted responses (potentials that need not be elicited using a physical stimulus) versus the evoked responses gathered in the other studies. This meant that they only used click stimuli, and subjects were required to count omitted clicks, in contrast with the frequency discrimination task used in the other studies. Although these two performance tasks seem similar, it made use of the actual absence of stimuli to elicit the auditory P300 responses, as no stimulus is needed to elicit an omitted potential. This protocol eliminates the effect of sensory neural hearing loss that could indirectly influence the results (Michalewski et al., 1982). Average amplitude findings reported in the encountered literature were relatively

equivalent to those reported in this study, varying between 3.6µV (Nourse, 2000) and 19.5 µV (Anderer et al., 1996).

The need for a clinic-specific normative database arises if the researcher is to reduce the number of variables that might affect the results (Hall, 2000). One of the objectives of the present study was to initiate the start of a clinic-specific normative data base. Latency and amplitude values of the present study compare favourably with results obtained by Theunissen (2002). Latency values for the P300 in both studies showed a difference of 3 ms and amplitude values showed a difference of 2 µV. These differences validate the reliability of the values obtained in the present study. A clinic-specific normative data base will enable future examiners to compare clinical findings to normative data obtained using the same protocol (Hall, 2000).

3.2. The variability and distribution of latencies and amplitudes of the auditory P300 evoked response

The second sub-aim was to determine the normal variation of the auditory P300 cortical evoked response.

A variety of calculations were executed to render a representation of the distribution and range of variability of all the data. The following descriptive statistics of each variable (P300 latencies and amplitudes and, in addition, also the latency and amplitude values of the ALLR's namely P100, N100 and P200) were provided:

- The minimum and maximum values and
- The standard deviation

- Percentiles

A visual presentation of the distribution (variability) of the latencies and amplitudes of the P300, P300 subtracted wave, P100, N100 and P200 can be seen in Figure 3.2 and 3.3.

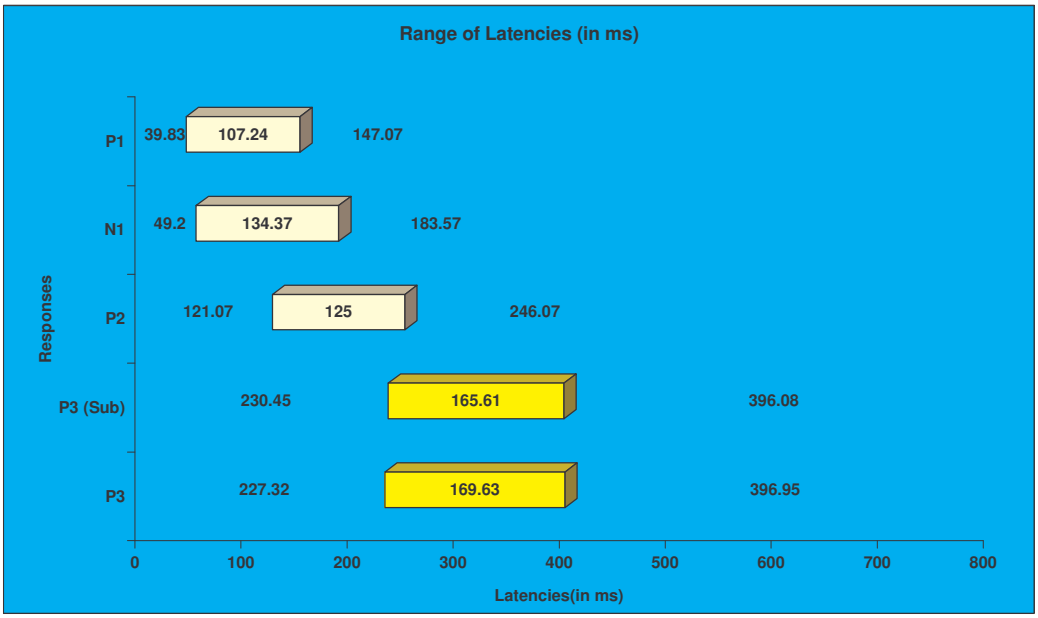


Figure 3.2: Findings on range of latencies for P1, N1, P2, P3 and P3 (Subtracted).

Figure 3.2 illustrates the minimum and maximum values of the P300 latency, found respectively at 227.32 ms and 396.95 ms. This indicates a range of about 169.63 ms. The P300 subtracted wave showed similar values with minimum and maximum values of 230.45 ms and 396.08 ms respectively, indicating a range of 165.61 ms. These ranges were larger than those reported for the P1, N1 and P2.

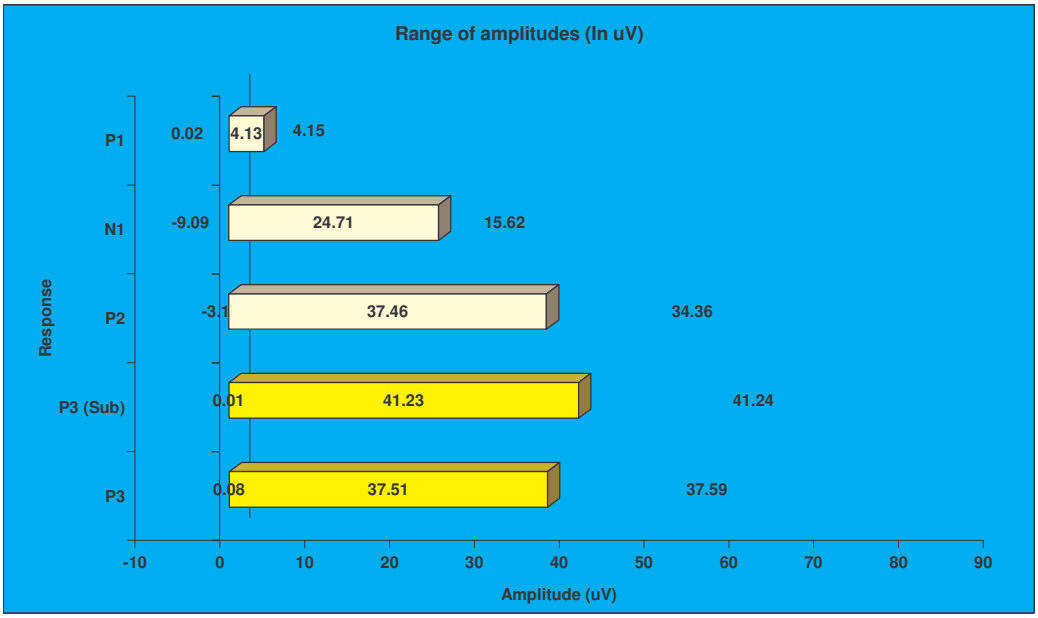


Figure 3.3: Findings on range of amplitudes for P1, N1, P2, P3 and P3 (Subtracted).

The range of amplitudes for the P300 was between 0.08 µV and 37.59 µV (a total range of 37.51 µV) and for the P300 subtracted wave was between 0.01 µV and 41.24 µV (a total range of 41.23). These values once again showed greater variability than those for P1, N1 and P2 values. These discrepancies are demonstrated by figures 3.2 and 3.3 and confirmed by the standard deviation values shown in Table 3.1.

The literature generally describes the P300 response as a large, positive wave occurring at approximately 300 ms after a rare or infrequent stimulus (Hall & Mueller, 1997; Musiek & Lee, 1999). Musiek et al (1994) describe abnormal P300 latencies as later than 350 ms, while Wilson (2000) estimates that latencies in normal adults should be between 250 and 380 ms. The present study recorded responses, which occurred after 350 ms in 19 normal adults tested (the maximum latency recorded at 396.95 ms). These findings suggest the guidelines provided by Wilson (2000) might be more appropriate for the clinical setting described in this study. In terms of amplitude, the

standard deviation of 6.1 µV (6.5µV for the P300 subtracted) is similar to that of the 7 µV reported by Wall et al. (1991). These values also compare favourably with the values reported by Salamat and McPherson (1999) (between 3.9 µV and 5 µV), Anderer et al. (1996) (values between 5.4 µV and 6.2 µV) and Theunissen (2002) (3.6 µV).

Salamat and McPherson (1999), using a continuous performance task, reported the range of P300 latencies and amplitudes for three different interstimulus intervals. Theunissen (2002) used the oddball paradigm and utilised the same test protocol as the present study. Once again, the differences and similarities in test protocols must be considered when comparing these findings to that of the present study (see section 3.1 above for a more detailed description of these two studies). A comparison of their findings with those of the present study is illustrated in Figure 3.4 (latency) and Figure 3.5 (amplitude).

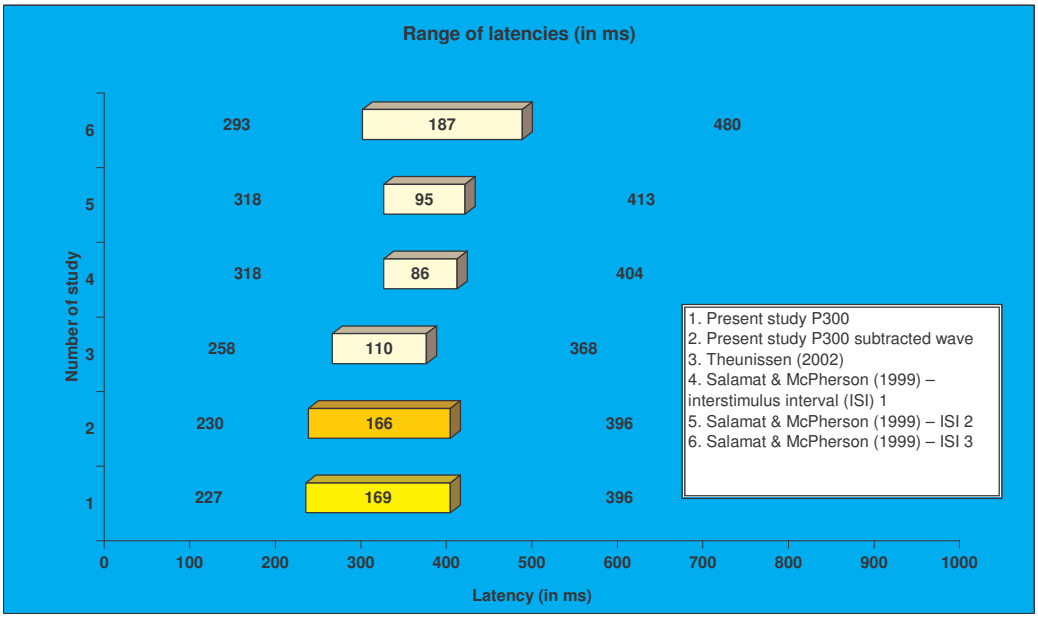


Figure 3.4: Comparison of the findings on the range of latencies of the present study to Salamat & McPherson (1999) and Theunissen (2002).

Figure 3.4 indicates that latencies reported in the present study are very similar to that of Salamat and McPherson (1999) and Theunissen (2002) in terms of range. Although there are differences in the absolute minimum and maximum latency values, there is a marked correspondence in terms of the size of the range of latencies.

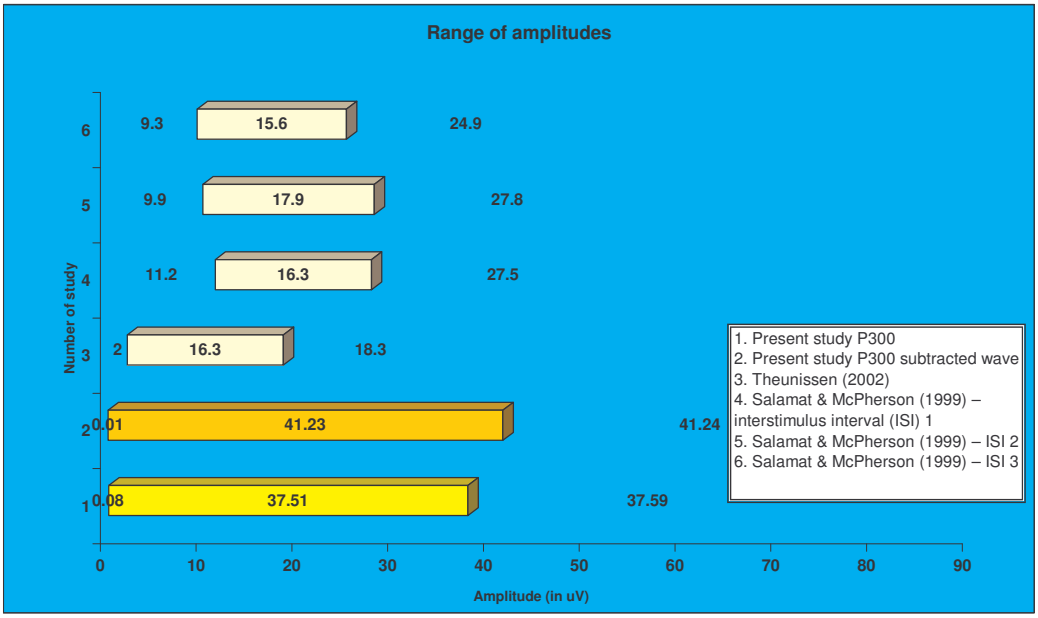


Figure 3.5: Comparison of the findings on the range of amplitudes of the present study to Salamat & McPherson (1999) and Theunissen (2002).

Figure 3.5 indicates a larger range of amplitude values in the present study than that found in the studies of Salamat and McPherson (1999) and Theunissen (2002). The minimum values of 0.01 and 0.08 for the P300 and the P300 subtracted wave respectively, were obtained by only two of the normal adults tested (n=100), thus only 2% of the total test population. Considering this, it can be said that comparing minimum and maximum values may be misleading. The standard deviation can be more useful to interpret these values. The standard deviation values of the present study were 6 µV for both the P300 and the P300 Subtracted wave. Theunissen (2002) reported a standard deviation value of 4µV.

Measures of relative standing (percentiles) can also be used to describe the shape of the distribution (Keller and Warrack, 2000). The advantage of this method is that it is not sensitive to extreme values and eliminates outliers (see Table 3.2). The P300 latencies presented with a range of values from the 25th percentile (first quartile) to 75th percentile (third quartile) of 287.48 ms to 342.17 compared to the P300 (subtracted) latencies range of 286.7 ms to 331.33 ms. The 25th percentile to 75th percentile value range for the P300 amplitudes were 2.28 µV to 9.69 µV compared to the P300 (subtracted) amplitude range of 2.6 µV to 9.41 µV.

This notable variability of the P300 waveform when compared to the P100, N100 and P200 can partially be explained by the very nature of the response. The P300 is described as an endogenous response dependent on subject factors such as attention (Hall, 1992), rather than being directly influenced by stimulus factors. The attention factors are, however, closely related to stimulus factors (Hall, 1992) such as rate, frequency and task complexity. These are factors that often vary from one clinical setting to another, creating remarkable discrepancies between test findings of different researchers (see Table 3.3).

In addition to the variance in the findings of different researchers, there is great inter-subject variability within this study in terms of latency and amplitude. Since the study is limited by age, gender and drugs and used the same stimulus and recording parameters for every subject, these differences need to be further investigated. The very nature of the P300 as an endogenous response dependent on subject factors such as attention, results in inter-subject variability, as the particular cognitive process required to create the response may vary, even within a normal population. Beydagi et al. (2000) investigated the correlation between working memory and the event-related potential in healthy subjects and found that variations in the recall time of the subjects yielded differences in P300 latencies. Motivation, personality and a number of other factors (briefly discussed below) may also influence the

P300 responses (Hall, 1992). An example is the psychological state of the subject (Musiek, Verkest & Gollegly, 1988). The present study is controlled for the presence of serious psychiatric illness in the selection criteria, but the exact state of mind of each subject was not evaluated prior to testing. The personality of a subject might also influence the P300. Vedeniapin et al. (2001) examined the relation between self-directedness, as a personality trait and the P300 response, and concluded that subjects with a low score on the self-directedness scale of the Temperament and Character Inventory had significant reduced P300 responses. Hostility and aggression can also have an effect on the P300, as illustrated in a study by Bond and Surguy (2000), who studied the effect of aggression in a normal population on P300 components. They found significant prolonged P300 latencies in more hostile or aggressive subjects.

These findings indicate that there are a great number of personal characteristics and psychological factors that might influence the P300 results. This may also give some explanation of the great inter-subject variability for the P300 response, even within a group of normal adult subjects. The clinical utility of the auditory P300 as a valid diagnostic measure in clinical audiology, however, remains questionable. It is self-evident that audiologists will not always be able to control these factors when using event-related potentials in the clinical setting. However, if a recorded sample can be compared to a clinic-specific normative database, it may serve as a useful tool as part of a test battery. It is important though, that the examiner takes an acceptable degree of variability into account.

The scope of this study did not include an investigation of the Auditory Late Latency Responses (ALLR). Due to the nature of recording technique involved in recording the Auditory P300, these values where available. The average latencies and amplitudes for ALLR's (P1, N1, and P2) can be seen in Appendix F in graphic format.

3.3. The Significance of gender

The third sub-aim was to establish if there are statistically significant differences between male and female subjects using the auditory P300 event related potentials (latency and amplitudes).

The mean latencies and amplitudes (P300 and P300 subtracted wave) as calculated separately for males and females are depicted below in Figure 3.6, 3.7, 3.8 and 3.9. After calculating the mean values for each group, the *Wilcoxon Rank Sum test* was performed to determine whether there is a statistically significant difference between each group for each variable (P300 & P300 subtracted wave latencies and amplitudes). This analysis gives a p-value which indicates the probability that the differences are not due to chance factors alone (Keller & Warrack, 2000).

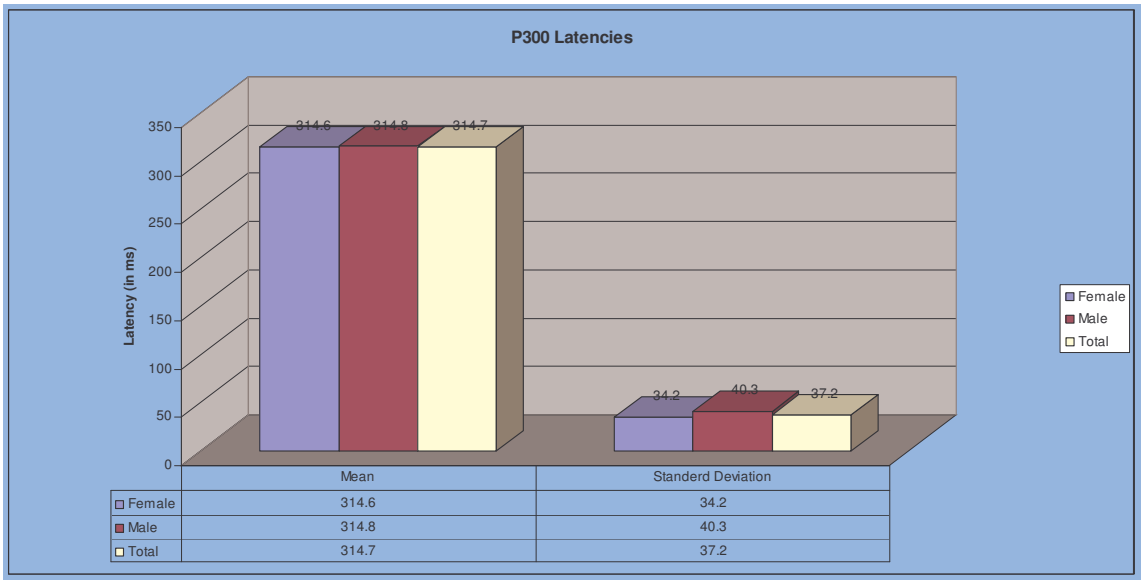


Figure 3.6: Gender differences for the P300 mean latencies.

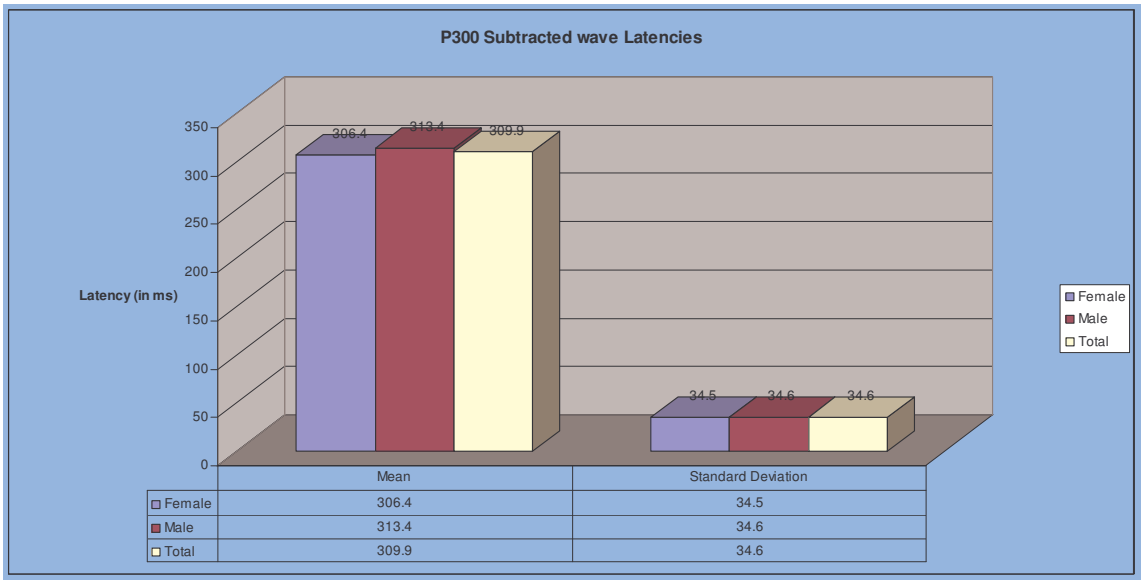


Figure 3.7: Gender differences for the P300 subtracted wave mean latencies.

Figure 3.6 and Figure 3.7 indicates the latency values for the P300 and P300 subtracted wave. No significant differences are indicated for either the female or male latencies. Standard deviations (also seen in Figure 3.6 & 3.7) for both female and male subjects showed only marginal differences. No significant effects of gender were observed for the latency of the P300 and P300 subtracted wave ($p < 0.05$). The p-values are indicated in Table 3.4.

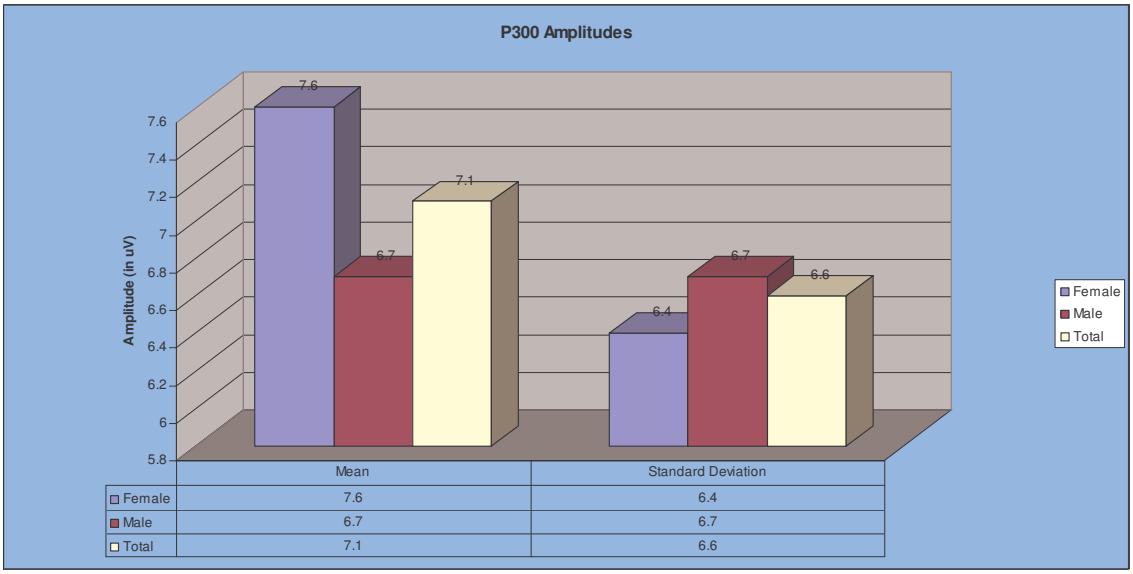


Figure 3.8: Gender differences for the P300 mean amplitudes.

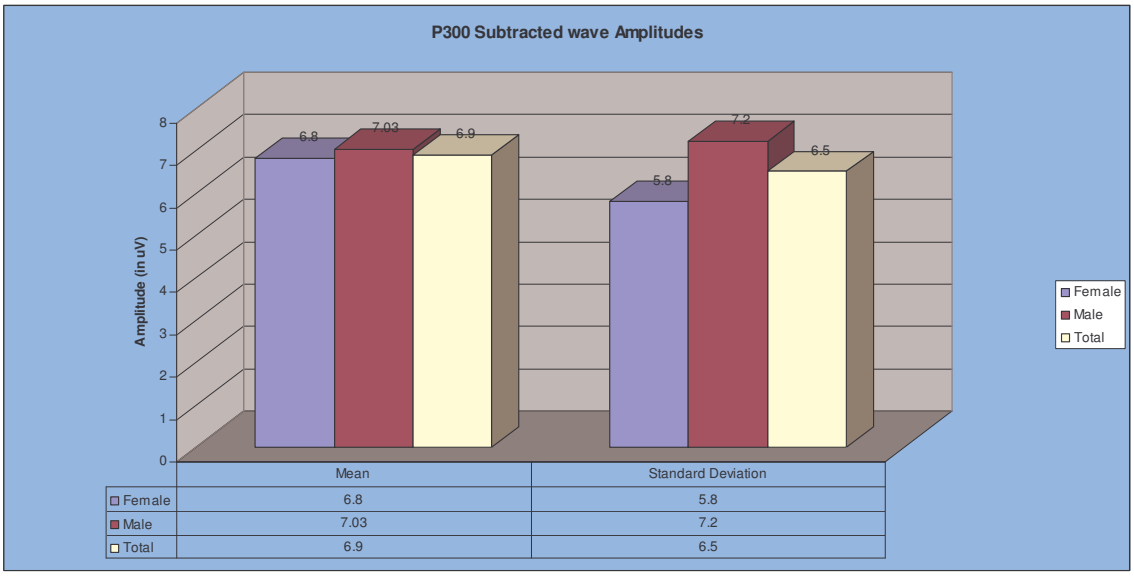


Figure 3.9: Gender differences for the P300 subtracted wave mean amplitudes.

Figure 3.8 and 3.9 indicates the amplitude values for the P300 and P300 subtracted wave. The amplitude values for the female subjects show larger P300 amplitudes (Figure 3.8). Interestingly, the female amplitude values for

the P300 subtracted wave show only a marginal difference from the male amplitude values (Figure 3.9). The standard deviation for both male and female subjects shows only marginal differences. Statistically, no significant difference was found for the amplitude values for male and female subjects (see Table 3.4 for p-values). No significant effect on gender was observed for the amplitude values of the P300 and P300 subtracted wave.

Table 3.4: p-values of the latencies and amplitudes of the P300 and P300 Subtracted wave.

Variable		*p-value*	*Statistically significant? (p< 0.05)*
P300	Latency	0.75	No
	Amplitude	0.35	No
P300 Subtracted Wave	Latency	0.22	No
	Amplitude	0.99	No

When examining the literature on the subject of gender effects on the P300, it becomes clear that this particular variable has rarely been investigated (Hall, 1992). However, some authors have reported a gender effect for one or more of the late responses. Hoffman & Polich (1999) reported that the P300 response tends to be larger in females than in males. Similar results were

found by Niwa and Hayashida (1993) and Hirayasu et al. (2000), who found larger P300 amplitudes in adult females compared to males. Other studies have also shown that P300 latencies vary as a function of age and gender (Ehlers, Wall, Garcia-Andrade & Phillips, 2001; Gölgeli, Süer, Ozesmi, Dolu, Ascioglu & Sahin, 1999; Bahramali, Gordon, Lagopoulos, Lim, Li, Leslie & Wright, 1999). However, Polich (1986), who examined the normal variation of the P300, found no significant differences in either latency or amplitude between males and females. Similarly, Hall (1992) and McPherson (1996) feel gender is not such a significant factor in P300 measurements as age.

The present study found marginal differences in latency and amplitude values for the P300 with female latencies shorter and amplitudes higher than that of their male counterparts. None of these differences were statistically significant. The study done by Theunissen (2002) utilising the same test protocol, yielded similar results.

According to Friedman et al. (1985), gender differences might be due to variations in processing strategies between males and females. Others attribute these differences to structural anatomic diversities between males and females (Steinmetz et al., 1995; Witelson & Kigar, 1992). A number of other studies mentioning gender effects on the P300 primarily focused on either the effect of ageing or the interaction between age and gender (Ehlers et al., 2001; Hirayasu et al., 2000; Gölgeli et al., 1999; Bahramali et al., 1999; Kugler et al., 1996; Kugler, 1996; Segalowitz & Barnes, 1993; Yamashita et al., 1991). Segalowitz and Barnes (1993) for instance, reported larger P300 amplitudes in females than in males in a young adolescent group, while in the older adolescent group (17 years), the males presented with larger amplitudes. The discrepancy in these findings is attributed to the differences in the maturity rate between males and females (Van Beijsterveldt et al., 1998). The present study did not explore this relationship as it controlled the age group of the subjects.

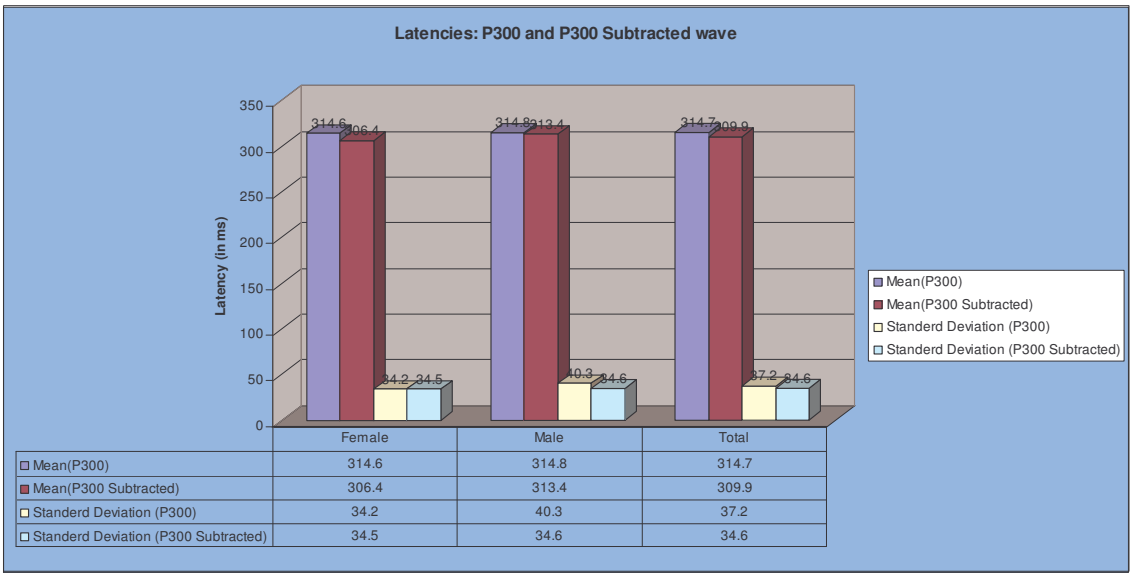
From the empirical evidence in this study, it is clear there is a need for further investigation into the interaction and effect of age and gender on the P300 response. The findings of such research can be utilised to build and strengthen a clinic-specific normative database and clarify the controversies around these variables, which could possibly influence clinical results.

3.4. The effect of the 'marking protocol' on the resulting P300 latencies and amplitudes

The last sub-aim was to determine if using a subtraction protocol (subtracting the common/frequent wave from the rare/infrequent wave to obtain a 'derived' P300) to mark the P300 has a statistical difference from marking the P300 on the rare/infrequent wave.

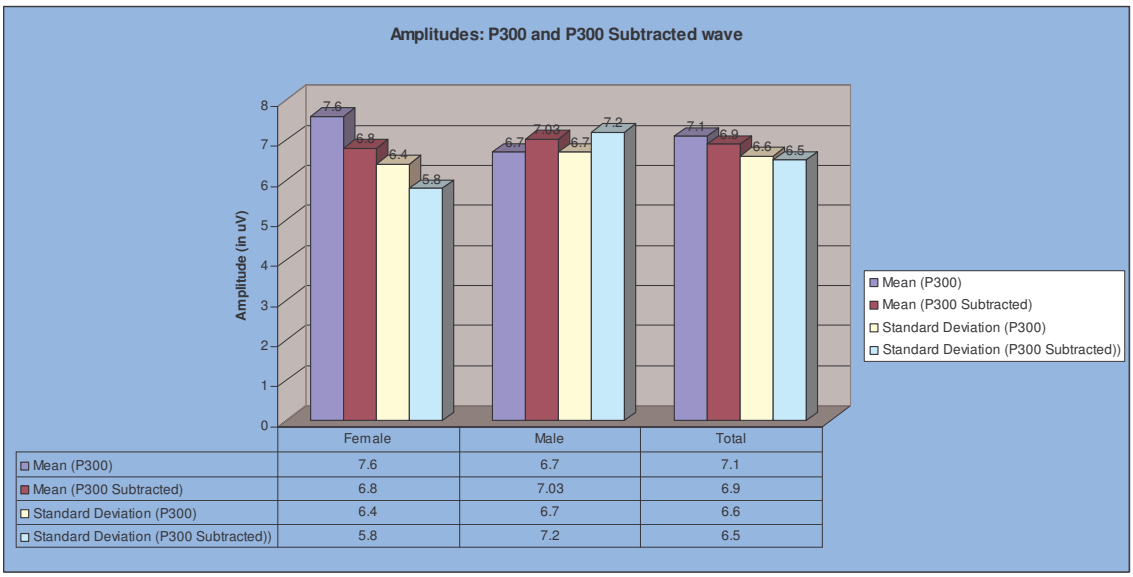
There are currently two different methods of marking and interpreting the resulting P300 response. The first is to mark the P300 as the largest positive response between 250 ms and 380 ms post stimulus on the infrequent or rare wave form (McPherson, 1996). The second method is to subtract the common/frequent wave from the rare/infrequent wave to obtain a 'derived' P300. The latter is used as part of a standard protocol in research done by Tremblay (2002).

The mean latencies and amplitudes calculated separately for the P300 and P300 Subtracted wave are depicted below in Figures 3.10 & 3.11.



	Female	Male	Total
Mean(P300)	314.6	314.8	314.7
Mean(P300 Subtracted)	306.4	313.4	309.9
Standerd Deviation (P300)	34.2	40.3	37.2
Standerd Deviation (P300 Subtracted)	34.5	34.6	34.6

Figure 3.10: Comparison between latencies for the P300 and the P300 subtracted wave.



	Female	Male	Total
Mean (P300)	7.6	6.7	7.1
Mean (P300 Subtracted)	6.8	7.03	6.9
Standard Deviation (P300)	6.4	6.7	6.6
Standard Deviation (P300 Subtracted))	5.8	7.2	6.5

Figure 3.11: Comparison between amplitudes for the P300 and the P300 subtracted wave.

As indicated by these figures, the mean latency and amplitude values show only marginal differences with female latencies consistently shorter and

amplitudes bigger than that of their male counterparts. No statistically significant differences were found for any of these variables. Similarly, the standard deviations for both the P300 and the P300 subtracted wave show only marginal, insignificant differences. No significant effect for the marking protocol/method was observed for the latencies and amplitudes of the P300 and P300 subtracted wave.

When examining the literature on the subject, it becomes clear that little or no information has been published regarding the subject. Furthermore, researchers tend not to disclose which method they have used when marking the P300 responses.

In light of these findings it can be concluded that either method is valid. What is essential is that the same method is used consistently throughout, especially with the aim of creating a clinic-specific normative database, or to be able to compare results to an existing clinic-specific database.

4. Conclusion

The P300 response depends on attention to and discrimination of stimulus differences. The main aim of this study was to determine the range of the latency and amplitude values of the auditory P300 evoked response across gender for a group of normal hearing young adults. This was achieved by determining the average values of the latencies and amplitudes of these waveforms and documenting the range of findings (mean, minimum, maximum and standard deviations). These findings are summarised in Table 4.1.

Table 4.1: Summary of average findings and range of P300 and P300 subtracted wave.

Variable		*Mean*	*Standard Deviation*	*25th Percentile*	*Median*	*75th Percentile*
P300	Latency (in ms)	314.70	37.20	287.28	311.7	342.17
	Amplitude (in µV)	7.1	6.6	2.28	4.54	9.69
P300 subtracted wave	Latency (in ms)	309.90	34.60	286.7	305.45	331.33
	Amplitude (in µV)	6.9	6.5	2.6	4.85	9.41

4.1. Critical evaluation of study

The implications of the clinical and research findings must be discussed in comparison with the strengths and limitations of the present study, and the P300 in general.

In the words of *George von Békesy*," One of the most important features of scientific research is the detection of errors. The writer believes that positive results and failures ought to be discussed together." (Von Békesy, 1960:7)

The present findings were consistent with a number of documented studies in the literature and had one of the largest sample sizes (n=100). The generalisation of the results of the present study was, however, limited by:

1. The age range of the research sample (18-30 years, mean age = 24)
2. The utilisation of only one specific test protocol.

In terms of sample size (n=100), a number of studies were found to use a similar number of subjects. For instance Anderer et al. (1997), tested 58 subjects, Boutros et al. (1997), tested 40 and Picton et al. (1984) tested 72 subjects. Some of the other studies used even smaller sample sizes, varying between 5 and 24 subjects (Theunissen, 2002; Nourse, 2000; Salamat & McPherson, 1999; Wall et al., 1991; Polich et al., 1985; Michalewaski et al., 1982). Thus, when comparing the current sample size to the literature, it appears a statistically sound sample size to establish a clinic-specific normative data base. Unlike the brainstem auditory evoked potentials, which are very stable with well established normative parameters, the long latency auditory evoked potentials are subject to variations from both extrinsic and intrinsic factors. Due to these variations, establishing a normative database requires precise specification of the stimuli, recording conditions, recording environment, subject state (including age and various biological and

psychological factors), and response tasks. According to McPherson (1996), a sample size of 20 would be considered the absolute minimum to establish a normative database, and a sample size of 50 subjects would prove to be a statistically sound number for establishing a normative database.

Within this sample size, all the subjects were within the age range of 18-30 years. Although this limited age range implies that the findings can only be compared to other findings from the same age group, it was essential to establish this age limit, as age is generally accepted to have a significant influence on the results of the P300. If a larger sample size (that includes subjects from a greater age range) can be selected in future, a division of subjects into different age groups could provide the researcher with age-specific normative data from many different age groups.

Concerning test protocol, the present study was conducted using only one specific test protocol. The same protocol was used to evaluate all the subjects, to rule out any influences that differences in protocol may have on the results (e.g. Lew & Polich, 1993; Mertens & Polich, 1997). Limitations in terms of time and equipment also influenced the decision to use a single protocol. However, the exploration of different protocols will be of great value in obtaining the most accurate and reliable results possible.

Owing to time and equipment constraints, the present study only recorded the relevant potentials using pure tone stimuli. If the full clinical value of the P300 as a diagnostic tool is to be exploited, a protocol utilising speech stimuli must be explored. In conventional audiometry, this will not only provide a means of confirming the results obtained from the pure tone evaluation, but will also provide an indication of the processing of speech information. Speech stimuli, especially naturally produced speech tokens, can be used to measure the neural detection of acoustic cues. In a study conducted by Tremblay et al. (2003) it was found that auditory event-related potentials evoked by naturally

produced speech sounds showed remarkable test/re-test reliability. Given this stability, any significant alterations in morphology would likely reflect changes in neural activation to speech, and not simply random variability. P300s elicited using naturally produced speech sounds could be used to assess changes in neural activity over time, after various types of rehabilitation such as cochlear implants, hearing aid amplification, second language training and auditory training (Tremblay et al., 2003; Tremblay & Krause, 2002). Obligatory (N1) and discriminative (MMN, P3) cortical ERPs may provide useful indices of improvement in audibility and discriminability of auditory stimuli provided by hearing aids for the difficult-to-test patients with hearing loss, as well as subsequent monitoring of the effectiveness of auditory training.

The present study only explored the recording of the P300 in the active or attentive state, but can also be recorded using a passive or avoidance state (Musiek & Lee 1999). In the avoidance situation, the P300 is either greatly reduced or absent. A passive P300 requires no active counting of the rare stimuli by the subject. On investigation of the literature available on P300 recordings, there is a great number of studies using the active or oddball condition (e.g. Boutros et al., 1997; Anderer et al., 1996; Wall et al., 1991; Jirsa & Clontz, 1990; Polich, Howard & Starr, 1985 Picton et al., 1984). Studies recording the passive condition are less common. Some researchers have found reduced P300 amplitudes in the passive condition (Pfefferbaum et al., 1985), while others found no significant difference between P300 latency and amplitude for the attentive (oddball) and passive tasks (Iwanami et al., 1996).

Ford et al. (1997) investigated automatic and effortful processing in ageing and dementia, using three different protocols for recording P300, of which one was a passive condition. They found that regardless of the attention given to the rare stimuli, the P300 was still smaller in elderly than in younger subjects. They concluded that the performance task had no effect on the latency of the P300. According to Hall and Mueller (1997), subject attention is important

when measuring the conventional, attentive P300 responses, but not essential when measuring the so-called earlier P3a response. These alternative options for recording the P300 must be explored in future research, as a protocol that requires less participation from the subject can be of great value in so-called 'difficult-to-test' populations.

'Difficult-to-test' populations are defined as patients who "cannot, for some or other reason, participate sufficiently in conventional testing procedures" (Schmulian, 2002:22). According to Hall (1992) these may be of any age group, as most of the pathologies precluding voluntary participation are not age related. Among these conditions are the following:

- Intellectual limitations that will result in unreliable test results;
- Emotional and psychological problems that may lead to inconsistent responses and
- Persons with suspected non-organic hearing loss.

A number of pathologies, of which patients can be classified as difficult-to-test, have been evaluated using the P300. For instance, the P300 has been used as a tool for the diagnosis of demeaning illnesses such as Alzheimer's disease (Fernandez et al., 2001). This particular condition may cause an intellectual impairment that could lead to unreliable results when using a protocol that requires wilful participation on the part of the subject.

A condition such as autism that has also been studied using the P300 (Ciesielki et al., 1990), may preclude voluntary participation due to the emotional component of the condition. If the passive recording condition of the P300 can be explored in order to establish a normative database for this protocol, this may serve as a reference of normality, and will be greatly beneficial when evaluating the populations that are unable to participate wilfully in the evaluation.

4.2. Recommendations for future research

The value of a clinic-specific normative database as suggested by Hall (2000) has already been established. Recordings from clinical populations may be compared to normative findings to determine whether the clinical findings fall within the range of normality as defined by the normative data. The present study's findings compare favourably with a study by Theunissen (2002) at the same clinic, utilising the same protocol. This study had a larger sample size which can be used in combination with the study done by Theunissen (2002) to establish the first clinic-specific normative database for the auditory P300 event-related potential at the University of Pretoria. Future research can utilise this normative database to compare results and expand the database to include more clinical populations. This will yield a larger, and therefore more reliable, normative database.

Having established a normative database, the auditory P300 can now be utilised for a variety of clinical purposes, including assessment of higher level auditory processing. Event-related potentials (ERP), in combination with behavioural measures, may be used to assess the higher level cognitive processing involved in the discrimination and identification of complex stimuli such as speech sounds. Electrophysiological and behavioural measures provide insight into the timing, strength and location of early and later cortical brain processes associated with auditory processing. Utilising these measurements may provide insight into how sensori-neural hearing loss alters the brain processes underlying auditory detection and discrimination (Oates, Kurtzberg & Stapells, 2002).

The susceptibility of the late latency responses to the subject's state of consciousness might make it less useful in routine estimation of hearing thresholds, but it is this very sensitivity to state of awareness that enables the clinician to use these measurements in evaluating the higher auditory functioning, such as auditory attention (Hall & Mueller, 1997) or recognition

and categorisation of sounds (McPherson, 1996). Its sensitivity to these higher auditory functions makes it useful in the evaluation of disorders that affect these skills, such as central auditory processing disorders (CAPD). CAPD generally presents with normal peripheral hearing. Consequently the traditional auditory tests for peripheral auditory function provide little or no insight into CAPD. Studies conducted by Jirsa and Clontz (1990) and Jirsa (1992) on the auditory P300 in children with Central Auditory Processing Disorders (CAPD) have been of great importance to point out the clinical value of these measures in providing some means of objective quantification of the disorder. These researches found significant delays in the latencies of the P300 potentials in children with CAPD. Jirsa (1992) compared behavioural changes resulting from intervention programs for CAPD, and concluded that P300 latencies and amplitudes are sensitive to changes in neural activity following an intervention program (Jirsa, 1992).

A further limitation of the use of P300s lies in the vast number of factors that may influence these responses. These include factors such as gender, age and medication that were controlled in the present study. Despite all the controls that were put in place for this study, considerable inter-subject variability still existed. This suggests that there are perhaps other unexplored variables that could influence the P300 latencies and amplitudes. These variables must be investigated in future research in order to determine their effect on the P300 potentials.

A comprehensive test battery and cross-check principal remains the most effect way to reduce the influences of variables and ensure a reliable and valid diagnosis (Gravel, 1994). According to *Hanley* “the test battery is the foundation of responsible and effective auditory assessment” (Hanley, 1986: 2).

4.3. A final thought

Having discussed the general advantages and limitations of the P300, the application of these measures in the current South African context must be reviewed. It may be argued that the recording of these potentials requires sophisticated equipment with large capital investment, which is not accessible to a great percentage of the population. The current shortage of these facilities must not force clinicians to be satisfied with less sophisticated methods. Audiology is a rapidly expanding, and developing science and audiology in South Africa can be no different. The clinical value of the auditory P300 evoked potentials must continually be explored and examined, as it has already been established that these potentials can be of great value in assessment of a variety of pathologies. The electrophysiological assessment of a disorder, such as CAPD may be of great value in a context where linguistic and culturally sensitive methods for assessing these disorders are not appropriate. Electrophysiological evaluation, such as auditory event-related potentials, is a low linguistically loaded assessment approach that is not sensitive to linguistic and cultural diversity. In these cases an understanding of the instructions for the performance task alone is required.

As scientists involved in the diagnosis and management of pathologies affecting any part of the complete auditory system, local audiologists have the responsibility to investigate any clinical tool that may be of value in delivering a responsible and accountable service to the population of South Africa.

Epilogue: "And the end of all our exploring will be to arrive where we started and know the place for the first time." (T.S. Eliot, 1888-1965)

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Appendix A: Consent Form

University of Pretoria
Pretoria 0002 Republic of South Africa Tel 012-420-2357
/ 012-420-2816 Fax 012-420-3517 http://www.up.ac.za
Department of Communication Pathology
Speech, Voice and Hearing Clinic

February 2004

Dear Sir / Madam,

Thank you for showing interest in this research project being conducted at the Hearing Clinic, Department of Communication Pathology at the University of Pretoria. We are currently undertaking clinical trials for the Auditory Event Related Potential (AERP) procedure (a state-of-the-art objective hearing perception test) and we need your assistance. We need to establish gender matched (male and female) norms for normal hearing ears and we kindly ask for your participation in this study.

Participation in this study will involve the following:

You will undergo a standard hearing evaluation (pure tone behavioural audiometry), where you are required to respond to sound stimulation. This procedure takes approximately 10 minutes.

An Auditory Event Related Potential test, using insert earphones, will follow. Your will be asked to lie down on a bed, with three electrodes attached to your head. You will be instructed to lie as quietly as possible with your eyes closed but awake. Subsequently, you will be instructed to count the infrequent stimuli (sounds) while simultaneously lifting your forefinger slightly every time you hear the infrequent stimuli/sounds. This procedure/test takes 20 minutes.

All the procedures (tests) are non-invasive and only the behavioural procedures require responses from you. All acquired information will be treated as confidential and no names will be used. A copy of your results will be made available to you, should you request it.

Thank you for your assistance.

Should you require any further information, you are welcome to contact us.

Yours sincerely

Prof. Brenda Louw	Mr De Wet Swanepoel	Me Ina Lombard
Head of Department	Research Supervisor	Researcher

University of Pretoria

Department Communication Pathology: Audiology

Name: _____ Occupation: _____.

Age: _____ Contact numbers: _____.

Date of birth: _____(mm/ dd/ yyyy/)

Please complete the following reply slip:

I _____, hereby agree to participate in this project and acknowledge that the data may be used for research purposes. I am aware that I can withdraw from this project, at any time, should I want to.

_____ _____

Date Signature

APPENDIX B: Case History Form

Medical/Audiological History Questionnaire

Name: _____

D.O.B:_____

Date: _____

Occupation:_____

Gender: M ف **F** ف

Subject identification no:

OTOSCOPY Tick if no significant problem ف

Right: Left:

AUDIOMETRY Tick if no significant problem ف

Is there any marked asymmetry?
Description:
Other comment:
Significant air-bone gap?
Description:

EAR DISEASE Tick if there is a significant problem ف

	Left	*Right*
Otalgia		
Discharge		
Perforations		
Ear Surgery		

IN CONFIDENCE

HISTORY Tick if there is a significant problem ف

Any previous hearing problems? *Left:* Description:
Right: Description:

HEARING Tick if there is significant problem ف

Onset: *Left*
Right
Noise Exposure:
Ototoxic drugs: Description:
Other: Description:

BALANCE

Dizziness: Description:

TINNITUS

Tinnitus: *Left:* Description:
Right: Description:

CURRENT MEDICATION

Please specify any current medication:

OTHER MEDICAL HISTORY/PROBLEMS

Please tick if no significant problem ف

Psychiatric problems: Description:
(Depression, schizophrenia)

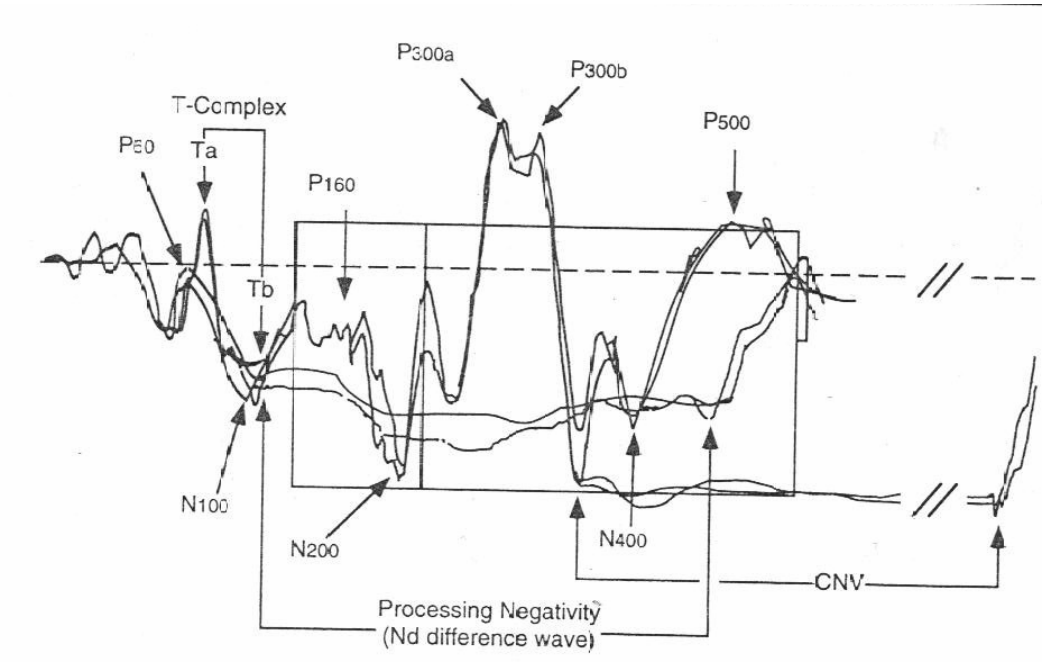
Organic mental disorders: Description:
(Epilepsy, dementia, head injury, stroke)

Alcoholism: Description:

Please specify any other problems:

IN CONFIDENCE

Appendix C: Graphic illustration of ALLR and AERP



Composite schematic of the components of the long latency auditory evoked potentials and the event-related potentials (N100, P160, N200, CNV, T-complex, Processing negativity)

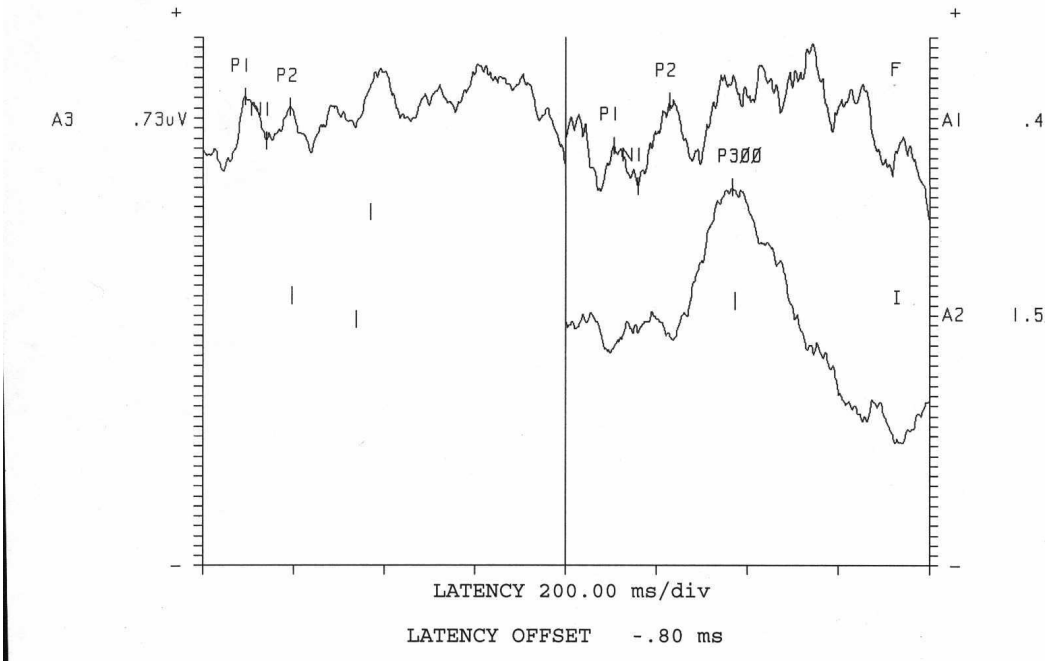
(From Late Potentials of the Auditory System, McPherson, 1996)

Appendix D: Example of results

B I O - L O G I C E V O K E D P O T E N T I A L R E P O R T

Patient:
Address:
Phone:

Date of Birth: 09/08/1978 Age: 0 year(s)
Sex: M File: LI011 ID #:
Physician:
Date: 02-17-04 Operator :



Appendix E: Results (Raw data)

P300 amplitude raw data (µV)

Female	Male	Total
12.73	2.69	12.73
18.76	3.25	18.76
8	7.75	8
8.2	5.27	8.2
2.77	6.2	2.77
7.37	8.04	7.37
5.68	0.48	5.68
0.97	2.31	0.97
2.26	22.49	2.26
2.65	13.98	2.65
1.74	13.64	1.74
10.74	12.26	10.74
1.75	5.75	1.75
0.61	8.66	0.61
0.25	9.68	0.25
5.25	8.85	5.25
6.69	2.29	6.69
6.69	0.18	6.69
1.13	3.94	1.13
1.56	0.41	1.56
8.86	2.43	8.86
8.86	2.24	8.86
7.18	13.49	7.18
5.26	9.73	5.26
25.33	20.11	25.33
23.51	6.11	23.51
7.13	1.24	7.13
7.13	0.69	7.13
0.08	37.59	0.08
0.08	10.16	0.08
7.98	9.94	7.98
7.98	2.88	7.98
9.95	2.88	9.95
9.95	1.75	9.95
6.16	1.75	6.16
6.16	5.14	6.16
8.06	5.14	8.06
8.07	2.52	8.07
0.97	2.52	0.97
0.97	12.79	0.97
11.12	12.79	11.12
11.12	2	11.12
4.13	2	4.13
4.13	6.82	4.13

4.29	6.82	4.29
4.29	1.66	4.29
15.31	1.66	15.31
15.31	3.74	15.31
22.68	3.74	22.68
22.68	3.74	22.68
		2.69
		3.25
		7.75
		5.27
		6.2
		8.04
		0.48
		2.31
		22.49
		13.98
		13.64
		12.26
		5.75
		8.66
		9.68
		8.85
		2.29
		0.18
		3.94
		0.41
		2.43
		2.24
		13.49
		9.73
		20.11
		6.11
		1.24
		0.69
		37.59
		10.16
		9.94
		2.88
		2.88
		1.75
		1.75
		5.14
		5.14
		2.52
		2.52
		12.79
		12.79
		2
		2
		6.82
		6.82
		1.66
		1.66
		3.74

3.74
3.74

P300 subtracted wave amplitude raw data (µV)

P300 Sub Amp Female	P300 Sub Amp Male	P300 Sub Amp Total
8	2.08	8
8	4.69	8
8.96	1.32	8.96
8.96	4.27	8.96
3.31	3.39	3.31
3.31	6.04	3.31
6.21	3.64	6.21
1.75	1.96	1.75
5.1	23.83	5.1
3.16	10.97	3.16
2.23	18.22	2.23
11.28	4.94	11.28
3.3	8.66	3.3
1.77	8.66	1.77
1.36	11.36	1.36
5.18	11.36	5.18
5.22	0.52	5.22
5.22	4.18	5.22
0.26	3.56	0.26
0.59	3.76	0.59
6	1.73	6
10.31	1.99	10.31
4.26	13.06	4.26
0.26	9.97	0.26
21.02	16.26	21.02
19.21	3.06	19.21
9.56	3.84	9.56
9.56	1.48	9.56
0.01	41.24	0.01
0.01	21.3	0.01
5.84	7.47	5.84
5.84	10.34	5.84
12.94	4.34	12.94
12.94	4.34	12.94
0.63	2.21	0.63
0.63	2.21	0.63
2.6	7.14	2.6
2.6	7.14	2.6
2.72	7.14	2.72
2.72	7.14	2.72
12.41	7.83	12.41
12.41	7.83	12.41
4.76	2.14	4.76

4.76	2.14	4.76
4.43	6.17	4.43
4.43	6.17	4.43
20.61	0.65	20.61
20.61	0.65	20.61
15.4	3.74	15.4
15.4	3.74	15.4
		2.08
		4.69
		1.32
		4.27
		3.39
		6.04
		3.64
		1.96
		23.83
		10.97
		18.22
		4.94
		8.66
		8.66
		11.36
		11.36
		0.52
		4.18
		3.56
		3.76
		1.73
		1.99
		13.06
		9.97
		16.26
		3.06
		3.84
		1.48
		41.24
		21.3
		7.47
		10.34
		4.34
		4.34
		2.21
		2.21
		7.14
		7.14
		7.14
		7.14
		7.83
		7.83
		2.14
		2.14
		6.17
		6.17
		0.65

0.65
3.74
3.74

P300 Latencies raw data (ms)

Male	Female	Total
271.08	330.45	271.08
283.56	346.08	283.56
311.7	336.7	311.7
336.7	346.08	336.7
255.45	274.2	255.45
246.07	267.95	246.07
308.58	324.2	308.58
305.45	314.83	305.45
364.83	349.2	364.83
367.95	339.83	367.95
311.7	267.95	311.7
311.7	292.95	311.7
330.45	333.58	330.45
355.45	330.45	355.45
302.33	305.45	302.33
283.58	227.32	283.58
355.45	283.58	355.45
386.7	283.58	386.7
352.33	274.2	352.33
355.45	271.08	355.45
314.83	333.58	314.83
339.83	333.58	339.83
274.2	346.08	274.2
286.7	352.33	286.7
364.83	358.58	364.83
396.95	392.95	396.95
302.33	305.45	302.33
324.2	305.45	324.2
374.2	302.33	374.2
327.33	302.33	327.33
314.83	336.7	314.83
308.58	336.7	308.58
264.95	333.58	264.95
267.95	333.58	267.95
252.32	299.2	252.32
252.32	299.2	252.32
302.33	299.2	302.33
302.33	299.2	302.33
352.33	336.7	352.33
352.33	336.7	352.33
311.7	264.83	311.7
311.7	264.83	311.7
289.83	302.33	289.83
289.83	302.33	289.83
236.7	380.45	236.7

236.7	380.45	236.7
342.95	274.2	342.95
342.95	274.2	342.95
352.33	321.08	352.33
352.33	321.08	352.33
		330.45
		346.08
		336.7
		346.08
		274.2
		267.95
		324.2
		314.83
		349.2
		339.83
		267.95
		292.95
		333.58
		330.45
		305.45
		227.32
		283.58
		283.58
		274.2
		271.08
		333.58
		333.58
		346.08
		352.33
		358.58
		392.95
		305.45
		305.45
		302.33
		302.33
		336.7
		336.7
		333.58
		333.58
		299.2
		299.2
		299.2
		299.2
		336.7
		336.7
		264.83
		264.83
		302.33
		302.33
		380.45
		380.45
		274.2
		274.2
		321.08

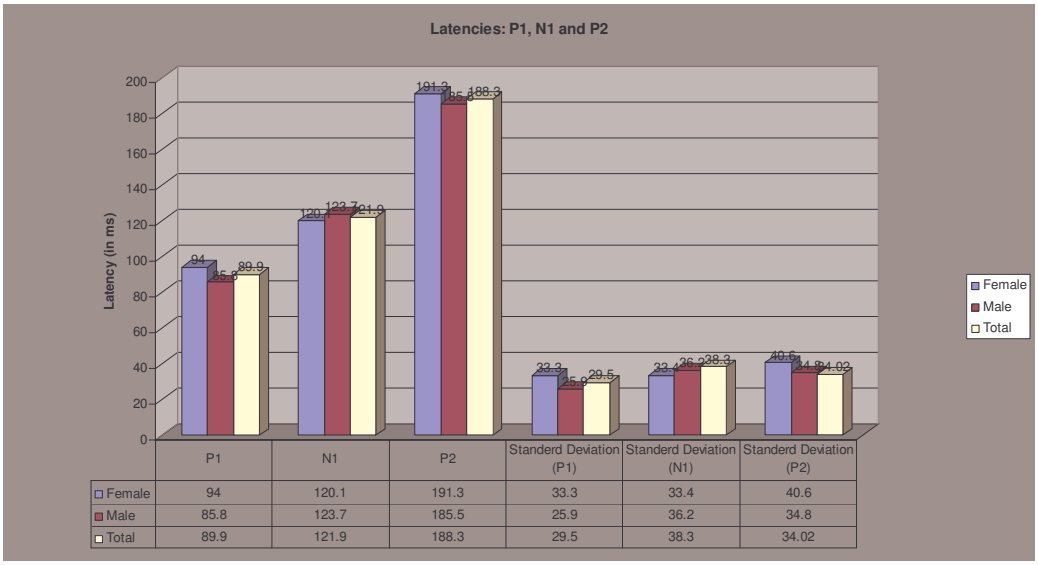
321.08

P300 subtracted wave latencies raw data (ms)

P300 Sub Lat Female	P300 Sub Lat Male	P300 Sub Lat Total
336.7	274.2	336.7
336.7	305.45	336.7
346.08	299.2	346.08
346.08	336.7	346.08
274.2	255.45	274.2
274.2	246.07	274.2
324.2	296.08	324.2
374.83	305.45	374.83
364.83	371.08	364.83
321.08	336.7	321.08
267.95	311.7	267.95
289.83	314.83	289.83
330.45	302.33	330.45
383.58	302.33	383.58
305.45	283.58	305.45
230.45	283.58	230.45
286.7	386.7	286.7
286.7	355.45	286.7
277.33	355.45	277.33
271.08	308.58	271.08
261.7	314.83	261.7
271.08	299.2	271.08
264.83	274.2	264.83
280.45	289.83	280.45
355.45	367.95	355.45
396.08	392.95	396.08
305.45	302.33	305.45
305.45	324.2	305.45
299.2	389.83	299.2
299.2	330.45	299.2
336.7	302.33	336.7
336.7	308.58	336.7
330.58	333.58	330.58
330.58	333.58	330.58
299.2	252.32	299.2
299.2	252.32	299.2
299.2	302.33	299.2
299.2	302.33	299.2
308.58	302.33	308.58
308.58	302.33	308.58
267.95	308.58	267.95
267.95	286.7	267.95
302.33	286.7	302.33
302.33	321.08	302.33
296.08	321.08	296.08
274.2	355.45	274.2

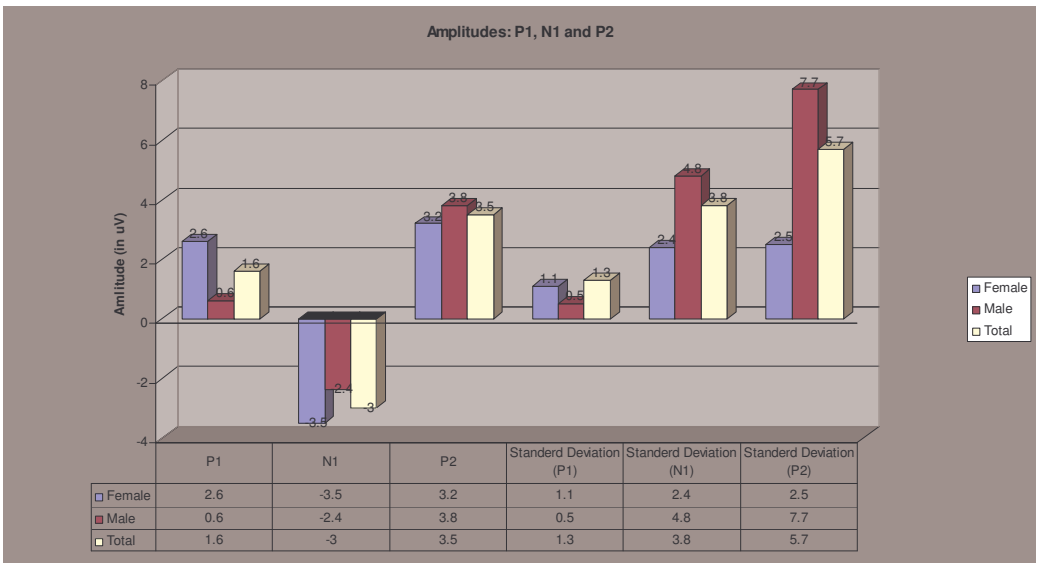
274.2	355.45	274.2
305.45	305.45	305.45
305.45	305.45	305.45
		274.2
		305.45
		299.2
		336.7
		255.45
		246.07
		296.08
		305.45
		371.08
		336.7
		311.7
		314.83
		302.33
		302.33
		283.58
		283.58
		386.7
		355.45
		355.45
		308.58
		314.83
		299.2
		274.2
		289.83
		367.95
		392.95
		302.33
		324.2
		389.83
		330.45
		302.33
		308.58
		333.58
		333.58
		252.32
		252.32
		302.33
		302.33
		302.33
		302.33
		308.58
		286.7
		286.7
		321.08
		321.08
		355.45
		355.45
		305.45
		305.45

Appendix F: Average latencies and amplitudes for the ALLR (P1, N1 and P2)



	P1	N1	P2	Standerd Deviation (P1)	Standerd Deviation (N1)	Standerd Deviation (P2)
Female	94	120.1	191.3	33.3	33.4	40.6
Male	85.8	123.7	185.5	25.9	36.2	34.8
Total	89.9	121.9	188.3	29.5	38.3	34.02

Average latency values for the P1, N1 and P2



	P1	N1	P2	Standerd Deviation (P1)	Standerd Deviation (N1)	Standerd Deviation (P2)
Female	2.6	-3.5	3.2	1.1	2.4	2.5
Male	0.6	-2.4	3.8	0.5	4.8	7.7
Total	1.6	-3	3.5	1.3	3.8	5.7

Average amplitude values for the P1, N1 and P2