Behavioural and Electrophysiological Measures of Electrode Discrimination in Adult Auditory Brainstem Implant Users

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Chapter 4: Event Related Potentials in Adult ABI Users

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Abstract

Auditory brainstem implants ABI are a recognised form of treatment in cases of neural hearing loss where amplification with conventional hearing aids or with cochlear implants (CI) is not beneficial. Using an electrode array surgically positioned in or on the ventral cochlear nucleus (VCN) in the brainstem, an ABI can stimulate neural pathways central to any damage so that auditory sensation may still be achieved. Outcomes are varied with an ABI and often poorer than those of CI users. A large part of ABI programming involves the evaluation of pitch variations between electrodes, and the benefit of spectral distinction is considered to be a benefit of multichannel implants. However, the auditory perceptual differences between ABI electrodes vary. This study therefore aimed to investigate place-pitch perception and judgements of non-tonotopic auditory perceptual differences between electrodes via both subjective and objective measures. For ABI users, understanding more about the auditory perceptual differences between electrodes may have clinical benefits during programming sessions.

Experiment one used psychophysical measures to investigate place-pitch perception and auditory perceptual differences between electrodes in ABI users, given that tonotopic ordering of electrodes is an overriding part of programming sessions and has been cited to have an effect on outcomes. Experiment one (Chapter 3) therefore had two aims: (a) to determine the relationship between place-pitch perception and speech outcomes in ABI users using their clinically-set maps; (b) to determine if auditory percepts other than pitch are related to electrode position for ABI users via a multidimensional scaling (MDS) procedure. Ten CI and 9 ABI users participated in experiment 1. CI and ABI speech perception scores were correlated with tonotopically accurate user maps and with more distinguishable pitch variations between electrodes. MDS analysis revealed that auditory percepts experienced via an ABI are different to those of a CI and that pitch perception is not likely to be the overriding auditory percept for an ABI user.

Experiment two used electrically-evoked event-related potentials (EERPs) to investigate auditory perceptual differences between implant electrodes. Experiment two (Chapter 4) therefore had two aims: a) to determine if electrophysiological measures of electrode discrimination correlate with behavioural measures of electrode discrimination in adult ABI users; b) to determine if electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users. N1, P2, MMN, P3a and P3b were elicited in ABI users. Difficulty in controlling for variations in auditory perception meant a wide range of ERP latencies were identified. The variations meant there were insufficient data to accurately test the hypothesis that P3b and MMN latency increases with increasing task difficulty in ABI users. A significant negative correlation was found with mean MMN latency and word and sentence scores in CI users and with P3a amplitude and word scores in ABI users. A significant relationship was also found between MMN latencies and behavioural measures of pitch discrimination between electrodes, providing some support for the hypothesis that electrophysiological measures of electrode discrimination may be related to behavioural measures of electrode discrimination.

This study has shown that electrophysiological measures of electrode discrimination are recordable in ABI users, but the relative uncertainty regarding the degree of perceptual difference to which they are elicited may limit their efficacy.

Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning

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Presentation of Alternative Format Thesis

The two experiments which comprise this thesis are presented as a series of two scientific articles rather than as part of a traditional thesis format. This research may have direct clinical applications for current and future NHS patients therefore timely publication in a peer reviewed journal was considered the most appropriate dissemination method for this study. The thesis format reflects the fact that the two experiments of this study are being prepared for submission to a peer reviewed audiology journal in 2013.

Due to the format of this thesis, some duplication will occur. The article-style chapters contain information which may also be contained in other sections of the thesis.

The main body of the thesis comprises the two experiments. These are introduced by a traditional-style introduction (Chapter 1) and selected background reading (Chapter 2) to provide a coherent background to the study rationale. The two experiments are detailed in Chapter 3 and Chapter 4, in an article-style of introduction, methods, results and conclusions. Finally, a traditional general discussion and conclusion (Chapter 5) draws the results together and suggests areas of future study.

Although publications do not generally contain numbered sections, the section numbering was continued throughout the two main experiment chapters for ease of navigation in the current thesis. Subheadings within Chapters 3 and 4 will remain in the précis of the chapters for submission for publication wherever relevant. Chapters 3 and 4 contain more in-depth information than can be contained in a précis for journal submission which may mean that some sub headings will not be required during preparation for journal submission. References are included within a single list at the end of the thesis rather than at the end of each of the two experimental chapters to maintain the consistency of thesis navigation and avoid duplication in the current format.

Acknowledgements

I would like to thank my supervisors Wael El-Deredy and Colette McKay for their unending support and guidance throughout this project. Their advice and encouragement has been invaluable and has seen this project to fruition. Thanks also to my advisor Richard Baker for his supportive advice and input and to my initial supervisor, Paul Boyd.

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Thanks to Cochlear Uk Ltd for the initial funding of this project, which made the research possible.

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List of Abbreviations

AB	Arthur Boothroyd
ABI	Auditory Brainstem Implant
ABR	Auditory Brainstem Response
AVCN	Antero-Ventral Cochlear Nucleus
BESA	Brain Electrical Source Analysis
CERP	Cortical Event-Related Potential
CI	Cochlear Implant
CUNY	City University of New York
dB	Decibel
DCN	Dorsal Cochlear Nucleus
EEG	Electroencephalography
EERP	Electrically-Evoked Event-Related Potential
ERP	Event-Related Potential
Hz	Hertz
ISI	Interstimulus Interval
MDS	Multi-dimensional Scaling
MMN	Mismatch Negativity
ms	Millisecond
NIC	Nucleus Implant Communicator™
µV	Microvolt

List of Equations

Chapter 1

Introduction

This study investigated electrode discrimination in adult auditory brainstem implant (ABI) users via both behavioural and electrophysiological assessments. A single channel auditory implant may conduct a certain amount of amplitude and temporal information via variations in pulse train intensity and duration. However, the benefit of multi-channel auditory implants is the spectral definition that may be conveyed through activation of electrodes sited near neural receptors that respond to different input frequencies. When the auditory perceptual difference following activation of different electrodes is complex, non-uniform or very small, the benefit of a multi-channel over a single-channel implant may be greatly reduced. For ABI users, understanding more about the auditory perceptual differences between electrodes may have clinical benefits during programming sessions. At present, particular attention is paid to pitch variations during programming. These may be difficult for a patient to judge, or may not be present at all. This study therefore aimed to investigate place-pitch perception and judgements of non-tonotopic auditory perceptual differences between electrodes via both subjective and objective measures.

1.1. Cochlear Implants and Auditory Brainstem Implants

Cochlear implants (CIs) are designed to produce electrical excitation in auditory nerve fibres for subjects with severe to profound hearing loss for whom conventional hearing aids provide limited or no benefit. In a CI, an electrode array positioned in the scala vestibuli of the cochlea is designed to mimic cochlear function by stimulating neural structures with a well-known tonotopicity to produce sensations with a clear tonotopic order. An external speech processor detects auditory input which is coded into appropriate electrical signals determined during individual programming sessions. The electrical signals activate the implanted electrodes which in turn stimulate the auditory nerve.

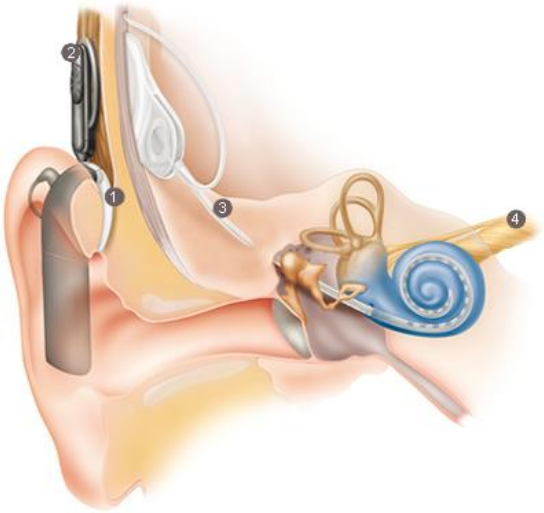


Figure 1.1. The external and internal components of a cochlear implant in-situ. Components include the external speech processor (1) and transmitter (2), and the internal package and electrode array (3). The array is implanted into the cochlea and activation of these electrodes causes stimulation of the auditory nerve (4). (Image from Cochlear Ltd)

Where auditory nerve damage or dysfunction exists, a CI is not useful. Using an electrode array surgically positioned in or on the ventral cochlear nucleus (VCN) in the brainstem, an auditory brainstem implant (ABI) can stimulate neural pathways central to any damage so that auditory sensation may still be achieved.

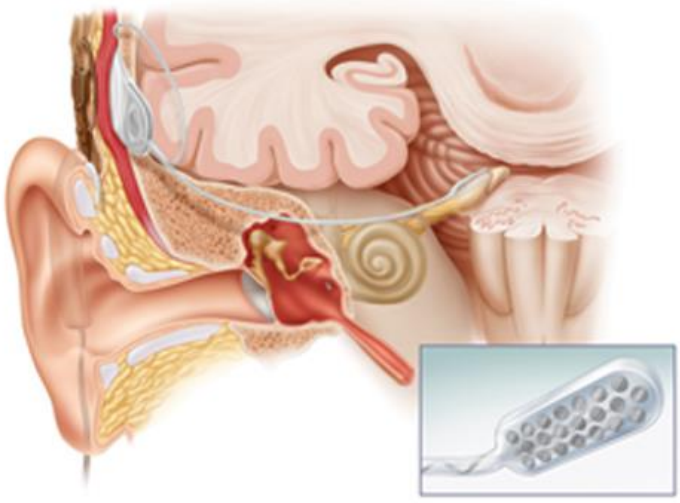
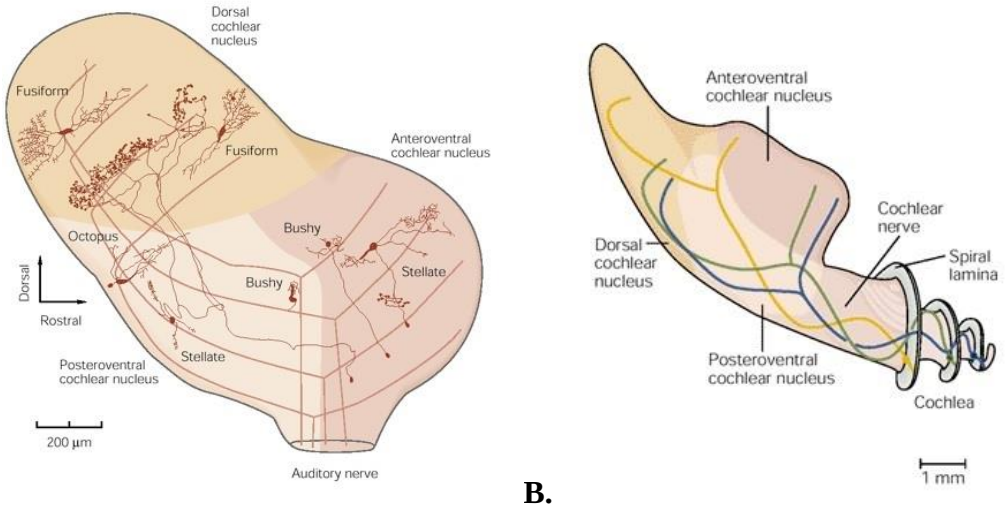


Figure 1.2. The internal and external components of an ABI in-situ. Here, the electrode array is placed on the surface of the ventral cochlea nucleus in the brainstem rather than being inserted into the cochlea. The electrode array itself (inset) contains 21 disc electrodes. (Image from Cochlear Ltd)

The cochlea nucleus (CN) has a more complex physiology than that of the cochlea. It consists of 3 main areas; the antero-ventral (AVCN), the postero-ventral (PVCN) and the dorsal nuclei (DCN). Each area contains several different types of specialised cells, each with characteristic reactions to auditory stimuli (Young, Spirou et al. 1992; Cant and Benson 2003). Some of these cells exhibit an excitatory response to stimuli, and some an inhibitory response (Young, Spirou et al. 1992; Cant and Benson 2003). Each area of the cochlea nuclei contains more or less of each particular cell type, meaning that each region of the cochlea nuclei may exhibit a different characteristic response to stimuli (Cant and Benson 2003).

The ABI electrode paddle is designed to be placed on the ventral cochlea nucleus, however it is likely that the distal parts of the array may be placed over the dorsal cochlear nucleus as well (Kanowitz, Shapiro et al. 2004). The tonotopicity of these structures, although well defined, is more complex than that of the cochlea itself. Nerve fibres terminate in the cochlea nuclei in strict tonotopic order, consistent with the tonotopicity of nerve fibres exiting the cochlea (Young, Spirou et al. 1992; McCreery, Shannon et al. 1998). However, the terminations run perpendicular to the cochlea nuclei surface, meaning that the ABI surface electrode will be located closer to some nerve fibres than others (McCreery, Shannon et al. 1998; Kanowitz, Shapiro et al. 2004).



A. **B.**

Figure 1.3. Arrangement of cell types (A) and neural terminations (A) and (B) within the cochlea nucleus. (A) CN structures and cell types are labelled. (B) The terminations of neurons corresponding to different frequencies are shown in yellow (high frequency), green (mid-frequency) and blue (low frequency). (Images from Hudspeth 2000)

Stimulation using ABI electrodes often does not exclusively result in auditory sensation, but may also cause dizziness, nausea, and taste and muscle sensations, even when ABI electrode array placement is considered optimal (Nevison, Laszig et al. 2002). As only electrodes providing auditory stimulation are activated following speech processor programming, the number of electrodes available for stimulation varies between patients. Whilst the number of active electrodes does affect performance (Colletti, Carner et al. 2005), those activated provide limited auditory information compared to that transmitted by a CI electrode (McCreery, Shannon et al. 1998; Colletti and Shannon 2005). Therefore, the benefit provided by an ABI can be extremely varied and it is currently not possible to predict how well someone may hear with their ABI in advance.

Currently, most ABI candidates in the Manchester Auditory Implant Centre are adult neurofibromatosis type II (NFII) patients. This condition causes multiple benign tumours to grow along nerve fibres. Tumour growth on the auditory nerve and subsequent tumour removal usually damages the auditory nerve, resulting in sudden hearing loss. This is quite different to the experience of most hearing aid and CI users who often have either a gradual or congenital hearing loss.

1.2 Event-related Potentials

A greater understanding of the electrical activity that occurs in the auditory system following activation of ABI electrodes would be beneficial in comparisons between implant user groups and natural activation of the auditory system. One method of investigating this is the use of event-related potentials (ERP).

When stimulated, nerves generate electrical activity which may be recorded via surface electrodes placed on the skin and connected to a recording system. An event-related potential (ERP) occurs when this electrical activity is time-locked to a stimulus. The response is therefore associated with a specific event (Luck 2005) and is found at a particular time-interval following event onset. For auditory ERPs, the event is an auditory signal. Electrically-evoked ERPs (EERP) may also be evoked via direct electrical stimulation of the nerve, for example in cochlear implant (CI) or auditory brainstem implant (ABI) users.

Auditory ERPs are classified as early, mid or late ERPs categorised by the post-stimulus onset time. Early auditory ERPs occur up to 10 ms post-stimulus onset, mid-latency from around 10 ms to 50 ms, and late are classed as occurring after this (Luck 2005). They have been extensively examined and their characteristics and components described in both normal hearing and hearing impaired individuals (Picton and Hillyard 1974; Moller, Jannetta et al. 1994; Sharma, Kraus et al. 1997; Firszt, Chambers et al. 2002a). Such research can suggest normative values for ERP waveform characteristics or morphology and some also suggest which neural sources components may originate from. Comparison of a recorded ERP component against pre-defined normative values can indicate if it is outside such values. Identification of an ERP component is therefore often interpreted as indication the integrity of neural structures and pathways up to and including the neural generators of that ERP component. EERPs recorded in implant users might therefore be useful in comparisons of auditory system excitation between user groups. Understanding the pattern of excitation occurring in the auditory system following ABI stimulation may help to indicate whether neural generators which have been identified in previous studies as being important for auditory sensation or speech perception are still functioning. EERP information might then be compared against outcome measures in the ABI patient group to determine any correlations.

Each ERP component may provide different amounts of information regarding auditory pathway integrity. It is widely accepted that the auditory brainstem response (ABR), being an early ERP, can indicate the integrity of auditory structures up to and including the termination of the lateral leminiscus in the brainstem (Moller, Jannetta et al. 1994), whilst later responses such as mid-latency ERPs may arise from the medial geniculate body and primary auditory cortex (Luck 2005). Therefore, as it is possible for auditory system damage to occur central to ABR generators, the presence of an ABR does not necessarily represent conscious auditory perception. In contrast, late auditory ERPs such as the auditory cortical evoked-response potential (CERP), mismatch negativity (MMN) and P3, are indicators of neural action in higher areas of the auditory pathway and as such are perhaps more useful when considering correlations to perception and useable auditory sensation.

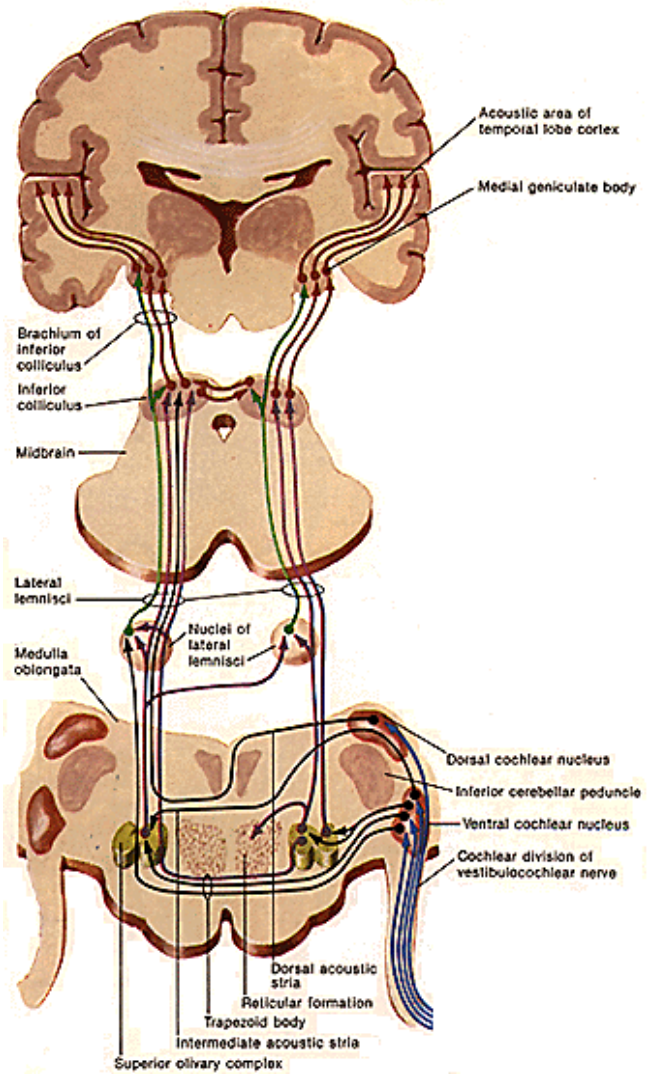


Figure 1.4. The auditory pathway, from the auditory nerve exiting the cochlear to the auditory cortex. Although only one auditory nerve (in blue, bottom right) and set of connections in the auditory pathway are labelled, connections are present bilaterally. (From http://www.ece.rice.edu/~dhj/pathway.html, where it was sourced from CIBA Collection of Medical Illustrations, Volume 1 (Netter 1953))

Any excitation to a stimulus may also be examined by imaging techniques like functional magnetic resonance imaging (fMRI) or positron emission tomography scanning (PET) (Luck 2005). Imaging techniques can indicate the topography of the stimulation more accurately, whilst the ERPs are more suited to the temporal aspects of the stimulation (Luck 2005). Knowing the post-stimulus onset time can indicate how far along the auditory pathway the signal has reached which helps in understanding whether a signal has reached higher processing areas. A study using imaging techniques might not provide the same information in as much detail. Due to the significance of temporal information in speech signals, ERP analysis may be more suited to investigations regarding speech outcomes than are imaging techniques.

1.2.1. Cortical Event-related Potential (CERP)

The CERP complex consists of several deflections labelled P1, N1, P2, and N2 (with P and N representing positive and negative deflections) occurring at approximately 50 ms, 100 ms, and 200 ms (not including N2) post-stimulus respectively (Wunderlich and Cone-Wesson 2006). The integrity of the auditory pathway affects the CERP (Wunderlich and Cone-Wesson 2006), and its presence indicates activation of cortical areas (Ponton, Eggermont et al. 2000). The CERP is therefore well suited to investigations in relation to ABI outcomes as its presence indicates that ABI stimulation is producing excitation of the highest auditory areas.

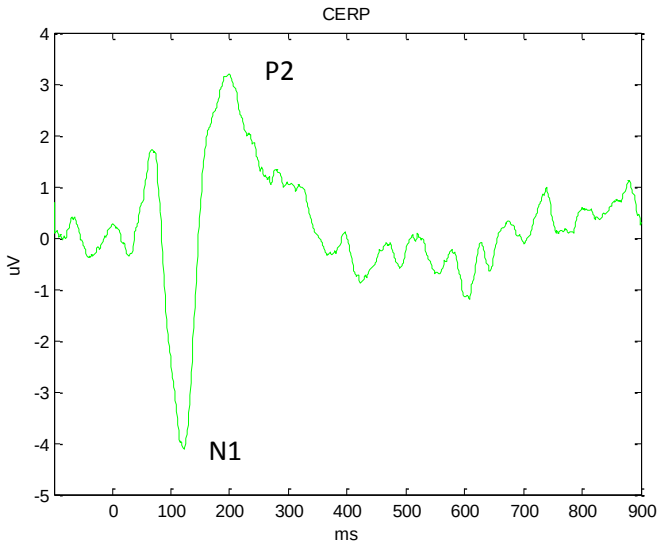


Figure 1.5. Example of a CERP trace recorded in a normal hearing individual during a pilot recording test for the present study. Positive is plotted up, with the x axis denoting time in ms and the y axis demoting amplitude in μV. The CERP itself is a negative deflection just after 100 ms (N1) and a positive deflection around 200 ms (P2).

1.2.2 Mismatch Negativity (MMN)

The MMN, a component of the N2, is elicited in response to a deviant or 'oddball' stimulus presented within a train of standard or frequent stimuli and manifests as a negative deflection approximately 160 to 220 ms after the onset of the random (oddball) stimulus (Luck 2005). The MMN reflects the processing of fine acoustic differences, and as attention to the stimulus is not required for MMN elicitation, it is thought that the MMN may indicate an automatic process in which a stimulus is compared the memory of the preceding stimuli (Naatanen, Brattico et al. 1992; Kraus and McGee 1994; Luck 2005). Despite not requiring conscious attention for elicitation of an MMN, a

perceptual difference must still exist for the deviant to be noticed when the memory traces of the deviant and standard are compared.

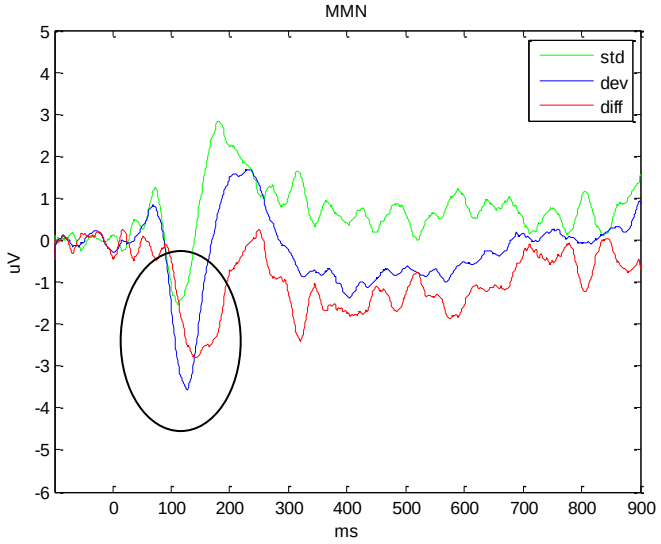


Figure 1.6. Example of a MMN trace recorded in a normal hearing individual during a pilot recording test for the present study. Positive is plotted up, with the x axis denoting time in ms and the y axis demoting amplitude in µV. The circle highlights the latency of interest. The MMN itself is the difference in the ERP response to the standard (green) stimulus and the deviant (blue) stimulus. Subtracting the standard from the deviant produces a difference trace (red) from which the MMN latency and amplitude are extracted.

1.2.3. P3b

The P3b, like the MMN, is elicited in response to a deviant or 'oddball' stimulus presented within a train of standard or frequent stimuli and is a positive deflection occurring approximately 300 ms after the onset of the random (oddball) stimulus (Luck 2005), although it may be as late as 900 ms (Rugg and Coles 1995). The P3b is only seen if the change in stimulus is task related (Luck 2005), i.e. the subject is attending to the stimuli. In the raw trace, the P3b manifests as a large positive wave only in response to the deviant stimuli, being absent following the frequent stimuli. P3b amplitude is greatest over the central or parietal scalp area and may be from 5 to 25 µV (Rugg and Coles 1995). It is more robust than the MMN and can be seen in cases where the MMN is not recordable (Kelly, Purdy et al. 2005). The P3b is a sub-component of the P3 or P300 ERP. The P300 ERP is influenced by attention, memory, expectation and auditory discrimination, and is thought to be a neural correlate of decision making or the processing of sequential information (Kraus and McGee 1994).

If the presentation of the random stimulus is not predictable, the response is of greater amplitude (Rugg and Coles 1995).

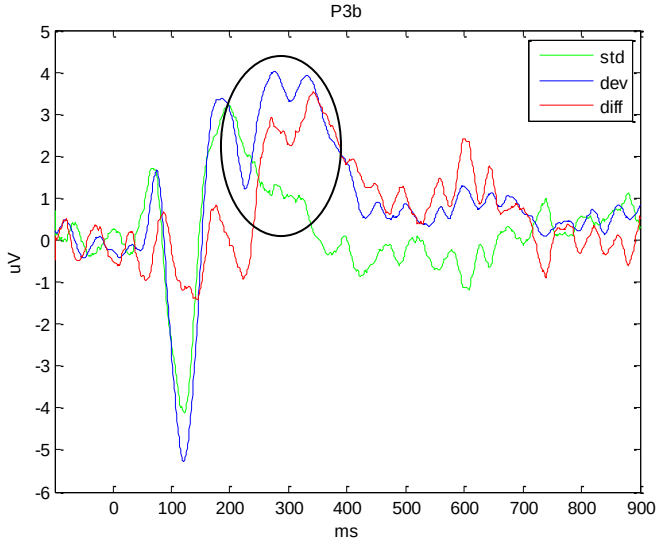


Figure 1.7. Example of a P3b trace recorded in a normal hearing individual during a pilot recording test for the present study. Positive is plotted up, with the x axis denoting time in ms and the y axis demoting amplitude in µV. The circle highlights the latency of interest. The P3b itself is the difference in the ERP response to the standard (green) stimulus and the deviant (blue) stimulus. P3b latency and amplitude are extracted from the deviant trace, although this figure does also show a difference trace for comparison purposes where standard has been subtracted from the deviant (red).

1.3. Research areas

As noted above, ABI outcomes vary greatly and are often poorer than those of CI users. Despite the increasing use of ABIs in the NHS, relatively few studies exist to examine these variations. A better understanding of ABI outcome variability would assist in rehabilitation for existing patients and development of future devices. Selected background reading, detailed in Chapter 2, highlights the areas for investigation.

A greater understanding of auditory system excitation in response to ABI stimulation may also help to increase the knowledge base in this field. ERPs have already been extensively examined in CI users in relation to outcomes but far fewer studies exist in relation to ABI users. Selected background reading in Chapter 2 details previous ERP investigations and highlights where ABI research may be useful.

Chapter 2

Selected Background Reading

2.1. Outcomes with Auditory Brainstem Implants

Whilst auditory brainstem implants (ABIs) function in much the same way as cochlear implants (CIs), functional outcomes vary greatly between the patient groups. An ABI can provide limited auditory information in most cases such that speech perception is poor compared to those with a multi-channel CI (McCreery, Shannon et al. 1998; Colletti and Shannon 2005). Despite their increasing use in the NHS, there have been relatively few published studies in the literature investigating ABI outcome variability. An increased understanding of outcome variability would be beneficial in aiding development of new ABI systems, practices and programming techniques.

ABI outcomes might be described in terms of reported functional benefit, speech perception test scores, or the number of active auditory electrodes (O'Driscoll 2012). The number of auditory electrodes may vary greatly. Studies report that an average of just under 50% of implanted electrodes may elicit auditory sensations at initial device programming, with around 5% of patients reporting no auditory sensation at all (Nevison, Laszig et al. 2002; Kanowitz, Shapiro et al. 2004; O'Driscoll, El-Deredy et al. 2011a; O'Driscoll, El-Deredy et al. 2011b; O'Driscoll 2012). The number of auditory electrodes is reported to affect outcomes (Kuchta, Otto et al. 2004; Colletti, Carner et al. 2005). Kuchta, Otto et al (2004) found that at least 3 tonotopically ordered electrodes were required for an ABI user to obtain satisfactory speech recognition scores. However, the limited relationship between the ABI surface electrode array and the perpendicular frequency gradient of the cochlear nucleus meant that no further benefit to speech scores was obtained with greater than 5 auditory electrodes (Kuchta, Otto et al. 2004).

Even with small numbers of electrodes, ABI users are able to report subjective benefit (Waring, Ponton et al. 1999). Two ABI users, each with 2 implanted electrodes reported receiving useful auditory perception from their implants in a study by Waring, Ponton et al. (1999). Unfortunately, no comment is made as to the nature of the percept or the degree of function it provided. User reports of functional benefit are relative and difficult to quantify or compare between patients. Listening skills can be mapped onto a listening hierarchy which describes a scale of increasing levels of auditory difficulty, beginning with detection, and moving through discrimination,

identification and then comprehension of sounds (Edwards and Estabrooks 2006). Positive thinking and expectations will affect reports of function (Galvin, Mok et al. 2008). Therefore, one user may have progressed along the listening hierarchy but is unable to appreciate it, whilst another may have limited function according to the heierachy but their personality allows for contentment with their device. For example, Kanowitz, Shapiro et al. (2004) describe 2 ABI non-users who reported no benefit despite discernible pitch differences and multiple auditory electrodes.

Standardised speech test scores may therefore be the most appropriate way to assess benefit. Speech score improvement is an accepted form of outcome measurement and various tests are cited in numerous studies (Nevison, Laszig et al. 2002; Kuchta, Otto et al. 2004; Colletti and Shannon 2005). Many found that the improvement in speech scores with ABI use was less than that found in CI users. However, Colleti, Carner et al. (2005) found that ABI outcomes have the potential to be comparable to those of CI users, depending on aetiology. They investigated outcomes in ABI users with either tumour or non-tumour pathology. Those in the tumour group consisted of 10 patients with NF2 and 3 with unilateral acoustic schwannoma in the only hearing ear. Of these 13 tumours, 7 were categorised as small, 3 medium and 3 large, with a size range from 4-50 mm (Colletti, Carner et al. 2005). Patients with a non-tumour pathology had either bilateral cochlear nerve aplasia (n=5), complete ossification of the cochleae (n=4), hearing loss following head trauma (n=6) or auditory neuropathy (n=1). They found that ABI users with non-tumour pathologies performed better in speech perception tasks after 1 year of use compared to those with tumour pathologies and concluded that tumour growth and removal affected cell structures important for speech perception (Colletti, Carner et al. 2005).

Although aetiology may be suggested as one factor limiting ABI performance (Colletti, Carner et al. 2005), ABI patients with NFII aetiologies present a wide range of outcomes, with a small amount achieving good open set speech perception (Lenarz, Moshrefi et al. 2001; Nevison, Laszig et al. 2002; Otto, Brackmann et al. 2002). Currently, ABI programming requires significant user co-operation, limiting the number of potential recipients according to co-operative ability. Two significant factors are the ability to indicate a perception of hearing against non-auditory stimulation for any given electrode activation, and the ability to indicate pitch variation to enable accurate

tonotopic ordering of input signals. Place-pitch perception of implanted CI electrodes may be assumed in normal cochlear anatomy but no systematic relationship exists between an ABI surface electrode array and the cochlear nucleus (Colletti, Fiorino et al. 2002), as noted in Section 1.1. Therefore, scaling is required (Colletti, Fiorino et al. 2002; Otto, Brackmann et al. 2002). Pitch scaling is not necessarily linear across ABI electrodes, with subjects often reporting many electrodes sounding similar or the same and significant pitch differences occurring infrequently (Kanowitz, Shapiro et al. 2004).

Previous studies have suggested that accurate tonotopic ordering of electrodes in the programming algorithm affects outcomes (Otto, Brackmann et al. 2002; Long, Nimmo-Smith et al. 2005). However, with pitch variations often variable between electrodes, the ease with which pitch differences can be identified will also vary. The overall range of pitch perceived is reported to be correlated with speech recognition (McCreery, Shannon et al. 1998). However, a large pitch range may still be associated with a number of electrodes that elicit very similar pitches within this range, accompanied by large 'gaps' between different groups of electrodes. ABI speech processor programming strategies assume a smooth and regular progression from low to high pitch percepts in the ordered electrodes. No investigations have so far investigated whether regular progression of pitch percepts across electrodes is correlated with outcomes.

An assumption often made is that pitch perception is the overriding percept experienced during stimulation of different ABI electrodes. Unlike a CI, the auditory percept experienced by ABI users is complex. Although device programming requires electrodes to be ordered tonotopically, it may be that whatever tonotopicity is experienced by an ABI user is overshadowed by non-tonotopic variations in auditory perception. Identification of variations in sounds is usually made via loudness, pitch or timbre. Timbre is generally used to describe the qualities or characteristics of sounds which might otherwise have the same pitch or loudness. For example a click may sound different to a bell, but be of a similar pitch. For ABI users, it may be that sounds are distinguishable by means of variations in timbre but this may not relate to strict tonotopic variation. No studies have yet investigated the degree to which non-tonotopic auditory percepts are experienced by ABI users, nor the relationship to speech outcomes. Perceptual variation has been investigated in CI users via multi-dimensional

scaling (MDS) techniques in which the user is asked to scale the degree of auditory perceptual difference between electrodes. Studies have shown that for CI users, pitch is the overriding percept (Collins and Throckmorton 2000) and the derived MDS stimulus space that corresponds with this may provide a predictable and reliable pattern of results (Henshall and McKay 2001). Given the emphasis placed on pitch ranking of electrode during ABI programming, investigation of the auditory perceptual differences experienced by ABI users during activation of different electrodes would be beneficial. Comparisons with the auditory perceptual differences experienced by CI users may assist in evaluating whether the presence of alternative auditory percepts is related to ABI outcomes.

2.2 Event-Related Potentials in implant users

A significant issue in the programming of ABIs is the co-operation required from the patient. If ERP features are shown to correspond with behavioural evaluations of auditory perception, there may be a possibility of objective ABI programming. ERPs have already been extensively described as a method of determining hearing threshold in normal hearing individuals (Lightfoot and Kennedy 2006), and have been shown to correspond with behavioural loudness in CI users (Firszt, Chambers et al. 2002a; Firszt, Chambers et al. 2002b). Conflicting reports exist regarding whether there is a relationship between CERP features and place pitch in both normal hearing (Picton, Woods et al. 1977; Verkindt, Bertrand et al. 1995) and CI groups (Firszt, Chambers et al. 2002b; Kelly, Purdy et al. 2005).

In ABI users, the most recorded ERP is the electrically-evoked ABR (EABR). This has been used intra-operatively to aid ABI placement (Waring 1996) and intra- and post-operatively to investigate correlations with behavioural thresholds of auditory sensation during device programming (O'Driscoll, El-Deredy et al. 2011a; O'Driscoll, El-Deredy et al. 2011b). There was a positive relationship between the number of EABR peaks and speech performance, but EABR thresholds were not found to correlate with behavioural thresholds during ABI programming for adult patients (O'Driscoll, El-Deredy et al. 2011a). In children, post-operative EABR thresholds were correlated with behavioural reactions, and threshold and maximum comfort levels where children were able to give reliable responses (O'Driscoll, El-Deredy et al. 2011b).

The CERP has also been investigated in ABI users. Waring et al. (1999) described two qualitatively different CERP recordings in two ABI users, surmising that tumour growth and removal allowed for activation of now separate ascending auditory pathways. More recently, O'Driscoll (2012) determined that dipole source modelling of group CERP features showed distinctions between auditory and non-auditory stimuli.

As a predictor of ABI outcomes, the CERP has been investigated once. O'Driscoll (2012) showed an association between larger P2 amplitudes and speech perception scores in ABI users. There was also a trend towards longer P2 latencies for poorer ABI users. Conversely, CERPs have been extensively examined in CI users in relation to outcomes, with varying results. Shorter N1 and P2 latencies have been found to correlate with higher speech perception scores in some studies (Makhdoum, Groenen et al. 1998; Kelly, Purdy et al. 2005) but not others (Firszt, Chambers et al. 2002a; Firszt, Chambers et al. 2002b). These conflicts suggest that further investigation of the CERP in relation to outcomes in ABI users should be undertaken before conclusions regarding its efficacy in ABI outcome prediction are drawn.

In addition to investigations regarding ABI speech outcomes, particular attention should also be given to the investigation of electrode discrimination in ABI users. Given that discrimination of sounds elicited via activation of different electrodes is not as straightforward in ABI users compared to CI users, investigation of ERPs relating to auditory discrimination may provide information regarding neural representation of electrode discrimination. ERPs such as the MMN and P3b are cited as indicating automatic and conscious perception of auditory change respectively (Naatanen, Brattico et al. 1992; Kraus and McGee 1994). ERP studies have already shown that MMN can be measured in individuals (Pekkonen, Rinne et al. 1995) and correlates well with behavioural auditory discrimination tasks (Naatanen, Brattico et al. 1992). In normal subjects, the MMN may occur in response to very small deviations, for example frequency deviations of 8 Hz or amplitude variations of 5 dB (Kraus and McGee 1994). If identified in ABI users, its presence may therefore indicate changes in the auditory percept of the eliciting stimulus.

The MMN has been successfully recorded in CI users. The presence of a sound-field evoked MMN was correlated with a better rating on scales of auditory perception and speech production for CI users (Sing, Liasis et al. 2004), and MMN identification was not always possible in poorer CI users (Kelly, Purdy et al. 2005). Its latency was negatively correlated with duration of implant use regardless of outcomes (Sing, Liasis et al. 2004) or with the presentation level required to discriminate between two words (Roman, Canevet et al. 2005). Its duration was found to be positively correlated with scores on word and sentence perception tests (HINT sentences and CNC words lists) (Kelly, Purdy et al. 2005). For CI users, MMN presence may therefore provide information regarding speech outcomes. This has not yet been investigated in ABI users.

The P3b has also been successfully recorded in CI users. Kubo, Yamamoto et al. (2001) found that the electrically evoked P3 latency was negatively correlated with the behavioural consonant recognition score. In addition, whilst the CERP latency does not change as a discrimination task becomes harder, the P3 latency does (Rugg and Coles 1995). This was taken to indicate that the P3 reflects evaluation of the incoming sound, a task important for speech perception (Kubo, Yamamoto et al. 2001). Kelly, Purdy et al. (2005) also report that poorer CI users showed recordable CERPs but not P3 responses.

Neither the MMN nor the P3b have yet been examined in ABI users. The fact that the P3b is elicited only following perceptual discrimination of a difference between stimuli means that, like the MMN, it is necessarily influenced by auditory discrimination. When considering that auditory discrimination is a requirement for speech perception, examination of this perceptual response in addition to the MMN's automatic measure of discrimination may prove useful in determining whether any detected auditory signals from an ABI that have elicited a CERP then undergo further perceptual processing.

2.3. Conclusions

This is not an exhaustive review of the literature in this field. However, the aim of this background reading was to determine the merit of the ideas underlying this study, and highlight why previous studies have so far failed to answer the question of what

excitation is happening during ABI stimulation and how this relates to speech perception outcomes. A review of further literature is unlikely to have generated vastly different conclusions.

The topic of ERPs and outcomes has been investigated in CI patients, but studies of ERPs in relation to outcomes in ABI patients are extremely limited. Therefore, this background reading does reference greater numbers of CI studies. One reason may be the significantly smaller numbers of willing and available ABI participants in comparison to CI patients in any implant clinic. Secondly, two quantitively different CERP morphologies have been reported in 2 different patients within a single study (Waring, Ponton et al. 1999). It may be that the anatomical differences which give rise to these differences are so great so as to prevent such ERP measures being consistent between ABI patients, meaning that inferences cannot be made to the wider ABI population.

This background reading has shown that ERPs are recordable in implant users, albeit CI users, and has indicated how they assist our understanding of outcomes amongst implant users. However, whilst the evidence indicates possible correlations between ERPs and CI outcomes, much still needs to be done in order to answer the same question for ABI users. Although CI studies of this nature suggest that atypical or 'poorer' ERP morphology correlates with poorer speech perception results (Gordon, Tanaka et al. 2005; Kelly, Purdy et al. 2005) the differences between the site of ABI and CI stimulation and the anatomical differences between CI and ABI patients means that inferences cannot be drawn from the CI data for ABI patients. It is therefore necessary to investigate ERPs and speech outcomes in ABI patients.

The emphasis on pitch identification during ABI programming suggests that understanding the auditory system's response to frequency deviations during ABI usage is important. As the MMN and P3b are considered as reflections of discrimination (see Sections 1.2.2. and 1.2.3.), then the absence of an MMN or P3b would be anticipated in cases where frequency deviations are not subjectively identified. Determining whether these ERPs relate to behavioural measures of frequency deviation would determine whether objective measures may be used to predict aspects of auditory sensation in an

ABI. Any correlations with speech perception may then indicate the extent of the role of frequency discrimination in speech perception with an ABI.

2.4 Study Aims

This study was divided into two experiments. Firstly, experiment one used psychophysical measures to investigate place-pitch perception and non-tonotopic auditory perceptual differences between electrodes in ABI users, given that tonotopic ordering of electrodes is an overriding part of programming sessions and has been cited to have an effect on outcomes. Experiment one (Chapter 3) therefore had two aims: (a) to determine the relationship between place-pitch perception and speech outcomes in ABI users using their clinically-set maps; (b) to determine if auditory percepts other than pitch are related to electrode position for ABI users via an MDS procedure.

Experiment two used ERPs to investigate auditory perceptual differences between implant electrodes. Experiment two (Chapter 4) therefore had two aims: a) to determine if electrophysiological measures of electrode discrimination correlate with behavioural measures of electrode discrimination in adult ABI users; b) to determine if electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users.

Chapter 3

Tonotopic Ordering of Electrodes in ABI Users Affects Speech Outcomes

3.1. Abstract

Background and aims

Activation of the electrodes on an auditory brainstem implant (ABI) does not produce sensations with a clear tonotopic order, unlike those produced by a cochlear implant (CI). Subjective pitch ranking of electrodes by ABI users shows significant variation in place-pitch perception between users and test methods. This study therefore had 2 objectives: (1) to determine the relationship between pitch perception and speech outcomes, (2) to determine if auditory percepts other than pitch are related to electrode position for ABI users.

Method

10 ABI and 9 CI patients from Manchester Auditory Implant Centre undertook a two-alternative forced choice pitch ranking task and a four-alternative forced choice multi-dimensional scaling (MDS) task. In each test, pairs of electrodes were sequentially activated and subjects were required to choose either (a) which of the two sounded higher in pitch, or (b) the degree of auditory perceptual difference between electrodes using a 4-point scale from 'no difference' to 'very different'. Stimulus level was the user's maximum comfortable current level following loudness balancing. Every combination of electrode pair was presented in each of the two tests. For the pitch ranking task, overall pitch ranks were assigned following completion of the whole test. Measured ranks were compared with the clinically-set map order and this relationship was compared with speech perception scores. For the perceptual difference task, MDS analyses were conducted to determine (a) the auditory perceptual relationships evoked by different electrode positions for each user, (b) the degree to which auditory perceptual differences between electrodes varies between ABI users and an average of CI users.

Results

Speech perception scores were correlated with the relationship between measured pitch ranks and map ranks in that CI or ABI users with greater agreement between measured pitch rank and clinical map ranks also had better scores in speech perception tests. MDS analyses indicated that pitch perception is not the overriding auditory percept experienced by ABI users, unlike CI users. For the ABI group, there was no significant correlation between speech scores and a more 'CI-like' MDS stimulus space.

Conclusions

Speech scores in ABI users are correlated with tonotopically ordered user maps and maps in which pitch variations are more reliably identified. ABI users also demonstrate consistency in identification of non-tonotopic auditory perceptual differences, although this is not related to speech scores. The pattern of auditory perceptual differences experienced by ABI users is significantly different to that experienced by CI users. There was no correlation between ABI speech scores and patterns of auditory discrimination that were more similar to those of CI users. This may indicate that the auditory perceptual differences experienced by ABI users are qualitatively different to those of CI users and are not dominated by pitch-perception. Clinical implications include the need to ensure effective pitch ranking at the outset of ABI usage and the possibility of including an MDS task to aid device programming. This information may assist in patient counselling regarding expectations and possible outcomes.

3.2 Introduction

Cochlear implants (CIs) are designed to produce electrical excitation in auditory nerve fibres for subjects with severe to profound hearing loss for whom conventional hearing aids provide limited or no benefit. In a CI, an electrode array is designed to mimic cochlear function by stimulating neural structures with a well-known tonotopicity to produce sensations with a clear tonotopic pitch order. However, where auditory nerve damage or dysfunction exists, a CI is not useful. Using an electrode array surgically positioned in or on the ventral cochlear nucleus (VCN) in the brainstem, an auditory brainstem implant (ABI) can stimulate neural pathways central to any damage so that auditory sensation may still be achieved. Whilst ABIs function in much the same way as CIs, functional outcomes vary greatly between the patient groups: an ABI can provide limited auditory information in most cases such that speech perception is poor compared to those with a multi-channel CI (Colletti and Shannon 2005).

Currently, most ABI candidates in the Manchester Auditory Implant Centre are adult neurofibromatosis type II (NFII) patients. This condition causes multiple benign tumours to grow along nerve fibres. Tumour growth on the auditory nerve and subsequent tumour removal usually damages the auditory nerve, resulting in sudden hearing loss. This is quite different to the experience of most hearing aid and CI users who often have either a gradual or congenital hearing loss.

The cochlea nucleus has a complex physiology, with less-understood neural processing and a more complex tonotopicity than that of structures within the cochlea. Stimulation using ABI electrodes often does not exclusively result in auditory sensation, but may also cause dizziness, nausea, and taste and muscle sensations, even when ABI electrode array placement is considered optimal. As only electrodes providing auditory stimulation are activated following speech processor programming, the number of electrodes available for stimulation varies between patients. Whilst the number of active electrodes does affect performance (Colletti, Carner et al. 2005), those activated provide limited auditory information compared to that transmitted by a CI electrode (Colletti and Shannon 2005). Therefore, the benefit provided by an ABI can be extremely varied and it is currently not possible to predict how well someone may hear with their ABI in advance.

Terminations of nerve fibres from the cochlear run parallel to the surface of the VCN such that the tonotopicity of the VCN does not lend itself to effective and straightforward tonotopic activation from a surface electrode array (McCreery, Shannon et al. 1998). Unlike a CI, subjective pitch ranking of electrodes by ABI users is required to provide a pitch rank order of active electrodes. Active electrodes located in the same position on the implanted array can be ranked differently between patients. One reason may be that due to the aetiology of ABI users, tumour growth and removal result in anatomical differences between users and as such stimulation of different nerve fibres (Waring, Ponton et al. 1999; Colletti and Shannon 2005). The pitch rank provided by a subject may also change upon repeat testing (Long, Nimmo-Smith et al. 2005). The difficulty is that changes in rank may not necessarily indicate a change in perception, but may be an indication of a subject's pitch-ranking abilities. Collins, Zwolan et al. (1997) found that pitch structures predicted by pitch ranking and pitch scaling tasks in CI users sometimes showed large discrepancies within subjects and that the derived pitch rank was not in strict tonotopic order according to electrode location. As an ABI pitch rank is not known before testing and is user-specific, poor ability to do a pitch ranking task (whether due to the subject finding pitch ranking a confusing concept, or due to unclear or small pitch differences) may result in a user map containing active electrodes incorrectly ranked in relation to the user's actual pitch percept. The relation between electrode frequency allocation and pitch perception has been suggested to have an effect on speech perception in both CI (Di Nardo, Scorpecci et al. 2010) and ABI users (Long, Nimmo-Smith et al. 2005). In a study cited by Long, Nimmo-Smith et al. (2005), ABI users were found to have better speech scores when using maps with electrodes allocated to a subjective pitch rank compared to those with electrodes assigned a random order. In addition, McCreery, Shannon et al. (1998) found that ABI users with the highest speech recognition scores also have the widest pitch range. These results indicate that accurate pitch perception and pitch ranking is important during ABI programming.

A limitation of pitch ranking tasks is the assumption that place pitch is the overriding perceptual difference between electrodes. Whilst a subject may find a pitch ranking task a confusing concept, or experience small and unclear pitch variations between electrodes, it may also be that that auditory percepts other than pitch create the overriding auditory perceptual differences between electrodes. This makes a pitch

ranking task difficult because a subject is being asked to rank electrodes according to only one aspect of a complex sound. However, in a multi-dimensional scaling (MDS) task, a subject is asked to categorise the difference between two items (in this case the auditory percept experienced following activation of a two different electrodes) based on the overall perceptual difference, or timbre, rather than being limited to answering only on the basis of pitch. Timbre is generally used to describe the qualities or characteristics of sounds which might otherwise have the same pitch or loudness. For example a click may sound different to a bell, but be of a similar pitch. For ABI users, it may be that sounds are distinguishable by means of variations in timbre but this may not relate to strict tonotopic variation. Analysis of MDS data results in a stimulus space that illustrates the relative degree of difference between stimuli.

MDS solutions are calculated using a dissimilarity matrix and solutions may include any number of dimensions to best describe the relation between electrode positions. The MDS solution that best describes the perceptual difference between electrode positions in CI users is a horseshoe shape in two dimensions (Collins and Throckmorton 2000). Electrodes are ordered along one dimension according to position on the array, with the two ends of the one-dimensional line curving into a horseshoe shape when viewed in 2 dimensions. This is not because two separate perceptual dimensions are present for CI users, but rather the horseshoe is a result of difficulty in accurately describing differences between stimuli with large degrees of auditory perceptual difference (Coxon 1982; Collins and Throckmorton 2000; Henshall and McKay 2001). Even for smaller data sets, a horseshoe is apparent when stimuli are easily distinguishable (McKay, McDermott et al. 1996). However, MDS solutions have not been obtained for ABI users. Given that the dominant percept in activation of different CI electrodes is accepted as being pitch (Collins and Throckmorton 2000), and that the MDS solution relating to this is predictable (Henshall and McKay 2001), investigating the similarities or differences between ABI and CI MDS solutions may prove useful in terms of understanding the auditory perceptual features of ABI electrodes. MDS data may also provide a more accurate way of determining the number of indistinguishable electrodes for a user. Where patients find pitch ranking difficult, this number may be overestimated when compared to results from MDS tasks (Collins and Throckmorton 2000).

3.3. Subjects and Methods

3.3.1. Subjects

Participant details for 9 CI (6 female, 3 male) and 10 ABI (4 female, 6 male) participants are presented in Table 1. All participants were post-lingually deafened and were recruited from the Manchester Auditory Implant Centre. By the end of the subject recruitment period of this study, The Manchester Auditory Implant Centre had implanted around 57 unilateral ABIs. Approximately 14 of this number were non-users of the device, 10 were sleepers (the device was implanted at the time of tumour removal for ease of surgery but residual contralateral hearing meant non-use of the device until required by hearing threshold deterioration), 4 were deceased and 2 had failed devices. This meant approximately 27 ABI recipients used their devices. The nature of NFII itself means that tumour growth can cause significant debilitative symptoms in many areas of the body, meaning not all ABI recipients are in a state of health conducive to study participation. Because of these and other personal factors, approximately 10 users were not suitable to be invited to participate, leaving a potential population size of 17. Despite this, the relatively small number of published studies involving ABI users necessitated the drive to complete this work with a small sample size. For comparison purposes, the CI user group consisted of a similar number of participants.

ABI users were implanted with the Cochlear Nucleus 21-channel ABI, which is based on the Cochlear Nucleus 24M Cochlear Implant. CI users were implanted with Cochlear Nucleus 24M or 24RE devices. All subjects except SR used the ACE processing strategy on a day to day basis (SR used SPEAK processing strategy), and all subjects used either 3G or Freedom speech processors.

ABI users	Age	Sex	Aetiology	ABI side	Switch on (mm/ yy)	Deafness duration (years)	Active electrodes	Pulse width (μs)	Inter-phase gap (μs)	Rate (pulses /s)
DB	28	M	NFII	R	05/08	0	8	150	45	250
EO	31	F	NFII	R	01/01	0	10	300	8	250
JD	22	F	NFII	R	09/04	0	7	50	7	900
GB	47	M	NFII	L	11/07	0	10	101	8	250
HW	25	F	NFII	L	05/09	0	10	25	8	1200
ML	47	M	NFII	R	01/06	2	16	50	8	720
PC	57	M	Bilateral vestibular schwannoma	R	02/09	0	10	25	8	900
RC	30	M	NFII	R	08/06	10	7	101	8	500
RH	19	M	NFII	R	03/05	0	9	50	8	900
SR	28	F	NFII	R	10/02	0	18	37	8	250
CI users	**Age**	**Sex**	**Aetiology**	**CI side**	**Switch on (mm/ yy)**	**Deafness duration (years)**	**Active electrodes**	**Pulse width (μs)**	**Inter-phase gap (μs)**	**Rate (pulses /s)**
AS	50	F	Ototoxic	R	12/04	12	16	25	8	1200
DT	43	M	Mumps	L	07/98	26	18	25	8	900
GC	41	F	Congenital progressive	R	12/04	10	22	25	8	900
JG	46	F	Meningitis	L	11/04	10	22	37	8	250
JR	40	F	Idiopathic progressive	L	03/02	2	22	25	8	1000
JW	43	M	Measles	L	09/00	5	22	25	8	1000
PM	34	M	Congenital progressive	R	06/04	5	22	25	8	1000
WM	51	F	Familial progressive	R	08/03	1	22	25	8	900
YW	58	F	Familial progressive	L	01/05	5	22	25	8	1000

Table 3.1. participant details, including parameters of the clinically-set maps

3.3.2. Apparatus setup

Test stimuli were computer generated using algorithms from Cochlear Nucleus Implant Communicator™ (NIC) software and a MATLAB interface. During the experimental procedures, test stimuli were presented directly from MATLAB to the patient's implant via a standard Cochlear clinical programming pod and Freedom speech processor. Prior to the experiment, comfortable loudness checks (C-level) and loudness balancing of all test stimuli were conducted using Cochlear's Custom Sound 2 clinical programming software and delivered via the same programming pod and speech processor.

3.3.3. Stimuli

Test stimuli were 125 ms duration pulse trains delivered at the patient's comfortably loud current level (C level). Pulse width, inter-phase gap and rate were the same as in their clinical map, and are shown in Table 3.1. above.

The nature of the forced choice pitch ranking and multidimensional scaling (MDS) tasks detailed below meant that testing a large number of electrodes resulted in a long test session with a very large number of stimuli to judge. The majority of recruited ABI users had a maximum of 10 active electrodes and all required testing due to uncertainty regarding auditory perceptual differences between them. To reduce fatigue a similar number of CI electrodes were chosen for investigation, as otherwise CI users would be subjected to excessively long and tiring test sessions. The assumed tonotopicity of the CI electrode array was used to allow testing of a section of the implanted electrode array. For all CI users except AS, tested electrodes were the 10 electrodes assigned to the lowest frequencies (most apical active electrodes). For AS, only the 8 most apical active electrodes were tested. This was because the initial test procedure required testing the 50% of active electrodes assigned the lowest frequency bands. The procedure was revised to include the 10 electrodes assigned the lowest frequency bands, regardless of whether this was more than 50% of the active electrodes.

3.3.4. Tests

3.3.4.a. Maximum current level check

Electrodes were activated individually and patients used a 7-point scale to indicate the loudness perceived, varying from 'first hearing' to 'too loud'. Stimulus levels were increased by the tester using step sizes of 2-5 current units until the patient response matched 'loud but comfortable'. For some ABI users, it was only possible to increase the stimulus to a 'medium' level on some electrodes due to non-auditory side-effects being introduced at higher current levels.

3.3.4.b. Loudness balancing

Following C-level checks, three electrodes allocated to adjacent frequency bands in the patient's map were activated in succession and the current level of the latter two stimuli were manually adjusted until the stimuli were perceived to be at the same loudness as the first. The third electrode in the sequence of three stimuli then became the first

(reference) stimulus in a further set of three. This process continued until all active electrodes had been balanced. A sweep of all electrodes at the balanced C levels was then conducted to check for further variations in loudness. Adjustments to stimulus current levels were made accordingly until the patient perceived all stimuli to be of equal and comfortable loudness. Where non-auditory side-effects prevented an increase of current to reach the desired sensation level, subjects were instructed to ignore the minor variation in loudness when considering their responses to the two main tasks outlined in Sections 3.3.4.d. and 3.3.4.e. below. Where this occurred, it was felt that balancing at the lower loudness level would result in more concentration being required on the part of the subject to perform the discrimination tasks. C-levels remained at the louder level for all applicable electrodes to avoid early fatigue and less accuracy in general discrimination.

3.3.4.c. Clinical pitch ranking of electrodes

All ABI users underwent a mid-point comparison pitch ranking technique in their standard clinical review sessions, based on the method originally described by Steinhaus (1950) and detailed in Long, Nimmo-Smith et al. (2005). In brief, a pitch judgement is required following activation of two electrodes in succession, with ranks being assigned to electrodes after each judgement and amended as judgements for new electrodes are made. To determine its place in the rank, an electrode is compared with another already assigned the middle pitch in the provisional rank (the first two electrodes activated for comparison are chosen randomly) and the higher pitch electrode is identified. The test electrode is then compared to an electrode ranked higher or lower in pitch than the original reference electrode, depending on the result of the first judgement. It is not compared against all possible electrodes, only those deemed relevant following previous judgements. In this way, electrodes are ranked based on single presentations of electrode-pairs and not all combinations of electrode-pairs are required to be activated. The presentation of all stimuli for this test is governed by computer software specifically designed for this purpose.

The above test was applied following C-levels checks during initial speech processor programming and again in subsequent programming sessions as required. Where pitch ranks altered upon retesting in subsequent appointments, clinical judgement was used in any decision to amend or retain programmed pitch ranks. Over time, this meant that

each ABI user underwent a personalised number of pitch ranking tests and map order amendments.

CI users did not undergo any clinical pitch ranking as the pitch rank of active electrodes is assumed due to known cochlear tonotopicity. All CI users in the current study used clinical maps with the standard electrode order for all active electrodes.

3.3.4.d. Forced-choice pitch ranking of electrodes

One ABI user (JD) chose not to complete this test. For all other subjects, stimuli were presented on two electrodes with a 200 ms inter-stimulus interval. The subject was asked to judge which sound was higher in pitch. The answer was typed by the patient directly onto the stimulus computer. Consistent with Otto, Brackman et al. (2002), all possible combinations of electrode pairs were activated, including pairs consisting of activation of the same electrode twice. Each pair was presented 8 times, except pairs containing the same electrode, which were presented only 4 times. For each pair of electrodes, the order of activation was balanced but in pseudo-random order. For a subject with 10 electrodes, a total number of 400 pairs were presented in pseudo-random order. Answers typed into the MATLAB programme were collated at the end of the test to form matrices containing the responses to all pair judgments, as illustrated in Figure 3.1. For each judgement, a count of 1 was added to the row corresponding to the higher pitched electrode. If e7 was judged as higher pitched than e2 in the pair e7-e2, the count would be added to the element (row-e7 column-e2) in the matrix. If e2 was judged as higher pitched than e7, the count was added to the element (row-e2 column-e7). Any matrix element may therefore have a maximum value of 8, except the diagonal elements, which contained always 4. For analysis, elements were summed across each row. The greater the sum of the elements in a row, the more often that electrode was judged as higher pitched than those it was compared to. Final pitch ranks were calculated by ranking these row sums.

electrode	2	4	5	7	8	10	11	13	14
2	4	2	0	1	0	1	3	0	3
4	6	4	1	1	0	0	0	0	0
5	8	7	4	0	1	2	0	1	0
7	7	7	8	4	1	3	3	1	0
8	8	8	7	7	4	4	1	1	1
10	7	8	6	5	4	4	4	1	3
11	5	8	8	5	7	4	4	5	2
13	8	8	7	7	7	7	3	4	5
14	5	8	8	8	7	5	6	3	4

Figure 3.1. the results matrix for ABI user RH. Row and column headings are the patient's electrodes. Electrodes are numbered according to location on the electrode array, not according to subjective pitch ranking or clinical map order. Comparisons between electrodes are indicated by the elements in the matrix. Highlighted values indicate examples of the total presentations for two electrode pairs. In these examples, e7 is judged consistently higher in pitch than e2 (yellow highlights: 7/8 higher), but is inconsistently judged against e11 (blue highlights: 3/8 higher, 5/8 lower than e11).

3.3.4.e. Perceptual difference task (Multidimensional Scaling, MDS)

One ABI user (SR) chose not to complete this test. For all other subjects, stimuli and presentation method remained the same as for the forced-choice pitch ranking task. Subjects were asked to judge the degree of difference between the two sounds. Instructions allowed judgments based on any factor, e.g. pitch, tone, richness, but to ignore any minor fluctuations in loudness levels. Answers were again typed directly into MATLAB by the patient and consisted of a 4-alternative-forced-choice. Options were:

1 They sound the same

2 I can't quite tell if they are the same or different

3 I can tell they are a little different

4 They are very different

The values 1 - 4 were collated in MATLAB matrices, with the answer value for each pair presented added to element corresponding to the row of the first electrode and column of the second electrode. As before, each possible electrode combination was presented 8 times (pairs containing the same electrode twice were presented 4 times), with the order of presentation balanced 50:50. This meant each element in the matrix represented 50% of the total presentations for each pair (except for the diagonal elements). Each element could contain a total value of between 4 and 16.

electrode	2	4	5	7	8	10	11	13	14
2	7	11	13	14	16	16	15	14	15
4	13	9	16	16	13	13	16	16	16
5	15	16	4	14	13	16	13	13	13
7	16	16	12	5	15	16	15	16	15
8	15	15	16	13	6	15	15	14	16
10	16	16	16	16	15	6	12	12	15
11	16	15	13	15	14	12	7	11	13
13	16	16	16	15	16	11	11	7	14
14	16	16	15	13	14	16	15	12	8

Figure 3.2. The MDS response matrix for RH

3.3.5. Analysis

For pitch ranking data, the derived pitch ranks were compared to the ranking in the user's maps. The degree to which these two ranks corresponded was then analysed with respect to clinically recorded AB word scores and CUNY sentence scores.

For MDS data, ALSCAL analysis was conducted on each matrix using SPSS software to produce a stimulus space showing the relative degree of auditory perceptual difference between electrodes. INDSCAL (individual differences) analysis was then used to determine similarities and differences between the derived stimulus configurations in different ABI subjects and between the two implant groups. First, a 'best fit' or 'ideal' stimulus space was created using the data from 8 of the 9 CI users (as INSDCAL analyses require all matrices to contain an equal number of elements, CI user AS was included only in analyses involving ABI users DB, JD and RC who had 8 or fewer electrodes). Next, using the CI INDSCAL stimulus space as a reference, data from one ABI user at a time was added into the INDSCAL to determine individual perceptual weights of the ABI data compared to those of the CI users. Individual weights from INDSCAL analyses were examined with respect to clinically recorded speech scores

As 10 electrodes were chosen for the majority of CI testing, only 10 of ABI subject ML's 16 active electrodes could be included in the INDSCAL analysis. These were the 10 active electrodes assigned the lowest frequency bands in ML's user map, chosen for consistency with the tested CI electrodes and the electrode order used during speech testing. Analysis was conducted to confirm that results would not be affected should

ML's 10 lowest pitch electrodes as defined by the pitch ranking task be included instead. The results of this comparison are shown in Section 3.4.2. below.

3.3.6. Speech scores

Pre-recorded AB word lists and CUNY sentences were presented in each subject's most recent standard clinical review appointment via PC and loudspeaker at a level of 70 dBA. Subjects were listening with the same maps they were using at the time of the psychophysical experiments in the present study. AB words were scored as percentage of phonemes correctly identified. CUNY sentences were scored as percentage of keywords correctly identified.

For ABI users, speech test stimuli were presented both with and without lipreading (i.e. audio alone, visual alone, and audiovisual). The audio alone score (A) can often show a floor effect. The degree of auditory benefit may therefore be derived from the audiovisual (AV) score for both AB words and CUNY sentences as shown in Equation 3.1:

$$\text{Improvement score} = (\text{AV score} - \text{V score})/(100 - \text{V score}) \quad (3.1)$$

This calculates the auditory benefit gained in the AV condition relative to the maximum improvement available considering the subject's lipreading (V) performance (Tye-Murray, Sommers et al. 2007) For ABI users, the calculated improvement scores for AB words and CUNY sentences were the speech scores included in statistical testing to avoid bias due to floor effects.

For CI users, speech test stimuli were presented without lipreading (i.e. audio alone). For CUNY sentences, stimuli were also presented in the presence of noise (Pink noise +10 dB SNR). For CI users, a ceiling effect can occur in an audio alone condition. Therefore, to avoid any bias, the speech in noise scores for CUNY sentences were used for statistical testing. A speech in noise score was not available for AB words, but no ceiling effect was seen in the AB word scores for the CI group (see Table 3.2. in results section 3.4.3.).

3.4. Results

The results for the pitch ranking task and the perceptual difference task are summarised in sections 3.4.1. and 3.4.2. Correlations with speech perception data are summarised in section 3.4.3.

3.4.1. Pitch ranking

Pitch ranks were created from the pitch ranking procedure by summing the elements in the matrix rows, i.e. summing the number of presentations in which an electrode was judged higher pitched in the pairs in which it was presented. The greater the sum of responses for any particular electrode, the closer its position was to the high-pitch end of the ranking. The correlation between the measured pitch ranking and the existing map rank was assessed for each subject and compared between groups. Within groups, qualitative examination of pitch ranking data showed 4 patterns in CI users and 3 in ABI users. Examples of these are shown in the Figures 3.3. and 3.4. below.

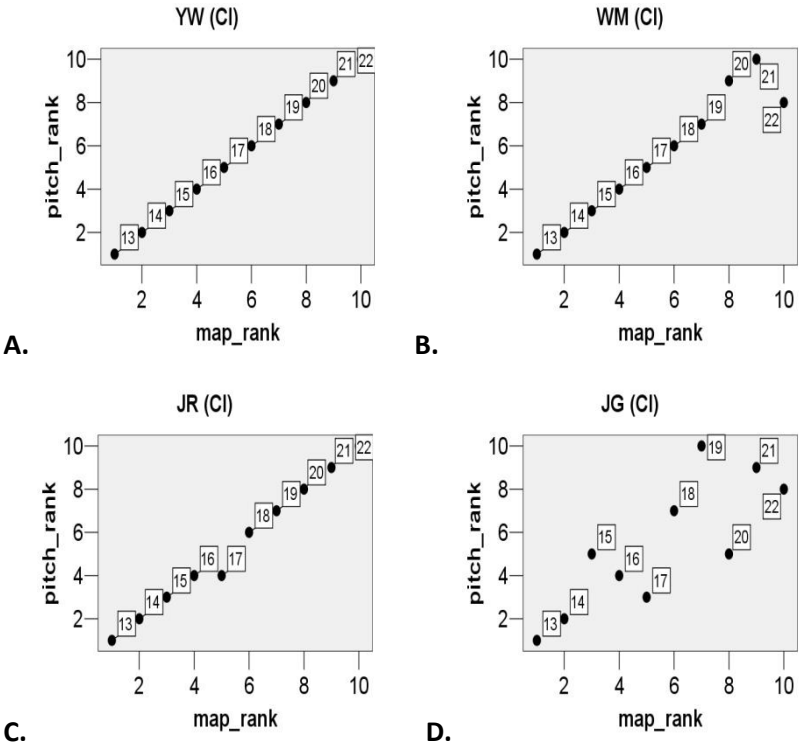


Figure 3.3. Four examples of pitch ranks plotted against the user map rank for CI users. A rank of 1 indicates highest pitch, and 10 indicates lowest pitch. Data points are labelled with active electrode number as labelled on the implanted array. **A.** Correlation of 1 between ranks (GC, JW, YW). **B.** Mis-matched ranks in low frequency electrodes (PM, WM). **C.** Mis-matched ranks in the middle frequency range (AS, JR). **D.** Mis-matched ranks across a wide range of the electrodes tested (DT, JG)

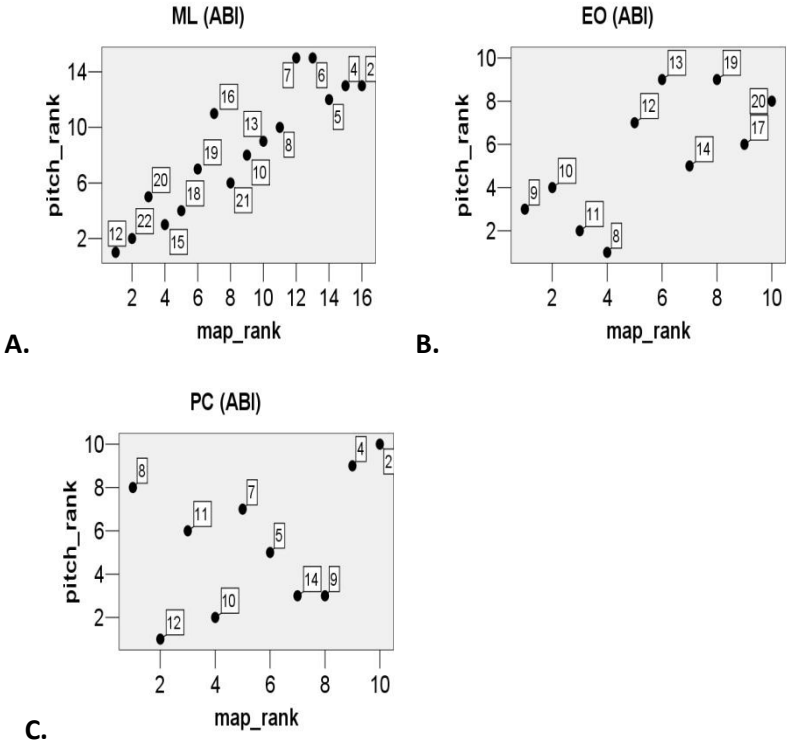


Figure 3.4. Three examples of pitch ranks plotted against the user map rank for ABI users. A rank of 1 indicates highest pitch, and 10 indicates lowest pitch. Data points are labelled with active electrode number as labelled on the implanted array. **A.** A relatively small number of mis-matched ranks across all electrodes such that a clear correlation is visually apparent (ML, RH, SR). **B.** A moderate number mis-matched ranks across all electrodes such that a clear correlation is less visually apparent (DB, EO, HW). **C.** Mis-matched ranks across a wide range of the electrodes tested (GB, PC, RC).

Visual inspection of the above figures suggests that the degree of correlation between the measured pitch rank and the user map rank decreases with each subsequently identified pattern. CI patterns A, B and C show a predominantly straight line, indicating a high degree of agreement between the two ranks. ABI pattern A might be classed as comparable to CI pattern C in that a degree of agreement is identifiable as the data points loosely fall around an identifiable straight line. CI pattern D and ABI pattern B might also be classed as comparable with each other in that no clear line is distinguishable but a general trend may be seen in the data points. Finally, ABI pattern C may be considered a pattern of its own as no trend can be seen within the data points at all.

The correlation between pitch rank and map rank was calculated for each subject and a box-plot summary is shown in Figure 3.5. with respect to implant type.

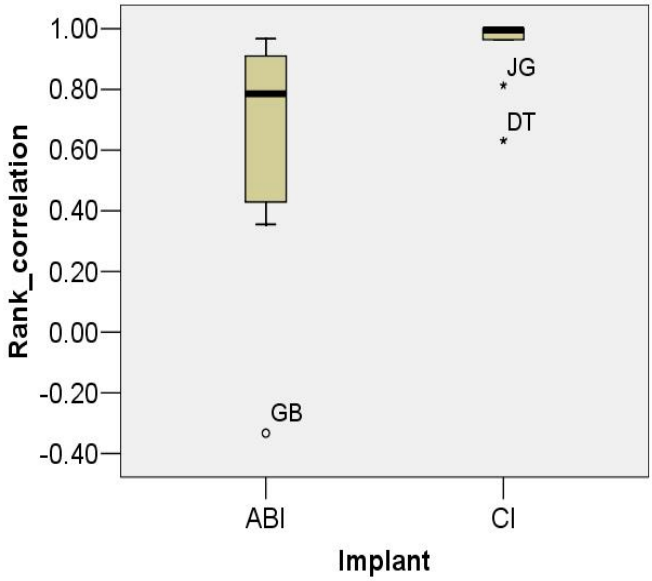


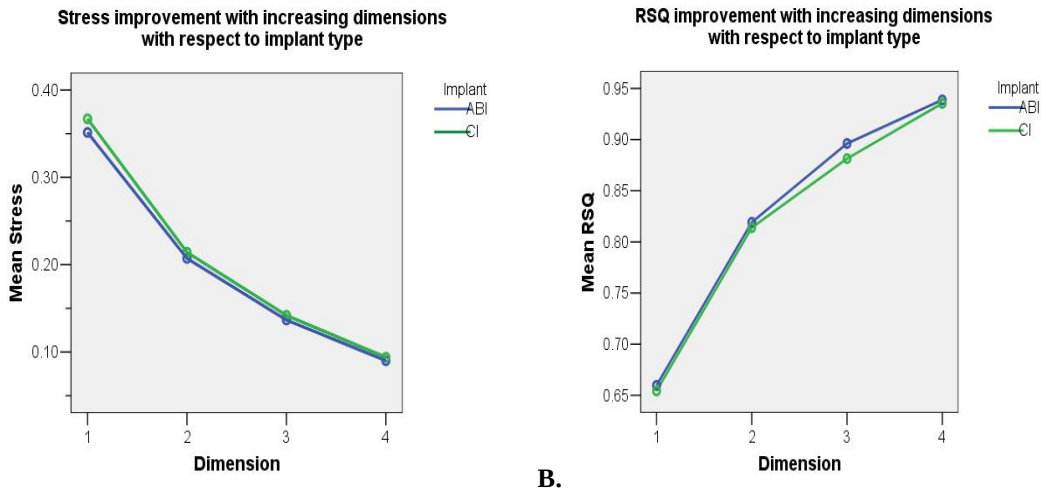
Figure 3.5. Pearson Correlations (labelled Rank Correlation) between measured pitch ranks and user map ranks for each implant type. Outliers are labelled.

The correlations were significant (p= <0.05) in all subjects except ABI users GB, PC and RC, and CI user DT. There was a significant difference in the within-group variance of the rank correlations between the two implant groups (F=6.065, p=0.026) but an independent sample T-Test showed no significant difference between the mean rank correlation of the two implant groups (ABI mean=0.618, CI mean=0.931, t=-2.150, p=0.059). As seen in Figure 3.5., it is visually apparent that the CI group have a greater mean rank correlation. However the presence of outliers increases the overall range of the CI group. This affects the statistical significance of the difference between implant groups.

3.4.2. Perceptual difference testing

MDS was conducted on the perceptual difference results matrix for each subject to produce stimulus spaces. The location of the data points within the stimulus space aim to represent as accurately as possible the perceived differences between the original stimuli. In MDS analyses, the goodness of fit of the stimulus space compared to the original data matrix is commonly defined in terms of RSQ or Stress. RSQ is the squared correlation, and shows the proportion of the variance of the best-fit data which the MDS stimulus space can account for (Umat 2005). Stress is the square root of a normalised 'residual sum of squares' and might be considered a 'badness of fit' measure in that a higher Stress indicates a poorer fit of the stimulus space to the original data

(Kruskal and Wish 1976). A stimulus space which well describes the distances between data in the original matrix will therefore show a high RSQ but a low Stress. The improvement in Stress and RSQ values with the number of stimulus space dimensions was used to estimate the appropriate number of ALSCAL dimensions for analysis. Figure 3.6. shows the mean Stress and RSQ values in relation to implant type.



A. **B.**

Figure 3.6. Stress (A) and RSQ (B) values with respect to implant type against number of dimensions.

Although the greatest change is seen between 1 and 2 dimensions there is no visible kneepoint to indicate which would be the appropriate number of dimensions to use. More than 2 dimensions may introduce analysis error in the cases of 2 ABI users who have only 7 active electrodes (JD and RC). The small number of data points in these cases means that a 4 dimensional solution is incalculable and a 3 dimensional solution, although calculable, may be unreliable because the number of data points is not large in relation to the number of parameters.

It has already been discussed that for CI users, the single dimension of place-pitch is best viewed in a two-dimensional MDS solution. As can be seen from Figure 3.7 below, the CI data collected in the current study is consistent with this. For comparison purposes, ABI data was viewed with the same number of dimensions.

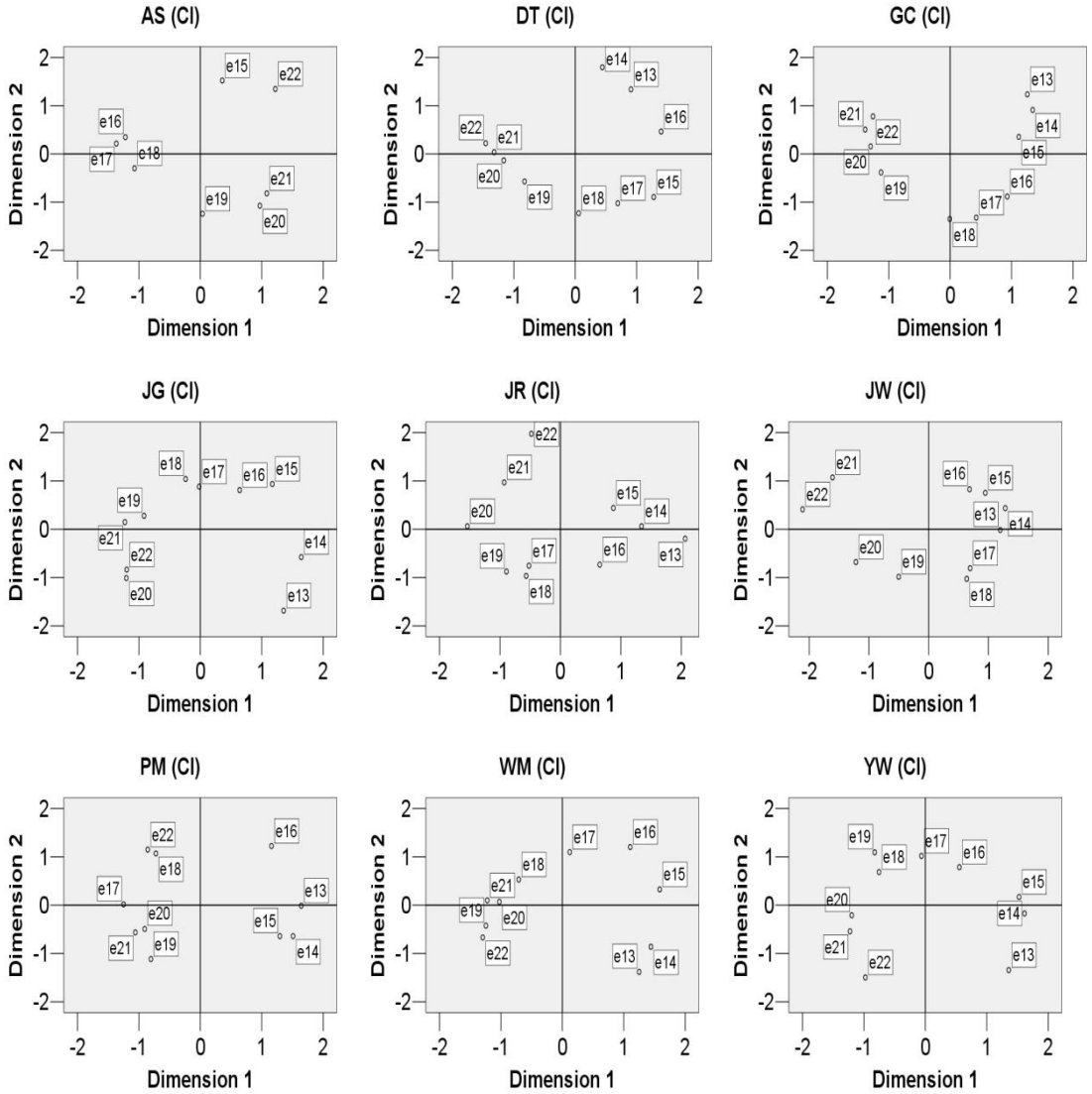


Figure 3.7. Elucidian distance models showing the derived stimulus configuration for 2 dimensional ALSCAL for each of the CI subjects. Electrodes are numbered according to their position within the map, which for CI users also indicates their position on the electrode array. Lower numbers indicate more basal electrodes.

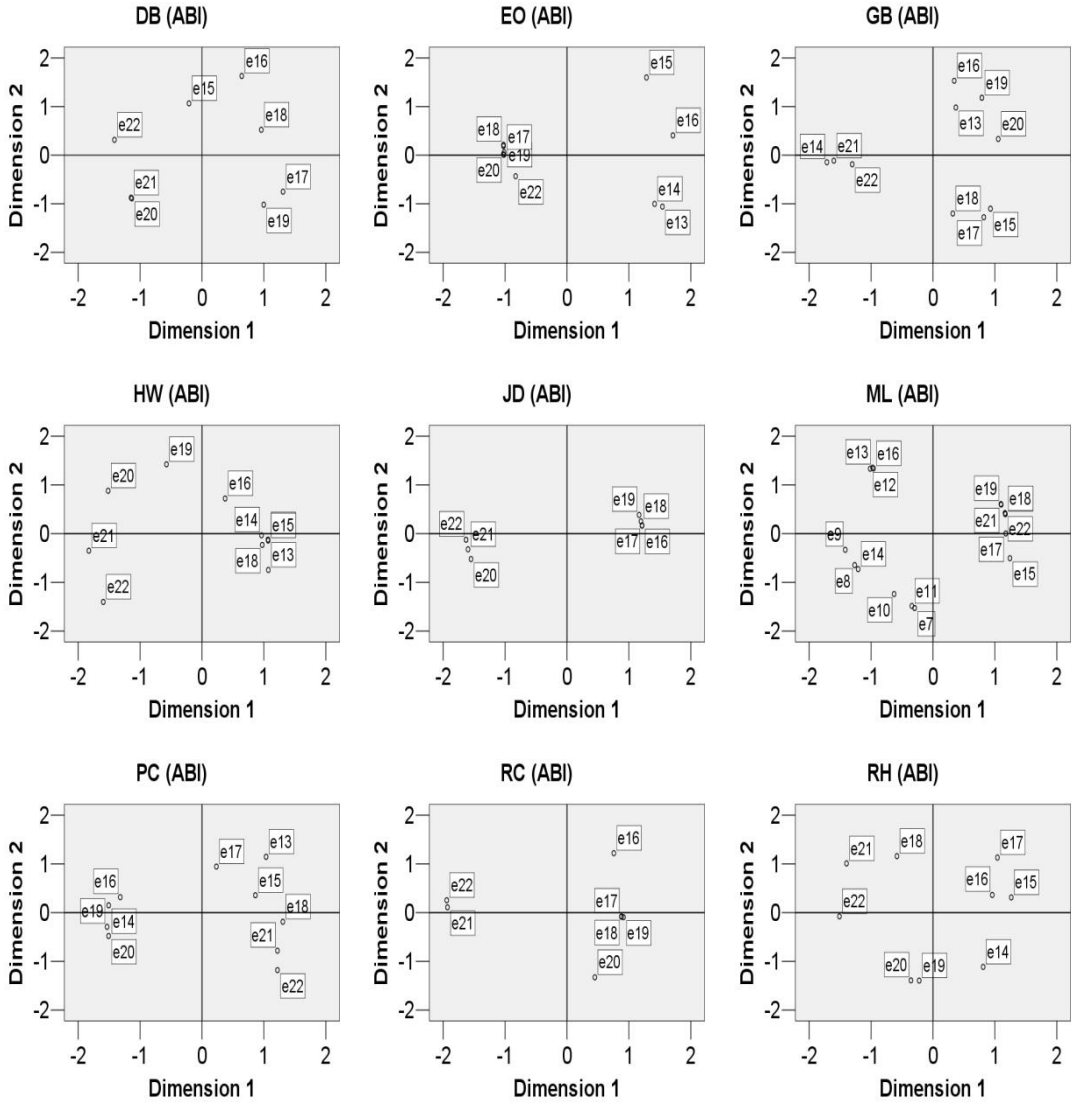


Figure 3.8. Elucidian distance models showing the derived stimulus configuration for 2 dimensional ALSCAL for each of the ABI subjects. Electrodes are numbered in the order in which they are on the subject's map and not with the named electrode location on the array. For example, e22 is the electrode assigned to the lowest frequency range in the clinical map, e21 is the electrode assigned to the next higher frequency range, regardless of its number on the electrode array.

Visual inspection of the above figures indicates that in most cases, the stimulus space of CI users might be described as a curve with relatively evenly distributed data points (electrodes) mostly arranged in map order. In contrast, ABI users often appear to have several data points closely packed together. This indicates electrodes which are not easily distinguishable from each other across a 2 dimensional ALSCAL solution but which, as a group, are distinguishable from other electrodes in the array. These 'clumps' of electrodes are not easily apparent in the CI data. Visual inspection indicates

that for ABI users, 'clumped' electrodes can be seen in the derived stimulus space of both good and poor users. For CI users, a relatively evenly distributed curve can be seen in the derived stimulus space of both good and poor users.

A measure of the goodness of fit of the data to the individual derived stimulus spaces, the RSQ value, was compared between implant groups. A higher RSQ indicates greater consistency across responses.

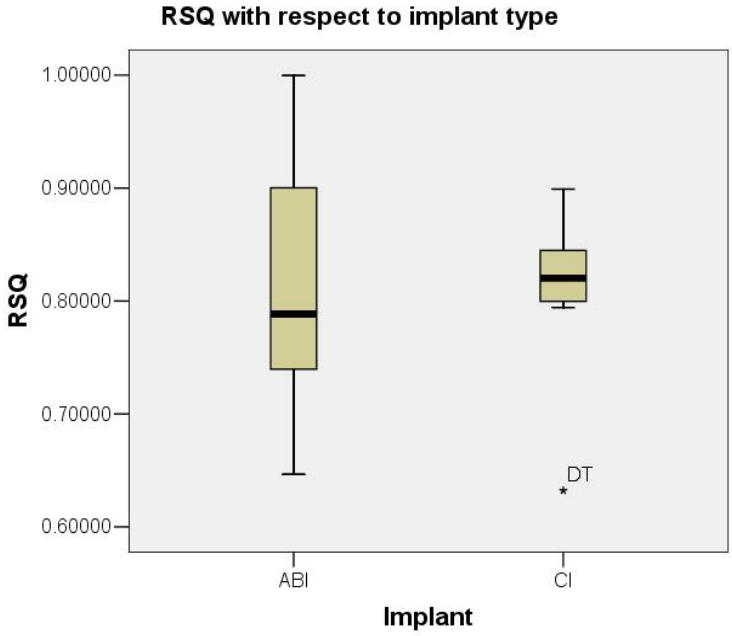
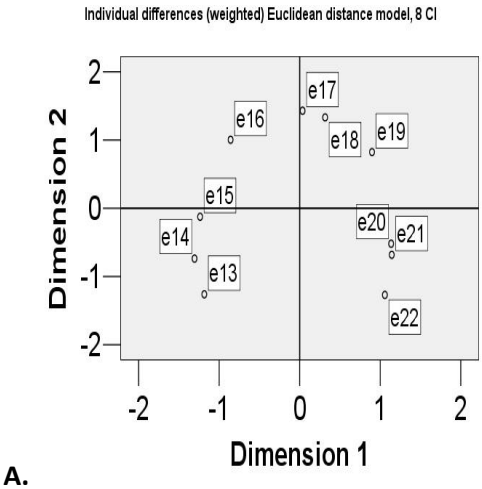


Figure 3.9. Boxplot of RSQ with respect to implant type.

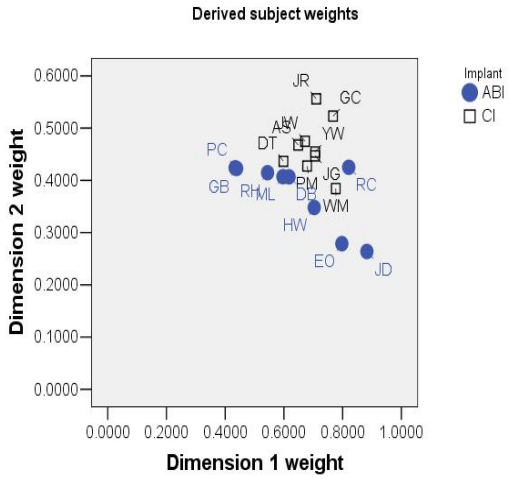
Levene's test for equality of variances confirmed there was no significant difference between the variances for the two implant groups for RSQ ($F=3.614$, $p=0.075$). It may be that the outlier, DT, skewed the CI data such that differences seen in the boxplot were reduced to a non-significant value. A T-test revealed no significant difference between the mean RSQ for the two implant groups (ABI mean=0.819, CI mean=0.814, $t=0.111$, $p=0.913$).

An average stimulus space was calculated via INDSCAL with data from 8 CI users (as noted above, CI user AS was included only in INDSCAL measures for ABI users with 8 or fewer active electrodes). Figure 3.10. shows the average INDSCAL, the derived subject weights for all subjects and weirdness values. Weights show the relative importance of a dimension on a subject's categorising of differences between

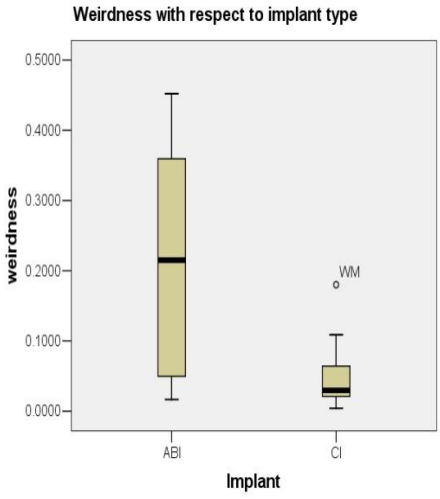
electrodes. Weirdness values show the discrepancy between the ratio of a subject's derived weights and the average ratio of weights of the group, i.e. how different a subject's weights are to everyone else in the comparison (in this case to members of the CI group). Subjects with weights close to the average have smaller weirdness values.



A.



B.



C.

Figure 3.10. A: Elucidian distance model showing the derived stimulus configuration for 2 dimensional ALSCAL for 8 CI subjects. Electrodes are numbered for the order in which they are on the subjects' map, which for CI users also corresponds with electrode location on the array. **B:** Derived subject weights, shown for each subject with respect to implant type. **C:** Boxplot of weirdness with respect to implant type.

Overall vector distance (calculated by $\sqrt{((\text{dimension 1 weight})^2 + (\text{dimension 2 weight})^2)}$) was used as a measure of how well each ABI data set fit the CI INDSCAL space. This and weirdness were examined with respect to implant type. Levene's test for equality of variances confirmed a significant difference exists between the variances

of the two implant groups for overall vector length (F=5.540, p=0.032) and weirdness (F=16.253, p=0.01). T-tests revealed that there was no significant difference between the two implant groups for overall vector distance (ABI mean= 0.760, CI mean=0.838, t=-1.768, p=0.104). However, there was a significant difference between the implant groups for weirdness (ABI mean=0.209, CI mean=0.055, t=9.844, $p<0.05$).

INSDCAL analysis was also conducted using ABI user ML's 10 lowest pitch electrodes as defined by the pitch ranking task rather than user map. The high correlation between map and pitch ranks for ML meant 9 of these 10 electrodes were the same. There was a difference in overall vector length for ML due to small change in dimension 1 weight (vector length with map order=0.72234, vector length with pitch order=0.70436), and a small change in weirdness (weirdness with map order=0.168, weirdness with pitch order=0.0173). Neither change resulted in a significant difference in the mean of ABI users between the two analyses (mean vector length with ML map order=0.7596, mean vector length with ML pitch order=0.7576, t=0.35, p=0.972; mean weirdness with ML map order=0.2086, mean weirdness with ML pitch order=0.2087, t=-0.001, p=0.999). Therefore, comparisons with speech tests were conducted using the original electrode configuration for ML.

3.4.3. Psychophysical results in relation to speech scores.

Speech scores for each study participant are shown in Table 3.2. Please see Section 3.3.6. for an explanation regarding the speech scores used for statistical analysis. For tables 3.2. to 3.7., any element marked with a dash indicates a value not tested.

ABI user	**Open set word list (audio, %)**	**Open set word list (audio-visual, %)**	**Word list calculated improvement**	**Open set sentences (audio, %)**	**Open set sentence (audio + noise, %)**	**Open set sentences (audio-visual, %)**	**Sentence list calculated improvement**
DB	0	80	0.545	0	-	63	0.532
EO	63	90	0.807	79	-	95	0.915
GB	0	52	0.20	0	-	4	0
HW	27	83	0.605	7	-	100	1.000
JD	21	69	0.24	0	-	57	0.411
ML	44	88	0.823	37	-	87	0.854
PC	9	53	0.254	0	-	5	0.050
RC	23	48	0.133	8	-	91	0.855
RH	46	92	0.88	85	-	100	1.000
SR	18	62	0.30	38	-	91	0.87
CI user							
AS	89	-	-	100	78	-	-
DT	36	-	-	34	25	-	-
GC	38	-	-	79	35	-	-
JG	34	-	-	37	12	-	-
JR	94	-	-	98	88	-	-
JW	77	-	-	97	75	-	-
PM	62	-	-	98	68	-	-
WM	74	-	-	100	90	-	-
YW	82	-	-	94	66	-	-

Table 3.2. Speech perception scores for study participants, recorded in their standard clinical review using the user maps that were being used at the time of the psychophysical testing.

Correlations between a subject's psychophysical test measures and clinically recorded speech scores were assessed. All correlations were calculated within implant type groups. Rank correlation (correlation between measured pitch ranking and map ranking) was analysed with respect speech scores to determine whether consistency across different measures of pitch ranking was related to outcomes. Rank correlation was significantly correlated with improvement speech scores for ABI users, and for word and sentence scores for CI users. Values are shown in Table 3.3.

	ABI		CI	
	Pearson correlation	**significance**	**Pearson correlation**	**significance**
Open set word list (audio)	-	-	0.673	0.047*
Open set word list calculated improvement	0.810	0.015*	-	-
Open set sentences (audio + noise)	-	-	0.690	0.040*
Open set sentences calculated improvement	0.802	0.009*	-	-

Table 3.3. The relationship between speech perception and consistency of pitch ranking. Starred elements indicate significant correlations.

Because a pitch rank does not indicate the degree of pitch difference between electrodes, a measure was derived to indicate how clearly defined the pitch differences were. This measure was the range of row-sums of the pitch ranking matrix, normalised to the number of electrodes used (Equation 3.2).

$$\text{Normalised range} = \frac{(\text{maximum sum of a row}) - (\text{minimum sum of a row})}{\text{no. of electrodes tested}} \quad (3.2)$$

The assumption was that subjects who experience a clear pitch variation between electrodes will have a larger range of row-sums because their responses to each electrode pair will be more consistent. For example, a perfectly discriminated stimulus set, and a consistent responder, would lead to zero row-sum for the lowest pitch electrode and the maximum row-sum (9x8 when using 10 electrodes) for the highest pitch electrode. Those with a poorer understanding of pitch ranking or a less well defined pitch variation would be less consistent in their rankings, meaning more equal row-sum scores across electrodes, and a smaller difference between the maximum and minimum row-sums. The hypothesis was that those with a more defined pitch or a greater ability to pitch rank (a greater row-sum maximum difference) would also have better speech scores. The normalised range scores were significantly correlated with both word and sentence scores for CI users, and for sentence improvement scores for ABI users. Results are shown in Table 3.4.

	ABI		CI	
	Pearson correlation	**significance**	**Pearson correlation**	**significance**
Open set word list (audio)	-	-	0.737	0.023*
Open set word list calculated improvement	0.136	0.728	-	-
Open set sentences (audio + noise)	-	-	0.845	0.004*
Open set sentences calculated improvement	0.695	0.038*	-	-

Table 3.4. The relationship between the normalised range score in the pitch ranking task and speech scores. Starred elements indicate significant correlations.

Because rank correlation was significantly correlated with speech scores, the MDS stimulus space was evaluated to see whether the stimulus space supported one or other of the pitch or map ranks. For CI users, an MDS pitch rank was derived from the horseshoe shape of the two-dimensional MDS solution where one could be identified, aided by the known tonopticity of the CI array (Figure 3.11). For ABI users, the tontopicity is not pre-determined and a horseshoe shape is not often apparent. Therefore MDS ranks were obtained on the basis of electrode position along dimension 1 due to a higher weight for dimension 1 than dimension 2 in all ABI users (Figure 3.12).

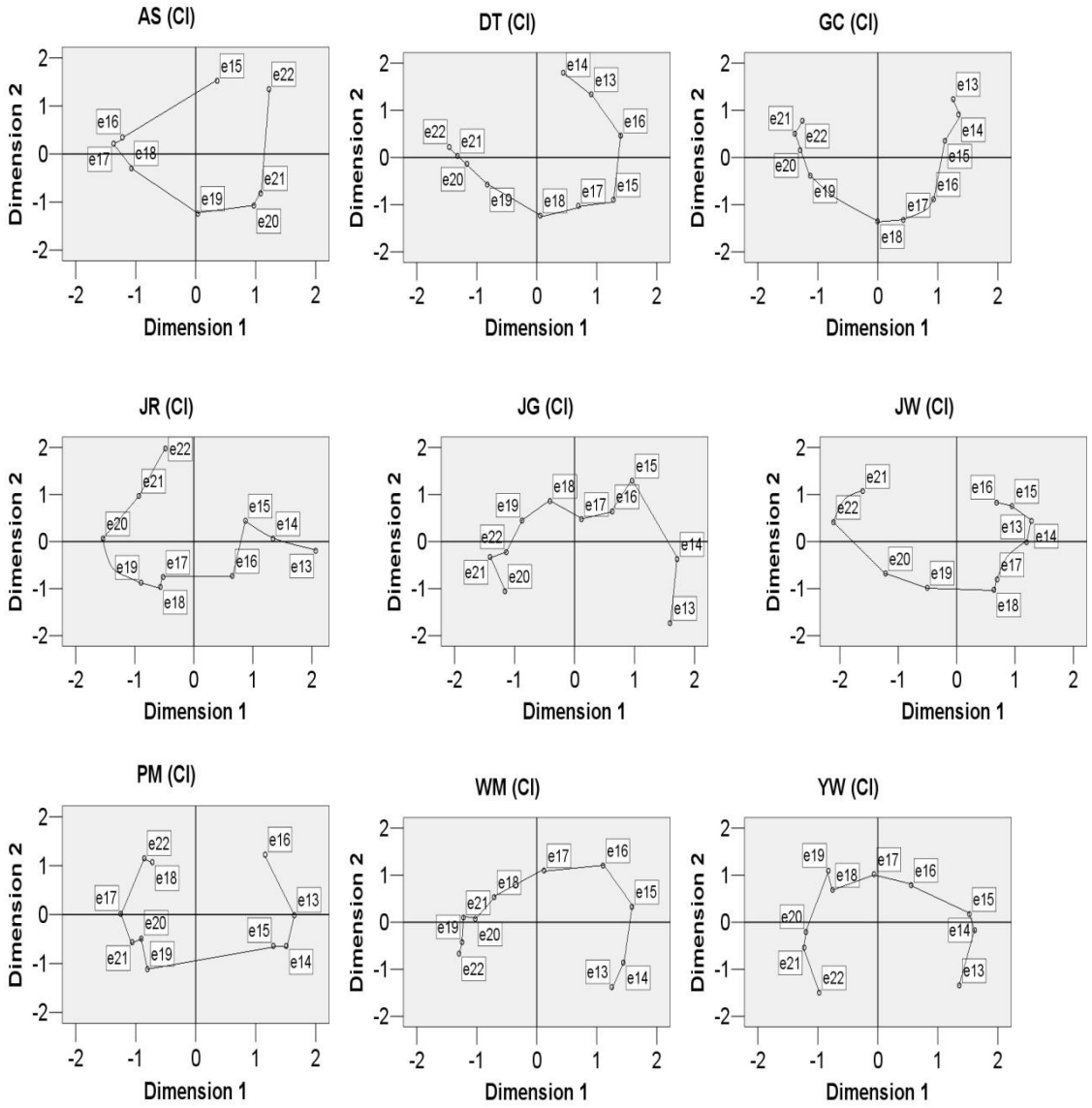


Figure 3.11. Elucidian distance models showing the derived stimulus configuration for 2 dimensional ALSCAL for each CI subject. Lines show the pitch rank derived from the MDS solution. Electrodes are numbered in the order in which they are on the subject's map, which also corresponds to the location on the array.

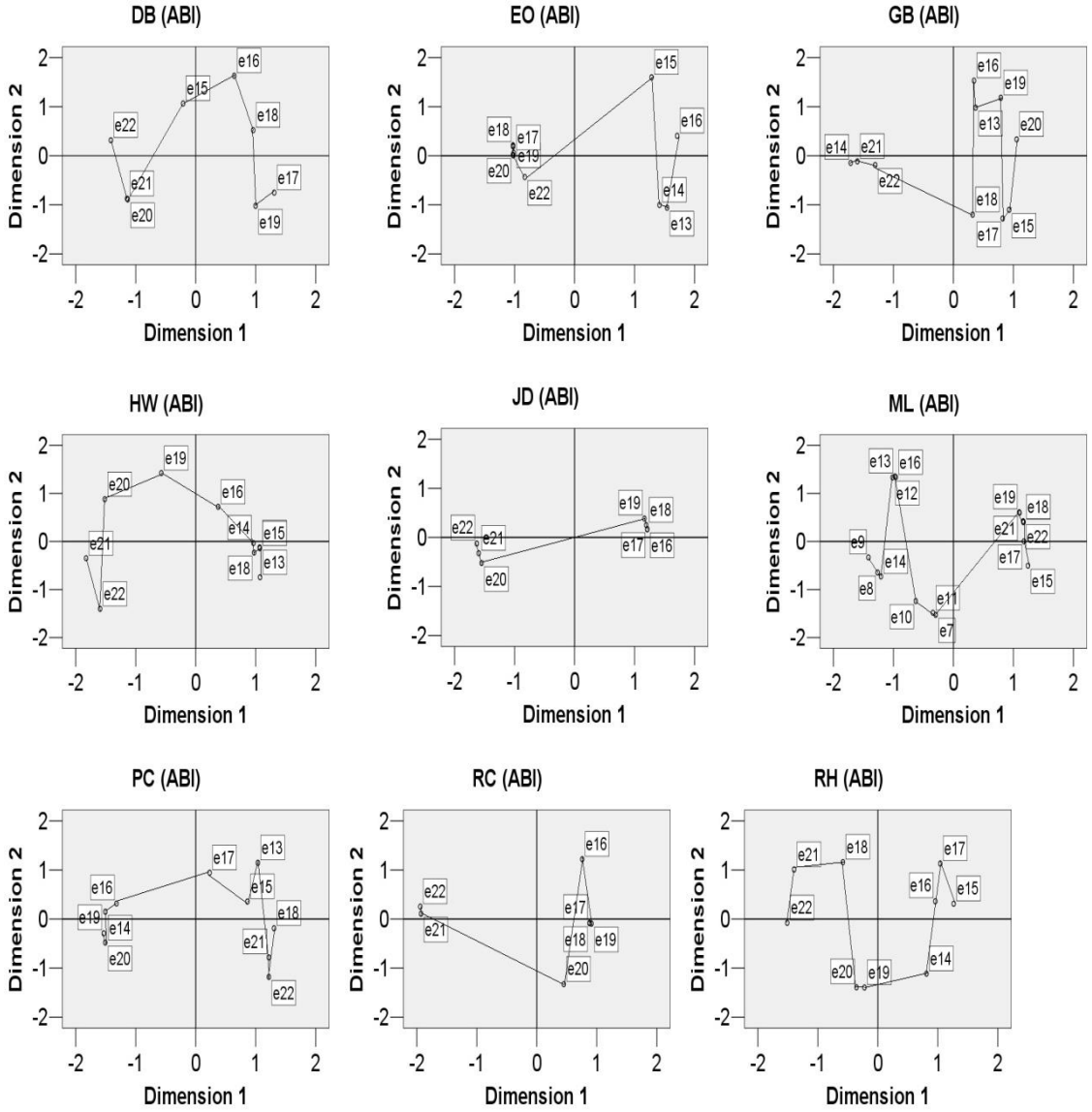


Figure 3.12. Elucidian distance models showing the derived stimulus configuration for 2 dimensional ALSCAL for each ABI subject. Lines show the pitch rank derived from the MDS solution. Electrodes are numbered in the order in which they are on the subject's map, which does not correspond to the location on the array. 22 denotes the lowest pitch electrode.

For ABI users, the MDS rank was significantly correlated with the map rank in 6 users (EO, HW, JD, ML, RC, RH, $p<0.05$) and with the pitch rank in 4 users (EO, ML, PC, RH, $p<0.05$). For 6 users, the MDS rank was more correlated with the map than the pitch rank (DB, GB, HW, ML, RC, RH). For 2 users it was more correlated with the pitch rank than the map rank (EO, PC). There was no pattern as to whether these cases were good users or poorer users. ABI user SR did not complete the MDS task and therefore was not included in this analysis. ABI user JD did not complete the pitch

ranking task and therefore was included only in the comparisons between the MDS ran and the map order.

For CI users, the MDS rank was significantly correlated with both the map order and pitch rank in all users (map order $p<0.005$, pitch rank $p<0.05$). The MDS rank was more correlated with the map order than pitch rank in 5 subjects (DT, JG, JR, PM, WM). For 4 users the correlation was equal (AS, GC, JW, YW). There was no pattern as to whether these cases were good users or poorer users.

The relation of the MDS rank and the map rank was then compared to speech scores for ABI users. As the map rank was the ranking used at the time of speech testing, the degree to which this agrees with the MDS ranking may indicate the accuracy of the map rank. This is because, whilst patients may be poor at understanding a pitch ranking task and therefore may provide an erroneous pitch ranking, the MDS procedure allows judgements based on any aspect of auditory perceptual difference between electrodes and might be more reliable (Collins and Throckmorton 2000). The hypothesis was that those users with more accurate maps (i.e. a higher degree of correlation between the MDS rank and the map rank) would also have higher speech scores. There was a significant correlation between sentence scores for ABI users and the degree of agreement between the MDS rank and the map rank (see Table 3.5.)

	ABI		**CI**	
	Pearson correlation	**significance**	**Pearson correlation**	**Significance**
Open set word list (audio)	-	-	0.066	0.866
Open set word list calculated improvement	0.339	0.372	-	-
Open set sentences (audio + noise)	-	-	-0.114	0.771
Open set sentences calculated improvement	0.741	0.022*	-	-

Table 3.5. The relationship between speech scores and the degree of agreement between MDS ranking and map ranks. Starred elements indicate significant correlations.

Because RSQ is a measure of the goodness of fit of the MDS data matrix to the derived stimulus space, it was compared to speech scores to determine if those subjects with consistency in their responses to the MDS task, i.e. a larger RSQ, also had better

outcomes. RSQ for the 2-dimensional MDS solution was not correlated with any speech score measures for either implant group. Values are shown in Table 3.6.

	ABI		CI	
	Pearson correlation	**significance**	**Pearson correlation**	**Significance**
Open set word list (audio)	-	-	0.391	0.298
Open set word list calculated improvement	-0.316	0.407	-	-
Open set sentences (audio + noise)	-	-	0.332	0.382
Open set sentences calculated improvement	0.005	0.989	-	-

Table 3.6. The relationship between speech perception and RSQ.

CI users are known to generally have better speech scores than ABI users. There were also visually apparent differences between the MDS solutions for ABI users and CI users. Because the MDS procedure examines the perceptual difference between electrodes, the degree of agreement between a subject's derived MDS stimulus space and that of an average CI user (i.e. the weirdness value) was compared to speech scores. The aim was to determine if ABI subjects with a more CI-like MDS solution also had better speech outcomes. There was no significant correlation between weirdness and speech scores (see Table 3.7.).

	ABI		CI	
	Pearson correlation	**significance**	**Pearson correlation**	**significance**
Open set word list (audio)	-	-	0.330	0.385
Open set word list calculated improvement	-0.421	0.259	-	-
Open set sentences (audio + noise)	-	-	0.440	0.236
Open set sentences calculated improvement	0.070	0.858	-	-

Table 3.7. The relationship between speech perception and weirdness.

3.5. Discussion and Clinical Implications

3.5.1. Discussion

The current study aimed to determine the relation between place-pitch perception and speech outcomes in ABI users. Results showed that the degree of correlation between two measures of ABI pitch ranking (our experimental method and the method used in the clinic to determine the ABI map rank) was correlated with speech scores. This indicates that the ability to detect and reliably define pitch differences between electrodes is related to outcomes. Because pitch variations between ABI electrodes

may very small and difficult to accurately judge, or may not even be present (Kanowitz, Shapiro et al. 2004), an ABI user with a low rank correlation may therefore have been inaccurate in one or both pitch ranking methods due to small or undefined pitch differences which make the task difficult. The poorer rank correlation may not therefore be because the one rank or method is less accurate than the other, but because no accurate rank is determinable.

Where ranks are determinable, the subject must be able to understand and perform the pitch ranking task. Instead of a difference in quantity (i.e. quieter or louder can easily be described as less or more), pitch differences might be described as a difference in quality (Stevens 1985). It does not lend itself naturally to being assigned a 'higher or lower' rank and can be difficult to describe to patients with no familiarity of judging it in the past. Some patients may therefore answer inaccurately during testing because they are not truly basing their judgements on pitch. This situation would also manifest as a poor correlation between pitch rank and map rank. This may be seen in CI subjects DT and JG. For CI users, it is generally assumed from cochlear mechanics that a systematic pitch variation exists between electrodes and as such, no clinical pitch ranking is conducted as standard. Baumann and Nobbe (2006) demonstrated that for all but the most apical electrodes, in a MEDEL Combi 40+ cochlear implant, electrodes do elicit an orderly and linear pitch variation when stimulated. Although for some CI users some of the active electrodes on the array can be found to be non-tonotopic upon testing (Henshall and McKay 2001), CI users DT and JG in the current study were seen to have particularly low correlations between standard map rank and measured pitch rank. The measured ranks would be highly unlikely as this would most likely indicate unusual anatomy or electrode placement anomalies, neither of which is the case for either subject (no ossification is reported for JG despite an aetiology of meningitis). Therefore, patient ability to complete the task is the most probable cause for the low correlation between measured pitch rank and assumed cochlear tonotopicity. If in these two cases we assume the map rank to be accurate, we cannot conclude that the poorer speech scores in these two users were due to inaccurate mapping. However it may be that ability to consistently identify pitch ranks is important for speech perception skills in daily life, or that these two skills are correlated with each other. It may be that, in these two CI cases, difficulty in the pitch ranking task highlights a general difficulty in accurately coding incoming signals which then translates into poorer speech perception.

For ABI users the pitch rank cannot be pre-assumed so it may be difficult to determine if a lower correlation between the map ranks and pitch ranks is due to subject ability for the task or an indeterminable pitch rank.

The normalised range of row-sum scores in the pitch ranking task gave a measure of the consistency of responses during pitch ranking. The normalised range score was correlated with all recorded speech scores for CI users, and for CUNY improvement scores for ABI users. This indicates that the ability to clearly rank variations in pitch (or perceive larger pitch differences) is related to some speech scores. These results may support previous studies who have suggested that improved speech scores are related to a larger perceived pitch range in CI (Dorman, Smith et al. 1990) or ABI (McCreery, Shannon et al. 1998) users, indicating that pitch perception is an important factor for users of either device.

Variation in pitch ranges between subjects may be one explanation for differences in MDS solutions between CI and ABI users. For CI users, an inability to determine differences between large perceptual distances causes the curving of an otherwise one-dimensional solution, assumed to be place-pitch (Collins and Throckmorton 2000). Where ABI data does not have the same curve, it may be because the differences between stimuli are never large enough to be subject to the same limiting effect. In this case, the entire MDS solution for the ABI user might be likened to a small portion of the CI horseshoe shape. For example, whilst RC has a larger normalised row-sum range score, and therefore consistently identifiable pitch differences, the MDS solution is better described as 'clumps' of electrodes rather than a horseshoe. The consistently identifiable pitch differences here may therefore be smaller than those perceived by CI users.

The 'clumping' of electrodes is not restricted to users with smaller normalised row-sum range scores. If ABI users with consistently identifiable pitch differences also show 'clumps' in MDS data, it may be that pitch is not the overriding auditory perceptual difference and so any identifiable pitch differences are actually relatively small when stimuli are judged according to overall sound quality. A further example of this can be seen in the RSQ data. High RSQ values were observed for all subjects, with no significant difference in the values between implant groups which indicates that ABI

users are able to consistently identify auditory perceptual differences between electrodes as well as CI users. However RSQ was not related to speech scores. This indicates that all users experience some structure to the auditory perceptual differences between electrodes but that general consistency in an MDS task is not related to speech outcomes. It may be that the auditory perceptual differences identified in the MDS task are not ones which are useful for speech perception.

Where auditory perceptual differences related to electrode position other than place-pitch exist, it is not known how many dimensions would be appropriate, or even whether these non-tonotopic auditory differences apply to all or some electrodes along the array (Collins and Throckmorton 2000). Whilst for CI users it might be assumed that any curvature is not necessarily indication of a separate perceptual dimension, this might not be assumed for ABI users who can describe a variety of sound percepts following stimulation of different implanted electrodes. INDSCAL analysis of the current study data showed a significant difference in the weirdness between the two implant groups using a 2 dimensional solution. This indicates that ABI MDS solutions are significantly different on average to those of CI users, possibly suggesting that interactions between pitch and other auditory percepts may be significantly different between implant groups.

Because place-pitch change is assumed to be the overriding auditory perceptual change experienced for CI users when electrode position is changed, one might expect that ABI users with more 'CI-like', curved 2 dimensional solution may also be experiencing reliable pitch variations. However, there were no significant correlations between weirdness and speech scores. This indicates that where ABI ALSCAL solutions are more similar to a CI user, (i.e. where weirdness is smaller) the definition of the auditory perceptual differences between electrodes may still be qualitatively different.

Investigations involving ABI users are inherently difficult due to other factors which cannot be controlled for such as differences in general health related to NFII, anatomy post-surgery, exact paddle location, and number of active electrodes. In addition, the relative number of patients for whom an ABI is suitable is small, therefore reducing sample sizes when conducting local rather than national or international studies.

Despite this, the current study has indicated areas where further consideration for research and clinical application may be appropriate.

3.5.2. Clinical Implications

If the relationship seen in the current study between speech scores and rank correlation was at least partially due to inaccuracy of the map ranking, or difficulty in pitch ranking, it would indicate that ensuring sufficient time during initial clinical mapping to evaluate pitch ranking accurately may assist in maximising ABI benefit. ABI users become accustomed to the frequency allocation of their map with use and any subsequent frequency re-allocation causing a shift, either basal or apical, can reduce performance (Friesen, Shannon et al. 1999). Therefore, an ABI user who may have changes in their active electrode configuration over time due to non-auditory stimulation must re-acclimatise to a new frequency allocation each time this occurs. The same is true for any frequency reallocation in response to changes in clinically-obtained pitch ranking data. Patients with little discernible pitch or those who have difficulty performing a pitch ranking task may present with an apparently changing pitch rank each time it is tested. In these cases a change in allocated frequencies may not necessarily indicate that a more accurate ranking was obtained but may instead increase acclimatisation time to the implant.

The existing clinical method of pitch ranking, based on the Steinhaus procedure, creates a rank as the test progresses. Each pitch ranking of an electrode pair actively affects subsequent selection of electrode pairs for comparison, such that some electrode pairs will not be presented as the ongoing ranking indicates they are not required. An error in judgment for one comparison may therefore cause a change in the ongoing ranking. Taking the average rank derived from a set of three runs of the test is recommended to reduce error (Long, Nimmo-Smith et al. 2005). For ABI users, the pitch rank of electrodes is previously unknown, so discrepancies between runs cannot indicate whether the ABI user has poor pitch ranking abilities or if there is no consistent pitch difference to rank. The pitch ranking procedure used in the current study therefore allowed all possible electrode comparisons to be made and a rank derived post-hoc from a greater number of multiple responses so that erroneous responses may have a smaller impact on the derived rank. The method described in the current study may therefore

provide more complete data for initial clinical mapping to assist confidence in assigning accurate ranks to active electrodes at an early stage in clinical programming.

For paediatric ABI patients, behavioural pitch ranking procedures cannot be performed, causing uncertainty in electrode to frequency allocation. For these patients, an objective measure related to pitch ranking is required. O'Driscoll (2012) measured auditory event-related potentials in response to stimulation of electrodes with known high, mid and low frequency percepts in adult CI and ABI patients to determine whether behaviourally measured pitch variations were related to objective electrophysiological measures. No significant difference was found in the latencies of the cortical event-related potential (CERP) in response to activation of electrodes assigned to different frequency inputs in adult ABI users.

For adult patients who are able to respond behaviourally, the correlation between speech scores and the degree of agreement in MDS and map ranks may also provide a useful measure during clinical mapping. The high RSQ for all patients in the current study indicates that consistent auditory perceptual differences of some type are available to users, even for those whose pitch ranking is poorly related between ranking procedures (for example ABI users DB and GB). It may be that a combination of MDS and a multiple comparison pitch ranking procedure can provide the best range of data for optimally mapping ABIs. This would require a large amount of clinic time and patient co-operation and concentration. However it would inform clinicians of not only the pitch rank of electrodes if one exists, but also the relative degree of auditory perceptual difference between them. If little or no auditory perceptual difference is noticed between several active electrodes then the activation of these in a user map may actually cause more confusion than information. In such a case, different inputs would all result in a very similar percept, creating a barrage of excitation without much perceptual difference to distinguish between variations in the input signal. An MDS procedure may therefore help identify if it is better to deactivate a number of these electrodes to keep active only those with a significant degree of difference. The idea of deactivating electrodes with little or no perceptual difference or that are not consistently tonotopically related to other electrodes was continued and examined in a study by McKay, Azadpour et al (2013) in which MDS data from the present study was used to

inform decisions regarding creation of experimental maps using fewer but more clearly distinguishable active electrodes.

3.6. Conclusions

This study has highlighted the importance of place-pitch pitch perception during initial ABI programming. Sentence and word improvement scores in ABI users are related to tonotopically ordered user maps and to maps in which pitch variations are more easily identified. This has fulfilled aim 1 of this study, in which the relationship between place-pitch perception and speech outcomes in ABI users was sought.

Where pitch variations are not accurately identified, either due to small pitch variations or pitch ranking ability, ABI users may still demonstrate consistency in identification of non-tonotopic auditory perceptual differences. This indicates that a range of auditory percepts are available to ABI users. Multidimensional scaling (MDS) analysis showed that the pattern of auditory perceptual differences experienced by ABI users is significantly different to that experienced by CI users. There was no correlation between ABI speech scores and patterns of auditory discrimination that were more similar to those of CI users. This may indicate that the auditory perceptual differences experienced by ABI users are qualitatively different to those of CI users and are not dominated by pitch-perception but instead may be more related to timbre. This has fulfilled aim 2 of this study which aimed to determine whether auditory percepts other than pitch are related to electrode position. Consistency in identification of non-tonotopic auditory perceptual differences is not related to speech scores.

Clinically, this study may have implications for the manner in which pitch ranking is derived. A method which involves multiple comparisons and includes comparisons between all available electrodes may provide information not only regarding an overall rank, but also the ease with which pitch variations were identified. This information may assist in patient counselling regarding expectations and possible outcomes. In addition, use of an MDS procedure may identify electrodes which are not easily discriminated. Following further research, this may influence the number of auditory electrodes chosen to remain active in a user map.

Chapter 4

Electrically-Evoked Event Related Potentials in Adult ABI Users

4.1. Abstract

Background and Aims

Studies of electrically and acoustically evoked event-related potentials (ERPs) in cochlear implant (CI) users have concluded that some features of the N1, P2, MMN and P3b are related to speech scores. Few studies have systematically investigated this in adult auditory brainstem implant (ABI) users. As ABI outcomes are variable, investigations regarding outcomes and auditory system excitation, such as ERPs, would help to expand the evidence base for this area of audiology. Drawing on the previous experiment in the current thesis, which found that some measures of electrode discrimination are correlated with speech scores in adult ABI users, the current study had two aims: a) to determine if electrophysiological measures of electrode discrimination correlate with behavioural measures of electrode discrimination in adult ABI users; b) to determine if features of electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users.

Method

Subjects were 9 ABI and 8 CI users who participated in experiment one of this thesis. All were users of Cochlear Ltd CI or ABI devices. Direct activation of individual implanted CI or ABI electrodes was conducted via a standard clinical programming interface in order to record N1, P2, MMN and P3b ERPs. The choice of activated electrodes for this study was based on multi-dimensional scaling (MDS) analysis from the previous experiment in this series. Two pairs of electrodes were selected for each subject: one provided a small auditory perceptual difference; one provided a medium auditory perceptual difference. Each pair was presented in an oddball paradigm to elicit a P3b and an MMN for each of the degrees of perceptual difference. Each deviant stimulus was also presented alone to elicit N1, P2 and to provide a baseline from which to identify MMN. Data were collected using a 64-channel Biosemi EEG system. Data preparation was conducted using BESA software and ERP extraction was conducted using MATLAB.

Results

N1, P2, MMN, P3a and P3b were elicited in ABI users, with N1 and P2 topographies comparable to CI users. Difficulty in controlling for variations in auditory perception meant a wide range of ERP latencies were identified. A trend was seen for longer P3b

latencies with increasing task difficulty, and where identified, longer MMN latencies with increasing task difficulty, MMN latency was significantly negatively correlated with normalised row-sum pitch ranking scores from the previous study in this series. With respect to speech scores, a significant negative correlation was seen between MMN latency and speech scores for CI users but not ABI users. A significant correlation was seen between P3a amplitude and word scores in ABI users along with a trend towards a negative correlation between P3a latency and speech scores. No significant relationships were seen between CERP or P3b data and speech scores.

Conclusions

The presence of MMN, P3a and P3b in ABI users indicates signal processing beyond initial cortical detection. The relationship between MMN latency and normalised row-sum pitch ranking scores and the trends seen in P3b and MMN latency changes suggest some support for the hypothesis that electrophysiological measures of electrode discrimination are related to behavioural measures of electrode discrimination. However, the small ABI user population available for study recruitment coupled with variations in identified ERP latencies and amplitudes meant there were insufficient data to accurately test this and so fulfil aim 1 of this study. Similarly, the hypothesis that electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users was not proven, although the presence of some trends and significant correlations means that neither was it completely disproven. This study has shown that electrophysiological measures of electrode discrimination are recordable in ABI users, but the relative uncertainty regarding the degree of auditory perceptual difference to which they are elicited may limit their efficacy.

4.2. Introduction

There is little in the scientific literature regarding auditory brainstem implant (ABI) outcomes and auditory system stimulation during ABI usage despite the fact that ABIs are being increasingly used in the NHS. Although studies have examined speech perception outcomes following ABI implantation (Nevison, Laszig et al. 2002; Colletti, Carner et al. 2005; Colletti and Shannon 2005), few have systematically examined mid and late event-related potentials (ERPs) in relation to this. However, mid and late electrically-evoked and soundfield-evoked ERPs have been examined in relation to speech perception abilities in cochlear implant (CI) patient groups. Despite some methodological differences, several studies have concluded that mid and late ERP morphology is often correlated with outcomes (Kubo, Yamamoto et al. 2001; Sing, Liasis et al. 2004; Gordon, Tanaka et al. 2005; Kelly, Purdy et al. 2005; Roman, Canevet et al. 2005; O'Driscoll 2012). Differences exist between the CI and ABI patient groups in terms of both site of electrical stimulation and auditory system anatomy. This means CI studies cannot be relied upon to infer what excitation is occurring during ABI stimulation. However, as the main source of ERP studies in relation to outcome measures in implant users, CI studies were drawn on to understand more about the manner in which they have been conducted and to aid in the design of the present study.

ERPs have been extensively examined and their characteristics and components described in both normal hearing and hearing impaired individuals (Picton and Hillyard 1974; Moller, Jannetta et al. 1994; Sharma, Kraus et al. 1997; Firszt, Chambers et al. 2002a). Such research can suggest normative values for ERP waveform characteristics or morphology and some also suggest which neural sources components may originate from. Comparison of a recorded ERP component against pre-defined normative values can indicate if it is outside such values. Identification of an ERP component is therefore interpreted as indication of the integrity of neural structures and pathways up to and including the neural generators of that ERP component.

Examination of auditory system excitation during activation of an ABI may therefore provide information regarding the integrity of the auditory system and its response to electrical stimulation that has a direct relevance to speech perception abilities. Colletti

and Shannon (2005) found that detection of an amplitude modulated signal was correlated with speech outcomes and was better in ABI users with non-tumour pathologies. They concluded that modulation detection was important for speech perception and that tumour growth and removal impeded the vascular supply of the cells important for this. ERPs such as mismatch negativity (MMN) and P3b may be considered as analogous to modulation detection because they are elicited to a change within a stream of stimuli. Studies have also shown that MMN correlates well with behavioural auditory discrimination tasks (Naatanen, Brattico et al. 1992). The previous experiment in the current series has already shown that behavioural measures of pitch variation are correlated with outcomes in ABI users. Therefore, examination of MMN presence and latency in ABI users may indicate user ability to detect changes in stimulus electrode.

In CI users, the presence of a sound-field evoked MMN was correlated with a better rating on scales of auditory perception and speech production (Category of Auditory Performance and Speech Intelligibility Rating) (Sing, Liasis et al. 2004). Identification of MMN was not always possible in poorer CI users (Kelly, Purdy et al. 2005). Its latency has been shown to be negatively correlated with duration of implant use regardless of outcomes (Sing, Liasis et al. 2004) or with the presentation level required to discriminate between two words (Roman, Canevet et al. 2005). Its duration was found to be positively correlated with scores on word and sentence perception tests (HINT sentences and CNC words lists) (Kelly, Purdy et al. 2005). One difficulty that may arise during MMN recording is the possible elicitation of a further ERP, the P3a. This is elicited when attention is drawn to the deviant stimulus in cases of an unexpected or very large stimulus change and may degrade an MMN (Kraus and McGee 1994). Despite this, MMN presence has been shown to provide information regarding CI speech outcomes. This has not yet been investigated in ABI users.

The late ERP, the cortical event-related potential (CERP), has already been investigated in ABI users. O'Driscoll (2012) recorded electrically-evoked CERP in adult CI and ABI users following activation of high, mid and low pitched electrodes, and different current levels. He found that the N1 and P2 latencies in CI users were negatively correlated with speech scores, and the P2 amplitude was positively correlated with ABI speech scores. No significant difference was found in the latencies or amplitudes of the

CERP recorded in response to electrodes of different pitches in ABI users. This may agree with the findings of Gordon et al. (2005), who found 3 distinct CERP morphologies across their CI patient group, each with a positive peak at differing latencies. Those with the shortest latency (identified as a 'Type 1' response) correlated with better open or closed set word discrimination, with increasing impairment of performance through Type 2 responses to Type 3 responses. Similarly, Kelly et al (2005) determined that P2 latencies were negatively correlated with speech scores in CI users. All these studies suggest that CERP latency is negatively correlated with speech scores.

With regard to the long-latency auditory-evoked ERP, P3, latencies were found to be longer in cochlear implant users with a 'fair' behavioural consonant recognition score compared to those with a good (>70%) score (Kubo, Yamamoto et al. 2001). Latency was not significantly different between these good users and a control group, and the authors surmised that P3 latency may indicate the time required for signal processing to occur. Kubo et al. (2001) also note from previous CI studies that whilst the CERP latency does not change as a discrimination task becomes harder, the P3 latency does. This was taken to indicate that the P3 reflects evaluation of the incoming sound, a task important for speech perception. Kelly et al. (2005) note that poorer CI users have been reported to have had recordable CERPs but not P3 responses. These results suggest that identification of a P3 and examination of its latency may indicate a CI subject's performance rating. This has not yet been investigated in ABI users.

Kubo et al. (2001) recorded ERPs and speech perception on several different occasions and found that the negative correlation between P3 latency and speech scores was stronger after 1 year of CI use compared to 6 months of implant use. Sing et al. (2004) also noted that the presence of a MMN in some of the poorer CI performers might indicate that given more or different rehabilitation, speech scores might improve with time. The suggestion was that the recorded ERPs are indicators of what the auditory system is capable of, and that rehabilitation is required in order to achieve that potential.

MMN, CERP and P3b may therefore be used to investigate different aspects of the auditory system. The sensory CERP indicates that auditory sensation is reaching different parts of the auditory pathway, and the MMN and P3 indicates automatic and

conscious change discrimination respectively. All can be recorded in response to the same stimulus, thus avoiding any compounding effects of stimulus differences on the recorded responses.

In ABI users, an electrically-evoked ERP (EERP) investigation will allow us to categorise the patterns of excitation that result from direct stimulation of a part of the auditory system whose mechanics are currently much less understood than those of the more peripheral regions. Comparisons with other user groups may help to categorise similarities or differences in auditory excitation following stimulation of different parts of the auditory system. Understanding the pattern of excitation occurring in the auditory system following ABI stimulation may help to indicate whether neural generators which have been identified in previous studies as being important for auditory sensation or speech perception are still functioning. As with CI studies, EERP information might then be compared against outcome measures in the ABI patient group to determine any correlations.

The previous experiment in this series showed that accurate pitch ranking and clearly determinable pitch variations are correlated with speech scores. Therefore, this experiment aimed to investigate electrophysiological measures of discrimination between electrodes to determine whether ERPs can support behavioural methods of electrode discrimination and show any correlation with clinically recorded speech scores. This investigation may assist in determining whether objective measures of electrode discrimination may be used to assist in clinical ABI programming. Such information would benefit users, such as paediatric patients, who are unable to provide the in-depth behavioural information that is required during programming.

4.3. Subjects and Methods

4.3.1. Subjects

Nine of the 10 ABI users and 8 of the 9 CI users who were recruited for experiment 1 of this study took part in the present experiment 2. One CI user (WM) and 1 ABI user (SR) who participated in experiment 1 declined to participate in experiment 2. Participant details are shown in Table 3.1. in the previous chapter. All participants were post-lingually deafened and were recruited from the Manchester Auditory Implant

Centre. As outlined in the previous chapter a relatively small number of ABI users were available for recruitment due to a small population size and additional factors such as ill-health due to NFII or non-use of the device. Single centre ABI studies may often be faced with such factors but the need for more ABI research necessitated the completion of this study with a relatively small sample size.

ABI users were implanted with the Cochlear Nucleus 21-channel ABI, which is based on the Cochlear Nucleus 24M Cochlear Implant. CI users were implanted with Cochlear Nucleus 24M or 24RE devices. All subjects used the ACE processing strategy on a day to day basis, and subjects used either 3G or Freedom speech processors.

4.3.2. Apparatus setup

As with experiment 1 of this series, described in Chapter 3, test stimuli were computer generated using algorithms from Cochlear Nucleus Implant Communicator (NIC) software and a MATLAB interface. During the experimental procedures, test stimuli were presented directly from MATLAB to the patient's implant via a standard Cochlear clinical programming pod and Freedom speech processor. Prior to the experiment, a comfortable loudness check (C-level) and loudness balancing of all test stimuli were conducted using Cochlear's Custom Sound 2 clinical programming software and delivered via the same programming pod and speech processor.

ERP testing took place in a quiet room, away from general public traffic. During all ERP recording, subjects watched a muted film of their choice with subtitles. Subjects sat in a reclining chair with headrest to try and minimise muscle movement and were asked to relax throughout.

ERP recording was via the Biosemi Active Two^{TM} 64-channel EEG recording system, using a 2068Hz sampling rate. A 5th order sinc low-pass anti-aliasing filter was applied during recording with -3 dB at 416.8 Hz (416.8 Hz is derived from 0.2035 multiplied by the sampling rate). Recordings with this system are referenced to a single reference during recording and can be re-referenced during analysis. A Biosemi headcap was used to secure the 64 pin-style Ag-AgCL electrodes within the standard 10-20 International System. Standard Biosemi electrode conducting gel was used maintain the quality of the electrode contact with the skin, ensuring electrode offsets were stable and

between ± 50 mV. During cap placement, all electrodes were positioned over the head away from the speech processor programming wire and coil. For every subject, the coil placement meant that 1 to 3 recording electrodes were compromised due to RF interference. This was minimised by separating electrode cables and the processor lead as much as possible. Further minimisation of artefact was conducted during preparation for analysis.

4.3.3. Stimuli

Test stimuli were 60 ms - duration pulse trains delivered at the patient's comfortably loud current level (C level). Pulse width, inter-phase gap and rate were the same as in their clinical map, and are shown in Table 3.1. in the previous chapter. The pulse trains were presented in runs of 20, 40, 100 or 200. Runs consisted of activation of either a single electrode, or a combination of two. The choice of tested electrode was based on results from results of the MDS task described in Chapter 3. Run parameters and electrode choice are detailed below.

4.3.4. Tests

4.3.4.a. Maximum current level check

The maximum current level check followed the same design as described in Section 3.3.4.a. Electrodes were activated individually and patients used a 7-point scale to indicate the loudness perceived, varying from 'first hearing' to 'too loud'. Stimuli levels were increased by the tester using step sizes of 2-5 current units until the patient response matched 'loud but comfortable'. Only the electrodes chosen for ERP testing were checked during this test.

4.3.4.b. Loudness balancing

The loudness balancing was a shortened version of the procedure described in Section 3.3.4.b. Following C-level checks, the electrodes chosen for ERP testing were activated in succession and the current levels of the latter stimuli were manually adjusted until the stimuli were perceived to be at the same loudness as the first.

4.3.4.c. P3b and MMN recording

To elicit P3b and MMN, two electrodes were activated in an oddball paradigm. Using the stimulus space co-ordinates from the 2-dimensional MDS solution in experiment 1,

two pairs of electrodes were chosen for each subject; one with a small auditory perceptual difference and one with a medium auditory perceptual difference. The 2-dimensional vector denoting the relative distance between the co-ordinates of electrodes within the pair (c) was calculated using Equation 4.1. where a and b denote the co-ordinates from the two electrodes within the pair.

$$c = \sqrt{(a^2 + b^2)} \qquad (4.1.)$$

Within subjects, the value of c was greater for the electrode pair with the medium auditory perceptual difference than the small auditory perceptual difference. The medium and small differences were subjectively confirmed by the participant following initial electrode identification. In some cases, no subjective difference in auditory perceptual difference of the two pairs could be reliably confirmed and the choice of electrodes was varied until a difference in size of auditory perceptual difference could reliably be confirmed. The actual vector length and the difference between the vectors of electrode pairs with a small or medium perceptual difference varied between subjects. As the distances in a stimulus space are only relative, equal values across patients did not mean an equal degree of perceptual difference. The location on the array of the chosen pair of electrodes also varied between patients.

Subject	Small auditory perceptual difference		Medium auditory perceptual difference	
	Standard Electrode	Deviant electrode	Standard Electrode	Deviant electrode
ABI subject				
DB	11	9	9	6
EO	17	20	11	10
JD	4	3	15	2
GB	7	4	7	10
HW	17	14	10	7
ML	12	22	13	10
PC	12	10	5	11
RC	4	3	9	6
RH	13	11	10	8
CI subject				
AS	15	16	17	22
DT	20	22	13	14
GC	13	15	18	22
JG	18	22	13	15
JR	14	13	18	21
JW	13	14	21	22
PM	17	18	21	22
YW	20	21	18	19

Table 4.1. Tested electrodes.

The electrode judged to be the higher pitched of the pair was presented as the standard and the electrode judged to be the lower pitched of the pair was presented as the deviant. Tested electrodes are shown in Table 4.1. Each of the two pairs of electrodes was presented within 2 different paradigms; once with the ISI and standard-deviant ratio for eliciting P3b and once with the ISI and standard-deviant ratio for eliciting MMN. Four oddball paradigms were therefore presented to each subject. Details of these paradigms are seen in Table 4.2. The ISIs were derived from Lightfoot and Kennedy (2006) and were amended for the current study due to limitations of the test equipment which did not allow for ISIs shorter than 1.7 ms.

Paradigm	Oddball runs		Deviant-alone runs (number of stimuli)	ISI (s)
	Number of standard stimuli	Number of deviant stimuli		
P3b; small auditory perceptual difference	80	20	20	1.8 +/- 15%
P3b; medium auditory perceptual difference	80	20	20	1.8+/- 15%
MMN; small auditory perceptual difference	150	50	50	1.7
MMN; medium auditory perceptual difference	150	50	50	1.7

Table 4.2. Paradigm parameters.

For each of the two run lengths, 5 lists were created to denote the order of standard and deviant stimuli. No deviant stimulus could follow another deviant and at least 4 standard stimuli were presented at the beginning of each run to create a strong memory trace of that stimulus. Other than these two rules, the order of standards and deviants within a list was pseudorandom. During testing, MATLAB software chose one of the 5 lists at random for each run. To ensure sufficient data collection, 3 to 4 runs of each paradigm were recorded. This provided a minimum of 60 or 150 recorded deviants in the P3b and MMN paradigms respectively. To elicit the P3b, subjects were asked to silently count the number of deviant stimuli presented in a run of 100 stimuli and were asked after each run how many they counted. To elicit the MMN, subjects were asked to ignore all sounds they heard.

4.3.4.d. Deviant-alone conditions

Runs consisting of only the deviant electrode in each of the four oddball paradigms were also presented. Runs contained 20 or 50 stimuli and maintained the ISI of the P3b and MMN paradigms respectively (see Table 4.2). Three or four runs of each deviant-alone paradigm were presented to ensure recording of a minimum of 60 or 150 deviant-alone responses in the P3b and MMN paradigms respectively. For the deviant-alone runs corresponding to the P3b paradigm, subjects were asked to count all stimuli silently and were asked the count at the end of each run. This was to maintain the level of attention to the stimulus throughout recording. For the deviant-alone runs corresponding to the MMN paradigm, subjects were asked to ignore all stimuli.

4.3.5 Analysis

Data were prepared in BESA and exported to MATLAB for peak data extraction. All data was down-sampled to 250 Hz before applying automatic artefact correction for blinks (+/-75 µV) and filtering. Filtering for all P3b paradigms (including deviant-alone runs) was between 0.1-20 Hz, and for all MMN paradigms was 0.3-30 Hz. The artefact rejection threshold during averaging was +/-75 µV. Significant artefact was seen in all channels for subject EO so EKG automatic artefact correction was applied with a threshold of +/-75 µV. All data were referenced to a common reference, made possible by the recording of 64 channels. Baseline correction was applied using 100 ms of the pre-stimulus recording. All data were treated as right sided stimulus. Therefore after BESA data preparation, the EEG electrode configuration was reversed upon exporting to MATLAB for the 8 patients who had a left sided implant.

Each of the four paradigms had four possible conditions; standard electrode, deviant electrode, deviant-alone and difference (deviant minus deviant-alone). For all but 2 subjects, this therefore resulted in 16 conditions being recorded (4 conditions in each of 4 paradigms). Subject DB decline to complete either MMN paradigm and subject JD declined to complete one of the two MMN paradigms.

Grand mean waveforms were created in MATLAB per implant group and per relevant condition. Grand mean topographies for each relevant condition per implant group identified an average time window, and the electrode at the centre of the topographical response of the ERP. The identified electrode varied depending on the chosen ERP. For example, the electrode central to the topography identified for the N1 is more frontal than that identified for the P3b, consistent with the documented topography in the literature (Rugg and Coles 1995; Wunderlich and Cone-Wesson 2006). To avoid fluctuations due to stimulus artefact or noise, ERP amplitude was not calculated using the identified electrode alone. Instead, the amplitude was the mean amplitude of the identified electrode and the 8 surrounding electrodes, averaged over a 30 ms time window. Any one of the cluster of 9 electrodes identified in the grand average was accepted as the centre electrode during ERP identification for individual subjects. Data from the 8 surrounding electrodes was then used to calculate the mean amplitude in the same way as in the grand mean data.

The extracted latency was taken as the peak latency of the centre electrode within a 30 ms time window around the identified ERP. Whilst grand mean EEG traces provided a mean time window, the individual time window for each subject was accepted outside of this if the topography of the suspected ERP was acceptable. ERP time window and centre electrode identification relied greatly on acceptable topography. This avoided accidental identification due to noise or stimulus artefact.

The recording of both standard and deviant-alone conditions resulted in 4 N1 and P2 conditions being recorded for each subject; one each from the standard and deviant within the P3b small auditory perceptual difference paradigm, and one each from the standard and deviant within the P3b medium auditory perceptual difference paradigm. N1 and P2 were not extracted from the MMN paradigm as the implanted electrodes stimulated within these paradigms were identical to the P3b paradigm, the only differences being attention to the stimuli, length of run and rate of stimulation. To reduce noise, the 4 N1 and P2 conditions were averaged so that one mean N1 and P2 could then be extracted for each subject. This was possible as no significant difference was found between CERP amplitudes or latencies recorded in response to activation of implanted ABI or CI electrodes assigned to medium or low frequencies (O'Driscoll 2012).

P3b latencies and amplitudes were extracted from the deviant EEG trace which was recorded during the oddball paradigm. This provided 2 P3b values, one for the small auditory perceptual difference paradigm and one for the medium auditory perceptual difference paradigm.

MMN latencies and amplitudes were extracted from the difference trace created from subtracting the deviant-alone recording from the deviant recording for each of the 2 MMN paradigms. This provided 2 P3b values, one for the small auditory perceptual difference paradigm and one for the medium auditory perceptual difference paradigm. The deviant was not compared to the standard from the same oddball run as in these recordings the standard stimulus was activation of a different implanted electrode. Using a deviant-alone paradigm for MMN identification avoided any possibility of variation between responses from different electrodes showing an artificial difference not related to MMN.

P3B and MMN latencies and amplitudes were examined with respect to paradigm (small auditory perceptual difference and medium auditory perceptual difference). All ERP latencies and amplitudes were examined with respect to clinically recorded AB word scores, CUNY sentence scores and results from behavioural measures of electrode discrimination described in experiment 1, Chapter 3 of this series.

4.3.6. Speech scores

Speech scores used during statistical analysis in this experiment of the study were the same as described in Section 3.3.6. Scores from AB word lists and CUNY sentences recorded during the latest clinic appointment were used as the speech perception scores against which ERP data was compared. For ABI users, the calculated improvement scores derived from the raw speech scores were used. For CI users, the speech-in-noise score for CUNY sentences and the speech-in-quiet score for AB word lists were used.

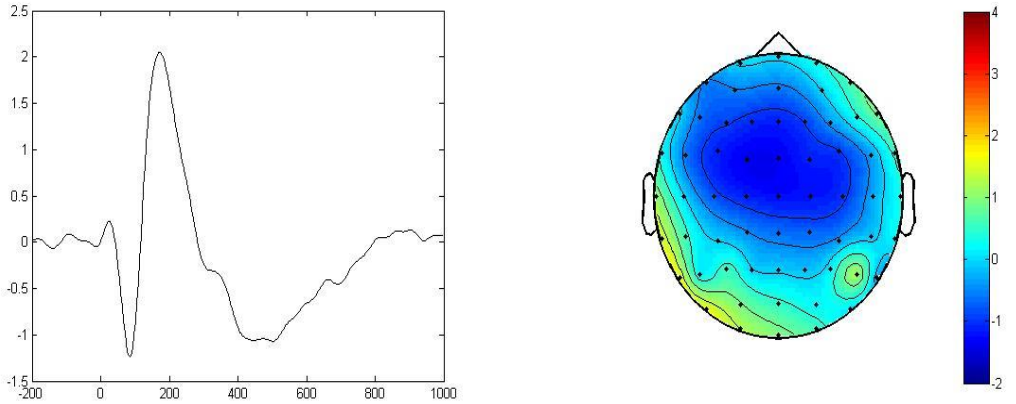
4.4. Results

The results for the ERP data are summarised in section 4.4.1. Correlations with speech perception data are summarised in section 4.4.2., and correlations with behavioural measures of discrimination are summarised in section 4.4.3.

4.4.1. ERP data

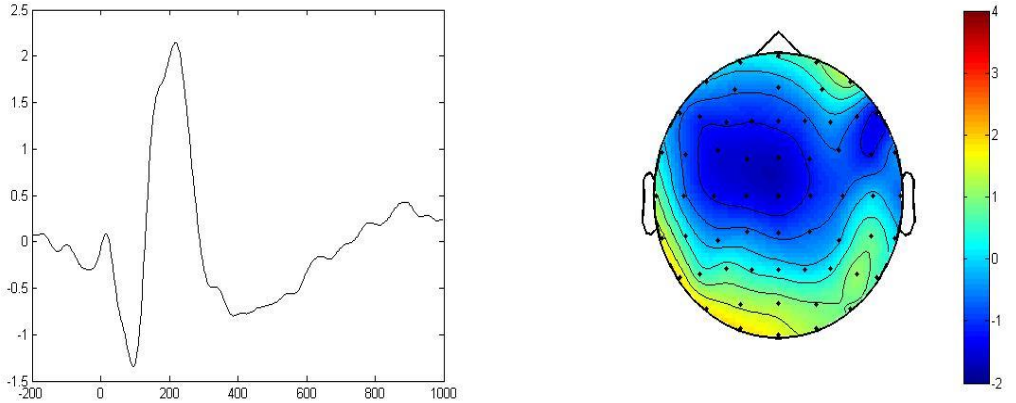
4.4.1.a N1

A mean N1 was identified in each subject. Grand mean waveforms were created for the N1 data for each implant group.



A. **B.**

Figure 4.1. Grand mean waveform (A) and topography (B) for the N1 for the CI group. The waveform (A) shows the mean of the centre electrode (Fz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (86 ms), with the colourbar denoting amplitude in µV.

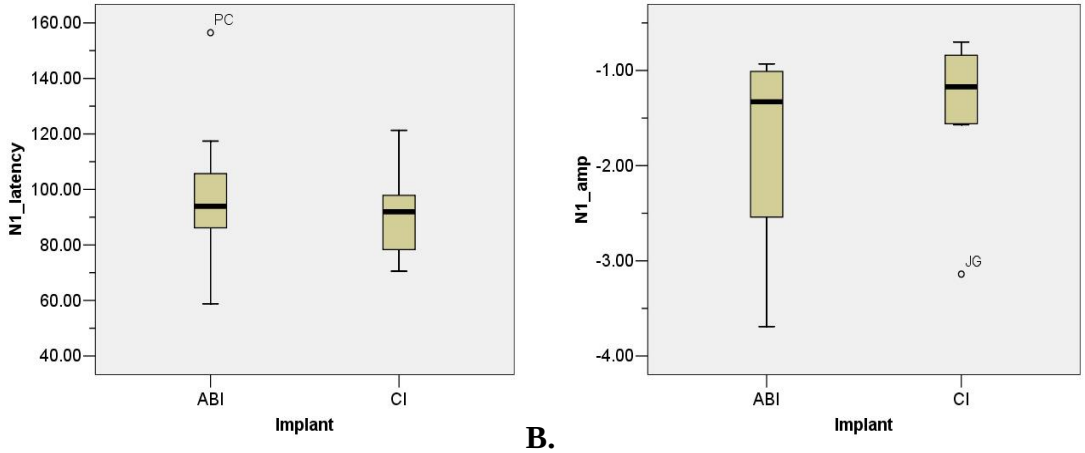


A. **B.**

Figure 4.2. Grand mean waveform (A) and topography (B) for the N1 for the ABI group. The waveform (A) shows the mean of the centre electrode (Fz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (94 ms), with the colourbar denoting amplitude in µV.

Levene's test of equality of variance showed no significant difference in the variance of the N1 latency between groups (F=1.010, p=0.331) and an independent samples T-Test showed no significant difference in the mean latency between groups (t=0.617, p=0.546). Similarly, there was no significant difference in the variance of the N1 amplitude between groups (F=1.201, p=0.290) and no significant difference in the mean amplitude between groups (t=-0.972, p=0.347). From visual inspection of Figure 4.3, it

may be that data from the outlier JG has affected the significance of any difference in the variance of N1 amplitude between groups.

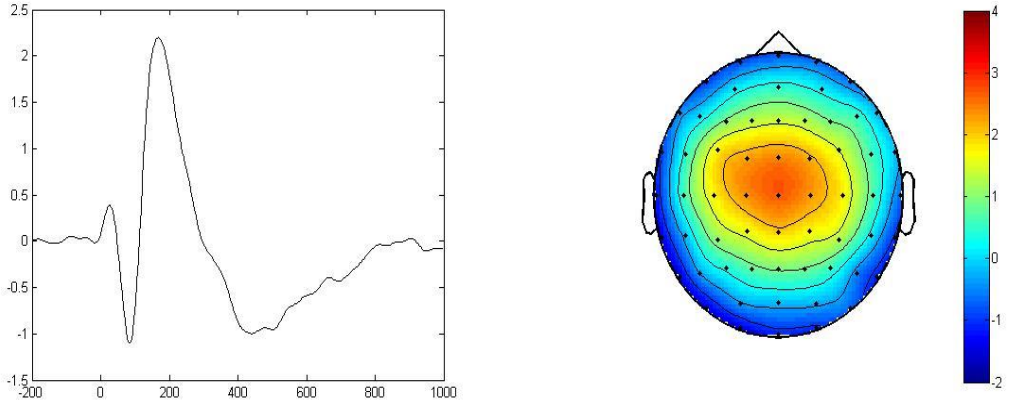


A. **B.**

Figure 4.3. Boxplots showing the range of N1 latencies and amplitudes between groups. **A.** Y axis shows time in ms. **B.** Y axis shows amplitude µV. Outliers are labelled.

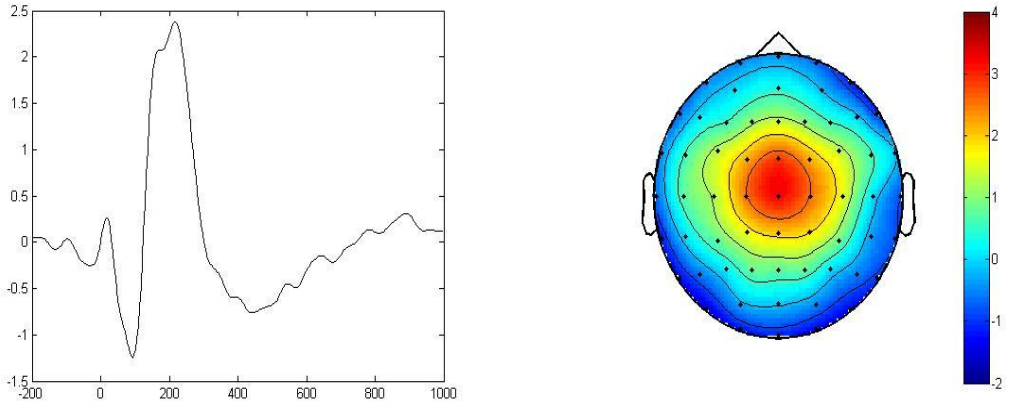
4.4.1.b. P2

A mean P2 was identified in each subject. Grand mean waveforms were created for the P2 data for each implant group.



A. **B.**

Figure 4.4. Grand mean waveform (A) and topography (B) for the P2 for the CI group. The waveform (A) shows the mean of the centre electrode (Cz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (168 ms), with the colourbar denoting amplitude in µV.



A. **B.**

Figure 4.5. Grand mean waveform (A) and topography (B) for the P2 for the ABI group. The waveform (A) shows the mean of the centre electrode (Cz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (219 ms), with the colourbar denoting amplitude in µV.

Levene's test of equality of variance showed no significant difference in the variance of the P2 latency between groups (F=4.391, p=0.054) and an independent samples T-Test showed no significant difference in the mean latency between groups (t=0.967, p=0.349). Similarly, there was no significant difference in the variance of the P2 amplitude between groups (F=1.059, p=0.320) and no significant difference in the mean amplitude between groups (t=-0.320, p=0.753).

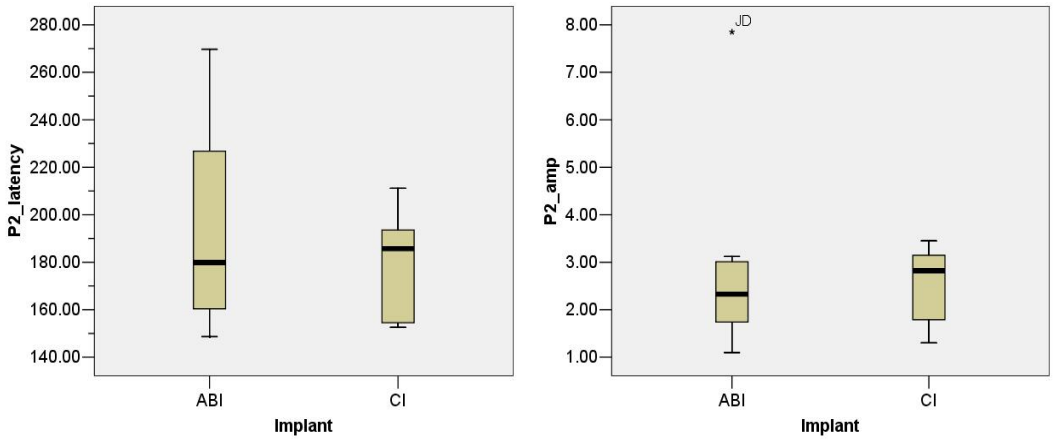


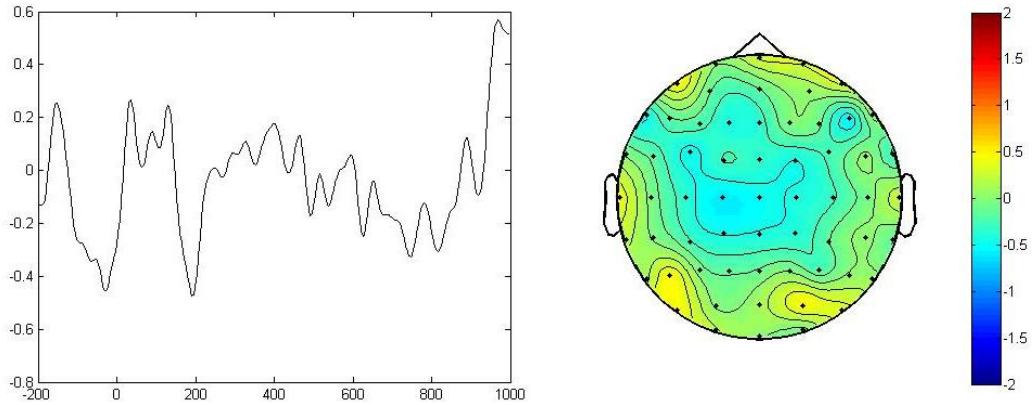
Figure 4.6. Boxplots showing the range of P2 latencies and amplitudes between groups. **A.** Y axis shows time in ms. **B.** Y axis shows amplitude µV. Outliers are labelled.

The extremely large standard deviation seen in the both implant groups for the latencies of both N1 (ABI group=27.41, CI group=16.01) and P2 (ABI group = 42.27, CI group =

22.27) significantly reduces the power of the small sample used in this study. As the difference in the variance of the P2 latency between groups is very close to a significant value, a larger sample size may have more reliably confirmed the presence or absence of any significant differences. However, the present ABI sample size was unavoidable due to participant availability.

4.4.1.c. MMN

A grand mean was created for each implant type per MMN paradigm. A grand mean difference trace was created from the grand mean of the standard trace subtracted from the grand mean of the deviant trace. Figure 4.7 shows the grand mean MMN identified in the small auditory perceptual difference paradigm for CI users.



A. **B.**

Figure 4.7. Grand mean waveform (A) and topography (B) for the MMN to a small perceptual difference for the CI group. The waveform (A) shows the mean of the centre electrode (Cz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (195 ms), with the colourbar denoting amplitude in µV.

MMN was not identified in every CI subject. For the small auditory difference paradigm, MMN was identified for 4 of the 8 CI users, and a P3a for the remaining 4. Grand means were created for these two sub-groups and are shown in Figure 4.8.

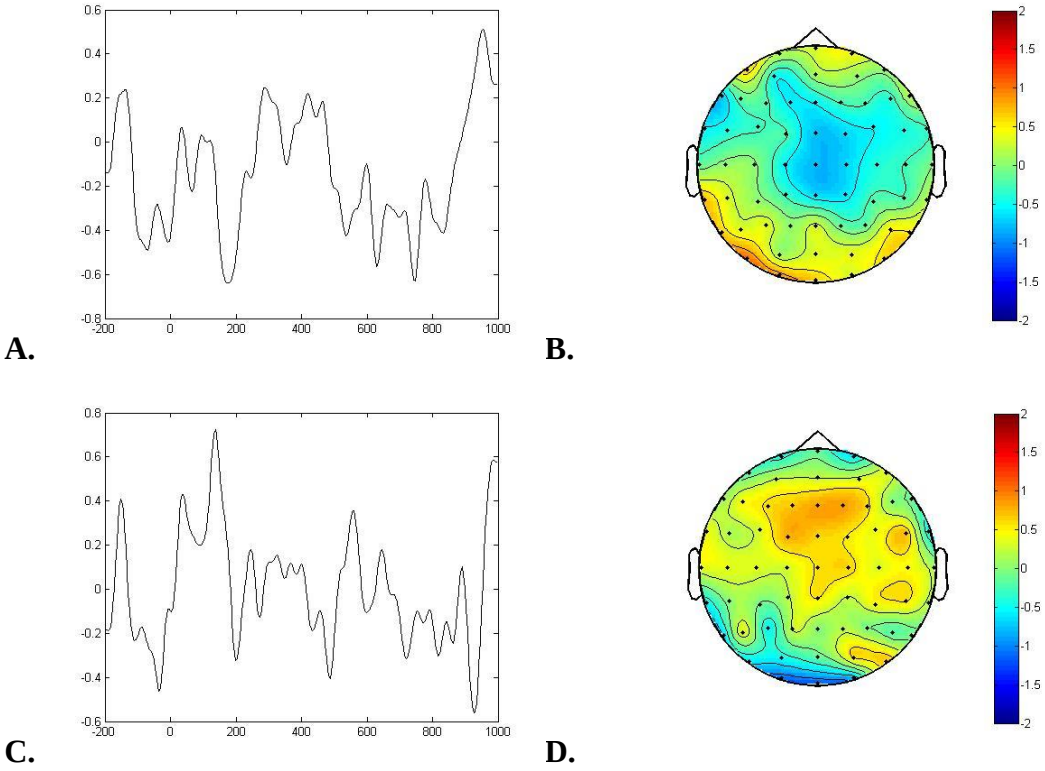
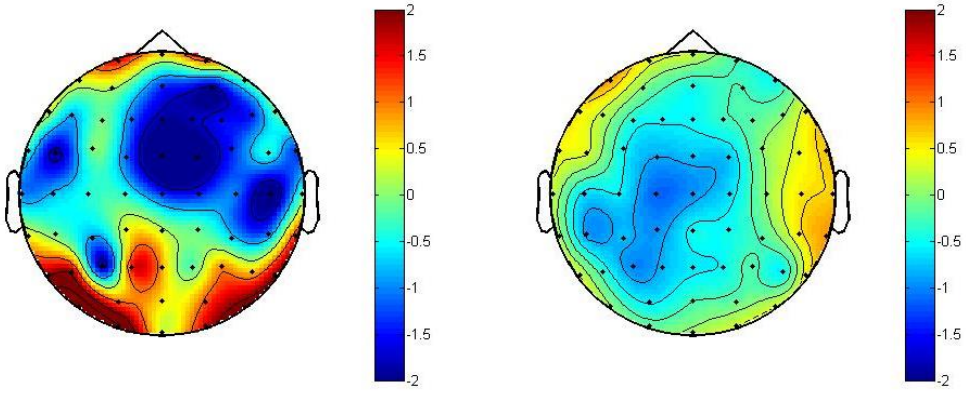


Figure 4.8 Grand mean waveforms (A and C) and topographies (B and D) for the MMN to a small auditory perceptual difference for the CI sub groups. The MMN subgroup is shown in A and B. The P3a sub group is shown in C and D. The waveforms (A and C) shows the mean of the centre electrode (Cz and FCz respectively) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topographies (B and D) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (164 ms and 133 ms respectively), with the colourbar denoting amplitude in µV.

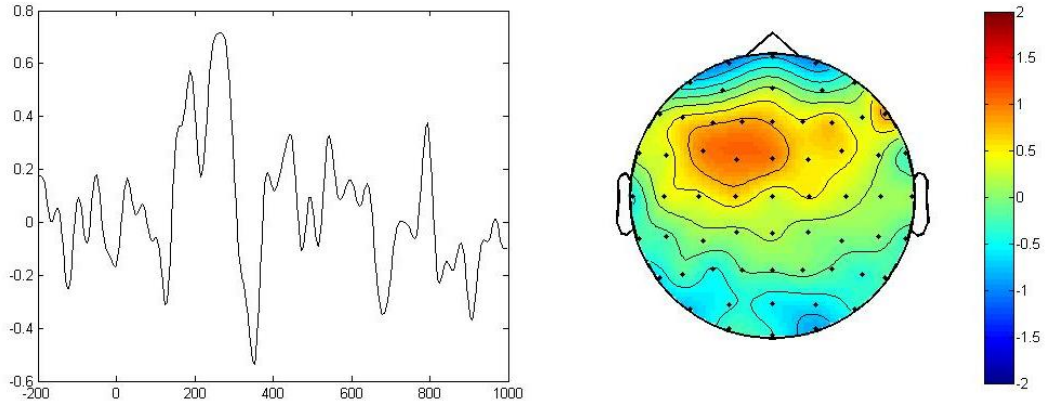
In the medium auditory difference paradigm, MMN was identified in 2 of the 8 CI users (JR and JW). The averaged EEG recordings for 4 CI users contained too much noise to reliably identify MMN (PM, YW). MMN was absent in the remaining 4 users (AS, DT, CG, JG). A grand mean for the 2 identified MMNs was not possible as the difference in MMN latency for JR and JW (140 ms and 94 ms respectively) caused smearing of traces and loss of identifiable ERP peak. The two individual traces are shown in Figure 4.9



A. **B.**

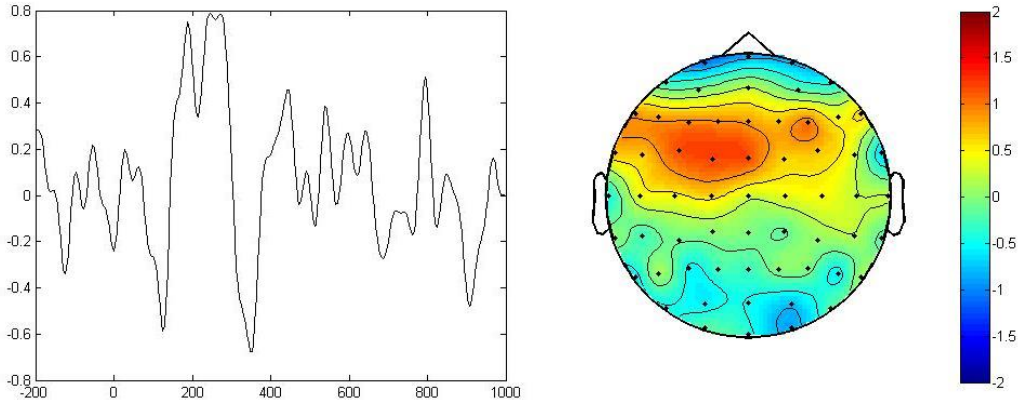
Figure 4.9. Topographies for MMN to the medium auditory difference paradigm for CI users JR (A) and JW (B). The topography shows the mean amplitude over 9 electrodes surrounding the identified ERP peak within a 30 ms time window around the identified latency, with the colourbar denoting amplitude in µV. (A) Peak electrode is FC2 and latency is 140 ms. (B) Peak electrode is FC1 and latency is 91 ms.

For the ABI group, MMN was identified in 2 users and P3a in 5 in the small auditory difference paradigm. One ABI user declined to participate in MMN recording and for 1 ABI user the average EEG trace was too noisy to reliably identify MMN presence or absence. The overall grand mean for the ABI group for the small auditory perceptual difference paradigm is shown in Figure 4.10. The grand mean for the P3a subgroup is shown in Figure 4.11. No grand mean was possible for the ABI MMN subgroup (ABI users EO and RH) as the latency difference between the two identified MMNs (218ms and 152ms respectively) meant a cancelling of the effect during averaging.



A. **B.**

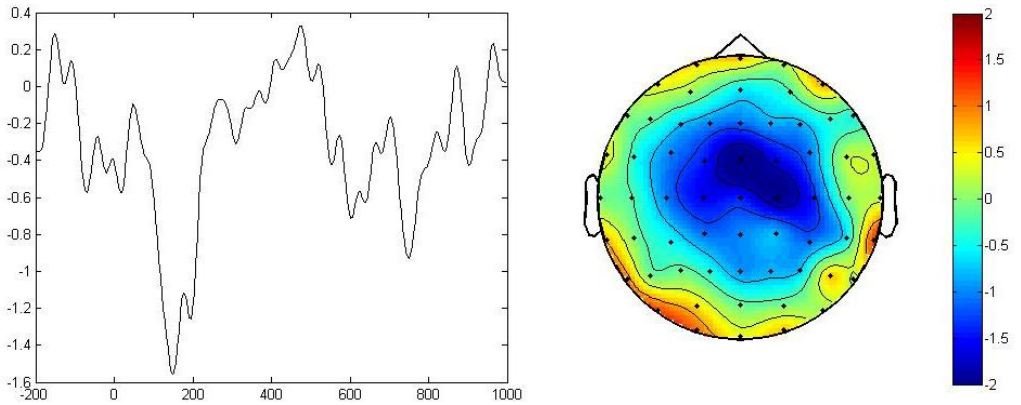
Figure 4.10. Grand mean waveform (A) and topography (B) showing an overall P3a to a small auditory perceptual difference for the ABI group. The waveform (A) shows the mean of the centre electrode (FCz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30ms time window around the identified latency (250ms), with the colourbar denoting amplitude in µV.



A. **B.**

Figure 4.11. Grand mean waveform (A) and topography (B) showing the P3a to a small auditory perceptual difference for the ABI P3a sub group. The waveform (A) shows the mean of the centre electrode (FCz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30ms time window around the identified latency (242ms), with the colourbar denoting amplitude in µV.

For the medium difference paradigm, MMN was identified in 6 ABI users. For 1 ABI user, the averaged EEG recording was too noisy to reliably identify MMN and 2 users declined to participate in the MMN recording. The grand mean MMN for the medium difference paradigm is shown in Figure 4.12



A. **B.**

Figure 4.12. Grand mean waveform (A) and topography (B) for the MMN to a medium perceptual difference for the ABI group. The waveform (A) shows the mean of the centre electrode (FCz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30ms time window around the identified latency (145ms), with the colourbar denoting amplitude in µV.

Where identified, MMN or P3a latencies varied, causing some smearing of identifiable peaks in the grand mean averages. The presence of both MMN and P3a in paradigms

designed to elicit MMN indicated that a range of auditory perceptual differences were experienced in response to the stimuli. An increase in MMN latency and decrease in amplitude was hypothesised with increasing task difficulty. Only CI user JW and 2 ABI users EO and RC had identifiable MMN in both the small and medium difference paradigm. Other users had one identifiable P3a and one MMN between the two paradigms (CI n=1, ABI n=3), or only 1 MMN or 1 P3a between the two paradigms (CI P3a n=3, CI MMN n=3, ABI P3a n=3, ABI MMN n=1). All subjects had at least one identifiable ERP from these two paradigms. However insufficient data was available to determine whether MMN latencies and amplitudes varied according to the hypothesis. Instead, all MMN data was evaluated together, as was P3b data (see Figure 4.13). In the three cases above where 2 MMN latencies and amplitudes were reported, the mean MMN latency and amplitude was taken for each user. In all three of these cases MMN latency was longer for the MMN small auditory difference paradigm, but amplitudes varied between paradigms.

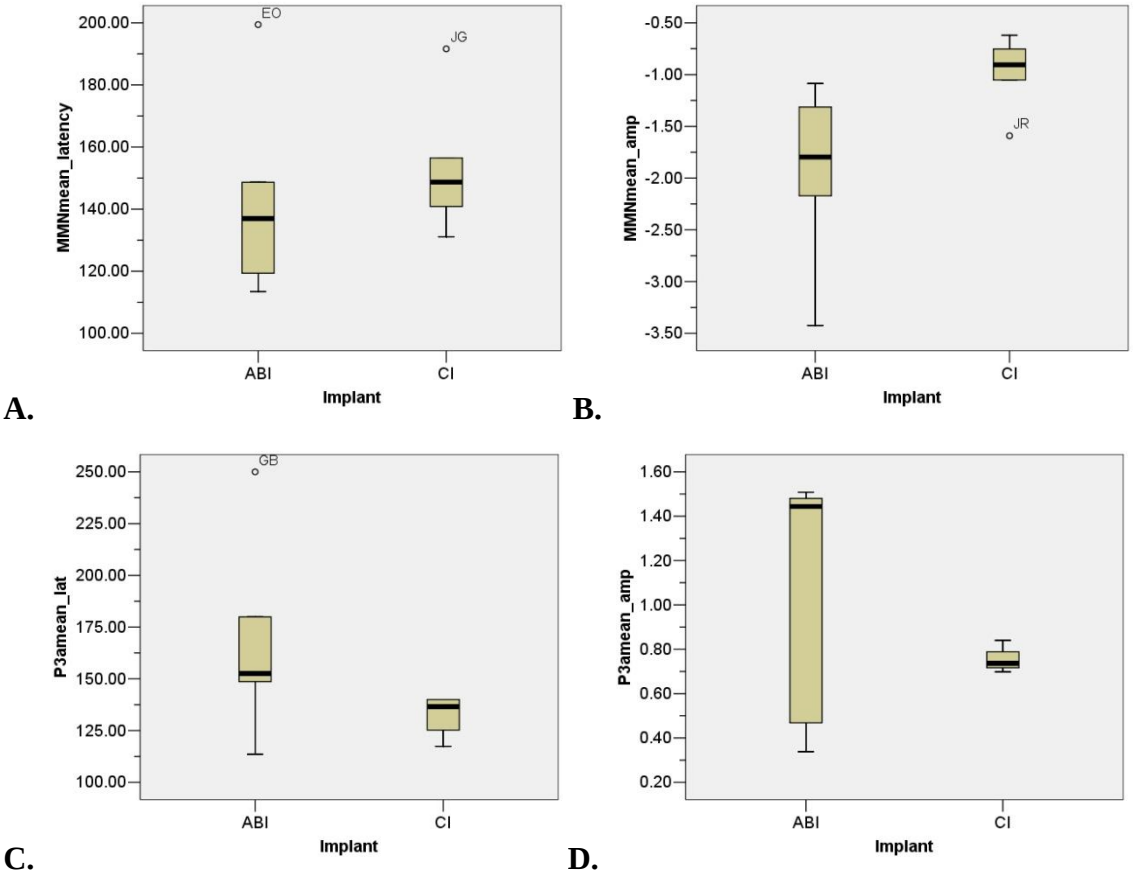
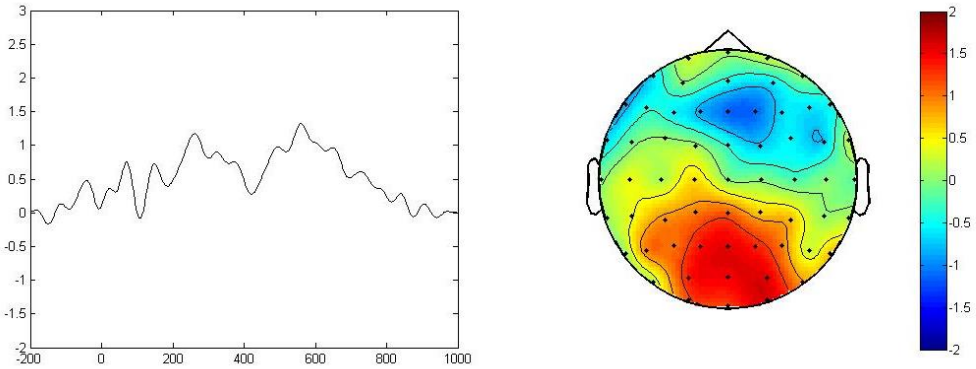


Figure 4.13. Boxplots showing the range of MMN and P3a latencies and amplitudes between groups. (A) and (C) show mean MMN and P3a latencies respectively, Y axis shows time in ms. (B) and (D) show mean MMN and P3a amplitude respectively, Y axis shows amplitude µV. Outliers are labelled.

Levene's test of equality of variance showed no significant difference in the variance of the MMN or P3a latencies between groups (MMN F=0.442, p=0.523, P3a F=3.519, p=0.103). An independent samples T-Test showed no significant difference in the mean MMN or P3a latency between groups (MMN t=-0.660, p=0.526, P3a t=1.379, p=0.210). There was a significant difference in the variance of the P3a amplitude between implant groups (F=49.853, p<0.001), but not the MMN amplitude (F=1.439, p=0.261). There was a just significant difference in the mean MMN amplitude between groups (t=-2.351, p=0.043) but not P3a amplitude (t=0.982, p=0.359). Visual inspection of Figure 4.13. indicates that due to the small sample sizes, outliers are likely to skew the significance of any differences.

4.4.1.d. P3b

A grand mean was created for each paradigm, per implant group. Figures 4.14. and 4.15. show the P3b identified in the ABI group within the small auditory perceptual difference paradigm.



A. **B.**

Figure 4.14. Grand mean waveform (A) and topography (B) showing the P3b to a small auditory perceptual difference for the ABI group. The waveform (A) shows the mean of the centre electrode (Pz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (559 ms), with the colourbar denoting amplitude in µV.

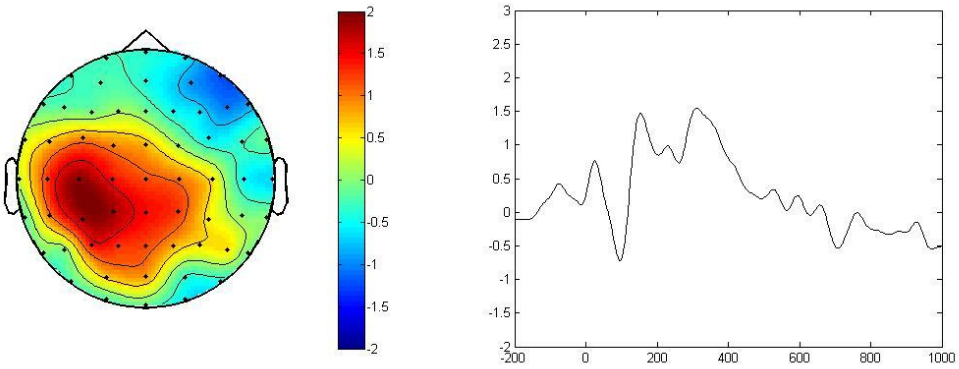
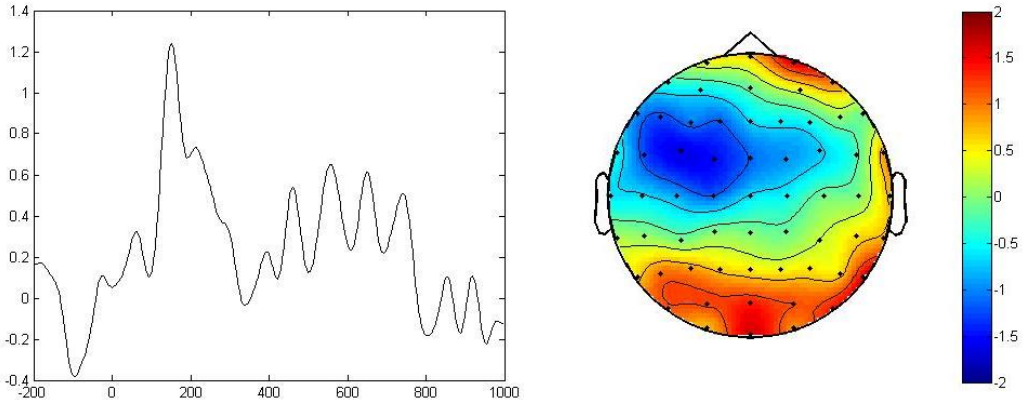


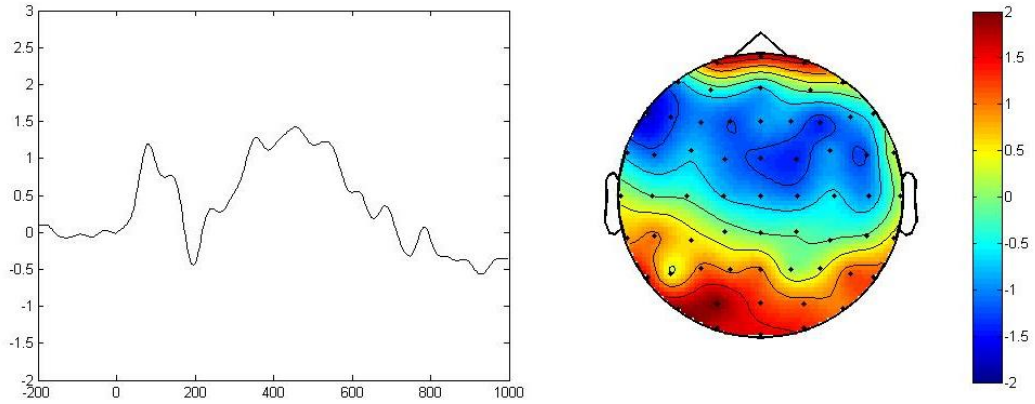
Figure 4.15. Grand mean waveform (A) and topography (B) showing the P3b to a medium auditory perceptual difference for the ABI group. The waveform (A) shows the mean of the centre electrode (CP1) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (305 ms), with the colourbar denoting amplitude in µV.

P3b identification was clearer in ABI users than CI users in general. P3b was not identified for one ABI user, DB, in the medium auditory perceptual difference paradigm due to noise in the averaged EEG recording. Large variability in latencies produced smearing in the CI grand mean.



A. **B.**

Figure 4.16. Grand mean waveform (A) and topography (B) showing the P3b to a small auditory perceptual difference for the CI group. The waveform (A) shows the mean of the centre electrode (POz) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (461 ms), with the colourbar denoting amplitude in µV.



A. **B.**

Figure 4.17. Grand mean waveform (A) and topography (B) showing the P3b to a medium uditory perceptual difference for the CI group. The waveform (A) shows the mean of the centre electrode (PO3) and the 8 surrounding electrodes, with the x axis denoting time in ms, and y axis denoting amplitude in µV. The topography (B) shows the mean amplitude over these averaged electrodes within a 30 ms time window around the identified latency (465 ms), with the colourbar denoting amplitude in µV.

Levene's test of equality of variance showed no significant difference in the variance of the P3b latencies to the small or medium paradigm between groups (P3b small F=0.814, p=0.381, P3b medium F=1.439, p=0.250). An independent samples T-Test showed no significant difference in the P3b latencies between groups (P3b small t=0.502, p=0.623, P3b medium t=0.588, p=0.566). There was no significant difference in the variance of the P3b amplitude for either paradigm between implant groups (P3b small F=0.236, p=0.634, P3b medium F=0.759, p=0.398). There was no significant difference in the mean P3b amplitude for either paradigm between implant groups (P3b small t=1.911, p=0.075, P3b medium F=0.737, p=0.473).

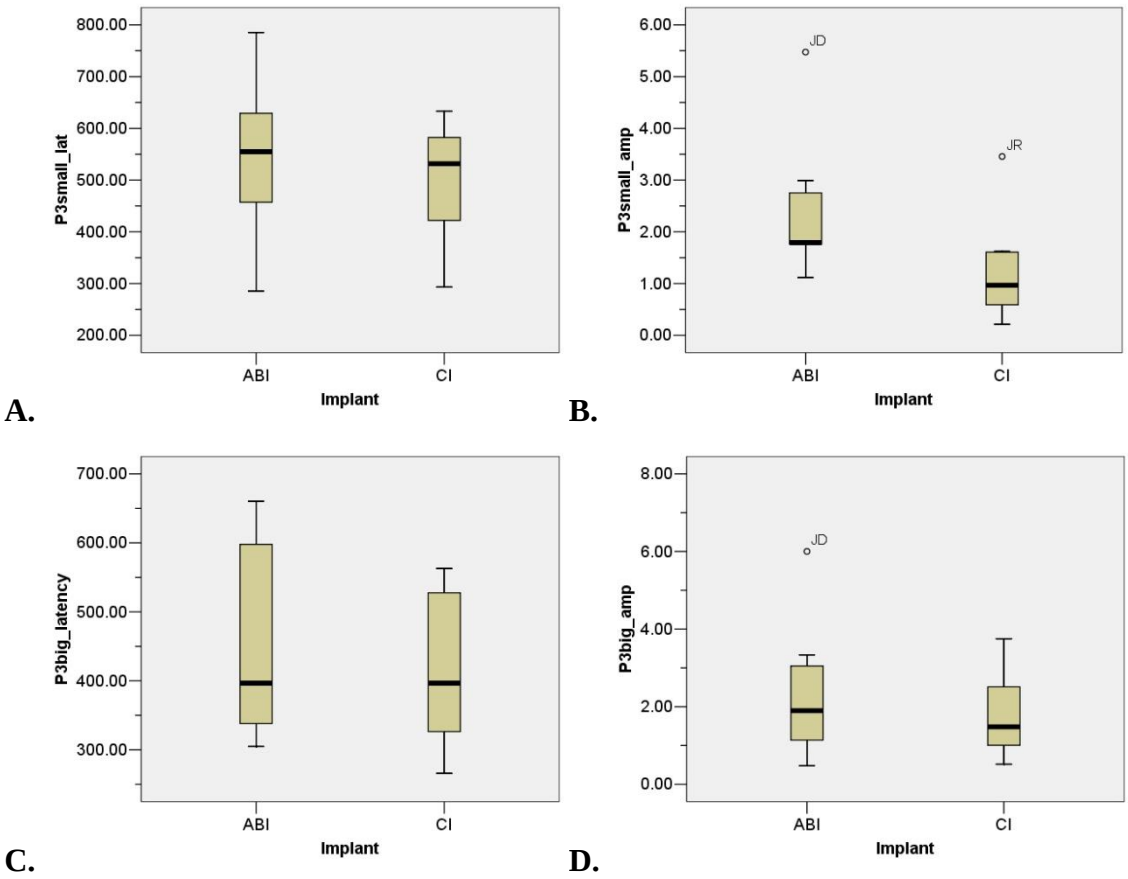


Figure 4.18. Boxplots showing the range of P3b latencies and amplitudes between groups and paradigms. (A) and (C) show P3b latencies to the small and medium paradigms respectively, Y axis shows time in ms. (B) and (D) show mean P3b amplitudes to the small and medium paradigms respectively, Y axis shows amplitude µV. Outliers are labelled.

It was hypothesised that an increase in task difficulty would result in an increase in latency and a decrease in amplitude of any identified P3b. Therefore, Equations 4.2. and 4.3. were used to determine the difference in values between the two perceptual difference conditions.

$$\underline{\text{Latency of P3b in small paradigm – Latency of P3b in medium paradigm}} \qquad (4.2.)$$

$$\underline{\text{Amplitude of P3b in medium paradigm – Amplitude of P3b in small paradigm}} \qquad (4.3.)$$

A one-sample T-Test was used to determine whether the resulting values were consistent with this hypothesis. There was no significant difference between the

difference in P3b latency or amplitude and a value of 0, indicating that there was no consistent difference in the amplitude or latency between the two perceptual difference conditions for either implant group.

CI users	ABI users		CI users	
	t	**significance**	**T**	**significance**
P3b latency change	1.667	0.134	2.297	0.061
P3b amplitude change	-0.726	0.488	0.840	0.429

Table 4.3. The relationship between 3b latency and amplitude changes with respect to paradigm in ABI and CI

The change in P3b latency is close to significance in the CI user group but not the ABI group. Visual inspection of Figure 4.19 shows that the ABI outlier EO is likely to have caused an effect on any significant differences due to the small sample sizes.

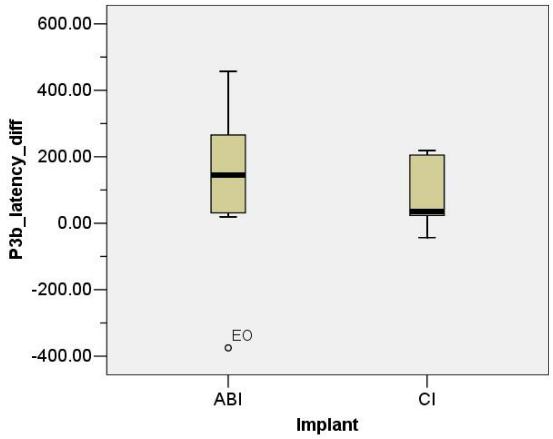


Figure 4.19. Boxplots showing the range of P3b latency variation between the small and medium perceptual difference paradigms, labelled by implant type. Y axis denotes time in ms.

4.4.2. Speech perception data

For each implant group, each subject's mean N1 and P2 amplitude and latency were compared with speech scores. There was no correlation between speech scores and ERP data for either implant group

CI users	AB words		CUNY sentences	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
N1 latency	-0.062	0.875	-0.383	0.309
N1 amplitude	0.325	0.394	-0.359	0.343
P2 latency	-0.240	0.535	-0.466	0.206
P2 amplitude	-0.328	0.389	-0.198	0.609
ABI users	**AB words**		**CUNY sentences**	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
N1 latency	0.269	0.519	0.250	0.550
N1 amplitude	0.278	0.506	0.467	0.243
P2 latency	-0.197	0.639	-0.349	0.397
P2 amplitude	0.112	0.792	0.101	0.813

Table 4.4. The relationship between speech scores and N1/P2 data for CI and ABI users

For each implant group, subjects' mean MMN and P3a latencies and amplitudes were compared with speech scores. MMN latency was negatively correlated with CI word and sentence scores. P3a amplitude was correlated with ABI word score improvement. There was also a trend towards a negative relationship between ABI P3a latency and word scores.

CI users	AB words		CUNY sentences	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
MMN latency	-0.908	0.033*	-0.936	0.019*
MMN amplitude	-0.582	0.303	-0.518	0.371
P3a latency	0.729	0.271	0.709	0.291
P3a amplitude	-0.603	0.397	-0.598	0.402
ABI users	**AB words**		**CUNY sentences**	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
MMN latency	0.311	0.549	-0.054	0.919
MMN amplitude	-0.239	0.649	-0.487	0.327
P3a latency	-0.823	0.087	-0.550	0.337
P3a amplitude	0.890	0.043*	-0.707	0.182

Table 4.5. The relationship between speech scores and MMN / P3a data for CI and ABI users

As no significant difference was found to P3b latencies and amplitudes for the small or medium auditory difference paradigms, a mean P3b latency and amplitude were derived for each subject from the two conditions to be compared against speech scores. There

was no significant correlation between the P3b latency or amplitude and speech scores in either implant group

CI users	**AB words**		**CUNY sentences**	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
Mean P3b latency	-0.214	0.611	-0.101	0.651
Mean P3b amplitude	0.526	0.181	-0.510	0.196
ABI users	**AB words**		**CUNY sentences**	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
Mean P3b latency	0.455	0.218	-0.017	0.966
Mean P3b amplitude	-0.305	0.425	0.007	0.987

Table 4.6. The relationship between speech scores and P3b data for CI and ABI users

4.4.3. Behavioural measures of electrode discrimination

MMN is reported as an indicator of automatic detection of changes in auditory stimuli. The previous study in this series found that a greater degree of change in the pitch variation between electrodes was related to speech scores in ABI and CI users. Therefore, the MMN and P3a latencies and amplitudes were compared with the normalised row-sum scores from the pitch ranking task described in Chapter 3 to determine whether electrophysiological measures of electrode discrimination have any relationship with behavioural measures of electrode discrimination. There was a significant negative correlation between MMN latency and normalised row-sum scores in both CI and ABI users.

	ABI Users		**CI users**	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
MMN latency	-0.829	0.041*	-0.936	0.019*
MMN amplitude	0.282	0.589	-0.437	0.462
P3a latency	-0.887	0.113	-0.032	0.968
P3a amplitude	-0.443	0.557	0.068	0.932

Table 4.7. The relationship between normalised row-sum scores during pitch ranking MMN / P3a data for CI and ABI users

The mean P3b latency and amplitude was also compared to the normalised row-sum scores. There was no significant correlation between the P3b latency or amplitude and speech scores in either implant group

	ABI Users		CI users	
	Pearson Correlation	**significance**	**Pearson Correlation**	**significance**
Mean P3b latency	-0.155	0.714	-0.394	0.335
Mean P3b amplitude	0.421	0.299	0.689	0.059

Table 4.8. The relationship between the normalised row-sum scores of the pitch ranking exercise and speech scores and P3b data for CI and ABI users

The electrodes chosen via Equation 4.1 for elicitation of P3b and MMN were examined with respect to the pitch confusion matrix to determine whether the pitch judgments were more consistent in the medium auditory difference electrode pair. Pitch judgements were varied across both implant groups, with no pattern regarding greater consistency in the medium difference pair. 3 ABI users judged the medium auditory difference pair more consistently in relation to pitch, whilst 3 judged the small auditory difference electrode pair more consistently and 3 judged both pairs equally inconsistently. Four CI users judged the medium auditory difference pair more consistently and 4 judged the small auditory difference pair more consistently

4.5. Discussion and clinical implications

4.5.1 Discussion

The relatively diffuse topographies and the noisy traces seen in MMN and P3b recordings highlight the difficulty associated in ERP identification. MMN, P3a and P3b latencies were very varied within both implant groups. Grand mean waveforms and topographies will therefore be shaped by participants with stronger responses and may not necessarily reflect individual effects. This is consistent with previous reports of the use of grand average data. Features present in individual ERP waveforms may sometimes be lost in the analysis of grand average data such that the grand average is not representative of the individual waveforms that it is derived from (Luck 2005).

One reason for the variation in identified latencies may be variations in the relative degree of auditory perceptual difference between users. As previously discussed, any qualification of perceptual difference is necessarily relative meaning that attempts to control for the degree of auditory perceptual difference between electrodes is limited. In addition, as electrodes themselves are discrete, there is no provision for decreasing

the size of the auditory perceptual difference in cases where all electrodes are easily discriminable.

The documented response habituation that occurs quickly when recording CERP (Lightfoot and Kennedy 2006) was one reason for using a minimal number of runs during recording sessions. However, more runs greatly improved the signal to noise ratio, as seen in the grand average of N1 and P2 responses, which is derived from 4 times as many runs as the grand averages for the P3b and MMN. Recording more runs for the ERPs elicited during oddball paradigms would significantly increase test time due to large number of standard stimuli that would need to be presented. This may be possible if a future study were to concentrate solely on elicitation of either the P3b or the MMN rather than record both.

Clear MMN and P3b were recordable in ABI users but inability to adequately control for variations in auditory perceptual differences between electrodes meant the expected increase in MMN and P3b latency and decrease in amplitude with increasing task difficulty was not reliably supported or refuted. For ABI users, the MMN small auditory difference paradigm elicited more P3a than MMN amongst users and the opposite was true for the medium auditory difference paradigm. As P3a is elicited in response to a large deviation in stimuli (Rugg and Coles 1995, Kraus and McGee 1994), this would suggest that the expected change in ERP morphology with increasing task difficulty was in fact reversed for the ABI group. In fact, the explanation is likely to be the limited control of the degree of auditory perceptual difference elicited by different electrodes.

There was a trend toward longer latencies for P3b elicited to the small perceptual difference paradigm but this was not statistically significant. The variation in identified latencies and the small sample size are likely to have affected this outcome. There was not only a large variation between subjects in identified P3b latencies, but also a wide variation in the degree of difference between the calculated differences in each subject's identified P3b. This is likely to have reduced the power of the statistical test. However, the trend towards longer latencies with increased task difficulty is in contrast to the trend towards P3a elicitation with the small difference paradigm. P3a elicitation

suggests an easier discrimination task, whilst the trend of longer P3b latencies suggests a more difficult task.

Electrically evoked late ERPs in CI subjects are reported to have significantly shorter latencies to acoustically-evoked late ERPs (Firszt, Chambers et al. 2002a). The ERPs themselves have been found to have arisen from the same neural generators despite the stimulation difference (Firszt, Chambers et al. 2002a). Some early N1 latencies were seen in the present study, which concurs with this. In particular, topographies for the N1 and P2 data were highly similar between subjects for each group, with individual topographies often deviating little from the grand mean. Such similarities despite large variation in ERP latencies appears to suggest that reliable N1 and P2 responses can be elicited from ABI users that are comparable to CI users. In contrast, P3b latencies, where identified were often later than the reported average latency of 300ms. However the recording of MMN, P3a and P3b in ABI users does indicate the presence of signal processing beyond initial cortical detection which is illustrated by CERP. The presence of these ERPs in poorer implant users might indicate that whilst certain auditory processing skills are harnessed in ABI use, they may not be ones useful for speech perception.

With respect to speech scores, there was a significant negative correlation with MMN latency and word and sentence scores in CI users, and between P3a amplitude and word scores in ABI users. The CI finding support the reports of previous studies which have documented a relationship between MMN data and speech scores (Kelly, Purdy et al 2005)

From previous studies, a negative correlation was anticipated between P2 amplitude and speech scores in ABI users (O'Driscoll 2012). In addition, CI studies have indicated a negative correlation between speech perception data and P2 latencies, and in some cases also N1 latencies (Kelly et al 2005, Gordon et al 2005, O'Driscoll 2012), but not for ABI users (O'Driscoll 2012). No correlation was found between N1 and P2 data and speech scores for either implant group during the present study. Discrepancies between the speech scores of interest and the method of ERP peak extraction may explain the conflict. This study has already noted the wide variation that is possible in identified

ERP latencies. Deriving a mean N1 and P2 latency for each implant user was designed to reduce that variability but does mean that some individual features of the identified ERP peaks may be lost. The difference in ERP extraction in this case may be one reason for conflict in statistical results between studies.

The statistically significant negative correlation between MMN latency and normalised row-sum scores of the pitch ranking task does go towards supporting the hypothesis that electrophysiological measures of discrimination between electrodes are related to behavioural measures of discrimination. The difficulty in identifying MMN in all subjects may indicate the need for future studies to amend paradigms to include more runs in an effort to reduce response variability.

This study has shown that electrophysiological measures of electrode discrimination are recordable in ABI users, but the relative uncertainty regarding the degree of perceptual difference to which they are elicited may limit their efficacy. One suggestion for variations in perceptual difference in ABI users may be the location of the ABI electrode array. As previously noted, the stimulation of different parts of the cochlear nucleus may give rise to different characteristic reactions. If both the VCN and the DCN are activated during ABI stimulation, it may result in complicated interactions between excitatory and inhibitory cells (Illing 2006). This would further complicate the percept experienced by ABI users and highlight the likelihood of individual differences.

The difficulties in controlling for the degree of auditory perceptual difference meant that ERPs designed to be recorded in response to changes in percept were poorly identified or showed variable latencies. However, this highlights the fact that despite attempts to characterise or quantify the degree of auditory perceptual difference between electrodes, individuals still experience a range of auditory percepts that are difficult to compare between subjects. This in itself may support the previously documented variations in ABI outcomes by indicating that users within implant groups are not experiencing the same qualities of sound despite using the same method of auditory stimulation.

4.5.2 Clinical Implications

The recording of late evoked potentials in ABI users, such as the CERP and P3b, confirm that for all subjects in this study, auditory information was conducted to cortical processing areas. Whilst for an adult implant user the subjective reporting of auditory sensation may provide that same information, this is not possible with paediatric ABI recipients. Any behavioural reaction to the electrical stimulation may indicate either auditory or non-auditory sensation. The ability to record electrically evoked N1 and P2 data that corresponds with other implant groups may prove highly beneficial in evaluating the presence of auditory electrodes during paediatric ABI programming. This idea has been further explored in O'Driscoll (2012). He investigated the difference in morphology of EERPs recorded in response to activation of auditory ABI electrodes and those which were known to cause non-auditory side-effects in adult ABI users. Atypical EERP morphology was found in 66% of ABI users who reported non-auditory side-effects (O'Driscoll 2012).

The identification of P3b in ABI users indicates conscious processing of detectable differences following activation of different electrodes. However, the relationship between pitch confusion and MDS vector size noted in section 4.4.3. confirms the complexity of the sensations elicited via auditory implants. Whilst MDS vectors indicate the relative ease of distinguishing between one pair of electrodes compared to another, the actual quality of sound perceived is not easily indicated. If pitch were the overriding percept, the pitch confusion matrices would show more consistency in judgments between pairs of electrodes deemed by the MDS vectors to be more easily distinguishable. This was not the case for the present data set. Consistency in pitch judgements was varied. As discussed in experiment 1 of this series, pitch judgements themselves may be prone to error depending on subject ability, actual pitch ranges, and the presence of a percept other than pitch. Clinically, the discrepancy between overall discrimination and clear pitch variation is significant due to the required pitch ordering of electrodes for programming.

4.6. Conclusions

In ABI users, reliable N1 and P2 are seen that are comparable to CI users. As identification of ERPs is often taken to indicate the integrity of the auditory pathway up

to the neural generators of that ERP component, CERP presence in ABI users may indicate that activation of an ABI electrode array is capable of stimulation of similar auditory structures to that of a CI electrode array. In addition, the presence of MMN, P3a and P3b in ABI users indicates signal processing beyond initial cortical detection. However, the trend towards larger variances for the ABI group for latencies or amplitudes of many of these identified ERPs may suggest that the stimulation of the auditory pathway following ABI activation may be more varied than with a CI.

Without outliers, a trend is seen for longer P3b latencies with increasing task difficulty, which goes some way to supporting the hypothesis that electrophysiological measures of electrode discrimination are related to behavioural measures of electrode discrimination. However, this trend conflicts with the identification of more P3a than MMN with a more difficult auditory perceptual task in ABI users. Too few MMN were identified to fully test the hypothesis that MMN latency increases with task difficulty. However, in those 3 implant users where sufficient MMN were identified, there was a trend towards increasing latency with task difficulty. Further to this, MMN latency was significantly negatively correlated with normalised row-sum pitch ranking scores from the previous study in this series. Larger normalised row-sum scores indicate a more easily defined pitch rank, i.e. an easier task. Similarly, a shorter MMN latency is hypothesised for an easier discrimination task. This study has therefore indicated that some electrophysiological measures of electrode discrimination are related with some behavioural measures of electrode discrimination, although this hypothesis was not able to be fully confirmed nor disputed.

With respect to electrophysiological measures of electrode discrimination and speech scores, a significant negative correlation was seen between MMN latency and speech scores for CI users but not ABI users. A significant correlation was seen between P3a amplitude and word scores in ABI users along with a trend towards a negative correlation between P3a latency and speech scores. No significant relationships were seen between CERP or P3b data and speech scores. The hypothesis that electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users was not therefore proven, although the presence of some trends and significant correlations means that neither was it completely disproven. Small sample sizes, due to the limited

ABI user population reduced the power of this study such that a multicentre study may be required to fully test the hypothesis.

Chapter 5

Discussion and Conclusions

5.1. Discussion

This study investigated both behavioural and electrophysiological measures of electrode discrimination in adult ABI users. Whilst variations in pulse train intensity and duration may convey some amplitude and temporal information via a single channel auditory implant, spectral definition is not possible. The benefit of multi-channel implants is the spectral definition gained via activation of electrodes sited near neural receptors that respond to different input frequencies. This multi-channel benefit is significantly reduced when the auditory perceptual difference following activation of different electrodes is complex, non-uniform or very small. For ABI users, understanding more about the auditory perceptual differences between electrodes may have clinical benefits during programming sessions. Particular attention is paid to pitch variations during programming, which may be difficult for a patient to judge, or may not be present at all. This study therefore aimed to investigate place-pitch perception and judgements of perceptual differences between electrodes via both subjective and objective measures.

Experiment 1 (Chapter 3) aimed to investigate place-pitch perception and judgements of perceptual differences between electrodes in ABI users via multidimensional scaling tasks. The experiment had 2 aims: (a) to determine the relationship between place-pitch perception and speech outcomes in ABI users using their clinically-set maps; (b) to determine if percepts other than pitch are related to electrode position for ABI users via an MDS procedure.

Speech outcomes were correlated with more clearly identified pitch variations between electrodes and also with a greater degree of correlation between measured and mapped electrode orders. Therefore, evaluation of a multiple-comparison pitch ranking task during initial programming may assist in predicting ABI performance. A further benefit of a multiple comparison pitch ranking task is the likelihood of identifying an accurate pitch rank, if one exists. This should reduce the need to adjust the pitch order of successive maps, which would otherwise increase acclimatisation time.

MDS analysis highlighted the complexity of ABI stimulation as pitch variations are unlikely to be the overriding auditory percept following ABI activation. Further work regarding auditory perception with an ABI should include qualitative evaluation such as

subject interviews and categorisation of the sounds perceived. Factor analysis of such data may then provide information regarding similarities of differences in sound quality judgements between good and poorer ABI users.

One difficulty with any experiment requiring subjective assessments is that judgments are not comparable between participants. Each participant brings their own experiences and views when asked to scale, rank or categorise items. Electrophysiological experiments may therefore be beneficial in reducing some of the subjective variability seen in behavioural experiments. Experiment 2 (Chapter 4) aimed to investigate perceptual differences between electrodes via electrophysiological measurements. The experiment had two aims: (a) to determine if electrophysiological measures of electrode discrimination correlate with behavioural measures of electrode discrimination in adult ABI users; (b) to determine if electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users.

Electrically-evoked CERPs were identified in each implant user, which is consistent with other EERP studies (Waring, Ponton et al. 1999; O'Driscoll 2012). N1,P2, MMN, P3a and P3b were elicited in ABI users. Difficulty in controlling for variations in auditory perception meant a wide range of ERP latencies were identified. The variations meant there were insufficient data to accurately test the hypothesis that P3b and MMN latency increases with increasing task difficulty in ABI users. With respect to speech scores, no relationship was found with N1 or P2 data and speech scores. A significant negative correlation was found with mean MMN latency and word and sentence scores in CI users and with P3a amplitude and word scores in ABI users. A significant relationship was also found between MMN latencies and behavioural measures of pitch discrimination between electrodes, providing some support for the hypothesis that some electrophysiological measures of electrode discrimination may be related to behavioural measures of electrode discrimination.

The large variability in EERP latency meant that the small sample size in the present study was very restricted in power. To significantly improve the power for any group effect to be reliably reported, multi-centre ABI recruitment is required. However, for any ERP data to be clinically useful, it would need to also be individually robust. The variability seen in the present study between subjects within the ABI implant group

indicates that clinical applications of ERP data may be limited. However, adjustments in study procedure may improve the signal to noise ratio and therefore overall EERP recordings. P3b was found to be more robust than MMN in CI users (Kelly et al 2005) and in the present study was found to be more robust for ABI users. Therefore, concentrating solely on P3b recordings would allow for a greater number of runs to be presented without a significant change to the overall test duration. Recordings may also benefit from electrical shielding of the test room.

With regard the variation in outcomes, a further consideration may be the introduction of more structured rehabilitation to aid confidence, concentration and development of listening skills. Rehabilitation manuals containing listening exercises for completion at home are routinely provided for new ABI users at the Manchester Auditory Implant Centre but attendance at regular therapy sessions during early use may assist in ensuring practice takes place and may guide the user. Studies have already noted that positive reinforcement and appropriate expectations are key to successful habilitation with a CI (Kampfe, Harrison et al. 1993). For ABI users, it has already been noted that poor perception of functional benefit hinders acclimatisation despite auditory perception and pitch perception indicating potential benefit (Kanowitz, Shapiro et al. 2004). Furthermore, the author's own clinical experience in rehabilitation of CI users receiving a sequential cochlear implant has highlighted the benefit that perseverance, confidence and auditory training can provide during acclimatisation to a new device. Acclimatisation to an ABI may be likened to the learning of a new language. Therefore a review of current training techniques and user input may assist in the development of more individualised training programmes to achieve the optimum outcomes for each ABI user.

5.2. Conclusions

This study series has investigated both behavioural and electrophysiological measures of auditory perceptual differences elicited from activation of ABI electrodes. Experiment 1 of this series (Chapter 3) has highlighted the importance of place-pitch pitch perception during initial ABI programming. Sentence and word improvement scores in ABI users are related to tonotopically ordered user maps and to maps in which pitch variations are more easily identified. In addition, multidimensional scaling (MDS)

analysis showed that the pattern of auditory perceptual differences experienced by ABI users, whist it may be consistent, is significantly different to that experienced by CI users. This may indicate that the auditory perceptual differences experienced by ABI users are qualitatively different to those of CI users and are not dominated by pitch-perception but instead may be more related to timbre.

Clinically, this may have implications for the manner in which pitch ranking is derived. A method which involves multiple comparisons and includes comparisons between all available electrodes may provide information not only regarding an overall rank, but also the ease with which pitch variations were identified. This information may assist in patient counselling regarding expectations and possible outcomes. In addition, use of an MDS procedure may identify electrodes which are not easily discriminated. Following further research, this may influence the number of auditory electrodes chosen to remain active in a user map.

Experiment 2 of this series (Chapter 4), investigated electrophysiological measures of auditory discrimination following activation of different ABI electrodes. In ABI users, reliable N1 and P2 are seen that are comparable to CI users. As identification of ERPs is often taken to indicate the integrity of the auditory pathway up to the neural generators of that ERP component, CERP presence in ABI users may indicate that activation of an ABI electrode array is capable of stimulation of similar auditory structures to that of a CI electrode array. The identification of MMN, P3a an P3b in ABI users indicates that activation of higher cortical areas are possible with ABI use and processing is occurring beyond simple cortical detection. However, the trend towards larger variances for the ABI group for latencies or amplitudes of many of these identified ERPs may suggest that the stimulation of the auditory pathway following ABI activation may be more varied than with a CI.

The trend towards longer P3b and MMN latencies with increasing task difficulty, along with the significant negative correlation between MMN latency and performance in a pitch ranking task indicates that some electrophysiological measures of electrode discrimination are related with some behavioural measures of electrode discrimination, although this hypothesis was not able to be fully confirmed nor disputed.

With respect to electrophysiological measures of electrode discrimination and speech scores, a significant negative correlation was seen between MMN latency and speech scores for CI users but not ABI users. A significant correlation was seen between P3a amplitude and word scores in ABI users along with a trend towards a negative correlation between P3a latency and speech scores. No significant relationships were seen between CERP or P3b data and speech scores. The hypothesis that electrically-evoked ERPs correlate with clinically recorded speech scores in adult ABI users was not therefore proven, although the presence of some trends and significant correlations means that neither was it completely disproven.

Overall, the small sample size resulting from a limited available ABI population reduces the power of the study findings, meaning not all study aims were fulfilled. This study has therefore indicated that further ABI research may require multicentre studies and ERP paradigm changes to improve signal to noise ratios sufficiently and record enough data to accurately test the relationships between ERPs, speech scores and behavioural measures of electrode discrimination.

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