CORTICAL PREDICTORS AND CORRELATES OF COCHLEAR IMPLANT OUTCOME: A LONGITUDINAL STUDY USING FUNCTIONAL NEAR-INFRARED SPECTROSCOPY

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ABSTRACT

While cochlear implants (CIs) have transformed the lives of hundreds of thousands of profoundly deaf individuals worldwide, the ability of individual patients to understand speech through their CI varies widely. The longitudinal study reported in this thesis aimed to investigate the role of cortical function and plasticity in helping to predict and explain variability in individual CI outcome.

Speech-evoked cortical activations, measured using functional near-infrared spectroscopy (fNIRS), and behavioural measures of speech perception were acquired in adult CI recipients before implantation through to six months after CI activation. As anticipated, cochlear implantation enabled the significant recovery of auditory speech perception over the first six months of CI use, yet individual performance varied widely across CI users.

fNIRS enabled the measurement of speech-evoked cortical activations from bilateral superior temporal cortex (STC) that were free from CI-generated artefacts. Cortical activation to visual speech measured before implantation was able to significantly predict future CI outcome measured following six months of CI use. This pre-implant measure of brain activity provided unique predictive value above that of well-established clinical characteristics, including the age-at-onset and duration of deafness.

When examining changes in cortical activation from before to after implantation, a greater increase in STC activation to visual speech was found to be related to better CI outcome. These visual-related changes also predicted changes in STC activation to auditory speech. These results highlight the importance of visual speech cues and coupling between the auditory and visual modalities during the recovery of auditory function with a CI. Together, the findings demonstrate the potential of fNIRS as a brain-imaging tool that is uniquely well-suited for use in cochlear implantation. Future applications of this technology could help to explain individual variability in CI success and to deliver more accurate clinical prognoses for CI candidates.

PUBLICATIONS

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DECLARATION

I certify that this is my own work, except where indicated by referencing. No part of this thesis has been submitted elsewhere for any other degree or qualification.

Carly Anderson Date

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LIST OF ABBREVIATIONS

AV	Audio-visual
BA	Brodmann's areas
BKB	Bamford-Kowal-Bench
CD	Cook's Distance
CI	Cochlear implant
CUNY	City University of New York
dB	Decibels
DW	Durbin-Watson
EEG	Electroencephalography
FDR	False discovery rate
fMRI	Functional magnetic resonance imaging
fNIRS	Functional near-infrared spectroscopy
GLM	General Linear Model
HA/s	Hearing aid/s
HbO	Oxygenated haemoglobin
HbR	Deoxygenated haemoglobin
HbT	Total haemoglobin
HL	Hearing loss
HRF	Haemodynamic response function
IHR	Institute of Hearing Research
kHz	Kilohertz
K-S	Kolmogorov-Smirnov test
LI	Laterality index
LIF	Left inferior frontal
LIFG	Left inferior frontal gyrus
LMM	Linear mixed model
MEG	Magnetoencephalography
NAIP	Nottingham Auditory Implant Programme
NH	Normal-hearing
NHBRU	Nottingham Hearing Biomedical Research Unit
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
PET	Positron emission tomography

RAU	Rationalised arcsine unit
ROC	Receiver operating characteristic
ROI/s	Region/s of interest
SNHL	Sensorineural hearing loss
SNR	Signal-to-noise ratio
SR	Studentized residuals
STC	Superior temporal cortex
STG	Superior temporal gyrus
STS	Superior temporal sulcus
UKCISG	UK Cochlear Implant Study Group
VIF	Variance inflation factor

1. THESIS OVERVIEW

1.1 INTRODUCTION

A cochlear implant is an auditory prosthesis that can partially restore a sensation of hearing to profoundly deaf individuals. Continued developments in cochlear implantation have enabled many individuals to benefit substantially from their CI and to achieve a good level of auditory speech perception ability (Summerfield & Marshall, 1995; Teoh et al., 2004; UK Cochlear Implant Study Group, UKCISG, 2004a). Despite this, other individuals receive far less benefit from their device as evidenced by the high level of individual variability in CI outcome that is consistently reported in the literature (Holden et al., 2013; Lazard et al., 2010a; Tyler et al., 1997). Clinical variables including peripheral, surgical and device-related factors have been shown to influence the level of speech perception achieved after implantation (Blamey et al., 2013; Lazard et al., 2012a; Summerfield & Marshall, 1995). However, these factors are only able to account for approximately 20% of the variability observed in CI outcome, and the amount of benefit that an individual might receive from a CI cannot currently be accurately predicted (Lazard et al., 2012a). Emerging evidence suggests that central factors, notably cortical function and plasticity, should be considered as important contributors to the variability observed in auditory speech perception following implantation (Buckley & Tobey, 2011; Lazard et al., 2012a, 2013; Lee et al., 2007a; Sandmann et al., 2012).

Following implantation, the ability to recruit bilateral auditory association cortices in response to auditory speech stimulation appears crucial for achieving proficient levels of auditory speech perception (Fujiki et al., 1999; Green et al., 2005; Mortensen et al., 2006). However, evidence of cortical plasticity has been observed in cases of profound deafness, whereby auditory brain regions can become more responsive to the intact senses such as vision (Finney et al., 2001; Lomber et al., 2010) and touch (Auer et al., 2007). Such evidence has generated much interest in how this 'cross-modal plasticity' may have a deleterious effect on auditory processing resources that could impact upon an individual's ability to perceive auditory speech information with a CI (Buckley & Tobey, 2011; Doucet et al., 2006; Lee et al., 2001; Sandmann et al., 2012). During periods of profound deafness, the communicative importance of visual speech can similarly result in the auditory association cortices becoming more responsive to visual speech information (Capek et al., 2008; Lee et al., 2007b). This cortical adaptation appears to underlie greater visual speech perception, or 'speechreading' abilities, thus providing a behavioural advantage for oral communication during periods of profound deafness (Capek et al., 2008; Lee et al., 2007b). Whilst there has been speculation that the use of visual language, such as speechreading and sign language, may compromise auditory processing resources during deafness (Lee et al., 2001), other authors have highlighted that the impact of speechreading on auditory cortical function and its relation

to future CI outcome remains unexamined (Campbell et al., 2014; Lyness et al., 2013).

Neuroimaging evidence obtained soon after cochlear implantation has demonstrated a negative relationship between cortical activation to visual speech within auditory brain regions and future CI outcome (Strelnikov et al., 2013). Such evidence alludes to the detrimental consequences of visual speech processing within temporal brain regions, but also to the potential value of such a cortical measure in helping to predict variability in CI outcome. Furthermore, evidence of a reduction in this speechreading activation with increased CI use may suggest that the reversal of such activations may be associated with successful auditory rehabilitation following cochlear implantation (Rouger et al., 2012). However, it is also thought that CI users may capitalise on a close coupling between the auditory and visual modalities, both at the behavioural (Rouger et al., 2007) and the cortical level (Doucet et al., 2006; Giraud et al., 2001a, 2001b; Strelnikov et al., 2015), to facilitate accurate perception of the novel and degraded auditory signal provided by the implant. Thus, given the multimodal propensity of the superior temporal cortices and the importance of visual and audio-visual speech perception for effective communication following deafness and cochlear implantation, understanding the interplay between the two sensory modalities within STC both before and after implantation may be essential for understanding and predicting individual variability in CI outcome.

Although cochlear implantation offers a unique opportunity to study the effects of auditory deprivation and its subsequent amelioration on cortical function and plasticity, such longitudinal examinations remain lacking largely due to methodological challenges. For instance, well-established neuroimaging techniques are either limited in their compatibility with the CI device or are not safe for repeated testing, often precluding functional imaging of the cortex during speech stimulation in CI users (Giraud et al., 2001b; Kim et al., 2015). One promising solution is functional near-infrared spectroscopy. fNIRS is a quiet, flexible and non-invasive neuroimaging technique which, owing to its optical nature, is fully compatible with CI devices (Sevy et al., 2010). This thesis looks to capitalise on the opportunity that fNIRS provides for safely acquiring cortical measurements during speech stimulation within the same individuals from pre- to post-implantation. The overall aim of this work was to understand whether cortical function before and after cochlear implantation could help to predict and explain the variability observed in CI outcome. Specifically, the longitudinal study reported in this thesis examines whether the responsiveness of auditory brain regions to visual and auditory speech before implantation may help to predict future success with a CI. Furthermore, whether subsequent adaptation of the auditory brain regions to speech information following cochlear implantation could help to explain the variability observed in CI outcome is investigated.

1.2 OVERVIEW OF FOLLOWING CHAPTERS

Chapter 2: The Role of Cortical Plasticity in Understanding Variability in Cochlear Implant Outcome: A Literature Review

This chapter comprises a review of the literature that the thesis is grounded in. The chapter first provides an outline of sensorineural hearing loss and a description of cochlear implantation as a rehabilitative option for profoundly deaf adults. The chapter presents evidence that the recovery of auditory speech perception varies drastically amongst adult CI users and the influence of key clinical characteristics is examined. The chapter highlights that much variability in CI outcome remains unexplained by such clinical characteristics, and the value of examining cortical function as an additional contributor and predictor of this variability is anticipated. Subsequently, evidence pertaining to the effects of cortical plasticity during deafness and its influence on CI outcome is examined. The chapter identifies that cortical predictors and correlates of variable CI outcome are not fully understood largely due to methodological challenges that preclude repeated cortical imaging throughout the CI process. Limitations of established neuroimaging techniques are outlined and, as a potential solution, the application of fNIRS with CI users is advocated. To familiarise the reader with this relatively novel neuroimaging modality, the principles, limitations and advantages of the technique are discussed. The chapter concludes by stating the aims of this thesis as arising from the literature review.

Chapter 3: Longitudinal Experiment Design and Methodology

This chapter describes the design and methodology of a longitudinal, neuroimaging and behavioural study of speech perception conducted with adult CI users and normal-hearing (NH) control subjects. The chapter provides details of participant recruitment, study design, and the experimental procedures employed. Responses to auditory, visual, and audio-visual speech were recorded bilaterally from the temporal cortex using fNIRS. Behavioural performance on measures of auditory, visual, and audio-visual speech perception was also assessed. Both neuroimaging and behavioural measures were acquired from the same individuals before cochlear implantation, one month after activation of the CI device, and six months after CI activation. The chapter outlines the preparation of neuroimaging and behavioural data and the definition of cortical regions of interest (ROIs) for subsequent statistical analyses.

Chapter 4: Evolution of Speech Perception Abilities Following Cochlear Implantation

This chapter reports behavioural performance on measures of auditory, visual, and audio-visual speech perception in CI users and NH control subjects. For each modality, the trajectory of performance from pre- to post-implantation is presented both at the individual and at the group level. The chapter employs a linear mixed model (LMM) approach to examine how performance differed

between the two experimental groups, how performance changed as a function of time, and whether any interactions were observed between the effects of group and time. The results demonstrate that cochlear implantation provided significant improvements to auditory and audio-visual speech perception abilities as soon as one month after CI activation in the current sample of CI users, with a further improvement with prolonged CI experience. Both before and after implantation, CI users were seen to have significantly enhanced speechreading abilities compared to NH individuals. Importantly, the results confirm that substantial between-subject variability in auditory speech perception existed following six months of CI use, thus lending to the investigation of the contribution of cortical factors to this observed variability in CI outcome.

Chapter 5: Speech-evoked Cortical Activation Before and After Cochlear Implantation

This chapter presents fNIRS measurements of cortical activation to auditory, visual and audio-visual speech acquired from CI users and NH control subjects. For each speech stimulation condition, group-level cortical activation maps are used to display patterns of significant cortical activation across the bilateral measurement array. Time course analyses within pre-defined superior temporal regions of interest illustrate the successful, artefact-free measurement of cortical activation elicited by auditory, visual and audio-visual speech following cochlear implantation. For each

modality, the chapter employs a ROI analysis using a LMM approach to examine group differences in the amplitude of cortical activation, changes in amplitude of cortical activation over time, and interactions between the effects of group and time on cortical activation. The results confirm the ability of fNIRS to repeatedly measure artefact-free cortical responses to speech throughout the CI process, and to detect group differences in cortical activation as well as changes over time, thus affording the subsequent examination of associations between speech-evoked cortical activation and auditory performance with a CI.

Chapter 6: Pre-implant Cortical Predictors of Future Cochlear Implant Outcome

This chapter examines the responsiveness of superior temporal brain regions to speech before implantation as a cortical predictor of future CI outcome. Due to the communicative importance of visual speech information during periods of profound deafness, the chapter first examines the predictive value of STC activation to visual speech before implantation. Regression analysis revealed that greater STC activation to visual speech before implantation was predictive of poorer auditory speech perception following six months of CI use. Furthermore, this pre-implant cortical measure was able to provide additional predictive value above that of known clinical characteristics including the age-at-onset and duration of auditory deprivation. The chapter also considered the potential clinical application of this pre-implant cortical measure in the prediction of

CI outcome, with high levels of specificity and sensitivity demonstrating its potential ability to classify those CI candidates who were likely to become non-proficient CI users with a high level of accuracy.

The second half of the chapter assessed hemispheric specialisation for auditory speech processing within STC before implantation. Specifically, regression analysis examined the extent to which auditory speech-evoked activation was left-lateralised within the superior temporal ROIs as a predictor of CI outcome. The results indicated that a more strongly left-lateralised response to auditory speech was predictive of better auditory performance following six months of CI use. However, a limitation of the laterality index employed here for quantifying hemispheric lateralisation meant that this could only be determined for individuals who displayed positive cortical activation values in response to auditory speech in both the left and right STC. Therefore, due to these practical limitations, the specificity and sensitivity of this cortical measure as a prognostic indicator were not explored, and subsequent exploration of this cortical measure in ensuing chapters was not deemed appropriate.

Chapter 7: Examining Cortical Plasticity Following Cochlear Implantation and Relation to Cochlear Implant Outcome

This chapter capitalises on the longitudinal nature of the current study by examining how superior temporal cortices adapt to the restoration of auditory inputs following cochlear implantation, and

how this plasticity relates to CI outcome. Given the negative predictive relationship demonstrated between amplitude of STC activation to visual speech before implantation and CI outcome in Chapter 6, Chapter 7 examines whether a reduction in STC activation to visual speech following implantation enables more proficient levels of auditory performance to be achieved with a CI. However, correlational analysis demonstrated that a greater increase, rather than reduction, in STC response to visual speech was associated with greater auditory performance following six months of CI use. Furthermore, a positive association between change in STC response to visual speech and change in STC response to auditory speech was observed following implantation, indicating coupling between the two modalities rather than a sensory shift when auditory inputs are reinstated. The chapter considers the importance of this apparent synergy between the two modalities during the recovery of auditory function following cochlear implantation. Consequentially, the examination of audio-visual speech integration in CI users was investigated in the following chapter.

Chapter 8: Integration of Auditory and Visual Speech Information Following Cochlear Implantation

This chapter examines the integration of auditory and visual speech information at the behavioural and cortical level in CI users following six months of CI use. The amount of perceptual benefit obtained from visual speech information in audio-visual conditions is

compared between CI users and NH individuals when auditory-only performance is approximately equated. In addition, how auditory and visual speech information is integrated with the superior temporal brain regions is examined by applying the additive model of multisensory integration to speech-evoked fNIRS measurements. Group comparisons suggest that CI users may derive greater perceptual benefit from visual speech cues in noisy audio-visual conditions compared to NH controls, although this finding was dependent on the exact means by which the level of this 'visual benefit' was quantified. Correlation analysis conducted between visual benefit and audio-visual integration within STC demonstrated differential functional relationships in the two groups that may be explained by the principle of inverse effectiveness.

Chapter 9: Summary and Discussion

This chapter presents a summary of the aims and main findings of the thesis, including: i) the recovery of speech perception abilities following implantation; ii) the ability of fNIRS to measure speech-evoked cortical activation before and after implantation; iii) cortical activation to visual speech as a pre-implant predictor of future CI outcome; iv) individual variability in post-implant cortical plasticity as a neural correlate of variable CI outcome; and v) integration of auditory and visual speech information at the behavioural and cortical level following cochlear implantation. The chapter provides a general discussion and interpretation of these results, including

limitations of the current research. Directions for future research are proposed and closing conclusions are made.

2. THE ROLE OF CORTICAL PLASTICITY IN VARIABLE COCHLEAR IMPLANT OUTCOMES: A LITERATURE REVIEW

2.1 INTRODUCTION

Cochlear implantation can be a highly successful rehabilitative option for ameliorating severe-to-profound sensorineural hearing loss and in significantly improving the ability to perceive auditory speech information (Summerfield & Marshall, 1995; Teoh et al., 2004; UKCISG, 2004a). However, the level of this clinical benefit obtained from cochlear implantation can vary drastically between CI recipients and remains largely unpredictable (Blamey et al., 1996, 2013; Green et al., 2007; Lazard et al., 2010a, 2012a). In clinical practice, the prognostic information available to healthcare professionals is currently insufficient to accurately inform patients of the anticipated clinical benefit of cochlear implantation and to set and manage their expectations most effectively. Therefore, a greater understanding of the factors that underlie and determine CI outcome is necessary to facilitate more realistic and accurate prognoses that in turn could enable improved counselling of patients' expectations and informed consent to treatment. This chapter first reviews the research to date regarding known influential clinical variables and the predictive value that they offer. Given the large proportion of variance in CI outcome left unaccounted for by these clinical characteristics and the influence

that they may exert on the central auditory processing system, the importance of examining the contribution of cortical factors to the observed variability in CI outcome is highlighted. Evidence of cortical adaptation during periods of profound deafness and the subsequent restoration of auditory inputs following cochlear implantation is examined. In particular, the effects of this cortical plasticity within the superior temporal cortices and the consequences for reaching proficient levels of auditory speech perception with a CI are discussed. This chapter concludes by outlining the current challenges faced in measuring cortical plasticity following deafness and the subsequent reintroduction of hearing through implantation using conventional neuroimaging techniques. Specifically, the promising application of functional near-infrared spectroscopy for studying auditory cortical function and plasticity in CI users over time is outlined.

2.2 VARIABILITY IN COCHLEAR IMPLANT OUTCOME

2.2.1 Sensorineural Hearing Loss and Cochlear Implantation

In the UK, approximately 11 million people are estimated to have some degree of hearing loss (HL) with approximately 900,000 estimated to have severe-to-profound deafness (Action on Hearing Loss, 2011). The functional, social, emotional and economic impact that HL and deafness can have on the individual is well acknowledged (World Health Organisation, 2015). However, it is important to recognise a distinction between those individuals with an acquired deafness and those who are congenitally deaf and

native sign language users, for whom deafness is not seen to impair functional abilities (Bond et al., 2009; Munoz-Baell & Ruiz, 2000). Damage to the cochlea is said to be the most common cause of HL in developed countries (Moore, 2007). In the case of severe-to-profound sensorineural hearing loss (SNHL), extensive damage or complete absence of the cochlear hair cells means that spiral ganglion neurons of the auditory nerve cannot be properly stimulated by acoustic information. Therefore, the transmission of incoming acoustic information from the peripheral to the central auditory system is greatly diminished. However, it is in the auditory brain regions where acoustic information must be processed in order to be perceived as sound. Subsequently, an individual with severe-to-profound SNHL displays a markedly reduced ability, or in some cases a complete inability, to perceive auditory speech information.

Typically, acoustic hearing aids (HAs) are an ineffective rehabilitative option for individuals with bilateral profound SNHL: often caused by damage of the inner ear hair cells, an amplification of acoustic signals by HAs provides limited or no benefit in transmitting the acoustic signal along the auditory nerve to the cortex. Alternatively, a CI can offer a more effective rehabilitation option as it bypasses the damaged elements within the cochlea by directly stimulating spiral ganglion neurons of the auditory nerve (see Figure 2.1 for more detailed information).

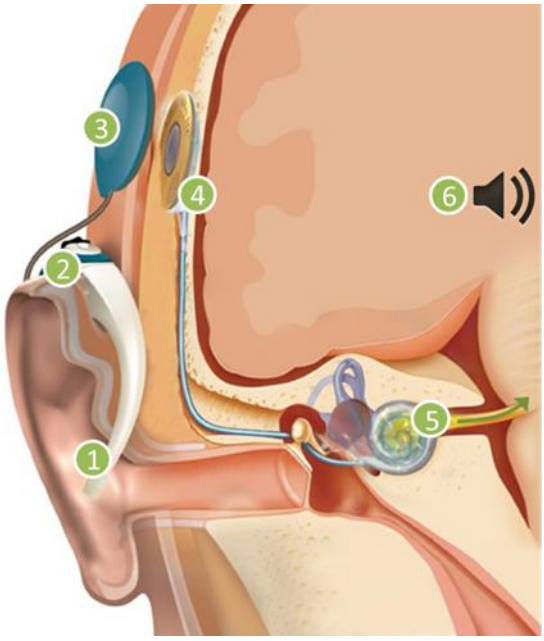


Figure 2.1: An illustration of how a cochlear implant works.1) The external microphone receives incoming acoustic information from the environment. 2) The over-ear speech processor analyses this acoustic information and converts it into digital information. 3) The magnetic external coil transmits the digital information to the internally implanted receiver. 4) The receiver converts the digital information into electrical signals that are transmitted down the electrode array. 5) The electrode array implanted within the cochlea stimulates the spiral ganglion neurons of the auditory nerve, bypassing the damaged cochlea hair cells. These electronic signals are then transmitted via the auditory nerve to the central auditory system. 6) The auditory brain regions process the electronic signals, resulting in the perception of sound. *(Adapted from Advanced Bionics:* http://www.advancedbionics.com/com/en/your_journey/what_is_a_cochlearimplantsystem.html*)*

In this way, a CI provides individuals with an opportunity for a partially restored, but artificial, sensation of hearing. In the UK, unilateral cochlear implantation for adults is deemed a cost-effective rehabilitative option (Bond et al., 2009; UKCISG, 2004a); however, not all adults with a severe-to-profound SNHL are suitable candidates for cochlear implantation and the CI candidacy assessment process involves a breadth of assessments conducted by a multidisciplinary team. Broadly speaking, the components of this multidisciplinary process include audiological, surgical, psychological, and rehabilitative assessment, all of which contribute

towards determining the candidate's suitability for implantation. In terms of governance, the National Institute for Health and Care Excellence guidelines (NICE, 2009) state that certain audiological criteria must be met. Firstly the candidate must have a profound bilateral deafness, defined as pure-tone hearing thresholds of more than 90 decibels hearing level (dB HL) at frequencies of 2 and 4 kilohertz (kHz) in both ears. Furthermore, the candidate must have a best-aided auditory word recognition score of 50% or less on the Bamford-Kowal-Bench (BKB) sentence test (Bench et al., 1979). Traditionally adult CI candidates were those individuals who had acquired deafness after the acquisition of native language (post-lingual deafness), as those individuals with pre-lingual and congenital deafness were thought not to benefit from implantation. However, due to continued developments in various aspects of the cochlear implantation process, it is now widely accepted that congenitally deaf and pre-lingually deaf individuals can gain substantial benefit from implantation, albeit lower than that achieved by traditional post-lingual recipients (Teoh et al., 2004).

It is acknowledged that various forms of benefit can be derived from cochlear implantation. For instance, typical audiological measures of 'CI benefit' or 'CI outcome' include the ability to accurately perceive auditory and audio-visual speech (sound supplemented by speechreading). Other audiological outcomes also include increased awareness or recognition of environmental sounds, reduction of tinnitus, ability to communicate using the telephone, watching the

television unaided by subtitles, and the appreciation of music (Cooper, 2006). Beyond such audiological outcomes, potential benefits of cochlear implantation include improved overall quality of life (Damen et al., 2007; Klop et al., 2007; UKCISG, 2004b), increased social interaction (Ross & Lyon, 2007), improved employment status and prospects (Chee et al., 2004; Fazel & Gray, 2007), and benefits to psychological well-being (Olze et al., 2011; Rembar et al., 2009; Summerfield & Marshall, 1995). Nonetheless, as a CI is an auditory rehabilitation device, and typical CI candidates seek restoration of functional aural communication abilities, the clinical benefit obtained from a CI is typically measured by improvements in auditory speech perception. In addition, empirical research studies commonly define performance on tests of auditory speech perception as the primary measure of CI outcome. Indeed, this thesis defines 'CI outcome' as the level of auditory speech perception achieved following cochlear implantation.

Several studies document significant improvements to adult CI users' word and sentence recognition abilities compared to their pre-implant best-aided abilities (Blamey et al., 2013; Gantz et al., 1993; Lazard et al., 2010a, 2012a; Summerfield & Marshall, 1995; Tyler et al., 1997; UKCISG, 2004a). Despite this, pronounced variability in CI outcome across adult recipients has been shown in both early (Blamey et al., 1992; Gantz et al., 1993; Summerfield & Marshall, 1995; Tyler et al., 1997) and more recent studies (Blamey et al., 2013; Lazard et al., 2010a, 2012a). Specifically, both the

rate and direction of the recovery of speech perception is seen to vary across individuals (Tyler et al., 1997, see Figure 2.2), and the ultimate level of auditory performance achieved can be seen to span the entire possible range (0—100 % correct, Lazard et al., 2010a, Figure 2.3). In some ways, this variation in CI outcome is not entirely surprising. Firstly, the CI provides an artificial sensation of hearing that is markedly different from that of natural hearing. Therefore, CI users have to acclimatize to and learn to process this novel and degraded sound signal (Tyler & Summerfield, 1996), and the ability to do so no doubt varies between individuals and as a function of time. Secondly, CI recipients are commonly heterogeneous in many clinical characteristics including the age-at-onset of deafness, the duration of deafness, etiology of deafness, level of usable residual hearing, and history of HA use (Blamey et al., 2013; Lazard et al., 2010a, 2012a; Summerfield & Marshall, 1995). All such factors undoubtedly give rise to a high level of inter-individual variability in CI outcome and the evidence pertaining to this is reviewed below.

2.2.2 Influence of Clinical Characteristics on Cochlear Implant Outcome

2.2.2.1 Aetiology of Deafness

The cause or aetiology of profound deafness in adults is notoriously difficult to establish: a nationwide study of cochlear implantation in the UK documented that, between 1990 and 1994, the majority of CI recipients (34%) had an aetiology classified as 'not known' and

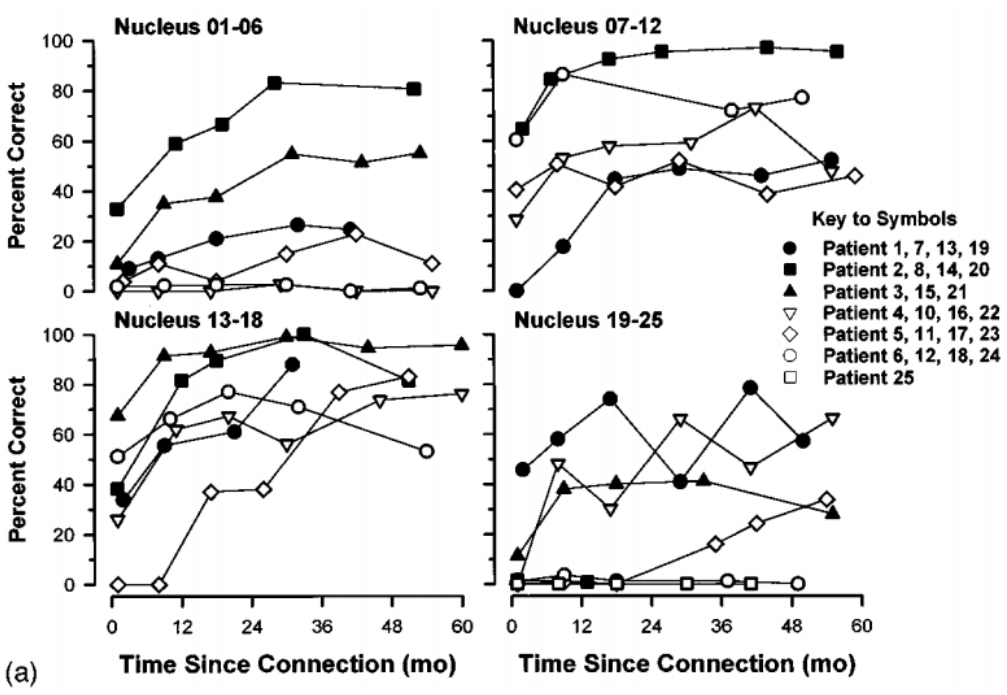


Figure 2.2: Variations in individual trajectories of auditory performance with a CI. Auditory sentence identification scores are shown as a function of CI use *Taken from Tyler et al. (1997).*

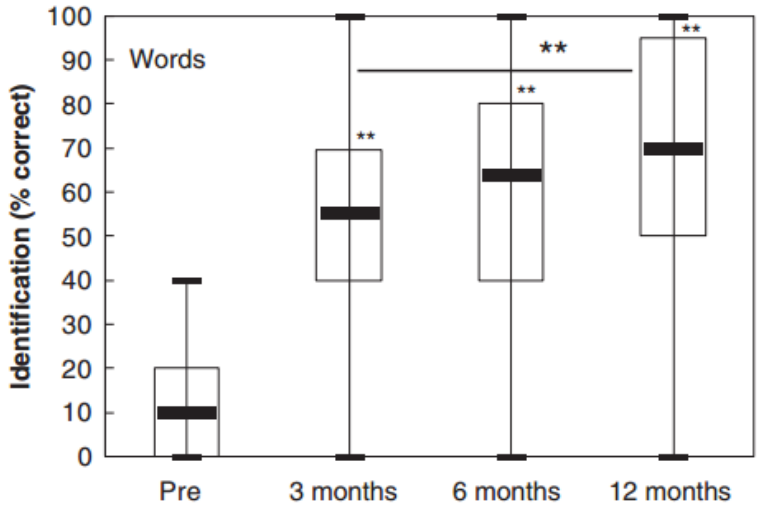


Figure 2.3: Variability in CI outcome in post-lingually deaf CI users. Auditory word identification scores are shown as a function of CI use. *Taken from Lazard et al. (2010)*.

15% as 'idiopathic' (Summerfield & Marshall, 1995). It is generally accepted amongst the literature and within clinical practice that the aetiology of deafness is not a useful predictor of outcome or the

most appropriate guide to candidature (Fielden, 2006; Summerfield & Marshall, 1995). However, certain aetiologies including meningitis (Green et al., 2007) and otosclerosis (Blamey et al., 1992) have been associated with poorer CI outcomes. This is likely due to the associated abnormal bone growth or ossification of the cochlea affecting both the electrode position and the depth of electrode insertion within the inner ear, which are known to influence CI outcome (Aschendorff et al., 2007; Blamey et al., 1992; Skinner et al., 2002, 2007; Yukawa et al., 2003).

2.2.2.2 Duration of Deafness

As with aetiology, it can prove difficult to reliably establish the duration of deafness prior to implantation, particularly if the progression of HL has been gradual. Despite this, the duration of severe-to-profound HL experienced prior to implantation has been commonly cited as a pre-implant predictor of CI outcome. For instance, significant, moderate-to-strong, negative correlations have been consistently observed between the duration of deafness and CI outcome in adults, with a longer period of deafness prior to implantation relating to poorer speech perception abilities (Blamey et al., 1996, 2013; Gomaa et al., 2003; Green et al., 2007; Hirschfelder et al., 2008; Holden et al., 2013; Summerfield & Marshall, 1995; UKCISG, 2004a). Green and colleagues (2007) classified 117 post-lingually deafened adult CI users as 'poor', 'average', or 'good' performers on a measure of speech perception. They found that the duration of deafness prior to implantation was

an independent predictor of CI outcome, with each additional year of deafness experienced prior to implantation increasing patients' chances of falling into a poorer performing group by 9%. Similarly, in a larger international study of 2251 post-lingually deafened CI users, Lazard and colleagues (2012a) demonstrated that, in the absence of HA use, auditory performance following cochlear implantation was significantly reduced by 0.83 percentage points with each additional year of severe-to-profound deafness experienced. One line of reasoning suggests that a longer duration of deafness may be detrimental to speech perception following implantation due to the degenerative effect of SNHL on the peripheral auditory system. For example, it has been suggested that duration of deafness is related to a reduction in spiral ganglion cells, and hence both factors are related to poorer CI outcome (Nadol et al., 1989). However, most histopathology studies in humans have found no clear relationship between the number of spiral ganglion cells and CI outcome (Fayad et al., 1991; Fayad & Linthicum, 2006; Khan et al., 2005; Nadol et al., 2001; Xu et al., 2012) suggesting that the duration of auditory deprivation may not exert its influence on CI outcome solely through the degeneration of the peripheral auditory system. Indeed, neuroimaging evidence from adult CI users has suggested the duration of auditory deprivation experienced before implantation may negatively impact on auditory performance with a CI by limiting the capability of superior temporal regions to be effectively stimulated by auditory speech. For instance, a longer duration of deafness prior to

implantation has been associated with a lower level of auditory speech-evoked activation within bilateral auditory association cortices following implantation (Green et al., 2005), and a lower level of activation within left posterior superior temporal regions during phonological processing (Lazard et al., 2013).

2.2.2.3 Age-at-Onset of Deafness

Whilst the duration of deafness is known to be an important factor in determining CI outcome, it is also acknowledged that the timing of deafness in relation to language acquisition is highly influential, and distinctions based on this onset of deafness are often made. In NH individuals, auditory experience begins prenatally (Hepper & Shahidullah, 1994) and can influence postnatal auditory development (DeCasper & Spence, 1986). Therefore, congenitally deaf individuals are known to have radically altered auditory and language experience from gestation compared with NH individuals. If the onset of deafness occurs after birth, but prior to language acquisition, this is referred to as pre-lingual deafness. Pre-lingually deaf individuals typically have some exposure to auditory input and experience spoken language during gestation, infancy and perhaps early childhood, but would not have fully acquired their native spoken language in conditions of normal auditory input. Conversely, when the onset of deafness occurs after the acquisition of language this is referred to as post-lingual deafness. In such cases, post-lingually deafened CI recipients experience typical

auditory development and acquire language under conditions of normal auditory input prior to the onset of deafness in later life.

Consequentially, the age-at-onset of deafness can be an important distinguishing factor in terms of rehabilitative options and CI efficacy: although advancements in cochlear implantation have enabled congenitally and pre-lingually deafened adolescents and adults to benefit from cochlear implantation (Schramm et al., 2002; Teoh et al., 2004), the maximal benefit achieved by these individuals is on average significantly lower than for post-lingually deafened adult CI recipients (Teoh et al., 2004). This is thought to be due to differences between the development of auditory cortical function during a sensitive period in infancy and early childhood (Kral & Sharma, 2012; Sharma et al., 2002; Sharma & Campbell, 2011). Indeed, congenitally and pre-lingually deafened children are known to achieve better speech and language outcomes when implantation takes place at an earlier age, preferably within the sensitive period to allow for normal development (Peterson et al., 2010; Sharma & Campbell, 2011; Snik et al., 1997). Moreover, neuroimaging evidence in adult CI users suggests the differential development of temporal-lobe speech processing networks in individuals depending on when the onset of deafness occurred in relation to language acquisition: specifically, speech-evoked activation within auditory association cortices has been found to be significantly reduced in pre-lingually deaf compared to post-lingually deaf individuals (Naito et al., 1997). Furthermore, the ability to

selectively recruit left STG in response to speech compared to multi-talker babble has been evidenced in post-lingually deaf adult CI users, but not pre-lingually deaf CI recipients (Petersen et al., 2013).

2.2.2.4 Residual Hearing and Hearing Aid Use

A higher level of pre-implant residual hearing may, theoretically, reflect a less impaired peripheral auditory system and thus could positively impact on future CI outcome. However, some studies have found no such evidence of a relationship between pre-operative, pure tone average hearing thresholds and auditory performance following implantation (Blamey et al., 1992; Gantz et al., 1993). Conversely, Gantz et al. (1993) demonstrate that the number of frequencies with a measurable hearing threshold was predictive of CI outcome, suggesting that the overall bandwidth of residual hearing may be important. Alternatively, it appears that a more meaningful measure, namely, 'usable' residual hearing, may be a more informative factor in explaining CI outcome. For instance, Gomaa et al. (2003) demonstrated that the level of pre-implant aided sentence recognition was positively associated with the level of post-implantation word recognition. The authors suggest that this preoperative usable residual hearing may be a protective factor against the degenerative effects of profound SNHL as it maintains both peripheral and central auditory pathways that are integral to successful speech perception with a CI. Similarly, Lazard et al. (2012a) quantified residual hearing as the pre-implant

hearing thresholds of the better ear, averaged across 500, 1000 and 2000 Hz and demonstrated that this level of residual hearing correlated strongly with pre-implant speech perception abilities. Furthermore, this measure reflecting the level of usable residual hearing was seen to have a consistent significant influence on CI outcome. Interestingly, implantation of the better ear or worse ear (in terms of pre-implant hearing thresholds) did not have an effect on CI outcome. Taking these results together, the authors concluded that successful speech perception with a CI may not rely on the peripheral status of the implanted ear. Rather they propose that the continued provision of auditory inputs, reflected by the level of usable residual hearing, may be crucial for maintaining central auditory pathways for the accurate processing of speech with a CI.

In line with this notion, it has been suggested that the pre-operative use of HAs could guard against, or modify, the detrimental effects of auditory deprivation. For instance, Lazard et al. (2012a) demonstrated that, in cases where bilateral hearing aids were worn prior to implantation, the detrimental effect of the duration of severe-to-profound hearing loss on the level of auditory speech perception achieved with a CI was reduced by almost one half. Studies have shown that residual hearing (Lambertz et al., 2005) and provision of enriched acoustic input following HL (Noreña & Eggermont, 2005) can protect against cortical plasticity and reorganisation, the extent of which may determine CI outcome

(Doucet et al., 2006; Lee et al., 2001; Sandmann et al., 2012). Complementary observations from neuroimaging studies in individuals with early-onset deafness confers that a greater duration of hearing aid use may guard against cortical reorganisation: specifically, Shiell et al. (2014) observed an inverse relationship between the duration of hearing aid use and the extent of cross-modal response to visual motion in superior temporal cortices, as well as the level of functional connectivity between auditory and visual brain regions.

2.2.3 Predictive Models of Cochlear Implant Outcome

As is clear from the above, CI recipients differ in many factors that, in combination, form individualistic profiles of each CI recipient and no doubt interact and influence the amount of benefit an individual is able to obtain from their CI. In isolation, the relationship between each of these factors and CI outcome can be elucidated, as reviewed in the previous section. However, by assessing these factors in combination, their collective ability to explain and predict CI outcome as well as their relative importance can be better understood. As data pertaining to the influential clinical characteristics of CI users are readily available from CI clinics, these factors are commonly incorporated and assessed by predictive models of CI outcome. For instance, Summerfield & Marshall's (1995) seminal evaluation of the UK's national Cochlear Implant Programme involved data collection from approximately 300 adult CI recipients prior to implantation. Of these, data were available for

approximately 170 recipients following nine months of implant use and for approximately 100 recipients 18 months post-implantation. One measure of CI performance used in this evaluation was a composite measure of ability to identify speech and environmental sounds nine months after implantation. Several step-wise multiple regression analyses were conducted with varying combinations of factors to determine their predictive value of CI performance. For example, one model demonstrated that 33% of the variance in CI performance was accounted for by recency of onset of profound deafness, pre-operative usable residual hearing (defined here as the benefit gained from HAs supplemented by speechreading), and pre-operative lip-reading ability. The authors suggest that such factors could be indicative of the importance of auditory nerve survival and responsiveness, ability to map phonological and linguistic representations onto incoming sounds, and ability to both attend to and centrally process sensory information for successful CI performance. However, despite this model incorporating factors relating to both peripheral and central processing, a large amount of variance in CI outcome (67%) still remained unexplained. The authors warned that none of their models were able to identify a combination of factors powerful enough to predict outcomes or guide candidacy criteria, thus highlighting the difficulties faced in forming an accurate prediction of CI outcome.

Similarly, Green et al. (2007) highlight that predicting CI outcomes from clinically available data remains problematic. In this study,

data were obtained from 117 adult CI users within the Manchester Cochlear Implant Programme. Using multivariate ordinal regression on a variety of clinically available factors, the authors identified the duration of deafness as the only independent predictor of CI outcome. Using a larger international multicentre data set, Blamey et al. (1996) conducted a retrospective study of 808 post-lingually deafened adult CI users. They first proposed a theoretical four-factor, three-stage model of auditory performance over time (see Figure 2.4). An analysis of variance using the General Linear Model (GLM) showed that the proposed four factors, including duration of profound deafness, age-at-onset of profound deafness, duration of implant use and aetiology, all had a significant effect on CI outcome. In combination, these factors accounted for 21% of the variance in outcome, with duration of deafness accounting for the largest proportion of the variance (13%). Due to inherent variability of the data, the variance arising from random factors was estimated to account for approximately 15% of the variance. Therefore, taking the four-factor model of auditory performance and the inherent variability of the data into account, approximately 64% of the variance in CI outcome remains unexplained by this model. Blamey et al. (2013) updated this model with a more recent and larger sample of 2251 post-lingually deaf adults who received a CI between 2003 and 2011.

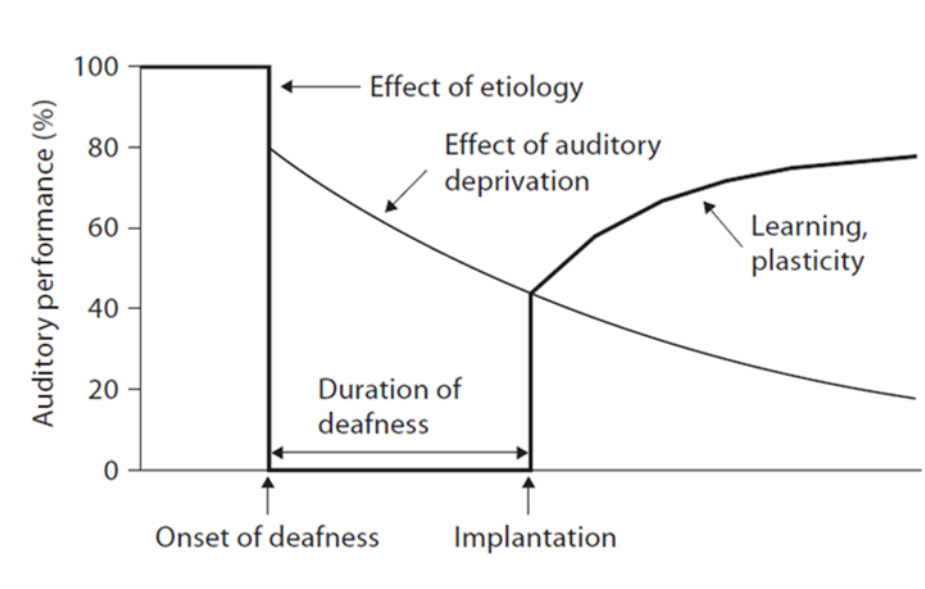


Figure 2.4: Blamey's (1996) theoretical three-stage model of auditory performance in a post-lingually deafened adult. The **bold** line represents the trajectory of auditory performance, beginning at 100% in Stage 1 of normal hearing and decreasing in Stage 2 at the onset of profound deafness. Stage 3 occurs at the time of cochlear implantation and includes a learning curve that incorporates the effects of surgical and device related factors and cortical reorganisation. The thin line represents potential auditory performance with a cochlear implant, incorporating the effect of etiology and duration of auditory deprivation on cochlear implant outcome. *Taken from Blamey et al. (2013).*

The original four factors (Blamey et al., 1996) were still seen to have a significant effect on CI outcome; however, these now were only seen to account for 10.5% of the variance in outcome compared to 21% in 1996. Furthermore, their relative importance had changed: the duration of profound HL was less important, aetiology had a smaller effect, and duration of CI experience had a greater effect with auditory performance improving more rapidly within the first year of CI use. These differences between the two studies are not necessarily surprising as more individuals with residual hearing are now being implanted due to the relaxation of candidacy criteria over time. In addition, there have been

technological advancements in both HA and CI devices, as well as improvements in surgical techniques and audiological management.

In acknowledgment of this, using the dataset of Blamey et al. (2013), Lazard et al. (2012a) investigated additional factors that they felt were more timely and reflective of current clinical populations, procedures and practices used within modern CI programmes. For instance, they included factors such as duration of moderate HL, residual hearing, HA use, CI brand and surgical approach. From these factors they determined that, in addition to the four factors identified by Blamey et al. (2013), auditory performance in quiet was most heavily influenced by duration of moderate HL, HA use through its mediating influence on the impact of duration of severe-to-profound HL (outlined in section 2.2.2.2), amount of residual hearing, CI brand and the percentage of active electrodes post-operatively. These most influential factors were incorporated into a nine-factor model that was able to account for 22% of the total variance in speech recognition with a CI, a larger proportion compared to the 10.5% of Blamey and colleagues' (2013) four-factor model. Lazard et al. (2012a) note that their updated model of auditory performance (Figure 2.5) incorporates newly identified factors, including duration of mild-to-moderate HL and duration of HA use, that may incorporate the effects of central reorganisation on CI outcome. For example, whilst cortical reorganisation of auditory brain regions has been documented in cases of

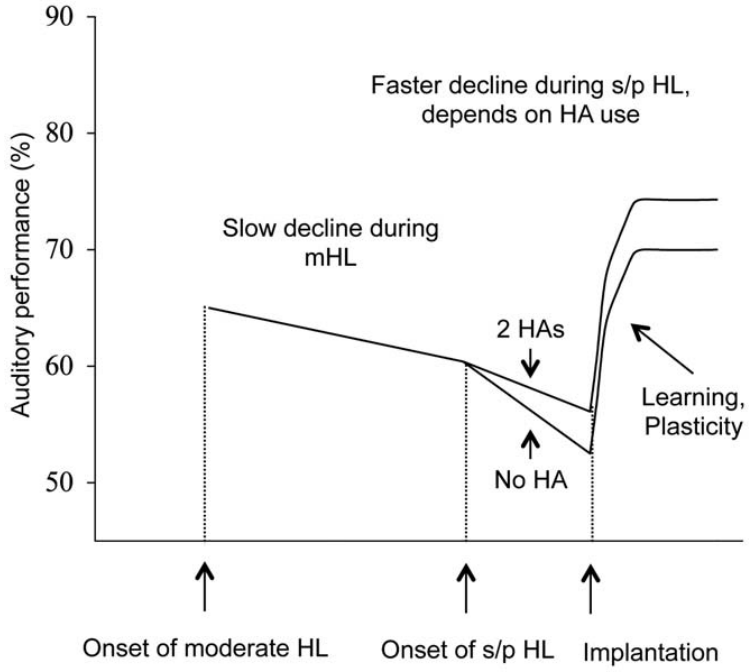


Figure 2.5: Lazard's (2012a) three-stage model of auditory performance over time for a typical postlingually deaf CI user. Moderate hearing loss and severe to profound hearing loss are labelled as mHL and s/p HL respectively, HA: hearing aid.

severe-to-profound HL (Fine et al., 2005; Finney et al., 2001), central modifications of temporal brain regions associated with poorer auditory performance in noise have also been evidenced in the early stages of adult-onset mild-to-moderate hearing loss (Campbell & Sharma, 2014). Furthermore, as discussed in section 2.2.2.4, the protective role of hearing aid use on central modifications has also been indicated (Shiell et al., 2014).

2.2.4 Summary

From the above review of the literature, it is clear that an extensive range of factors can influence how much benefit an individual receives from their CI. This highlights the difficulty and complexity that researchers and clinicians face in accurately predicting CI outcome. Factors relating to clinically-relevant, pre-, peri- and

post-operative factors have been investigated most heavily as these data are uniformly collected across cochlear implant programmes. Models of auditory performance have been crucial in enabling us to understand the relative importance of these particular factors in CI success, providing information that can help to guide the assessment process within the clinic and to inform candidates' expectations (Blamey et al., 1996, 2013; Green et al., 2007; Lazard et al., 2012a; Summerfield & Marshall, 1995). However, the large proportion of variance in outcome left unexplained by these models suggest that investigating factors beyond the typical clinical variables may prove fruitful if a more comprehensive understanding of what determines CI outcome is to be achieved. In particular, the ability of the brain to process auditory speech information provided by the implant may be an influential factor (Green et al., 2005; Naito et al., 1997; Petersen et al., 2013). Indeed, the importance of understanding the role of such central factors in influencing and predicting CI outcome is becoming increasingly acknowledged amongst the field (Lawler et al., 2015; Lazard et al., 2012b; Wilson et al., 2011). More timely predictive models of CI outcome have begun to incorporate the effects of clinical characteristics, such as duration of mild-to-moderate HL and duration of HA use, that may exert their influence on the central as well as the peripheral auditory system (Lazard et al., 2012a). In doing so, this model accounted for a greater proportion of the variance in CI outcome compared to other comparable models (Blamey et al., 1996, 2013). In this way, a complex interplay between clinical characteristic of the listener

may influence CI outcome that, at least in part, may reflect effects on the central auditory processing system. Thus, more direct measurement of cortical function, which is not currently conducted in CI clinics, may be crucial if the relationship between central factors and variable speech perception abilities following implantation is to be fully elucidated.

2.3 CORTICAL PREDICTORS AND CORRELATES OF COCHLEAR IMPLANT OUTCOME

2.3.1 Adaptation of the Brain to Sensory Loss

The structural and functional organisation of the human brain was once assumed to be largely fixed in nature, with change only possible through normal development and maturation in childhood. However, it is now widely accepted that the brain's organisation is malleable and susceptible to events occurring in the individual's environment, even during adolescence and throughout adulthood. For instance, a plethora of research has demonstrated the brain's ability to change its organisation in response to perceptual learning (Draganski et al., 2004; Lövdén et al., 2013), environmental enrichment (Rosenzweig & Bennett, 1996), sensory deprivation (Bavelier & Neville, 2002; Holtmaat & Svoboda, 2009; Rauschecker, 1995, 1999) and injury and rehabilitation (Wieloch & Nikolich, 2006). The brain's ability to modify its structural and/or functional organisation in response to such events is referred to as 'cortical plasticity' (Bavelier & Neville, 2002; Merabet & Pascual-Leone, 2010). Of particular interest and relevance to this thesis is how the

brain adapts to altered sensory inputs and sensory experience, and how this can manifest at the behavioural level. Early sensory experience is crucial for the normal development of cortical areas that support sensory functions (Carvell & Simons, 1996; Meredith & Allman, 2012; Simons & Land, 1987). The reduction or absence of sensory input is known to impact on the cortical development of the juvenile brain (Kral et al., 2005) and can also induce changes in the adult brain (Allman et al., 2009; Lazard et al., 2013). Of note, sensory deprivation in one modality can strongly impact on other intact modalities at both the cortical and behavioural level. At the cortical level, brain regions normally associated with the deprived modality can become more sensitive to other intact modalities (e.g. Auer et al., 2007; Finney et al., 2001). In such cases, the deprived sensory cortices are said to be 'recruited' by other intact modalities, often referred to as 'cross-modal reorganisation' or 'cross-modal plasticity' (Bavelier & Neville, 2002). At the behavioural level, these cortical changes in the deprived modality can result in functionally-relevant and compensatory behaviour in the other intact sensory modalities, as illustrated in Figure 2.6 (Cohen et al., 1997; Gougoux et al., 2005; Lomber et al., 2010; Merabet & Pascual-Leone, 2010). Although these adaptations to sensory loss are compensatory during deprived periods, there is a risk that such changes may be detrimental when the deprived modality is subsequently reinstated (Kral & Eggermont, 2007; Sandmann et al., 2012). Cochlear implantation of profoundly deaf individuals offers a unique

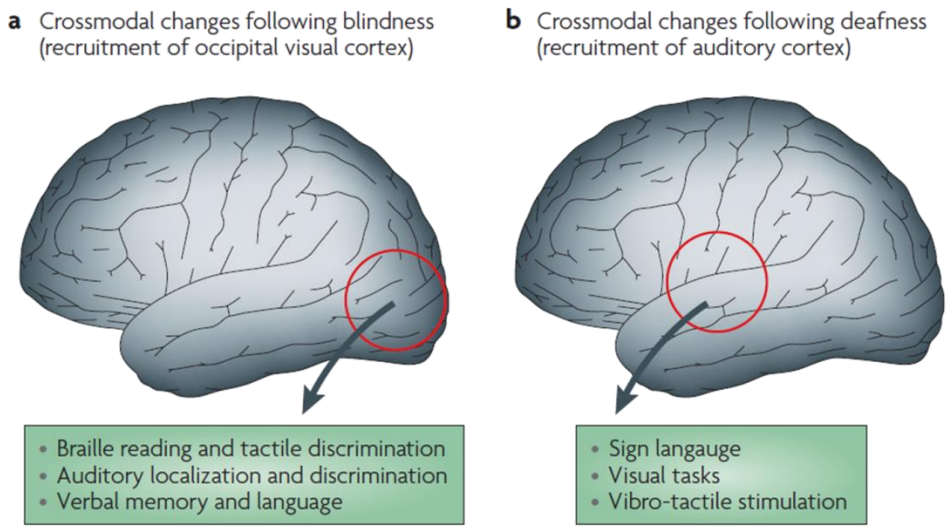


Figure 2.6: A schematic representation of cross-modal changes following sensory deprivation. a) visual brain regions being recruited for non-visual processes in blind individuals; b) auditory brain regions recruited for non-auditory processes in deaf individuals. *Taken from Merabet & Pascual-Leone (2010).*

opportunity to understand cortical changes following auditory deprivation and subsequent auditory restoration, as well as the behavioural correlates of such cortical plasticity.

2.3.1.1 Cortical Plasticity Following Deafness

In the case of auditory deprivation, deaf individuals show adaptive changes and strategies in order to effectively interact with their environment. For instance, enhanced or 'supranormal' non-auditory abilities have been evidenced in deaf compared to NH individuals. These include enhanced peripheral visual attention (Bavelier et al., 2000, 2006; Neville & Lawson, 1987), superior visual speech perception abilities (Auer & Bernstein, 2007) and heightened tactile sensitivity (Levänen & Hamdorf, 2001). Neuroimaging studies have suggested that cross-modal activation within the auditory brain regions may support behavioural enhancements observed in deaf

individuals. For example, Auer et al. (2007) provide evidence using functional magnetic resonance imaging (fMRI) of greater and more widespread activation to vibrotactile stimulation of the hand within bilateral auditory brain regions of deaf adults compared to NH controls. The authors speculate that this cross-modal reorganisation, whereby auditory brain regions become more responsive to somatosensory input, may underlie the superior tactile sensitivity thresholds of deaf individuals that have been demonstrated elsewhere (Levänen & Hamdorf, 2001).

In a similar way, compared to NH controls, greater cross-modal responses to visual motion stimuli have been observed within right auditory brain regions of congenitally deaf individuals (Fine et al., 2005; Finney et al., 2001; Sadato et al., 2005). For instance, a seminal study by Finney et al. (2001) showed activation within right primary and secondary auditory cortices of congenitally deaf, but not hearing, individuals in response to a visual moving dot pattern. Whilst these findings suggest that cross-modal plasticity in auditory brain regions may be driven by auditory deprivation, disentangling the effects of deafness from other confounding factors can be problematic. Notably, sign language is a visual method of communication that involves visual motion processing, and is the native and preferred language of many congenitally deaf individuals (Sutton-Spence & Woll, 1999). Therefore, it is plausible that heightened responsiveness to visual stimuli in auditory brain regions and enhanced visual motion detection abilities may be mediated by

sign language experience rather than auditory deprivation per se. In an attempt to distinguish between these effects, Fine et al. (2005) demonstrated that visual motion stimuli evoked significant activation in right primary and secondary auditory cortices (Brodmann's areas, BA 41, 42 and 22) of deaf native signers but not of hearing native signers or hearing non-signers. These findings suggest that the cross-modal responsiveness of the right auditory brain regions to visual stimuli in deaf adults is driven by auditory deprivation rather than sign language experience. Further to this, Cardin et al. (2013) demonstrated dissociation between the effects of sign language experience and sensory experience on cortical plasticity in congenitally deaf adults: plasticity effects in the left superior temporal cortex were associated with sign language experience and thought to be of linguistic origin, whereas plasticity effects in the right superior temporal cortex were associated with auditory deprivation and thought to be of a sensory nature.

These plasticity effects are thought to prove functional during periods of profound deafness by underlying supranormal visual abilities. Formative evidence of this comes from Lomber et al. (2010) who used a cortical cooling technique to create temporary deactivations in the auditory cortex of congenitally deaf cats. In doing so, Lomber and colleagues demonstrated that deactivation of the posterior auditory cortex and dorsal zone eliminated superior visual localisation and motion detection abilities respectively, indicating a causal relationship whereby these auditory brain regions

had been recruited to support enhanced visual performance. Of further interest, the deactivation of primary auditory areas did not modify the cats' visual performance, demonstrating that primary auditory brain regions were not recruited for visual processing and may not have undergone cross-modal reorganisation. In line with this, higher-order association cortices are thought to be more susceptible to cross-modal reorganisation following sensory loss than are primary sensory cortices (Kral et al., 2003; Lomber et al., 2010; Meredith et al., 2011). It has been recognised that the higher-order association cortices support perceptual functions that are shared by different sensory modalities, and in this way the association cortices may be more susceptible to receiving and processing inputs from different sensory modalities (Dormal & Collignon, 2011; Lomber et al., 2010; Meredith et al., 2011). For instance, it has been said that right temporal-lobe activation to visual motion stimuli observed in deaf individuals likely reflects a right temporal-lobe propensity for auditory motion processing (Baumgart et al., 1999) that, in the absence of auditory input, re-allocates auditory resources to visual motion processing (Sadato et al., 2005). Whilst the mechanisms underlying cortical plasticity following deafness remain uncertain and may differ depending on the nature of the plasticity effects, plausible mechanisms include enhancement of existing cortico-cortical pathways (either directly between sensory cortices or via projections from multimodal brain regions), change in input from thalamic structures to the cortex, as well as a combination of synaptic pruning, strengthening, and

unmasking of these connections (Bavelier & Neville, 2002; Pascual-Leone et al., 2005; Rauschecker, 1995).

2.3.1.2 Implications for Auditory Rehabilitation

Whilst cortical plasticity may be beneficial during periods of profound deafness, subsequent restoration of auditory input into an altered central auditory system may prove problematic for establishing proficient auditory function. Indeed, neuroimaging studies have sought to understand the impact of deafness-related modifications within auditory brain regions on future CI outcome. In a seminal study using positron emission tomography (PET), Lee et al. (2001) examined the pre-implant resting-state cortical metabolism of pre-lingually deaf children. It was shown that the size of the hypometabolic area, thought to indicate lack of cross-modal responses, in bilateral primary (BA 41) and association auditory cortices (BA 22/42) was strongly and positively correlated with post-implant auditory speech perception abilities. These findings have been taken as evidence that a high-level of cross-modal responsivity before implantation may have a detrimental impact on future CI outcome. Although it is somewhat speculative to infer level of cross-modal response from an indirect measure such as resting state metabolism, these results were amongst the first to indicate the potential prognostic value of cortical factors in CI outcome.

Studies conducted following implantation have also indicated the detrimental role of cross-modal plasticity on CI outcome. In particular, electrophysiological techniques have been employed to measure of the extent of cross-modal activations within the auditory cortex of adult CI users. For instance, using electroencephalography (EEG), Sandmann et al. (2012) demonstrated enhanced visual evoked potentials over the right auditory brain regions of post-lingually deafened adult CI users compared to NH controls when presented with reversing chequerboard images. This level of visually-evoked activation was modulated by the visual luminance ratio of the stimulus, suggesting functionally-relevant visual responses within the right temporal brain regions. Of particular note, the amplitude of visually-evoked activation was inversely related to CI users' speech perception abilities in quiet and in noise. This lends support to the notion that a high level of cross-modal plasticity within temporal auditory brain regions may limit the ability of the auditory cortex to process the novel auditory input provided by the CI, thus resulting in poor CI outcome. Buckley and Tobey (2011) also provide corroborating EEG evidence of an association between greater visually-evoked activation over the right temporal lobe and poorer auditory speech perception abilities with a CI. It is interesting that this association between cross-modal response and CI outcome was observed only in pre-lingually deaf CI users and not in post-lingually deaf CI users. However, the duration of deafness was not associated with the amplitude of cross-modal response (Buckley & Tobey, 2011), as has

also been indicated in previous studies (Desai et al., 2007; Lee et al., 2007b; Suh et al., 2009). Together these findings suggest that when the onset of deafness occurred, rather than duration of auditory deprivation, may be more influential on the extent of cortical plasticity that takes place within the auditory brain regions of deaf individuals and the association with future CI outcome (Buckley & Tobey, 2011).

2.3.2 Plasticity within Superior Temporal Cortices during Deafness and Following Cochlear Implantation

In cases of normal sensory input, auditory association cortex is known to be multimodal in nature: alongside physiological evidence for the existence of non-auditory and multisensory neurons within the auditory association areas of hearing ferrets (Bizley et al., 2007; Bizley & King, 2008), human neuroimaging studies have provided evidence of superior temporal-lobe activations to silent visual speech (Calvert et al., 1997; Capek et al., 2008; Hall et al., 2005; MacSweeney et al., 2000), visual sign language (Sadato et al., 2005), and have implicated these regions in the multisensory integration of object information (Beauchamp et al., 2004; Werner & Noppeney, 2010) and audio-visual speech information (Benoit et al., 2010; Calvert et al., 2000; Szycik et al., 2012). During deafness, when the auditory modality is severely degraded and unreliable on its own, individuals come to rely on visual modes of communication such as speechreading, sign language, and the integration of visual speech information with the degraded auditory

input (Auer & Bernstein, 2007; Lyness et al., 2013; Rouger et al., 2007, 2008; Sutton-Spence & Woll, 1999; Woll, 2012). Given the multimodal propensity of the superior temporal cortices, when auditory input is deprived it is possible for 'meta-modal' plasticity to take place, whereby a shift in the dominant input modality can occur and these multi-modal sensory brain regions can come to favour the visual modality (Lazard et al., 2014). Therefore, understanding how an increased reliance on the visual modality for communication purposes during deafness could result in plasticity within the superior temporal brain regions, and the impact of this on auditory rehabilitation when input is restored, is of key interest in this thesis. The following section will first describe the involvement of the superior temporal regions in achieving proficient levels of auditory speech perception with a CI. Next, the impact of deafness on the processing of visual speech within the superior temporal regions, and the implications of this on future auditory rehabilitation, will be reviewed.

2.3.2.1 Role of Superior Temporal Cortices in Auditory Speech Perception

In hearing individuals, auditory speech perception involves a complex and widespread cortical network covering temporal, parietal, pre-motor and inferior frontal areas connected via dorsal and ventral pathways (illustrated in Figure 2.7, Berwick et al., 2013; Friederici, 2011; Hickok & Poeppel, 2007). At earlier stages of

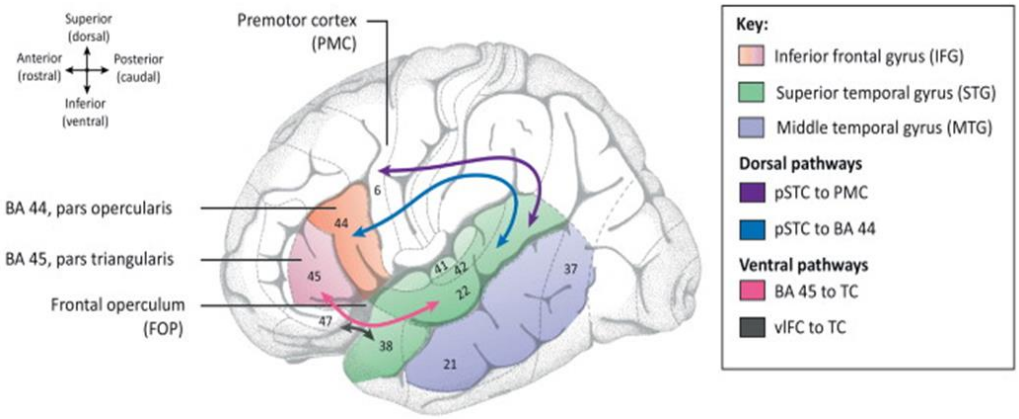


Figure 2.7: Illustration of the fronto-temporal network implicated in auditory speech perception, labelled by Brodmann's areas (BA). *Taken from Berwick et al. (2013).*

speech processing, the auditory association cortices (BA 22/42), comprising the middle to posterior portions of the bilateral superior temporal gyri, are known to be heavily involved in analysing the acoustic and phonetic properties of the auditory speech signal (see Figure 2.8, Binder et al., 1994, 2000; Hickok & Poeppel, 2007; Lazard et al., 2014). At later stages of speech processing, a left-hemisphere specialisation is observed: for instance, the posterior portion of the left superior temporal gyrus (STG, BA 22), known as 'Wernicke's area', has been identified as the interface between the processing of speech sounds and the subsequent retrieval of internal word representations from long-term memory (Wise et al., 2001), a feature that is integral to successful understanding of auditory speech information. Furthermore, these left superior temporal regions are said to be connected via the left- hemisphere dominant dorsal stream to the left inferior frontal gyrus (LIFG), also referred to as Broca's area (BA 44/45). This is known as the articulatory network that is thought to be involved in higher-level

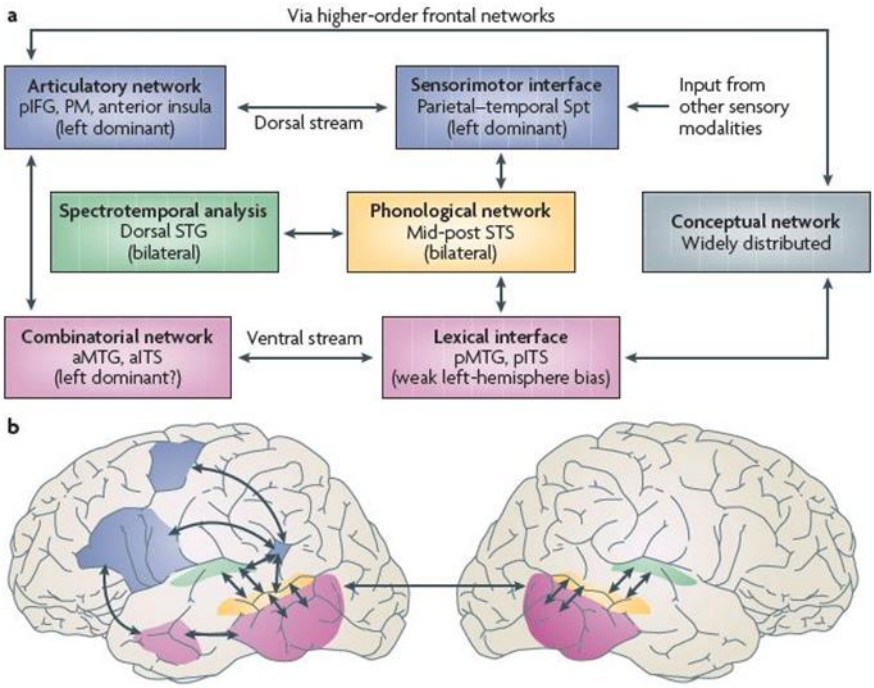


Figure 2.8: A schematic of cortical regions and associated linguistic functions. **a)** A schematic diagram of the dual-stream model of the functional anatomy of language; **b)** approximate anatomical locations of the dual stream model components. *Taken from Hickok and Poeppel (2007).*

speech perception functions such as accessing stored auditory representations from memory and the use of predictive strategies for accurate comprehension (Berwick et al., 2013; Fiebach et al., 2001, 2005; Friederici, 2002, 2011; Hickok & Poeppel, 2007).

A large body of evidence suggests that the left hemisphere is specialized for language processing irrespective of the sensory input modality, i.e. auditory inputs for oral communication, visual inputs either used for speechreading or for communication through sign language (Corina, 1999; Hickok et al., 1998; MacSweeney et al., 2008a; Neville et al., 1998; Petitto et al., 2000; Sakai et al., 2005). This left-hemispheric specialization seems resilient to auditory deprivation. For instance, in cases of congenital deafness, the left

superior temporal cortex is seen to undergo plasticity whilst maintaining its linguistic function, evidenced by the cortical processing of sign language in these regions (Cardin et al., 2013). Likewise, this left-hemispheric specialization seems unaffected by the progressive loss of oral communication in cases of post-lingual deafness. Specifically, postlingually deaf individuals, even after years of profound deafness, are seen to preserve the left dominance for phonology processing (Lazard et al., 2010b, 2012c). Furthermore, as the side of cochlear implantation is not seen to impact on auditory performance with a CI in postlingually deafened adults (Blamey et al., 2015), it seems that the incoming auditory information is still able to be analyzed and segregated to the most relevant hemisphere for linguistic processing.

Following unilateral cochlear implantation in pre- and post-lingually deaf adults, cortical activations measured using positron emission tomography (PET) have been observed bilaterally within the superior temporal brain regions during story comprehension (Green et al., 2005) and when listening to sequential speech sentences relative to silence (Fujiki et al., 1999), white noise (Mortensen et al., 2006; Naito et al., 1995), and multi-talker babble (Mortensen et al., 2006; Petersen et al., 2013). These auditory speech-evoked activations have not only been evidenced in experienced CI users with more than two years of CI use (Green et al., 2005) but also in relatively inexperienced CI users within the first few months following activation of their CI device (Green et al., 2005; Petersen

et al., 2013). Such PET studies have suggested that the successful stimulation of auditory association cortices through the CI may be an important factor in achieving proficient auditory speech perception. For instance, CI users with 'high' and 'low' levels of auditory speech comprehension have been distinguished based on their differing levels of speech-evoked activation within the superior temporal cortices and left inferior frontal cortex (Mortensen et al., 2006). In addition, Green et al. (2005) showed a positive correlation between the strength of activation to speech within bilateral auditory association areas and auditory performance on a sentence recognition test. Similarly, Fujiki et al. (1999) provided evidence of an association between greater speech-evoked activation within the left and the right auditory association areas and greater consonant recognition score, albeit with stronger correlations for consonant, vowel and sentence recognition evident in the left temporal lobe (Fujiki et al., 1999). These findings demonstrate that the recruitment of superior temporal cortices following implantation, and perhaps the left hemisphere in particular, may be crucial in order to successfully process and understand the auditory speech signal provided by the implant.

Evidence has also indicated that deafness may impact on the development of left-hemisphere specialisation for auditory speech processing, with post-lingually deaf CI users demonstrating speech-specific responses within the left STC that were not evident in pre-lingual deaf CI users (Petersen et al., 2013). Interestingly,

available evidence in postlingually deaf CI users suggests that maintaining the left-hemispheric specialisation for auditory speech processing may be an important cortical factor in CI success. For instance, greater activation to speech compared to multi-talker babble within the left temporal gyrus has been observed in CI users with high levels of speech comprehension; however this was not evident in CI users with low levels of speech comprehension, indicating greater functional specialisation of and ability to successfully recruit these brain regions for speech processing in rehabilitated CI users (Mortensen et al., 2006). In line with this notion, Giraud et al. (2001a) observed greater phonology-specific activation within left posterior superior temporal regions of hearing control subjects compared to postlingually deaf adult CI users, thus suggesting decreased specialisation for speech processing in CI recipients. However, Giraud et al. (2001b) also provide evidence of the development of speech-specific activation with increased cochlear implant use, particularly within left superior temporal regions. From their findings, the authors suggest that left hemisphere language specialisation may be impacted on by deafness, yet could be subsequently reinstated with increased CI experience (Giraud et al., 2001a, 2001b).

Indeed, maintaining the left-hemisphere specialisation for higher-level speech processing functions, such as accessing stored auditory phonological representations, has been suggested as an important factor in CI success (Lazard et al., 2013). Using fMRI prior to

implantation, Lazard et al. (2013) examined the functional organisation of bilateral posterior temporal cortices in postlingually deaf CI candidates. Cortical activations were measured during a memory task that evoked environmental sound imagery, typically right-hemisphere specialised, and a phonological task that involved accessing auditory speech representations from memory, typically left-hemisphere specialised (Hickok & Poeppel, 2007; Lazard et al., 2012c, 2014). Evidence of functional cortical reorganisation was demonstrated whereby left-hemisphere specialised phonological processing came to be supported by analogous contralateral regions in the right hemisphere (Lazard et al., 2013). In addition, this was accompanied by a decrease in activation to environmental sound processing within the right hemisphere. Lazard and colleagues suggest that this contralateral reorganisation during deafness may be driven by communication needs, as environmental sound processing is less important to maintain compared to the accessing of phonological representations for maintaining interpersonal communication and social interactions. Furthermore, right and left temporal reorganisations were associated with a longer duration of bilateral hearing loss, thus suggesting the effects of post-lingual deafness on central plasticity within bilateral posterior temporal cortices (Lazard et al., 2013). Importantly, Lazard et al. (2013) observed that greater phonological activity in right temporal regions prior to implantation was associated with poorer CI outcome following six months of CI use, whereas greater phonological activity in the left temporal regions was positively correlated with

future CI outcome, indicating that maintaining dedicated hemispheric specialization during deafness may be important for future CI success. In this way, examining pre-implant cortical measures of temporal-lobe function could help to prospectively identify those individuals at risk of poor CI outcome.

Although not the focus of this review, it should be noted that, in addition to the temporal auditory association cortices, neuroimaging studies have also examined the involvement of the left inferior frontal (LIF) regions during auditory speech perception in CI users. However, the available evidence is conflicting: whilst some studies have demonstrated that better CI outcomes are associated with greater recruitment of LIF regions (Lee et al., 2007a; Mortensen et al., 2006) others have observed no such relationship (Fujiki et al., 1999). Such contradictory results are likely due to differences between studies in the complexity of speech material presented during cortical imaging and the strategies employed by individual CI users (Fiebach et al., 2001, 2005; Friederici, 2002). In addition, it has been suggested that activation of LIF regions by CI users could be due to the degraded nature of the speech signal delivered by the CI and may reflect heightened attention to the auditory signal (Giraud & Truy, 2002; Giraud et al., 2000). In line with this explanation, it has been demonstrated that NH listeners display heightened activation in LIF regions during attention to degraded speech compared to clear speech stimuli, suggesting that activation of the LIF region may represent a neural correlate of effortful

listening (Wild et al., 2012), which would be anticipated during auditory speech processing with a CI.

2.3.2.2 Implications of Visual Speech Processing within Superior Temporal Cortices

Informed by existing studies and definitions (Calvert & Campbell, 2003; Hall et al., 2005; Summerfield, 1992), this thesis defines visual speech processing, or 'speechreading', as the ability to perceive and understand speech, without audition, from viewing the talker's linguistic facial movements. Speechreading entails analysis and identification of each linguistic facial configuration (viseme) that is associated with a corresponding speech sound (phoneme; Woll, 2012). In this way, visual speech has to be processed, identified and mapped onto stored internal sound representations in order for meaning to be extracted from the visual speech cue.

In NH individuals, it is widely accepted that visual speech can elicit activations in auditory association areas within the bilateral superior temporal cortices (Bernstein et al., 2002; Calvert et al., 1997; Calvert & Campbell, 2003; MacSweeney et al., 2000, 2002), with greater levels of activation commonly observed in the left temporal regions (Calvert & Campbell, 2003; Hall et al., 2005; MacSweeney et al., 2002). Furthermore, individual subject analyses of fMRI data have demonstrated a positive association between the level of activation in the left STG during a speechreading task and the level of speechreading proficiency (Hall et al., 2005). Whilst there

remains some debate over the cortical mechanisms underlying these superior temporal activations to visual speech, it seems most likely that visual input is received via higher order multisensory convergence sites such as the superior temporal sulcus (STS) rather than via direct visual inputs into the auditory brain regions (Besle et al., 2008; Callan et al., 2003; Calvert et al., 1999, 2000; Pekkola et al., 2005). Alternatively, it has been proposed that visually evoked responses could represent indirect activations either due to the anticipation of hearing auditory information when viewing its visual counterpart (Pekkola et al., 2005), via inner speech where acoustic representations are accessed and mapped onto the observed visual speech gestures (Hall et al., 2005; McGuire et al., 1996; Shergill et al., 2001), or by imagining the sound of the talker's voice (auditory verbal imagery, Jäncke & Shah, 2004; McGuire et al., 1996). Regardless of the exact processes that this activation may reflect, evidence suggests that a facilitative interaction exists between auditory and visual speech information both at the behavioural level (Bernstein et al., 2004; Grant et al., 1998; Ross et al., 2007; Sumby & Pollack, 1954) and at the cortical level, particularly within posterior portions of STS (Beauchamp et al., 2010; Benoit et al., 2010; Campbell, 2008; Nath & Beauchamp, 2012; Szycik et al., 2012).

Unsurprisingly, adults with early-onset (Auer & Bernstein, 2007; Bernstein et al., 2000; Ellis et al., 2001) and late-onset deafness (Rouger et al., 2007) are seen to display a greater level of

speechreading proficiency compared to NH listeners, providing an adaptive strategy for supporting spoken communication. Neuroimaging studies have sought to understand whether this behavioural adaptation is also accompanied by alterations at the cortical level during profound deafness. Indeed, fMRI studies have provided corroborating evidence of enhanced speechreading activations within left posterior superior temporal regions of congenitally (Capek et al., 2008) and post-lingually deaf individuals (Lee et al., 2007b) that is positively related to individual speechreading skill. These adaptations may reflect deafness-related plasticity, whereby the left auditory association areas come to more heavily process visual speech information and support greater levels of speechreading proficiency in the absence of auditory input (Lee et al., 2007b; MacSweeney et al., 2002). Furthermore, it is interesting to note that these functional adaptations are evident in some postlingually deaf individuals soon after the onset of deafness and thereby do not appear to require long periods of auditory deprivation for these plasticity effects to arise, presumably drawing on latent multi-modal connections (Lee et al., 2007b).

Whilst an enhanced recruitment of the left superior temporal regions for visual speechreading may be beneficial for communication purposes during deafness, it is possible that such cortical adaptations could consequentially result in the modification of left-hemisphere auditory processing resources and thus impact on auditory speech perception ability. However, the effects of

speechreading during deafness on temporal-lobe function and its relation to future CI outcome remains largely unexamined yet a topic of intense debate (Campbell et al., 2014; Lyness et al., 2013). Moreover, evidence of the existence and direction of a functional link between speechreading proficiency during post-lingual deafness and CI outcome remains inconsistent and poorly explained (Gantz et al., 1993; Hay-McCutcheon et al., 2005; Holden et al., 2013; Summerfield & Marshall, 1995). However, as speechreading shares a left predominant temporo-parieto-frontal network including the posterior left superior temporal regions (Calvert & Campbell, 2003; Hall et al., 2005; Lee et al., 2007b), STC activations to visual speech may reflect activation elicited by amodal linguistic analysis such as phonological processing (Hall et al., 2005), a cognitive function that is implicated in successful speechreading (Andersson et al., 2001; Lyxell et al., 2003). In this way it could be alternatively hypothesised that recruitment of these cortical regions for speechreading prior to implantation in postlingually deafened individuals could help to maintain phonological representations and the left hemispheric specialisation for phonological processing, with the potential to guard against the effects of maladaptive central plasticity and promote optimal CI outcome.

Furthermore, given the multi-modal rather than sensory-specific nature of the posterior superior temporal regions for language processing (Petitto et al., 2000; Straube et al., 2012) and their involvement in audio-visual speech integration (Beauchamp et al.,

2010; Lee & Noppeney, 2011; Nath & Beauchamp, 2012; Szycik et al., 2012; Wright et al., 2003), it is possible that enhanced STC activation to visual speech could reflect an enhanced synergy between auditory and visual speech representations that may be beneficial when trying to decipher the novel and degraded auditory input provided by the implant. Indeed, regardless of improved auditory speech perception abilities, CI users continue to show enhanced speechreading abilities (Rouger et al., 2007) and a high level of reliance on visual speech information in audio-visual speech conditions (Desai et al., 2007; Rouger et al., 2008; Schorr et al., 2005). Moreover, an enhanced ability to integrate auditory and visual speech information has been demonstrated in CI users compared to that of NH listeners (Rouger et al., 2007). At the cortical level, evidence has suggested that CI users with proficient auditory speech perception abilities may capitalise on enhanced levels of visual-cortex activity to compensate for the degraded auditory input provided by the implant (Doucet et al., 2006; Strelnikov et al., 2010, 2013). For instance, higher levels of visual cortex activation during speechreading at an early stage post-implantation have been associated with higher levels of auditory speech perception ability following six months of CI use, suggesting the beneficial role of visual speech input for auditory rehabilitation (Strelnikov et al., 2013).

Giraud et al. (2001a) also provide evidence of an enhanced audio-visual synergy in CI users at the cortical level: analogous to

superior temporal-lobe activations to visual speech, greater levels of activation within the visual cortex (BA18/V2) when listening to meaningful sounds, including speech, were observed in CI users compared to NH controls. Furthermore, the amplitude of this activation was positively correlated with speechreading proficiency and was seen to increase with a greater duration of CI use (Giraud et al., 2001a). The authors propose that this recruitment of the visual cortex for auditory perception may reflect enhanced synergy between the two modalities in CI users, and that a progressive refinement in coupling between auditory and visual speech representations with increased CI use could offer a facilitative mechanism for the rehabilitation of auditory speech perception abilities. Likewise, enhanced activations to visual speech in the STC following implantation may reflect a developed AV synergy that could be beneficial for the recovery of auditory function. However, currently there are no available neuroimaging studies that have examined the impact of deafness and subsequent implantation on the interplay between the processing of auditory and visual speech information within STC and the relation to CI outcome.

Unlike the left hemisphere, there appears to be no clear evidence that a greater level of activation within right posterior superior temporal regions is associated with speechreading proficiency either in NH individuals (Hall et al., 2005), nor when enhanced in deaf individuals (Capek et al., 2008; Lee et al., 2007b) or CI users (Rouger et al., 2012). Therefore, visual speech-related plasticity

effects within the right temporal lobe following deafness do not seem to provide a behavioural advantage for communication, unlike neural plasticity within the left temporal cortex (Capek et al., 2008; Lee et al., 2007b). These findings seem to support the notion that deafness-related plasticity observed in the left temporal lobe may reflect linguistic processing (Cardin et al., 2013; MacSweeney et al., 2004), whereas plasticity effects in the right temporal lobe may reflect visual motion processing (Fine et al., 2005; Finney et al., 2001). Importantly, existing evidence suggests that the involvement of right temporal lobe for basic visual processing may be detrimental to CI outcome, likely due to the depletion of auditory resources (Buckley & Tobey, 2011; Sandmann et al., 2012).

Although activation to visual speech in posterior portions of the right superior temporal lobe is not thought to underlie individual variability in speechreading skill (Capek et al., 2008; Hall et al., 2005; Lee et al., 2007b; Rouger et al., 2012), alternatively, enhanced activation within the right middle temporal gyrus of congenitally deaf individuals (Capek et al., 2008) and right anterior STS of post-lingually deaf CI users (Rouger et al., 2012) has been associated with a higher level of speechreading proficiency. Furthermore, this meta-modal plasticity observed within the right anterior STS of adult CI users is seen to decrease from an early to late stage post-implantation, nearing the activation levels observed in NH controls (Rouger et al., 2012). Rouger and colleagues suggest that this reduction in speechreading activation is indicative

of a reversal of a maladaptive 'cross-modal' reorganisation of the right superior temporal regions, which may enable greater recovery of auditory speech perception abilities with increased CI use. However, these findings should be interpreted with caution as the lack of corresponding repeated measurement data from NH control subjects means that it is not possible to attribute changes in activation over time solely to the CI rehabilitation process. Furthermore, a subsequent study indicated that the level of speechreading activation within the right middle STS/STG at an early stage post-implantation was negatively correlated with future auditory speech understanding abilities following six months of CI use (Strelnikov et al., 2013). Together these results suggest that recruitment of the anterior to middle portions of the right superior temporal lobe for visual speech processing may have a detrimental effect on auditory rehabilitation (Strelnikov et al., 2013), as has been previously indicated by the effects of basic visual processing in the right temporal regions (Buckley & Tobey, 2011; Sandmann et al., 2012), but that these effects may be reversible following increased CI use (Rouger et al., 2012).

2.3.3 Summary

Following cochlear implantation, the ability of the superior temporal cortices to respond effectively to the re-instated auditory input seems an important factor in achieving proficient levels of auditory speech perception (Fujiki et al., 1999; Green et al., 2005; Mortensen et al., 2006). However, higher-order cortices such as

these auditory association regions are thought to be particularly susceptible to cortical modifications during deafness, perhaps due to their multi-modal propensity (Dormal & Collignon, 2011; Kral et al., 2003; Lomber et al., 2010; Meredith et al., 2011). In particular, meta-modal plasticity can take place whereby superior temporal brain regions can become more responsive to visual cues when auditory inputs are deprived (Capek et al., 2008, 2010; Lazard et al., 2014; Lee et al., 2007b). Such cortical plasticity effects may underlie compensatory behavioural benefits during deafness that aid communication (Lee et al., 2007b; Suh et al., 2009). However, emerging evidence suggests that cortical plasticity and reorganisation within STC can impact on the typical functional organisation of auditory processing resources (Lazard et al., 2013), and could prove to be maladaptive for auditory speech processing abilities when auditory input is later reinstated by cochlear implantation (Lazard et al., 2013; Strelnikov et al., 2013).

Alternatively, it is possible, yet currently speculative, that speechreading prior to implantation may prove beneficial to future CI outcome by maintaining amodal linguistic functions and left-hemispheric specialisation for speech processing. In addition, speechreading could help to maintain a close cooperation between the auditory and visual modality that CI users are thought to capitalise on, both at the behavioural (Rouger et al., 2007) and the cortical level (Giraud et al., 2001a, 2001b; Strelnikov et al., 2015), during auditory rehabilitation. However, from the evidence to date,

it is not clear whether these plasticity effects are fully or even partially reversible over time post-implantation. Neither is it understood whether the reversal of visually-evoked activations within the temporal lobe corresponds to an increased responsivity to auditory speech cues and restoration of auditory speech perception. It seems possible that the variability observed in CI outcome may result from individual differences in the brain's ability to adapt to increased auditory inputs provided by cochlear implantation and to lose the compensatory effects developed during deafness (Chen et al., 2015a). Yet this remains largely speculative due to the scarcity of longitudinal follow-ups of temporal auditory rewiring and audio-visual interactions in the same individuals. Such studies currently remain scarce due to methodological challenges encountered when applying neuroimaging modalities to CI populations.

2.4 EXAMINING CORTICAL PLASTICITY FOLLOWING COCHLEAR IMPLANTATION

2.4.1 Limitations of Conventional Neuroimaging Techniques

The above review has highlighted the need for longitudinal studies to assess the functional link between auditory performance with a CI and the cortical adaptations that take place during deafness and following cochlear implantation. Unfortunately, it proves notoriously challenging to obtain measures of cortical function repeatedly, and safely, over a short time period in CI users due to various methodological limitations of conventional neuroimaging modalities. For instance, fMRI involves the use of a high magnetic field and

therefore is not compatible with the magnetic component of CI device. Whilst it is possible for CI users to safely undergo MRI scanning at low-power 1.5 Tesla if the CI device is tightly bound (Crane et al., 2010), large artefacts are generated ipsilateral to the implant thus preventing imaging of large regions of temporal cortex (see Figure 2.9, Crane et al., 2010; Kim et al., 2015). As shown in Figure 2.10, the size of the artefact can be reduced by surgically removing the implanted magnet (Kim et al., 2015). However, not only does this create risk and inconvenience to the CI user that would be unjustified for most research purposes, but it also precludes auditory stimulation through the CI and thus imaging of auditory cortical function. Even with the use of protective head bandages during low power MRI scanning, adverse events are still experienced including pain and discomfort due to heating of the implanted electrical component, magnet displacement and demagnetisation (Kim et al., 2015). Therefore, fMRI is not deemed fully compatible or safe for use in such research with CI users.

Alternatively, neuroimaging techniques such as electroencephalography (EEG) and magnetoencephalography (MEG) are safe for use with CI users. However, EEG and MEG respectively involve the measurement of electrical currents and magnetic fields produced by cortical activity. Therefore, evoked potentials acquired using such techniques are often plagued by electric and magnetic artefacts produced by the electronic and magnetic components of the CI device. For instance, in the case of EEG, electrical

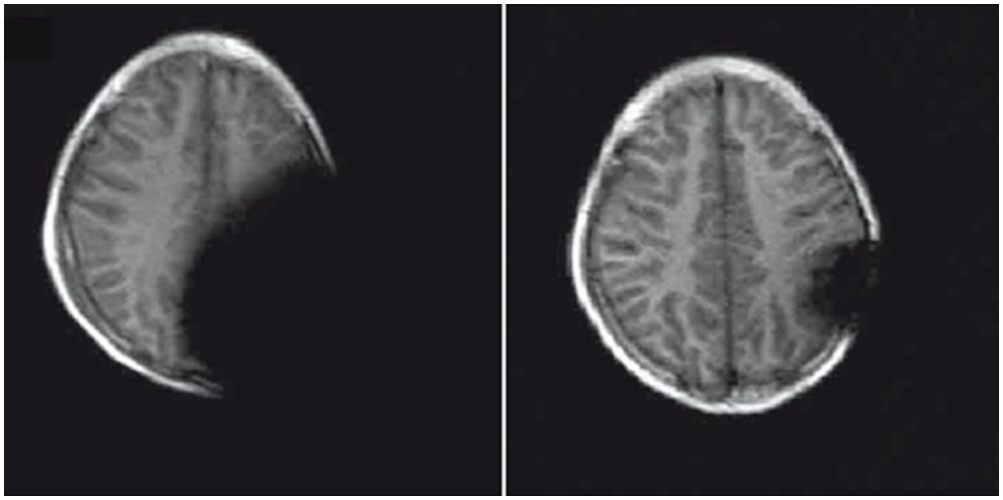


Figure 2.9: CI device-related artefact during MRI scanning. Images were acquired with (left) and without (right) the CI internal magnet in place. *Taken from Kim et al. (2015).*

stimulation from the CI generates electrical artefacts in the EEG signal that are thus time-locked to the presentation of the auditory stimulus (see Figure 2.10, Debener et al., 2008; Gilley et al., 2006). In order to minimise these artefacts, the duration of auditory stimulation is often limited in the order of hundreds of milliseconds (e.g. Chen et al., 2015b; Debener et al., 2008; Gilley et al., 2006; Sharma et al., 2002). As a consequence, the presentation of spoken words or sentences is precluded, meaning such techniques are unable to provide information about the cortical processing of speech at the level of word identification and sentence comprehension. Signal processing techniques such as independent component analysis have been deemed effective in recovering auditory evoked potentials (AEPs) elicited by tones and white noise (see Figure 2.11, Debener et al., 2008), environmental sounds (Viola et al., 2011), and synthesized syllables (Gilley et al., 2006) from CI-related artefacts. However, Martin (2007) found that such

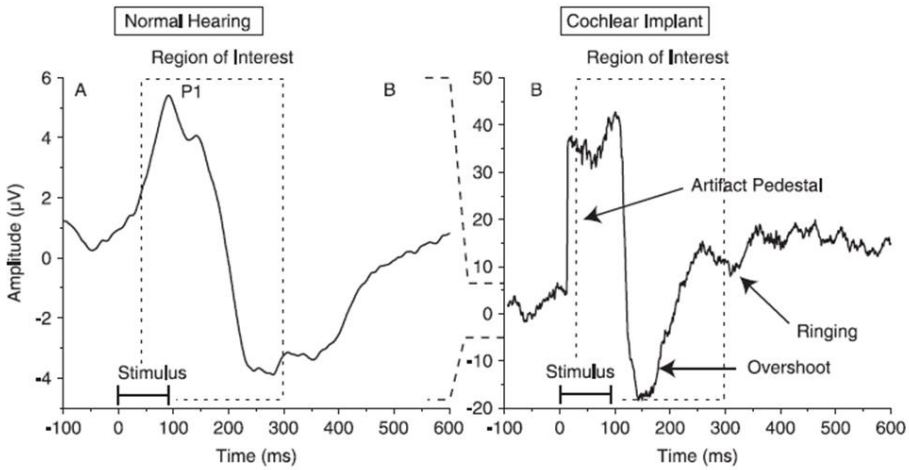


Figure 2.10: CI-generated artefact in EEG measurements. A cortical auditory evoked potential of a normal-hearing child is shown on the left in comparison to that of a CI user shown on the right. *Taken from Gilley et al. (2006).*

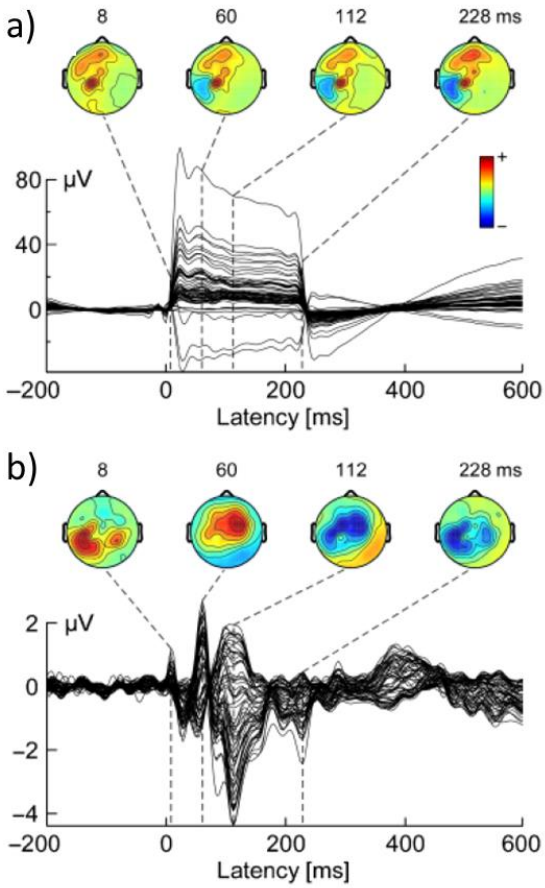


Figure 2.11: Example of EEG artefact removal. Auditory evoked potentials in CI users a) before ICA artefact removal, and b) after ICA removal. *Taken from Debener et al. (2008).*

techniques were not successful in removing the CI-related artefact from EAPs elicited by synthesised vowel stimulation, highlighting that such issues can prove problematic in CI users. Moreover, even in cases where the CI artefact during speech stimulation can be successfully removed from the EEG signal, the integrity of the resultant AEPs and preservation of important information about the speech-evoked neural response in CI users is largely unknown.

In contrast to the above methods, PET can be used to measure changes in cerebral blood flow and metabolism as a result of neuronal activity. As PET does not rely on electrical or magnetic cortical signal, it enables artefact-free functional imaging in CI users and is seen to be the most commonly used neuroimaging technique in CI research (Giraud et al., 2001b). However, one major drawback of PET is its invasive nature, involving the injection of a radioactive tracer isotope into the bloodstream (for example, fluorodeoxyglucose). This requires a high level of tolerance from the subject and means that its use is restricted to approximately one exposure per year, unless the dose, and consequentially the number of sampling sessions, is reduced (Giraud et al., 2001b). Indeed, existing PET studies that have conducted more than one post-operative scan over the first eight months of CI use have noted that the design of stimulus presentation paradigms, specifically the number of stimulation conditions, can be somewhat constrained due to limitations set by European legislation (Strelnikov et al., 2015). Moreover, its use is forbidden in the European community in

paediatric populations and is very restrictive for women in their childbearing years. Therefore, the repeated use of PET within the same individual is constrained and can limit the adequate assessment of cortical changes, which are thought to occur rapidly following the receipt of a CI (Rouger et al., 2012).

2.4.2 Principles of Functional Near-Infrared Spectroscopy

Near-infrared spectroscopy is a non-invasive optical neuroimaging technique that offers a promising solution to the aforementioned issues associated with performing brain imaging with CI recipients (Lawler et al., 2015; Saliba et al., 2016; Sevy et al., 2010). As a functional neuroimaging technique, fNIRS is used to measure functional haemodynamic responses in both the infant and adult brain. Specifically, fNIRS is based on the principle of neurovascular coupling whereby an increase in neuronal activation and metabolic demand of the cells provokes an increase in local cerebral blood flow (CBF) and oxygen delivery for consumption by the active cells (Villringer & Chance, 1997). This can be likened to fMRI that also measures cerebral haemodynamics, namely the blood oxygenated level-dependent (BOLD) signal that has been shown to correlate well with temporo-spatial characteristics of the fNIRS signal (Steinbrink et al., 2006; Toronov et al., 2007). In this way, fNIRS does not provide a direct measure of neuronal activation: rather it measures the consequential haemodynamic response comprising stimulus-evoked changes in levels of oxygenated haemoglobin

(HbO) and deoxygenated haemoglobin (HbR) in the blood (see Figure 2.12).

In order to measure these changes in HbO and HbR concentrations, fibre-optic bundles named optodes are placed on the subject's scalp (see Figure 2.13). Emitter probes emit the near-infrared light through the scalp and into the cortex (see Figure 2.14). Continuous wave NIRS systems emit two frequencies of near-infrared light that are coupled with the absorption properties of HbO and HbR (Lloyd-Fox et al., 2010). Thus, the amount of light that returns to the detector probes gives a measure of how much light has been absorbed by the chromophores at an anatomical region located between each emitter-detector pair, referred to as a measurement channel (see Figure 2.15). From this measure of optical density, the quantities of HbO and HbR are then derived. However, the attenuation of the light emitted is not only due to absorption by the two chromophores, but also due to the scattering of light within the cortex. Therefore, when the raw measures of optical density are converted to a change in chromophore concentration (ΔHbO or ΔHbR), the modified Beer-Lambert Law is applied to account for these scattering effects (Huppert et al., 2009). It is therefore important to note that fNIRS does not provide an absolute measure of chromophore quantities within the brain: rather, it measures the change in chromophore concentrations in response to an event such as auditory stimulation. fNIRS measurements are also known to be more sensitive to changes nearer the scalp where systemic signals

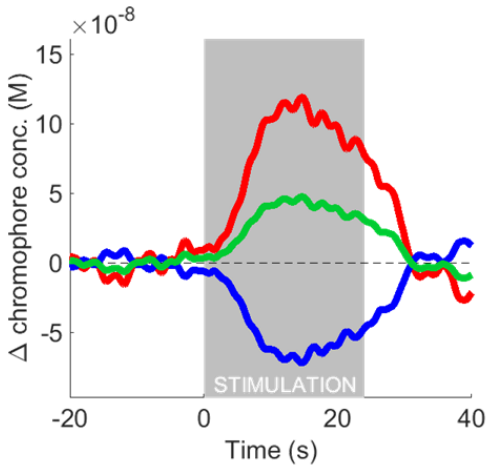


Figure 2.12: A typical fNIRS response to functional brain activation. This illustrates an increase in oxygenated haemoglobin (**HbO**) due to increased neuronal activity and an increase in oxygen delivery. This is accompanied by a smaller relative decrease in deoxygenated haemoglobin (**HbR**). As this increase in oxygen delivery exceeds the increase in oxygen consumption by the active cells, this leads to an overall increase in the total haemoglobin levels (**HbT**). *Adapted from Lawler et al. (2015).*



Figure 2.13: A picture of a 3x3 fNIRS optode array. This is used to measure cortical activation bilaterally from the participant's temporal brain regions. *Taken from Lawler et al. (2015).*

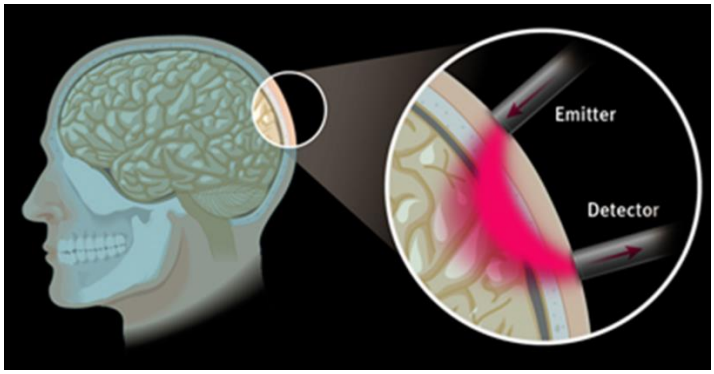


Figure 2.14: The pathway of infrared light into the cortex between an emitter and detector optode.
Source: http://www.psy.plymouth.ac.uk/research/Wsimpson/interests/fNIRS.jpg

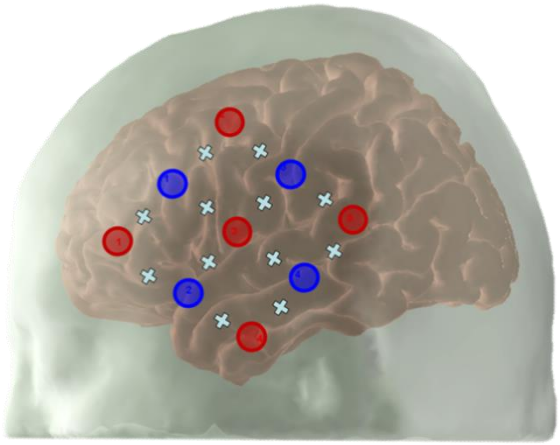


Figure 2.15: A schematic of a 3x3 NIRS optode array. Emitters are depicted in **red**, detectors in **blue**, and measurement channels are represented as crosses. *Adapted from Lawler et al. (2015).*

such as heart rate and blood pressure are present (Boas et al., 2004). Therefore, interference from systemic vascular changes can impede the attribution of the measured fNIRS signal to a functional haemodynamic response in the cortex. However, separation of the fNIRS signal into estimates of the systemic and functional response can be effective for removing physiological noise and extracting the functional component from the fNIRS signal (Yamada et al., 2012).

Overall, fNIRS offers a useful set of compromises when considering its temporo-spatial characteristics in comparison to other well-established neuroimaging techniques (see Figure 2.16; Lloyd-Fox et al., 2010). For instance, in comparison to methods such as EEG with a high temporal resolution, fNIRS is limited somewhat by the sluggish nature of the haemodynamic response. However, in comparison to the temporal resolution of fMRI, fNIRS has a higher sampling rate and can therefore acquire measurements more rapidly and provide a more comprehensive picture of the

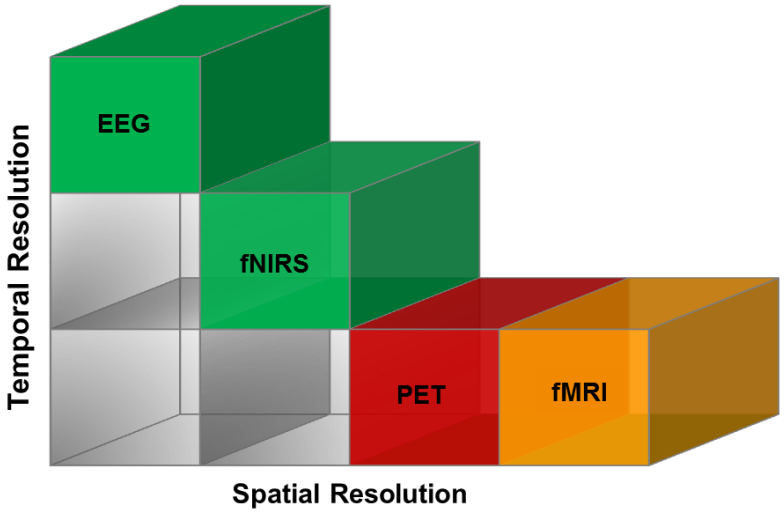


Figure 2.16: The temporal and spatial resolution of fNIRS compared with other conventional neuroimaging techniques. The degree of subject tolerance needed is indicated in **green** (low), **orange** (medium) and **red** (high). *Adapted from Lloyd-Fox et al. (2010).*

haemodynamic response (Huppert et al., 2006; Lloyd-Fox et al., 2010). The spatial sensitivity of fNIRS is limited by the depth penetration of light into the cortex (Toronov et al., 2007), as well as light absorption and scattering by the skull and the cerebrospinal fluid (Okada & Delpy, 2003). Furthermore, fNIRS does not permit imaging of the underlying brain anatomy, meaning that it is not possible to localise the precise anatomical origin of cortical activations, or to account for individual differences. However, ongoing technological advancements that address such drawbacks, including the use of 3D digitizers and spatial-registration software, now enable more accurate estimation of the anatomical source of cortical activation measured using fNIRS and help to reduce variability across subjects (Singh et al., 2005; Tak & Ye, 2014; Tsuzuki et al., 2012; Tsuzuki & Dan, 2014).

2.4.3 The Promising Application of Functional Near-infrared Spectroscopy

In addition to the above mentioned temporo-spatial characteristics, fNIRS offers several pertinent advantages for use in both adult and paediatric populations. Firstly, fNIRS is intrinsically quiet, making it particularly adept and ecologically valid when studying auditory function. Secondly, by its non-invasive and portable nature, fNIRS requires the lowest level of subject tolerance compared to alternative neuroimaging techniques such as PET and fMRI (illustrated in Figure 2.16) as the injection of a radioactive tracer and horizontal placement into a constrained scanning environment is not required. The technique also offers a relatively high level of resilience to subjects' head and body movements (Piper et al., 2014). Thus fNIRS offers the opportunity for safe and flexible repeated testing across a variety of subject populations. As such, fNIRS has generated much interest in the field of developmental neuroscience due to its ability to measure brain activity in children and infants without the need for sedation. For instance fNIRS has been applied to the study of paediatric sensory function and perceptual development (Taga et al., 2003; Watanabe et al., 2013), language acquisition (Gervain et al., 2008; Homae et al., 2011), social-cognitive function (Csibra et al., 2004; Minagawa-Kawai et al., 2009; Southgate et al., 2014) and the assessment and early identification of neuro-developmental disorders (Lloyd-Fox et al., 2013; Negoro et al., 2010; Zhu et al., 2014). Moreover, these advantageous features of fNIRS have enabled bed-side monitoring

of cerebral haemodynamics and the assessment of clinical outcomes in a range of fields including, but not limited to, psychiatry, oncology, and clinical neurology (Ehlis et al., 2014; Hirsch et al., 2009; Jean-Pierre, 2014; Obrig, 2014).

Pertinent to this thesis, it has been demonstrated that fNIRS is fully compatible with a CI. Sevy et al. (2010) provided the first report of the successful use of fNIRS in paediatric CI recipients. Using a four-channel fNIRS system, cortical activation within bilateral temporal brain regions was measured during presentation of speech stimuli comprising 20 second segments of vignettes from a children's story. The study demonstrated that fNIRS was able to detect significant levels of auditory speech-evoked activation in a group of paediatric CI recipients on the day of CI activation, and in another group with more than four months of CI use. Crucially, these auditory speech-evoked fNIRS recordings were free from any CI-generated artefacts that are known to contaminate EEG recordings. Overall, Sevy and colleagues' findings indicated the suitability of fNIRS for examining speech-evoked cortical activation in paediatric CI users without the need to limit the stimulation paradigm or to employ aggressive artefact removal techniques that are often required by techniques such as EEG.

Since Sevy and colleagues' report, fNIRS has been applied in adult CI users to study brain activity during low-level visual stimulation, as well as linguistic and non-linguistic auditory stimulation (Bisconti

et al., 2015; Chen et al., 2015a; Olds et al., 2015). However, to date, little is known about the functional link between auditory speech-evoked cortical activation measured using fNIRS and auditory performance: only two recent studies that had sought to understand these relationships in NH adults (Pollonini et al., 2014) and adult CI users (Olds et al., 2015) could be identified. Pollonini et al. (2014) examined whether fNIRS could detect differences in speech-evoked activation when normally-hearing adults listened to clear speech or to speech that was degraded to simulate listening through a cochlear implant. The results demonstrated that clear speech elicited a significantly larger area of temporal-lobe activation in both hemispheres compared to degraded speech. This study provides initial evidence to suggest that fNIRS can detect differences in cortical activations elicited by speech stimuli of varying levels of intelligibility in a group of NH adults. Further to this, Olds et al. (2015) went on to investigate the relationship between fNIRS measurements of speech-evoked cortical activation and behavioural measures of speech perception in postlingually deaf adult CI users. The study demonstrated that the extent of speech-evoked activation within the lateral temporal lobe/STG in each hemisphere, expressed as an activation area ratio for normal to scrambled speech, was positively correlated with auditory word and sentence recognition scores (Olds et al., 2015). Although further work is imperative, the findings to date are encouraging for the future use of fNIRS to objectively assess the quality of the speech signal delivered by the implant to auditory brain regions and for

understanding the neural substrates of variable CI outcome (Olds et al., 2015; Pollonini et al., 2014).

Crucially, emerging evidence should be highlighted when considering the practical applicability of fNIRS for assessing and monitoring cortical plasticity and audio-visual interactions both before and after implantation (Chen et al., 2015a; Dewey & Hartley, 2015; Wiggins & Hartley, 2015). These studies provide the first demonstrations of the ability of fNIRS to measure audio-visual interactions within the occipital cortex of hearing adults (Wiggins & Hartley, 2015), cross-modal responses within the temporal brain regions of deaf individuals (Dewey & Hartley, 2015), and cross-modal responses in both the occipital and temporal lobes of CI users (Chen et al., 2015a). Specifically, Dewey and Hartley reported enhanced cortical activations to a visual motion stimulus within the right temporal lobe of profoundly deaf individuals compared to hearing controls, illustrating the feasibility of fNIRS for detecting cross-modal activations during deafness that have previously been reported in fMRI studies (Fine et al., 2005; Finney et al., 2001). In postlingually deafened adult CI recipients, Chen et al. (2015a) observed cross-modal activations in temporal and occipital brain regions using fNIRS. Chen and colleagues identified that a greater level of cross-modal activation to basic visual stimulation within the auditory cortex (maladaptive reorganisation), relative to the level of cross-modal activation to auditory speech within the visual cortex (beneficial reorganisation), was related to poorer auditory

performance on a speech in noise task. The authors conclude that reorganisation within temporal and occipital brain regions may jointly influence auditory performance with a CI, and that an optimal balance between beneficial and maladaptive plasticity effects may be an important factor in determining CI outcome. Furthermore, the authors recognise the need for longitudinal studies in order to understand the impact of cortical plasticity that takes place both before and after cochlear implantation on CI outcome (Chen et al., 2015a).

Certainly, the current review suggests that longitudinal measurements acquired within the same individuals from pre- to post-implantation are vital if the relationship between cortical plasticity and CI outcome is to be fully elucidated. However, the measurements must be sufficiently reproducible in order to reliably attribute changes in cortical activation to the CI rehabilitation process. Existing studies that have examined the test-retest reliability of fNIRS measurements in adults during basic visual stimulation (Plichta et al., 2006), verbal fluency tasks (Kakimoto et al., 2009; Schecklmann et al., 2008), and during auditory and visual social stimulation in infants (Blasi et al., 2014), have reported good reproducibility of fNIRS measurements across test sessions when responses are assessed at the group level and averaged over a small number of channels overlying a cortical region of interest. However, it should be noted that the reliability of fNIRS measurements at an individual level has typically been shown to be

highly variable between people (Blasi et al., 2014; Kakimoto et al., 2009; Plichta et al., 2006; Schecklmann et al., 2008).

2.4.4 Summary

The brain's capacity for the reversal of maladaptive plasticity effects and the development of beneficial audio-visual interactions within temporal brain regions following implantation remains largely unexamined as performing repeated cortical imaging in CI recipients proves challenging: well-established neuroimaging techniques, including fMRI, EEG, MEG and PET, are all either limited in their compatibility with CI devices or are generally not well suited to longitudinal research for safety reasons (Gilley et al., 2006; Giraud et al., 2001b; Kim et al., 2015). Unlike these techniques, fNIRS is unaffected by CI-generated artefacts (Sevy et al., 2010) and is well-suited to unrestricted longitudinal functional imaging in CI users, whatever their age (Lawler et al., 2015; Saliba et al., 2016; Sevy et al., 2010). Recent reports also attest to the exciting opportunity that fNIRS provides for the study of cortical function and plasticity in deaf adults and CI users (Chen et al., 2015a; Dewey & Hartley, 2015; Olds et al., 2015), as well as audio-visual interactions in adults (Wiggins & Hartley, 2015) and infants (Watanabe et al., 2013). Therefore, in conjunction with behavioural measures of speech perception, fNIRS offers a powerful tool to identify cortical predictors and correlates of variable CI outcome.

2.5 AIMS OF THE THESIS

The premise of this review is that adult CI users' auditory speech perception abilities remain highly variable and unpredictable. This chapter has reviewed evidence of the influence that clinical characteristics of the CI recipient can have in determining the amount of benefit derived from cochlear implantation. The available evidence suggests that the accurate prediction of CI outcome cannot currently be achieved based solely on this routinely available clinical data. The review presented a growing body of evidence that suggested cortical plasticity within auditory brain regions could be an important factor in understanding and predicting how much benefit an individual will receive from their CI. Specifically, cortical adaptations to deafness, perhaps due to an increased reliance of visual speech processing, may impact on the integrity of the superior temporal cortices and hence on future CI outcome. Following implantation, the limited available evidence suggests that the reversal of deafness-related plasticity effects may be possible and may be key to the recovery of auditory function. The implications of cortical plasticity on the synergistic use of auditory and visual speech information following implantation were also discussed.

To date, methodological challenges have precluded the longitudinal examination of cortical function and plasticity during deafness and following the restoration of hearing through cochlear implantation. More recently, the promising application of fNIRS in studying

auditory cortical function in CI users has been recognised. Therefore, in conjunction with behavioural measures of speech perception, fNIRS offers a powerful tool to elucidate the relationship between pre-implant cortical function, cortical plasticity following implantation, and the recovery of auditory speech perception in CI recipients. Despite this, the author is unaware of any such empirical examinations within the literature. Resultantly, the specific aims of this thesis are:

i. To assess the recovery of auditory speech perception following cochlear implantation and to evaluate the level of between-subject variability in CI outcome within a representative sample of adult CI recipients.
ii. To evaluate the suitability of fNIRS for acquiring repeated measurements of speech-evoked activation from the superior temporal brain regions of adult CI users during periods of profound deafness and throughout the subsequent CI rehabilitation process.
iii. To examine the pre-implant responsiveness of the superior temporal brain regions to auditory and visual speech stimulation as cortical predictors of future CI outcome.
iv. To examine cortical plasticity within superior temporal brain regions following cochlear implantation and how this relates to CI outcome.
v. To examine the perceptual benefit that CI users obtain from visual speech information in audio-visual conditions and how

auditory and visual speech information is integrated within the superior temporal brain regions following implantation.

3. LONGITUDINAL EXPERIMENT DESIGN AND METHODOLOGY

3.1 INTRODUCTION

This chapter describes the design and methodology of a longitudinal study conducted with a group of adult CI users and NH control subjects. In line with the overall aims of this thesis, the current observational study was designed to examine speech-evoked cortical activation both before and after cochlear implantation and to determine associations to individuals' speech perception abilities. Specifically, fNIRS was used to measure cortical activation to auditory, visual, and audio-visual speech from superior temporal brain regions. In addition, behavioural measures of auditory, visual, and audio-visual speech perception ability were employed. All measures were obtained in the same individuals before implantation, one month after CI activation, and six months after CI activation, as well as at corresponding time points with NH individuals. Preliminary analyses and preparation of behavioural and neuroimaging data are also described.

3.2 ETHICAL APPROVAL

The study was approved by the Nottingham 1 Research Ethics Committee (REC reference: 12/EM/0016) and was sponsored by Nottingham University Hospitals NHS Trust (Research & Innovation reference: 11IH007). All participants gave written informed consent before taking part. Participants were recruited into the study

between January and October 2014, with data collection conducted between January 2014 and July 2015.

3.3 PARTICIPANTS

A group of profoundly deaf adult CI recipients and a group of adult hearing control subjects were recruited to this study. Common inclusion criteria across both groups were:

1) Native English speakers
2) Self-reported normal or corrected-to-normal vision
3) At least 18 years of age
4) Able to travel to and take part in all study assessments

Any known language, cognitive, motor disorders and previous brain injuries were defined as exclusion criteria.

3.3.1 Cochlear Implant Users

Seventeen profoundly deaf adult CI recipients were recruited to the study from the Nottingham Auditory Implant Program (NAIP). Additional inclusion criteria were: 1) deemed a suitable candidate for cochlear implantation by NAIP's clinical team; and 2) consented to receive a CI. Relevant information regarding participants' clinical history of deafness was gathered from the NAIP's patient files. A measure of self-reported health utility was obtained for each participant before and six months after cochlear implantation using the Health Utilities Index Mark III (Feeny et al., 1995). The Edinburgh Handedness Inventory (Oldfield, 1971) was used to provide a measure of handedness for each participant.

3.3.2 Normal-hearing Control Subjects

Seventeen control subjects were recruited to enable between-group comparisons to be made in the current study. Such between-group comparisons were desirable in order to understand whether any observed differences in cortical activation and performance could be attributable to differences in hearing status of the groups, as well as whether any changes over time could be attributed to the CI rehabilitation process rather than learning effects and/or measurement error. The recruitment of control subjects was staggered across the recruitment timeline in an effort to approximately match the group's mean age to that of the CI users who were being recruited to the study. Participants were largely recruited from the National Institute for Health Research Nottingham Hearing Biomedical Research Unit's (NIHR NHBRU's) participant database, as well as advertisement through word-of-mouth by existing participants.

An additional inclusion criterion was normal hearing thresholds, defined here as average pure-tone air-conduction hearing thresholds of ≤20 dB across frequencies 0.5, 1, 2 and 4 kHz in both ears. For each participant, pure-tone air-conduction threshold audiometry was conducted in line with British Society of Audiology recommended procedures (2011) at the beginning of the first testing session to confirm normal hearing thresholds. The

Edinburgh Handedness Inventory (Oldfield, 1971) was used to provide a measure of handedness for each participant.

3.3.3 Determining Sample Size

Ideally the current study would have been powered to detect a statistical relationship between cortical activation measured before implantation using fNIRS and auditory speech perception measured after implantation. However, no data were available from which an estimate of the strength of such a relationship could be derived. As characterising the extent to which auditory function recovers following implantation was also a key aim of this thesis, the study was powered to detect expected changes from pre- to post-implantation on widely used clinical outcomes. A national study of outcomes following implantation conducted by the UKCISG (2004a) obtained measures for a battery of clinical outcomes. In order to be conservative, the smallest effect size reported in that study for the change from pre-implantation to nine months post-implantation (0.66 of a standard deviation) was used to determine the required sample size.

The G*Power 3 statistical power analysis program (Faul et al., 2007) indicated that a sample size of 16 was required to detect an effect size of 0.66 SD at an alpha of 0.05 and with 80% power using a repeated-measures t-test. A sample of 16 participants also appeared reasonable for a study involving repeated fNIRS measurements when compared to other longitudinal studies in the

literature (e.g. Plichta et al., 2006, n=12; Schecklmann et al., 2008, n=15). To allow for attrition due to the longitudinal nature of the current study and in anticipation of unsatisfactory fNIRS data being acquired from some participants (Lloyd-Fox et al., 2010), a recruitment target of 24 CI users was set, should this have been achievable in the planned recruitment timeframe.

3.4 DESIGN

A longitudinal repeated-measures design was employed. The same tests were administered to all participants at three time points. The timelines of the research testing sessions are illustrated in Figure 3.1 and Figure 3.2 for the CI users and NH controls respectively.

3.4.1 Test Intervals

For CI users, the first testing session (T0) took place at their earliest convenience after having consented to receive a CI, but before undergoing CI surgery ('pre-implantation'). At T0, CI users were tested in their best-aided condition, i.e. wearing their preferred listening devices. The second testing session (T1) was conducted approximately one month after activation of the CI device. At T1, CI users were tested wearing their preferred listening devices (i.e. CI and optional contralateral HA). The third testing session (T2) was conducted approximately six months after CI activation. Again participants were tested wearing their preferred listening devices. NH control subjects were also tested at three time points. The retest intervals were set to mirror those of the CI group as closely

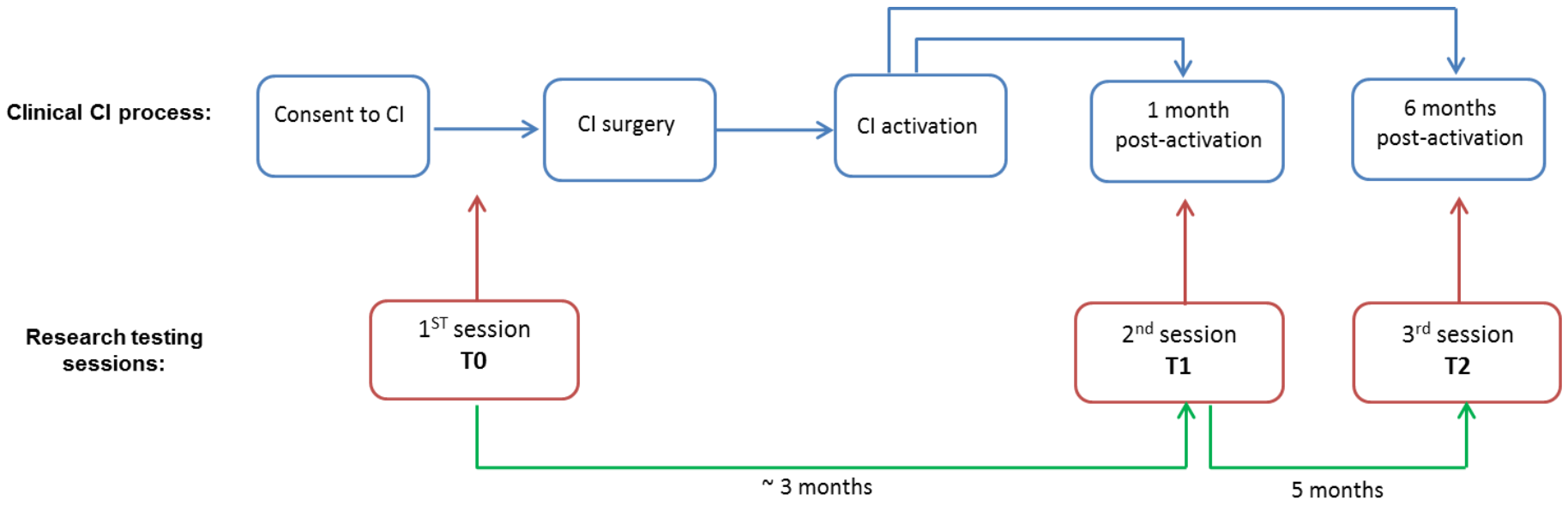


Figure 3.1: A schematic of the clinical CI process and the timeline of research testing sessions

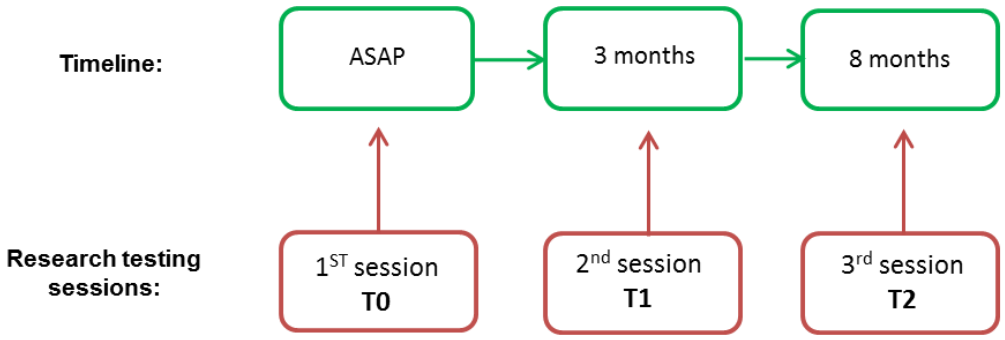


Figure 3.2: Timeline of research testing sessions for normal-hearing control participants

as was pragmatically possible given the variation in waiting times for the CI operation and device activation.

3.4.2 Order of Testing

At each time point and for each participant, all neuroimaging and behavioural tests were conducted within the same testing session. In each testing session, the tests were performed in the following order:

1) fNIRS scanning (approximate duration 45 minutes)
2) Speech perception testing in quiet (approximate duration 45 minutes)
3) Speech perception testing in noise (approximate duration 20 minutes)

In total, each testing session took between two and three hours to complete, including breaks when needed.

3.4.3 Testing Conditions

All neuroimaging and behavioural testing was carried out in a double-walled sound-attenuated room (IAC Ltd, Hampshire UK),

with fabric-lined walls, a mineral tile ceiling and carpeted floor. During fNIRS scanning, all lights were switched off with a lamp in the adjoining control room providing ambient light through the viewing window. During behavioural testing, lights were switched on to aid communication between the participant and researcher. A steady room temperature (23°) was maintained to provide comfortable testing conditions for the participants. For all tests, participants were seated in front of a visual display unit (VDU) at a viewing distance of one metre, with a centrally located Genelec 8030A loudspeaker mounted immediately above and behind the VDU. All stimuli were presented, and scored where appropriate, using the MATLAB® computing environment (Release 2014b, The MathWorks, Natick, MA). Visual components of the stimuli were presented on the VDU. To reflect the typical level of conversational speech, auditory components were presented through the loudspeaker at 65 dB SPL (A-weighted root-mean-square level averaged over the duration of each sentence) measured at the listening position with the participant absent using a Brüel & Kjær 2250 sound level meter and free-field microphone (Type 4189). Participants were provided with a booklet of written instructions (Appendix A) and were instructed to read the appropriate page prior to the commencement of each test. Details of neuroimaging and behavioural testing are described below in the order in which they were conducted.

3.5 FNIRS TESTING

Speech-evoked haemodynamic responses were acquired bilaterally using a continuous-wave fNIRS system (ETG-4000, Hitachi Medical Co., Japan, see Figure 3.3). The ETG-4000 is a commercial system that emits a continuous beam of light into the cortex and samples at a rate of 10Hz. The system measures simultaneously at two different wavelengths, 695 and 830 nm, to allow for the separate measurement of changes in HbO and HbR concentrations and to reduce cross-talk error between the two (Boas et al., 2004; Sato et al., 2004). The two 3x3 optode arrays together comprised ten emitter and eight detector optodes with a fixed inter-optode distance of 30mm (illustrated in Figure 3.4), providing a penetration depth into the brain of approximately 15mm (Gibson et al., 2005; Strangman et al., 2014). This resulted in a total of 24 measurement channels, with 12 used to measure speech-evoked cortical activation from the left hemisphere and 12 used to simultaneously measure from the right hemisphere. A dense sound-absorbing screen was placed between the fNIRS equipment and the participant to minimise the steady fan noise generated by the equipment. This resulted in a steady ambient noise level of 38 dB SPL (A-weighted). The fNIRS experimental set-up is displayed in Figure 3.5 and the procedure is detailed below.

3.5.1 Stimuli and Presentation Paradigm

The Institute of Hearing Research (IHR) Number Sentences (Hall et al., 2005) were presented as speech stimuli during the acquisition of



Figure 3.3: The Hitachi continuous wave ETG-4000 Optical Topography System.
Taken from: http://www.hitachi-medical.co.jp/english/products/opt/etg4000/

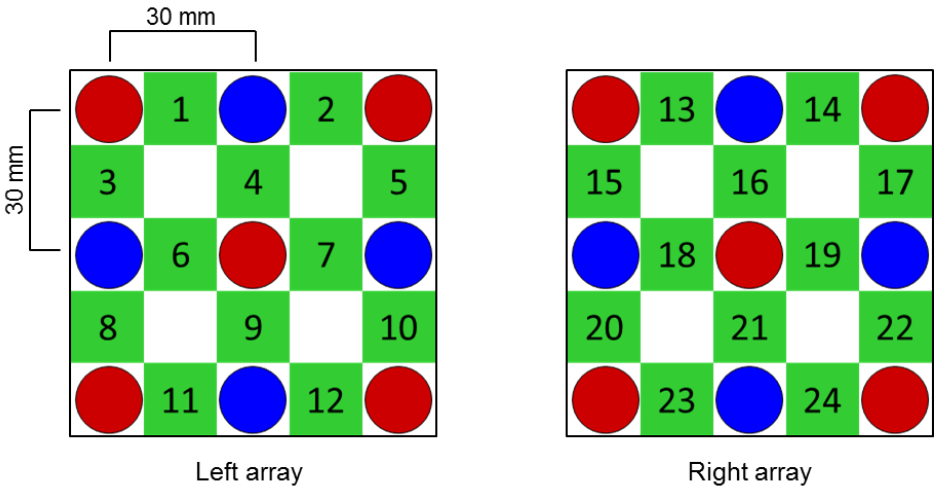


Figure 3.4: A schematic of the bilateral 3x3 NIRS optode array employed.
Emitters are depicted in **red** and detectors in **blue**. Emitter-detector distance is indicated as 30mm. The 24 measurement channels are represented in **green** and labelled numerically.

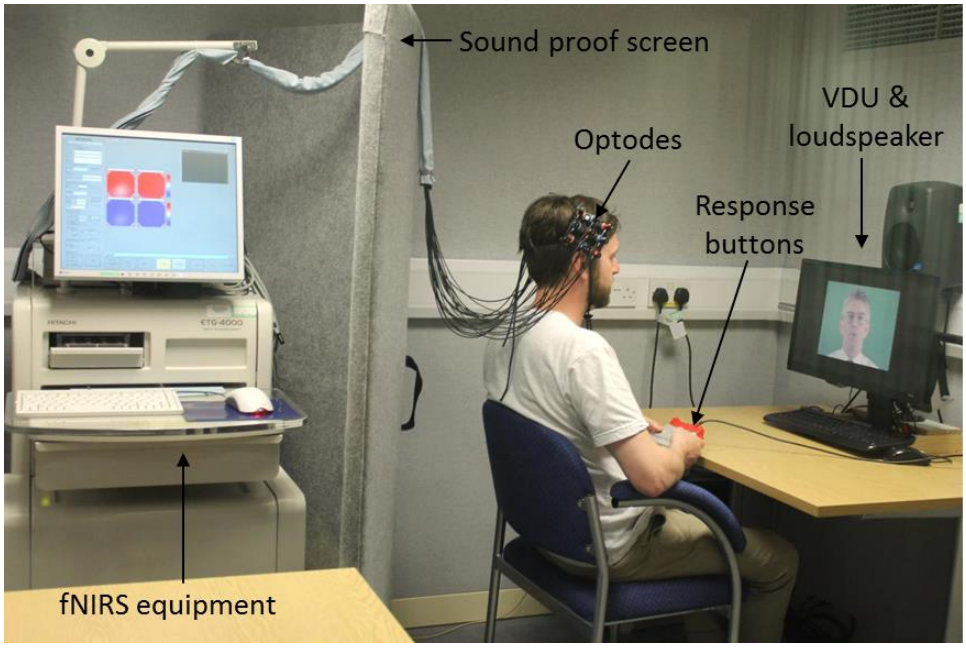


Figure 3.5: The fNIRS experimental set-up in a sound-attenuated room.

fNIRS measurements. This corpus was developed by Hall and colleagues (2005) through modification of the original IHR Audiovisual Adaptive Sentence Lists (Macleod & Summerfield, 1990) by incorporating a number between one and ten into each sentence. For example, the original sentence "The puppy chased the ball" became "One puppy chased the ball". One hundred of these modified IHR Number Sentences were digitally recorded in audio-visual format and were spoken by both a male and female talker. Sentences in which the original key words were modified or removed as a result of this modification process were excluded: for example, the two keywords "very" and "early" in "The lunch was very early" were omitted to create "The lunch was at six o'clock". Thus, the speech material used in this fNIRS experiment comprised digital audio-visual recordings of 90 IHR Number Sentences, each spoken by both a male and female talker. Each of these 90 IHR

Number Sentences contained between four and seven words and all included three keywords. As the sentences were uniform in their number of keywords they were particularly suited for random presentation within the fNIRS experimental paradigm. Furthermore, this corpus has previously been used to successfully elicit auditory and visual speech-evoked activation in auditory brain regions as measured using fMRI (Hall et al., 2005). Pilot experiments confirm that stimulus-evoked responses were obtainable using fNIRS at both the individual and group level (see Appendix B).

The speech material was presented in three stimulation conditions, auditory-only (A-ONLY), visual-only (i.e. silent speechreading, V-ONLY) and audio-visual (AV). Thirty sentences were randomly selected without replacement for presentation in each of these three conditions, with the restriction that an equal number were spoken by the male and female talker in each condition. Figure 3.6 shows freeze-frame clips of each of the three conditions. In the AV condition, both the auditory and visual components of the sentence recordings were presented congruently (Figure 3.6a). In the V-ONLY condition, the visual component of the recording was shown but the auditory component was muted (Figure 3.6b). In the A-ONLY condition, the auditory component was presented but the visual component was not shown; the background remained uniform and a fixation cross was presented in place of the talker's mouth (Figure 3.6c). Rest periods consisted of this uniform background and

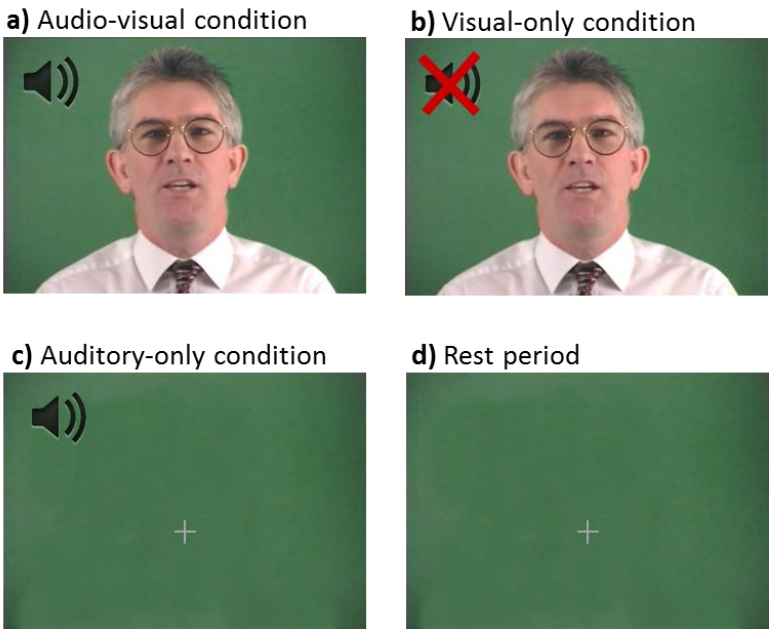


Figure 3.6: Freeze-frame clips of the IHR Number Sentences to illustrate the differences between the three speech conditions and the rest period presented to participants.

fixation cross with no visual or auditory components presented (Figure 3.6d).

The speech stimuli were presented in a block-design paradigm interleaved with rest periods, illustrated in Figure 3.7. Each block comprised six concatenated sentences, evenly spaced to fill a 24s block duration. Five blocks were presented for each of the three conditions (A-ONLY, V-ONLY and AV) interleaved in a random order. During these blocks, the participants were instructed to attend to the talker and to always try to understand what the talker was saying. Participants were instructed to look at the fixation cross when the talker's face was not presented on the VDU. The subsequent rest periods allowed for the haemodynamic response elicited by the stimulation block to return to a baseline level.



Figure 3.7: Schematic representation of one cycle of the block-design stimulus presentation paradigm

The durations of the rest periods were randomly varied between 20 and 40s in 5s increments. During the rest periods, participants were instructed to relax, look at the fixation cross, and to try to remain still. Two attentional trials were presented at random, and therefore unpredictable, positions within the sequence of 15 blocks to encourage active attention to the speech stimuli whilst minimising possible response artefacts throughout the experiment. Two seconds after the cessation of the randomly-chosen blocks, two alternative words were presented on either side of the fixation cross. Participants were asked to press one of two buttons to indicate which word had been spoken in the immediately preceding sentence in a two-alternative forced-choice task. The response period automatically timed out if no button press was registered within 15s, although in practice a response was always given within this time period. Following the participant's response, an additional 5s rest was inserted prior to the start of the rest period proper. The duration of the experimental run totalled approximately 15 minutes.

3.5.2 Procedure

3.5.2.1 Familiarisation Run

Participants first completed a short familiarisation run to demonstrate, and ensure that they understood, the main experimental procedure. During the familiarisation session, one block of each of the three conditions (A-ONLY, V-ONLY and AV) was presented. In order to avoid pre-exposure to the experimental stimuli, the familiarisation blocks comprised speech material (BKB

sentences, Bench et al., 1979) that were different to the material presented during the fNIRS measurements and the subsequent behavioural testing. Following each stimulation block, an example of the attentional control task was also presented.

3.5.2.2 Optode Placement

Following completion of the familiarisation run, the two 3×3 optode arrays were placed bilaterally over the subject's temporal lobes. The optode arrays were positioned on the participants' head so as to ensure good coverage of superior temporal regions, where association auditory cortices are located. Optode positioning was guided by the International 10-20 System (Jasper, 1958) to promote consistency across participants and test sessions. Specifically, on each side, the lowermost source optode was placed as close as possible to the preauricular point, with the uppermost source optode aligned towards position Cz (see Figure 3.8). Consistency of optode positioning across test sessions at the individual level was further ensured by reference to photographs taken during the previous testing session.

To evaluate the consistency of optode positioning across individuals, the procedure was piloted on six adult volunteers who did not take part in the main study. After positioning the arrays as described above, the optode positions, plus anatomical surface landmarks, were recorded using the Hitachi ETG-4000's electromagnetic 3D

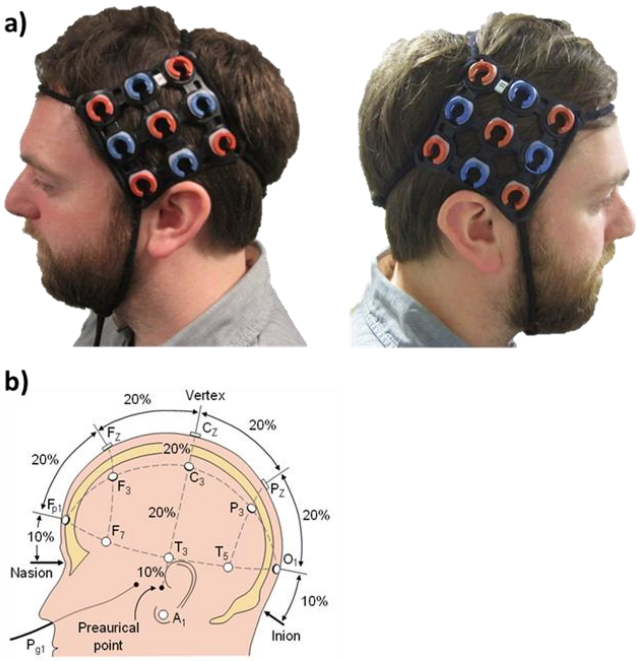


Figure 3.8: Placement of the fNIRS measurement array.
a) Photo of the bilateral optode placement used with the emitter optode locations shown in red and detector optode locations in blue; **b)** Schematic of the international 10-20 positioning system, illustrating the preaurical point and Cz point that was used to guide optode placement.

Probe Positioning Unit. For each volunteer, the digitized optode positions were registered to a standard atlas brain ('Colin27', Collins et al., 1998) using the AtlasViewer tool (Aasted et al., 2015), allowing their locations to be visualized relative to underlying cortical anatomy. Figure 3.9 shows the spread in registered optode positions across the six volunteers. The standard deviation in the position of each optode was between 2.9 and 8.8 mm. This was considered a satisfactory level of consistency in optode positioning between individuals, given the relatively modest spatial resolution of fNIRS measurements obtained with a source-detector spacing of 30 mm. The information available from the spatial registrations suggested that this optode-array position provided good coverage of the superior temporal brain regions; the mean position of the

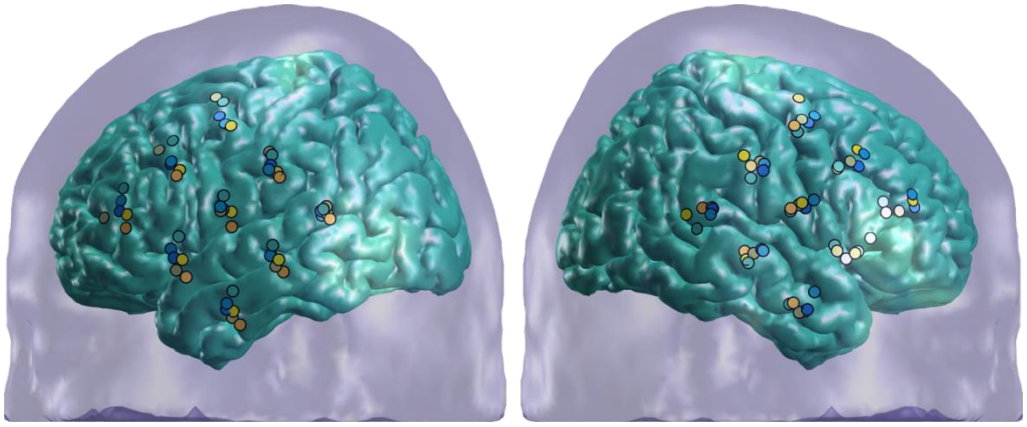


Figure 3.9: Variability in optode positioning across six volunteers, registered to standard brain atlas and colour coded by subject.

optodes and measurement channels are shown in Figure 3.10. To illustrate the position of the optode array in relation to the fronto-temporal speech processing network, existing schematics from the literature are overlaid with the approximate average optode locations in Figure 3.11 and Figure 3.12. The positioning of the optode array was also considered suitable as it avoided placement directly over the internally implanted receiver and external coil of the CI device, which is typically located more posteriorly. Figure 3.13 shows the placement of the optode array on a participant's head whilst wearing their CI device.

Once the arrays had been positioned, the optodes were connected and the Hitachi ETG-4000's 'Auto Gain' function was used to verify that the correct level of light intensity was being output and detected by each source-detector pair. Once the status of the optodes was deemed satisfactory, a crepe bandage was wrapped around the arrays to secure them to the participant's head. Participants were asked to sit as still as possible to reduce the

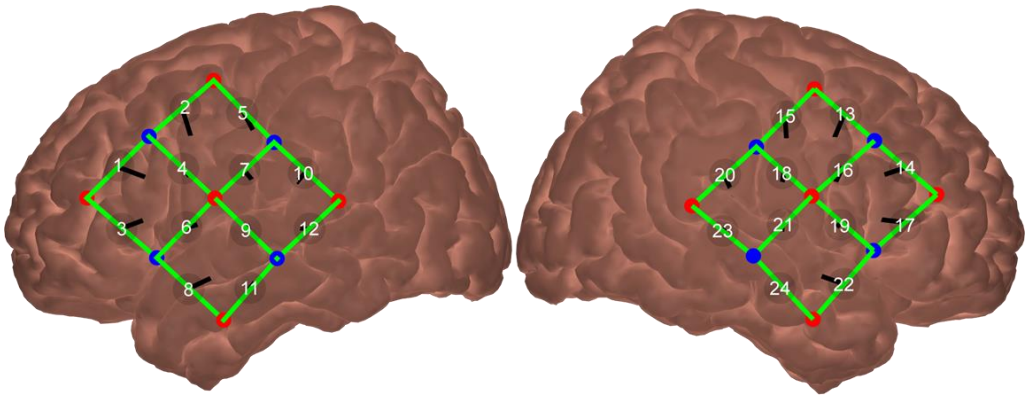


Figure 3.10: Mean position of optodes and measurement channels projected to cortical surface. Measurement channels are labelled numerically, source optodes are indicated in red and detector optodes are indicated in blue.

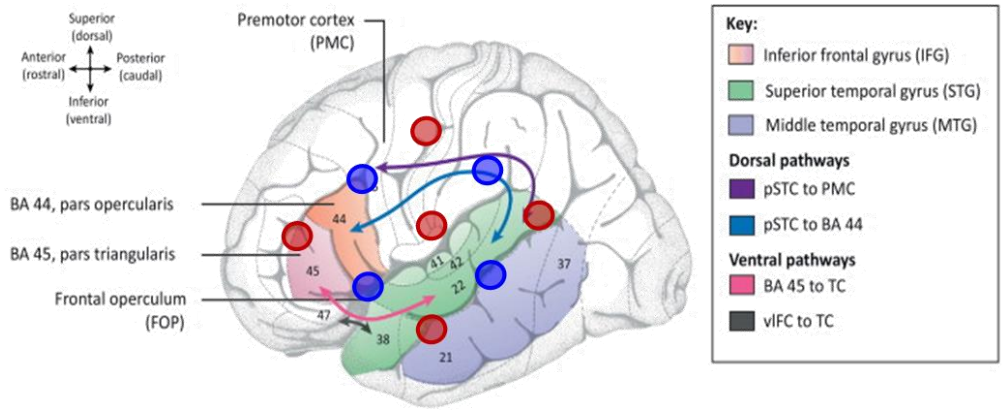


Figure 3.11: A schematic of the fronto-temporal network implicated in auditory speech perception overlaid with approximate optode locations (red and blue circles), and numbered by Brodmann's areas (BA). Adapted from Berwick et al., (2013).

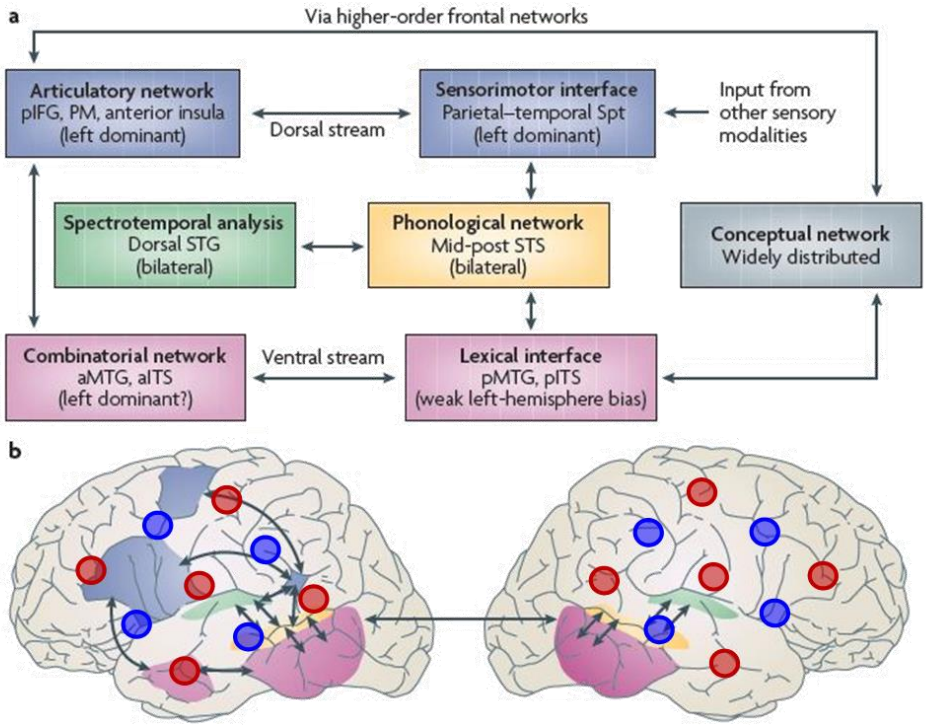


Figure 3.12: Anatomical locations of the dual stream model components overlaid with approximate optode locations (red and blue circles). Adapted from Hickok and Poeppel (2007).



Figure 3.13: Typical placement of the optode array around CI device.

occurrence of motion artefacts throughout the duration of the fNIRS measurements. Pilot testing suggested that use of a crepe bandage was an effective preventative method for minimising optode-scalp

decoupling and thus possibly of reducing artefacts and improving the quality of the raw measurement signal at source (see Figure 3.14 for example).

3.5.2.3 Acquisition of fNIRS Measurements

Following optode placement, the researcher left the sound-proofed room and the experimental run was initiated. Throughout the duration of the block-design paradigm, speech-evoked haemodynamic responses were simultaneously measured from both the left and right temporal lobes using the ETG-4000 continuous-wave fNIRS system. The researcher observed the experimental run from the control room through an adjoining glass window to monitor the participant's behaviour. Any significant observations regarding participant movement and compliance were documented in the participant's testing notes. On completion of the experimental run, acquisition of fNIRS measurements ceased and the researcher re-entered the sound-proofed room to remove the fNIRS optodes from the participants head.

3.6 SPEECH PERCEPTION TESTING IN QUIET

As in the fNIRS scanning, speech perception testing was conducted in A-ONLY, V-ONLY and AV conditions to provide a measure of auditory, visual and audio-visual speech perception ability.

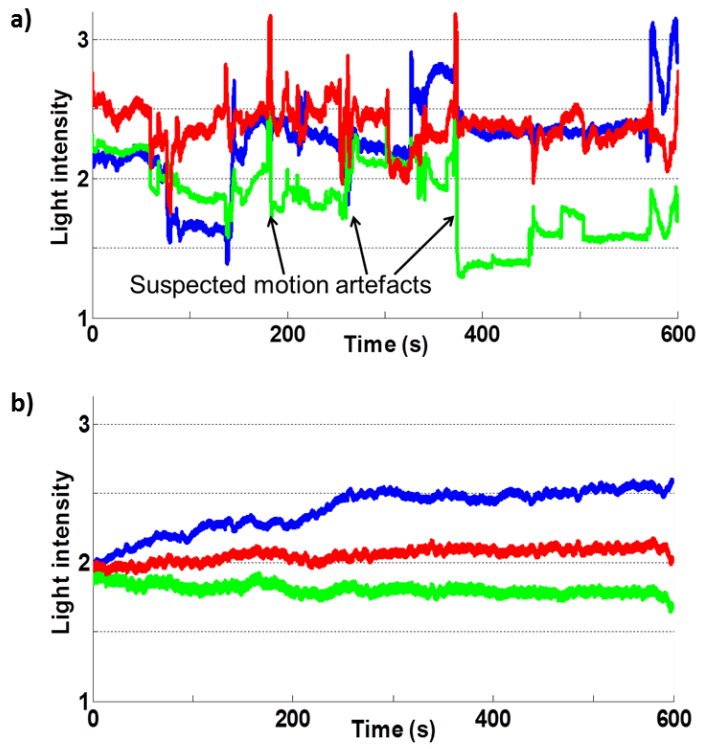


Figure 3.14: Example of motion artefacts with and without bandaging. Raw levels of light intensity measured at three channels are indicated in blue, red and green, across the duration of a pilot experiment (N=1): **a)** an example of suspected motion artefacts and optode-scalp decoupling without bandaging **b)** an example of the reduction of motion artefacts and optode-scalp decoupling using bandaging.

Following fNIRS testing, the Hitachi ETG-4000 system remained switched on behind the dense sound-absorbing screen. Therefore, the steady ambient noise level of 38 dB SPL (A-weighted) remained constant through the neuroimaging and behavioural measurements as participants completed all tests in the same seated position.

3.6.1 Stimuli

The CUNY Sentence Lists (Boothroyd et al., 1985) were employed to obtain a measure of speech perception ability. The reasons for employing the CUNY corpus were threefold. Firstly, this corpus was not presented during fNIRS scanning, thus limiting training effects. Secondly, the CUNY sentences are typically more varied in length

and content. Therefore the sentences are arguably less predictable than other speech corpuses available in audio-visual format (e.g. BKB sentences) and were felt to provide a more ecologically valid measure of ability. Thirdly, the CUNY Sentence Lists are currently used by CI programs across the UK (e.g. Craddock et al., 2016; Kumar et al., 2016) and have been employed in a national study of the effectiveness of unilateral cochlear implantation (UKCISG, 2004a), thus allowing for the collection here of clinically–relevant and comparable data. The CUNY Sentence Lists include 25 standardised lists each comprising 12 sentences that vary in length and topic. Each list contains between 101 and 103 words spoken by a male talker. Two different CUNY lists (i.e. 24 sentences) were randomly selected without replacement for presentation in each of the three conditions (A-ONLY, V-ONLY, and AV).

The choice of the CUNY corpus to assess speech perception was based in part on its routine use as a clinical outcome measure and also to avoid learning effects across testing sessions, as the IHR Number Sentences were presented during brain imaging. Therefore, comparisons between the fNIRS measurements and speech perception outcomes would be based on different sentence materials. Speech intelligibility was also measured using the IHR Number Sentences solely to confirm that the pattern of auditory recovery across participants was similar regardless of the speech corpus used.

3.6.2 Procedure

The three stimulation conditions (A-ONLY, V-ONLY and AV) were tested in a random order. Prior to the first trial of each stimulation condition, the researcher informed the participant whether they would only hear, only see, or both see and hear the man talking. Within each condition, the 24 sentences were presented in a random order. Each trial was initiated by the researcher using a response box. After each sentence presentation, the participant was instructed to repeat back all words that they were able to identify. All words correctly reported by the participant were recorded by the researcher on a scoring laptop before initiation of the next trial. The scoring method ignored errors of case or declensions. All participants responded verbally, however, in instances where the verbal response of the CI users could not be fully understood, clarification was made using British Sign Language.

3.6.2.1 Familiarisation Run

Prior to commencement of the speech perception testing, all participants completed a short familiarisation run to demonstrate, and ensure that they understood, the behavioural testing procedure. During the familiarisation session, three sentences were presented in each of the three conditions. BKB sentences (Bench et al., 1979) were employed during the familiarisation run in order to avoid pre-exposure to the CUNY corpus employed during the subsequent behavioural testing.

3.7 SPEECH PERCEPTION TESTING IN NOISE

Measures of A-ONLY and AV speech perception in noise were employed in order to estimate the amount of benefit participants derived from visual speech information in audio-visual conditions compared to auditory-only, referred to here as 'visual benefit':

Visual benefit = AV – A-ONLY

CUNY sentences were presented in A-ONLY and AV conditions at a fixed signal-to-noise ratio (SNR, dB). The SNR was determined individually for each participant to approximate the SNR at which they would perform at 50% correct in A-ONLY conditions. This method was employed in an attempt to bring performance away from ceiling and floor so that visual benefit could be quantified, and in an attempt to equalize levels of A-ONLY performance across all participants. Due to the limited number of CUNY sentences and the necessity to avoid familiarisation effects, BKB sentences were used in the adaptive procedure described below to estimate the SNR at which speech perception testing in noise was subsequently conducted.

3.7.1 Adaptive Routine

3.7.1.1 Stimuli

BKB Sentences (Bench et al., 1979) were employed as the speech stimuli for use in the adaptive procedure. The BKB corpus is recorded in an auditory format and consists of 20 lists containing 16 sentences per list, with three or four keywords in each sentence to

total 50 keywords in each list. The long-term average A-weighted level was normalised across all individual sentences. A steady speech-shaped noise, fixed in level over time, was produced with a long-term average spectrum matched to that of the BKB sentences (see Figure 3.15). This was presented as background noise in order to optimally mask the speech sentences. Two BKB sentence lists were randomly selected without replacement and the resulting 32 sentences were presented in a random order in the A-ONLY condition. Each sentence was presented with a random sample of the speech-shaped background noise at the appropriate SNR as outlined below.

3.7.1.2 Procedure

A one-up, one-down adaptive procedure was employed to measure the SNR at which A-ONLY performance was 50% correct. Testing began by presenting a BKB sentence in noise at an SNR of -16dB for control subjects, and -6dB for patients. The participant was required to repeat any words that they could identify. A loose keyword scoring method was employed and if two or three keywords were repeated correctly by the participant then the trial was scored as correct. If a trial was scored as correct, the subsequent sentence was presented at an SNR that was reduced by a predetermined step-size; whereas, if a trial was scored as incorrect, the sentence was presented at an SNR that was increased by the same predetermined step-size.

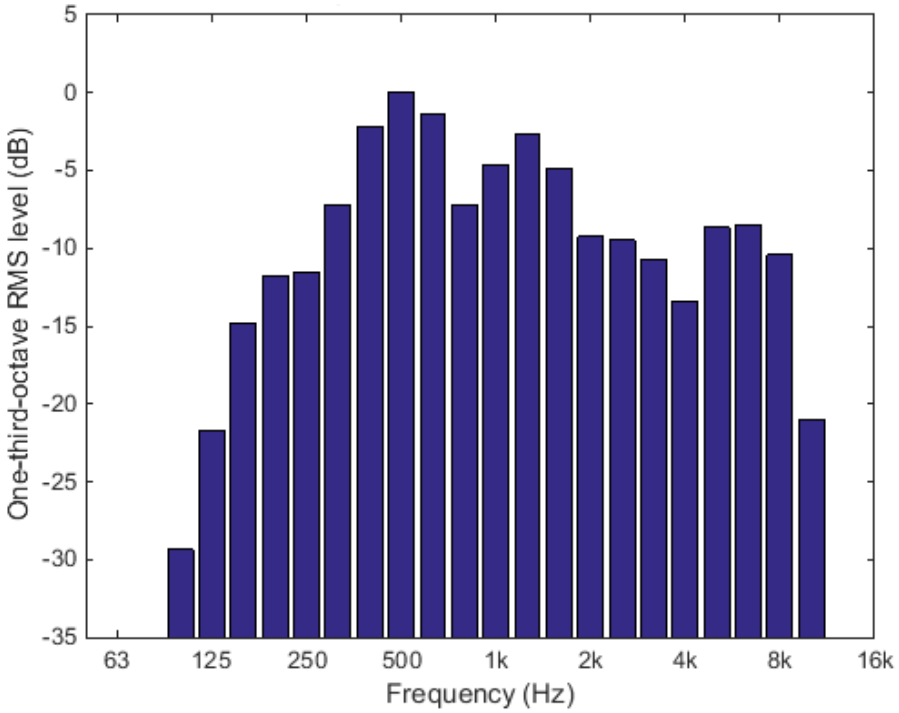


Figure 3.15: Spectrum of the generated BKB steady speech-shaped noise in one-third-octave bands to allow comparison with long-term average speech spectra (Byrne et al., 1994).

This adaptive routine made efficient use of the limited number of sentences available (Plomp & Mimpen, 1979). Specifically, the first sentence was presented at a SNR at which it was unlikely that the participant would report it correctly. The same sentence was then presented repeatedly at an increasing SNR until it was reported correctly. When it was reported correctly, the procedure then moved on to presenting the next trial. For the NH control subjects, the step-size was set to 4dB for the first trial, and 2dB for all subsequent trials. For the CI users, the step-size was set to 6dB for the first trial, and 2dB for all subsequent trials. The suitability of these step sizes for measuring a steady adaptive track was confirmed by pilot testing. For each of the 32 trials, the SNR at which the stimulus was presented was stored, and the final SNR

was calculated by averaging the SNRs over the last 20 trials. If a participant scored an incorrect trial three times consecutively at an SNR of 36dB, then it was presumed that the SNR at which A-ONLY performance was 50% correct could not be measured and testing was terminated at this point.

3.7.2 Testing in Noise

3.7.2.1 Stimuli

Two different CUNY lists were presented in each of the two conditions (A-ONLY and AV). These lists were randomly selected from the available lists, excluding those that had previously been presented during speech perception testing in quiet. This ensured that the same lists were never presented more than once during the same testing session. Each sentence was presented with a random sample of a steady speech-shaped background noise, fixed in level over time, which had a long-term average spectrum matched to that of the CUNY sentences (see Figure 3.16). The speech stimuli were presented at a SNR 2 dB below the final SNR previously calculated using the adaptive procedure. Pilot testing indicated that presenting the speech stimuli at this SNR was suitable for ensuring that A-ONLY performance would be close to 50% correct when measuring performance using the CUNY sentence lists.

3.7.2.2 Procedure

The CUNY speech material was presented in A-ONLY and AV conditions. These conditions were tested in a randomly selected

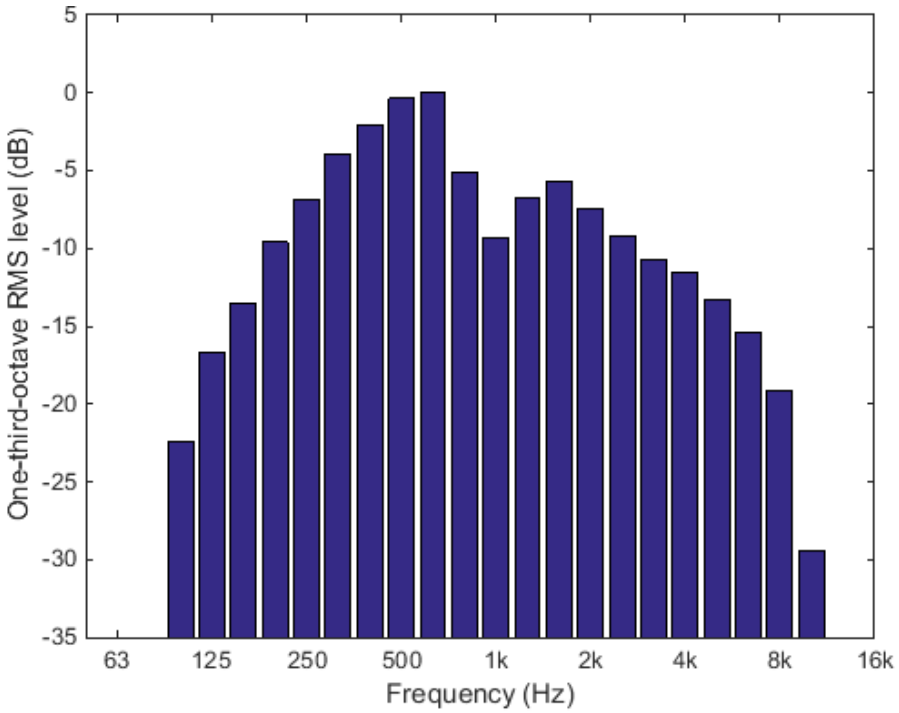


Figure 3.16: Spectrum of the generated CUNY steady speech-shaped noise in one-third-octave bands to allow comparison with long-term average speech spectra (Byrne et al., 1994).

order. Before each condition commenced, participants were told whether they would only hear, or both see and hear the talker. Within each condition, 24 sentences from two different CUNY lists were presented with noise in a random order. As with the previous behavioural testing procedures, one sentence was presented at a time and trials were initiated by the researcher. For each trial, participants verbally repeated all words that they were able to identify. All words correctly identified were recorded by the researcher on the scoring laptop before initiating the next trial.

3.8 ANALYSIS OF BEHAVIOURAL DATA

For each condition, performance on the CUNY Sentence Lists in quiet was quantified as the percentage of *all words* reported

correctly (% correct). This was based on the routine scoring procedure employed in both clinical (personal observations made in the NAIP) and research settings (e.g. UKCISG, 2004a). In order to address anticipated ceiling and floor effects and to make the performance data more suitable for statistical analysis, the rationalised arcsine transform (Studebaker, 1985) was applied using Matlab. Firstly the arcsine transform (T) was applied as follows:

$$T = \text{arcsine}\sqrt{\frac{X}{N+1}} + \text{arcsine}\sqrt{\frac{X+1}{N+1}}$$

The 'asin' function in Matlab was used to return the inverse sine (arcsine) for each value of X, where X represents the total number of words reported correctly and N represents the total number of words presented. This was then transformed linearly:

$$R = 46.47324337T - 23$$

where R indicates the resulting rationalised arcsine-transformed score (rationalised arcsine unit, RAU). This transformation extends the original percent correct scale outwards in both directions from 50%, creating bigger differences as the extremes of the range are approached. Consequently, this transformation makes the rationalised arcsine scale linear and additive in its proportions whilst producing values close to that of the original percentage scores (Studebaker, 1985). Thus, the transformed data (RAUs) were subjected to subsequent statistical testing that is outlined throughout the thesis.

3.9 ANALYSIS OF FNIRS DATA

3.9.1 Pre-processing Steps

Raw fNIRS recordings were exported from the Hitachi ETG-4000 into MATLAB for use with routines provided in the HOMER2 package (Huppert et al., 2009) and custom scripts. To prepare the recordings for subsequent analyses they were subjected to a set of processing steps. The order of these processing steps is illustrated in Figure 3.17 and each step is described in detail below.

First, to quantify changes in the amount of light absorbed, the raw light intensity measurements were normalized and converted to changes in optical density (Huppert et al., 2009). Wavelet motion correction was then performed to reduce the impact of motion artefacts on the fNIRS signal. Motion artefacts typically manifest as abrupt spikes in the fNIRS signal due to movement and subsequent decoupling between the optodes and the scalp. By avoiding the need to reject contaminated trials from the data, and instead processing the signals to directly suppress artefacts, wavelet filtering can enhance data yield and has emerged as a favourable approach for use with fNIRS data (Brigadoi et al., 2014; Cooper et al., 2012; Molavi & Dumont, 2012). The HOMER2 hmrMotionCorrectWavelet function (based on Molavi and Dumont, 2012) was used which assumes that the wavelet coefficients have a Gaussian probability distribution and so applies a probability threshold to remove outlying wavelet coefficients that are assumed to correspond to motion artefacts.

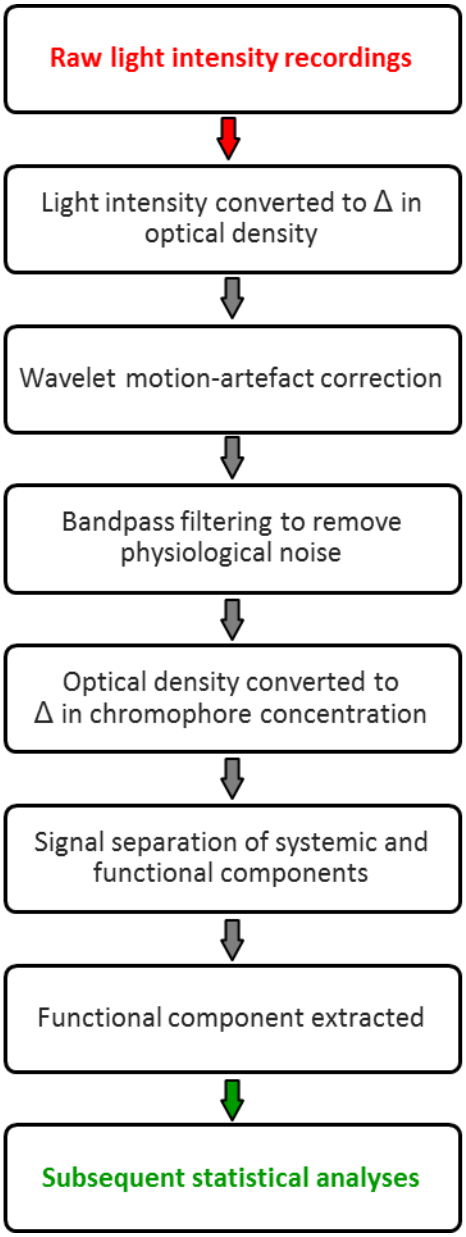


Figure 3.17: Summary of fNIRS signal processing steps that preceded further statistical analyses.

A probability threshold was set to exclude coefficients lying more than 1.5 inter-quartile ranges below the first quartile or above the third quartile. This is a criterion commonly used to detect statistical outliers, but is likely a more conservative approach in comparison to existing fNIRS studies (Brigadoi et al., 2014; Cooper et al., 2012; Molavi & Dumont, 2012; Wiggins & Hartley, 2015). An example of

the effect on wavelet filtering on the fNIRS signal is provided in Figure 3.18 (Wiggins & Hartley, 2015).

Following motion-artefact correction, a bandpass filter of 0.01–0.5 Hz was applied to reduce sources of noise in the data. This filter was selected to remove high-frequency cardiac oscillations, as well as low-frequency physiological noise including respiration and blood pressure changes. The fNIRS signal was next converted into estimates of changes in chromophore concentrations, specifically oxygenated and deoxygenated haemoglobin, using the modified Beer-Lambert law with a default differential path-length factor of six (Huppert et al., 2009). As light does not travel through the cortex in a straight path, the differential path-length factor accounts for these scattering effects in the estimation of haemoglobin changes. As bandpass filtering is unable to remove all physiological noise from fNIRS recordings (Huppert et al., 2009), the haemodynamic signal separation method of Yamada et al. (2012) was also applied. This algorithm separates the fNIRS signal into estimates of the functional and systemic components, based on expected differences in the correlation between HbO and HbR in each component. Specifically, a positive correlation between changes in HbO and HbR is assumed in the systemic component, whereas a negative correlation is assumed in the functional component. Figure 3.19 provides a representative example of the application of this algorithm to fNIRS data (Wiggins & Hartley, 2015).

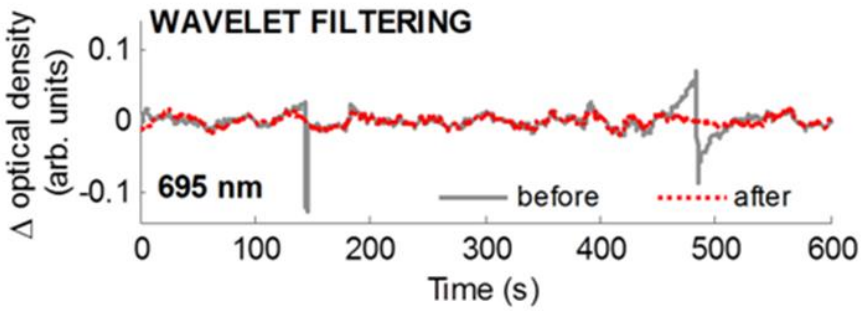


Figure 3.18: An example of the effect of wavelet filtering on the optical signal. Spikes in the optical signal are identified as motion artefacts and are removed, whilst uncontaminated parts of the original signal are left unchanged. *Taken from Wiggins & Hartley (2015).*

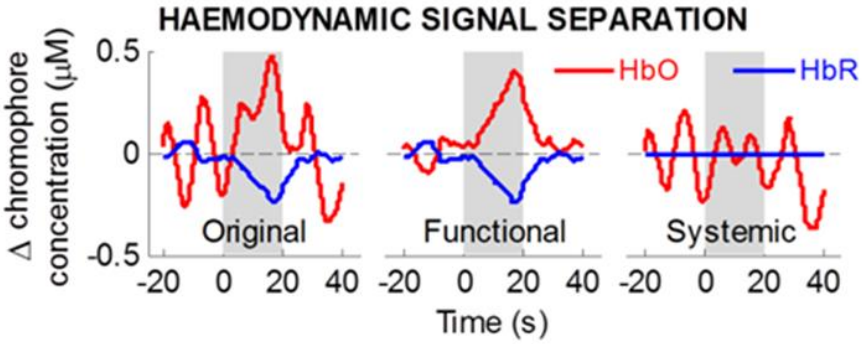


Figure 3.19: An example of the haemodynamic signal separation method applied to the fNIRS signal. The original haemodynamic response function shows contamination by physiological noise. The application of the separation technique extracts a plausible functional component from the original response, and provides an estimate of the interference from systemic noise. *Taken from Wiggins & Hartley (2015).*

The estimated functional component of the fNIRS signal was extracted and subjected to subsequent processing as detailed below.

3.9.2 Quantifying Amplitude of Cortical Activation

In order to quantify the level of cortical speech-evoked response, the pre-processed fNIRS signal was subjected to an ordinary least squares (OLS) general linear model (GLM). The GLM design matrix included three boxcar regressors, one for each of the three

stimulation conditions. The two response periods following the two attentional trials were also modelled in the design matrix as isolated events occurring at the time the two words were presented on screen. These were convolved with the canonical hemodynamic response function provided in SPM8 [http://www.fil.ion.ucl.ac.uk/spm]. No HRF derivatives were included in the GLM analysis as preliminary analysis of a subset of the data did not indicate any benefit of doing so. The beta weights of the canonical HRF term were extracted at each measurement channel, for each stimulation condition, and for all participants. As described in section 3.9.1, Yamada et al.'s (2012) haemodynamic signal separation method employed here assumes a fixed linear relationship between HbO and HbR in the functional response. Therefore, the results of all statistical analyses are identical regardless of whether conducted on the beta weights extracted for the HbO or HbR parameter. For simplicity in future results chapters, only results pertaining to the beta estimates of the HbO parameter of the functional component are presented. These beta weights were used to quantify the amplitude of speech-evoked cortical activation and were subjected to further statistical analyses that are specified in subsequent results chapters.

3.9.3 Defining Cortical Regions of Interest

Whist the primary auditory cortex is located medially in the depths of the lateral sulcus (Penhune et al., 1996), secondary auditory regions, including BA 22 and 42, that are important for speech

processing (see section 2.3.2.1) are located more laterally (Friederici, 2011). Therefore, the limited depth sensitivity of fNIRS means that the measurement of cortical activation from more lateral regions of the cortex, including auditory association cortices, would be anticipated, whereas fNIRS measurements would be far less sensitive to cortical activation from medially located primary auditory brain regions (Strangman et al., 2013). In order to assess the sensitivity of our fNIRS measurements to the underlying cortical regions using the AtlasViewer tool (Aasted et al., 2015), a Monte-Carlo code for simulating the probabilistic path of photon migration through an adult human head ('tMCimg', Boas et al., 2002) was run with 1×10^7 simulated photons launched from each optode position (as recommended by Aasted et al., 2015). This enabled us to estimate the spatial distribution of photons across the cortical regions covered by our optode array. The resultant spatial sensitivity profiles of each individual measurement channel are shown in Figure 3.20.

Visual inspection of these sensitivity profiles suggested that channels #9, 10 and 12, located over the left hemisphere, and channels #21, 23 and 24, located over the right hemisphere, provided sufficient sensitivity to the posterior superior temporal cortices, including coverage of auditory association areas BA 22/42 (see Figure 3.11 and Figure 3.12). Furthermore, existing studies have indicated that fNIRS measurements are more reliable when

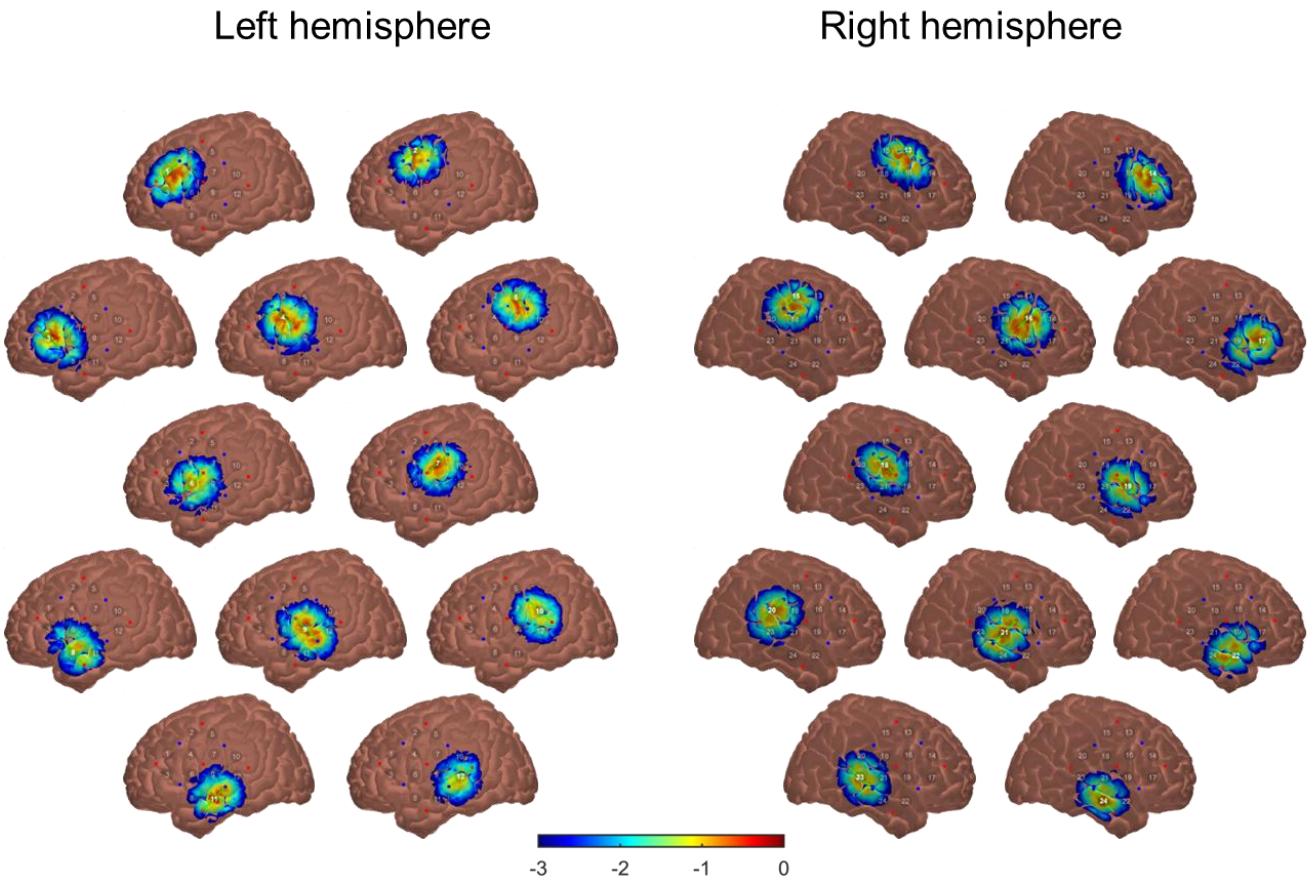


Figure 3.20: Spatial sensitivity profiles for each individual measurement channel over the left and right hemisphere, displayed in accordance with the optode array design. The colour scale depicts relative sensitivity logarithmically from 0.001 to 1.

averaged over a small number of channels that overlie a cortical region of interest (Plichta et al., 2006; Schecklmann et al., 2008). Therefore, these measurement channels (#9/10/12 and #21/23/24) were pre-defined as the left and right superior temporal ROI respectively. The aggregate sensitivity profiles for these temporal ROIs are shown in Figure 3.21. Whilst these ROIs were defined based on achieving optimal coverage of the posterior portion of STC, due to the limited spatial resolution of fNIRS, as well as the 3cm source-detector distance employed here, it is acknowledged that these ROIs will also be sensitive to haemodynamic changes occurring in neighbouring cortical regions. Therefore, although the term 'STC activation' is used throughout the thesis, this reference is made loosely to reflect the intended ROI coverage as no claims can be made about the exact anatomical origin of the cortical activations that we observed.

As speech stimuli can activate diverse cortical regions across the temporal, parietal and prefrontal lobes (Friederici, 2011; Hickok & Poeppel, 2007), the optode design employed here did not provided coverage of cortical areas with sufficient distance from the cortical regions where speech-evoked activations were expected. For this reason, a non-ROI was not defined as doing so would not have aided the assessment of the regional selectivity to speech-evoked activation (Aslin, 2012).

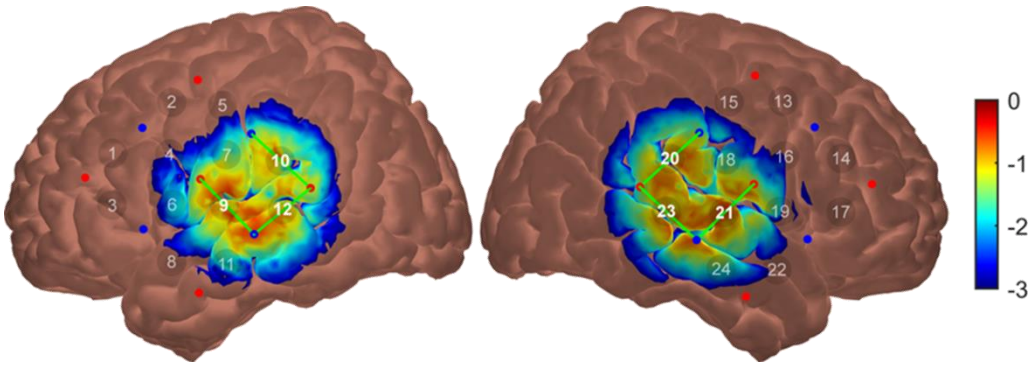


Figure 3.21: Aggregate spatial sensitivity profiles for the regions of interest over the left (channels #9, 10 and 12) and right (channels #20, 21, and 23) hemispheres. The colour scale depicts relative sensitivity logarithmically from 0.001 to 1.

3.10 SUMMARY

The current chapter has outlined the design and methodology of a longitudinal neuroimaging and behavioural experiment conducted to assess changes in speech-evoked cortical activation and speech perception abilities from pre- to post-implantation. Neuroimaging and behavioural data were collected from the same CI users before implantation, one month after CI activation and six months after CI activation, as well as from NH control subjects at three parallel time points. Specifically, this chapter has outlined how fNIRS was employed to measure cortical activation to auditory, visual and audio-visual speech bilaterally from predefined superior temporal regions of interest. Correspondingly, the use of behavioural tests to provide a measure of auditory, visual, and audio-visual speech perception ability in quiet listening conditions has been outlined. Furthermore, speech perception testing in noise was conducted to estimate the amount of benefit derived from visual speech information in audio-visual conditions. Finally, the chapter described methods involved in the preparation of neuroimaging and

behavioural data for subsequent statistical testing conducted in future chapters.

4. EVOLUTION OF SPEECH PERCEPTION ABILITIES FOLLOWING COCHLEAR IMPLANTATION

4.1 INTRODUCTION

The current chapter presents auditory, visual and audio-visual speech perception data obtained from CI users and NH control subjects in quiet testing conditions. The chapter examines the evolution of these speech perception abilities from before implantation, to one month, and six months after CI activation. In keeping with the overall aims of the thesis, the chapter aims to evaluate the level of between-subject variability observed in the recovery of auditory speech perception in a local population of CI users and compare this variability to that previously reported in the literature. Group differences in speech perception abilities between CI users and NH controls are also explored. Furthermore, the chapter aims to determine how the effects of time on performance differ between CI users and NH controls in order to understand whether any observed changes in performance over time can be attributed to the receipt of and increased experience with a CI, rather than learning effects associated with repeated testing. Note that correlations between behavioural performance and clinical characteristics are not explored here but are examined later in Chapter 6.

4.2 ANALYSIS

In order to examine performance on behavioural tests of auditory (A-ONLY), visual (V-ONLY) and audio-visual (AV) speech perception, the transformed speech perception data (RAUs, see section 3.8 for details) for each of the three conditions were subjected to statistical testing using a linear mixed model (LMM). A LMM is a parametric linear model that offers a particularly useful and flexible approach for analysing longitudinal data. Of particular relevance to the data in the current study, LMMs are able to give accurate estimates of the fixed effect of predictor variables whilst incorporating and accounting for the random effects that are often inherent in repeated-measures designs (Seltman, 2012). In addition, when a subject has a data value that is 'missing at random' LMMs include all available observations for each subject rather than omitting the subject entirely from the analysis, thus maximising the use of the available data (West et al., 2007). In order to estimate the fixed effect of experimental group (CI users and NH controls) and time relative to implantation (before implantation, one month after CI activation, and six months after CI activation) on performance, a LMM was employed with two fixed factors of 'group' and 'time'. In addition, a 'group – time' interaction term was specified in order to understand whether an effect of time on performance differed between the two groups. Specifically, if a group – time interaction indicated that performance increased over time in the CI group but remained stable in the NH group, this would suggest an effect specific to the CI process.

Due to the repeated measures design employed, measurement values obtained from the same participant are highly likely to be correlated rather than independent from each other. This within-participant covariance was incorporated into the fixed effect estimation by specifying 'participant' as a variable. In addition, it was expected that there would be a high level of between-subject variability in auditory, visual, and audio-visual speech perception abilities (Auer & Bernstein, 2007; Bernstein et al., 2000; Hay-McCutcheon et al., 2005; Lazard et al., 2010a; Rouger et al., 2007; Summerfield & Marshall, 1995), as well as variability in the rate and direction of change in these speech perception abilities over time (Hay-McCutcheon et al., 2005; Tyler et al., 1997). Therefore, a random intercept effect and a random effect of time were also specified within the model to facilitate the estimation of the fixed effect of 'group' and 'time' whilst accounting for between-subject variability.

4.3 RESULTS

4.3.1 Description of the Samples

4.3.1.1 CI Users

All seventeen participants were deemed suitable candidates for cochlear implantation by NAIP's clinical team and had consented to receive a CI prior to being recruited to the study. At the time of recruitment, the NAIP's process for determining eligibility for implantation was based on whether either ear met the NICE criteria

(2009) in addition to an overall assessment of need. The group comprised nine male and eight female participants with a mean age of 58 years (range 36 – 78 years) at the time of their first testing session. Fourteen individuals were identified as right handed by the Edinburgh Handedness Inventory (Oldfield, 1971). Table 4.1 presents a summary of clinical characteristics for this sample of CI users. Apart from cases of congenital deafness, the duration of bilateral profound deafness was unable to be determined for the majority of participants due to the progressive nature of their HL. However, more reliable information was available to estimate the duration of bilateral HL before implantation, defined as the duration from when participants first received bilateral HAs up until the time of the first testing session, which ranged from 4 months to 59 years. For the majority of participants (n=12) the onset of bilateral HL occurred during adulthood (age 20 – 65 years) and therefore after native language acquisition (post-lingual deafness). Two participants reported congenital deafness before the acquisition of native language (pre-lingual deafness), and three participants reported that the onset of bilateral HL occurred during childhood (aged three to five years), likely during the period of language acquisition (peri-lingual deafness). In terms of communication mode, one congenitally deaf participant reported using British Sign Language; however, all participants stated that spoken English was both their native language and preferred method of communication, with a reliance on speechreading. All participants received a Cochlear™ Nucleus® 6 device with CP910 sound processor that

Table 4.1: Summary of clinical characteristics of CI users

a)	b)	c)	d)	e)	f)	g) Left HT		h) Right HT		i)	j)
ID	**Aetiology**	**Onset HL**	**Duration HL**	**Age**	**Ear CI**	**2kHz**	**4kHz**	**2kHz**	**4kHz**	**Handedness**	**Hand LI**
CI_01	Immune Deficiency Virus	51	10 months	52	Right	80	85	120	>115	Right	95
CI_02	Unknown	Birth	37	37	Right	105	110	95	110	Right	100
CI_03	Noise-induced	44	23	67	Right	105	>120	110	>120	Right	100
CI_04	Unknown	24	40	64	Left	>120	>120	>120	>120	Right	80
CI_05	Unknown	20	39	59	Right	80	75	115	>120	Right	60
CI_06	Maternal rubella	Birth	38	38	Right	120	120	115	110	Right	95
CI_07	Otosclerosis	25	25	50	Right	115	90	115	105	Right	95
CI_08	Mastoidectomy	52	8	60	Left	105	>120	90	110	Left	-100
CI_09	Noise-induced	45	33	78	Right	>120	>120	>120	>120	Right	100
CI_10	Mastoidectomy	30	40	70	Left	>120	>120	>120	>120	Right	100
CI_11	Rubella	3	54	57	Right	80	90	120	>120	Right	100
CI_12	Unknown	5	59	64	Left	120	>120	110	110	Left	-100
CI_13	Unknown	4	32	36	Right	115	>120	115	>120	Right	80
CI_14	Unknown	65	11	76	Left	95	110	70	75	Left	-40
CI_15	Unknown	42	4 months	43	Left	>120	>120	120	>120	Right	100
CI_16	Unknown	43	35	78	Left	>120	>120	120	>120	Right	80
CI_17	Unknown	25	28	53	Right	75	90	>120	>120	Right	75

Column **a)** Participant ID; **b)** Aetiology of onset of hearing loss; **c)** Age-at-onset of bilateral hearing loss (years); **d)** Duration of bilateral hearing loss (years, unless otherwise stated); **e)** Age at time of CI surgery (years); **f)** Ear implanted; **g)** Unaided hearing threshold (dB) for left ear at frequencies 2 and 4kHz; **h)** Unaided hearing threshold (dB) for left ear at frequencies 2 and 4kHz; **i)** Dominant hand; **j)** Handedness laterality index (LI).

employed the advanced combination encoder (ACE™) stimulation strategy, with ten participants implanted in the right ear and seven implanted in the left ear. None of the participants experienced any complications during their CI surgery and no abnormalities were identified on post-operative scanning. Furthermore, for all participants, no electrodes were located outside of the cochlea and post-operative impedances were within normal range on all electrodes. For one participant, activation of the device was delayed by one week due to an infection around the surgical site of incision. All participants were stimulated in monopolar configuration and comfort and threshold levels were estimated for each electrode position by the clinical team according to standard clinical protocols. Self-reported information obtained using the Health Utilities Index Mark III (Feeny et al., 1995) indicated a significant increase in health utility across the group of CI users from pre-implantation to six months post-CI activation (mean change = 0.15, 95% confidence interval = 0.06 – 0.24).

As outlined in section 3.4.1, participants were tested before implantation (T0), one month after CI activation (T1), and six months after CI activation (T2). The study's testing timeline is provided in Figure 4.1. T0 took place at the participant's earliest convenience before undergoing the cochlear implant surgery. On average, T1 took place 33 days (range = 26 – 43 days) after CI activation and T2 took place 6.1 months (range = 5.3 – 7.1 months) after CI activation (shown in Table 4.2). In all three

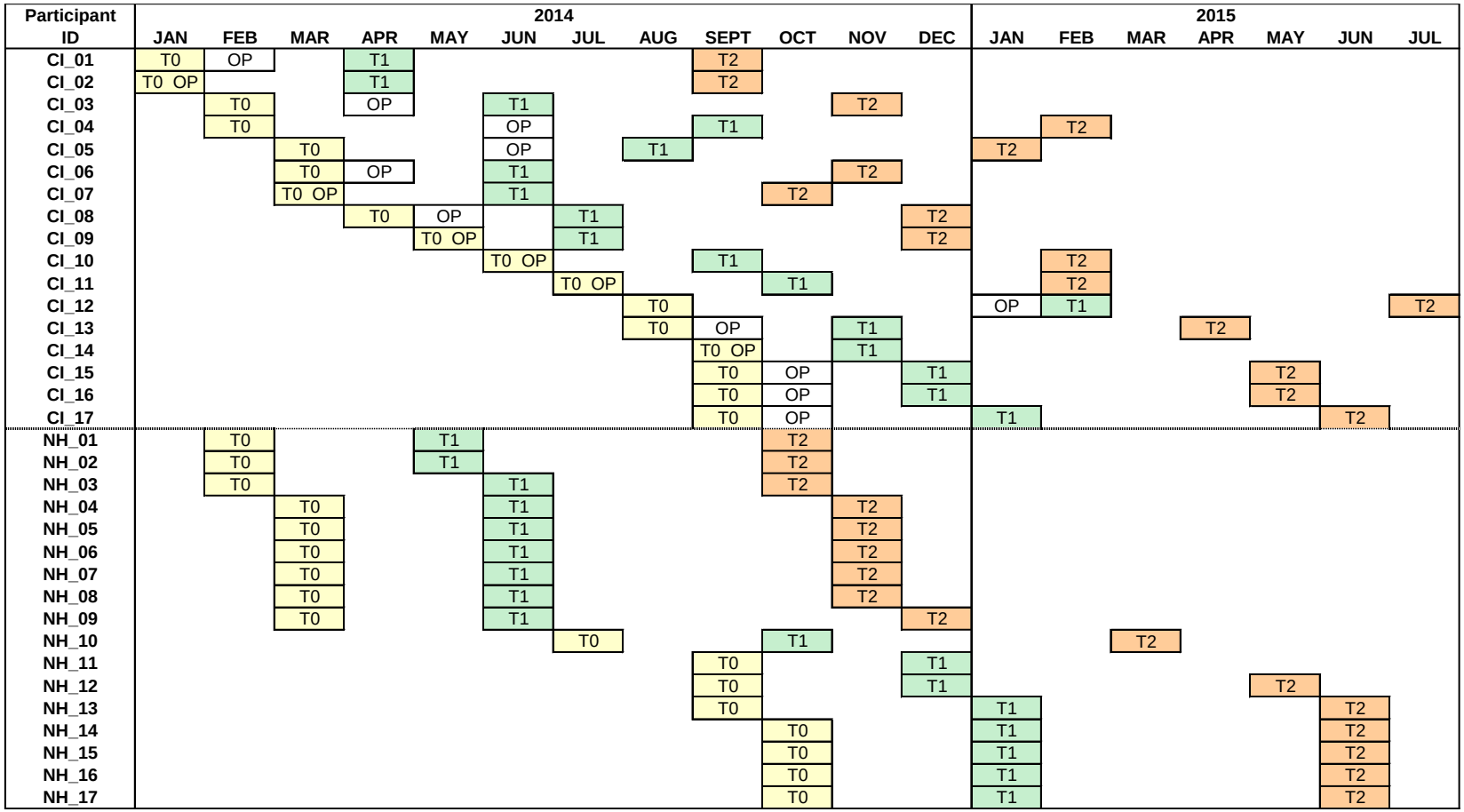


Figure 4.1: Recruitment and testing timeline for all study participants. T0, T1 and T2 denote the month in which the 1st, 2nd, and 3rd testing session took place respectively, with CI operations denoted as 'OP'.

Table 4.2: Summary of listening devices worn during testing sessions

a) ID	b) Ear CI	c) T1 CI use	d) T2 CI use	e) T0 HA	f) T1 HA	g) T2 HA
CI_01	Right	32	6.1	Left	✓	✓
CI_02	Right	42	7.1	Bilateral	✓	✓
CI_03	Right	26	6.2	None	×	×
CI_04	Left	31	6.1	Bilateral	✓	✓
CI_05	Right	34	6.4	Left	×	×
CI_06	Right	27	6.5	Bilateral	✓	✓
CI_07	Right	35	5.3	Bilateral	✓	✓
CI_08	Left	26	6.0	Bilateral	✓	✓
CI_09	Right	30	5.7	Bilateral	✓	×
CI_10	Left	26	6.1	Left	×	×
CI_11	Right	43	6.0	Right	×	×
CI_12	Left	28	6.0	Bilateral	✓	✓
CI_13	Right	43	6.5	None	×	×
CI_14	Left	35	-	Right	✓	-
CI_15	Left	29	6.1	Left	×	×
CI_16	Left	31	6.1	Bilateral	×	×
CI_17	Right	34	6.0	Bilateral	✓	✓
Mean (SD)		**32.5 (5.8) days**	**6.1 (0.4) months**			

Column **a)** Participant ID; **b)** Ear implanted; **c)** Duration of CI use at T1 since CI activation (days); **d)** Duration of CI use at T2 since CI activation (months); **e)** Side of acoustic hearing aid use at T0; **f)** Contralateral hearing aid worn with CI device at T1; **g)** Contralateral hearing aid worn with CI device at T2.

testing sessions, participants were tested wearing their preferred listening devices (see Table 4.2). It can be seen from Table 4.2 that acoustic HA use varied amongst subjects during pre-implant testing (T0), and that contralateral HA use varied amongst subjects in both post-implantation testing sessions (T1 and T2).

4.3.1.2 NH Controls

The seventeen NH participants recruited to the study comprised 11 females and six males with a mean age of 57 years (range 26 – 75 years). Pure-tone audiometry confirmed that all participants had hearing thresholds within normal levels, defined here as average pure-tone hearing thresholds of ≤20 dB across frequencies 0.5, 1, 2 and 4 kHz in both ears. Fifteen individuals were identified as right handed by the Edinburgh Handedness Inventory (Oldfield, 1971). A summary of the characteristics of the group of NH control subjects is provided in Table 4.3. Similar to the CI group, NH controls were also tested at three time points. The NH controls subjects' session retest intervals closely mirrored those of the CI users. Details of the retest intervals for both CI users and NH controls are provided in Table 4.4.

4.3.2 Missing Data

The number of participants with missing data values for each testing condition at each time point is summarised in Table 4.5. Missing data were treated as missing at random for the purpose of the LMM analysis. It can be seen from Table 4.5 that all 17 CI users underwent behavioural speech perception testing in A-ONLY, V-ONLY and AV conditions at T0. At T1, the same 17 CI users underwent behavioural testing; however, for participant 'CI_02' testing was terminated before completion due to illness, resulting in one missing data value for the V-ONLY and AV condition. At T2, 16 CI users completed all behavioural testing; participant 'CI_14' was

Table 4.3: Summary of characteristics of normal-hearing control subjects

a)	b)	c) Average HT		d)	e)
ID	**Age**	**Left**	**Right**	**Handedness**	**LI**
NH_01	31	8.75	7.5	Right	95
NH_02	50	11.25	3.75	Right	90
NH_03	28	2.5	0	Right	100
NH_04	67	11.25	7.5	Left	-100
NH_05	67	13.75	16.25	Right	100
NH_06	29	1.25	1.25	Right	50
NH_07	65	8.75	16.25	Right	90
NH_08	66	10	7.5	Right	65
NH_09	26	11.25	7.5	Right	65
NH_10	62	18.75	12.5	Right	100
NH_11	65	20	16.25	Left	-100
NH_12	69	15	17.5	Right	100
NH_13	63	12.5	11.25	Right	90
NH_14	58	7.5	7.5	Right	100
NH_15	75	8.75	11.25	Right	60
NH_16	70	15	11.25	Right	100
NH_17	71	10	16.25	Right	100

Column **a)** Participant ID; **b)** Age at first testing session (years); **c)** average pure-tone hearing thresholds (dB) across frequencies 0.5, 1, 2 and 4 kHz in the left and right ear; **d)** Dominant hand; **e)** Handedness laterality index (LI)

Table 4.4: Summary of retest interval durations

Group	T0 - T1 Retest interval (months)	T1 – T2 Retest interval (months)
CI	3.27 (1.28)	5.06 (0.37)
NH	3.06 (0.19)	5.02 (0.23)

Mean (SD) retest interval duration between the first (T0) and second testing session (T1), and between the second (T1) and third (T2) testing session for both groups of participants.

Table 4.5: Summary of missing behavioural data

Group	Testing session	Condition		
		A-ONLY	V-ONLY	AV
CI	T0	0 (n=17)	0 (n=17)	0 (n=17)
	T1	0 (n=17)	1 (n=16)	1 (n=16)
	T2	1 (n=16)	1 (n=16)	1 (n=16)
NH	T0	0 (n=17)	0 (n=17)	0 (n=17)
	T1	0 (n=17)	0 (n=17)	0 (n=17)
	T2	1 (n=16)	1 (n=16)	1 (n=16)

The number of participants with missing data values is indicated for each speech perception measure. Total sample sizes are shown in parentheses.

withdrawn from the study due to having a stroke between T1 and T2 that classified them as ineligible. Table 4.5 shows that all seventeen control subjects completed all behavioural testing at both T0 and T1. However, 16 control subjects were tested at T2 due to attrition.

4.3.3 Model Diagnostics

Following LMM analysis for each condition, the model's residuals were examined by visual inspection of histograms, Q-Q plots and use of the Kolmogorov-Smirnov (K-S) test. Together these diagnostics confirmed that the LMM's residuals were normally distributed for the V-ONLY condition. The deviations from normality in the other conditions were found to be due to ceiling effects, which by their nature could not be corrected for by transforming the data using the rationalised arcsine transform (as described in section 3.8). The implications for these violations of assumptions are that

the effects of time on A-ONLY and AV performance may not have been accurately estimated by the LMM analysis in the NH group, and may have not been accurately estimated for AV performance in the CI group.

4.3.4 Auditory Speech Perception

The non-transformed A-ONLY performance scores (% correct) for each participant are displayed as a function of time in Figure 4.2. Auditory performance before implantation (T0) was seen to range from 0—98% correct across the sample of CI candidates. This high level of between-subject variability reflects the heterogeneity of the current sample of CI candidates and the fact that participants were tested binaurally in their best-aided condition, whereas the NAIP's process for determining eligibility was based on whether either ear met criteria for implantation. As anticipated, a high level of variability in auditory performance was observed across the group of CI users, with performance ranging from 1—100% correct after six months of CI use. Some participants (n=5) were seen to perform near to or at ceiling (performance >95% correct) at T1 and T2, indicating that their improvement in auditory speech perception from pre- to post-implantation may not have been fully quantified here due to ceiling effects. Figure 4.2 shows the trajectory of A-ONLY performance over time to vary between individuals. As anticipated, ceiling effects were observed in the NH group, with mean A-ONLY performance greater than 99% at all three time points and negligible between-subject variability.

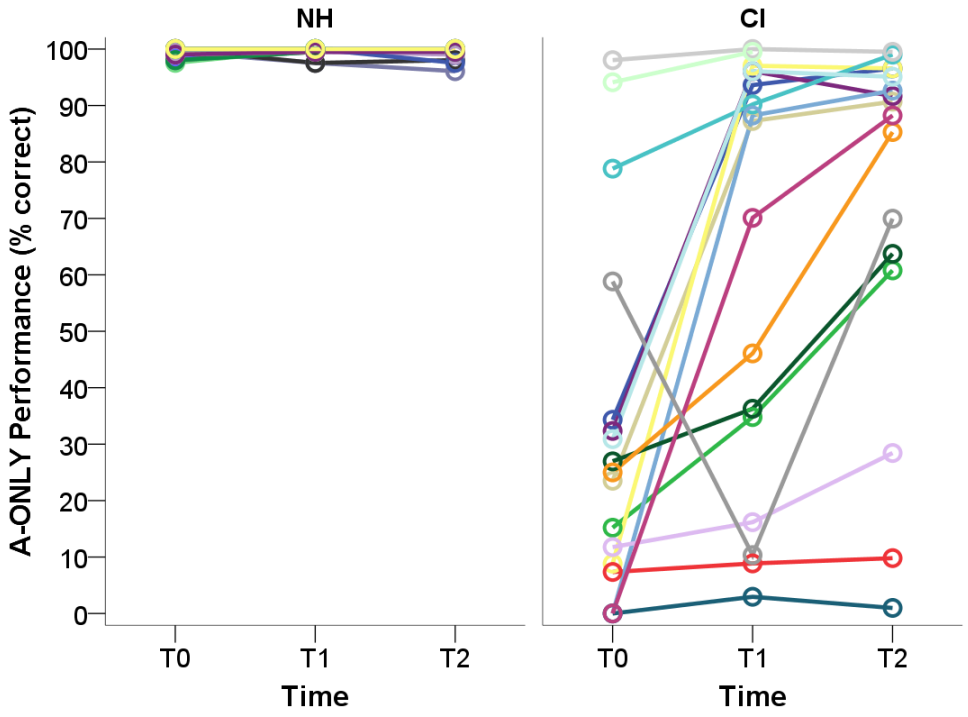


Figure 4.2: Line graph showing individual trajectories of auditory performance Line graph is panelled by group (NH controls and CI users) with A-ONLY performance (percentage of words correctly identified) plotted as a function of time. Individual lines are colour coded by participant.

LMM analysis of the transformed data (RAUs) indicated a significant main effect of group ($F_{1,31.76}$=44.95, p<.001) and a main effect of time ($F_{2,31.73}$=18.95, p<.001) on A-ONLY performance. Importantly, the model also revealed a significant group – time interaction ($F_{2,31.73}$=19.85, p<.001), indicating that time had a differential effect on A-ONLY performance depending on group. This interaction was explored further by conducting a separate LMM for each group. This analysis showed a significant main effect of time on A-ONLY performance in the CI group ($F_{2,15.84}$=20.69, p<.001) but not in the NH group ($F_{2,15.93}$=1.85, p=.19). Figure 4.3 displays mean A-ONLY performance as a function of time for both groups with the significant effect of time indicated. Post-hoc pairwise comparisons

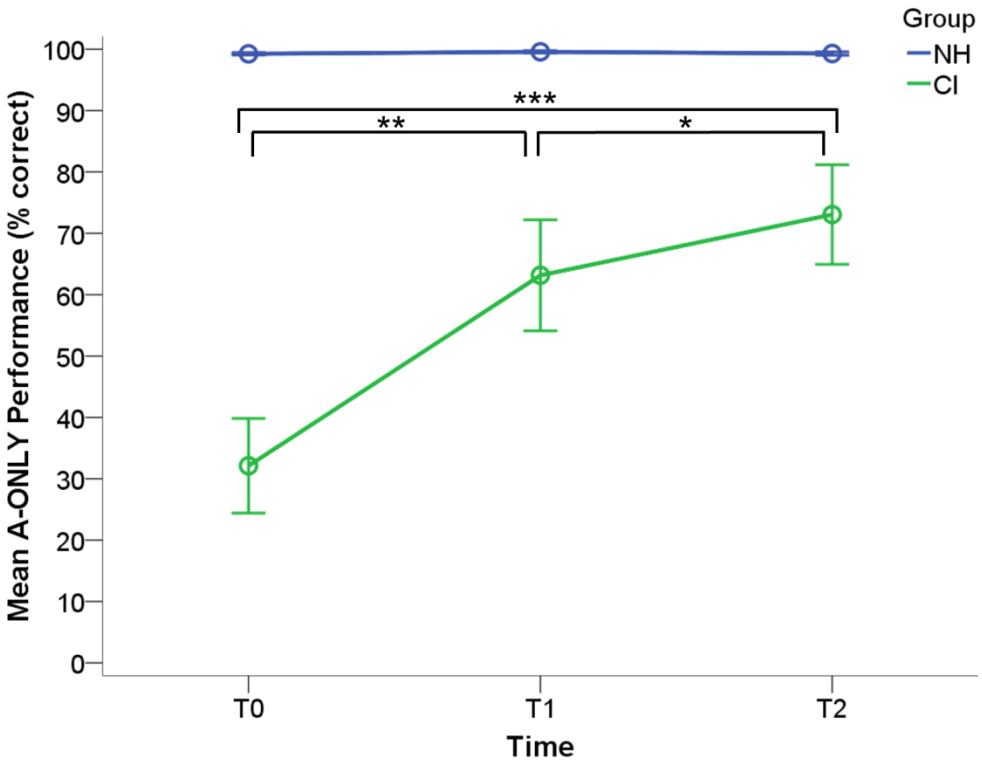


Figure 4.3: Line graph showing mean auditory performance
Mean A-ONLY performance (percentage of words correctly identified) is plotted as a function of time with lines colour coded by group. Error bars represent ± 1 standard error. Asterisks denote a significant difference in performance between time points based on the LMM's estimated marginal means of the transformed data (*p<.05, **p<.01, ***p<.001, Bonferroni corrected).

of the estimated marginal means (Bonferroni corrected) indicated that A-ONLY performance of CI users improved significantly between T0 and T2 (mean difference=50.00 RAUs, p<.001), with an initial significant increase observed between T0 and T1 (mean difference=37.29 RAUs, p<.01), and a further significant mean increase of 12.72 RAUs observed between T1 and T2 (p<.05). A similar pattern of performance was found for the IHR Sentences. Analogous versions of Figures 4.2 and 4.3 showing these data are provided in Appendix C, section 10.3.1.

4.3.5 Visual Speech Perception

The non-transformed V-ONLY performance scores (% correct) for each participant are displayed as a function of time in Figure 4.4. Between-subject variability in visual performance was observed in CI users both before and after implantation (T0: range=0 – 57%; T1: range=0 – 58%; T2: range=0 – 51%). A lower level of between-subject variability in performance was observed in NH controls (T0: range=0 – 28%; T1: range=0 – 37%; T2: range=0 – 29%). Furthermore, floor effects were marked in the NH group with approximately 80% of participants performing below 10% correct at all three time points.

LMM analysis of the transformed data (RAUs) indicated a significant main effect of group ($F_{1,31.90}$=8.93, p<.01), with the CI group displaying greater speechreading abilities compared to the NH group (mean difference=18.36 RAUs). No main effect of time ($F_{2,29.16}$=1.48, p=.25), nor a group – time interaction ($F_{2,29.16}$=.06, p=.94), was observed. In order to confirm whether the group effect was present both before and after cochlear implantation, separate LMMs were conducted at each time point. This post-hoc analysis confirmed that the main effect of group was present during periods of profound deafness (T0: $F_{1, 32}$=7.42, p<.05), soon after CI activation (T1: $F_{1, 31}$ = 6.78, p<.05), and following six months of experience with a CI (T2: $F_{1, 30}$=10.31, p<.01). Figure 4.5 displays mean V-ONLY performance for NH controls and CI users as a function of time with significant effects of group indicated.

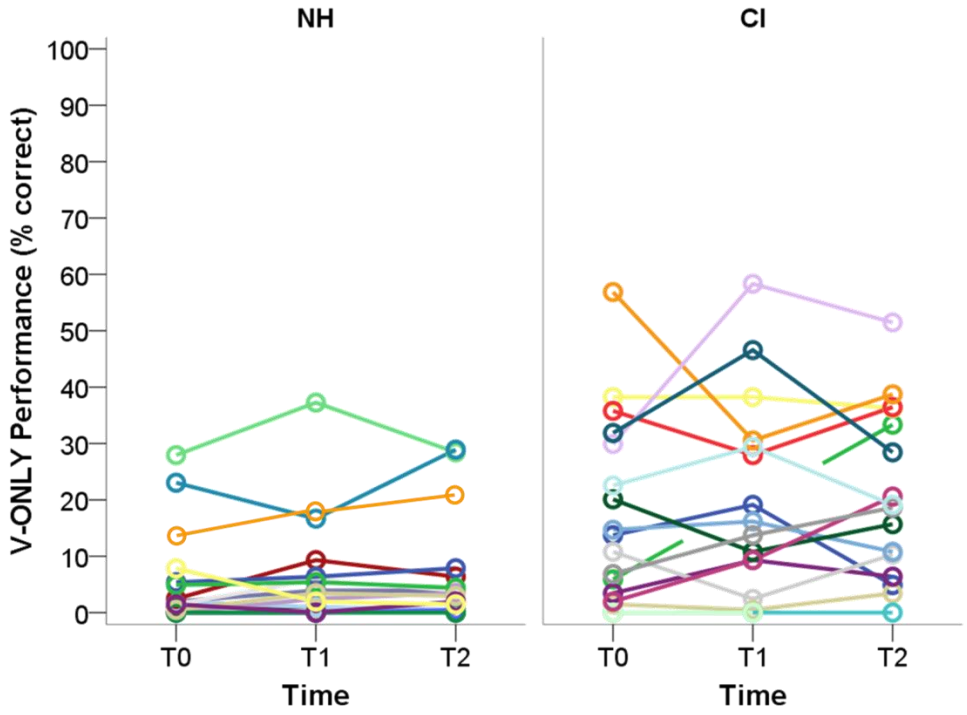


Figure 4.4: Line graph showing individual trajectories of visual performance
Line graph is panelled by group (NH controls and CI users) with V-ONLY performance (percentage of words correctly identified) plotted as a function of time. Individual lines are colour coded by participant.

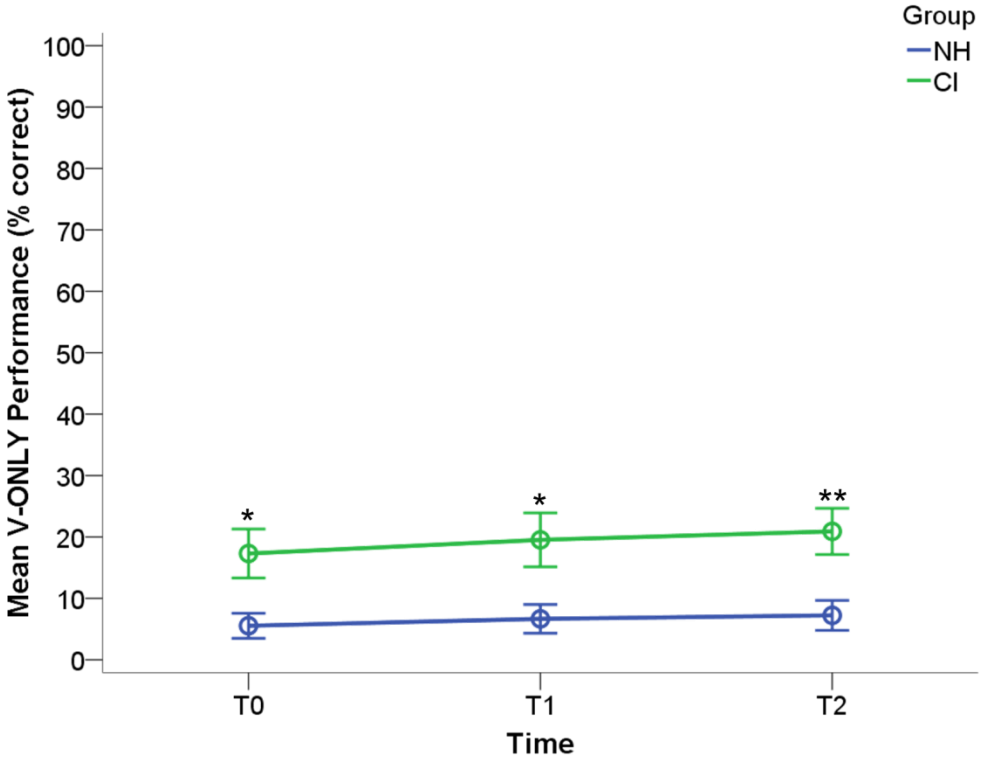


Figure 4.5: Line graph showing mean visual performance
Mean V-ONLY performance (percentage of words correctly identified) is plotted as a function of time with lines colour coded by group. Error bars represent ± 1 standard error. Asterisks denote a significant group difference based on the LMM's estimated marginal means of the transformed data (*p<.05, **p<.01, Bonferroni corrected).

A similar pattern of performance was found for the IHR Sentences. Analogous versions of Figures 4.4 and 4.5 showing these data are provided in Appendix C, section 10.3.2.

4.3.6 Audio-Visual Speech Perception

The non-transformed AV performance scores (% correct) for each participant are displayed as a function of time in Figure 4.6. Before implantation, audio-visual speech perception ability was seen to vary widely across the group of CI users (13—100% correct). Following six months of CI use, variability in AV performance was reduced but still evident (range=56—100% correct). Figure 4.6 shows that the trajectory of AV performance over time also varied between individuals. Ceiling effects were observed following implantation with approximately 50% of CI users performing above 95% correct at T1 and 56% performing above 95% correct at T2. As anticipated, NH control subjects performed at ceiling throughout, with mean AV performance greater than 98% correct at all three time points and negligible between-subject variability observed (see Figure 4.6).

LMM analysis of the transformed data (RAUs) indicated a significant main effect of group ($F_{1,32.02}$=24.29, p<.001) and time ($F_{2,31.54}$=12.39, p<.001) on AV performance. Importantly, the model revealed a significant group – time interaction ($F_{2,31.54}$=8.47, p<.01), indicating that time had a differential effect on AV performance depending on group. This interaction was further

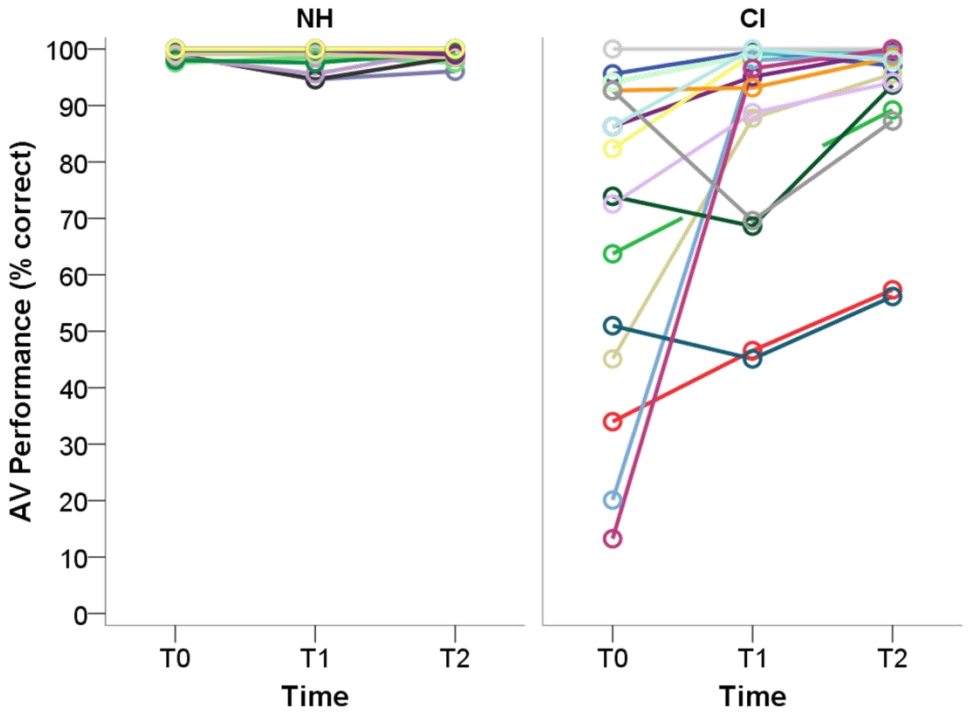


Figure 4.6: Line graph showing individual trajectories of audio-visual performance. Line graph is panelled by group (NH controls and CI users) with AV performance (percentage of words correctly identified) plotted as a function of time. Individual lines are colour coded by participant.

explored by conducting a separate LMM for each group. This revealed a significant effect of time in the CI group ($F_{2,15.53}$=11.54, p<.01) but not in the NH group ($F_{2,2.66}$=1.86, p=.31). Figure 4.7 displays mean AV performance as a function of time for both groups with significant effects of time indicated. Post-hoc pairwise comparisons of the estimated marginal means (Bonferroni corrected) indicated that AV performance of CI users improved significantly between T0 and T2 (mean difference=29.38 RAUs, p<.01), with an initial significant increase observed between T0 and T1 (mean difference=20.75 RAUs, p<.05), and a further significant mean increase between T1 and T2 (mean difference=8.63 RAUs, p<.05).

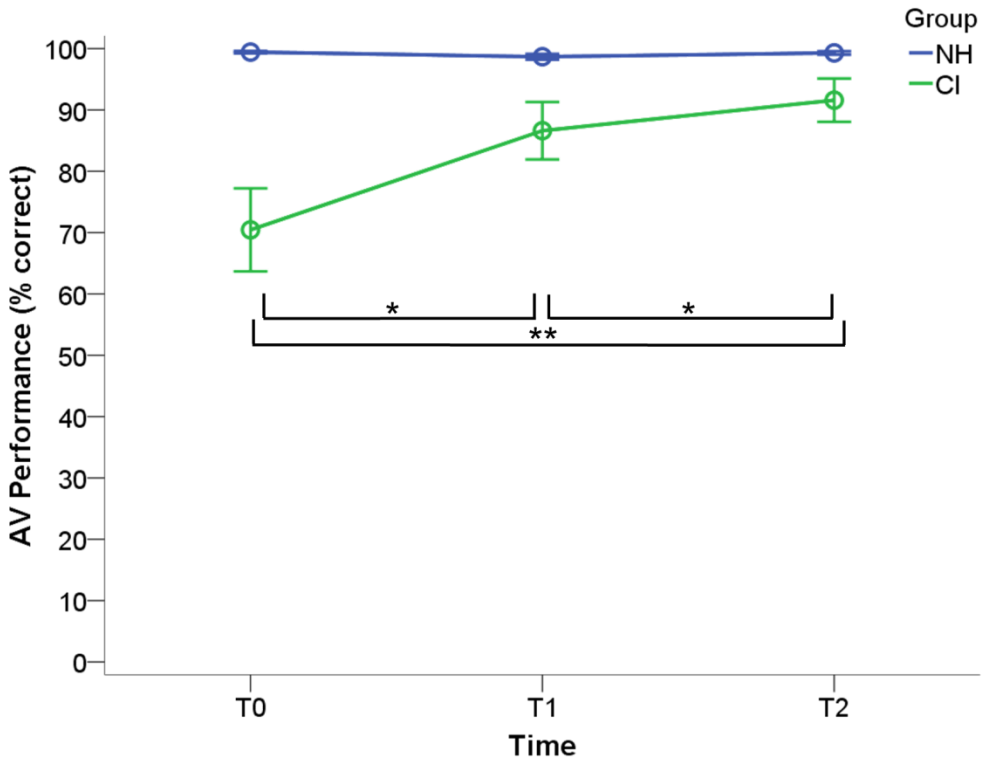


Figure 4.7: Line graph showing mean audio-visual performance
Mean AV performance (percentage of words correctly identified) is plotted as a function of time with lines colour coded by group. Error bars represent ± 1 standard error. Asterisks denote a significant difference in performance between time points based on the LMM's estimated marginal means of the transformed data (*p<.05, **p<.01, Bonferroni corrected).

A similar pattern of performance was found for the IHR Sentences. Analogous versions of Figures 4.6 and 4.7 showing these data are provided in Appendix C, section 10.3.3.

4.4 DISCUSSION

The behavioural data presented in the current chapter illustrate the significant benefits that cochlear implantation can provide to profoundly deaf individuals. Specifically, significant improvements in auditory performance were observed as soon as one month after CI activation, with further improvements over the following five months of CI use. This is consistent with existing reports of the

benefits that cochlear implantation can provide for auditory speech perception (Blamey et al., 2013; Gantz et al., 1993; Lazard et al., 2010a, 2012a; Summerfield & Marshall, 1995; Tyler et al., 1997), particularly over the initial six month period (Lenarz et al., 2012; Rouger et al., 2007). As anticipated, a high level of variability was observed in CI outcome, with auditory performance six months post-CI activation spanning almost the entire possible range (1—100 % correct) across the group of CI users. This is in line with existing reports (Gantz et al., 1993; Lazard et al., 2010a; Summerfield & Marshall, 1995) and confirms that variability in CI outcome is evident and pronounced within the current local cohort of CI users. In addition, between-subject variability was also observed in the rate and direction of change in auditory performance over time. This is consistent with available data from adult CI recipients (Dorman et al., 1990; Hay-McCutcheon et al., 2005; Tyler et al., 1997) and demonstrates individual differences in the recovery of auditory speech perception over the first six months post-implantation.

Given the observed significant improvements in auditory performance, it is perhaps unsurprising that similar improvements were likewise observed in audio-visual performance, also consistent with previous reports (Rouger et al., 2007; Summerfield & Marshall, 1995). As anticipated, many CI users (approximately 50%) in the current study were seen to achieve levels of audio-visual performance above 95% correct as soon as one month after

implantation. Some CI users were seen to perform at ceiling in both A-ONLY and AV conditions, with ceiling effects in audio-visual performance particularly marked following six months of CI use. Therefore, it is unlikely that the full extent of improvements in auditory and audio-visual speech perception gained from implantation were estimated here. This highlights an inherent problem when conducting speech perception testing in quiet listening conditions with a constrained 0 – 100% correct performance scale. Furthermore, as anticipated, there was no evidence of any significant change in A-ONLY and AV performance of NH control subjects over time. Evidence of significant group – time interaction indicated that the improvements observed in CI users' A-ONLY and AV performance were attributable to the CI rehabilitation process. However, as noted in section 4.3.3, it is possible that the accurate estimation of any improvements in performance gained by the NH control subjects due to repeated exposure and learning effects may have been precluded by the marked ceiling effects encountered at all three time points.

Existing studies have demonstrated enhanced speechreading abilities in adults with early-onset deafness (Auer & Bernstein, 2007; Bernstein et al., 2000; Ellis et al., 2001) and post-lingual deafness (Rouger et al., 2007) compared to NH listeners. Consistent with these reports, the current findings indicated significantly greater speechreading performance in profoundly deaf adults prior to cochlear implantation compared to NH control

subjects. This enhanced performance may reflect an increased reliance on visual speech information and a behavioural adaptation to aid spoken communication during periods of auditory deprivation (Auer & Bernstein, 2007). However, the current findings also demonstrated a high level of variability in visual performance of the CI group, indicating individual differences in speechreading ability within the current sample of deaf adults similar to that which has been reported elsewhere (Auer & Bernstein, 2007). The variability in speechreading skill observed here may reflect the known heterogeneity of the current sample of CI users in terms of their clinical history of deafness, spoken language experience and associated differences in their level of reliance on visual speech cues (Auer & Bernstein, 2007), as well as individual differences in perceptual and cognitive factors (Andersson et al., 2001; Lyxell et al., 2003). The poorer speechreading abilities and marked floor effects observed in the NH control group were anticipated as NH subjects do not commonly have to decipher visual speech cues in the absence of corresponding auditory information, and have been seen to rely more heavily on auditory speech cues in ambiguous audio-visual conditions (Desai et al., 2007). Notably, the two NH individuals who displayed the greatest level of speechreading skill within the current group (see Figure 4.4) both reported working in noisy environments. Thus reliance on visual speech cues and speechreading proficiency may have been necessary for effective communication in day-to-day life for these NH individuals. Indeed, individual differences in speechreading ability of NH individuals

observed here is consistent with reports in the literature (Auer & Bernstein, 2007; Bernstein et al., 2000; Ellis et al., 2001; Hall et al., 2005; Macleod & Summerfield, 1987). In line with available longitudinal evidence in post-lingually deaf CI users (Rouger et al., 2007), the current findings indicated that speechreading abilities remained enhanced above that of the NH individuals across both of the post-implantation testing sessions. This may reflect the continued importance of and reliance on visual speech cues that has been demonstrated in CI users (Desai et al., 2007; Rouger et al., 2007, 2008; Schorr et al., 2005), likely due to the benefits that corresponding visual speech information can provide to help decipher the degraded auditory input provided by the implant (Bergeson et al., 2003; Lachs et al., 2001; Moody-Antonio et al., 2005; Rouger et al., 2007).

4.5 CHAPTER SUMMARY

The current chapter examined the evolution of auditory, visual and audio-visual speech perception abilities from pre- to post-implantation at both the individual and group level. The findings demonstrate the significant improvements that cochlear implantation can provide to auditory and audio-visual speech perception following profound deafness. As anticipated, substantial between-subject variability was observed in auditory speech perception following six months of CI use, thus confirming variability in CI outcome in the current sample of CI users and warranting exploration of contributory and predictive factors in future chapters

of the thesis. In the NH control group, no evidence of significant learning effects due to repeated exposure to the experimental stimuli was seen. However, ceiling effects in both the auditory and audio-visual conditions, as well as floor effects in the visual condition, could have conceivably masked any such training effects. Prior to implantation, CI candidates on average displayed enhanced speechreading abilities compared to NH listeners, likely reflecting a behavioural adaptation to deafness due to a strong reliance on visual speech information during periods of auditory deprivation. This greater level of speechreading proficiency was seen to be maintained following implantation, suggesting the continued reliance and importance of visual speech information even when auditory input is reinstated. However, individual variability in performance was observed at all time points within the group of CI users, indicating that individual differences in speechreading skill and the reliance on visual speech information exist both during periods of profound deafness and during the recovery of auditory function.

5. SPEECH-EVOKED CORTICAL ACTIVATION BEFORE AND AFTER COCHLEAR IMPLANTATION

5.1 INTRODUCTION

The current chapter presents fNIRS measurements of cortical activation to auditory, visual and audio-visual speech acquired from bilateral superior temporal brain regions of CI users and NH control subjects. The chapter aims to evaluate the ability of fNIRS to detect cortical responses to speech within auditory brain regions that are free from CI-generated artefacts when listening with a cochlear implant. Group-level cortical activation patterns, as well as the time course and amplitude of activation within predefined superior temporal ROIs, are examined in both groups. In order to understand the impact of profound deafness and subsequent cochlear implantation on cortical responses to speech, the chapter employs an LMM approach to determine any group differences in amplitude of cortical activation as well as any changes over time from pre- to post-implantation. Furthermore, the chapter aims to determine how the effect of time may differ between CI users and NH control subjects in order to identify changes in cortical activation associated with the recovery of hearing following cochlear implantation. Note that correlations between cortical activations, behavioural performance and clinical characteristics are examined in subsequent chapters.

5.2 ANALYSIS

In order to examine cortical responses to auditory (A-ONLY), visual (V-ONLY) and audio-visual (AV) speech, beta weights representing the amplitude of cortical activation for each condition were extracted for each measurement channel across the bilateral array (see section 3.9.2 for details) and were subjected to statistical testing described below.

5.2.1 Cortical Activation Maps

For each condition, group-level cortical activation maps were produced to visualise patterns of significant speech-evoked cortical activation bilaterally across the fNIRS measurement arrays. Single sample, one-tailed *t*-tests were conducted on the beta weights in order to detect measurement channels that displayed significant levels of cortical speech-evoked activation compared to rest. However, by testing for significant activation in all 24 individual measurement channels, multiple comparisons are conducted and the risk of Type I error is increased. To correct for multiple comparisons, a false discovery rate (FDR) procedure has been proposed for use with fNIRS data that appears to offer a less conservative, and therefore more powerful, approach in comparison to Bonferroni correction (Singh & Dan, 2006). Therefore, the FDR correction procedure was employed here at $\alpha = 0.05$.

5.2.2 Region of Interest Analysis

For each condition, the time course of cortical activation within the predefined ROIs (see section 3.9.3 for details) was plotted. This enabled the visualisation of speech-evoked hemodynamic responses to determine whether plausible, artefact-free, HRFs had been obtained in each condition. For each measurement channel, the time course of HbO and HbR concentration changes as well as HbT levels were block-averaged using the HOMER2 hmrBlockAvg function (Huppert et al., 2009). For each condition these were then averaged over the relevant measurement channels to produce separate time courses for the left and right ROIs.

Following the use of a GLM approach (see section 3.9.2), the resultant beta weights representing the amplitude of cortical activation were averaged across the ROI measurement channels for each group. These beta weights were analysed separately for the left and right ROI using a LMM similar to that described in section 4.2. Each model included two fixed factors of 'group' and 'time' in order to estimate the fixed effect of experimental group (CI users and NH controls) and time relative to implantation (before implantation, one month after CI activation, and six months after CI activation) on speech-evoked cortical activation. In addition, a 'group – time' interaction term was specified in order to understand whether an effect of time on cortical activation differed between the two groups. Specifically, if a group – time interaction indicated that speech-evoked cortical activation changed over time in the CI group

but remained comparatively stable in the NH group, this would identify changes associated with the CI rehabilitation process. Due to the repeated measures design, 'participant' was specified as a variable to incorporate within-participant covariance into the fixed effect estimation. Furthermore, a random intercept effect and random effect of time were included to facilitate the estimation of the fixed effect of 'group' and 'time' whilst accounting for possible between-subject variability in the overall fNIRS signal strength and the trajectory of signal strength over time.

5.3 RESULTS

5.3.1 Missing Data

As previously described in section 4.3.1.1, seventeen CI users participated in this study (see Table 4.1 for a summary of their clinical characteristics). fNIRS measurements were acquired for all 17 CI users before implantation (T0) and one month after CI activation (T1). Following the withdrawal of participant CI_14 from the study for reasons outline in section 4.3.2, fNIRS measurement were subsequently acquired for 16 CI users six months after CI activation (T2). Similarly, 17 NH controls subjects underwent fNIRS testing at T0 and T1, with retest intervals set to closely mirror those of the CI users (see Table 4.4 for details). Due to attrition, fNIRS measurements were acquired for 16 NH control subjects at T2.

One CI user (CI_04) was excluded from fNIRS analysis due to concerns over the quality of the acquired fNIRS measurements.

These concerns were documented by the researcher in the participant's testing notes at the time of scanning, and were later confirmed by visual examination of the data. The number of missing data values at each time point following these participant exclusions is summarised in Table 5.1. In a small number of cases the analysis procedure failed to produce valid numerical values for the chromophore concentration changes, typically because of poor quality in the raw fNIRS signals; channels suffering from this issue were excluded from further analysis. These 'bad channels' were evident across three participants, the details of which are provided in Table 5.2. It was documented in the researcher's testing notes that bad channels for NH_06 and CI_17 were due to poor source-detector pairings that were 'under-gain', likely due to poor optode-scalp coupling and the attenuation of light by dark hair. However, CI_10 presented an unusual case in which the positioning of the optode array overlaid the individual's CI coil (see Figure 5.1). In this instance, a source optode could not be connected; therefore it was not possible to acquire measurements from channels #10 and #12 for this participant.

5.3.2 Model Diagnostics

For each LMM analysis conducted, the model's residuals were assessed by examining histograms, Q-Q plots, as well as the K-S test. Overall, this examination suggested that the residuals in the A-ONLY and AV conditions were approximately normally distributed. However, there was evidence of a deviation from normality for the

Table 5.1: Summary of missing fNIRS data

Group	Testing session	Missing
NH	T0	0 (n=17)
	T1	0 (n=17)
	T2	1 (n=16)
CI	T0	1 (n=16)
	T1	1 (n=16)
	T2	2 (n=15)

The number of participants with missing fNIRS data following participant exclusions is indicated for each testing session. Total sample sizes are shown in parentheses.

Table 5.2: Details of excluded fNIRS measurement channels

Participant ID	Testing session		
	T0	T1	T2
CI_10	-	#10, #12	#10, #12
CI_17	#3, #5, #8, #10	-	-
NH_06	#10, #12	-	-

Measurement channel numbers are indicated that were excluded due to the absence of valid numerical values in the fNIRS raw chromophore concentration data.

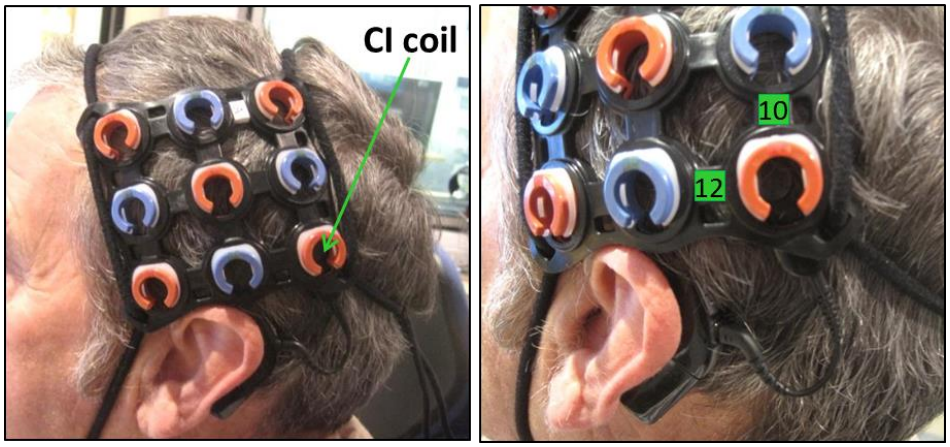


Figure 5.1: Pictures showing the overlapping placement of the fNIRS optode array and CI coil. This precluded the use of the corresponding red source optode and associated measurement channels #10 and #12 that are highlighted here in green.

residuals of the LMM conducted for the left ROI in the V-ONLY condition, which appeared to be driven by skew within the NH group. This violation of normality may have affected the accuracy with which the model estimated parameters within the left ROI in this condition.

5.3.3 Cortical Activation to Auditory Speech

Figure 5.2 displays the group-level cortical activation maps for the A-ONLY condition. Significantly activated channels revealed by one-tailed *t*-tests ($p<.05$, FDR corrected) are highlighted. Across the group of CI users, no measurement channels showed significant activation before implantation (T0) or one month after CI activation (T1). However, following six months of CI use (T2), activation measured at channel #12 over the left superior temporal regions was seen to reach significance. Consistently across all time points, a greater number of measurement channels were found to be significantly activated over the superior temporal regions of the NH group compared to that of the CI group. The locations of these significantly activated channels aligned well with the predefined ROIs. In addition to these superior temporal activations, channel #2, seemingly located over pre-central motor regions, also showed significant activation at T1.

Figure 5.3 shows the group-averaged time course of activation within the left and right ROIs for each group and test session. These plots indicate that plausible HRFs elicited by auditory speech

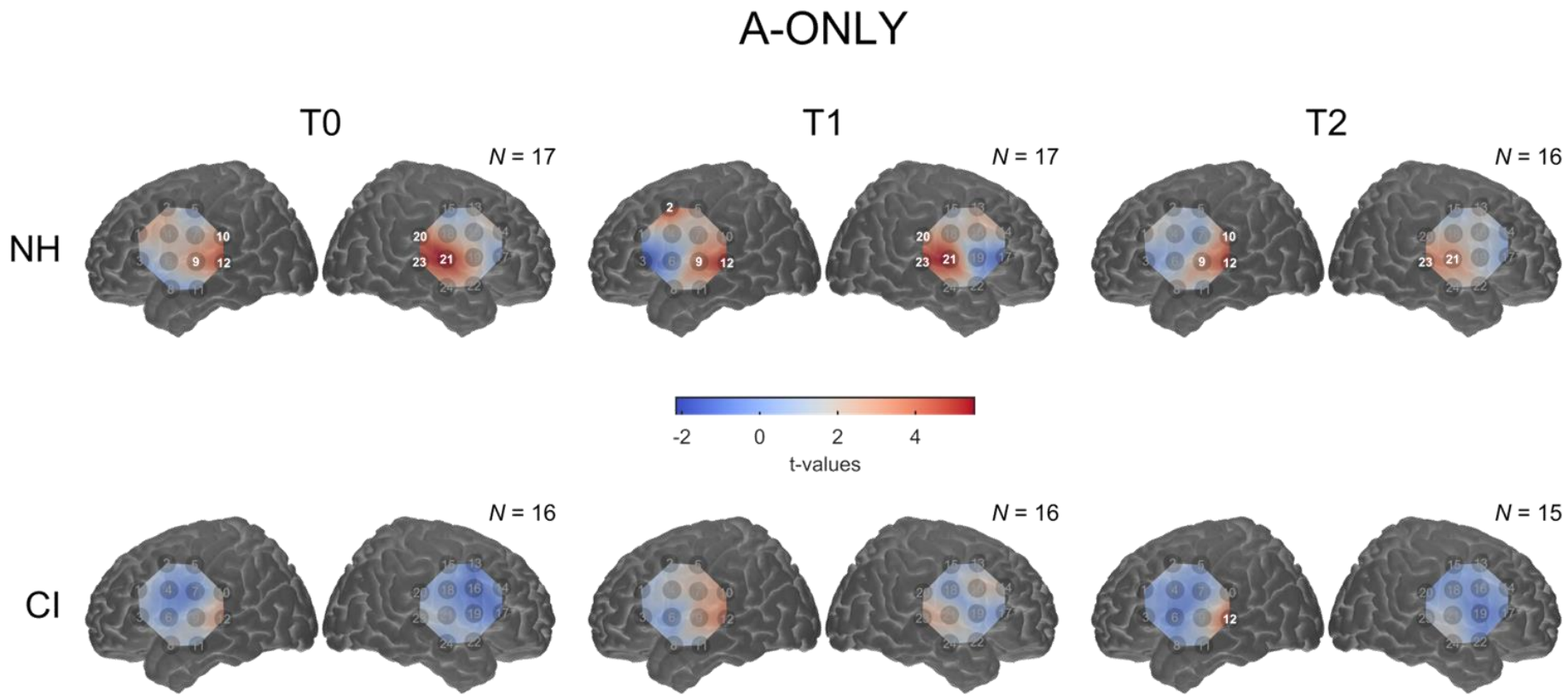


Figure 5.2: Group-level cortical activation map for auditory speech. Amplitude of cortical activation to auditory speech is colour coded by *t*-value. Significantly activated channels releveled by one-tailed *t*-tests ($p<.05$, FDR corrected) are highlighted.

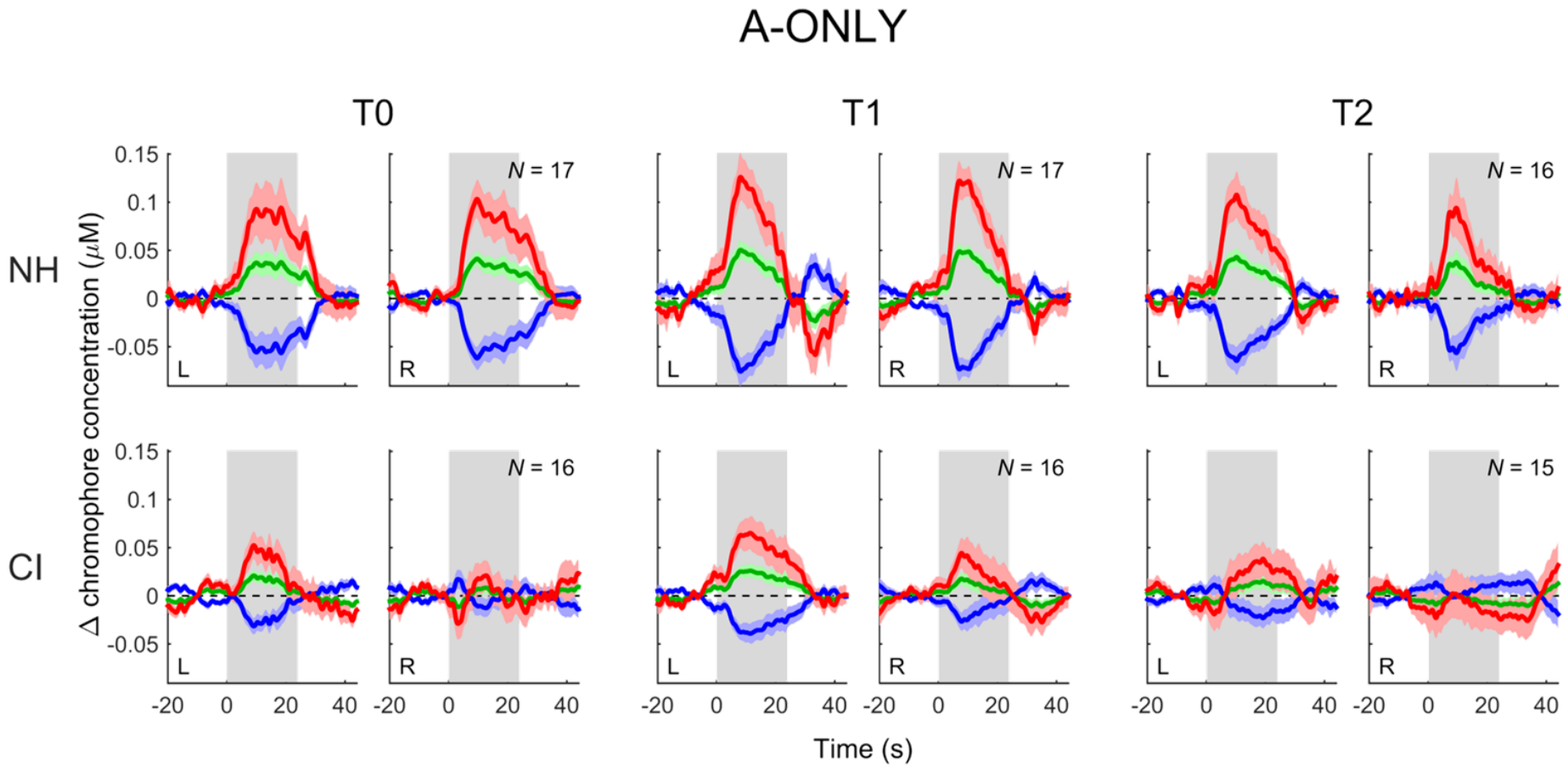


Figure 5.3: Group-averaged time courses of activation to auditory speech. Changes in **HbO** and **HbR** concentration, as well as **HbT** levels, are shown for the left (L) and right (R) ROI during the presentation of auditory speech (stimulation period indicated by shaded grey region). Coloured shading indicates ± 1 standard error across participants.

were acquired from the superior temporal brain regions of NH controls and CI users, with an increase in HbO and a simultaneous decrease in HbR concentration observed reflecting the canonical HRF. Importantly, it can be seen that these STC responses acquired from the CI group after implantation are free from any CI device-related artefacts.

Mean beta weights for the left and right ROI are displayed for each group as a function of time in Figure 5.4. LMM analysis of beta weights within the left ROI revealed a significant main effect of group on amplitude of cortical activation ($F_{1,29.82}$=6.51, p<.05), with NH controls displaying significantly greater activation to auditory speech compared to CI users. The LMM revealed no evidence of an effect of time on the amplitude of cortical activation ($F_{2,28.75}$=.76, p=.48), nor a group – time interaction effect ($F_{2,28.75}$=.06, p=.94). Similarly, LMM analysis of the right ROI indicated a significant main effect of group ($F_{1,31.05}$= 3.66, p<.001), with greater cortical activation observed in the NH group compared to the CI group (mean difference in beta weight =0.047). Again, no significant main effect of time on cortical activation ($F_{2,30.03}$=1.92, p=.17), nor a group – time interaction effect was observed ($F_{2,30.03}$=.43, p=.65).

Whilst existing PET studies provide some evidence to suggest greater activations to auditory speech are observed in the hemisphere contralateral to the side of implantation (Giraud et al., 2001b; Green et al., 2008; Naito et al., 1997), others have shown

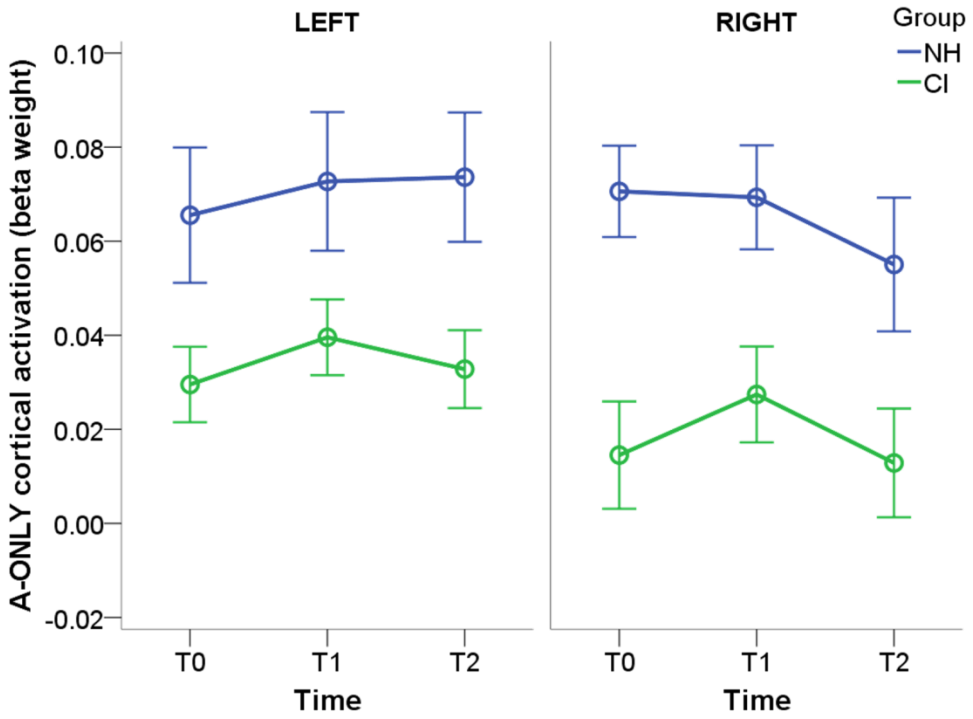


Figure 5.4: Line graph showing mean amplitude of cortical activation to auditory speech. Line graph is panelled by ROI, with mean A-ONLY cortical activation (beta weight) plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error.

no clear effects using PET (Łukaszewicz-Moszyńska et al., 2014) and fNIRS (Sevy et al., 2010). Furthermore, as there may be a tendency for CI users to display greater auditory speech-evoked activation within the left STC (Coez et al., 2014; Fujiki et al., 1999; Giraud et al., 2001b; Naito et al., 1997), it is possible that whether activation is seen to be greater in the contralateral or ipsilateral hemisphere may in fact differ depending on the side-of-implantation. To examine this in experienced CI users, a LMM analysis of the beta weights acquired after six months of CI use (T2) was conducted.

To examine whether the amplitude of cortical activation was greater in the hemisphere contralateral to or ipsilateral to the side-of-

implantation, and whether this effect differed depending on the side-of-implantation, a fixed effect of 'hemisphere' (contralateral or ipsilateral), 'side' (left or right ear implanted), and a 'hemisphere – side' interaction term were specified. The LMM analysis did not indicate a significant effect of hemisphere ($F_{1,13}$=.13, p=.73), thus providing no evidence that the amplitude of cortical activation significantly differed between the contralateral and ipsilateral hemisphere following implantation. Furthermore, there was no main effect of side-of-implantation ($F_{1,13}$=.38, p=.55), indicating that the amplitude of bilateral STC activation did not significantly differ between individuals who were implanted in the left ear or the right ear.

Visual inspection of the mean beta weights plotted in Figure 5.5 appears to suggest that individuals implanted in the left ear showed greater activation to auditory speech in the ipsilateral hemisphere compared to the contralateral hemisphere. Conversely, the data appeared to show that individuals implanted in the right ear displayed greater activation in the contralateral hemisphere compared to the ipsilateral hemisphere. However, the LMM analysis did not reveal a significant hemisphere – side interaction effect ($F_{1,13}$=2.42, p=.14), thus providing no evidence of an effect of hemisphere that differed depending on the side-of-implantation. It should be noted that participants were tested free-field in their best aided condition, that is, wearing their CI device and contralateral HA

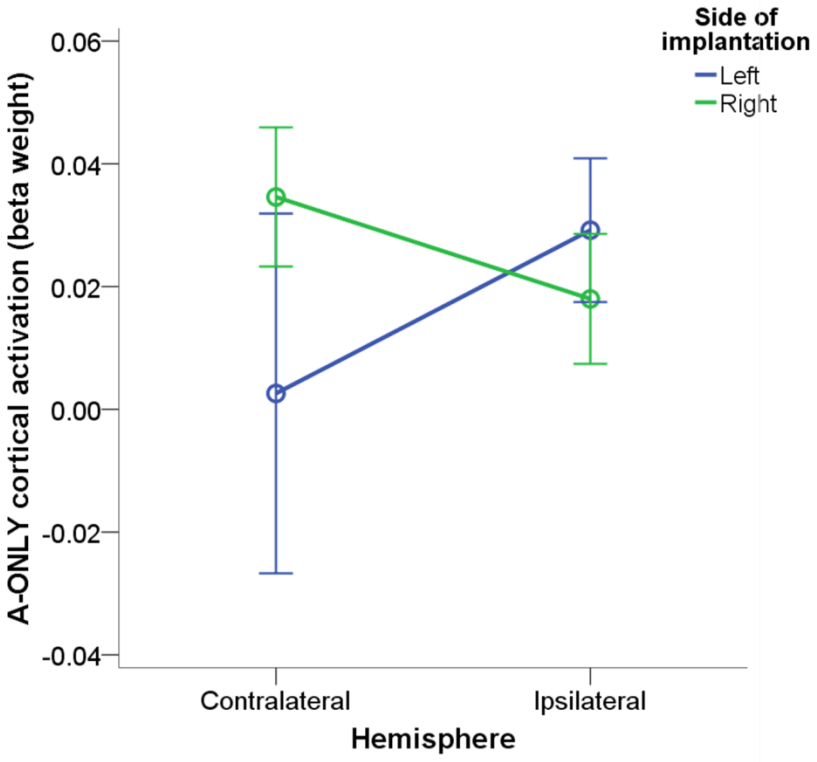


Figure 5.5: Line graph showing mean amplitude of contralateral and ipsilateral activation to auditory speech (beta weight). Lines are colour coded by side of implantation. Error bars represent ± 1 standard error.

if appropriate and preferred. Therefore, the amplitude of cortical activation assessed here may not only reflect the electrical auditory stimulation provided by the implant.

5.3.4 Cortical Activation to Visual Speech

Figure 5.6 displays the group-level cortical activation maps for the V-ONLY condition, with significantly activated measurement channels highlighted. Whilst the colour maps indicate evidence of cortical activations to visual speech over superior temporal regions of NH controls at T0 and T1, none of these channels were seen to reach significance. However, measurement channels #10 and #12 within the left ROI were found to be significantly activated at T2.

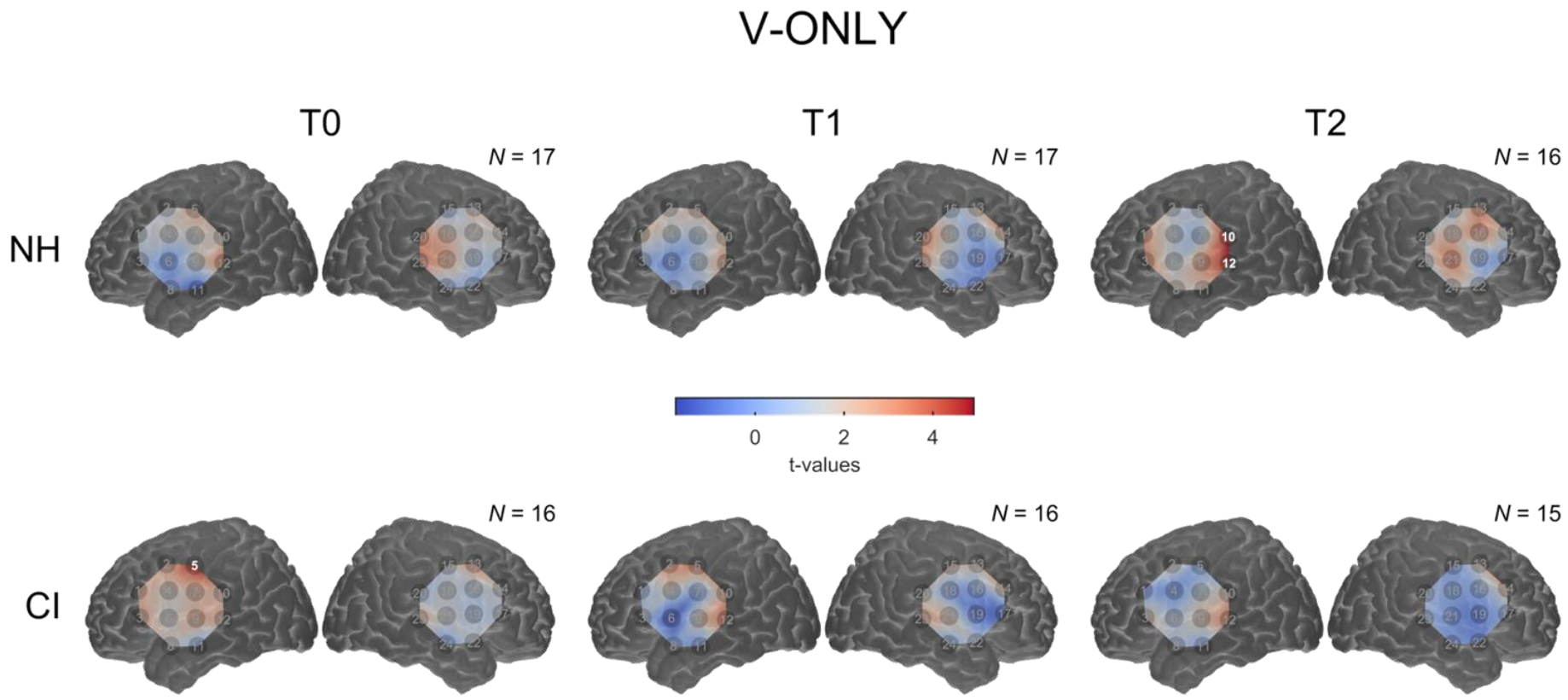


Figure 5.6: Group-level cortical activation map for visual speech. Amplitude of cortical activation to visual speech is colour coded by *t*-value. Significantly activated channels releveled by one-tailed *t*-tests ($p<.05$, FDR corrected) are highlighted.

Conversely, no measurement channels were seen to be significantly activated over STC across the group of CI users at any time point. However, channel #5 thought to be located over post-central motor regions was seen to be significantly activated before implantation.

Figure 5.7 shows the group-averaged time course of activation within the left and right ROIs for each group and test session. Visual inspection of these time courses indicates that plausible HRFs were elicited by visual speech within superior temporal regions of both the NH and CI group. Whilst these plots suggest that the NH controls may have displayed greater cortical activation compared to CI users, LMM analysis of the beta weights revealed no evidence of a significant main effect of group on amplitude of cortical activation in the left ($F_{1,42.83}$=.01, p=.95) or the right ROI ($F_{1,27.29}$=.88, p=.36). In addition, the LMM showed no significant main effect of time on amplitude of cortical activation ($F_{2,22.71}$=.09, p=.92), nor a group – time interaction ($F_{2,22,71}$=1.43, p=.26) within the left ROI.

Conversely, LMM analysis of the right ROI did indicate a significant main effect of time on amplitude of cortical activation ($F_{2,23.04}$=4.81, p<.05) but revealed no evidence of a significant group – time interaction ($F_{2,23.04}$=.29, p=.75). Visual inspection of the mean beta weights presented in Figure 5.8 suggests that a decrease in cortical activation within the right ROI at T2 may have driven this main effect of time. Post-hoc pairwise comparisons of the estimated marginal means (Bonferroni corrected) indeed revealed a

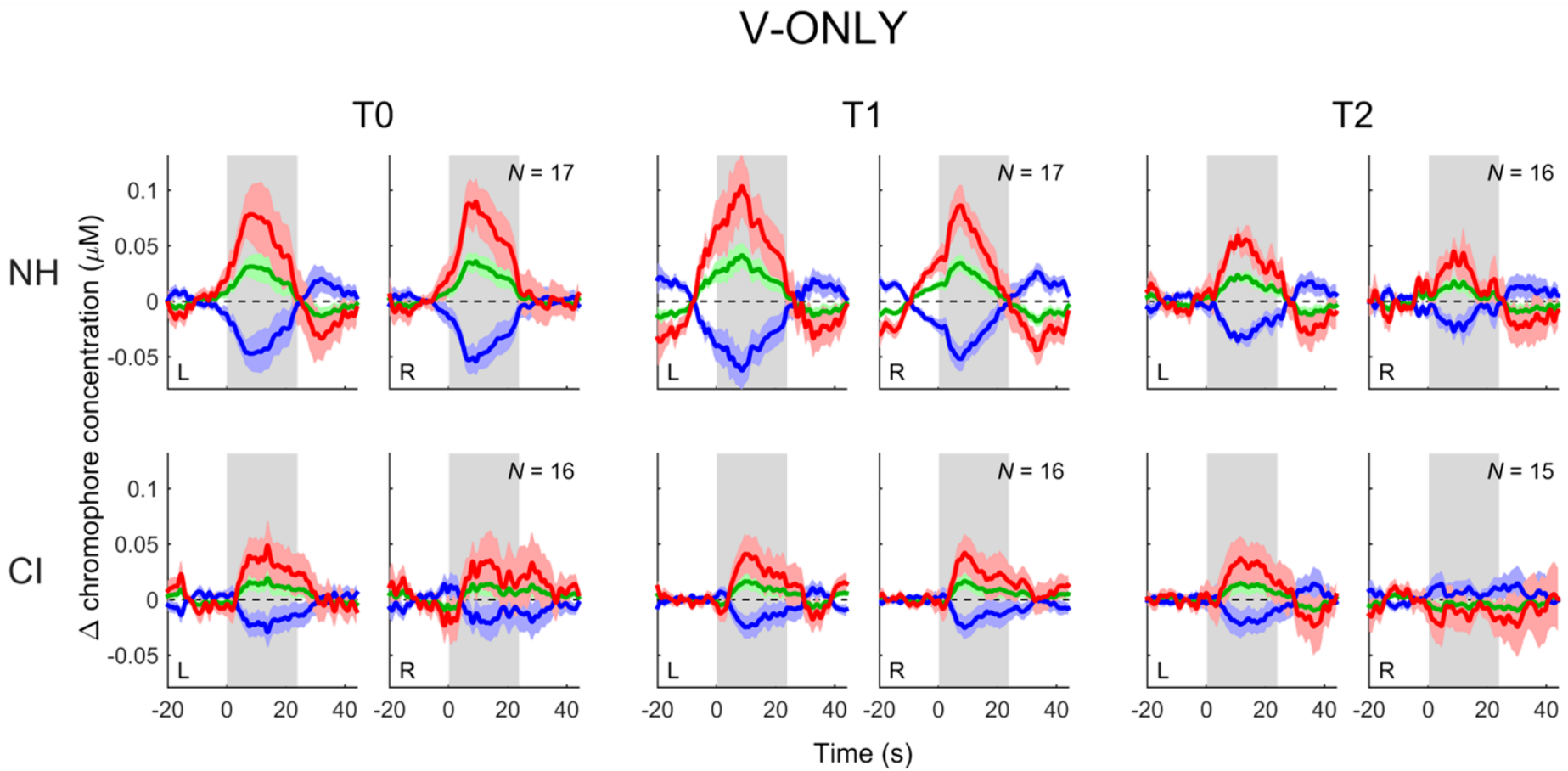


Figure 5.7: Group-averaged time courses of activation to visual speech. Changes in **HbO** and **HbR** concentration, as well as **HbT** levels, are shown for the left (L) and right (R) ROI during the presentation of visual speech (stimulation period indicated by shaded grey region). Coloured shading indicates ± 1 standard error across participants.

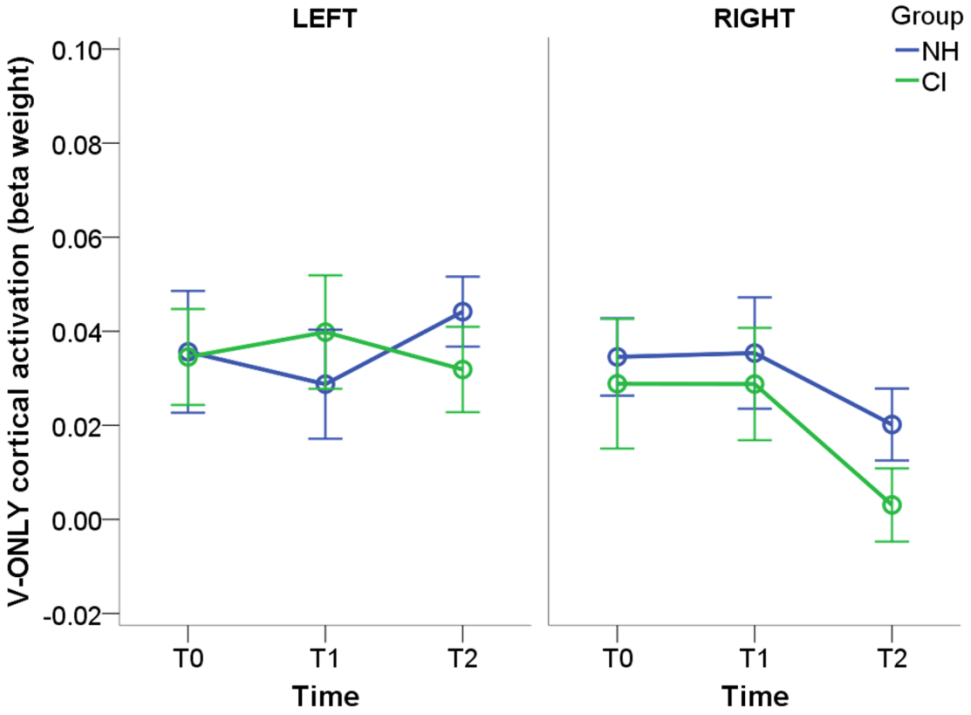


Figure 5.8: Line graph showing mean amplitude of cortical activation to visual speech. Line graph is panelled by ROI, with mean V-ONLY cortical activation (beta weight) plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error.

near-significant decrease in cortical activation to visual speech from T0 to T2 (p=.058), and from T1 to T2 (p=.056), but no significant difference in activation between T0 and T1 (p=1).

5.3.5 Cortical Activation to Audio-Visual Speech

Figure 5.9 displays the group-level cortical activation maps for the AV condition, with significantly activated measurement channels highlighted. At all three time points, a greater number of significantly activated channels was observed across the group of NH controls compared to CI users. Some variation was observed over time in the number and location of significantly activated channels across the NH group. However, the measurement

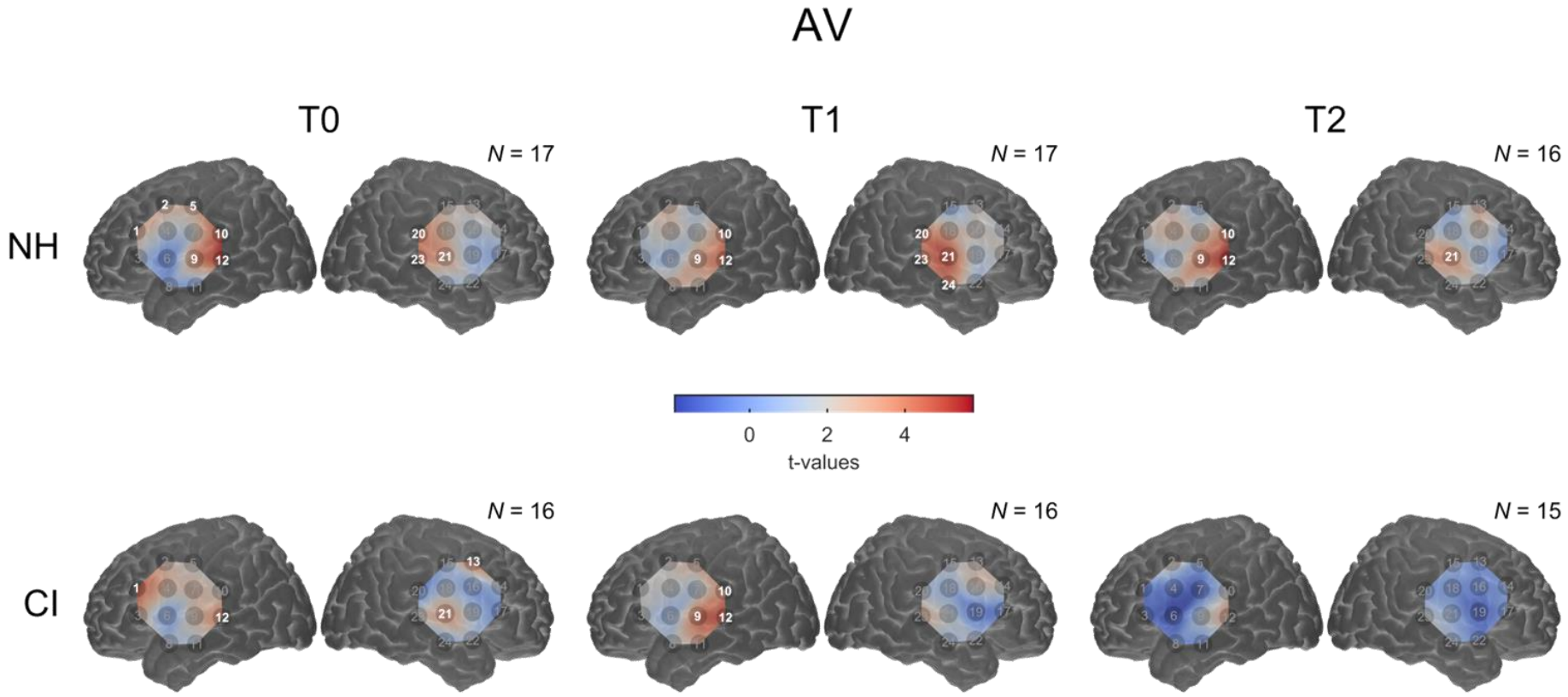


Figure 5.9: Group-level cortical activation map for audio-visual speech. Amplitude of cortical activation to audio-visual speech is colour coded by *t*-value. Significantly activated channels releveled by one-tailed *t*-tests ($p<.05$, FDR corrected) are highlighted.

channels that were seen to be consistently activated across test sessions were those that aligned with the predefined ROIs. In comparison, superior temporal-lobe responses appeared to be more variable in the CI group over time. In addition to these activations, significant activations were observed over the left frontal regions (channel #1) and the right post-central regions (#13) across the group of CI users before implantation (T0). The NH group were also seen to display significant activations over the left post-central and frontal regions at this time point (channels #1, 2, and 5).

Figure 5.10 shows the group-averaged time course of activation within the left and right ROIs for each group and test session. These plots indicate that plausible HRFs were elicited by audio-visual speech within the superior temporal brain regions of both NH controls and CI users. Furthermore, Figure 5.10 suggests that the NH group demonstrate greater activation to audio-visual speech compared to the CI group, particularly in the right ROI. Indeed, LMM analysis of the right ROI revealed a significant main effect of group ($F_{1,30.50}$=9.12, p<.01), with NH controls displaying significantly greater cortical activation in response to audio-visual speech compared to CI users. However, no significant main effect of time ($F_{2,29.91}$=2.71, p=.08), nor a group – time interaction effect ($F_{2,29.91}$=.15, p=.87) was observed. LMM analysis of the left ROI indicated that there was no significant main effect of group ($F_{1,30.79}$=2.77, p=.11), time ($F_{2,30.17}$=1.59, p=.22), nor a group – time interaction ($F_{2,30.17}$=1.47, p=.25) on the amplitude of cortical

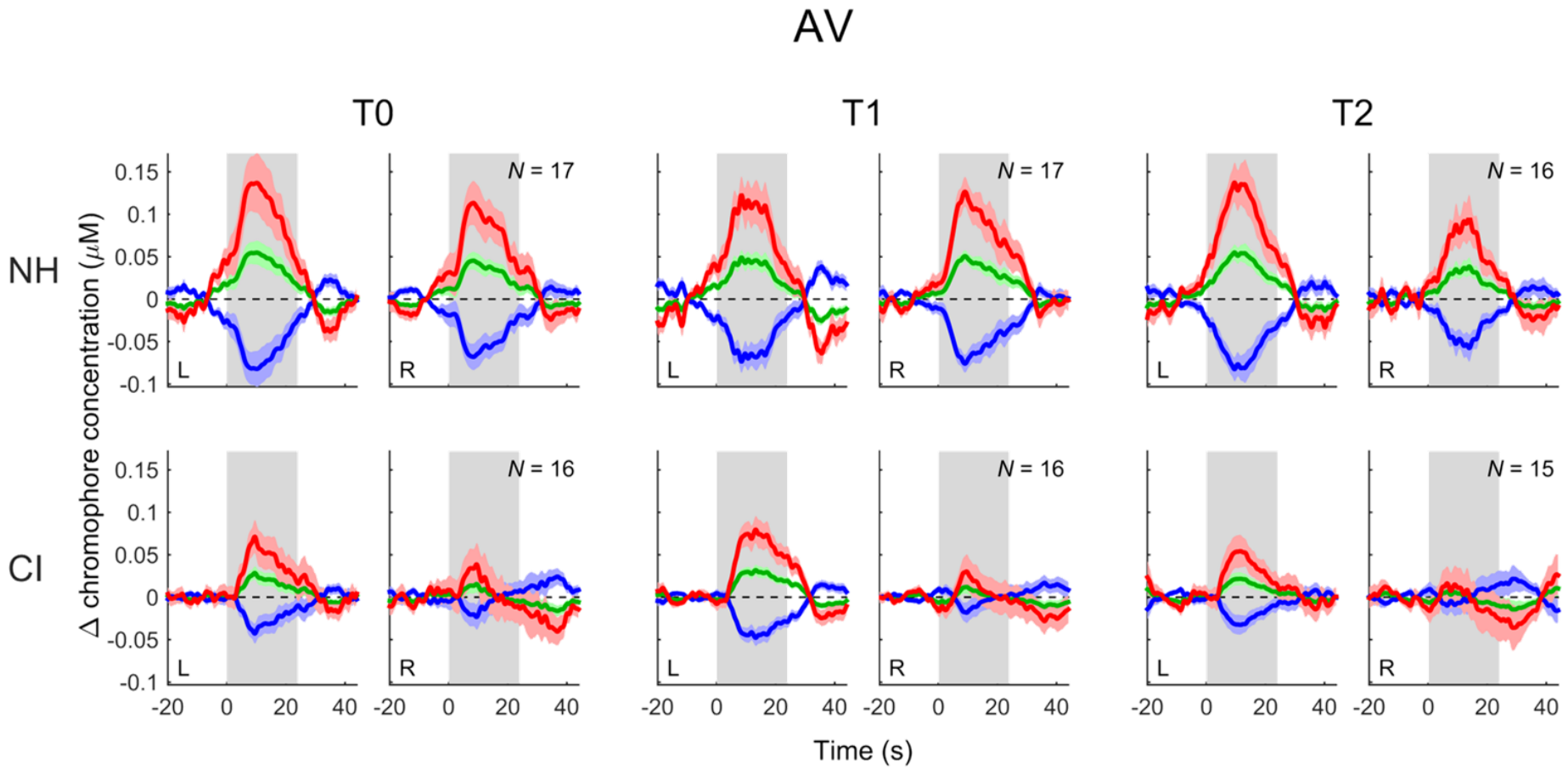


Figure 5.10: Group-averaged time courses of activation to audio-visual speech. Changes in **HbO** and **HbR** concentration, as well as **HbT** levels, are shown for the left (L) and right (R) ROI during the presentation of audio-visual speech (stimulation period indicated by shaded grey region). Coloured shading indicates ± 1 standard error across participants.

activation. Mean beta weights for the left and right ROI are displayed for each group as a function of time in Figure 5.11.

5.4 DISCUSSION

5.4.1 Capability of fNIRS to Detect Speech-evoked Cortical Activation

The current results are amongst the first demonstrations of the capability of fNIRS to successfully measure artefact-free haemodynamic responses to auditory speech over the bilateral auditory cortex of adult CI recipients, reports of which have only recently begun to emerge in the literature (Bisconti et al., 2015; Chen et al., 2015a; Olds et al., 2015). Whilst activation across the group of CI users was largely non-significant at each time point after correcting for multiple comparisons across 24 measurement channels, the topographical patterns and time courses of activation demonstrate the measurement of auditory speech-evoked activation over posterior superior temporal brain regions. These findings are consistent with previous neuroimaging evidence that has implicated these regions in the processing of auditory speech in adult CI users (Coez et al., 2008; Giraud et al., 2001c; Green et al., 2008; Green et al., 2005; Olds et al., 2015). As anticipated from existing fNIRS studies of auditory speech-evoked activations in NH adults (Pollonini et al., 2014; Sato et al., 1999; Sevy et al., 2010), significant group-level cortical activations to auditory speech were observed primarily and consistently over bilateral superior temporal regions in the NH control group, aligning well with the predefined ROIs. In addition to

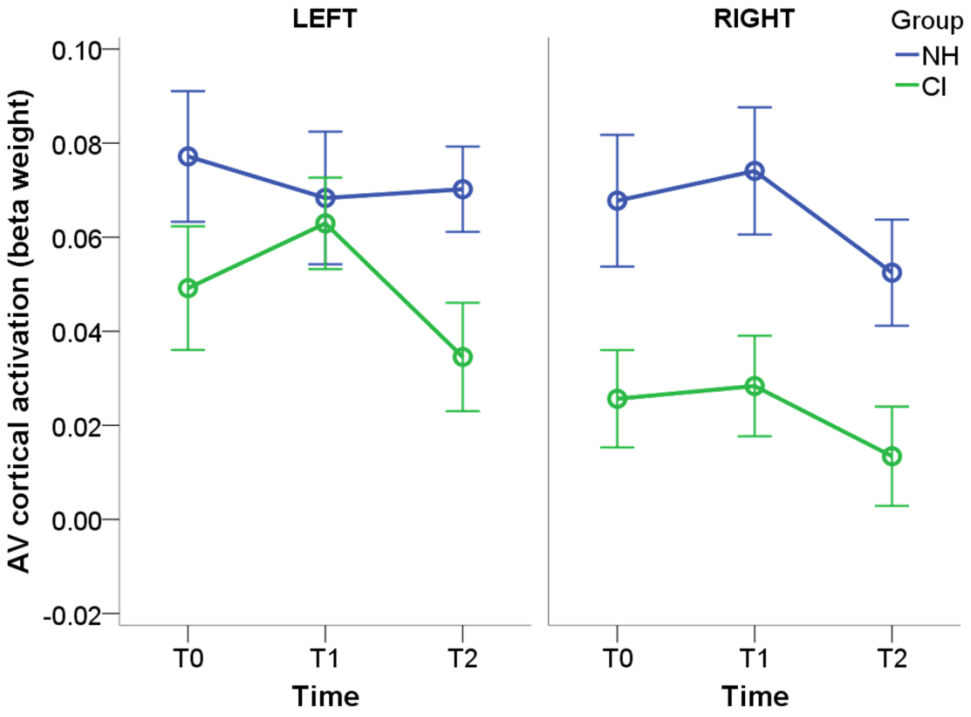


Figure 5.11: Line graph showing mean amplitude of cortical activation to audio-visual speech. Line graph is panelled by ROI, with mean AV cortical activation (beta weight) plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error.

evidence of temporal-lobe responses to auditory speech, significant cortical activation was also observed at a measurement channel believed to be located over pre-central motor regions of NH controls. Although this area was not a predefined cortical region of interest, the significant activation observed here is anatomically plausible given that an extensive cortical network, including motor regions and the dorsal pathway, is recruited by NH listeners to process auditory speech information (Friederici, 2011; Hickok & Poeppel, 2007; Pulvermuller et al., 2006).

Silent visual speech information was also seen to elicit canonical haemodynamic responses within the superior temporal brain regions

of NH controls and CI users at all time points. These observations are in line with existing reports of superior temporal-lobe activations during silent speechreading in NH listeners (Calvert et al., 1997; Hall et al., 2005; MacSweeney et al., 2000), profoundly deaf adults (Capek et al., 2008; Lee et al., 2007b) and adult CI users (Rouger et al., 2012; Strelnikov et al., 2013), illustrating the multi-modal nature of these brain regions. Furthermore, cortical activations to visual speech were largely non-significant at the group-level, with evidence of substantial between-subject variability in the amplitude of cortical activation. This is largely consistent with fMRI evidence suggesting that these features may reflect individual variability in the speechreading networks of both NH (Hall et al., 2005) and profoundly deaf adults (MacSweeney et al., 2001).

It is possible that STC activation to visual speech may not reflect direct sensory processing of visual inputs, but rather may reflect amodal language processes such as phonological processing of speech information (Andersson et al., 2001; Calvert et al., 2000; Lyxell et al., 2003; MacSweeney et al., 2000), and the accessing of stored auditory speech representations to enable successful speechreading (Hall et al., 2005), both processes which are known to involve posterior superior temporal brain regions (Hickok & Poeppel, 2007; Lazard et al., 2012b; Wise et al., 2001). Furthermore, it is possible that cortical activations to visual speech within auditory association areas reflect indirect activations due to the inherent link between auditory and visual speech information

(Hall et al., 2005). For instance, viewing someone silently talking may elicit activation within bilateral auditory association cortices, as has been demonstrated with auditory verbal imagery (Jäncke et al., 2004; Shergill et al., 2001), and anticipation of hearing the talker's voice (Pekkola et al., 2005). Whilst it is probable that the demands of the speechreading task employed here elicited activations reflecting different perceptual and linguistic processes, it is possible that such processes as outlined above may be altered by the absence of auditory inputs during periods of profound deafness, and are likely to be altered by subsequent restoration of auditory inputs through cochlear implantation. The current study provides the first known demonstration of the feasibility of fNIRS as a method for assessing speechreading activation both before and after cochlear implantation.

Given the aforementioned observations of cortical activations to auditory and visual speech information measured in both NH controls and CI users, it is unsurprising that audio-visual speech also appeared to elicit canonical haemodynamic responses across all test sessions. Cortical activation maps indicated significant group-level activations across a wide-spread cortical network, including temporal, pre-frontal and motor regions. This is in line with existing observations of the processing of the unimodal auditory and visual speech constituents in these cortical regions (Friederici, 2011; Hall et al., 2005; Hickok & Poeppel, 2007; Pulvermüller et al., 2006), and with evidence that the dorsal stream, an articulatory network

connecting superior temporal regions with pre-motor cortex and posterior inferior frontal regions, may provide an interface between the auditory and articulatory representations of speech (Friderici, 2011; Hickok & Poeppel, 2007; Pulvermüller et al., 2006). More specifically, significant group-level activations in response to audio-visual speech were consistently observed bilaterally within the predefined superior temporal regions of NH controls, as was anticipated based on the existing literature of audio-visual speech processing (Callan et al., 2003; Campbell, 2008; Nath & Beauchamp, 2012). Significant group-level temporal-lobe activations were also observed in CI users both before implantation and one month after CI activation. Whilst no neuroimaging studies examining cortical activations to audio-visual speech in profoundly deaf adults could be identified, the current observations made following implantation are consistent with available reports of superior temporal-lobe activation to audio-visual speech in adult CI users (Strelnikov et al., 2013, 2015).

5.4.2 Group Differences in Speech-evoked Cortical Activation

The NH group displayed significantly greater cortical response to auditory speech within the left and the right ROIs compared to the CI group across all time points. These observed group differences are consistent with existing evidence of significantly greater temporal-lobe activations to auditory speech in NH control subjects compared to CI users (Coez et al., 2008; Giraud et al., 2001c). An existing fNIRS examination of auditory cortex activation in NH

control subjects demonstrated strongest cortical activation to clear intelligible speech and reduced level of cortical activation to speech that was degraded using a cochlear implant simulation (Pollonini et al., 2014). In this way, the current group differences detected here may reflect the difference in the intelligibility of the auditory speech sentences perceived by NH listeners and CI users. There are also contrary reports in the literature that CI users display more extensive and greater activations to auditory speech within the temporal brain regions compared to NH controls (Limb et al., 2009; Wong et al., 1999), as well as greater recruitment of the LIF regions (Jiwani et al., 2016; Mortensen et al., 2006), thought to reflect the greater cognitive demands experienced by CI users and enhanced cortical processing requirements to enable successful speech processing of the degraded auditory input provided by the implant. Whilst the current results provide no such evidence of enhanced speech-evoked activation over bilateral frontal, temporal or parietal cortices in CI users compared to NH controls, this is in line with an existing fNIRS study of speech comprehension in adult CI users (Bisconti et al., 2015).

Despite the significant group difference in behavioural speechreading abilities described in the previous chapter (see 4.3.5), no group differences in the amplitude of cortical response to visual speech were observed in the left or right ROIs. Although non-significant, a trend could be seen in the right ROI whereby CI users displayed lower levels of cortical activation compared to NH

controls consistently across all test sessions. Conflicting evidence exists in the fMRI literature regarding differences in superior temporal-lobe activations to visual speech between normal-hearing listeners and profoundly deaf individuals, likely due to differences in speechreading tasks employed and variability in factors relating to the clinical history of deafness across the samples. For instance, whilst some studies have demonstrated significantly greater speechreading activation in bilateral STC of congenitally (Capek et al., 2008) and post-lingually deafened individuals compared to NH control subjects (Lee et al., 2007b), conversely others have demonstrated this group difference in the opposite direction (MacSweeney et al., 2002). In a post-implantation PET study, Rouger and colleagues (2012) observed significantly greater cortical activations to visual speech in CI users following one month of CI use compared to NH controls, although this was evidenced in anterior portions of the right STC rather than the more posterior region studied here. The anticipation of greater speechreading activation in deaf individuals and CI users may be most intuitive given the importance of visual speech inputs when auditory inputs are unreliable (Desai et al., 2007; Rouger et al., 2008; Schorr et al., 2005), as well as evidence of enhanced speechreading abilities compared to NH controls reported in the current study (see 4.3.5) and in the existing literature (Auer & Bernstein, 2007; Bernstein et al., 2000; Ellis et al., 2001; Rouger et al., 2007). However, individual differences in speechreading proficiency have been observed in both NH and deaf individuals (Bernstein et al., 2000;

Auer & Bernstein, 2007) and were also evidenced in the current sample (see section 4.3.5). It is therefore possible that this may be reflected in between-subjects variations in the strength of speechreading activation (Capek et al., 2008; Hall et al., 2005; Lee et al., 2007b), thus potentially precluding any clear evidence of an overall significant difference at the group level. Furthermore, cortical activations to audio-visual speech were seen to be significantly enhanced in NH controls compared to CI users within the right ROI; however, no group difference was detected within the left ROI. This pattern of results likely arises due to an average of the group effects observed in both the unimodal A-ONLY and V-ONLY conditions as outlined above when the two modalities were presented in combination in the AV condition.

5.4.3 Effects of Time on Speech-evoked Cortical Activation

The current findings provide no evidence to suggest that group-level STC activation to auditory speech changed as a function of time from pre-implantation to six months after CI activation. Whilst no existing studies of the evolution of speech-evoked cortical activation from pre- to post-implantation were able to be identified, the current findings are in line with existing longitudinal PET evidence following implantation, whereby whole-brain analysis indicated no significant effect of time on speech-evoked cortical activation over the first six months of CI use (Petersen et al., 2013). Similarly, using PET, Green and colleagues (2008) reported no evidence of change in bilateral auditory cortex activation from an early stage

(approximately one month) to late stage (approximately 12 months) following implantation. With regards to cortical activation to audio-visual speech, the current results similarly indicate no significant change in STC activation over time at the group-level. Whilst there is some evidence of greater cortical activation to audio-visual speech following eight months of CI use compared to activation following one week of CI use, this was observed within the left middle temporal brain regions (Strelnikov et al., 2015) as opposed to the posterior superior temporal regions studied here.

Although temporal-lobe responses to auditory and audio-visual speech were not seen to vary as a function of time, cortical responses to visual speech in the right superior temporal regions were seen to significantly decrease over time. Specifically, this decrease in cortical activation to visual speech occurred across both groups at T2. For the CI users, such an observation is indeed consistent with the only available longitudinal evidence that has demonstrated a decrease in cortical activation to visual speech within the right anterior STS from one week to eight months after CI activation (Rouger et al., 2012), despite the difference in the anterior compared to posterior ROI employed here. Rouger and colleagues (2012) interpret this reduction in speechreading activation with increased CI use as evidence of the reversal of 'abnormal cross-modal activations'. However, in their absence of corresponding repeated measurements in normal-hearing controls, and given that no evidence of a significant group – time interaction

was observed here, the current findings highlight that caution must be exercised in concluding whether such effects of time are truly associated with the CI rehabilitation process. Rather, it appears more plausible that the observed decrease in right STC activation to visual speech observed here across both NH controls and CI users may reflect a change in a process that was common to both groups. For instance, both NH and CI participants may have become more familiar with the IHR speech corpus presented during the fNIRS scanning due to repeated exposure over time. For this reason, the speechreading strategies that participants employed may have in turn altered from lower-level segmental and phonetic analysis of the speech information that typically recruits superior temporal regions, (Friederici, 2002, 2011; Hickok & Poepell, 2007; Jäncke et al., 2002; MacSweeney et al., 2002), to higher-level processing, such as mapping articulatory gestures to stored auditory representations from memory and the use of predictive strategies, that typically involves more wide-spread networks including LIF regions (Fiebach et al., 2001, 2005; Friederici, 2002, 2011; Hall et al., 2005; Hickok & Poepell, 2007). Whilst this may offer a plausible explanation for the decrease in cortical activation to visual speech observed across both groups, such a notion remains speculative as the positioning of the measurement array in the current study was not designed for optimal coverage of the LIF regions, precluding examination of the association between LIF activation and speechreading ability.

5.5 CHAPTER SUMMARY

This chapter has demonstrated the successful application of fNIRS in measuring artefact-free cortical activation to auditory, visual and audio-visual speech information in adult CI recipients and NH control subjects. Consistent with existing PET studies, NH listeners displayed significantly greater cortical activation to auditory speech within the predefined region of the left and right superior temporal cortex compared to CI users. Furthermore there was no evidence of a significant change in amplitude of auditory speech-evoked cortical activation over time. Following six months of CI use, cortical activation to visual speech was seen to decrease significantly within the right superior temporal ROI; however, this effect was not specific to the group of CI users and therefore may reflect a global change across both groups, for instance in the speechreading strategies employed and cortical resources used over time due to familiarisation effects. The variability observed in strength of speech-evoked cortical activation across the group of CI users may lend itself to subsequent investigations of the contribution of cortical factors to variability observed in CI outcome. Importantly, the current study provides one of the first investigations of the development of speech-evoked cortical activation from pre- to post-implantation. The current chapter demonstrates that fNIRS can offer a safe and fully compatible tool for monitoring responsiveness of the STC speech processing networks repeatedly in the same individuals during periods of profound deafness and throughout the subsequent CI rehabilitation process.

6. PRE-IMPLANT CORTICAL PREDICTORS OF FUTURE COCHLEAR IMPLANT OUTCOME

6.1 INTRODUCTION

This chapter aims to establish whether the responsiveness of superior temporal cortices to speech stimulation before implantation could help to predict future CI outcome. Due to the communicative importance of visual speech information during deafness, the first half of this chapter examines STC activation to visual speech before implantation as a potential predictor of auditory speech perception abilities following six months of CI use. Regression analyses are used to assess the extent to which cortical activation to visual speech before implantation can help to explain the observed variability in CI outcome, and to understand if such a cortical measure can provide any unique predictive value above that of routinely available clinical data. Furthermore, measures of sensitivity and specificity are examined to demonstrate how a pre-implant cortical measure could be implemented in clinical practice to aid in CI prognosis. The second half of the chapter examines the responsiveness of STC to auditory speech information before implantation. Specifically, the extent to which auditory speech-evoked cortical activation is lateralised to the left hemisphere is examined as a potential predictor of future CI outcome. The prognostic value and practical limitations of this laterality measure are also discussed.

6.2 CORTICAL ACTIVATION TO VISUAL SPEECH

6.2.1 Rationale

In NH individuals, the superior temporal brain regions are known to be responsive to both auditory and visual speech stimulation (Callan et al., 2003; Calvert et al., 1997; Hall et al., 2005; MacSweeney et al., 2000). In cases of profound deafness when the brain is deprived of auditory inputs, meta-modal plasticity may occur whereby these multi-modal brain regions come to favour the more dominant visual modality (Lazard et al., 2014). For instance, compared to NH individuals, greater cortical activations to visual speech have been observed within bilateral superior temporal regions in pre-lingually (Capek et al., 2008, 2010) and post-lingually deaf individuals (Lee et al., 2007b)[1]. Suh and colleagues (2009) also provide evidence of faster neural processing of visual speech information within the superior temporal cortex of post-lingually deaf adults compared to control subjects. Such cortical modifications during periods of profound deafness may provide a behavioural advantage by supporting higher levels of speechreading proficiency (Capek et al., 2008, 2010; Lee et al., 2007b; Suh et al., 2009). Whilst this cortical plasticity may prove beneficial for communication purposes during periods of auditory deprivation, evidence suggests that cortical modifications within the temporal brain regions could have a detrimental effect on auditory rehabilitation with a CI due to depletion or reorganisation of

[1] Note that in the present data set no group-level differences existed (see Chapter 5).

auditory processing resources (Buckley & Tobey, 2011; Lazard et al., 2013, 2014; Sandmann et al., 2012; Strelnikov et al., 2013). In this way, a negative relationship between STC activation to visual speech stimulation before implantation and future CI outcome may be anticipated. Alternatively, stimulation of these brain regions by visual speech cues during deafness could help to preserve amodal linguistic functions such as phonological processing and a close association between auditory and visual speech representations that may be important for CI success (Giraud et al., 2001a, 2001b; Lazard et al., 2013, see section 2.3.2 and 2.3.3 for a more comprehensive argument). In this way, a positive relationship between STC activation to visual speech stimulation before implantation and future CI outcome may be anticipated. However, several authors have noted the absence of empirical examinations of the impact of deafness on the processing of visual speech within the STC, and the subsequent impact on auditory speech processing abilities with a CI (Anderson et al., in press; Campbell et al., 2014; Lyness et al., 2013). Therefore, whilst there is theoretical grounding to believe that the strength of STC activation to visual speech measured before implantation could help to explain individual variability in future CI outcome, the notion remains speculative and the direction of any predictive relationship uncertain.

6.2.2 Analyses

For each participant, CI outcome was quantified as auditory performance on the CUNY sentence test in quiet conditions (transformed RAU data) measured six months after CI activation. CI outcome was defined here as the dependent variable and referred to throughout as 'AUDITORY[+6]'. For each participant, STC activation to visual speech was quantified as the amplitude of cortical activation (beta weight) elicited by visual-only speech sentences before implantation. Whilst some studies have suggested that the involvement of right temporal lobe for basic visual processing may be detrimental to CI outcome (Buckley & Tobey, 2011; Sandmann et al., 2012), it is not clear to what extent this applies when using visual speech stimulation. Furthermore, as Chapter 5 revealed evidence of STC activations to visual speech bilaterally, here beta weights were averaged across the predefined right and left ROIs to obtain a measure of bilateral STC activation. Bilateral STC response to visual speech before implantation was defined as the predictor variable and is referred to throughout as 'V_RESPONSE[pre]'. Prior to all statistical testing, histograms and the K-S test were used to examine whether the distribution of each variable significantly differed from normality. The appropriate parametric or non-parametric tests were selected accordingly based on whether the variables of interest met the relevant parametric assumptions. The statistical tests conducted are specified in the relevant sections throughout.

6.2.3 Results

6.2.3.1 Description of the Samples

Data for V_RESPONSE[pre] and AUDITORY[+6] were available for 15 CI users. Table 6.1 provides a revised summary table of the clinical characteristics of the 15 CI users included in the current analyses. Whilst this chapter focusses on examining cortical predictors of CI outcome, data obtained from the NH control group (n=16) is provided for purposes of comparison and discussion where appropriate.

6.2.3.2 Cortical Activation to Visual Speech Predicts CI Outcome

Bivariate linear regression analysis was performed to test whether bilateral STC response to visual speech before implantation was predictive of future CI outcome. Normality of the distribution of V_RESPONSE[pre] data was confirmed. Whilst the K-S test indicated that the distribution of AUDITORY[+6] data did not significantly differ from normality, visual inspection of the histogram did indicate slight negative skew, despite the rationalised arcsine transformation of the raw performance data. This skew was somewhat anticipated given the significant benefits that cochlear implantation can provide, particularly within the first six months following implantation (Lenarz et al., 2012). However, post-hoc diagnostic measures verified that the assumptions of bivariate linear regression were met: a scatterplot indicated linearity between the predictor and dependent variable, and visual inspection of histograms and normal P-P plots indicated that the standardised

Table 6.1: Revised summary of clinical characteristics for the current sample of CI users (n=15)

a) ID	b) Aetiology	c) Onset HL	d) Duration HL	e) Age	f) T0 HA	g) Ear CI	h) T2 CI use	i) T2 HA	j) Handedness	k) Hand LI
CI_01	Immune Deficiency Virus	51	10 months	52	Left	Right	6.1	✓	Right	95
CI_02	Unknown	Birth	37	37	Bilateral	Right	7.1	✓	Right	100
CI_03	Noise-induced	44	23	67	None	Right	6.2	×	Right	100
CI_05	Unknown	20	39	59	Left	Right	6.4	×	Right	60
CI_06	Maternal rubella	Birth	38	38	Bilateral	Right	6.5	✓	Right	95
CI_07	Otosclerosis	25	25	50	Bilateral	Right	5.3	✓	Right	95
CI_08	Mastoidectomy	52	8	60	Bilateral	Left	6.0	✓	Left	-100
CI_09	Noise-induced	45	33	78	Bilateral	Right	5.7	×	Right	100
CI_10	Mastoidectomy	30	40	70	Left	Left	6.1	×	Right	100
CI_11	Rubella	3	54	57	Right	Right	6.0	×	Right	100
CI_12	Unknown	5	59	64	Bilateral	Left	6.0	✓	Left	-100
CI_13	Unknown	4	32	36	None	Right	6.5	×	Right	80
CI_15	Unknown	42	4 months	43	Left	Left	6.1	×	Right	100
CI_16	Unknown	43	35	78	Bilateral	Left	6.1	×	Right	80
CI_17	Unknown	25	28	53	Bilateral	Right	6.0	✓	Right	75
Mean (SD)							**6.1 (0.4)**			

Column **a)** Participant ID; **b)** Aetiology of onset of hearing loss; **c)** Age-at- onset of bilateral hearing loss (years); **d)** Duration of bilateral hearing loss (years, unless otherwise stated); **e)** Age at time of CI surgery (years); **f)**; Side of acoustic hearing aid use at T0; **g)** Side of cochlear implantation; **h)** Duration of CI use at T2 since CI activation (months); **i)** Contralateral hearing aid worn with CI device at T2; **j)** Dominant hand; **k)** Handedness laterality index (LI).

residuals of the regression model were normally distributed and that the assumption of homoscedasticity was met.

The regression analysis revealed that V_RESPONSE[pre] was significantly predictive of AUDITORY[+6], $F_{(1,13)}$=16.59, p<.01, and was able to explain 56% of the variance observed (R^2=.56), with an adjusted R^2 of .53 indicating good generalizability of the regression model (see Table 6.2, Model A). Figure 6.1 illustrates that a negative relationship existed (Pearson's correlation coefficient r=-.75, p<.01, 2-tailed), whereby individuals showing greater bilateral STC response to visual speech before implantation were seen to display poorer auditory speech perception abilities following six months of CI use. Separate regression analysis of cortical activation within the left and right ROI (V_RESPONSE_LEFT[pre] and V_RESPONSE_RIGHT[pre] respectively) confirmed that this predictive relationship was not predominantly driven by either the left or the right STC and that the direction of the effect was the same for each hemisphere (see Table 6.2, Model B and C). Bivariate correlation analysis revealed no evidence that STC activation to visual speech before implantation was related to STC activation to auditory speech before implantation (bilateral: r=.38, p=.17; left: r=.27, p=.33; right: r=.10, p=.72, all 2-tailed).

Table 6.2: Summary of bivariate regression statistics for activation to visual speech in the prediction of CI outcome

Dependent *AUDITORY[+6]*	**R^2**	**Adj. R^2**	***F***	***b***	**SE *b***	***β***	***t***
Model A	.56	.53	16.59**				
Constant				99.88	9.30	-	10.74***
V_RESPONSE[pre]				-743.47	182.56	-.75	-4.07**
Model B	.46	.41	10.85**				
Constant				98.49	10.58	-	9.31***
V_RESPONSE_LEFT[pre]				-642.91	195.16	-.68	-3.29**
Model C	.30	.25	5.69*				
Constant				86.78	10.10	-	8.59***
V_RESPONSE_RIGHT[pre]				-384.50	161.24	-.55	-2.39*

Model A = bilateral ROI, Model B = left ROI, and Model C = right ROI activation to visual speech before implantation. *p<.05, **p<.01, ***p<.001

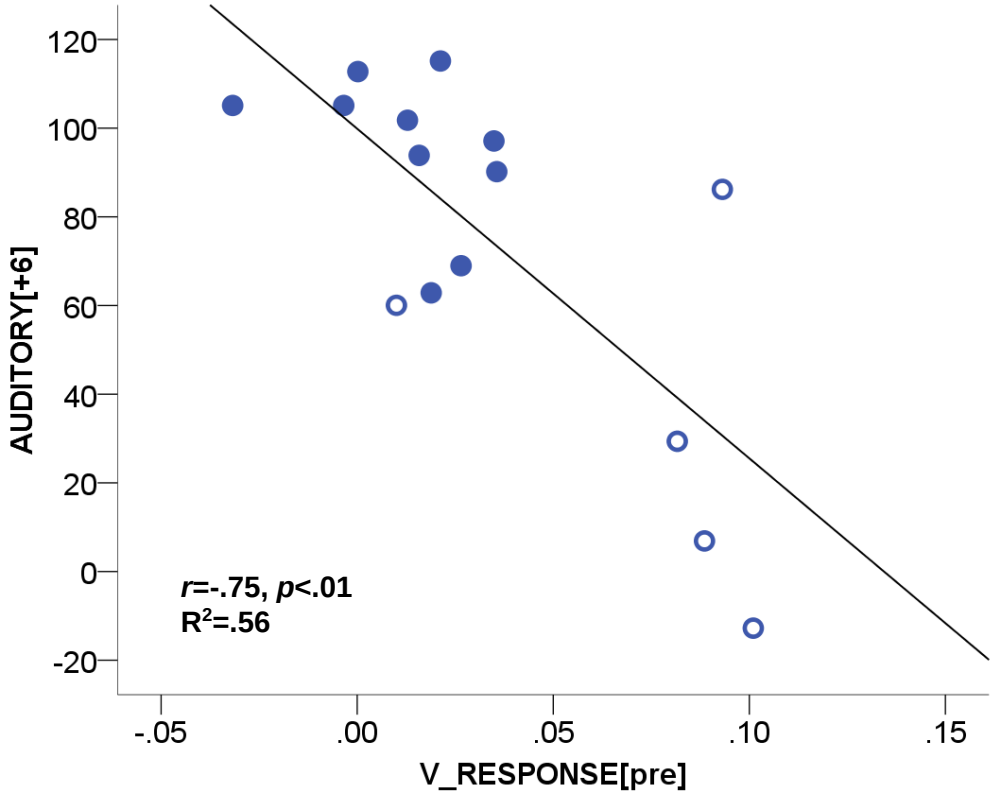


Figure 6.1:Scatterplot of bilateral STC activation to visual speech before implantation and future CI outcome, with regression line shown. Filled markers represent data obtained from post-lingually deaf CI users, and open markers represent data obtained from pre- and peri-lingually deaf CI users.

6.2.3.3 Examining the Influence of Mediating Factors

It can be seen in Figure 6.1 that those individuals displaying the highest levels of V_RESPONSE[pre] and the lowest levels of AUDITORY[+6] were pre- and peri-lingually deafened, whereas individuals displaying the lowest levels of V_RESPONSE[pre] and the highest levels of AUDITORY[+6] were predominantly post-lingually deafened. It is therefore important to consider the possible mediating influence of key clinical characteristics, such as the age-at-onset and duration of deafness that are known to influence CI outcome (Blamey et al., 2013; Green et al., 2007; Lazard et al., 2012a; Summerfield & Marshall, 1995; Teoh et al., 2004). In

addition, existing research has demonstrated positive associations between speechreading ability and the amplitude of temporal-lobe response to visual speech in pre-lingually (Capek et al., 2008, 2010) and post-lingually deaf adults (Lee et al., 2007b), as well as both negative (Hay-McCutceon et al., 2005) and positive (Gantz et al., 1993) associations between speechreading ability and CI outcome. Therefore, the age-at-onset of bilateral HL (ONSET), the duration of bilateral HL (DURATION), and speechreading ability before implantation (SPEECHREAD[pre]) were considered here as potential covariates that could mediate the predictive relationship between V_RESPONSE[pre] and AUDITORY[+6]. Indeed, associations were observed in the anticipated directions between these potential covariates and the dependent and predictor variable, although not all associations were seen to reach significance (Pearson's correlation coefficients summarised in Table 6.3).

Given the limited sample size here relative to the number of potential covariates, it was deemed inappropriate to employ a hierarchical multiple regression model to estimate the incremental predictive value of V_RESPONSE[pre] over the proportion of variance in CI outcome that could be explained by all three covariates combined. As an alternative approach, separate hierarchical linear regressions were conducted for each covariate to estimate the ability of V_RESPONSE[pre] to predict outcome independently of ONSET (Model 1), DURATION (Model 2), and SPEACHREAD[pre] (Model 3).

Table 6.3: Pearson's correlation coefficients (*r*) between covariates and the predictor and dependent variables

		Covariates			Predictor	Dependent
		ONSET	DURATION	SPEECHREAD[pre]	V_RESPONSE[pre]	AUDITORY[+6]
Covariates	ONSET	-	-.72**	-.56*	-.63*	.67**
	DURATION		-	.60*	.55*	-.46 (*p*=.09)
	SPEECHREAD[pre]			-	.57*	-.40 (*p*=.14)
Predictor	V_RESPONSE[pre]				-	-.75**
Dependent	AUDITORY[+6]					**-**

*p<.05, **p<.01, 2-tailed (not corrected for multiple comparisons)

For each model, the covariate of interest was first entered as a predictor variable into Block 1, with V_RESPONSE[pre] then entered as a predictor into Block 2 of the model. For all three models, histogram and scatterplots confirmed that the standardised residuals were normally distributed and the assumption of homoscedasticity was met. Furthermore, the Durbin-Watson (DW) statistic indicated that the assumption of independent errors was met (range=2.3 – 2.5) and the variance inflation factor (VIF) indicated that multicollinearity between the predictor variables in Block 2 of the models was not problematic (range=1.4 – 1.6). All regression models indicated that including V_RESPONSE[pre] as a predictor added significant incremental predictive value to the model above that of each of the covariates, with V_RESPONSE[pre] accounting for an additional 18% of the variance that remained unexplained in Model 1, 35% in Model 2, and 40% in Model 3. Furthermore, for V_RESPONSE[pre] the standardised beta coefficients (β) in Block 2 of the models were seen to be significant, indicating that V_RESPONSE[pre] was a significant individual predictor of CI outcome. Table 6.4, Table 6.5, and Table 6.6 provide summaries of the relevant regression statistics for Models 1 – 3 respectively.

Table 6.4: Summary of hierarchical regression statistics when controlling for age-at-onset of bilateral HL

Dependent *AUDITORY[+6]*		**R^2**	**Adj. R^2**	***F***	**ΔR^2**	**ΔF**	***b***	**SE *b***	***β***	***t***
Model 1	**Block 1**	.44	.40	10.40**	-	-				
	Constant						40.24	13.29	-	3.03*
	ONSET						1.33	.41	.67	3.23**
	Block 2	.63	.56	10.00**	.18	5.78*				
	Constant						76.16	18.77	-	4.06**
	ONSET						.65	.45	.33	1.44 (*p*=.18)
	V_RESPONSE[pre]						-541.12	224.99	-.55	-2.41*

*p<.05, **p<.01

Table 6.5: Summary of hierarchical regression statistics when controlling for duration of bilateral HL

Dependent *AUDITORY[+6]*		**R^2**	**Adj. R^2**	***F***	**ΔR^2**	**ΔF**	***b***	**SE *b***	***β***	***t***
Model 2	**Block 1**	.21	.15	3.45 (*p*=.09)	-	-				
	Constant						106.77	19.56	-	5.46**
	DURATION						-1.06	.57	-.46	-1.86 (*p*=.09)
	Block 2	.56	.49	7.75*	.35	9.73*				
	Constant						103.30	15.17	-	6.81**
	DURATION						-.15	.53	-.07	-.29 (*p*=.78)
	V_RESPONSE[pre]						-707.02	226.63	-.71	-3.12*

*p<.01, **p<.001

Table 6.6: Summary of hierarchical regression statistics when controlling for pre-implant speechreading ability

Dependent *AUDITORY[+6]*		**R^2**	**Adj. R^2**	***F***	**ΔR^2**	**ΔF**	***b***	**SE *b***	***β***	***t***
Model 3	**Block 1**	.16	.09	2.46 (*p*=.14)	-	-				
	Constant						86.48	12.17	-	7.11**
	SPEECHREAD[pre]						-.74	.47	-.40	-1.57 (*p*=.14)
	Block 2	.56	.49	7.70*	.40	11.03*				
	Constant						99.43	9.94	-	10.00**
	SPEECHREAD[pre]						.08	.43	.05	.19 (*p*=.85)
	V_RESPONSE[pre]						-768.87	231.47	-.77	-3.32*

*p<.01, **p<.001

6.2.3.4 Demonstration of Potential Clinical Application

The aforementioned predictive value of bilateral STC response to visual speech suggests that, in principle, measures of cortical activation acquired before implantation could aid in the more accurate prognosis of CI outcome. However, if such cortical recordings are to be usefully applied in clinical practice, the accuracy of the measure to predict good and poor CI outcome must be established. Here we examine the sensitivity and specificity of V_RESPONSE[pre] to correctly classify CI candidates as future 'proficient' and 'non-proficient' CI users to demonstrate how such a cortical measure could be applied for use in clinical practice. Whilst defining 'proficient' and 'non-proficient' levels of speech perception is not straightforward in practice, clinically it may be important to identify those individuals who are unlikely to be able to achieve speech perception abilities above that of the criteria for implantation. Here, the current CI candidacy criteria (NICE, 2009) of 50% speech intelligibility was therefore employed as the threshold for defining 'proficient' and 'non-proficient' CI outcome. Based on this threshold, the sensitivity and specificity of V_RESPONSE[pre] to identify individuals likely to become non-proficient CI users was estimated. In the current context, 'sensitivity' quantifies the ability of V_RESPONSE[pre] to correctly classify individuals likely to become non-proficient CI users, whereas, 'specificity' quantifies the ability of V_RESPONSE[pre] to correctly classify those likely to become proficient CI users (see Table 6.7). A receiver operating characteristic (ROC) curve was

Table 6.7: Table illustrating sensitivity and specificity calculations

CI Outcome	Pre-implant Cortical Measure		Calculations
	Low Response (negative)	**High Response** (positive)	
Proficient (negative)	a (True negative)	b (False positive)	Specificity: a / (a+b)
Non-proficient (positive)	c (False negative)	d (True positive)	Sensitivity: d / (d+c)

Adapted from Parikh et al. (2008).

used to determine a cut-off value for V_RESPONSE[pre] whereby the trade-off between the level of sensitivity and specificity was optimal (Figure 6.2). This analysis determined an optimal cut-off value of 0.059 beta weight, with individuals displaying V_RESPONSE[pre] values above or below this threshold referred to as having a 'high response' or 'low response' respectively (Figure 6.3). Applying this criterion, V_RESPONSE[pre] was seen to have a sensitivity level of 100%, meaning that V_RESPONSE[pre] was able to correctly classify 100% of non-proficient CI users based on them having a high level of bilateral STC response to visual speech before implantation. V_RESPONSE[pre] was also seen to have a high level of specificity (92%), meaning that it was able to correctly classify 92% of proficient CI users based on these individuals having a low level of STC response to visual speech before implantation. However, V_RESPONSE[pre] incorrectly classified one CI user (8% of the group) as non-proficient when they were in fact seen to become a proficient CI user. The area under the ROC curve was .94 (95% confidence interval=.82 – 1.0, $p<.05$), indicating that, with

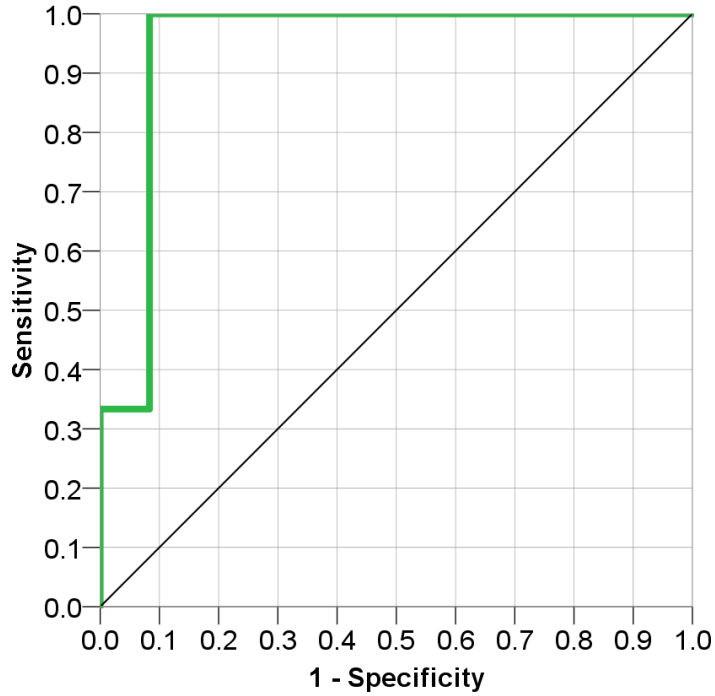


Figure 6.2: Receiver operating characteristic curve displaying the sensitivity (true positive rate) and 1 - specificity (false positive rate) values used to determine an optimal cut-off value for V_RESPONSE[pre].

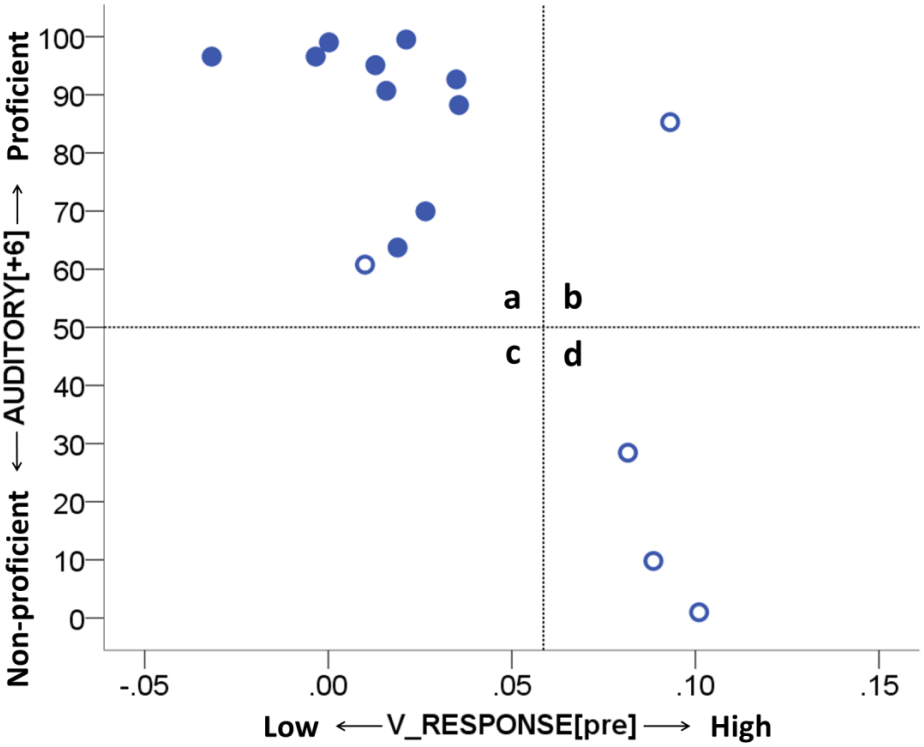


Figure 6.3: Scatterplot showing cut-off values for 'high' and 'low' cortical activation to visual speech, and 'proficient' and 'non-proficient' auditory performance. Data points falling within quadrant **a**= true negatives, **b**= false positives, **c**= false negatives, **d**= true positives. Filled markers represent data obtained from post-lingually deaf CI users, and open markers represent data obtained from pre- and peri-lingually deaf CI users.

the current thresholds applied, V_RESPONSE[pre] was able to predict whether a CI candidate would be a proficient or non-proficient CI user six months after CI-activation with a high degree of accuracy. However caution should be exercised over these findings due to the relatively small sample size, and therefore the limited number of cut-off points that could be calculated for the ROC analysis. A similar investigation employing a larger sample of CI users would be important to determine levels of sensitivity, specificity and the optimal measurement thresholds for enabling accurate predictions of CI outcome to be made.

6.2.4 Discussion

Previous fMRI studies conducted with congenitally (Capek et al., 2008) and post-lingually deaf individuals (Lee et al., 2007b) have suggested that greater recruitment of posterior superior temporal brain regions for speechreading may provide a behavioural advantage for speechreading ability. Whilst, at the group-level, STC response to visual speech was not seen to be significantly enhanced in deaf individuals compared to NH control subjects (see section 5.4.2 for further discussion), correlations conducted here indicate that greater activation to visual speech within bilateral STC was associated with a longer duration and earlier onset of auditory deprivation (see Table 6.3). Furthermore, as indicated in Table 6.3, a moderate positive association was evidenced between amplitude of cortical activation and speechreading proficiency before

implantation, suggesting that bilateral STC response to visual speech may have been behaviourally relevant in profoundly deaf individuals. While the same analysis here revealed no such relationship between amplitude of cortical activation and speechreading ability in NH controls (r=.02, p=.95, 2-tailed, n=16), it remains possible that no effect was observed due to floor effects in the behavioural data. Although one cannot infer causation from these associations, the current findings suggest that greater bilateral STC activation to visual speech before implantation may represent a cortical adaptation to deafness by providing a behavioural advantage for spoken communication. However, the results here also demonstrate that stronger STC activation to visual speech before implantation was significantly predictive of poorer auditory speech perception after six months of CI use, and was able to account for a significant proportion of the variability observed in CI outcome. Whilst existing research has provided evidence of a negative relationship between the extent of temporal-lobe response to non-linguistic visual stimuli and CI outcome (Buckley & Tobey., 2011; Doucet et al., 2006; Sandmann et al., 2012), to the author's knowledge, the current results provide the first neuroimaging evidence of the impact of deafness on temporal-lobe response to visual speech and the relationship with future CI outcome.

Correlational analysis provided no evidence to suggest that the predictive relationship observed here between bilateral STC activation to visual speech and CI outcome was driven solely by the

left or the right hemisphere. However, existing literature has suggested that a distinction may exist between the mechanisms driving plasticity effects within the two hemispheres, with right temporal-lobe plasticity said to be driven by sensory experience and left temporal-lobe plasticity driven by linguistic experience (Cardin et al., 2013; Fine et al., 2005). Indeed, in the current context of visual speech processing, it has been demonstrated that greater responsivity to visual speech within the left posterior superior temporal brain region is functionally related to greater speechreading ability in profoundly deaf individuals, whereas greater responsivity to visual speech within the right posterior superior temporal brain regions appears to offer no such communicative advantage (Capek et al., 2008, 2010; Lee et al., 2007b). In line with this notion, amplitude of left, but not right, STC response to visual speech before implantation was associated with speechreading ability (left: r=.62, p<.05; right: r=.35, p=.20, both 2-tailed). This suggests that, in the absence of auditory input, the left STC may still retain its linguistic function regardless of modality as has been previously demonstrated (Capek et al., 2008, 2010; Cardin et al., 2013; Lee et al., 2007b).

It has been speculated that the processing of non-linguistic visual inputs (Buckley & Tobey., 2011; Doucet et al., 2006; Sandmann et al., 2012) and visual speech information (Rouger et al., 2012; Strelnikov et al., 2013) within temporal brain regions of CI users negatively influence CI outcome through a deleterious effect on

auditory processing resources. However, the current data provide no evidence that responsiveness of bilateral STC to visual speech before implantation was inversely related to the responsiveness of bilateral STC to auditory speech either before or after implantation (T0: r=.38, p=.17; T1: r=.14, p=.61; T2: r=-.03, p=.93, all 2-tailed)[2]. Thus, these findings provide no evidence to suggest that the processing of visual speech cues within temporal brain regions during deafness limited the capacity of these brain regions to respond to auditory speech, nor precluded activation of these regions by auditory speech when later stimulated with an implant.

Although the mechanisms driving the observed predictive relationship remain uncertain, it seems likely that the relationship between bilateral STC response to visual speech before implantation and future CI outcome is mediated by other interrelated sensory and linguistic factors. Hence, whether bilateral STC activation to visual speech before implantation was able to offer any predictive value above that provided by influential clinical characteristics of the listener was also examined here. Existing key evidence that CI outcome remains largely unpredictable from routinely available clinical data pertains to post-lingually deafened CI users (Blamey et al., 2013; Lazard et al., 2010a, 2012a). Therefore, in the current sample comprising both pre- and post-lingually deaf individuals, it

[2] Note that no relationship existed at any time point for either the right hemisphere (T0: r=.10, p=.72; T1: r=.18, p=.52; T2: r=-.13, p=.64, all 2-tailed) or the left hemisphere (T0: r=.27, p=.33; T1: r=.34, p=.22; T2: r=-.01, p=.98, all 2-tailed) when examined separately.

may be anticipated that the age-at-onset of deafness could offer greater value in predicting CI outcome compared to that which has been estimated only from post-lingually deaf individuals. Amongst the clinical covariates examined here, the age-at-onset of bilateral HL was the only non-cortical factor that was able to significantly predict future CI outcome and was seen to correlate most highly with amplitude of STC activation to visual speech. Importantly, the current findings indicate that STC activation to visual speech was able to provide unique predictive value above each of the clinical factors examined, including the age-at-onset of bilateral HL. However, due to the relatively limited sample size, it was not possible to determine whether this cortical measure could offer further explanatory power above all of these clinical factors combined. Furthermore, section 6.2.3.4 demonstrated that the strength of STC activation to visual speech was able to predict whether an individual would become a proficient or non-proficient CI user to a high level of accuracy, although the need for further examination in a larger sample of CI users was highlighted. Such future research could help to understand whether brain imaging using fNIRS could support more accurate prognoses above that achievable using available clinical data.

Overall, the current findings suggest that, with future developments, fNIRS may become an effective prognostic tool to be used clinically. Such an objective indicator may be particularly beneficial for paediatric CI recipients: as implantation typically takes

place in early infancy and years before the development of language (personal communication, Doug Hartley), a prognostic tool that is fully compatible with a CI and child-friendly could help to help identify individuals early on in the implantation process who may be at risk of developing poor language outcomes. Future research including examinations of patient, parental and clinical acceptability of such a tool, as well as economic evaluation, would be amongst many of the necessary steps towards developing fNIRS as a prognostic tool. Whilst this chapter focusses on predicting absolute CI outcomes, clinically, the amount of benefit that an individual is likely to gain from cochlear implantation compared to their pre-implant aided ability may also be an important consideration. Indeed this could be examined by calculating the pre-post change in auditory performance and looking to verify if this level of benefit received could be predicted by the prognostic test. However, as the current sample comprised candidates that scored above the CI candidacy criteria at pre-implantation as well as post-implant ceiling effects in performance, employing a measure of pre-post change here would not have accurately quantified the level of benefit gained from implantation.

6.3 LATERALISATION OF CORTICAL ACTIVATION TO AUDITORY SPEECH

6.3.1 Rationale

In NH listeners, cortical activations to auditory speech stimulation are observed within the superior temporal cortices (Binder et al.,

2000; Friederici, 2011; Hickok & Poeppel, 2007; Vouloumanos et al., 2001). Whilst earlier stages of auditory speech processing such as basic acoustic analysis of the speech signal are known to take place bilaterally in primary auditory and early association cortices (Hickok et al., 2008; Hickok & Poeppel, 2007, Lazard et al., 2014), higher-level stages of processing tend to show left hemispheric dominance that extends to a frontal network (Friederici 2002; Hickok & Poeppel, 2007). Neuroimaging studies, when controlling for the acoustic complexity of the speech signal, have demonstrated 'speech-specific' processing within the left temporal-lobe of normal-hearing listeners, suggesting these regions may be associated with the comprehension of intelligible speech (Narain et al., 2003; Scott et al., 2000, 2006). As discussed in greater detail in section 2.3.2.1, maintenance of left-hemispheric specialisation for auditory speech processing may be an important factor for CI success. Specifically, evidence has indicated that proficient CI users show greater speech-specific activation within the left temporal gyrus compared to non-proficient CI users (Mortensen et al., 2006). Furthermore, decreased functional specialisation of, and ability to successfully recruit, left temporal brain regions for speech processing has been observed in CI users compared to NH controls (Giraud et al., 2001c). Moreover, cortical reorganisation of left-hemisphere specialised phonological processing to contralateral right hemispheric regions has been observed in profoundly deaf individuals prior to implantation (Lazard et al., 2013). Importantly, greater phonological activity in right temporal regions prior to

implantation was associated with poorer CI outcome following six months of CI use, whereas greater phonological activity in the left temporal regions was positively correlated with future CI outcome.

The first half of this chapter provided evidence that greater bilateral STC response to visual speech was associated with greater speechreading ability. This functional relationship was strongly driven by the left STC, a finding that is in line with existing evidence of a left hemisphere specialisation for language processing regardless of sensory input modality (Corina et al., 1999; Hickok et al., 1998; MacSweeney et al., 2008a; Neville et al., 1998; Petitto et al., 2000; Rönnberg et al., 2000; Sakai et al., 2005). However, STC activation to visual speech was also seen to be negatively predictive of future CI outcome. Therefore, it is possible that plasticity effects driven by recruitment of left superior temporal regions for processing of visual speech during periods of profound deafness may subsequently impact on left-hemisphere specialisation for auditory speech processing. However, the relative contribution of the left temporal cortex during the processing of auditory speech information before implantation, as well as its relation to visual speech processing and future CI outcome, remains largely unexamined. Based on the available evidence and current findings outlined in section 6.2 above, it could be anticipated that a more strongly left-lateralised temporal-lobe response to auditory speech before implantation may be predictive of more proficient auditory speech perception following cochlear implantation.

6.3.2 Analyses

Functional neuroimaging studies including fMRI and fNIRS have commonly calculated a laterality index (LI) in order to quantify the side and strength of hemispheric lateralisation during auditory speech processing (Binder et al., 1996; Jansen et al., 2006; Seghier, 2008; Shimoda et al., 2008; Watanabe et al., 1998; Watson et al., 2004). Specifically, the LI estimates the difference in cortical response magnitude between the left (L) and the right (R) hemisphere, expressed as a proportion of the total bilateral response magnitude (L - R / L + R). Thus, the LI yields values ranging between +1 and -1, with values nearer to +1 indicating a more strongly left-lateralised response, values close to zero indicating an approximately symmetrical response, and negative values indicating a more strongly right-lateralised response. Accordingly, here $L_{RESPONSE}$ denotes the amplitude of cortical response to auditory speech (beta weight) within the predefined left ROI, and $R_{RESPONSE}$ denotes the amplitude of cortical response to auditory speech (beta weight) within the predefined right ROI. Hemispheric lateralisation of temporal-lobe response to auditory speech before implantation 'LI[pre]' was therefore estimated for each participant using the following calculation:

$$LI[pre] = (L_{RESPONSE} - R_{RESPONSE}) / (L_{RESPONSE} + R_{RESPONSE})$$

LI[pre] was thus defined as the predictor variable.

As specified in section 6.2.2, CI outcome, quantified as auditory performance six months post-CI activation 'AUDITORY[+6]', was

defined as the dependent variable. Prior to all statistical testing, histograms and the K-S test were used to examine whether the distribution of each variable significantly differed from normality. The appropriate parametric or non-parametric tests were selected accordingly based on whether the variables of interest met the relevant parametric assumptions. The statistical tests conducted are specified in the relevant sections throughout.

6.3.3 Results

6.3.3.1 Missing Data

A caveat of the LI calculation employed here is that only positive cortical response amplitudes can be included in the calculation to ensure that a meaningful LI value is produced (Binder et al., 1996; Jansen et al., 2006; Seghier, 2008; Shimoda et al., 2008; Watanabe et al., 1998; Watson et al., 2004). As a result, it was only possible to estimate LIs for nine CI users as they displayed positive beta weight response values in response to auditory speech within both the left and the right ROIs. Table 6.8 provides a revised summary of clinical characteristics for the current sub-sample of CI users following these exclusions.

6.3.3.2 Lateralisation of Cortical Activation to Auditory Speech Predicts CI Outcome

It was confirmed that the distribution of both LI[pre] and AUDITORY[+6] data did not significantly differ from normality and a scatterplot suggested that a linear relationship existed between

Table 6.8: Summary of clinical characteristics for the current sub-sample of CI users (n=9)

a) ID	b) Aetiology	c) Onset HL	d) Duration HL	e) Age	f) T0 HA	g) Ear CI	h) T2 CI use	i) T2 HA	j) Handedness	k) Hand LI	l) LI[pre]
CI_02	Unknown	Birth	37	37	Bilateral	Right	7.1	✓	Right	100	-.03
CI_03	Noise-induced	44	23	67	None	Right	6.2	×	Right	100	.13
CI_06	Maternal rubella	Birth	38	38	Bilateral	Right	6.5	✓	Right	95	.72
CI_07	Otosclerosis	25	25	50	Bilateral	Right	5.3	✓	Right	95	.49
CI_10	Mastoidectomy	30	40	70	Left	Left	6.1	×	Right	100	.08
CI_11	Rubella	3	54	57	Right	Right	6.0	×	Right	100	.04
CI_12	Unknown	5	59	64	Bilateral	Left	6.0	✓	Left	-100	-.30
CI_13	Unknown	4	32	36	None	Right	6.5	×	Right	80	-.42
CI_17	Unknown	25	28	53	Bilateral	Right	6.0	✓	Right	75	.38
Mean (SD)							**6.2 (0.5)**				

Column **a)** Participant ID; **b)** Aetiology of onset of hearing loss; **c)** Age-at-onset of bilateral hearing loss (years); **d)** Duration of bilateral hearing loss (years); **e)** Age at time of CI surgery (years); **f)**; Side of acoustic hearing aid use at T0; **g)** Side of cochlear implantation; **h)** Duration of CI use at T2 since CI activation (months); **i)** Contralateral hearing aid worn with CI device at T2; **j)** Dominant hand; **k)** Handedness laterality index (LI); **l)** Hemispheric laterality index at T0.

these two variables. Therefore, a bivariate linear regression was performed to test whether the lateralisation of temporal-lobe response to auditory speech before implantation was predictive of future CI outcome. The regression analysis revealed that LI[pre] was not significantly predictive of AUDITORY[+6], $F_{(1,7)}$=1.22, p=.31 (see Table 6.9, Model A). However, visual examination of the standardised residuals of the regression model using a histogram and scatterplots demonstrated that the model's residuals were not normally distributed and that the assumption of homoscedasticity was not met. Furthermore, Figure 6.4 shows a scatterplot of the relationship between the predictor and dependent variable that highlights the presence of an extreme case, which warranted further investigation. Indeed, examination of two diagnostic statistics, Cook's Distance (CD)and Studentized Residuals (SR), identified this data point as an influential case relative to the commonly applied thresholds, with CD > 1 and SR < -2.5 (see Figure 6.5).

To assess the extent to which this case may have unduly affected the regression model, the analysis was conducted again but with this case (CI_06) removed (Model B, Table 6.9). This regression analysis yielded markedly different results, indicating that LI[pre] significantly predicted AUDITORY[+6], $F_{(1,6)}$=48.65, p<.001. Furthermore, this model was able to explain 89% of the variance observed in CI outcome (R^2=.89), with an adjusted R^2 of .87 indicating good generalizability of the regression model. Figure 6.6

Table 6.9: Summary of bivariate regression statistics for lateralisation of cortical activation to auditory speech in the prediction of CI outcome

Dependent *AUDITORY[+6]*	**R^2**	**Adj. R^2**	***F***	***b***	**SE *b***	***β***	***t***
Model A (n=9)	.15	.03	1.22 (*p*=.31)				
Constant				54.47	15.31	-	3.56*
LI[pre]				46.33	41.90	.39	1.11 (*p*=.31)
Model B (n=8)	.89	.87	48.65**				
Constant				60.74	5.36	-	11.33**
LI[pre]				127.78	18.32	.94	6.98**

*$p<.01$, **$p<.001$

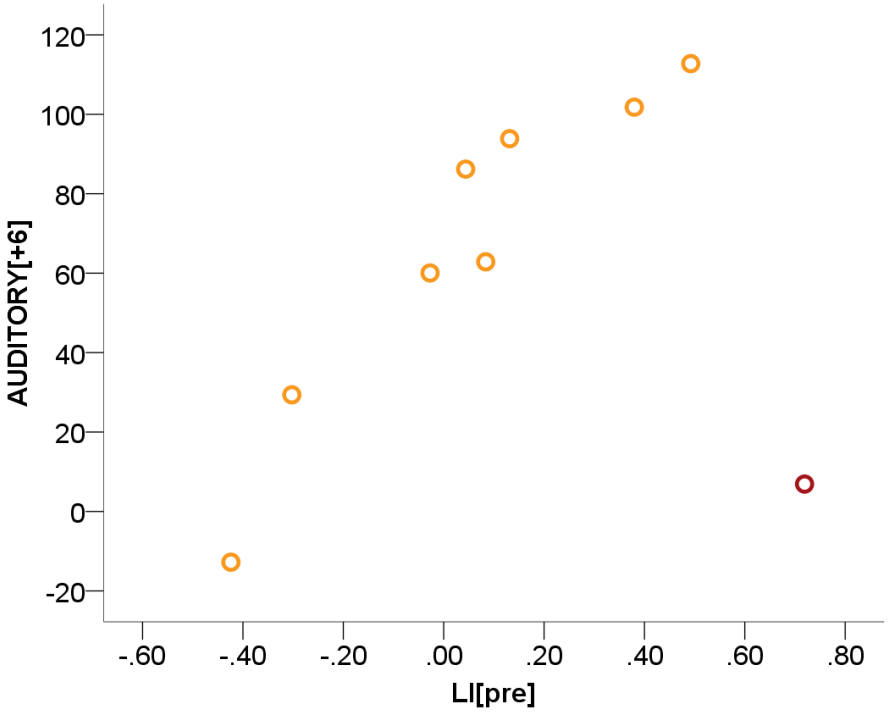


Figure 6.4:Scatterplot showing suspected outlier in relationship between lateralisation of cortical activation to auditory speech and future CI outcome(n=9). Suspected outlier observation is highlighted in red.

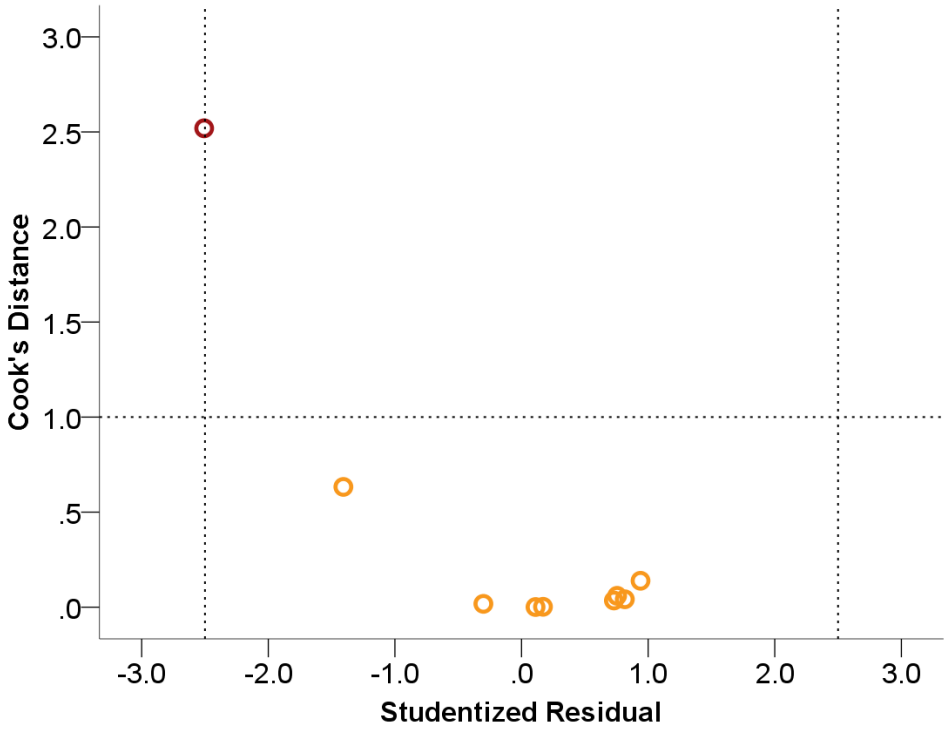


Figure 6.5: Scatterplot of Studentized Residuals and Cook's Distance values for the sample (n=9), with thresholds indicated by dotted lines and the influential case highlighted in red.

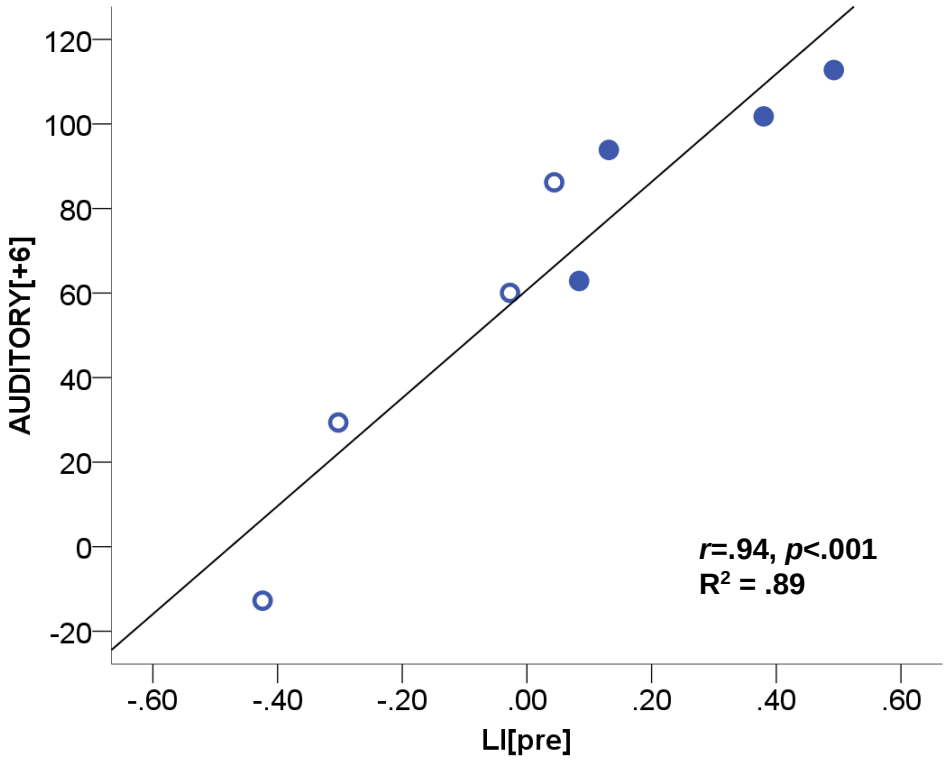


Figure 6.6: Scatterplot of lateralisation of cortical response to auditory speech and future CI outcome, with the outlier now excluded (n=8) and regression line shown. Filled markers represent data obtained from post-lingually deaf CI users, and open markers represent data obtained from pre- and peri-lingually deaf CI users.

illustrates that a strong positive association existed (r=.94, p<.001, 2-tailed), whereby individuals showing a more strongly left-lateralised temporal-lobe response to auditory speech before implantation were seen to display greater auditory speech perception ability following six months of CI use. However, due to participant exclusions and the resultant small sample size (n=8), caution should be exercised over these findings.

To examine whether hemispheric lateralisation of STC activation to auditory speech was related to the amplitude of left STC activation to visual speech before implantation, bivariate correlational analysis between LI[pre] and V_RESPONSE_LEFT[pre] was conducted. This

analysis indicated a negative, but non-significant, correlation (r=-.66, p=.07, 2-tailed). Furthermore, visual inspection of this relationship suggested that the trend was likely spurious due to the small sample size (see Figure 6.7).

6.3.3.3 Examining the Influence of Mediating Factors

It can be seen from Figure 6.6 that post-lingually deaf individuals typically showed left lateralisation, whereas pre- and peri-lingually deaf individuals typically showed right lateralisation. This suggests that other pre-implant clinical characteristics of the CI user, such as the age-at-onset and duration of deafness that are known to influence CI outcome (current findings reported in section 6.2.3.3; Blamey et al., 2013; Green et al., 2007; Lazard et al., 2012a; Summerfield & Marshall, 1995; Teoh et al., 2004), may mediate the observed predictive relationship between LI[pre] and AUDITORY[+6]. Furthermore, pre-operative aided auditory speech perception ability has been shown to influence CI outcome (Lazard et al., 2012a) and was anticipated to relate to LI[pre] here. Therefore, the likely interrelated factors of age-at-onset of bilateral HL (ONSET), the duration of bilateral HL (DURATION), and aided auditory speech perception ability before implantation (AUDITORY[pre]) were considered here as potential covariates that could mediate the predictive relationship between LI[pre] and AUDITORY[+6]. Relationships between these potential covariates and the predictor and dependent variable were estimated using Pearson's correlation coefficient r.

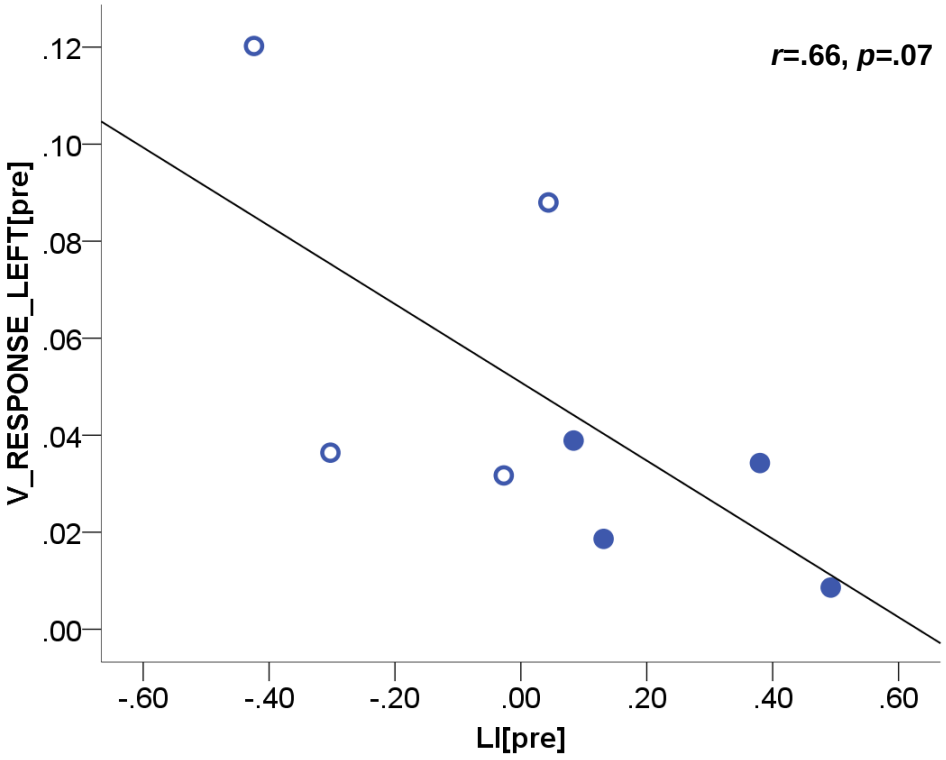


Figure 6.7: Scatterplot of lateralisation of cortical activation to auditory speech and activation to visual speech within the left ROI. Filled markers represent data obtained from post-lingually deaf CI users, and open markers represent data obtained from pre- and peri-lingually deaf CI users.

These associations are summarised in Table 6.10. While relationships between these variables were generally in the expected directions, not all associations were seen to reach significance perhaps due to the limited sample size (n=8).

As in section 6.2.3.3, separate hierarchical linear regressions were conducted to estimate the ability of LI[pre] to predict AUDITORY[+6] independently of ONSET (Model 1), DURATION (Model 2), and AUDITORY[pre] (Model 3). For each model, the covariate of interest was first entered as a predictor variable into Block 1, with LI[pre] then entered as a predictor into Block 2 of the model. For all three models, the assumption of independent errors

Table 6.10: Pearson's correlation coefficients (*r*) between covariates and the predictor and dependent variables

			Covariates		Predictor	Dependent
		ONSET	DURATION	AUDITORY[pre]	LI[pre]	AUDITORY[+6]
Covariates	ONSET	-	-.63 (*p*=.09)	.46 (*p*=.25)	.59 (*p*=.12)	.56 (*p*=.15)
	DURATION		-	-.31 (*p*=.46)	-.52 (*p*=.19)	-.35 (*p*=.40)
	AUDITORY[pre]			-	.90*	.86*
Predictor	LI[pre]				-	.94**
Dependent	AUDITORY[+6]					**-**

*p<.01, **p<.001, 2-tailed (not corrected for multiple comparisons).

was met (DW=2.04 – 2.11). For Models 1 and 2, the VIF indicated that multicollinearity between the predictor variables in Block 2 was not problematic (VIF=1.4 and 1.5). However, for Model 3 the correlation between the variables AUDITORY[pre] and LI[pre] was high (r=.90, p<.01), raising concern over multicollinearity in the model. However, the VIF (5.3) was less than 10, indicating that although a moderate degree of multicollinearity did exist this was not a cause for concern, especially since attempting to reduce this by eliminating a predictor variable would result in improper hypothesis testing here (Field, 2009; O'brien, 2007). All three regression models indicated that including LI[pre] as a predictor added significant incremental predictive value to the model above that of each of the covariates, with LI[pre] accounting for an additional 58% of the variance that remained unexplained by the covariate in Model 1, 80% in Model 2, and 15% in Model 3. Furthermore, for LI[pre] in each model, the standardised beta coefficients (β) were seen to be significant, indicating that LI[pre] was a significant individual predictor of CI outcome. Perhaps unsurprisingly given the correlation coefficients provided in Table 6.10, AUDITORY[pre] was the only covariate that, when examined alone (Model 3, Block 1), significantly predicted CI outcome. Table 6.11, Table 6.12, and Table 6.13 summarise the relevant regression statistics for Models 1 – 3 respectively.

Table 6.11: Summary of hierarchical regression statistics when controlling for age-at-onset of bilateral HL

Dependent *AUDITORY[+6]*		**R^2**	**Adj. R^2**	***F***	**ΔR^2**	**ΔF**	***b***	**SE *b***	***β***	***t***
Model 1	**Block 1**	.32	.20	2.77 (*p*=.15)	-	-				
	Constant						42.94	19.89	-	2.11 (*p*=.08)
	ONSET						1.46	.88	.56	1.66 (*p*=.15)
	Block 2	.89	.85	20.28*	.58	26.18*				
	Constant						60.47	9.44	-	6.41*
	ONSET						.02	.48	.01	.04 (*p*=.97)
	LI[pre]						127.27	24.87	.94	5.12*

*p<.01

Table 6.12: Summary of hierarchical regression statistics when controlling for duration of bilateral HL

Dependent *AUDITORY[+6]*		R^2	Adj. R^2	*F*	ΔR^2	ΔF	*b*	SE *b*	*β*	*t*
Model 2	**Block 1**	.12	-.03	.83 (*p*=.40)						
	Constant						107.82	47.42	-	2.27 (*p*=.06)
	DURATION						-1.10	1.21	-.35	-.91 (*p*=.40)
	Block 2	.92	.88	27.47*	.80	47.64*				
	Constant						37.80	18.95	-	1.99 (*p*=.10)
	DURATION						.60	.48	.19	1.26 (*p*=.26)
	LI[pre]						141.09	20.44	1.04	6.90*

*p<.001

Table 6.13: Summary of hierarchical regression statistics when controlling for pre-implant auditory performance

Dependent *AUDITORY[+6]*		**R^2**	**Adj. R^2**	***F***	**ΔR^2**	**ΔF**	***b***	**SE *b***	***β***	***t***
Model 3	**Block 1**	.74	.69	16.80**	-	-				
	Constant						35.20	11.24	-	3.13*
	AUDITORY[pre]						1.31	.32	.86	4.10**
	Block 2	.89	.85	20.36**	.15	7.03*				
	Constant						59.31	12.07	-	4.91**
	AUDITORY[pre]						.07	.52	.05	.14 (*p*=.90)
	LI[pre]						122.15	46.08	.90	2.65*

*p<.05, **p<.01

6.3.4 Discussion

This second half of the chapter aimed to understand whether the extent to which temporal-lobe activation to auditory speech was left-lateralised before implantation was associated with auditory speech perception abilities following six months of CI use. A laterality index (LI) was calculated to quantify the relative contribution of the right and left temporal cortices during auditory speech processing, with larger positive values indicating a more strongly left-lateralised response. A strong positive relationship was revealed between LI and aided auditory speech perception abilities when both were measured before implantation (r= .90, p<.01, 2-tailed, n=8), which may suggest that the LI provided a behaviourally relevant cortical measure of auditory speech processing. In comparison, it is interesting to note that the absolute amplitude of left temporal-lobe response to auditory speech before implantation did not correlate as strongly with baseline auditory speech perception abilities in the current sub-sample of CI users (r= .58, p=.13, 2-tailed, n=8). This suggests that, by calculating LI rather than examining the raw amplitude of auditory speech-evoked activation, we may have obtained a measure of cortical activation more directly relevant to auditory speech processing.

The current findings provide the first known evidence that a more strongly left-lateralised response to auditory speech stimulation measured within superior temporal brain regions before

implantation may be predictive of better auditory speech perception abilities following six months of CI use. Furthermore, it was observed in Figure 6.6 that post-lingually deafened individuals typically showed left lateralisation, whereas pre- and per-lingually deafened individuals typically showed right lateralisation before implantation. These observations may suggest that the relative contributions of the superior temporal cortices for the processing of auditory speech information may develop differently depending when the onset of auditory deprivation occurs in relation to language acquisition. However, in the absence of group comparisons such a notion is only speculative here, and future research with a larger sample should look to compare temporal-lobe lateralisation of speech-evoked activation between groups of post-lingually and pre-lingually deaf individuals in order to examine this. In this way, it is important to consider additional factors that may be mediating the predictive relationship that has been evidenced here. For instance, correlations reported in Table 6.10 indicate that pre-implant auditory speech perception ability was a significant predictor of better CI outcome (r= .86, p<.01, 2-tailed, n=8)[3] and was also strongly positively related to pre-implant LI (r= .90, p<.01, 2-tailed, n=8). Given the strength of this correlation between the lateralisation of cortical responses to auditory speech and auditory performance before implantation, it is possible that these two variables were proxies for one another. However, the

[3] Note that this relationship did not hold true across the wider sample of CI users considered earlier in this chapter (n=15, r=.49, p=.07, 2-tailed).

analysis conducted here indicated that, after controlling for the effects of baseline auditory ability, pre-implant LI remained a significant predictor of outcome and was able to provide unique predictive power explaining an additional 15% of the variance. In addition, examination of other potential mediating factors, including the age-at-onset and duration of bilateral HL, demonstrated that pre-implant hemispheric lateralisation to auditory speech provided additional predictive value above that of each of these covariates. Whilst inferences are somewhat limited due to the small sample size, the current findings suggest that this pre-implant cortical measure of hemispheric lateralisation for auditory speech processing could provide useful information in the prediction of CI outcome as an adjunct to routine clinical factors.

The results presented in the first half of this chapter suggest that greater recruitment of left superior temporal brain regions for visual speech processing may provide a behavioural advantage for speechreading ability during deafness. It was speculated based on existing literature in section 6.3.1 that greater left STC activation to visual speech before implantation may consequentially result in a more weakly left-lateralised STC response to auditory speech. However, the current findings provided no strong evidence of an inverse relationship between left STC activation to visual speech and hemispheric lateralisation to auditory speech before implantation. It would also be of interest to examine the relationship between the extent to which STC activation to auditory speech is left-lateralised

and the extent to which STC activation to visual speech is left-lateralised before implantation. However, such an analysis was not possible here as the presence of negative cortical response amplitudes to visual speech in either the right or the left ROI reduced the sample for which a LI for visual speech could be calculated to n=3.

It should be noted that temporal-lobe response to auditory speech was not seen to be typically left-lateralised in the current sample of NH controls; rather, for the 16 participants who had calculable LIs at T0, the data followed an approximately normal distribution, with nine individuals displaying right-lateralised activation, and seven individuals displaying left-lateralised activation (LIs ranged from -.82 to .53). This variation is not entirely surprising considering that in NH listeners bilateral STC is involved in the basic acoustic analysis of the auditory speech signal, with a left-hemispheric dominance often evidenced only in more dispersed fronto-temporal networks involved in higher-level stages of speech understanding (Hickok & Poeppel, 2007). Although left temporal-lobe dominance was not the typical pattern of activation observed in NH controls here, it does not negate the fact that a more strongly left-lateralised response to auditory speech measured in the current sample of CI users before implantation was related to both baseline and future auditory performance.

Unfortunately, a caveat of the LI calculation employed here is that this measure of lateralisation can only be estimated for those individuals displaying positive activation in both temporal cortices; including negative cortical activation values produces extreme LI values outside of the -1 to 1 scale. Here this resulted in a reduced sample size and so caution is exercised over the current findings as it is possible that the associations demonstrated could be spurious. Specifically, from a sample of 15 CI users, seven individuals were seen to have negative activation values in either the left or the right temporal ROI before implantation. This is perhaps unsurprising given that the participants were profoundly deaf and therefore these negative activation values may represent a genuine absence of cortical response to auditory speech stimulation. However, there appeared to be no common factor, such as HA use or baseline auditory speech perception ability, amongst these individuals for whom negative activation values were obtained. In addition, a LI was not calculable for one NH control subject and so it remains possible that negative activation values may have been due to individual anatomical factors that reduced the ability to record haemodynamic changes, or that they may even represent meaningful cortical deactivations.

For the above reasons, employing this LI measure to quantify hemispheric lateralisation to auditory speech is unlikely to provide a clinically useful prognostic indicator of CI outcome. Therefore, sensitivity and specificity analyses for this pre-implant cortical

measure were not conducted here. Despite these inherent caveats, this is the first known study to investigate cerebral lateralisation during the processing of auditory speech information following deafness and to demonstrate the implications of this on future rehabilitation with a CI. The current results provide an important contribution to knowledge by suggesting the importance of a more strongly left-lateralised temporal-lobe response to auditory speech before implantation for future CI outcome, warranting further investigation in a larger sample of CI users. Furthermore, whilst this cortical measure as it stands may not prove directly useful as a prognostic indicator, such findings lend some support to existing preliminary suggestions of the use of cognitive training to help promote particular processing strategies and functional organisation of temporal-lobe networks prior to implantation (Lazard et al., 2010b , 2012b), which may in turn aid in the more proficient recovery of auditory function following implantation.

6.4 CHAPTER SUMMARY

This chapter provides the first known empirical investigation of the relationship between temporal-lobe activation to auditory and visual speech, measured before implantation, and future auditory speech perception abilities following cochlear implantation. Before implantation, greater response to visual speech within auditory brain regions was associated with greater speechreading ability. Specifically, left superior temporal brain regions appeared to maintain their linguistic function for the processing of visual speech

in the absence of reliable auditory speech inputs. Stronger cortical activation to visual speech before implantation was significantly predictive of poorer auditory speech perception following six months of CI use. However, there was no evidence to suggest that the processing of visual speech within superior temporal brain regions was to the detriment of the responsiveness of these brain regions to auditory speech. Furthermore, a more strongly left-lateralised response to auditory speech was significantly predictive of better auditory speech perception following six months of CI use, although this could only be examined in a limited sub-sample of CI users. There was no strong evidence to suggest that greater activation to visual speech within left STC was associated with a more weakly left-lateralised response to auditory speech. Importantly, both pre-implant cortical measures examined here were able to provide unique value above that of influential clinical variables, such as age-at-onset and duration of deafness, in the prediction of CI outcome. The results presented in this chapter indicate that fNIRS may hold promise as a clinical tool that, with future developments and in combination with existing clinical measures, could deliver more accurate prognoses for CI candidates.

7. CORTICAL PLASTICITY FOLLOWING COCHLEAR IMPLANTATION AND ITS RELATION TO COCHLEAR IMPLANT OUTCOME

7.1 INTRODUCTION

Chapter 6 demonstrated that, prior to implantation, greater bilateral STC activation to visual speech was associated with a higher level of speechreading proficiency. Whilst greater visually-evoked activation may have offered a behavioural advantage prior to implantation, it was also predictive of poorer auditory speech perception abilities following six months of CI use. This chapter describes how this temporal-lobe response to visual speech alters after cochlear implantation, which was possible due to the longitudinal study design. Correlational analysis is used to explore how change in STC activation to visual speech from pre-implantation to six months post-CI activation relates to CI outcome. Given the multi-modal propensity of the superior temporal brain regions, the relationship between change in temporal-lobe responses to visual and auditory speech following implantation is examined. Furthermore, as visual speech information remains important following cochlear implantation, the impact of these post-implant cortical modifications on CI users' speechreading abilities is also explored.

7.2 RATIONALE

Results presented in section 6.2 indicated that greater STC activation to visual speech occurred in cases of an earlier age-at-onset and greater duration of HL and was related to higher levels of speechreading proficiency. It was suggested that this may reflect cortical plasticity within the STC, whereby responsiveness to visual speech information is increased when auditory inputs are impoverished in order to support proficiency in spoken communication. Whilst this plasticity may have been beneficial before implantation, evidence of a negative relationship with future CI outcome suggested this plasticity may have an adverse effect on auditory speech perception after hearing was reinstated. In a similar way, an existing PET study demonstrated a negative association between temporal-lobe activation to visual speech measured soon after CI activation and later-stage speech perception abilities (Strelnikov et al., 2013). Furthermore, PET evidence has also demonstrated a reduction in right temporal-lobe response to visual speech from an early stage (approximately one week) to a later stage (approximately 8 months) after implantation (Rouger et al., 2012). Therefore, a post-implant reversal of this seemingly detrimental temporal-lobe response to visual speech may reflect the ability of these multi-modal temporal brain regions to adapt to the increased auditory inputs provided by the implant. From the current evidence presented in Chapter 6 together with existing reports within the literature, it could be anticipated that a decrease in STC activation to visual speech from pre- to post-implantation

may be associated with increased responsiveness of STC to auditory speech. Furthermore, this visual-to-auditory sensory shift may be associated with better CI outcome, as evidence suggests that greater temporal-lobe response to auditory speech following implantation may be crucial for achieving proficient levels of auditory speech perception (Coez et al., 2008; Fujiki et al., 1999; Green et al., 2005; Naito et al., 1997). However, due to compatibility issues between conventional neuroimaging techniques and the CI device, longitudinal neuroimaging studies examining such cortical plasticity from pre- to post-implantation remain scarce. As such, no study could be identified that has examined the dynamic between temporal-lobe response to visual and auditory speech following implantation and how this relates to the recovery of auditory function with a CI.

Given that, in the current sample, greater STC response to visual speech was related to higher levels of speechreading proficiency before implantation, it is important to understand the impact that a reduction in STC activation following implantation could have on speechreading ability. At the behavioural level, CI users are known to maintain enhanced speechreading abilities (Rouger et al., 2007, current results reported in Chapter 4) and to still rely heavily on visual speech information in audio-visual conditions despite the increased auditory input provided by the CI (Desai et al., 2007; Kaiser et al., 2003; Rouger et al., 2007, 2008; Schorr et al., 2005; Song et al., 2014). Behavioural evidence in paediatric CI users has

also suggested the benefits that visual speech can provide to auditory-only abilities, likely by providing access to spoken language structure and enabling the development of amodal general communication skills that can transfer between the visual and auditory modality following cochlear implantation (Bergeson et al., 2005; Lachs et al., 2001). At the cortical level, these cross-correlations and cooperation between the auditory and visual modalities has been evidenced during speech perception in adult CI users. For instance, the recruitment of the visual cortex during the processing of auditory speech information has been demonstrated (Giraud et al., 2001a) along with evidence of a tight coupling between occipital and temporal-lobe activations following implantation (Strelnikov et al., 2015). In an analogous way, greater temporal-lobe response to visual speech may represent a close coupling between the two modalities at the cortical level, which CI users may capitalise on to compensate for the degraded auditory input and aid proficient auditory speech perception. Therefore, it could alternatively be anticipated that an increase in STC response to visual speech from pre- to post-implantation may reflect a facilitative link between the two modalities that could be beneficial to CI outcome. In summary, whilst there is theoretical grounding to believe that changes in temporal-lobe response to visual speech following implantation may be important in understanding variable CI outcome, it remains unclear whether a reversal or proliferation of such activation enables proficient levels of auditory speech perception to be achieved following implantation.

7.3 ANALYSES

Consistent with Chapter 6, CI outcome was quantified for each participant as auditory performance (transformed data, RAUs) on the CUNY sentence test in quiet conditions measured six months post-CI activation, also referred to here as AUDITORY[+6]. Change in bilateral STC activation to visual speech, V_RESPONSE[change], was also calculated for each participant as follows:

V_RESPONSE[change] = V_RESPONSE[+6] - V_RESPONSE[pre]

where V_RESPONSE[+6] denotes the amplitude of cortical response to visual speech (beta weight) within the predefined bilateral ROI six months post-CI activation, and V_RESPONSE[pre] denotes the amplitude of cortical response to visual speech (beta weight) within the predefined bilateral ROI before implantation (consistent with section 6.2.2). In the same way, change in bilateral STC activation to auditory speech, A_RESPONSE[change], was calculated as the difference between A_RESPONSE[+6] and A_RESPONSE[pre]. All variables comprised interval-level data, and the K-S test and visual inspection of histograms indicated that the distributions of data did not significantly violate assumptions of normality. Therefore, the parametric statistic Pearson's correlation coefficient (*r*) was used to estimate the direction and strength of each of the bivariate linear relationships examined throughout the chapter.

7.4 RESULTS

7.4.1 Description of the Sample

Consistent with data presented in Chapter 6, both neuroimaging and behavioural data before implantation and six months post-CI activation were available for 15 CI users (see Table 6.1 for details of the sample) who were included in all analyses presented in this chapter.

7.4.2 Change in Cortical Activation to Visual Speech and Relation to CI Outcome

The direction and level of change in bilateral STC activation to visual speech following implantation, V_RESPONSE[change], was seen to vary across the group of CI users: nine CI users displayed a negative V_RESPONSE[change] value, indicating a decrease in cortical response from pre-implantation to six months post-CI activation, whereas six CI users displayed a positive V_RESPONSE[change] value, indicating an increase in cortical response over time. A paired-sample t-test indicated that there was no significant change in the amplitude of bilateral STC activation to visual speech from pre-implantation (mean amplitude in beta weight=.034, *SE*=.010) to six months post-CI activation (mean amplitude in beta weight=.017, *SE*=.007) across the group of CI users, $t(14)=-1.44$, $p=.17$, 2-tailed, (see Figure 7.1).

To examine whether change in bilateral STC activation to visual speech following implantation was related to CI outcome, bivariate

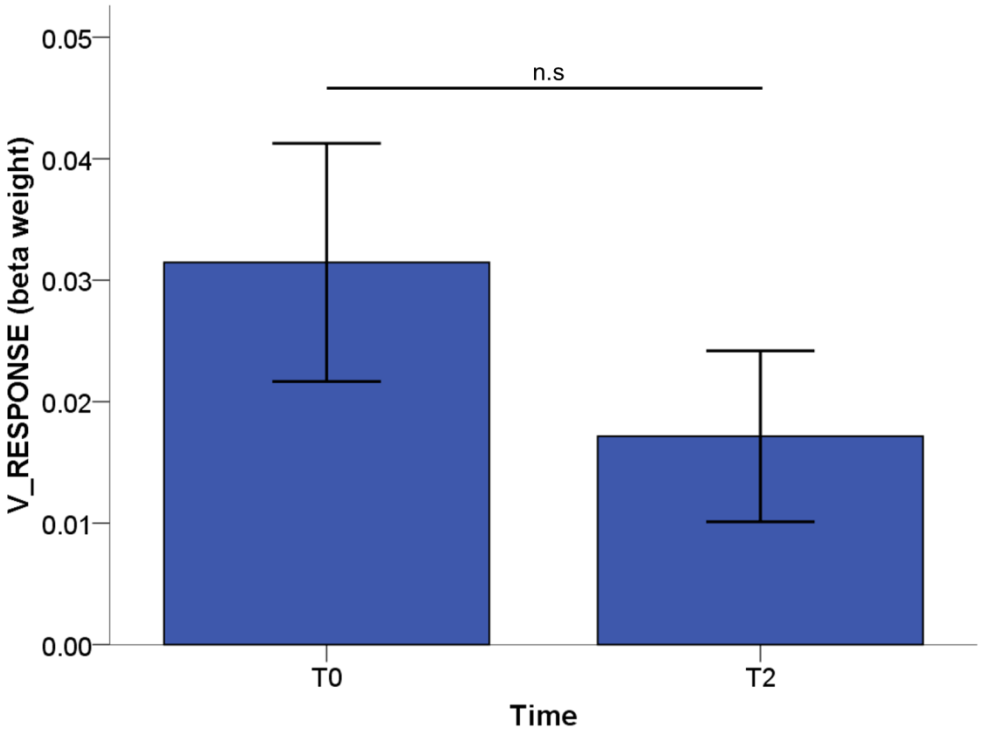


Figure 7.1: Bar graph displaying mean amplitude of cortical activation to visual speech (beta weight) plotted for T0 (before implantation) and T2 (six months post-CI). Error bars represent ± 1 standard error. n.s = non-significant difference between time points.

correlation analysis was conducted. This revealed that V_RESPONSE[change] was significantly and positively related to CI outcome, AUDITORY[+6], r=.77, p<.01, 2-tailed (see Figure 7.2) and was able to explain 59% of the variance observed (R^2=.59). Specifically, the greater the increase in STC activation to visual speech the greater the level of auditory performance achieved following six months of CI use. In addition, separate bivariate correlation analyses conducted between CI outcome and the change in cortical response to visual speech within the left and the right STC confirmed that this relationship was not predominantly driven by one hemisphere, and that the direction of the relationship was

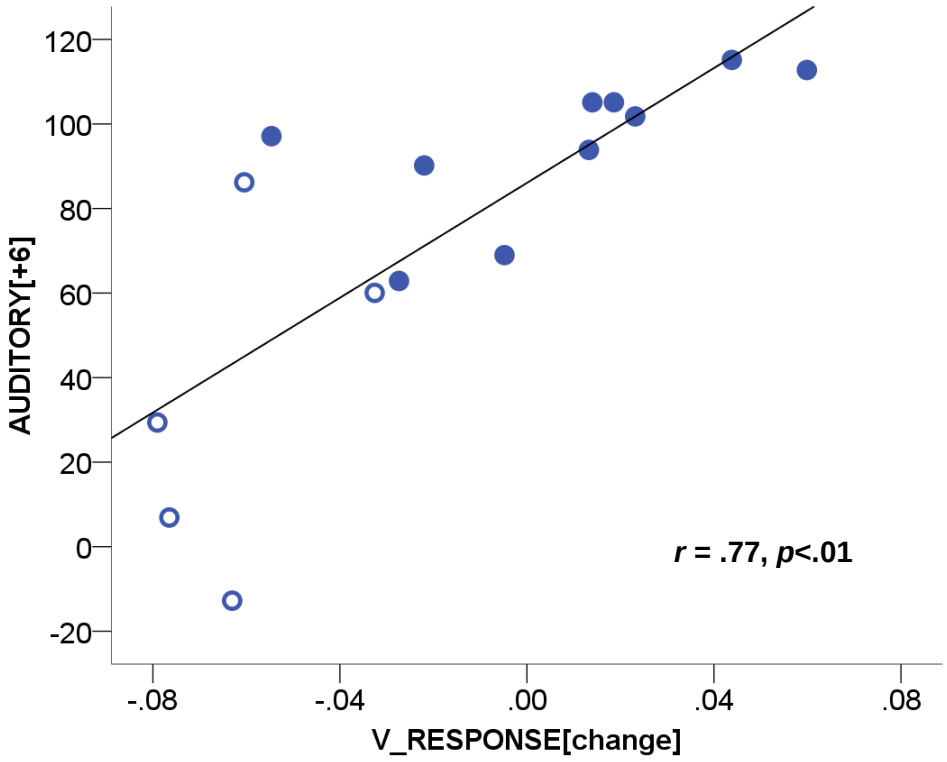


Figure 7.2: Scatterplot of the change in cortical activation to visual speech from pre- to post-implantation and CI outcome, with the regression line shown. Filled markers represent post-lingually deaf CI users, and open markers represent pre- and peri-lingually deaf CI users.

the same for each hemisphere (left: r=.63, p<.05; right: r=.73, p<.01, both 2-tailed). Overall these findings suggest that a greater increase in bilateral STC response to visual speech following implantation is associated with better CI outcome.

It should be noted that whilst some CI users (n=9) showed a decrease in cortical response to visual speech following implantation, auditory performance was seen to improve for all 15 CI users over the same period of time. Therefore, a decrease in STC response to visual speech did not appear to preclude an improvement in auditory performance following implantation. Indeed, bivariate correlation analysis conducted across the sample

of CI users (n=15) indicated that no significant relationship existed between change in STC activation to visual speech, V_RESPONSE[change], and change in auditory performance from pre-implantation to six months post-CI activation, AUDITORY[change], r=.12, p=.66, 2-tailed. Therefore, the current results provide no evidence to suggest that a greater increase in STC activation to visual speech directly relates to a greater improvement in auditory speech perception from pre- to post-implantation at the individual level. However, it is possible that the level of improvement in auditory performance following implantation was not accurately or fully quantified for all participants due to the ceiling effects encountered (see section 4.3.4 for further details).

7.4.3 Relationship with Speechreading Ability

Section 6.2 demonstrated that a greater STC activation to visual speech before implantation may have been adaptive as it was positively related to speechreading proficiency during periods of profound deafness (r=.57, p<.05, 2-tailed). However, bivariate correlation analysis conducted here revealed a negative relationship between V_RESPONSE[pre] and V_RESPONSE[change], r=-.80, p<.001, 2-tailed, indicating that those individuals who displayed greater STC activation to visual speech before implantation also tended to display the greatest decrease in STC activation to visual speech following implantation (see Figure 7.3). Therefore, it is important to confirm whether a decrease in this speechreading activation from pre- to post-implantation has a detrimental impact

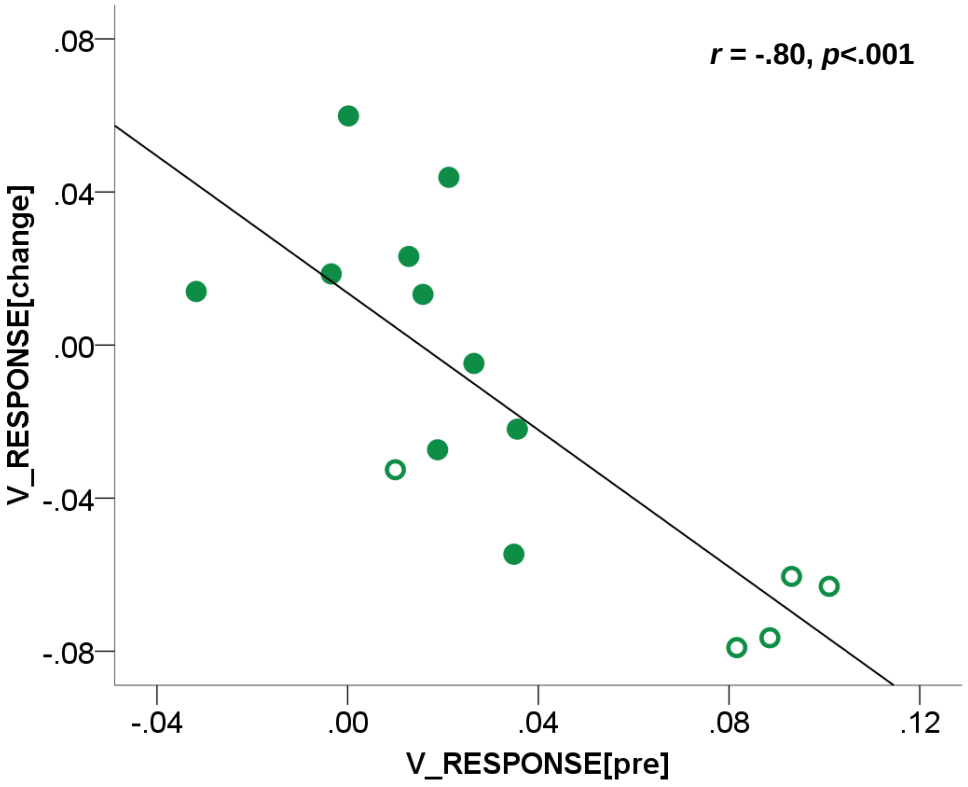


Figure 7.3: Scatterplot of cortical activation to visual speech before implantation and post-CI change in cortical activation to visual speech, with the regression line shown. Filled markers represent post-lingually deaf CI users, and open markers represent pre- and peri-lingually deaf CI users.

on these individuals' speechreading abilities. A paired-samples *t*-test revealed no evidence of a significant reduction in speechreading abilities from pre-implantation (*M*=20.4 RAUs, *SE*=7.0) to six months post-CI activation (*M*=28.3 RAUs, *SE*=4.6), *t*(8)=1.32, *p*=.22, 2-tailed, for those CI users who displayed a decrease in bilateral STC response to visual speech over this time period (n=9, see Figure 7.4). Therefore, the current results provide no evidence to suggest that a reduction in bilateral STC activation to visual speech following implantation negatively impacts on speechreading proficiency. Furthermore, looking across the whole group of CI users (n=15), change in STC activation to visual speech was not

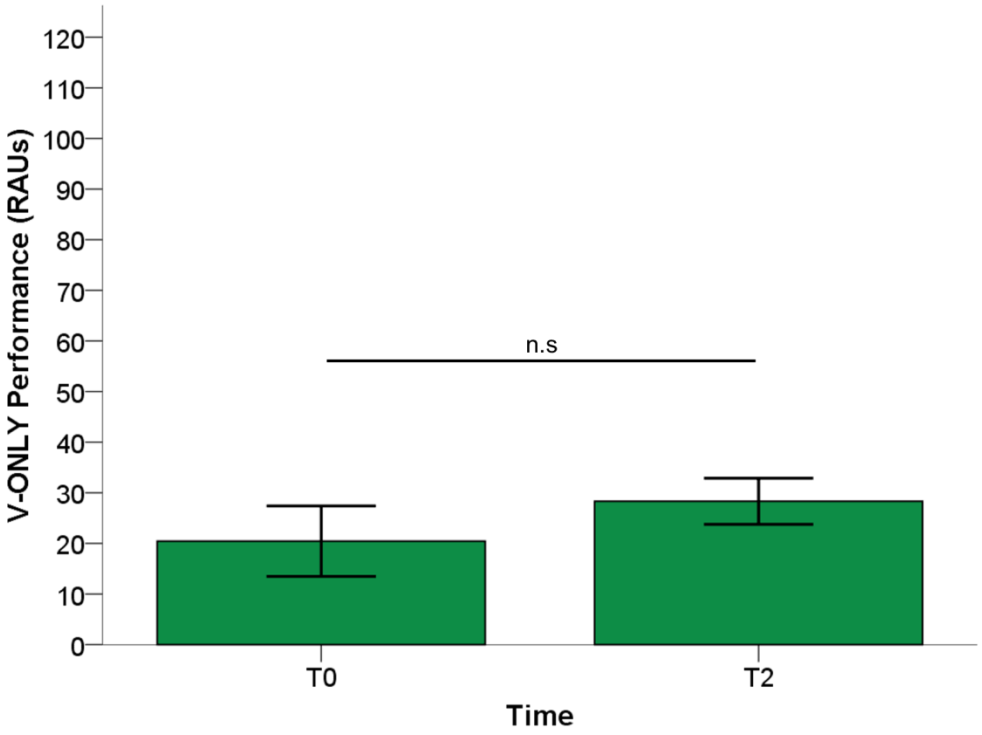


Figure 7.4: Bar graph displaying mean speechreading ability (n=9) plotted for T0 (before implantation) and T2 (six months post-CI). Error bars represent ± 1 standard error. n.s = non-significant difference between time points.

associated with change in speechreading ability, r=-.13, p=.65, 2-tailed (see Figure 7.5), thus providing no evidence of a functional relationship between post-implant alterations in cortical response to visual speech and a reduction in speechreading ability at the individual level.

7.4.4 Relationship with Change in Cortical Activation to Auditory Speech

Given the multi-modal propensity of the superior temporal cortices, it is important to understand how changes in STC response to visual speech following implantation may relate to changes in STC response to auditory speech. Following the recovery of auditory

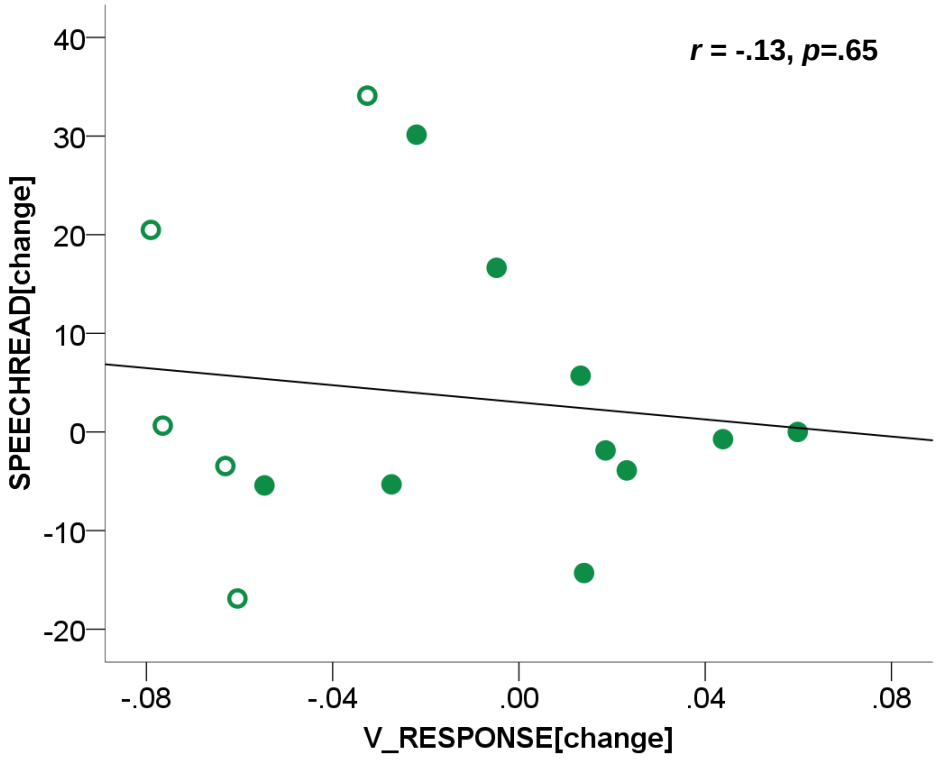


Figure 7.5: Scatterplot of post-CI change in cortical activation to visual speech and post-CI change in speechreading ability, with the regression line shown. Filled markers represent post-lingually deaf CI users, and open markers represent pre- and peri-lingually deaf CI users.

function, an inverse relationship between the two modalities may be anticipated with an increase in activation to auditory speech corresponding to a relative decrease in activation to visual speech. Conversely, considering existing evidence of a synergy between the two modalities following implantation (Giraud et al., 2001a; Strelnikov et al., 2015, outlined in section 7.2) together with the current evidence that a greater increase in STC response to visual speech relates to better CI outcome (section 7.4.2), a positive relationship between the two sensory modalities may be anticipated. To examine this, bivariate correlation analysis was conducted and revealed a positive, moderate association between change in bilateral STC response to visual speech, V_RESPONSE[change], and

change in bilateral STC response to auditory speech from pre- to post-implantation, A_RESPONSE[change][4], r=.51, p<.05, 2-tailed. Specifically, CI users who displayed a greater increase in cortical activation to visual speech following implantation tended to display a greater increase in cortical activation to auditory speech, whereas CI users displaying a greater decrease in one modality also tended to show a greater decrease in the other modality (see Figure 7.6). These findings provide evidence that the two modalities develop in a parallel manner following implantation, rather than displaying a visual-to-auditory sensory shift within the bilateral superior temporal brain regions of this group of CI users.

It can also be seen in Figure 7.6 that those CI users who displayed the greatest decrease in STC activation to both auditory and visual speech were pre-lingually deafened, whereas those showing the greatest increase were post-lingually deafened. Therefore it is possible that characteristics relating to the individual's clinical history of deafness may influence the direction and the extent of change in speech-evoked cortical activation following implantation. Indeed, both change in STC activation to visual speech and change in STC activation to auditory speech were seen to correlate with the age-at-onset (visual: r=.59, p<.05; auditory: r=.62, p<.05, both 2-tailed) and the duration of bilateral HL prior to implantation (visual: r=-.58, p<.05; auditory: r=-.61, p<.05, both 2-tailed).

[4] Note that A_RESPONSE[change] was not significantly correlated with CI outcome (AUDITORY[+6]), r=.37, p=.17, 2-tailed.

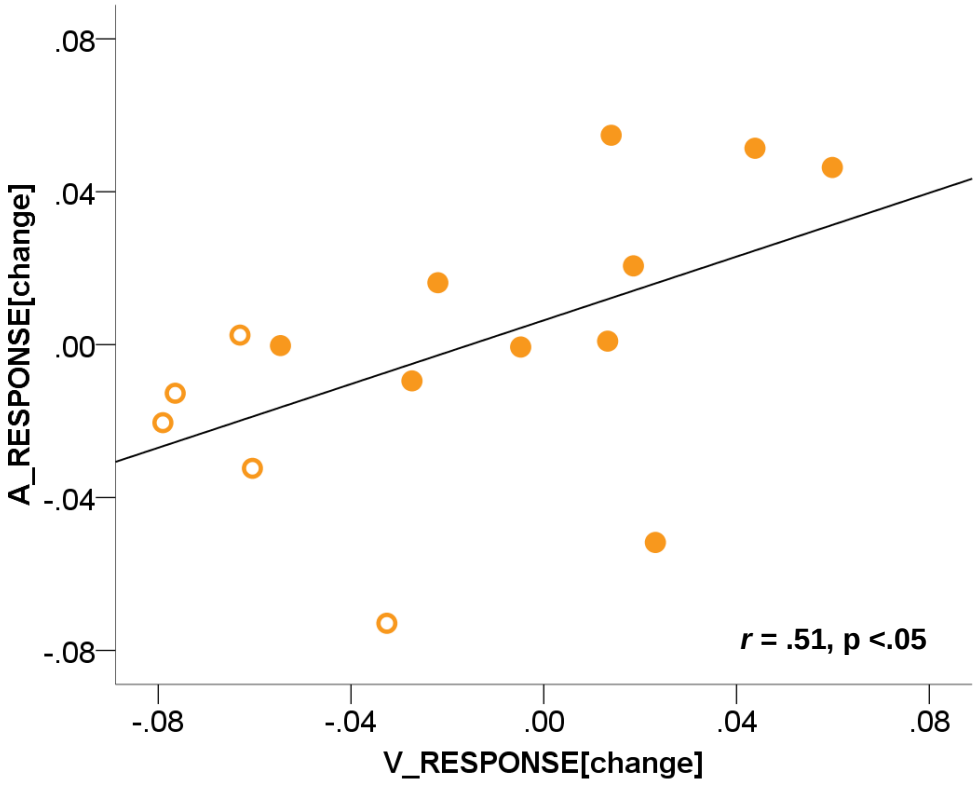


Figure 7.6: Scatterplot of the change in cortical activation to visual speech, and the change in cortical activation to auditory speech from pre- to post-implantation, with the regression line shown. Filled markers represent post-lingually deaf CI users, and open markers represent pre- and peri-lingually deaf CI users.

7.5 DISCUSSION

Prior to this chapter, Chapter 6 demonstrated that greater STC activation to visual speech before implantation predicted poorer CI outcome. An observation that a reduction in temporal-lobe response to visual speech from an early to later stage of implantation has caused some authors to speculate that a reversal of this visually-evoked activation may enable the recovery of auditory function (Rouger et al., 2012). The current chapter thus examined changes in activation to visual speech within the superior temporal brain regions from pre- to post implantation, capitalising on the ability to study cortical plasticity within the same CI users that fNIRS affords. The change in STC activation to visual speech

was seen to vary widely across individuals from a reduction to an increase of varying amounts. Contrary to previous speculation within the published literature (Rouger et al., 2012), correlation analysis indicated that a greater increase in STC activation to visual speech following implantation was related to a greater level of auditory performance six months post-CI activation. This provides the first investigation known to the author of the role of visual speech processing and cortical plasticity following implantation in CI success. Importantly, the findings provide evidence to suggest that a greater proliferation rather than reversal of temporal-lobe response to visual speech from pre- to post-implantation is associated with better CI outcome. This lends some support to the emerging debate that the recruitment of the language networks by the visual modality during auditory rehabilitation does not necessarily have maladaptive effects, and may offer a facilitative link between the two modalities that could promote auditory recovery (Heimler et al., 2014).

It is possible that superior temporal-lobe responses when viewing silent visual speech cues may reflect indirect activation by processes such as inner speech, auditory imagery, and the anticipation of hearing complementary auditory speech information due to the inherent correspondence that exists between auditory and visual speech representations (Hall et al., 2005). In this way, a greater increase in STC activation to visual speech observed here may reflect more strongly formed associations and the use of audio-

visual strategies following implantation. Accordingly, a more refined audio-visual synergy may enable individuals to successfully decipher the degraded auditory input provided by their device and to become more proficient CI users. Indeed, behavioural evidence has suggested the use of compensatory and enhanced audio-visual speech perception strategies during the recovery of auditory function in adult CI users (Rouger et al., 2007) as well as the benefits of inherent cross-correlations between visual and auditory speech representations for auditory language outcomes in paediatric CI users (Bergeson et al., 2005; Lachs et al., 2001). The current findings may therefore provide evidence at the cortical level of the beneficial role of visual speech and audio-visual associations for CI outcome in adult recipients. However, as with the interpretation of any bivariate relationship, causation cannot be inferred from the current findings. For instance, it is possible that the most proficient CI users were better able to form clear and accurate associations between auditory and visual speech representations, thus resulting in a greater proliferation of STC activation to visual speech following implantation.

Given the involvement of the superior temporal cortices in the successful processing of auditory speech information following implantation (Coez et al., 2008; Fujiki et al., 1999; Green et al., 2005; Naito et al., 1997), the dynamics of post-implant changes in STC activation to visual speech and auditory speech information were also examined here. The findings demonstrated a positive

association between change in STC activation to visual speech and change in STC activation to auditory speech from pre- to post-implantation. Therefore the current investigation provides no evidence of a visual-to-auditory sensory shift within bilateral superior temporal brain regions following reafferentation of auditory inputs, but rather indicates coupling between the two modalities that may lend further support to the notion of an AV synergy at the cortical level. Indeed, in NH listeners, the current posterior superior temporal regions of interest are known to be involved in the integration of auditory and visual speech information (Lee & Noppeney, 2011; Szycik et al., 2012; Wright et al., 2003). Although existing neuroimaging studies have suggested the existence of an audio-visual synergy following implantation (Giraud et al., 2001a; Rouger et al., 2012; Strelnikov et al., 2015), the current findings provide the first known evidence of a synergistic change in auditory and visual speech-evoked activation within bilateral posterior superior temporal cortices from pre- to post-implantation. Evidence of this coupling between the two modalities in adult CI users may suggest the importance of an audio-visual synergy at the cortical level over the first six months of the CI rehabilitation process. Furthermore, this apparent coupling between change in activation to auditory and visual speech was not evident over the same time period in NH controls (r=.09, p=.74, 2-tailed, n=16), suggesting that this audio-visual synergy is specific to the CI rehabilitation process and thus may reflect a cortical adaptation to cochlear implantation. However, it cannot be established here

whether this is a sensory-specific phenomenon or whether it reflects a more general cognitive function, such as attention, that is common to both sensory modalities and may also alter from pre- to post-implantation.

The examination of associations between changes in speech-evoked cortical activations over time and well-established clinical factors, including the age-at-onset and duration of auditory deprivation, indicated that how the cortex adapts following implantation may be influenced by these key clinical characteristics of the CI user. Specifically, an earlier age-at-onset and a greater duration of bilateral HL were related to a greater decrease in STC activation to both auditory and visual speech following implantation. Therefore, sensory experience of the listener prior to implantation may influence the extent to which the superior temporal cortices can adapt following cochlear implantation. Subsequently, it is possible that the age-at-onset and duration of auditory deprivation may exert their well-established detrimental influence on CI outcome by placing constraints on such post-implant cortical plasticity. However, reassuringly no CI user showed a reduction in auditory performance following implantation. Furthermore the level of change in STC activation to visual speech did not directly correlate with the level of change in auditory ability. The findings thus provide no evidence that post-CI changes in cortical activation to visual speech precluded the recovery of auditory function following implantation.

Similarly, the findings provided no evidence to suggest that a decrease in STC activation to visual speech following implantation was detrimental to CI users' speechreading abilities. However, given that a functional relationship was observed between bilateral STC response to visual speech and speechreading ability before implantation (r=.57, p<.05, 2-tailed, see section 6.2.3.3), the absence of a functional relationship between change in STC response to visual speech and change in speechreading abilities is somewhat surprising. Interestingly, there was also no evidence of a functional relationship between bilateral STC activation to visual speech and speechreading ability following six months of CI use (r=-.26, p=.34, 2-tailed). As suggested by Strelnikov and colleagues (2015), it is possible that the reliance on visual speech information during periods of profound deafness may then shift towards more of a reliance on audio-visual speech integration when auditory speech inputs are increased following cochlear implantation. Therefore, it is possible that STC activation to visual speech observed here following implantation may reflect indirect activation by audio-visual processes rather than direct activation by the processing of linguistic visual inputs following implantation, hence the lack of functional relationships with speechreading ability. In this way, cochlear implantation may impact on the temporal-lobe speechreading networks, whereby the superior temporal cortices may no longer be as heavily recruited for the processing of visual speech information. However, as speechreading abilities are

maintained following implantation (see current results presented in section 4.3.5; Rouger et al., 2007) it is possible that other cortical regions, for instance the left inferior frontal regions (see section 5.4.3 for further discussion), may be recruited for the processing of visual speech information as has been suggested by an existing PET study (Rouger et al., 2012).

7.6 CHAPTER SUMMARY

This chapter has capitalised on the longitudinal nature of the current study by examining plasticity within superior temporal brain regions from pre-implantation to six months post-CI activation. Specifically, whether a reversal of STC activation to visual speech was related to greater auditory speech perception following six months of CI use was examined. The current findings provided no evidence of a positive relationship between the reversal of STC activation to visual speech and CI outcome. Rather, a greater proliferation of STC activation to visual speech was associated with better CI outcome. The current findings may indicate the facilitative role of visual speech information, as evidenced at the cortical level, in achieving proficient levels of auditory performance following implantation. The chapter proposes that a greater increase in temporal-lobe response to visual speech may indicate greater coupling between auditory and visual speech information at the cortical level, which CI users may capitalise on to enable more proficient auditory speech perception abilities to be achieved. Further to this, examination of the dynamic between STC activation to visual and auditory speech

provided evidence of a parallel change between the two modalities from pre- to post-implantation, rather than a trade-off relationship. Specifically, a greater increase in STC activation to visual speech corresponded to a greater increase in STC activation to auditory speech. This apparent coupling between the two sensory modalities may reflect the importance and use of audio-visual strategies during the recovery of auditory function following cochlear implantation. Lastly, the chapter provided evidence that a longer duration of deafness and an earlier age-at-onset of deafness were associated with a smaller increase (or greater decrease) in STC activation to both auditory and visual speech from pre- to post-implantation. These findings suggest that the individual's auditory experience prior to implantation could influence, and in these cases constrain, their future capacity for cortical plasticity that appears important for CI success.

8. INTEGRATION OF AUDITORY AND VISUAL SPEECH INFORMATION FOLLOWING COCHLEAR IMPLANTATION

8.1 INTRODUCTION

The results presented in Chapter 7 provided evidence that STC activation to auditory and visual speech information developed in a parallel manner following implantation. In natural face-to-face communication, CI users continue to rely heavily on the use of visual speech cues to decipher the degraded auditory signal provided by the implant (Rouger et al., 2007; Strelnikov et al., 2009). However, little is known about the cortical mechanisms that underlie this adaptive behavioural strategy. This chapter investigates the amount of benefit that visual speech information provides in audio-visual compared to auditory-only speech perception. Group comparisons are made to understand whether CI users obtain a greater level of visual benefit compared to NH listeners when auditory-only performance is approximately equated across the two groups. Multisensory interactions are then examined by applying the additive model to fNIRS measurements in order to understand how auditory and visual speech signals are integrated within the STC of NH individuals and CI users. Correlational analyses are subsequently conducted in order to examine the relationship between this physiological measure of audio-visual integration and the perceptual benefit gained from combining the

two sensory modalities. Lastly, whether the level of visual benefit obtained and audio-visual integration relate to CI success is examined.

8.2 RATIONALE

Natural communication is multi-modal in nature: in our day-to-day lives, both auditory and visual speech cues are utilised together to form an accurate understanding of what the talker is saying. The well-known McGurk effect illustrates that visual speech information can influence the overall speech percept in ambiguous audio-visual conditions even when auditory signals are clear (McGurk & MacDonald, 1976). It is also widely documented that speech perception is markedly enhanced by congruent visual speech information at intermediate levels of auditory distortion (Ma et al., 2009; Ross et al., 2007) and when auditory conditions are severely degraded (Bernstein et al., 2004; Sumby & Pollack, 1954). Indeed this perceptual benefit received from visual speech information has been evidenced in individuals with HL (Grant et al., 1998; Massaro & Cohen, 1999), paediatric CI users (Bergeson et al., 2003; Lachs et al., 2001), as well as congenitally (Moody-Antonio et al., 2005) and postlingually deaf adult CI users (Desai et al., 2007; Rouger et al., 2007). Despite significant improvements that can be made to auditory speech perception abilities following cochlear implantation, the implant delivers degraded and novel auditory information, thus visual speech information remains important as a compensatory mechanism following implantation. For instance, studies that have

employed the McGurk effect to examine audio-visual integration in CI users have consistently demonstrated their reliance on visual speech information in ambiguous audio-visual conditions (Desai et al., 2007; Rouger et al., 2008; Schorr et al., 2005), likely reflecting the use of compensatory strategies due to the impoverished auditory cues. In a longitudinal evaluation of speech perception, Rouger and colleagues (2007) demonstrated that, when equalising for levels of auditory performance between CI users and NH controls by using degraded auditory stimuli, CI users gained significantly more perceptual benefit from visual speech information in audio-visual conditions compared to control subjects. Whilst evidence has shown that this ability to derive more benefit from visual speech information may be driven by greater speechreading abilities in NH listeners (MacLeod & Summerfield, 1987, 1990) and individuals with acquired SNHL (Grant et al., 1998), Rouger and colleagues (2007) demonstrate through the use of computational models that post-lingually deafened CI users may also be more highly skilled at integrating the two modalities.

Neuroimaging studies have sought to explore the cortical mechanisms that may underlie the perceptual benefit derived from the integration of auditory and visual speech information. In NH listeners, a plethora of research has identified the superior temporal sulcus (STS) as a multisensory cortical binding site (Beauchamp et al., 2010; Benoit et al., 2010; Callan et al., 2003; Calvert et al., 2000, 2001; Werner & Noppeney, 2010, 2011), with some studies

implicating the left posterior STS in the integration of auditory and visual speech information (Beauchamp et al., 2010; Nath & Beauchamp, 2012) and others suggesting involvement of bilateral posterior portions of the STS (Lee & Noppeney, 2011; Szycik et al., 2012; Wright et al., 2003). During the presentation of congruent auditory and visual speech information, Song and colleagues (2015) observed both visual and auditory cortical activation, including the multisensory STS, in NH controls; whereas cortical activation was primarily observed in visual brain regions of CI users and was seen to be reduced in auditory regions compared to controls (Song et al., 2015). This may indicate visual-reliance in CI users at the cortical level when processing audio-visual speech inputs (Song et al., 2015).

Similarly, greater levels of occipital activation have been observed in proficient CI users compared to non-proficient CI users and NH controls (Doucet et al., 2006). Doucet and colleagues (2006) suggest that proficient CI users may capitalise on this enhanced visual activation to compensate for the degraded auditory signal, thus indicating the facilitative role of vision at the cortical level. Furthermore, PET imaging studies have evidenced enhanced activation within the visual cortex during auditory speech perception in rehabilitated CI users compared to NH controls (Giraud et al., 2001a; Giraud & Truy, 2002), as well as close coupling between left temporal and occipital lobe activation in CI users (Strelnikov et al., 2015). From such evidence it has been speculated that this

apparent synergy between the two modalities may reflect CI users' continued reliance on visual and audio-visual strategies that may be beneficial for the recovery of auditory function following implantation (Doucet et al., 2006; Giraud et al., 2001a; Strelnikov et al., 2015). However, this notion remains to be directly investigated.

In summary, existing evidence suggests the facilitative role of vision at both the cortical and perceptual level following implantation. However, little is known about the relationship between the two. Thus, the current chapter aims to understand the perceptual benefit that CI users derive from visual speech information when combined with degraded auditory signals. Specifically it is anticipated that CI users will obtain more benefit from visual speech cues compared to NH controls at a matched level of auditory-only performance. Secondly, the chapter examines how auditory and visual speech signals are integrated within the superior temporal cortices of CI users and NH controls, and whether this physiological measure of audio-visual integration corresponds to the degree of perceptual benefit gained from visual speech information. Lastly, whether visual benefit and audio-visual integration relate to levels of auditory proficiency following cochlear implantation is explored.

8.3 ANALYSIS METHODS

BKB sentences were presented in auditory-only format, masked by speech-shaped background noise. The sentences were employed in

an adaptive procedure to measure the SNR at which auditory performance was 50% correct. Subsequently, for each participant, speech perception testing in noise was conducted at the predetermined SNR (dB) in auditory (A-ONLY) and audio-visual (AV) conditions. For each condition, performance was quantified as the percentage of words reported correctly by the participant. Section 3.7 contains further details of speech perception testing in noise.

Here, the difference between AV and A-ONLY performance in noise (% correct) was calculated to estimate the amount of benefit derived from visual speech information in AV conditions, referred to here as 'visual benefit'. Whilst it would be of interest to understand whether visual benefit changes as a function of CI use, speech perception testing in noise data was only obtainable for five CI users across all three testing sessions. As data values were missing for the poorer CI performers due to the inability to measure the SNR at which A-ONLY performance was 50% correct, the missing data values could not be classed as 'missing at random'. Therefore, it is not possible to statistically model the effects of group and time using the linear mixed model approach. Instead, the analyses presented here focused on data obtained six months after CI activation (T2) as the largest amount of data was available at this time point and CI users had the longest duration of experience in using their device. Prior to all statistical testing, descriptive statistics were used to examine assumptions of normality, homogeneity of variance, and the presence of tied data values

where appropriate. Parametric or non-parametric tests were then selected accordingly based on whether the variables of interest met the relevant parametric assumptions. The statistical tests conducted are specified in the relevant sections throughout.

8.4 RESULTS

8.4.1 Description of the Samples

At T2, for all sixteen NH control subjects, the SNRs at which A-ONLY performance was 50% correct were calculated (range from -9.8dB to -6.2 dB) and subsequent speech perception testing in noise data were obtained. For CI users, SNRs could only be determined for eleven individuals (range from -6.0dB to 14.2 dB). Due to one CI user (CI_03) experiencing discomfort during testing, ten CI users went on to complete the speech perception in noise testing. Following these exclusions, a revised summary of the clinical characteristics of CI participants in the current analysis sample is provided in Table 8.1.

8.4.2 Perceptual Benefit

As outlined in section 3.7, speech perception testing in noise was conducted at a predetermined SNR in order to bring A-ONLY performance in noise close to 50% correct. This was done in an effort to equalise A-ONLY performance across all participants and to enable the amount of benefit that visual speech information provides to AV performance to be quantified (i.e. visual benefit = AV − A-ONLY). This measure of visual benefit was calculated for

Table 8.1: Summary of clinical characteristics for the current sub-sample of CI users

a) ID	b) Aetiology	c) Onset HL	d) Duration HL	e) Age	f) Implant side	g) T2 CI use	h) T2 HA	i) Handedness
CI_01	Immune Deficiency Virus	51	10 months	52	Right	6.1	✓	Right
CI_05	Unknown	20	39	59	Right	6.4	×	Right
CI_07	Otosclerosis	25	25	50	Right	5.3	✓	Right
CI_08	Mastoidectomy	52	8	60	Left	6.0	✓	Left
CI_09	Noise-induced	45	33	78	Right	5.7	×	Right
CI_10	Mastoidectomy	30	40	70	Left	6.1	×	Right
CI_11	Rubella	3	54	57	Right	6.0	×	Right
CI_15	Unknown	42	4 months	43	Left	6.1	×	Right
CI_16	Unknown	43	35	78	Left	6.1	×	Right
CI_17	Unknown	25	28	53	Right	6.0	✓	Right
N=10						**Mean (SD) = 6.0 (0.3)**		

Column **a)** Participant ID; **b)** Aetiology of onset of hearing loss; **c)** Age-at- onset of bilateral hearing loss (years); **d)** Duration of bilateral hearing loss (years, unless otherwise stated); **e)** Age at time of CI surgery (years); **f)** Side of cochlear implantation; **g)** Duration of CI use at T2 since CI activation (months); **h)** Contralateral hearing aid worn with CI device at T2; **i)** Dominant hand.

each participant. All participants were seen to obtain perceptual benefit from visual speech information, with visual benefit ranging between 16% and 65% in NH subjects and between 19% and 69% in CI users (see Figure 8.1). A Mann-Whitney U test revealed no significant difference in visual benefit obtained by CI users (Median=40.3%) compared to NH controls (Median= 41.8%), U=74, z=-32, p=.75, r=-.06 (2-tailed) [5]. However, whilst the procedure employed for bringing A-ONLY performance in noise close to 50% correct had the intended effect in the CI group (median=53%), the procedure appeared to be unsuccessful in the NH control group (median=30%) and substantial variability in performance was observed within both groups (see Figure 8.2). Furthermore, a Mann-Whitney U test revealed that A-ONLY performance significantly differed between the two groups, U=24, z=-2.95, p<.01, r=-.58 (2-tailed), indicating that this procedure was not successful in equating auditory performance. Comparing visual benefit across individuals when auditory performance has not been equated can be problematic as the amount of visual benefit obtained is known to differ depending on levels of A-ONLY performance (Ma et al., 2009; Ross et al., 2007). Therefore, due to unequal auditory performance between groups, and for more direct comparison to previous findings reported in the literature, the following calculation was used to provide a measure of visual benefit

[5] The effect size '*r*' was calculated for the Mann-Whitney U test using the following formula: $r = \frac{Z}{\sqrt{N}}$

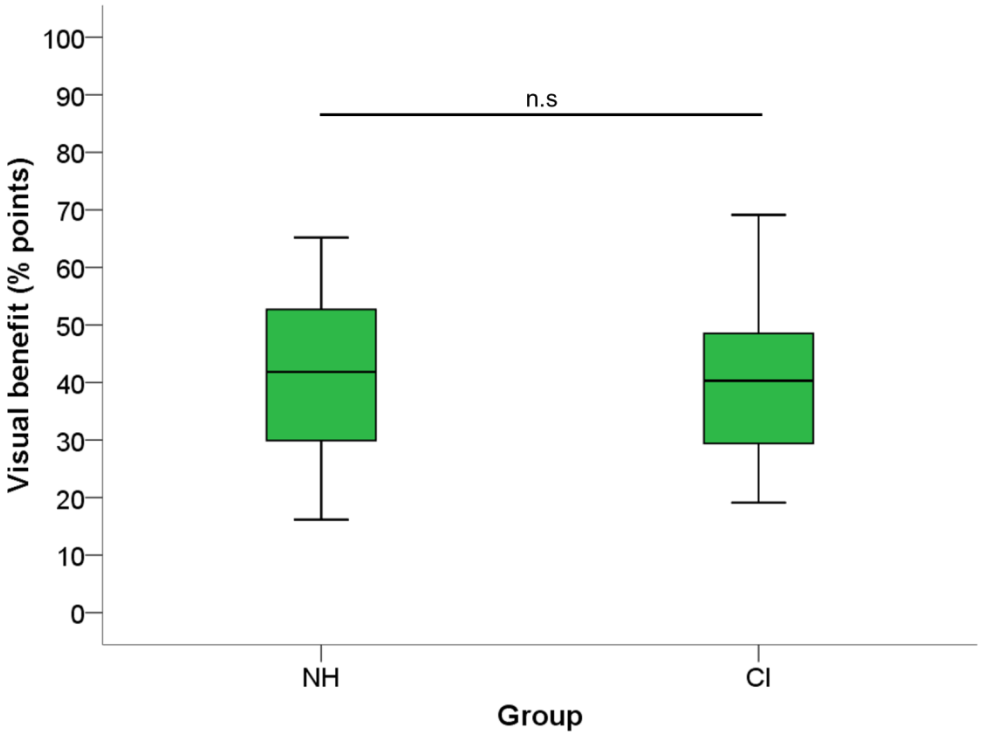


Figure 8.1: Box plot displaying visual benefit (% point difference between AV and A-ONLY performance) for NH controls and CI users. n.s = non-significant difference between groups.

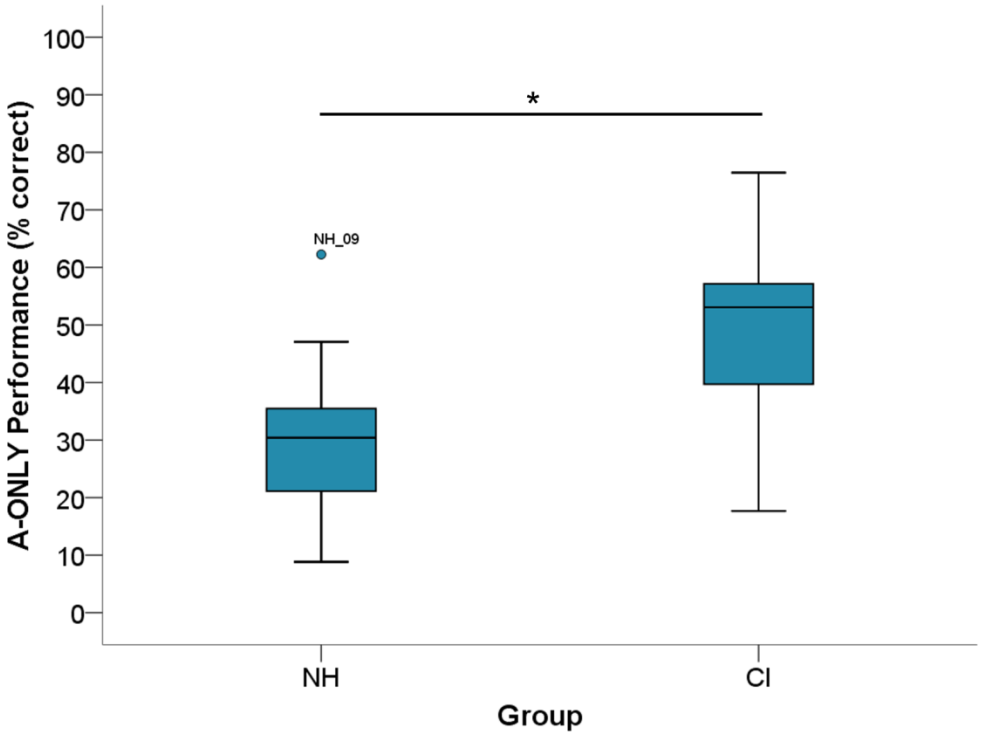


Figure 8.2: Boxplot displaying A-ONLY performance in noise (% of words correctly identified) for normal-hearing controls (NH) and CI users (CI). *p<.01, 2-tailed.

that was normalised for residual differences in auditory performance:

$$\text{Visual benefit} = (\text{AV} - \text{A-ONLY}) / (100 - \text{A-ONLY})$$

This calculation is commonly employed by studies examining visual benefit in NH listeners and CI recipients as it enables the contribution of visual speech information to be compared across individuals with differing levels of A-only performance (Desai et al., 2007; Grant et al., 1998; Hay-McCutcheon et al., 2005; Kaiser et al., 2003; Ross et al., 2007; Rouger et al., 2007; Sommers et al., 2005; Sumby & Pollack, 1954). This normalised measure of visual benefit is thus expressed as a proportion, with values closer to 1 indicating a greater amount of benefit received from visual speech information.

As with the un-normalised measure of visual benefit, all participants were seen to obtain perceptual benefit from visual speech information, with normalised visual benefit scores ranging between 0.25 and 0.91 in NH subjects and between 0.57 and 0.93 in CI users (see Figure 8.3). However, a Mann-Whitney U test conducted on the normalised scores revealed that CI users did obtain significantly greater visual benefit (Median = 0.83) compared to NH controls (Median= 0.64), U=29, z=-2.69, p<.01, r=-.53 (2-tailed). This finding replicates existing evidence provided by Rouger and colleagues (2007) and may suggest that CI users are better able to utilise and combine visual with auditory speech information to

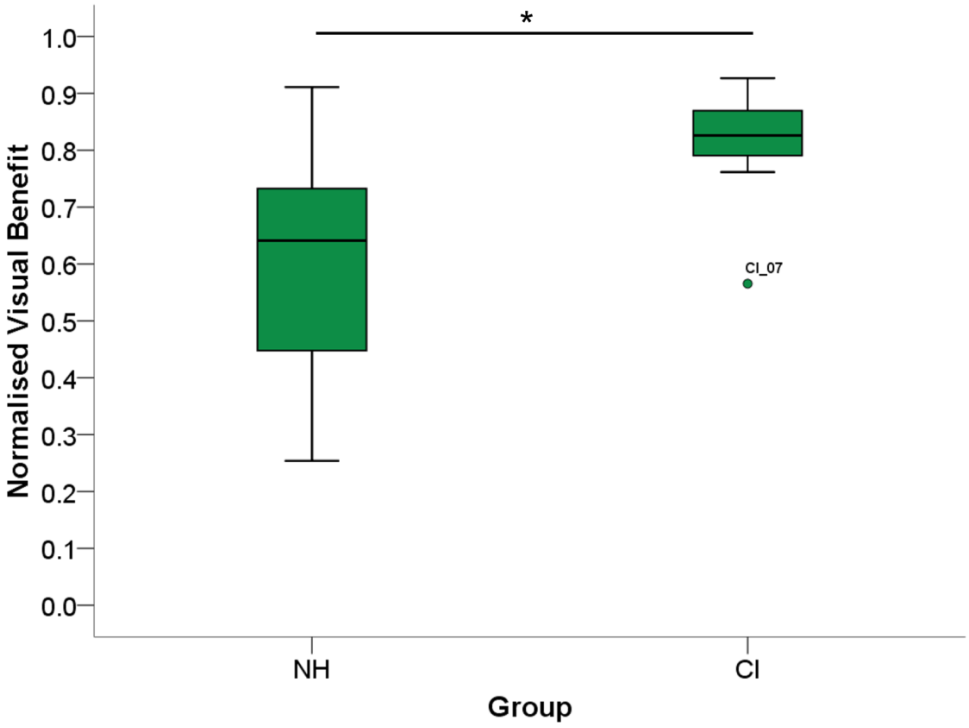


Figure 8.3: Boxplot displaying the proportion of benefit obtained from visual speech information in audio-visual conditions relative to auditory-only performance, for normal-hearing controls (NH) and CI users (CI). *p<.01, 2-tailed.

enhance speech perception in audio-visual conditions. However, it should be noted that this group difference was dependent on the method used to quantify visual benefit, being significant only when visual benefit was normalised for residual differences in auditory performance. As auditory performance was significantly greater for CI users than NH controls (Figure 8.2), it is possible the calculation used to normalise visual benefit used could have biased the results towards CI users displaying greater visual benefit compared to NH controls. Conversely, ceiling effects were observed in AV performance in noise that were particularly apparent in the CI group (CI: median=91.7%; NH: median=76.2%; see Figure 8.4).

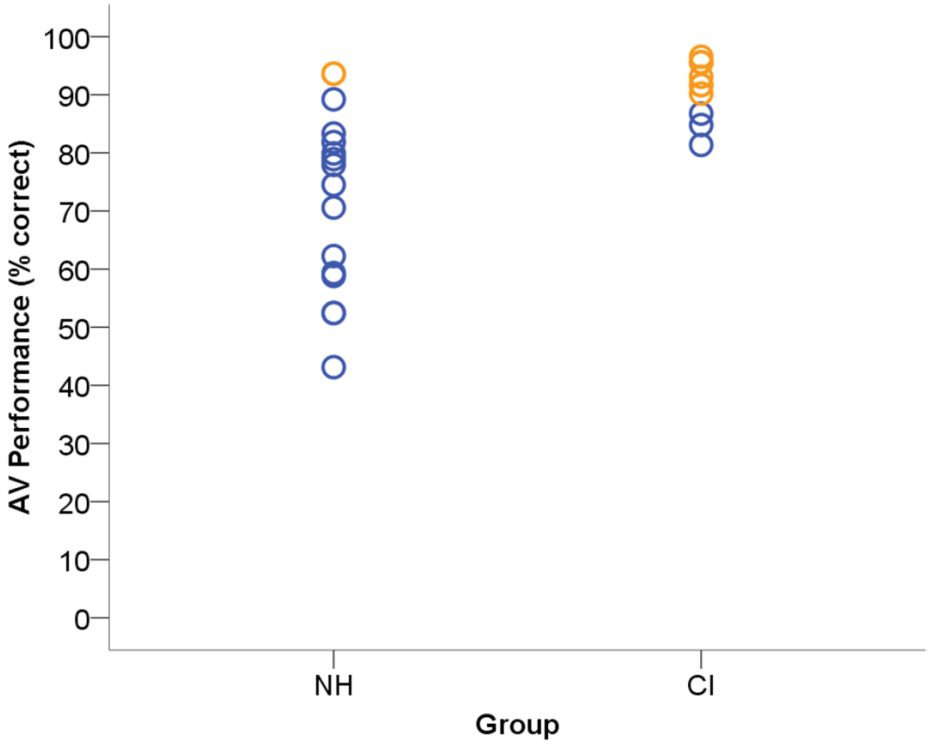


Figure 8.4: AV performance in noise (% of words correctly identified) for normal-hearing controls (NH) and CI users (CI). Orange circles represent participants with AV scores ≥90%, blue circles represent participants with AV scores <90%.

Therefore the amount of gain in performance that these participants could have obtained from visual speech information in audio-visual conditions may have in fact been constrained, and therefore underestimated by both the un-normalised and normalised measures of visual benefit.

Existing evidence demonstrates that speechreading ability is strongly and positively associated with the level of visual benefit obtained by NH listeners (MacLeod & Summerfield, 1987, 1990) and individuals with acquired SNHL (Grant et al., 1998). Therefore it is possible that the current sample of CI users may have derived greater benefit from visual speech information in audio-visual conditions compared to the NH control group due to enhanced

speechreading abilities. Indeed, section 4.3.5 demonstrated that CI users (n=16) displayed significantly greater speechreading abilities (V-ONLY performance in quiet, RAU) compared to NH controls at T2. Here, a Mann-Whitney U test also confirmed greater speechreading abilities in the current sub-sample of CI users (Median=16.9_{RAU}) compared to NH controls (Median=-4.5_{RAU}), U=38, z=-2.22, p<.05, r=-.44 (2-tailed). Bivariate correlation analysis (Spearman's correlation coefficient, r_S) revealed that speechreading ability was significantly positively associated with visual benefit in CI users (r_S=.64, p<.05, 2-tailed), accounting for 40% of the variance observed in visual benefit, and in NH controls (r_S=.52, p<.05, 2-tailed), accounting for 27% of the variance observed in visual benefit. Scatterplots of the relationship between speechreading ability and visual benefit in CI users and NH controls are provided in Figure 8.5 and Figure 8.6 respectively. Together these results suggest that the ability to utilise visual speech information in audio-visual conditions is related to an individual's level of speechreading ability, therefore the greater level of visual benefit observed in CI users compared to NH controls may have been driven by their enhanced speechreading abilities.

8.4.3 Audio-Visual Speech Integration within Superior Temporal Cortices

Functional neuroimaging studies commonly employ the 'additive model' to examine the neural mechanisms of audio-visual

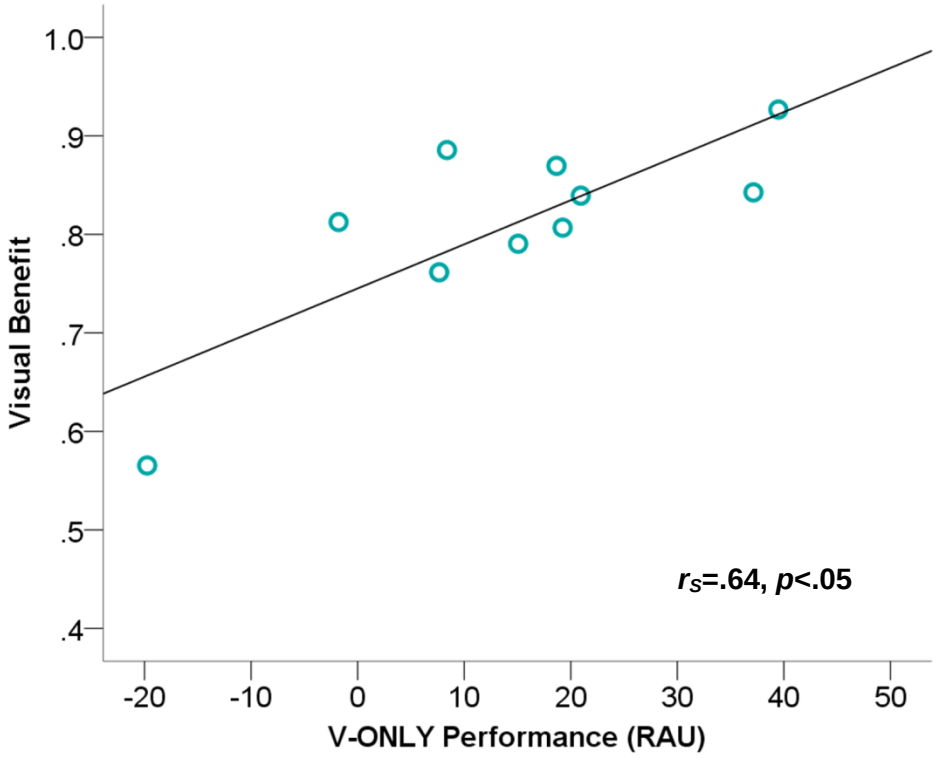


Figure 8.5: Scatterplot of relationship between speechreading ability and visual benefit in CI users.

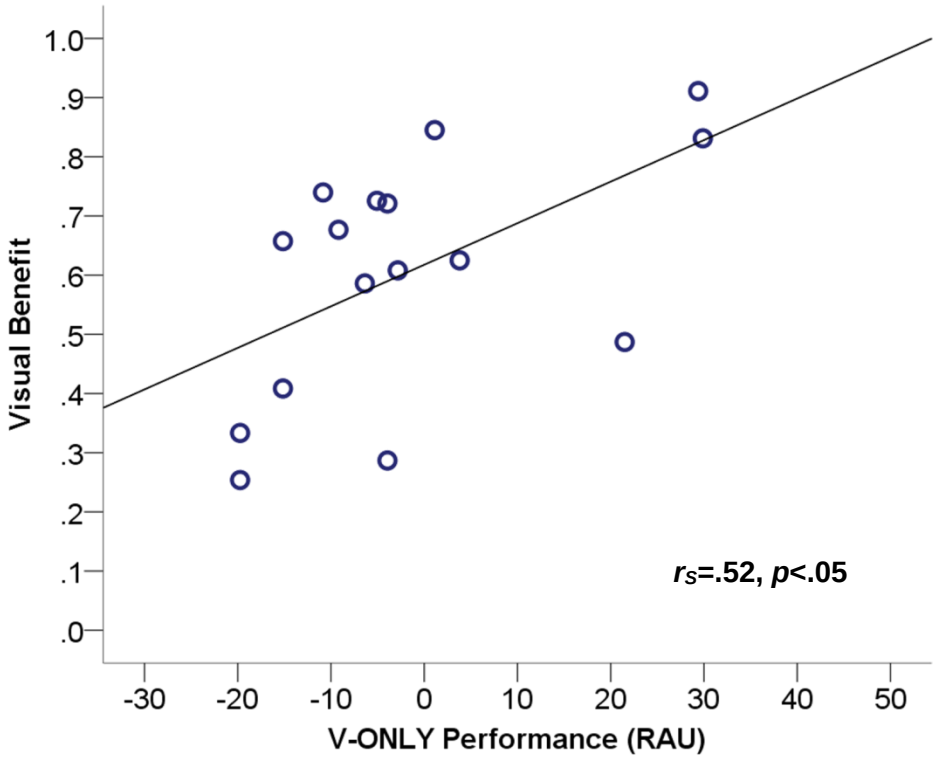


Figure 8.6: Scatterplot of relationship between speechreading ability and visual benefit in NH controls.

integration (Besle et al., 2004; Calvert & Thesen, 2004; Laurienti et al., 2005). Originating from the work of Stein's group on the response enhancement of multisensory neurons (Meredith & Stein, 1983, 1986; Stein & Stanford, 2008), the additive model predicts that a multisensory response is equal to the simple summation of its component unimodal responses. If the neural response to an audio-visual stimulus ($AV_{RESPONSE}$) is equal to the sum of the responses elicited separately by the unimodal auditory ($A_{RESPONSE}$) and visual stimuli ($V_{RESPONSE}$), i.e. $AV_{RESPONSE} = A_{RESPONSE} + V_{RESPONSE}$, then this would suggest independent processing of the two modalities and provides no evidence of multisensory integration. However, if the multisensory response exceeds this prediction then this represents response enhancement, and the neural computation underlying multisensory integration is said to be 'supra-additive' ($AV_{RESPONSE} > A_{RESPONSE} + V_{RESPONSE}$). Alternatively, if the multisensory response falls below the summative prediction this is indicative of a 'sub-additive' neural computation ($AV_{RESPONSE} < A_{RESPONSE} + V_{RESPONSE}$). The principle of inverse effectiveness states that response enhancement increases as the effectiveness of the unimodal input decreases (Meredith & Stein, 1986; Stein & Stanford, 2008). Although an extensive fronto-temporal network is thought to be involved in audio-visual speech integration (Lee & Noppeney, 2011; Sugihara et al., 2006), the STS has been implicated as a cortical binding site and is often the focal region for neuroimaging investigations of audio-visual speech integration (Beauchamp et al., 2010; Calvert et al., 2001; Lee & Noppeney, 2011; Stevenson & James, 2009; Syzick

et al., 2012; Wright et al., 2003). Indeed, both supra-additive and sub-additive integration profiles within bilateral STS have been demonstrated in line with the principle of inverse effectiveness during the integration of audio-visual speech information (Lee & Noppeney, 2011; Stevenson & James., 2009) and audio-visual object information (Stevenson & James., 2009; Werner & Noppeney, 2010).

In the present study, speech-evoked responses to A-ONLY, V-ONLY and AV speech sentences in quiet conditions were recorded from bilateral superior temporal cortices using fNIRS (see section 3.5 for methodological details). The predefined ROIs examined here are located over the posterior STC and appear to include coverage of STS (see Figure 3.21). However, due to the poor spatial resolution of fNIRS, it is not possible to ascertain, and cannot be claimed, that the cortical responses observed here originated from STS. Moreover, due to the limited depth sensitivity of fNIRS, the measurements obtained from these regions would likely be less sensitive to cortical activation within the sulci (see section 3.9.3). Here, the following calculation was used to determine the nature of audio-visual integration at the cortical level:

$$\text{AV Integration} = AV_{RESPONSE} - (A_{RESPONSE}+V_{RESPONSE})$$

where $AV_{RESPONSE}$ represents the amplitude of cortical response (beta weight) elicited by audio-visual speech stimulation within the bilateral ROI (detailed in section 3.9.3). Accordingly, $A_{RESPONSE}$ represents the amplitude of cortical response elicited by auditory-

only speech stimulation, and $V_{RESPONSE}$ represents the amplitude of cortical response elicited by visual-only speech stimulation. Thus a positive AV integration value indicates a supra-additive effect, whereas a negative AV integration value indicates a sub-additive effect. This physiological measure of AV integration was calculated for each participant.

Figure 8.7 displays the group-level cortical activation maps for the AV integration response contrast [$AV_{RESPONSE} - (A_{RESPONSE}+V_{RESPONSE})$]. Two-tailed *t*-tests (FDR corrected, $p<.05$, see section 5.2.1) revealed that no individual measurement channels deviated significantly from additivity (i.e. from zero) either within or outside of the pre-defined ROI. The fact that contrast t-values were mostly negative suggests that largely sub-additive effects were observed across both groups. Figure 8.8 displays participants' individual AV integration response profiles within the bilateral temporal-lobe ROI, indicating that only three control subjects and four CI users displayed a supra-additive AV integration response. These current findings are in line with existing studies that have demonstrated primarily sub-additive interactions and a lack of supra-additive interactions within the fronto-temporal networks (Lee & Noppeney., 2011; Sugihara et al., 2006), and within bilateral STS during AV speech stimulation in NH individuals when unimodal signals are clear (Lee & Noppeney., 2011; Stevenson & James, 2009; Werner & Noppeney, 2011); however no existing studies of cortical AV

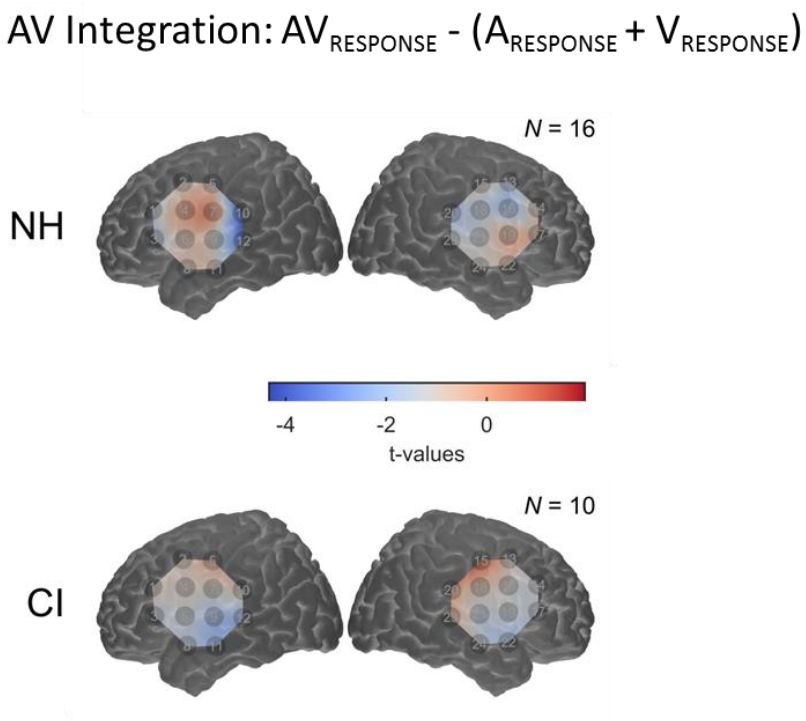


Figure 8.7: Group-level cortical activation map showing cortical activity for AV integration colour coded by *t*-value. No channels showed significant activation in the normal-hearing control group (NH) or the CI group (CI) (p<.05, FDR corrected).

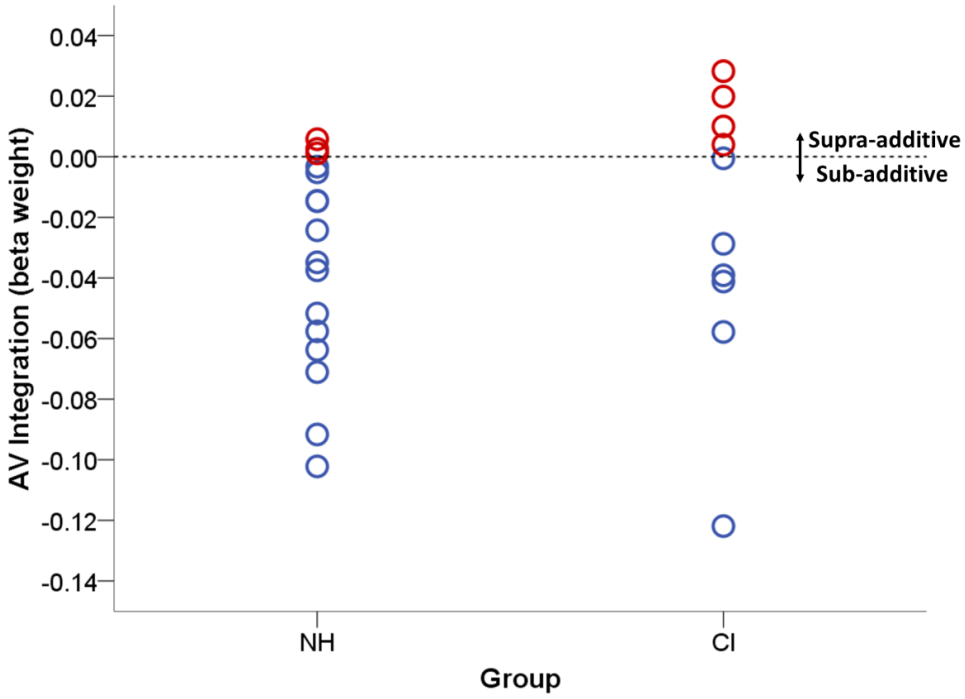


Figure 8.8: AV integration for each participant [$AV_{RESPONSE}$ - ($A_{RESPONSE}$ + $V_{RESPONSE}$)] measured within the bilateral ROI. The data are plotted for the normal-hearing controls (NH) and CI users (CI). Red circles represent those participants who displayed a supra-additive AV integration response, blue circles represent those participants who displayed sub-additive AV integration response. Y-axis reference line (zero) indicates the amplitude of AV integration response as predicted by the additive model.

interactions in CI users were identified. To understand if AV integration differed between CI users (Median = $-.015_{BETA}$) and NH controls (Median= $-.030_{BETA}$), a Mann-Whitney U test was conducted but revealed no evidence of a significant difference between AV integration values across the two groups, U=60, z=-1.05, p=.31, r=-.21 (2-tailed), see Figure 8.9.

8.4.4 Neural Correlates of Perceptual Benefit

Stein and colleagues' work on multisensory integration states that perceptual benefits are greatest when there is greater multisensory response enhancement (Meredith & Stein, 1986; Stein & Stanford, 2008). Therefore, it could be anticipated here that greater AV integration (i.e. a more positive value towards greater supra-additivity) would relate to greater perceptual gain (i.e. a higher proportion of visual benefit). However, sub-additivity is also known to play a role in audio-visual speech integration within regions of the STG and STS, at least in NH listeners (Wright et al., 2003). Thus, Spearman's correlations were conducted here to examine the relationship between the physiological measure of AV integration and the normalised measure of visual benefit. These revealed a negative association between AV integration and visual benefit in the control group (r_S=-.49, p=.05, 2-tailed). Whilst this association narrowly missed significance at the two-tailed level (p=.05), this trend indicates that a more negative AV integration value, indicating a greater sub-additive effect, related to a greater level of visual benefit obtained in the control group (displayed in Figure 8.10).

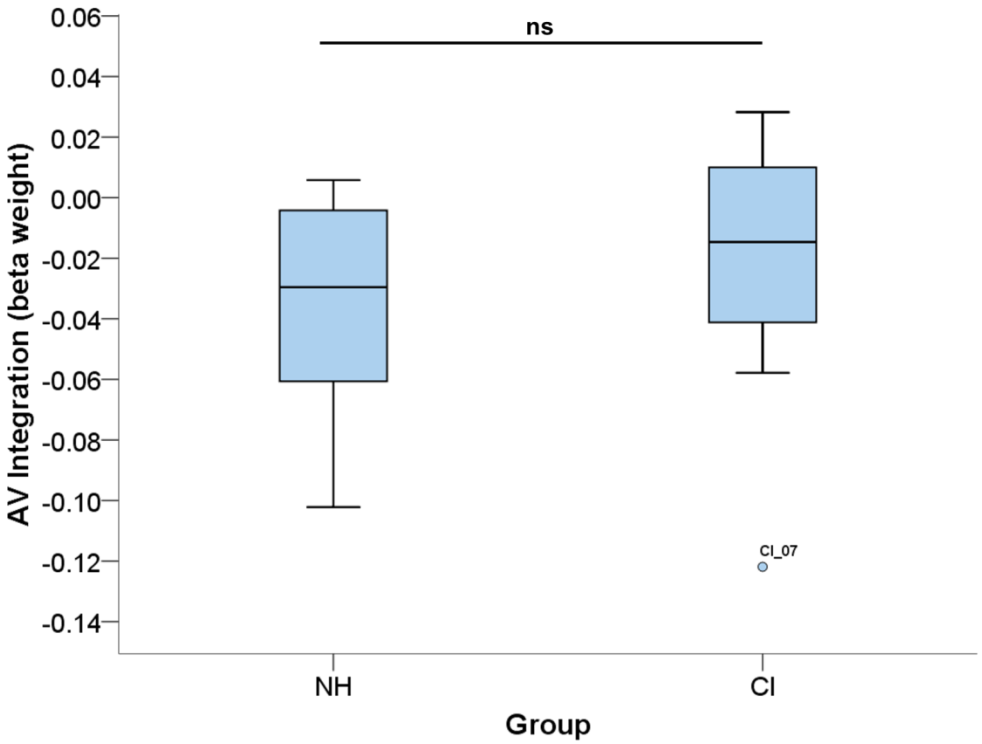


Figure 8.9: Boxplot of AV integration [$AV_{RESPONSE}$ - ($A_{RESPONSE}$ + $V_{RESPONSE}$)] measured within the bilateral ROI, plotted for normal-hearing controls (NH) and CI users (CI), ns = non-significant.

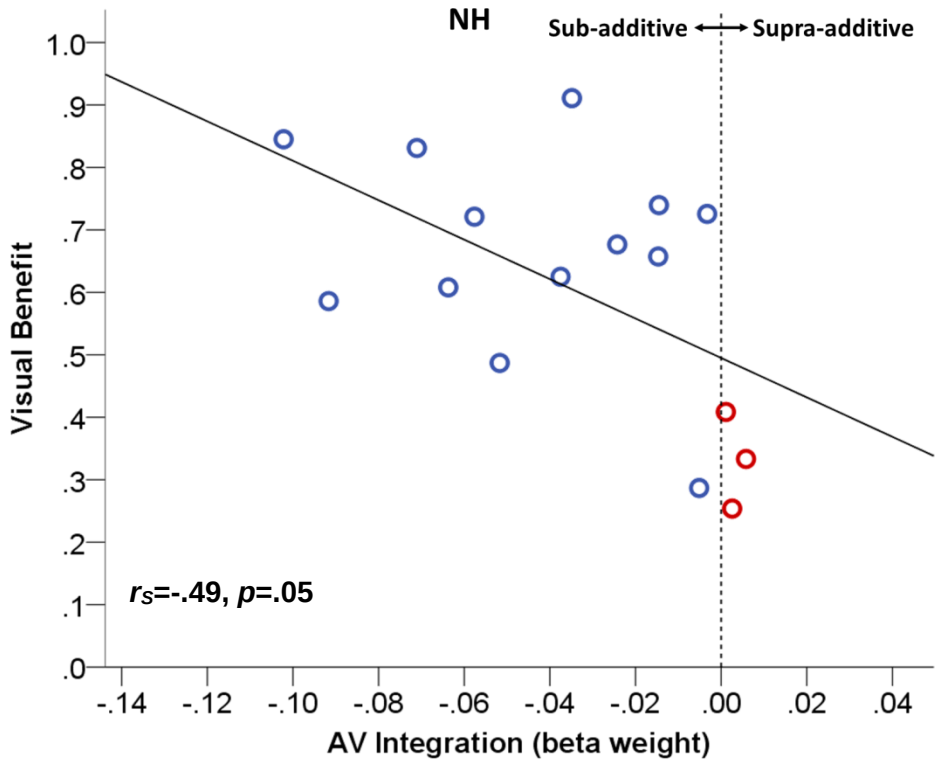


Figure 8.10: Scatterplot of relationship between AV integration and visual benefit obtained by NH controls. Red circles represent those participants who displayed a supra-additive AV integration response, blue circles represent those participants who displayed sub-additive AV integration.

Furthermore, separate analysis of the left and right temporal cortices indicated that this correlation was predominantly driven by the left hemisphere (left: r_S=-.49, p=.05; right: r_S=-.15, p=.57, both 2-tailed). This is in line with evidence from NH individuals that has implicated the left posterior STS in the integration of auditory and visual speech information (Campbell, 2008; Nath & Beauchamp, 2012) and has even suggested its causal role (Beauchamp et al., 2010). Conversely, in the CI group, a positive correlation was demonstrated between bilateral AV integration and visual benefit (r_S=.73, p=.02, 2-tailed). A scatterplot of this relationship is shown in Figure 8.11 where it can be seen that greater AV integration related to a greater level of visual benefit. Furthermore, separate correlation analyses of the left and the right temporal cortices indicated that a significant positive correlation existed in both hemispheres in the CI group (left: r_S=.71, p=.02; right: r_S=.77, p=.009, both 2-tailed).

This evidence of a differential relationship between AV integration and visual benefit in NH controls and CI users may be in line with the principle of inverse effectiveness. As fNIRS testing was conducted in quiet conditions, the auditory modality alone would have provided reliable information for NH listeners to accurately perceive the audio-visual speech stimuli. Evidence has indeed suggested that when unimodal inputs are effective, subadditivity may reflect more efficient processing of audio-visual speech information (Lee & Noppeney, 2011). Conversely, for the CI users,

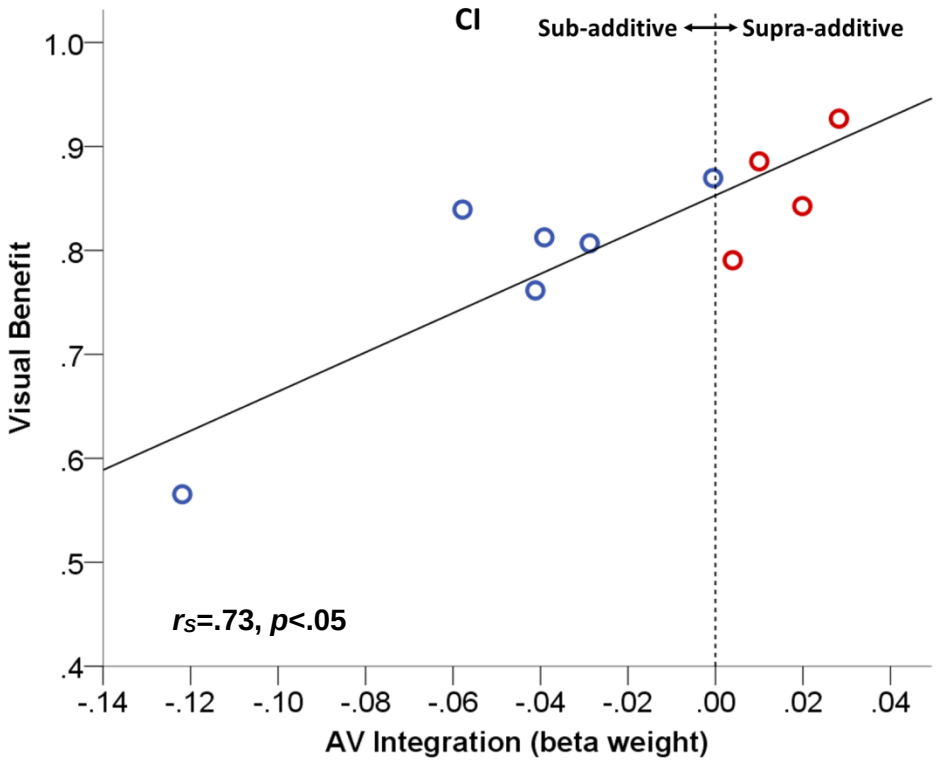


Figure 8.11: Scatterplot of relationship between AV integration and visual benefit obtained by CI users. Red circles represent those participants who displayed a supra-additive AV integration response, blue circles represent those participants who displayed sub-additive AV intgration.

auditory inputs provided by the implant remain degraded and so CI users may not have been able to perceive the audio-visual speech stimuli based on the ineffective auditory input alone. Therefore, the supra-additive integration of ineffective unimodal inputs may enable more efficient processing of audio-visual speech information in CI users. Indeed, inverse effectiveness has been evidenced within the STS, with supra-additive effects only observed at decreased SNRs of AV speech stimulation corresponding to reduced levels of unimodal intelligibility, but not at greater SNRs when unimodal signals are more highly intelligible (Stevenson & James, 2009). In this way, the inherent difference in stimulus intelligibility between the two groups during fNIRS scanning may have played a key role in

determining the differential relevance of the integration response profiles in each group.

8.4.5 Relation to Cochlear Implant Outcome

Existing research with paediatric CI users suggests the benefits of providing access to the structure of spoken language through the use of visual language, such as cued speech (Kos et al., 2009) and speechreading (Bergeson et al., 2003; 2005), for optimising auditory language outcomes following implantation. Furthermore, associations between the level of benefit gained from visual speech information and auditory speech perception and production abilities have been evidenced in paediatric CI recipients (Lachs et al., 2001). Lachs and colleagues (2001) suggest these associations may reflect common language skills such as phonological processing that can be provided by either the auditory or visual modality. In this way the authors suggest that the inherent cross-correlations between auditory and visual speech information could be exploited to enhance these general skills to thus improve auditory outcomes following cochlear implantation. Following a similar notion, it has been speculated in adults that the use of AV strategies and a synergy between the two modalities evidenced at the cortical level may be beneficial to auditory speech perception abilities following implantation (Doucet et al., 2006; Giraud et al., 2001a; Strelnikov et al., 2015), yet this remains to be examined. Therefore, whether the physiological measure of audio-visual integration and the

behavioural measure of visual benefit are related to auditory performance following implantation (CI outcome) is examined here.

Spearman's correlation analysis revealed no evidence of an association between normalised visual benefit and CI outcome, 'AUDITORY[+6]', (r_s =-.51, p=.14, 2-tailed, see Figure 8.12), or between AV integration and CI outcome (r_s =-.47, p=.17, 2-tailed, see Figure 8.13). However the sub-sample tested here likely comprised the most proficient CI users of the group as SNRs were able to be determined for these participants and they were able to complete speech perception testing in noise. Indeed, all participants displayed auditory performance in quiet scores greater than 60% correct (Median=93.9%, range=63.7 – 99.5%). Therefore, it remains possible that such associations may be evident when examining a more heterogeneous group of CI users that comprises individuals with lower auditory speech perception abilities. As such, the current results are limited only to proficient CI users.

8.5 DISCUSSION

This chapter estimated the amount of benefit that NH listeners and CI users derived from visual speech information by measuring the difference between AV and A-ONLY performance when auditory signals were degraded by the addition of noise. Behaviourally, all participants benefitted from the presentation of visual speech cues with the corresponding degraded auditory signal. As anticipated, CI

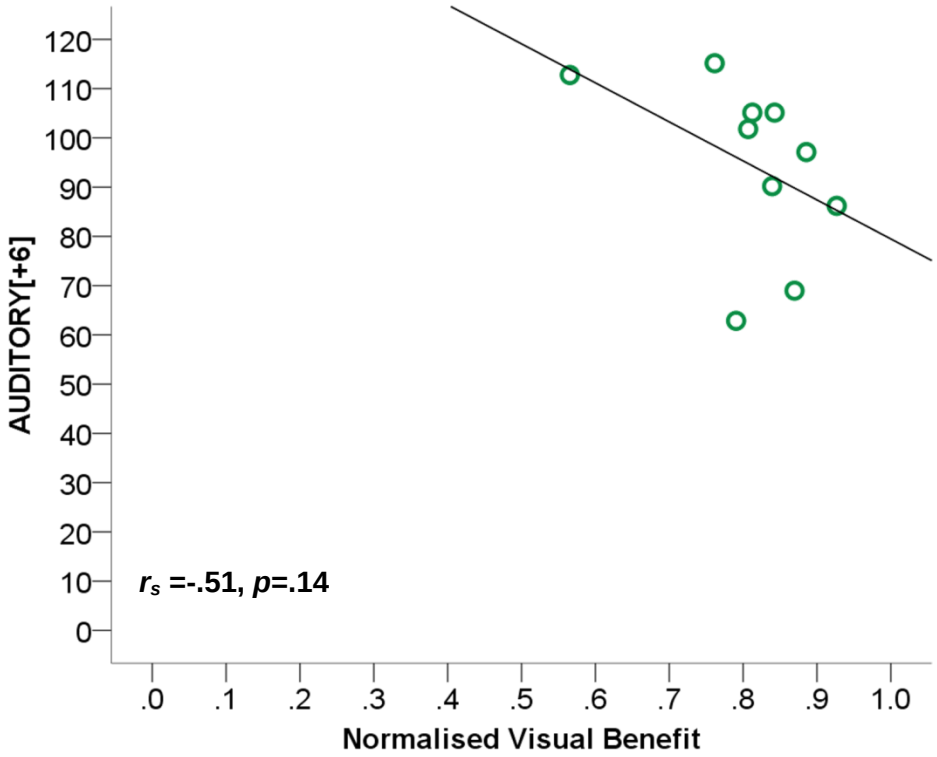


Figure 8.12: Scatterplot of relationship between normalised visual benefit and CI outcome

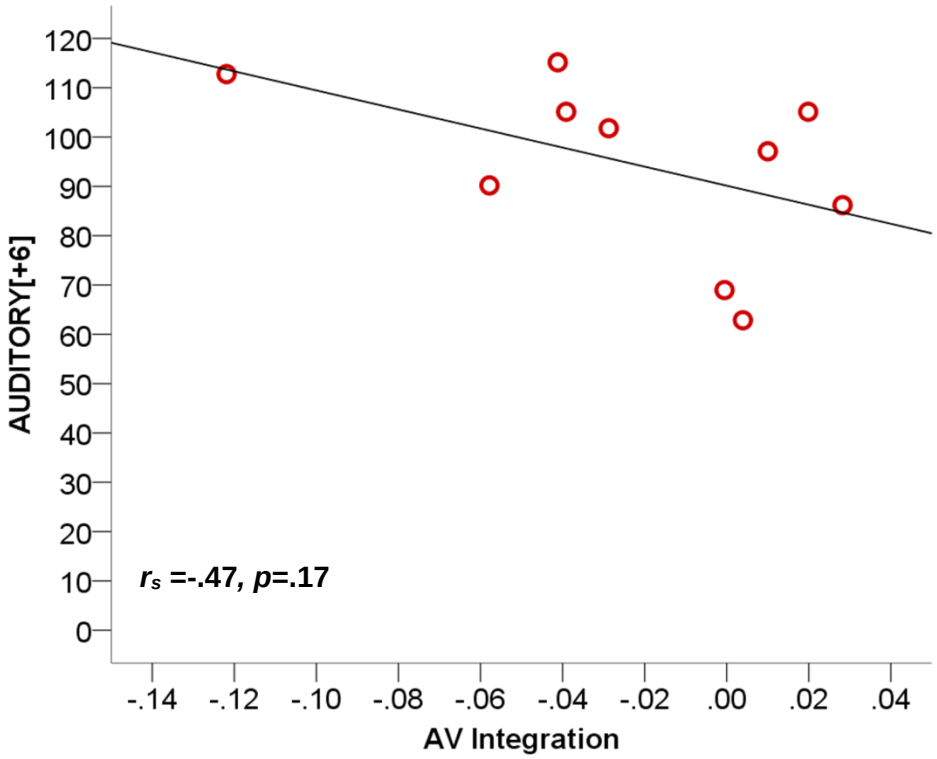


Figure 8.13: Scatterplot of relationship between AV integration and CI outcome

users were seen to gain a significantly greater amount of visual benefit compared to NH controls. This may reflect CI users' continued reliance on visual speech information and use of compensatory behavioural strategies to enable proficient face-to-face communication under challenging listening situations. However, this group difference was dependent on the exact means by which visual benefit was quantified. Specifically, a significant group difference existed only when residual differences in auditory performance between groups were taken into account using the normalised calculation of visual benefit, which many existing studies have employed (Desai et al., 2007; Grant et al., 1998; Hay-McCutcheon et al., 2005; Kaiser et al., 2003; Ross et al., 2007; Rouger et al., 2007; Sommers et al., 2005; Sumby & Pollack, 1954). Whilst it is possible that this calculation may have biased the degree of visual benefit obtained in favour of CI users displaying greater levels compared to NH controls, it is also possible that visual benefit was not fully quantified due to the ceiling effects observed in AV performance that was particularly problematic in CI users.

Indeed, the limitations of comparing absolute levels of AV and A-ONLY performance have been acknowledged, with the constraints of a bounded percent correct scale meaning this method is inadequate for truly estimating the perceptual benefit that visual speech cues can provide (MacLeod & Summerfield, 1990). During the experimental design phase, quantifying the difference between A-ONLY and AV by measuring SRTs was considered as an alternative

procedure to avoid these limitations. However, the procedure was not implemented due to concerns over whether reliable A-ONLY thresholds at 50% correct could be obtained because, for some CI users, performance may not reach that level even in quiet. It was also anticipated that measuring AV SRTs at 50% correct may not have been possible because the performance of some CI users exceeds that level using visual speech cues alone. Such complexities highlight the inherent issues when conducting psychophysical tests with CI populations and in adequately matching the auditory conditions of NH controls to enable valid between-group comparisons to be made.

Despite these methodological limitations, the results presented in this chapter do suggest that adult CI users rely heavily on and gain significant benefit from visual speech cues for enhancing speech perception when auditory information is degraded. In particular, this ability to utilise visual speech cues together with the degraded auditory signal was positively correlated with speechreading proficiency, as has previously been demonstrated in NH controls (MacLeod & Summerfield, 1987, 1990) and individuals with SNHL (Grant et al., 1998). Therefore, greater speechreading ability per se may contribute to gaining a greater amount of perceptual benefit in adverse audio-visual conditions. In this way it is possible, although speculative, that speechreading training could provide perceptual benefits to face-to-face communication in challenging listening situations that are commonly encountered in CI users' day-

to-day lives. Interestingly, recent behavioural and physiological evidence in early-deafened, bilaterally implanted ferrets has demonstrated that intermodal training with visual and auditory cues on separate trials can in fact improve localisation abilities with auditory cues alone, as well as neural sensitivity to sound localisation cues within the auditory cortex (Isaiah et al., 2014). Although this animal model suggests the facilitative role of vision in restoring auditory function following cochlear implantation (Isaiah et al., 2014; Isaiah & Hartley, 2015), the long-term benefits and any potential detrimental effects of both intermodal training (interleaved auditory and visual cues) and multisensory training (congruent auditory and visual cues) remain to be established along with the cortical plasticity effects that may accompany this perceptual training (Noel & Thelen, 2015). Whilst the current findings provide no evidence to suggest that audio-visual processes at the behavioural and cortical level provide benefit to CI success, equally they provide no evidence to suggest that a deleterious relationship exists.

Here the additive model was applied to speech-evoked haemodynamic responses acquired in quiet conditions in order to investigate the neural mechanisms of AV integration. Sub-additive AV interactions were primarily observed within bilateral superior temporal brain regions of both NH listeners and CI users. This is in line with existing studies that have demonstrated largely sub-additive AV interaction effects within bilateral STS of NH controls

(Lee & Noppeney., 2011; Stevenson & James, 2009; Werner & Noppeney, 2011). However this is the first study known to the author that has determined temporal-lobe AV speech interactions in CI users. It is important to acknowledge that the application of the additive model for estimating AV interactions from haemodynamic signals carries numerous limitations and issues of interpretation. Namely, since the additive model was based on single-cell recordings (Meredith & Stein, 1983, 1986), there are concerns regarding the validity of applying it to large and heterogeneous neuronal populations in the human cortex, and haemodynamic responses; the latter representing a step further removed from neuronal activity (Calvert & Thesen, 2004; Laurienti et al., 2005; Logothetis et al., 2001).

Compared to fMRI, these concerns are exaggerated with fNIRS as it samples from a more diffuse population. Thus, it is possible that the application of the additive model in the current study may have resulted in biased and even incomplete estimations of audio-visual speech interactions in the superior temporal cortices. For instance, the calculation AV-(A+V) can be biased towards identifying sub-additive interactions: due to the presence of non-sensory activity that is common to all stimulation conditions, such as attention and higher-order linguistic processes, adding two of these activities (A+V) but only subtracting from one (AV) in the calculation [AV-(A+V)] will result in identification of a spurious sub-additive effect (Besle et al., 2004). Furthermore, another concern is non-sensory

activation including effort and attention to stimuli that may vary across the three conditions due to differences in intelligibility. Therefore, estimating AV integration by calculating AV-(A+V) is likely to reflect differences in effort and attention across the stimulation conditions rather than purely multisensory processing and integration. Secondly, it has been demonstrated that different integration response profiles arise at the onset and offset on transient stimulations events (Werner & Noppeney, 2011). Therefore block-design paradigms for continuous speech stimulation, as employed here, are unlikely to fully characterise these intricacies of audio-visual speech interactions (Werner & Noppeney, 2011) and are not recommended for use with the additive model (Besle et al., 2004). Lastly, it has been demonstrated that visual stimuli can result in cortical deactivations in auditory brain regions (Laurienti et al., 2002), therefore summing negative and positive unimodal response values could lead to spurious supra-additive effects when subtracted from positive bimodal values (Calvert & Thesen, 2004; Laurienti et al., 2002).

For these reasons, issues of interpretation arise, and it cannot be claimed here that supra-additive computations represent a cortical mechanism of true convergence between the modalities. Rather it has been suggested that supra-additivity may simply reflect increased perceptibility due to the presence of two modalities compared to one (Calvert & Thesen, 2004; Laurienti et al., 2005). Indeed, here a greater AV integration response value (i.e. towards

greater supra-additivity) in CI users was seen to correlate with a greater degree of perceptual benefit gained in AV conditions. Conversely, in NH controls, a smaller AV integration response value (i.e. towards greater sub-additivity) was seen to correlate with a greater degree of perceptual benefit gained in AV conditions. These findings could be explained by the principle of inverse effectiveness (Meredith & Stein, 1986; Stein & Stanford, 2008). For instance, visual speech information alone does not enable proficient speech perception for either group of participants. Therefore, as auditory signals are also degraded for CI users, greater response enhancement in AV conditions enables a greater level of perceptual benefit to be obtained. However, for NH controls, auditory signals are salient and provide reliable information about the speech percept on their own. Therefore, sub-additivity may reflect a more efficient mechanism for processing AV speech in NH listeners, hence correlating with greater levels of perceptual benefit (Lee & Noppeney, 2011). In this way, the inherent difference in the effectiveness of auditory speech signals received by CI users and NH controls may result in different AV interactions within superior temporal brain regions during audio-visual speech perception.

8.6 CHAPTER SUMMARY

This chapter provides a novel investigation of the benefit gained from visual speech information during audio-visual speech perception and the neural substrates of this perceptual benefit following cochlear implantation. Speech perception ability was seen

to be enhanced by the presence of visual speech information in both NH listeners and CI users following six months of CI use. CI users were seen to derive a significantly larger amount of benefit from the presence of visual speech information when combined with degraded auditory signals compared to NH controls, although this was dependent on the method used to quantify visual benefit. A greater level of visual benefit obtained in audio-visual conditions was associated with greater speechreading abilities in both groups, suggesting that the ability to extract and perceive visual speech information per se may provide benefits for face-to-face communication in difficult listening situations. Examination of cortical audio-visual integration response profiles demonstrated that, in CI users, a greater level of perceptual benefit obtained from visual speech information was associated with a greater AV integration response within bilateral superior temporal cortices. Conversely, a greater level of perceptual benefit obtained from visual speech information in NH controls was associated with a smaller AV integration response, which was solely driven by activation within the left superior temporal cortex. Furthermore, the observed difference in the behavioural relevance of the cortical AV integration response between CI users and NH listeners may reflect inverse effectiveness due to fundamental differences in the effectiveness of unimodal inputs between the two groups. The perceptual benefit and the potential neural substrates of audio-visual speech integration identified throughout this chapter were not seen to be related to CI outcome, thus providing no evidence of

either beneficial or detrimental links between these multisensory processes and the recovery of auditory function following cochlear implantation.

9. SUMMARY AND DISCUSSION

9.1 RESEARCH AIMS

The overall goal of this thesis was to examine speech-evoked cortical activations within superior temporal cortices of profoundly deaf adults before and after cochlear implantation, and to investigate whether such measures of cortical function and plasticity could help to predict and explain individual variability in CI outcome. To address this, a group of adult CI users and NH individuals underwent longitudinal neuroimaging and behavioural speech testing. The first aim of the thesis was to examine the recovery of auditory speech perception abilities following cochlear implantation, and to evaluate the level of between-subject variability in CI outcome within the current sample of CI users following six months of CI use. Chapter four explored behavioural performance on auditory, visual and audio-visual speech perception tests and compared performance between NH individuals and CI users as well as over time. The second aim of the thesis was to establish the capability of fNIRS to repeatedly acquire artefact-free cortical activations to auditory, visual and audio-visual speech from superior temporal cortices before and after cochlear implantation. Chapter five compared the overall magnitude of speech-evoked cortical activation between NH individuals and CI users, and examined how these speech-evoked cortical activations changed from pre- to post-implantation.

Following these two fundamental steps, the third aim of the thesis was to investigate whether speech-evoked cortical activation measured before implantation was able to predict future CI outcome. This aim was addressed in Chapter six, which examined the predictive relationship between STC activation to visual speech and future CI outcome, as well as the extent to which STC activations to auditory speech were left-lateralised and the predictive value of this measure. The fourth aim of the thesis was to investigate the relationship between post-CI changes in speech-evoked cortical activation and CI outcome. Specifically, Chapter 7 examined the relationship between change in STC activation to visual speech and CI outcome, as well as how post-CI change in STC activation to visual speech related to post-CI change in STC activation to auditory speech. The final aim of the thesis was to investigate the amount of perceptual benefit that NH individuals and CI users derive from visual speech cues in audio-visual conditions, and how the two sensory modalities are integrated within the superior temporal cortices. Chapter eight compared the level of visual benefit obtained by experienced CI users and NH controls after approximately equating auditory-only performance. Furthermore, the relationship between the level of visual benefit obtained and audio-visual integration in STC was examined.

9.2 SUMMARY OF FINDINGS

9.2.1 Main Findings of Chapter 4

1) For profoundly deaf individuals, auditory performance in quiet listening conditions significantly improved over the first six months of CI use compared to their best-aided pre-implant auditory performance.

2) Following six months of CI use, auditory speech perception ability (CI outcome) varied widely between individuals, with auditory performance across the group spanning nearly the entire possible range from one to 100% correct. Individual differences in the trajectory of auditory performance over time were also observed.

3) Profoundly deaf individuals were more proficient speechreaders compared to NH individuals both before and after implantation, although individual variability in speechreading performance was observed across both groups.

9.2.2 Main Findings of Chapter 5

1) Cortical activations to auditory, visual, and audio-visual speech were successfully acquired bilaterally from the superior temporal cortices of CI users and NH controls using fNIRS. The absence of CI device-related artefacts in the fNIRS recordings confirmed the capability of fNIRS to

measure cortical activation from CI users both before and after cochlear implantation.

2) Overall, NH control subjects displayed greater cortical activation to auditory speech in the predefined posterior regions of the left and right STC compared to CI users. This group difference in amplitude of cortical activation was also observed within the right STC ROI in response to audio-visual speech. The amplitude of STC activation to visual speech was not seen to differ significantly between NH individuals and CI patients.

3) Amplitude of cortical activation to auditory and audio-visual speech was not seen to change as a function of increased CI use, nor as a function of time in the NH control group. In contrast, cortical activation to visual speech within the right ROI was seen to decrease following six months of CI use. Since this effect was observed across both NH individuals and CI users it could not be attributed to the implantation process.

9.2.3 Main Findings of Chapter 6

1) Greater cortical activation to visual speech measured from bilateral superior temporal ROIs before implantation was predictive of poorer auditory speech perception following six months of CI use.

2) Greater activation to visual speech before implantation was related to greater speechreading proficiency, longer duration of bilateral HL, and earlier age-at-onset of bilateral HL. However, STC activation to visual speech before implantation was able to provide unique predictive value above each of these clinical factors.

3) Preliminary examination suggested that such a pre-implant cortical measure may be able to predict future success with a CI with a high level of sensitivity and specificity. However this needs confirming in a larger sample of CI users.

4) A more strongly left-lateralised response to auditory speech within superior temporal cortices before implantation was predictive of better auditory performance following six months of CI use.

5) The extent to which cortical activation to auditory speech was left lateralised before implantation was able to provide unique predictive value above that of pre-implant auditory performance, as well as the duration and age-at-onset of bilateral HL. However, the unavoidable reduction in sample size (n=8), due to the means of quantifying hemispheric lateralisation, limited the validity and applicability of this cortical measure.

9.2.4 Main Findings of Chapter 7

1) A greater increase in bilateral STC activation to visual speech from pre- to six months post-implantation was associated with better CI outcome.

2) Change in STC activation to visual speech and auditory speech following implantation was positively correlated, indicating a synergistic relationship between the two modalities, rather than a visual-to-auditory sensory shift.

3) For both sensory modalities, a greater post-implantation increase in STC activation was associated with a shorter duration of bilateral HL and a later age-at-onset of bilateral HL, suggesting that these well-established clinical characteristics may influence the individual's future capacity for cortical plasticity that may be important for CI success.

9.2.5 Main Findings of Chapter 8

1) CI users derived a significantly greater level of visual benefit compared to NH listeners when auditory-only performance was approximately equated across the two groups. However, this group difference was dependent on the method used to quantify the level of visual benefit, being significant only when residual differences in auditory-only performance between groups were taken into account when calculating visual benefit.

2) Application of the additive model of multisensory integration to bilateral STC activations indicated that fNIRS responses were primarily sub-additive in both groups.

3) For NH individuals and CI users, this physiological measure of AV integration was correlated with the level of visual benefit. However, the direction of this relationship differed between the two groups, likely due to inherent difference in stimulus intelligibility between the two groups.

9.3 GENERAL DISCUSSION

9.3.1 Suitability of fNIRS for Assessing Cortical Activation during Speech Stimulation with a Cochlear Implant

The results of Chapter 5 provide confirmation of the suitability of fNIRS for measuring cortical responses to speech stimulation in adults with cochlear implants. Importantly, time-course analysis revealed that fNIRS recordings were unaffected by artefacts generated by the CI device that are known to impede recordings obtained by other, more conventional, neuroimaging techniques such as EEG (Debener et al., 2008; Gilley et al., 2006). Following Sevy and colleagues' demonstration of the ability of fNIRS to measure artefact-free speech-evoked cortical activations in paediatric CI users in 2010, reports of the successful application of fNIRS in adult CI populations have recently begun to emerge in the literature, yet remain scarce (Bisconti et al., 2015; Chen et al., 2015a; Olds et al., 2015). Whilst the current study adds to this relatively limited number of existing studies, moreover, it provides

an important and unique demonstration of the feasibility of using fNIRS repeatedly with the same individuals throughout the cochlear implant process. In particular, throughout the current study, no adverse events occurred such as participant discomfort due to optode placement over the newly implanted CI device or by the placement of elastic straps near to the surgical site of incision. Furthermore, the fact that no participants withdrew from the study may reflect the low-level of participant tolerance that was demanded by the fNIRS scanning procedure employed here. Therefore, due to its non-invasive, safe and CI–compatible nature, fNIRS provides an attractive alternative to invasive methods such as PET that is currently most commonly employed for cortical imaging in CI users (e.g. Aggarwal & Green, 2012; Giraud et al., 2001b; Green et al., 2008; Petersen et al., 2013; Rouger et al., 2012; Strelnikov et al., 2015) but is limited for repeated use due to the cumulative effect of radionuclide exposure. Thus, fNIRS may provide an ideal tool for imaging cortical function in CI users longitudinally and furthering our currently limited understanding of cortical plasticity following implantation, and its role in the recovery of auditory speech perception.

Considering the clinical applicability of fNIRS, existing studies have demonstrated its potential as an objective measure of speech perception ability in adult CI users (Pollonini et al., 2014; Olds et al., 2015). Whilst examining the use of fNIRS as an objective measure of speech perception was not the aim of the current

research, the results of Chapter 5 do suggest that fNIRS was able to detect differences in auditory-speech evoked cortical activation at the group-level between NH listeners and CI users, possibly reflecting inherent differences in the intelligibility of the speech signal provided by a normally functioning cochlea compared to a CI. However, practical issues that arose during the current study highlighted potential limitations of the applicability of fNIRS at the individual level. For instance, surgical placement of the implant differed between individuals and in one instance precluded measurement from two fNIRS channels within the STC ROIs. Furthermore, likely due to attenuation by dark or thick hair, inadequate levels of light intensity being transmitted and received between source-detector pairs caused the exclusion of some fNIRS recordings (see Table 5.2). Thus, the current longitudinal application of fNIRS highlights that practical constraints may in some instances limit the use of fNIRS for certain individuals, which is important when considering its suitability as a clinical tool for monitoring individual outcomes. However, the development of hair-penetrating brush optodes is likely to help improve this situation in the future (Khan et al., 2012).

9.3.2 Predicting Cochlear Implant Outcome from Speech-evoked Activations

The results of Chapter 6 indicate that greater STC activation to visual speech before implantation was associated with greater speechreading proficiency and was predictive of poorer auditory

speech perception abilities following six months of CI use. Previous reviews of the literature have highlighted that the effect of speechreading on cortical function during profound deafness and its relation to future success with a CI had until now remained unexamined (Campbell et al., 2014; Lyness et al., 2013). The current study thus provides an original examination of speechreading activation as a pre-implant cortical predictor of CI success and represents an important contribution to the existing knowledge base. Specifically, evidence of a deleterious relationship between the extent of cross-modal plasticity within auditory brain regions and future CI outcome have been revealed by studies of resting-state metabolism (Lee et al., 2001; Lee et al., 2007a) and functional activations evoked by low-level visual stimuli (Buckley & Tobey, 2011; Doucet et al., 2006; Sandmann et al., 2012). Such evidence has fuelled speculations (as noted by Campbell et al., 2014; Lyness et al., 2013) that the use of visual language may in the same way occupy and thus compromise the ability of auditory brain regions to successfully process auditory inputs, thus limiting future CI success. This has been somewhat supported by a preliminary indication that speechreading activation measured soon after CI activation negatively predicts later CI outcome (Strelnikov et al., 2013).

Whilst the findings presented in Chapter 6 indeed indicate an inverse relationship between visual speech-evoked STC activation prior to implantation and future CI outcome, importantly, the

examination of STC activation to both auditory and visual speech revealed no evidence of an inverse relationship between the two sensory modalities. In addition, there was no evidence to suggest that speechreading ability before implantation was predictive of auditory-only performance, corroborating existing reports based on auditory-only word identification in larger samples (Holden et al., 2013). Similarly, Summerfield and Marshall (1995) found no evidence of a relationship between pre-implant speechreading ability and a composite measure of the ability to identify speech and environmental sounds following nine months of CI use. Therefore, the current findings provide no evidence to suggest that the use of speechreading as a compensatory strategy during deafness, and the processing of visual speech within STC, limited the successful recovery of hearing through cochlear implantation due to the compromise of auditory speech processing resources. Existing evidence in fact stresses the importance of access to language regardless of modality for future linguistic ability (Mayberry et al., 2002) and for the critical establishment of amodal neural networks, such as those involved in phonological processing that can support future language learning (MacSweeney et al., 2008b). The findings of Chapter 6 suggest that the posterior regions of the left STC may maintain their linguistic function during deafness by being recruited for the processing of visual speech information. Similar findings have been evidenced in deaf BSL users, whereby these cortical regions are recruited to extract meaning and phonological information from sign language, thus undergoing plasticity but

maintaining linguistic function (Cardin et al., 2013). In this way, phonological processing (thought to be an important cognitive skill for achieving proficient levels of sentence-based speechreading, Andersson et al., 2001) of visual speech information within STC may enable maintenance of these amodal language networks in the absence of reliable auditory speech inputs. Of course, such interpretations are only speculative here in the absence of appropriate phonological tasks employed during fNIRS scanning.

With the aforementioned in mind, it is possible that the inverse relationship observed in Chapter 6 between STC activation to visual speech and CI outcome may not be due to the colonization of modality-specific auditory speech processing resources; rather, the predictive relationship may be mediated by other interrelated factors that adversely influence the ability to perceive auditory speech inputs provided by a CI. For instance, the data were suggestive of a possible split into two groups (see Figure 6.1), one comprising only prelingually deaf individuals who displayed the poorest CI outcome and greatest activation to visual speech, and the other comprising primarily postlingually deaf individuals who displayed the greatest CI outcome and lowest activation to visual speech. Furthermore, the age-at-onset of bilateral HL was the only non-cortical factor examined here relating to the CI users' clinical history of deafness that was seen to correlate positively with the amplitude of cortical activation to visual speech and that was able to independently predict CI outcome. It is therefore possible that the

age-at-onset of deafness may contribute to variability in CI outcome through the effects it exerts on the STC language networks.

Existing PET studies of adult CI recipients provide evidence to suggest that the language networks may develop differently in pre-lingually compared to post-lingually deafened individuals (Naito et al., 1995, 1997; Petersen et al., 2013), and that cross-modal plasticity may exert effects on CI outcome in pre-lingually but not post-lingually deaf CI users (Buckley & Tobey, 2011). In this way, the use of direct cortical measures of the integrity of the language networks may enable more accurate prognosis of CI outcome. Indeed, Chapter 6 demonstrated that the amplitude of STC activation to visual speech before implantation was able to provide additional predictive value after the influence of the age-at-onset of bilateral HL on CI outcome had been accounted for. These current findings may suggest that a direct measure of cortical function acquired before implantation, such as that employed here, may provide additional key information about the development of the language networks in profoundly deaf individuals and the potential of these to adapt to electrical stimulation, which could contribute to the more accurate prediction of CI outcome. Furthermore, Fujiwara et al. (2008) employed a similar visual language task during PET scanning of profoundly deaf children. Their findings provide a rudimentary indication that cortical activation to visual speech could provide objective information about the differential development and function of language networks in profoundly deaf children

(Fujiwara et al., 2008). The use of a visual language task may also avoid the issues associated with using an auditory language task to assess cortical function in a heterogeneous group of profoundly deaf individuals, such as those encountered in the examination of LI in Chapter 6. Future research should therefore assess whether cortical imaging with visual language tasks could provide meaningful information about the speech processing networks prior to implantation that could inform prognosis.

9.3.3 The Association between Cortical Plasticity and Speech Perception after Cochlear Implantation

To investigate cortical plasticity following implantation, Chapter 7 compared speech-evoked activation acquired before implantation to that acquired six months after CI-activation. The results of Chapter 7 indicated that the direction and degree of post-CI change in bilateral STC activation to visual speech varied across the group of CI users. Specifically, a significant positive correlation was observed with CI outcome, whereby a greater relative increase in STC activation to visual speech following implantation was associated with more proficient auditory speech perception following six months of CI use. Thus, individual variability in this post-CI change in cortical activation was able to explain a proportion (59%) of the variability observed in CI outcome. Importantly, existing evidence has suggested a reduction in right STC activation to visual speech from an early to a later stage following implantation (Rouger et al., 2012). Whilst group-level analysis presented in Chapter 5

replicated these findings of a reduction in right STC response to visual speech at 6 months post-CI activation, this effect of time was evident across both groups (NH listeners and CI users). Furthermore, the lack of a group – time interaction indicates that this effect of time was not specific to the CI rehabilitation process, thus challenging the validity of Rouger and colleagues' study that did not collect repeated measurements in NH controls. The authors speculated that the reversal of speechreading activation enabled the recovery of auditory function by allowing for audio-visual integration to take place. In the current study, analysis at the individual level indicated that in fact the opposite was true: CI users who displayed the greater increase in STC activation to visual speech also displayed the higher level of auditory performance with a CI. The current findings indicate that examining cortical plasticity at the individual level could contribute to a better understanding of the role of cortical factors in variable CI outcome.

Importantly, to the author's knowledge, the current study provides an original demonstration of the ability of fNIRS to detect changes in cortical activation from pre- to post-implantation that are functionally related to CI performance. Therefore, from a methodological perspective, the findings confirm that fNIRS offers a safe and non-invasive tool for studying functionally-relevant cortical plasticity in adult CI users. Such a measure of cortical function in CI users has implications for monitoring progress post-operatively, particularly in difficult-to-test populations, such as young children

and individuals with complex needs, where behavioural assessment of speech perception may be unreliable or not possible. The potential clinical applications are discussed further in section 9.5.1.

Following the receipt of a CI, individuals need to learn to match the new auditory speech inputs onto their existing stored auditory representations as well as to form new associations with visual speech cues (Strelnikov et al., 2009). PET studies have also indicated that the recovery of auditory speech perception may place demands on visual processing in both adult (Doucet et al., 2006; Giraud et al., 2001a; Giraud et al., 2001b) and paediatric CI recipients (Kang et al., 2004), supposedly indicating a facilitative mechanism between the sensory modalities after implantation. It is possible that a greater increase in STC activation to visual speech observed in the present study may reflect greater development and more refined association between the two modalities, which may provide benefits when deciphering the degraded auditory speech signal. Further to this, a moderate positive correlation was observed between post-CI change in activation to auditory and visual speech. This provides evidence that cortical activation to speech developed in parallel between the two modalities, and may suggest that a synergistic relationship between audition and vision exists following implantation. There was thus no evidence to suggest a trade-off between the processing of auditory and visual speech information. It is therefore possible that this parallel change in bilateral STC activation to visual and auditory speech after

implantation may reflect the importance of audio-visual strategies during the recovering of auditory function. Furthermore, due to the shared variance between the change in STC activation to auditory and visual speech, these post-CI changes may reflect plasticity changes of linguistic networks that are thought to be amodal rather than sensory-specific (MacSweeney et al., 2008a; MacSweeney et al., 2008b; Petitto et al., 2000; Straube et al., 2012).

The direction and degree of post-CI change in STC activation to auditory and visual speech were both associated with duration and age-at-onset of bilateral HL. Specifically, a longer duration of deafness and an earlier age-at-onset related to a lesser increase, or a greater decrease, in speech-evoked activation from pre- to post-implantation. In this way, it seems that language systems may be modifiable, but to varying degrees, depending on when the cortical networks supporting language developed relative to the onset of deafness and how they have been modified by sustained deprivation of auditory input. Evidence suggests that such associations between auditory and visual speech are largely formed during a sensitive period that occurs in early childhood, with a lack of auditory inputs during this sensitive period resulting in weak and inconsistent audio-visual binding abilities in paediatric CI users (Schorr et al., 2005). Therefore, CI users in the current sample with a pre- or peri-lingual onset of deafness may not have successfully formed strong associations between auditory and visual speech representations during this sensitive period. Hence, as adult

CI recipients, they may be less able to form associations between auditory and visual speech cues. Furthermore, greater deterioration of phonological representations and processing ability has been evidenced with a longer duration of auditory deprivation (Lazard et al., 2010b; Lyxell et al., 1998, 2003), and could thus impact on the ability to form associative links between the two modalities. In this way, the individual's clinical history of deafness may constrain the extent of adaptive cortical plasticity observed following implantation, thus limiting the amount of CI benefit obtained.

It is interesting to note that those individuals displaying greater STC activation to visual speech before implantation were also seen to show the smallest increase, or greater decrease, in STC activation to visual speech following implantation. Recall that Chapter 6 revealed no evidence to suggest that the processing of visual speech information within STC compromised its responsiveness to auditory inputs. In addition, Chapter 7 revealed no evidence to suggest that the reversal of STC activation to visual speech was essential for the restoration of auditory inputs or function. Taken together, the current findings may suggest that STC activation to visual speech both before and after implantation is unlikely to be directly detrimental to CI success. Rather, it is possible that success with a CI may largely depend on the ability of the STC linguistic processing resources to adapt to implantation, and that STC activation to visual speech before implantation may have acted as a proxy for this here. Overall these findings indicate that

assessing cortical plasticity post-operatively may be crucial in order to more fully understand the contribution of cortical factors to individual variability in CI outcome.

9.4 LIMITATIONS

9.4.1 Observational Longitudinal Approach

As one of the overall aims of the thesis was to examine cortical plasticity in CI users, an observational longitudinal approach was employed as the most appropriate way to detect changes in cortical activation over time whilst CI experience increased. However, due to this observational approach, several factors could have changed over this period of time that were not, or were unable to be, controlled for. For instance, no manipulation or control was exerted over factors such as the subjects' HA use and mapping of the CI devices. It is therefore possible that amplitude of cortical activation may have reflected this variability in individuals' HA use, CI MAPs, and thus the overall level of auditory stimulation provided and perception of sound intensity. Secondly, it is important to note that the potential effects of any global changes were not controlled for over time. For instance, other non-auditory, higher-level processes such as attention and effort could have varied as a function of increased CI use, potentially influencing both cortical activation and CI outcome. Indeed, existing studies have shown that attention can modulate the amplitude of cortical response to auditory (Grady et al., 1997; Pugh et al., 1996) and visual speech (Pekkola et al., 2006) within superior temporal brain regions. Therefore, a greater

increase in speech-evoked activation from pre- to post-implantation may reflect a greater increase in attention to speech information. Individuals who are more attentive and commit more effort to deciphering the auditory signal may be more engaged with their rehabilitation, a factor which has been shown to predict greater success with a CI (Knutson et al., 1991). In addition, it is possible that any change in cortical activation over time may also reflect confounds of the repeated-measures design, such as learning effects due to familiarisation with the testing protocol and materials.

Furthermore, the correlational approach taken here to explore relationships between cortical and behavioural measures does not allow causation to be inferred. Specifically, whilst cortical adaptations to auditory re-afferentation may underlie perceptual improvements, it is also possible that improvements in perceptual abilities due to increased CI use feedback to modify cortical activations over time (Giraud et al., 2001b). Nevertheless, changes in cortical activation (specifically in response to visual speech, reported in Chapter 7) were correlated with both the individual's clinical history of deafness and auditory performance, indicating that these changes were functionally relevant despite the aforementioned uncontrolled factors. Moreover, the findings reported in Chapter 6 are potentially of clinical significance in that cortical responses measured before implantation were able to predict behavioural outcome measured at a later point in time, and could lead into the development of clinically useful tools.

9.4.2 Quantifying Recovery of Auditory Speech Perception

Whilst the current study aimed to quantify recovery of speech perception ability following implantation, Chapter 4 indicated that some participants performed at or near to ceiling as soon as one month after CI activation, with ceiling effects also observed six months after CI activation. Therefore, for some individuals, it was not possible to accurately or fully estimate their level of auditory performance with a CI due to the constraints of speech perception testing in quiet conditions and use of a percent correct measurement scale. Whilst this could be addressed by conducting speech perception testing in noise, Chapter 8 indicated potential problems that are associated with such methods, including participant discomfort. This highlights the inherent difficulties associated with measuring changes in and absolute performance in such a heterogeneous group of CI users.

Existing studies have demonstrated that performance can continue to improve beyond the first six months of CI use (Lazard et al., 2012a; Tyler et al., 1997; UKCISG, 2004a). Therefore, the current study's findings may not extend to predicting longer-term outcomes. Conversely, evidence exists for a critical learning phase over the first six months, after which no significant improvements to auditory performance are seen (Lenarz et al., 2012; Rouger et al., 2007). For instance, a recent estimate indicating that auditory performance reaches a stable plateau by 6.3 months, with auditory

performance rising to 90% of the final level reached at two years by 6.9 months post-CI activation (Holden et al., 2013). As plasticity of the language networks can also occur rapidly (Lee et al., 2007b; Rouger et al., 2012; Thulborn et al., 1999) it was preferable in the current study to repeatedly measure both cortical activation and performance in this initial and important period of recovery. In addition, pragmatically, this was an ambitious yet achievable target within the time constraints of the PhD. It is also important to note that, due to the controlled experimental conditions and sentence tests employed here, it is likely that measures of performance were not reflective of the individual's ability in every-day listening situations. Therefore, use of more ecologically valid tests would improve the validity and generalisability of future findings. An exciting prospect for future fNIRS research with CI users is the recent advent of portable fNIRS systems (Ayaz et al., 2013; Piper et al., 2014) that could be used to image cortical function during speech perception in naturalistic situations.

9.4.3 Measurement of Speech-evoked Cortical Activation

A pertinent drawback of fNIRS is that it does not permit imaging of the underlying anatomy of the brain, meaning that individual differences in anatomy were not accounted for in the present study. In the current study, as the optodes were placed in relation to anatomical surface landmarks, it is likely that variability existed across subjects in the exact origin of cortical responses. Furthermore, due to both the limited spatial resolution of fNIRS

(Lloyd-Fox et al., 2010; Okada & Delpy, 2003; Toronov et al., 2007) and the 3cm separation between source and detector optodes of the measurement array employed here, it is not possible to localise the precise cortical origin of activations. Therefore, whilst loose reference is made to posterior superior temporal cortices as the regions of interest throughout the thesis, it is possible that fNIRS measurements were sensitive to haemodynamic changes occurring in neighbouring cortical regions. Whilst several technological advancements now enable more accurate estimation of the anatomical source of cortical activation through the use of 3D digitizers and spatial-registration software (Singh et al., 2005; Tak & Ye, 2014; Tsuzuki et al., 2012; Tsuzuki & Dan, 2014), it was not possible to utilise the Hitachi ETG-4000's magnetic 3D Probe Positioning Unit in the current study as a pilot study indicated that measurements were adversely affected, likely due to the sound-attenuated room's metal doors being in close vicinity of the magnetic receiver and transmitter unit. Given that CI candidates undergo MRI scanning prior to implantation, the ability of future fNIRS studies to localise the origin of cortical activations may be improved by the co-registration of digitized optode positions to the pre-implant anatomical image.

Regardless of the accuracy with which the origins of cortical activations can be localised, the task of identifying those aspects of cortical activation that are specific to speech processing would be facilitated by the use of suitable control conditions, such as

spectrally-rotated speech or signal correlated noise to control for the spectro-temporal properties of the auditory speech signal (Scott et al., 2000; Stoppelman et al., 2013). Indeed, existing research has demonstrated that the extent to which STC is activated by speech stimuli compared to unintelligible control stimuli may correlate with CI outcome (Olds et al., 2015), and that such a 'speech-specific' response may distinguish proficient rehabilitated CI users from non-proficient inexperienced CI users (Giraud et al., 2001b). However, non-speech control stimuli were not used in the present study due to fNIRS scanning time constraints: a trade-off exists between the duration of the stimulus presentation paradigm and level of subject comfort, fatigue, compliance, and occurrence of motion artefacts within the data (Orihuela-Espina et al., 2010).

9.4.4 Sample of Cochlear Implant Users

The relatively restricted sample size of the current group of CI users precluded the assessment of the predictive value of multiple pre-implantation factors. In particular, in Chapter 6 it was not possible to conduct multiple linear regression analyses to meaningfully examine how much variability in CI outcome pre-implant cortical activation was able to explain relative to that explained by several known influential clinical factors (Blamey et al., 2013; Lazard et al., 2012a). However, as the aim of the current study was not to build a comprehensive predictive model of CI performance incorporating both cortical and clinical factors, the study was not powered for this purpose. Instead, the study was powered to detect changes in

performance over time (see section 3.3.3), which were indeed evident in the current sample (reported in section 4.3.4). Furthermore, although restricted in some senses, the current sample size is relatively large compared to existing longitudinal neuroimaging studies with CI users that are often seen to employ samples of less than 10 and in the absence of repeated-measures control data (Green et al., 2008; Strelnikov et al., 2013, 2015; Rouger et al., 2012). Therefore the current findings based on data obtained from 100 testing sessions conducted with NH controls and CI users across three time points should not be undervalued in their contribution to the field. Furthermore, the CI users who participated in this study were seen to be heterogeneous in terms of their clinical history of deafness as well as other individual factors (see Table 4.1). Whilst the heterogeneity of the sample may not favour 'clean' interpretation of the data, the current sample may be more representative of CI candidates that present across UK clinics, therefore potentially enhancing the generalisability of the current results.

9.5 DIRECTIONS FOR FUTURE RESEARCH

9.5.1 Future Clinical Applications in Cochlear Implantation

The findings presented throughout this thesis indicate the ability of fNIRS to measure speech-evoked cortical activations and associated functional relationships with auditory speech perception abilities in adult CI users. Importantly, the current study demonstrated that fNIRS measurements of brain activity obtained before implantation

were able to predict future CI outcome. Moreover, fNIRS measurements were able to offer unique predictive value above well-established clinical characteristics, indicating the potential of fNIRS as a tool to improve and deliver more accurate clinical prognoses for CI candidates. However, caution should be exercised in drawing firm conclusions as the current study provides the first known examination of the prognostic value of brain imaging using fNIRS in cochlear implantation.

Building on these preliminary but promising results, future work should look to determine in a larger sample of CI users whether brain imaging using fNIRS could offer unique predictive value when the combined influence of well-established clinical characteristics are accounted for (e.g. duration of bilateral HL, age-at-onset of HL and speechreading ability). This could be examined in future studies using multiple linear regression analyses to estimate: 1) the proportion of variability in CI outcome explained known clinical factors; and 2) the additional proportion of variance accounted for by neural measures (i.e. amplitude of STC activation to speechreading). A pertinent research question would be whether fNIRS is able to offer incremental predictive value above well-established clinical characteristics for both pre-lingually and post-lingually deaf individuals. Therefore, future research should aim to recruit sufficient numbers of these two populations in order for the aforementioned predictive analysis to be carried out separately for each group of CI candidates. The current study indicated high

levels of sensitivity (100%) and specificity (92%) of the cortical measure for identifying poorly performing CI users. However, another important step towards the development of fNIRS as a prognostic tool includes confirming these levels of sensitivity and specificity in a larger sample of CI users. Depending on these future developments and results, such a tool could help to improve prognostic information and thus enable clinicians, patients, and parents to better set and modify their expectations about potential outcomes.

Furthermore, the current study demonstrated the suitability of fNIRS for repeated testing of cortical function following implantation. Together this alludes to the potential application of fNIRS in clinical practice, for example in the monitoring of post-operative outcomes. However, to date, little is known about the relationship between auditory speech-evoked cortical activation measured using fNIRS and behavioural measures of auditory speech perception ability with a CI. Specifically, only two recent studies were able to be identified that had sought to understand these relationships in NH individuals (Pollonini et al., 2014) and CI users (Olds et al., 2015). Pollonini and colleagues' investigation in NH listeners indicated the ability of fNIRS to detect differences in cortical activations elicited by clear and degraded speech stimuli of varying levels of intelligibility, and thus could provide an objective measure of the quality of the speech signal that the individual is hearing. Further to this, the same group went on to demonstrate a

relationship between fNIRS measurements of speech-evoked cortical activation and behavioural measures of speech perception ability in adult CI users (Olds et al., 2015). Specifically, the extent of STG activation, expressed as a ratio of activation elicited by normal speech to activation elicited by scrambled speech, positively correlated with auditory word and sentence recognition scores. Together these two studies indicate the potential of fNIRS to identify whether speech is activating temporal auditory brain regions, and importantly that it could be used to identify patterns of cortical activation that could help to indicate whether CI users are able to accurately perceive the speech signal being delivered by their CI device.

Future research that builds on these studies and contributes toward the development of fNIRS as an objective measure of speech perception could be of particular use in paediatric CI populations. Behavioural speech perception testing is not possible with young children and infants as the speech and language skills required to perform such tests are not acquired until a later stage of development. Furthermore, behavioural audiological assessments used with children are often unsuccessful at eliciting behavioural responses, which can also often be difficult to reliably interpret. Therefore, the use of a CI-compatible and infant-friendly method such as fNIRS for assessing whether speech information is reaching and stimulating the language networks in a typical way could be of significant clinical use for monitoring CI outcomes, and perhaps for

guiding effective CI programming, prior to the acquisition of spoken language. Future research should aim to characterise patterns of cortical activation in children elicited by speech stimuli of varying levels of intelligibility. This research aim could be addressed by using noise-vocoder simulations of CI stimulation in NH children. Based on existing work in adults (Olds et al., 2015; Pollonini et al., 2014) it would be hypothesised that STC activation to noise-vocoder simulations of intelligible speech would be greater than that elicited by noise-vocoder simulations of degraded and/or unintelligible speech.

Another pertinent research question to address would be whether children with good and poor CI outcomes can be differentiated based on their patterns of speech-evoked cortical activations. This could be examined by recruiting older children who are capable of performing behavioural speech perception tests (for instance eight years old) who have no known speech, language, motor, or cognitive disorders. Two groups of children of a similar age would need to be tested including: 1) children with good speech understanding following cochlear implantation (e.g. performing above 50% correct on measures on auditory speech perception); and 2) children with poor speech understanding following cochlear implantation (e.g. performing below 50% correct on measures on auditory speech perception). It would be hypothesised that the group-averaged amplitude of STC activation elicited by auditory speech stimulation compared to a speech control stimuli (for

instance, spectrally-rotated speech) would be greater in good CI users compared to reduced levels of activation in poor CI users.

Identification of any such group-level differences in patterns of speech-evoked cortical activation that distinguish those children with good and poor CI outcomes could furthermore help to identify an early prognostic marker of future CI outcome for individual candidates. For instance, if reduced STC activation in children with a CI was identified as a neural signature of poor clinical outcome, fNIRS scanning could be used to help identify individuals at risk of performing poorly with a CI at the earliest possible stage. Thus, this could enable rehabilitation resources to be directed most appropriately and to inform parental expectations of outcome years before behavioural testing may be possible. Furthermore, evidence from studies involving neonates suggests that a propensity for left-hemisphere lateralised responses to auditory speech in the temporal lobes exists from the early stages of development (Gervain et al., 2008; Pena et al., 2003). However, studies of neurodevelopmental disorders such as autism (Bigler et al., 2007; De Fossé et al., 2004; Escalante-Mead et al., 2003) and specific language impairment (Bishop, 2013; de Guibert et al., 2011) have demonstrated a relationship between atypical cerebral lateralisation and language impairment. Likewise, auditory deprivation is known to impact on the development of neural mechanisms that support language skills in children (Eggermont & Ponton, 2003; Gilley et al., 2008; Kral & Sharma, 2012; Sharma & Dorman, 2006). It could therefore be

hypothesised that the extent to which speech-evoked activation is left lateralised may be reduced or absent in children with poor speech perception after implantation. To examine this, future fNIRS studies should look to determine the extent to which cortical activation to speech is left-lateralised in NH children, children who use a cochlear implant but who have good speech perception abilities, and children who use a cochlear implant but who have poor speech perception abilities.

The aforementioned clinical application of fNIRS as a prognostic indicator and an objective tool to monitor CI outcome could of course only be implemented by clinicians if it is deemed pragmatic to do so. For instance, the cost-effectiveness of such a clinical tool would need to be assessed; that is, can the costs of implementing fNIRS scanning as part of routine pre-operative assessment be justified based on the benefits that could be gained by delivering more accurate prognoses. In addition, whether it is acceptable and viable to fit this into existing clinical practice and pathways would need to be established. Moreover, the acceptability of this brain imaging technique for routine use throughout the pre-operative assessment and post-operative rehabilitation process to CI candidates and parents of paediatric recipients should be explored. To address these questions, future research could employ qualitative approaches through the use of focus groups and semi-structured interviews with these various stakeholders to understand

how acceptable and feasible it may be to translate these findings into clinical practice.

9.5.2 Understanding the Contribution of Frontal Cortical Regions to Variable CI Outcome

The ability to understand auditory speech information involves a wide-spread fronto-temporal cortical network connected via dorsal and ventral pathways (Berwick et al., 2013; Friederici, 2011; Hickok & Poeppel, 2007). Specifically, the left inferior frontal gyrus (LIFG), including Broca's area (BA 44/45), is involved in higher-level speech perception functions such as accessing semantic information, phonological working memory and the use of predictive strategies to accurately recover meaning from the speech signal (Berwick et al., 2013; Fiebach et al., 2001, 2005; Friederici, 2002; 2011; Hickok & Poeppel, 2000, 2007). The LIFG is also thought to be implicated in compensating for degraded auditory input (Davis & Johnsrude, 2003) and activity in this region has been identified as a possible neural correlate of effortful listening (Wild et al., 2012), both of which are higher-level cognitive processes likely employed by CI users during auditory speech perception (Hughes & Galvin, 2013; Pals et al., 2013). Existing research with CI users has indeed provided evidence that CI users additionally recruit the LIFG during auditory speech stimulation and may thus reflect the use of compensatory strategies at the cortical level (Giraud & Truy, 2002; Giraud et al., 2000; Mortensen et al., 2006). Furthermore, studies of resting-state activation (Strelnikov et al., 2010), auditory speech-

evoked activation (Petersen et al., 2013), and visual speech-evoked activation (Rouger et al., 2012) have indicated the gradual reactivation of Broca's area with increased CI use in post-lingually deaf individuals.

The current findings presented in Chapters 6 and 7 indicate that activation within superior temporal brain regions can explain a proportion of variability observed in CI outcome but that residual variability still exists. Therefore, in order to achieve a more thorough understanding of the neural basis of individual variability in CI outcome, future fNIRS experiments should look to examine whether the recruitment of LIF regions may be an important contributory factor to auditory recovery in CI users. This could be achieved most efficiently by conducting a cross-sectional study in experienced CI users and exploring correlations between auditory speech-evoked activation in the LIFG and auditory performance with a CI. It would be hypothesised that CI users with higher levels of auditory performance would show a greater level of activation and recruitment of LIFG when listening to auditory speech, whereas CI users with lower levels of auditory performance would show a smaller levels of activation and recruitment of LIFG when listening to auditory speech.

In the current study the placement of the fNIRS measurement array was seen to provide coverage of LIF regions (measurement channels #3 and 6, see Figure 3.20) as well as the predefined STC

ROIs. However, as the aim of the thesis was to examine STC activation given its relevance in auditory speech processing of CI users, the positioning of the measurement array was not designed for optimal coverage of the LIFG. Furthermore, significant auditory speech-evoked activation was not observed over channels #3 and 6 in the NH control group (see Figure 5.2) and exploratory time course analysis also indicated that plausible HRFs were not successfully recorded from this cortical region (Appendix D). Indeed the absence of LIFG activation has been documented by existing neuroimaging studies with CI users and may be due to the passive listening task employed (Naito et al., 1995; Wong et al., 1999). Therefore future research in this area should employ active listening tasks during fNIRS scanning. For instance, employing an event-related design, whereby a short sentence is presented followed immediately by a forced choice task (yes/no) asking whether the word presented on the screen had featured in the sentence, would help to encourage active listening and to maintain attention more so than a block design paradigm.

9.5.3 Investigating Associations between Auditory and Visual Speech during the Recovery of Auditory Function

Behaviourally, CI users are seen to employ adaptive visual and audio-visual speech perception strategies in order to facilitate understanding of the degraded auditory signal provided by the implant (Rouger et al., 2007; Strelnikov et al., 2009). At the cortical level, existing PET studies conducted in CI users have

indicated the recruitment of visual cortices during auditory speech perception (Giraud et al., 2001a; Giraud & Truy, 2002) and have suggested a 'mutual reinforcement' between the two modalities following implantation (Giraud et al., 2001b). The findings presented in Chapter 7 provided evidence to suggest that STC activation to auditory and visual speech developed in a parallel manner over the first six months of CI use. Whilst the current results may support existing suggestions of a beneficial coupling between the two modalities during CI rehabilitation, a more direct examination of whether this audio-visual association may support proficient auditory speech perception would be desirable.

For instance, recent evidence has suggested a tight coupling between cortical activation within the left superior temporal and occipital cortex in relatively experienced and proficient CI users, although this was only demonstrated in a small group (n=8; Strelnikov et al., 2015). The authors interpret this as a synergistic neural mechanism enabling the recovery of auditory speech perception following implantation. However, this cortical activation was a collective measure of activation elicited by visual speech, audio-visual speech, a motor control task, and during rest, thus making it challenging to infer what this activation actually reflects. Furthermore, the relationship with auditory performance was not investigated. Therefore, future research would benefit from examining the nature and extent of coupling between temporal and occipital-lobe activation to auditory speech stimulation in

experienced CI users (i.e. following three years of CI use). Such a study should aim to examine whether the strength of this coupling differs between a group of CI users with poor speech perception abilities, and a group of CI users with good speech perception abilities. It would be hypothesised that proficient CI users would display a strong positive correlation between temporal and occipital-lobe activations while processing auditory speech information, whereas non-proficient CI users would display a weaker, or even absent, level of temporo-occipital coupling to auditory speech stimulation.

Such future research could thus help to understand whether a close coupling between the auditory and visual modalities contributes to CI success, and could help to inform effective rehabilitation strategies. For instance, adult CI rehabilitation largely focuses on training and improving auditory-only abilities (personal observations of speech and language therapy clinics in NAIP). However, such evidence may pave the way for development of audio-visual training strategies to promote these inherent links between auditory and visual speech, which preliminary evidence suggests may provide benefits to auditory-only performance (Bernstein et al., 2013).

9.6 CONCLUSIONS

Individual CI recipients vary drastically in their ability to perceive auditory speech information with a CI. Cortical activation elicited by visual speech measured prior to implantation may offer important

information about the integrity of the speech-processing networks and likely future success with a CI. The use of such cortical measures could offer a supplementary aid to the routinely available clinical information and help to more accurately predict individual outcomes. Individual differences in the ability of the cortex to adapt to cochlear implantation may provide a neural basis for the individual variability observed in CI outcome. Close association at the cortical level between auditory and visual speech cues may provide an important mechanism for auditory recovery during the crucial first months of cochlear implant use. Future research should look to determine whether this synergistic link between the sensory modalities could be capitalised on by training interventions to optimise auditory outcomes. The results reported throughout this thesis suggest that functional near-infrared spectroscopy is an adept tool for imaging behaviourally relevant, multimodal language function and plasticity in the same individuals both before and after cochlear implantation, bearing promise for its growing application with both adult and paediatric CI users.

10. APPENDICES

10.1 APPENDIX A: INSTRUCTION BOOKLET

NIRS

The machine:

- The machine that we use to measure brain responses is called NIRS.
- It works by shining light into the brain.
- It tells us how much oxygen some parts of your brain are using.

The cap:

The cap fits comfortably on your head as shown in the picture below.



Small lights clip onto the cap and the lights sit on your scalp.



- Wearing the cap on your head is not painful.
- It is important to keep still when wearing the cap. Please do not make any sudden head movements so as not to damage the wires.
- I will softly wrap a bandage around the lights on your head. This will hold the cap in place so that it does not move during the experiment.

The experiment:

- You will see and hear someone talking on the computer screen and the NIRS will measure how much oxygen your brain is using.
- First we will do a practice.

1

Practice for NIRS Experiment

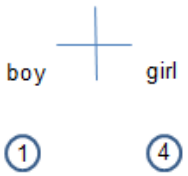
This is a practice so that you know what to expect in the real NIRS experiment.

The speech sentences:

- There will be a man talking. He will say some sentences one after the other.
- Sometimes you will **only hear** the man talking and will not see his face.
- Other times you will **only see** the man talking and not hear his voice.
- At other times you will **both see and hear** the man talking at the same time.
- You may find some parts of the test difficult, but it is very important that you try to understand what the man is saying.

The task:

- Sometimes, after the man has finished talking a cross will appear on the screen and two words will appear on either side of the cross. Like this:



- Please use the numbered buttons to show which word you think the man said.
- For example, press (1) if you think the man said "boy". Or press (4) if you think the man said "girl".
- You will not be asked to do this every time after the man has spoken so do not worry if words do not appear on the screen.
- However, it is important that you are **always** trying to understand what the man is saying. This is because you could be asked what you think he said at **any** time.

Rest period:

- When the man is not talking, there will be a cross on the screen and nothing will happen for a length of time.
- Please keep looking at the cross and try to sit still and relax during this time.

Do you have any questions?

2

NIRS Test

This experiment will be like the practice that you have just seen.

The speech sentences:

- Each sentence will be spoken by either a female or a male talker.
- You may find some parts of the test difficult, but it is very important that you **always try** to understand what the talker is saying.
- It is very important that you keep as still as possible throughout the whole experiment. Please do not make any sudden head movements.
- Remember to relax but to stay still when nothing is happening.
- This experiment will last about 15 minutes.

The response buttons:

- Please hold the buttons in your lap and make sure that you are not touching the table.
- Please do not look down at the buttons when you need to use them. Please keep looking at the screen.

To begin:

- Please wait until I have closed the door and turned the lights off.
- When I have turned the lights off, please press buttons 1 and 4 at the same time to begin the experiment.
- I will be watching through the window so if you need assistance raise your arm and I will see you.

Do you have any questions?

3

Practice with Speech Tests

Now we are going to do some speech tests. First I will show you a practice block so that you can see what you will need to do.

The speech sentences:

- As before, you will sometimes **only hear** the man talking and will not see his face.
- Other times you will **only see** the man talking and not hear his voice.
- At other times you will **both see and hear** the man talking at the same time.
- I will not tell you when this will change so please always look at the screen so that you do not miss any of the sentences.
- You may find some parts of the test difficult, but it is very important that you **always try** to understand what the man is saying

The task:

- After the man has finished saying a sentence, please repeat back to me what you think he said.
- It does not matter if you cannot repeat the whole sentence.
- Please repeat back **any** words that you think the talker said, no matter how strange these may seem.
- Some of these sentences will be very hard and are meant to push your abilities.
- Please do not worry if you find it difficult, this is normal. Please just try to do your best.
- Please just say "pass" or "no" if you do not know what the talker said.
- I will not tell you if your answer is right or wrong. We will just keep moving through the sentences at a steady pace.

Do you have any questions?

4

Speech Test 1

This test will be like the practice that you just did. This time it will be the male and female talker that you saw in the NIRS experiment.

To remind you:

- Please always look at the screen so that you do not miss any of the sentences.
- You may find some parts of the test difficult, but it is very important that you **always try** to understand what the talker is saying.
- After the talker has finished saying a sentence, please repeat back to me what you think they said.
- It does not matter if you cannot repeat the whole sentence.
- Please repeat back **any** words that you think the talker said, no matter how strange these may seem.

Do you have any questions?

5

Speech Test 2

We will now do the same again but this time the talker will be a different man.

The speech sentences:

- Please always look at the screen so that you do not miss any of the sentences.
- You may find some parts of the test difficult, but it is very important that you **always try** to understand what the talker is saying.

The task:

- After the man has finished saying a sentence, please repeat back to me what you think he said.
- It does not matter if you cannot repeat the whole sentence.
- Please repeat back **any** words that you think the talker said, no matter how strange these may seem.
- Some of these sentences will be very hard and are meant to push your abilities.
- Please do not worry if you find it difficult, this is normal. Please just try to do your best.
- Please just say "pass" or "no" if you do not know what the talker said.
- I will not tell you if your answer is right or wrong. We will just keep moving through the sentences at a steady pace.

Do you have any questions?

6

Speech Test 3

The speech sentences:

- In this test you will **only hear** the man talking. You will not see him.
- There will also be **background noise** present.
- At times it may be very difficult to hear what the man is saying. It is very important that you **always try** to understand what the talker is saying.
- Please do not worry if you find it difficult, this is normal. Please just try to do your best.

The task:

- Please repeat back **any** words that you think the talker said, no matter how strange these may seem.
- Just say "pass" or "no" if you do not know what the talker said.
- I will not tell you if your answer is right or wrong. We will just keep moving through at a steady pace.

Do you have any questions?

7

Speech Test 4

This is the last test! This will be like the previous test as there will be **background noise** present.

The speech sentences:

- In this test you will **either hear** the man, **or both see and hear** the man at the same time. I will tell you which.
- Please always look at the screen so that you do not miss any of the sentences.
- At times it may be very difficult to hear what the man is saying. It is very important that you **always try** to understand what the talker is saying.

The task:

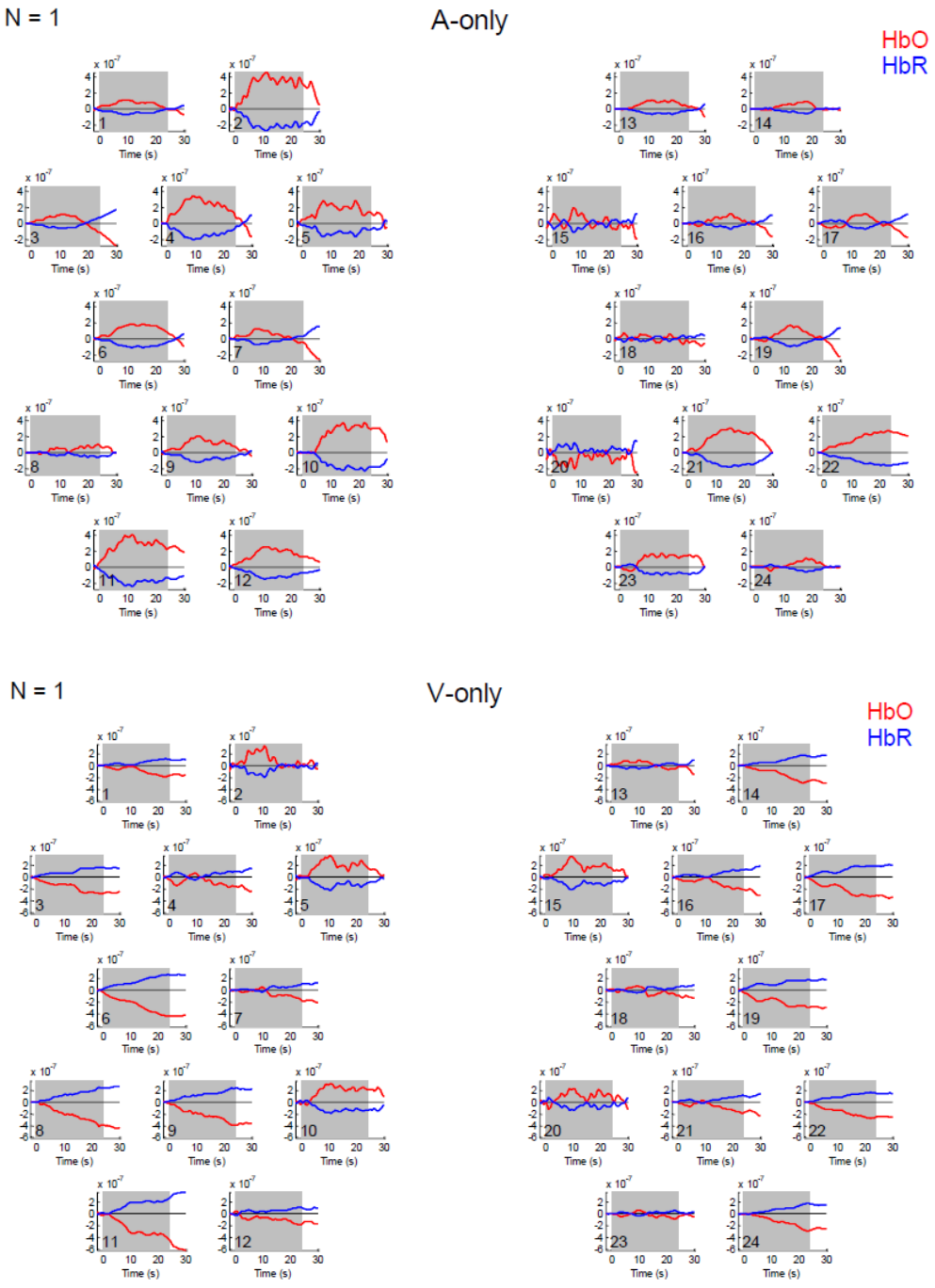
- After the man has finished saying a sentence, please repeat back to me what you think he said.
- It does not matter if you cannot repeat the whole sentence.
- Please repeat back **any** words that you think the talker said, no matter how strange these may seem.
- The test will be difficult and is meant to push your abilities.
- Please do not worry if you find it difficult, this is normal. Please just try to do your best.
- Please just say "pass" or "no" if you do not know what the talker said.
- I will not tell you if your answer is right or wrong. We will just keep moving through the sentences at a steady pace.

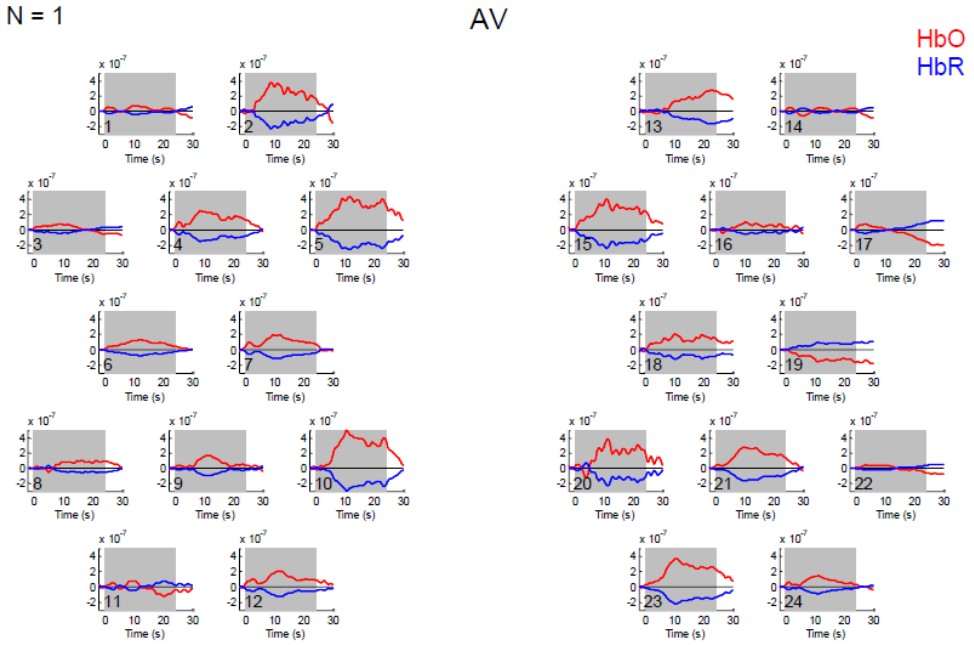
Do you have any questions?

8

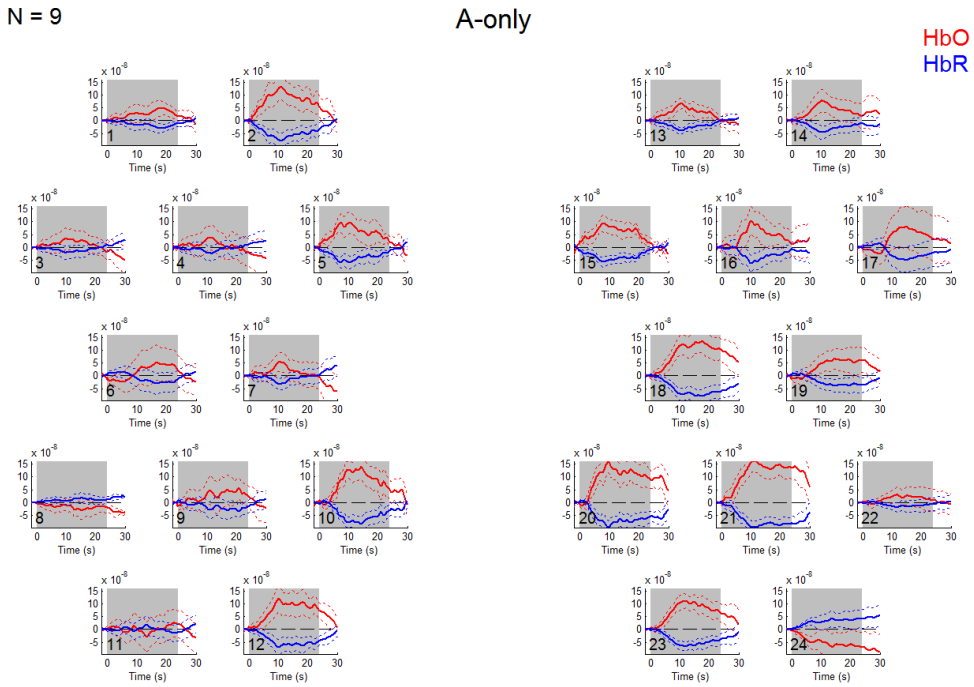
10.2 APPENDIX B: PILOT TESTING FNIRS MEASUREMENTS

An example of block-averaged haemodynamic responses for the A-ONLY, V-ONLY and AV conditions recorded bilaterally from one individual during pilot testing. Measurement channels covering the left and right hemisphere are shown on the left and the right respectively:





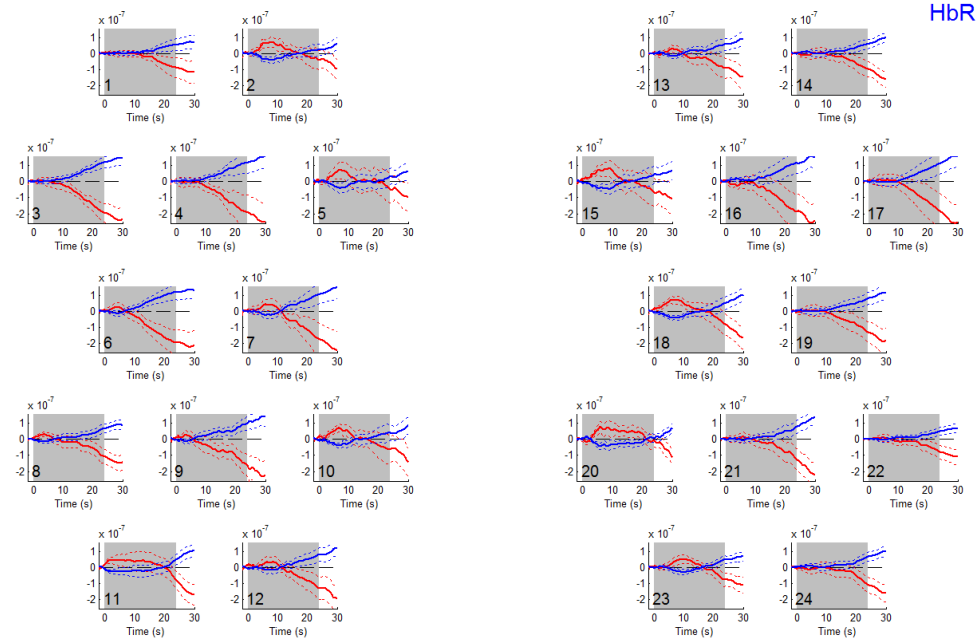
Group-averaged haemodynamic responses for the A-ONLY, V-ONLY and AV conditions recorded bilaterally during pilot testing. Measurement channels covering the left and right hemisphere are shown on the left and the right respectively:



N = 9

V-only

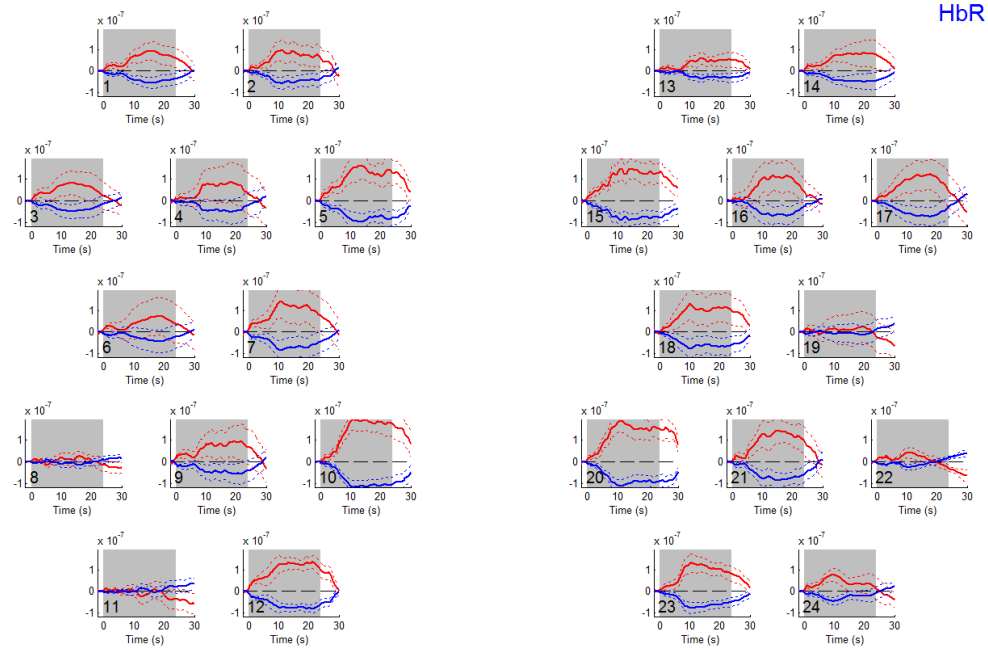
HbO
HbR



N = 9

AV

HbO
HbR



10.3 APPENDIX C: BEHAVIOURAL PERFORMANCE MEASURED USING THE IHR NUMBER SENTENCES

10.3.1 Auditory Speech Perception

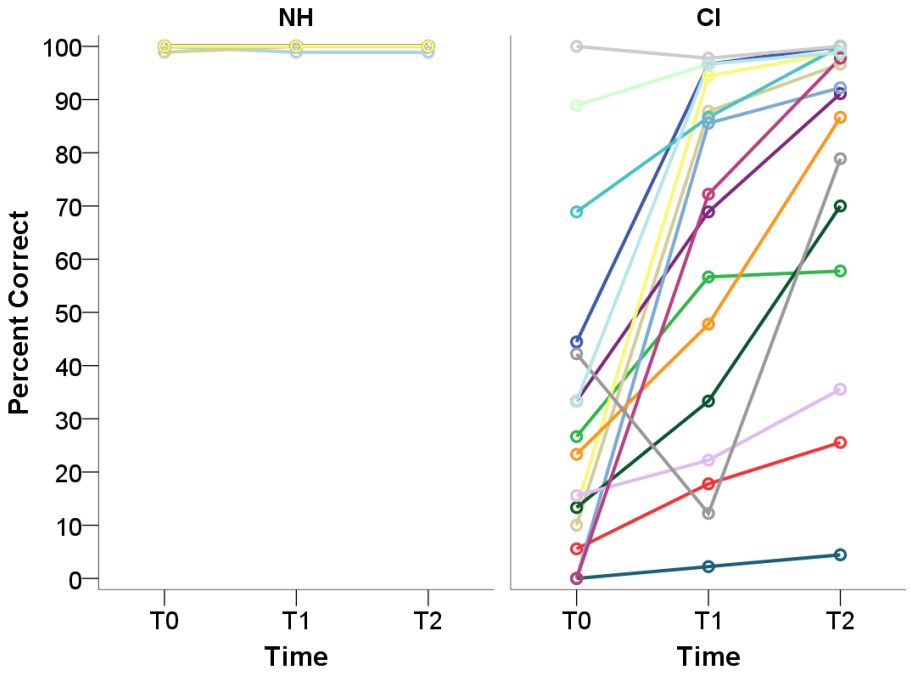


Figure C1: Percentage of words correctly identified on the IHR Number Sentences presented in the auditory-only condition. Auditory performance is plotted as a function of time with individual lines colour coded by participant.

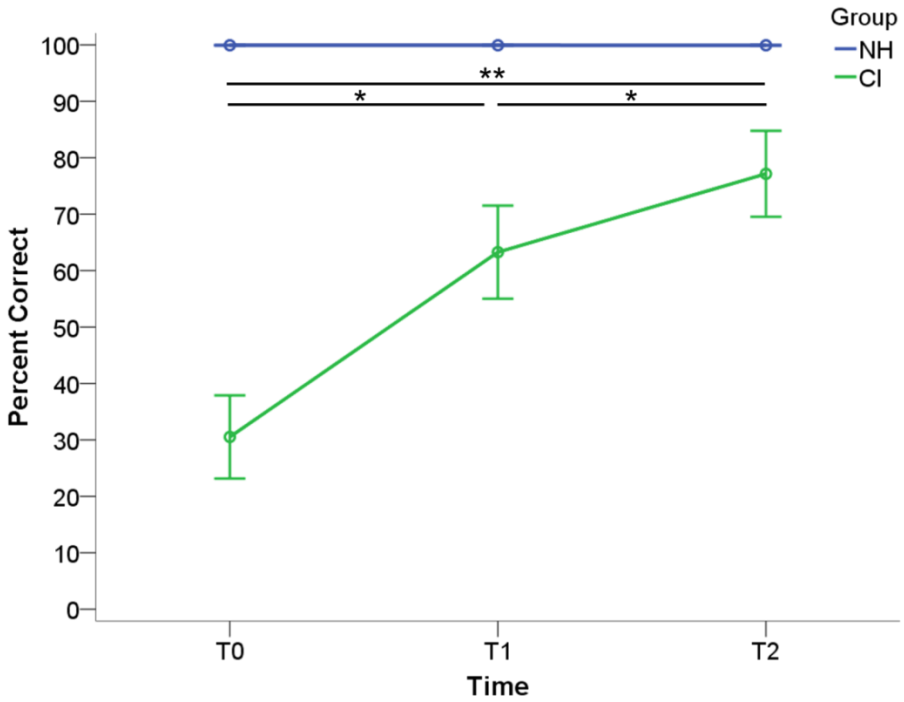


Figure C2: Mean percentage of words correctly identified on the IHR Number Sentences presented in the auditory-only condition. Mean auditory performance is plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error. Asterisks denote significant differences between time points in the CI group based on the transformed data (*p<.005, **p<.001).

10.3.2 Visual Speech Perception

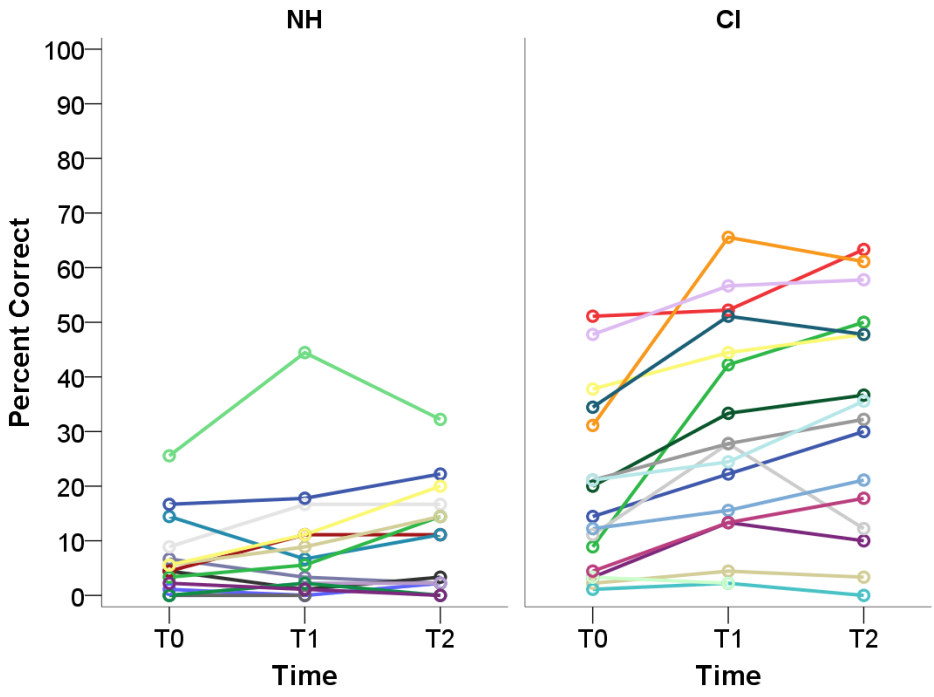


Figure C3: Percentage of words correctly identified on the IHR Number Sentences in the visual-only condition. Speechreading performance is plotted as a function of time with individual lines colour coded by participant.

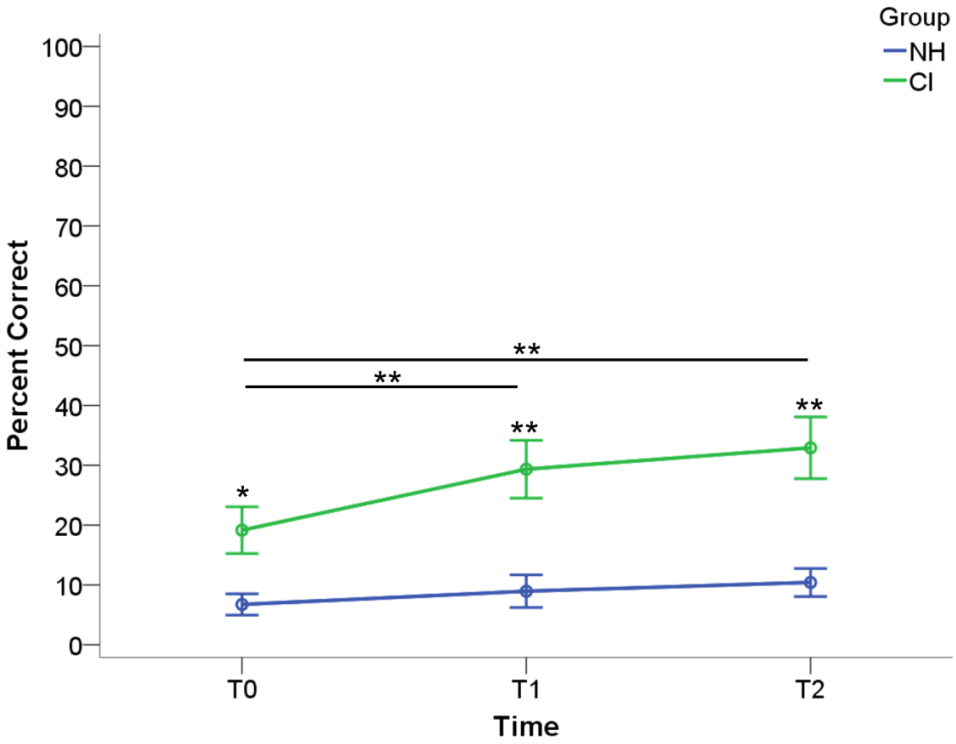


Figure C4: Mean percentage of words correctly identified on the IHR Number Sentences in the visual-only condition. Mean speechreading performance is plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error. Asterisks denote significant group differences and differences between time points in the CI group, based on the transformed data (*p<.05, **p<.005).

10.3.3 Audio-Visual Speech Perception

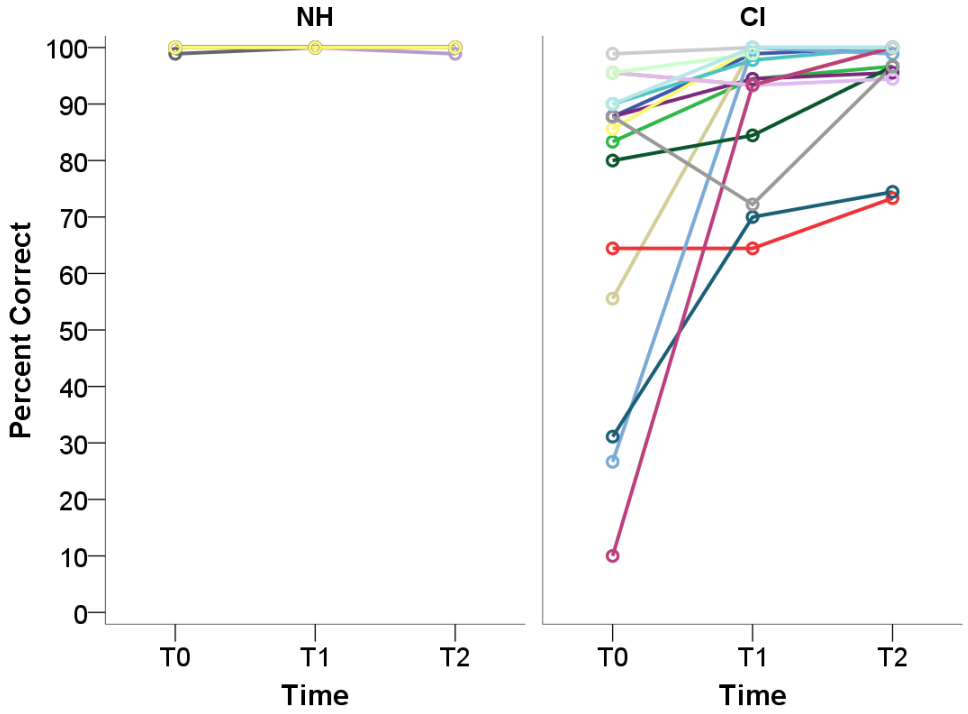


Figure C5: Percentage of words correctly identified on the IHR Number Sentences presented in the audio-visual condition. Audio-visual performance is plotted as a function of time with individual lines colour coded by participant.

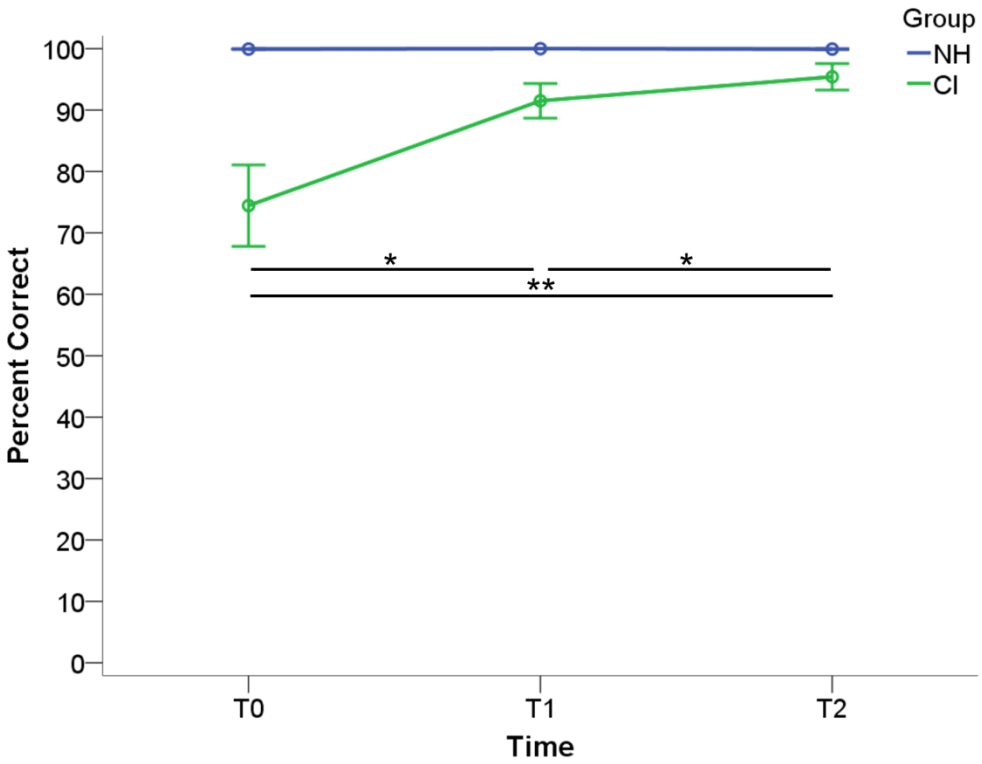


Figure C6: Mean percentage of words correctly identified on the IHR Number Sentences presented in the audio-visual condition. Mean audio-visual performance is plotted as a function of time and colour coded by group. Error bars represent ± 1 standard error. Asterisks denote significant differences between time points in the CI group based on the transformed data (*p<.05, **p<.005).

10.4 APPENDIX D: TIME COURSE OF LIFG ACTIVATION TO AUDITORY SPEECH

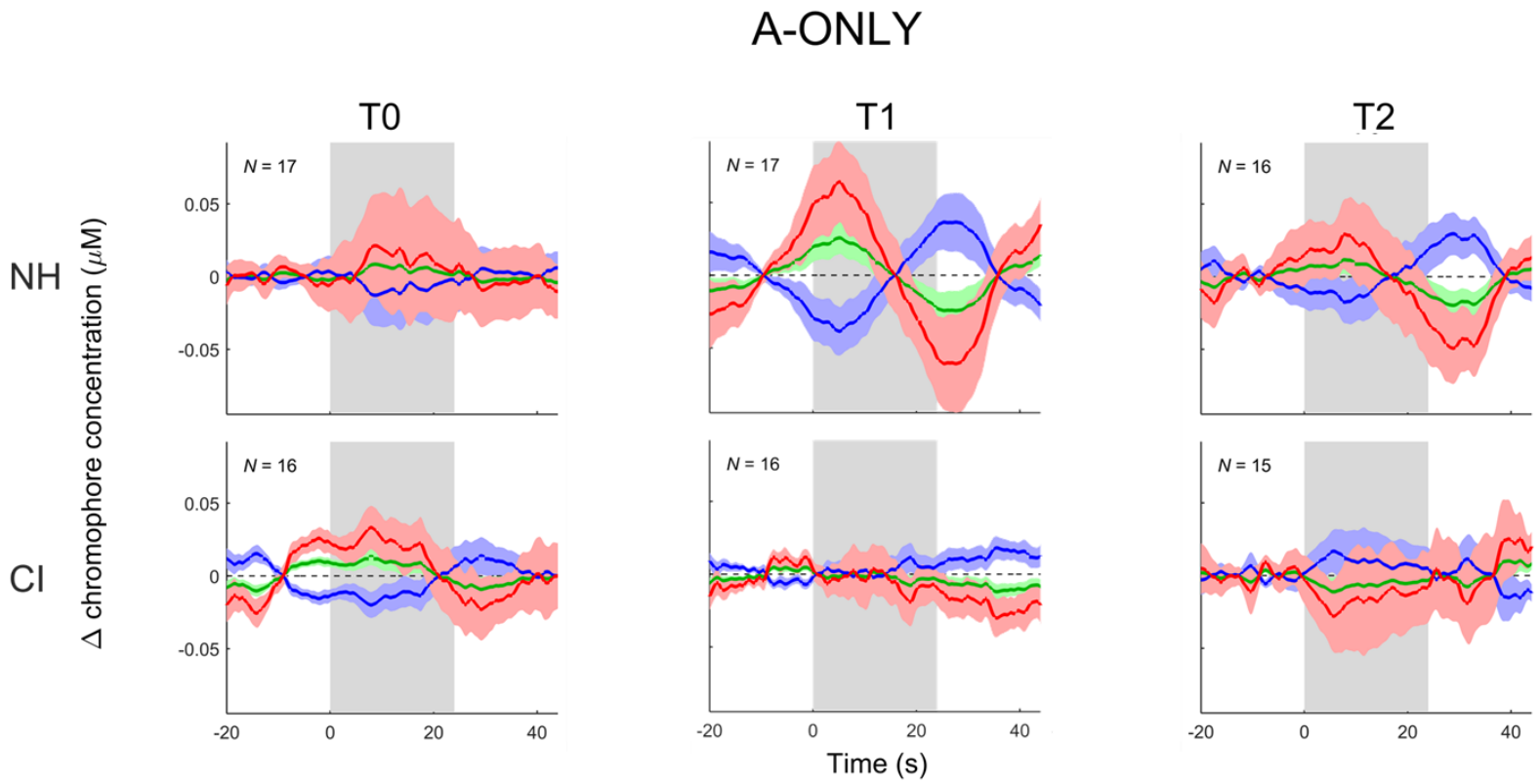


Figure D1: Group-averaged time courses showing changes in **HbO** and **HbR** concentration, as well as **HbT** levels, within the LIFG (channel #3 & 6) during the presentation of auditory speech (stimulation period indicated by shaded grey region). Coloured shading indicates ± 1 standard error across participants.

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