Developing a Means of Marking and Assessing Impairments in the Processing of Linguistic Prosody in Parkinson's Disease

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Declaration of Author's Rights

This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

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List of Publications

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List of Abbreviations

ACE-III – Addenbrooke's Cognitive Examination 3rd edition.

EEG – Electroencephalogram

EF – Executive Function

ERP – Event-Related Potential

GDS-30 – Geriatric Depression Scale with 30 Questions

H&Y – Hoehn and Yahr

H&YI – Hoehn and Yahr Stage 1

H&YII – Hoehn and Yahr Stage 2

H&YIII – Hoehn and Yahr Stage 3

HS – Healthy Senior, abbreviation used for the healthy cohort of older participants

IPB – Intonational Phrase Boundary

IPB-0 – Incongruent prosody condition with no IPBs

IPB-1 – Congruent prosody condition with 1 IPB

IPB-2 – Incongruent prosody condition with 2 IPBs

MDS - International Parkinson's and Movement Disorder Society

MMN – Mismatch Negativity

MC Simulation – Monte Carlo Simulation

MCC – Multiple Comparison Correction

N100 – negative component occurring 100ms after a stimulus

nP3 – novelty P3

PEP – Prosodic Expectancy Positivity

PD – Parkinson's disease

RAN – Right-Anterior Negative

RON – Reorientation Negative

RT – Response Time

SP – Switch Positive

WCST – Wisconsin Card Sorting Task

WM – Working Memory

Abstract

Introduction

People with Parkinson's disease (PD) may present with an impaired ability to interpret prosody. There are few studies examining perception of non-emotional prosody in PD and fewer still using event-related potentials (ERPs) to do so. ERPS are the electroencephalogram (EEG) response to stimuli. These are typically named as either P (positive) or N (negative) followed by the time at which they occur (e.g. N100, a negative component typically peaking 100ms after a stimulus). The lack of ERP studies examining linguistic prosody may be due to it having many functions and due to its subtle effect meaning the processing of linguistic prosody is difficult to capture on an EEG. The current study presents a means of eliciting markers for the processing of linguistic prosody in healthy persons and people with PD. This has the purpose of providing a means of examining prosodic perception in PD. The protocol was validated by testing on a primary cohort of healthy older persons, a smaller cohort of healthy younger persons and on two people with PD.

Method

Three cohorts took part in the study, a healthy senior (HS) cohort aged 59 and older (n=36); a younger Pilot cohort, aged 22-30 (n=8); and 2 people with PD (age 81 and 76; Hoehn and Yahr stages 3 and 1) who were analysed as case studies. The HS cohort and participants with PD were screened for dementia and mild cognitive impairment using the ACE-III and depression using the GDS-30. The protocol consisted of an EEG task combined with two behavioural tasks. Adapted from a study by Eckstein and Friederici (2005), intonational phrase boundaries (IPBs) were used to make two forms of incongruous prosody. There was an IPB-2 condition in which two IPBs were present and an IPB-0 condition in which the IPB was absent. The behavioural tasks were an Identification Task and Discrimination Task in which participants listened to utterances and were asked to identify incongruous prosody or say if two utterances heard back to back had the same or different prosody. During the EEG, participants carried out a Probe Task in which they listened to the utterances and then answered if a displayed word was the last word they heard in the sentence. The IPB-2 condition aimed to elicit the attention capture and orientation components the N100, P3a, reorientation negative (RON), and evoked frontal delta. The IPB-0 condition aimed to elicit the prosody reanalysis components the right-anterior negative (RAN) and the prosodic expectancy positive (PEP).

Results

The Pilot cohort elicited a P3a in the IPB-2 condition and a PEP and RAN in the IPB-0 condition.

The HS cohort elicited an N100, P3a, RON, and, evoked delta in the IPB-2 condition. In addition to this they elicited a switch-positive (SP) and parietal alpha suppression due to the task demands. The IPB-0 condition failed to elicit a RAN or PEP in the HS cohort.

The two participants with PD performed similarly to the healthy cohort in the behavioural tasks. In the IPB-2 condition one those participants did not elicit any ERP components but did elicit weakly significant increase in delta power at electrode FCz only. The other participant with PD elicited a P3a and a weakly significant SP and RON. In the IPB-0 condition one participant with PD elicited a weakly significant RAN. The other did not elicit a RAN nor PEP.

Discussion

The current study successfully elicited the full range of attentional components therefore these can be used to mark various stages in the processing of prosody. The prosodic reanalysis components, the PEP and RAN were absent in the HS cohort but were present in the Pilot cohort. There may therefore be an age effect on how the incongruent prosody was interpreted or processed in older persons. If this is confirmed with future work, it would mean they are inappropriate for use in the study of linguistic prosody in older patient groups.

Conclusion

The current study successfully elicited attentional markers in response to linguistic prosody in a novel way in healthy older persons. Testing in a small number of people with PD gave a preliminary indication that these can be used to examine the perception of linguistic prosody PD. The study failed to elicit the RAN and PEP in healthy older persons and this may be due to an age effect.

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Chapter 1

Introduction

1 Introduction

This thesis explores the perception of speech in Parkinson's disease (PD) using electroencephalogram (EEG) markers. EEG markers have a long history of providing a way studying a breadth of symptoms occurring in numerous pathologies. The temporal resolution of EEG means that multifaceted processes can be broken down into their constituent parts. This makes them a non-intrusive means of determining the underlying causes of symptoms. The current study makes use of this EEG technology to provide a novel means of eliciting markers to examine an as yet untreated and under-explored symptom of Parkinson's disease (PD): the impaired processing of linguistic prosody.

Idiopathic PD is the world's fastest growing neurological disorder (Dorsey et al. 2018). The approximate incidence of PD in over 60s in the UK in 2018 was 17,068 (112 per 100,000 over 60s) and this is expected to increase by approximately 70% to 29,309 by 2065. PD is recognisable by its movement and speech symptoms. A diagnosis of parkinsonism is recommended when bradykinesia (slowness of movement) is present in combination with either resting tremor, rigidity or both (Postuma and Berg 2016). It is estimated that when these core symptoms become recognisable that PD has already moderately progressed (Braak et al. 2003, Hawkes, Del Tredici and Braak 2010, Berg et al. 2014). There are therefore a diverse range of axial motor symptoms and non-motor symptoms present from the earliest stages of the disease which require treatment and management. Among these symptoms are impairments in the production (Rusz et al. 2011) and perception (Peron et al. 2012) of speech prosody. Speech is made up of semantics (the words used and their meaning), syntax (the underlying structure of the sentence and its grammar), and prosody. Prosody is the modulation of the suprasegmental speech parameters. This modulation is achieved by manipulating the fundamental frequency (pitch), duration and intensity of the vocalisation. In practice, prosody can distinguish sincerity from irony, distinguish a question from a statement, stress important information and convey the affective state of the speaker. Prosody having such a broad role means that it conveys much of a speaker's intended meaning, making it essential to the conveyance of and interpretation of spoken communications. Prosody when conveying the emotional state of a speaker is often referred to as *affective* or *emotional prosody* in literature. Saying something with a happy or angry or disgusted tone of voice is making use of emotional prosody. Prosody, when not used to convey emotion, most often comes under the umbrella term of *linguistic prosody*. Linguistic prosody serves a number of essential speech functions. A noticeable example of the use of linguistic prosody in every day speech is in conveying if an utterance is a statement or question. A question is signalled to the listener by increasing the pitch of the utterance towards the end of the sentence creating a rising intonation. Another important use of linguistic prosody in speech is to highlight new or important information in a sentence. When important or anomalous information is not stressed using prosody, the information

may go unnoticed by the listener (Karimi and Ferreira 2016). In this way, linguistic prosody plays a crucial role in capturing and guiding the listener's attention. Linguistic prosody is also used for structuring and segmentation. Segmentation is achieved using prosodic boundaries. Prosodic boundaries group words of an utterance into sub-groups and are signified by a drop in pitch, a lengthening of the last word prior to the boundary, and a pause following this word. After the pause, there is a resetting of the pitch contour and the intensity (volume) of the speech. These prosodic boundaries essentially act as vocal commas and full-stops. Amplifying or attenuating the cues used to form these boundaries strengthens or weakens the salience of the boundary (Wagner and Watson 2010). The strength of the boundary indicates the boundary type, with the *intonational phrase boundary* (IPB) being the strongest. The intonational phrase boundary signals the end of an intonational phrase - the largest of the prosodic groupings (Silverman et al., 1992) and is the boundary most akin to a full-stop in speech.

Impaired processing of emotional prosody has been observed repeatedly in PD. There is debate over whether this is a deficit in prosodic perception per se or a deficit in emotional processing that results in an impaired ability to detect emotion from facial expressions as well as from speech (Coundouris et al. 2019, Kwan and Whitehill 2011, Gray and Tickle-Degnen 2010). The presence (or lack) of impaired processing of linguistic prosody in PD is a more contentious topic. There are fewer studies examining non-emotional prosody in PD and those that do exist report conflicting results over the specific functions of linguistic prosody (if any) that are impaired (Section 2.5). PD is a heterogeneous disease with not only a diverse presentation of symptoms but diverse underlying physiology (Sauerbier et al. 2016, Marras and Chaudhuri 2016)). There is scepticism in the literature over whether these differences go as far as to represent distinct subtypes (or if they do, whether classifying them as such has diagnostic value) (Obeso et al. 2017, Berg et al. 2014, Boeve et al. 2016), however establishing markers of heterogeneity is recognised as an important step in increasing understanding of the disease and its varying prognoses (Obeso et al. 2017). Given that PD is heterogeneous, it stands to reason that people with PD will have a heterogeneous response to linguistic prosody. Mixed or conflicting reports in the literature concerning how people with PD interpret prosody are therefore to be expected but is something which is, nonetheless, given little consideration in the prosody literature so far.

The current study examines the perception of linguistic prosody and its electroencephalographic (EEG) markers. EEG is the process of measuring the voltage coming from the scalp. Event-Related potentials (ERPs) are a specific type of EEG recording in which the EEG is time-locked to a specific event or trigger. This event is often a visual or auditory cue, for example the display of an image or the playing of a pure tone. These cues elicit a waveform called an event-related potential (ERP). Much of an EEG

recording is noise, therefore to extract an ERP, events are repeated numerous times and the EEG split into epochs and averaged together. Any component of the EEG signal that is not time-locked to the event will be attenuated in the averaging process. This leaves behind a waveform consisting of peaks and troughs and these make up the ERP. The way in which the amplitude, location or latency of these peaks and troughs changes with different stimulus types or between different patient groups can be used to make inferences about the how the stimulus is processed. The presence or absence of ERPs can also be used to mark whether a certain process has occurred or not. ERPs are often given names related to their latency and whether they are positive (have a positive voltage) or negative (have a negative voltage). An *N100* (sometimes *N1*), for example, is a negative component that peaks at approximately 100ms and a *P200* (sometimes a *P2*) is a positive component that peaks at approximately 200ms. Other ERPs have names related to where on the scalp they occur (termed the topography or location of the component) or related to the process or cue that elicits them. An example of an ERP named after the location at which it occurs is the *right-anterior negative* (*RAN*), a negative ERP that occurs on the right anterior of the scalp. An example of a component named after the process that it marks is the *prosodic expectancy positive* (*PEP*). This a positive component that occurs in response to a sudden and unexpected change in prosody. ERPs can be used as signposts for different stages in the processing of a stimulus. They are therefore a useful tool in the study of the processing of prosody as they can be used to distinguish impairments in pre-attentive and sensory processing from impairments in later attentional and cognitive processes. A deficit in one of or a combination of any of these processes could result in impaired prosodic processing and knowing which can inform how the impairment should be treated.

Linguistic prosody has a subtle effect, so to capture the processing of linguistic prosody through the noise of an EEG requires careful manipulation of stimuli and of the task being used. The current study presents a methodology for examining the perception of linguistic prosody by manipulating its role in the guiding of attention and building prosodic expectations. The aim of this study is to develop a protocol that can be used to elicit EEG marker(s) for the processing of linguistic prosody for use in people with PD and to test this protocol on case studies.

1.1 Thesis Structure

Chapter 2 is the Literature Review. The Literature Review lays out the case for studying linguistic prosody in its own right by outlining the differences in physiological response to emotional and linguistic prosody. From there it outlines the different subtypes of PD to show why the existence of these subtypes needs to be considered in any study of the perception of prosody in PD and why this might account for the varied reports of how people with PD perceive prosody. Sections 2.6 and 2.7 of the Literature Review deal with the EEG markers of attention capture and orientation and of prosodic reanalysis. It is these markers that the current study aims to elicit, so a review is given of the tasks that elicit them, the underlying principles and theories of these tasks, and what the markers elicited by these tasks are able to tell us about the processing of prosody. This lays the foundation for the final task design used in the current study. The Literature Review concludes with a statement of the current study's aims and research question. Chapter 3 lays out the methodology used in the current study, with details of the prosody and tasks that are used and how these interact to elicit the desired effect. Chapter 4 presents the results. Pilot results are presented in this section as they provide an important comparison with the older cohort. The results of the main cohort are presented in two parts, one dealing with each of the two prosodic conditions used. Finally, the PD case studies are presented individually. Chapter 5 is the discussion which discusses the results of the current study with reference to the three research questions that the current study seeks to address. Chapter 6 is the conclusions. This chapter summarises the findings of the current study and their limitation before laying out the future work that the current study lays the groundwork for.

Chapter 2

Literature Review

2 Literature Review

2.1 Introduction

The study examines linguistic prosody using event-related potentials and event-related oscillations. The review first lays out important differences in the processing of linguistic and emotional prosody and how these differences present themselves on an EEG. The review then gives an overview of the current literature on PD with particular emphasis on prosody in PD and disease heterogeneity. This review argues that while there is a rich literature to draw from in both of these areas, there is very little literature examining them both together. The next section outlines how the functions of linguistic prosody can be manipulated to elicit an EEG response. It shows that in manipulating these processes, not only can EEG markers be produced but that a number of open questions about how attention is captured and controlled can be answered using these markers.

2.2 Physiological differences between emotional and linguistic prosodic processing

This section introduces the physiological differences between the processing of linguistic and emotional prosody. While emotional prosody and linguistic prosody make use of the same speech parameters, the discussion in this section highlights that the regions responsible for the processing of these parameters is different depending on the type of prosody being listened to and that these regions are interdependent but distinct. The purpose of this is to show the importance of studying linguistic prosody in its own right. If the processing of linguistic prosody and the processing of emotional prosody are distinct then a person might be impaired in one but not necessarily the other. This outline allows us to make predictions about how linguistic prosody processing might manifest itself in the EEG compared to emotional prosodic processing. This section also shows how task effects and top-down considerations are important factors that influence the EEG response to linguistic prosody. As linguistic prosody has an important relationship with semantics and syntax, altering how the task draws the participant's attention to these speech elements is a way of provoking an EEG response. Outlining this gives us information on how to manipulate the task to minimise the confounding influence of other speech and language features.

EEG studies show that the activation pattern to emotional prosody often differs to that of linguistic prosody. There is a wealth of behavioural (Wolfe and Ross 1987, Gorelick and Ross 1987, Blonder, Bowers and Heilman 1990, Starkstein et al. 1994, Heilman, Scholes and Watson 1975, Godfrey and Grimshaw 2016) and imaging data (Buchanan et al. 2000, Wildgruber et al. 2002, Mitchell et al. 2003) indicating a right-hemisphere preference for the processing of emotional prosody. Data from pathological populations bear this out. Studies working with survivors of right-hemisphere stroke show they are impaired in identifying emotion using prosody (Dara et al. 2014, Sheppard et al. 2020).

Dara et al. (2014) go as far as to present evidence that an impairment in identifying emotion from prosody may serve as a reliable marker for acute right-hemisphere dysfunction. Studies in hemispheric PD converge with these findings, showing that people with PD with left-sided motor symptoms (implied right-sided pathology) are impaired in the identification of emotion from prosody and persons with right-sided motor symptoms are not (Garrido-Vasquez et al. 2013, Ventura et al. 2012). A right-hemisphere preference for the processing of emotional prosody has therefore been shown in both behavioural and EEG tasks in healthy and patient groups.

The processing of linguistic prosody by contrast is not clearly lateralised. While people with right-hemisphere damage are often found to be unable to process emotional prosody, inhibited processing of linguistic prosody has been found in people with both right-hemisphere and left-hemisphere damage (Witteman et al. 2011, Friederici 2011). Linguistic prosody serves many purposes and each of these is linked to a different combination of prosodic cues. For example, distinguishing a question from a statement requires manipulation of the global pitch contour of an utterance. Syllable stress, word stress and phrase boundaries, on the other hand use more localised changes in pitch. Some studies suppose that how prosody is lateralised in the brain depends on the cues being used to decode that prosody. Different studies present different data on which cue features determine how prosodic processing will be lateralised. It is most commonly supposed that the right-hemisphere has a preference for continuous cues (such as those used to distinguish a statement from a question) and the left-hemisphere a preference for discrete or short-term cues (such as word stress) (Vanlancker and Sidtis 1992, Zatorre et al. 1992, Tong et al. 2005, Johnsrude, Penhune and Zatorre 2000, Patel et al. 2008). Other studies suppose that spectral structure (the intensity and volume of the speech) (Schoenwiesner, Ruebsamen and von Cramon 2005, Zatorre and Belin 2001) or whether the cues are segmental or suprasegmental (Friederici and Alter 2004, Friederici 2011) are the determining factor.

The theory that the nature/type of cue is the determining factor in lateralisation has been challenged by studies that show a left-hemisphere preference for processing of language and meaning, regardless of the duration or segmental/suprasegmental nature of the cue conveying that meaning. McGettigan and Scott (2012) argue that even defining cues as short-lasting or long-lasting is misguided as there is no easy or consistent way to define the difference. Moreover, phonetic information, something that is often associated with the left-hemisphere, is not necessarily conveyed over a short time-period and can even be conveyed by suprasegmental features (especially in tone languages). They conclude that the left-hemisphere has no preference for any particular cue but a specific preference for the encoding of speech and language information. Kreitewolf, Friederici and von Kriegstein (2014) present data indicating that linguistic prosody processing has a left-hemisphere preference when compared with processing of emotional prosody but a rightward preference when compared with a non-speech and

non-linguistic task. Their data suggest that linguistic prosodic processing is not hemisphere specific and that there is a right-hemisphere preference for the processing of suprasegmental pitch contours when used to decode prosody and left-hemisphere preference for the processing of suprasegmental speech cues when they are used to enhance the processing of lexical or semantic content. Data from tone languages give the clearest demonstration of this. In tone languages, two (or more) lexically identical words may have different meanings depending on the pattern of pitch used when pronouncing the word (for example, rising, dropping or flat intonation). This specific use of pitch to signal the meaning of the word is called *tone*. Gandour et al. (1998) found that the processing of suprasegmental changes in pitch is left lateralised when that pitch pattern determines the meaning of the word. Chien et al. (2019) compared the processing of tone (conveyance of meaning) and intonation (distinguishing statements from questions) in German and Mandarin speakers. They found that tone processing was bilateral in both speakers. Intonation processing (a more commonly tested linguistic prosody feature) was right-lateralised, but only when explicit evaluation of the intonation was required. This shows the right-hemisphere is used when making categorical judgements of prosody but that both hemispheres are used when making categorical judgements of semantic meaning, even when this is conveyed by the prosodic manipulation of tone. This converges with a study into the processing of intonational phrase boundaries. IPBs serve a different function from tone or intonation but the processing of IPBs is similarly left-lateralised when their presence is essential to determining the meaning of a sentence but are otherwise right-lateralised (van der Burght et al. 2019).

How the EEG response to prosody is lateralised is not the only topographical difference between linguistic and emotional prosody. Prosody is used to build expectations that facilitate rapid speech processing. When these expectations are violated, a measurable ERP response occurs. When this ERP occurs in response to linguistic prosody, it is elicited parietally. When this ERP occurs in response to emotional prosody, it is elicited frontally (Paulmann, Jessen and Kotz 2012). This shows that emotional and linguistic prosody engage different regions of the brain even in the absence of an explicit evaluative judgement.

In summary, the right-hemisphere has a preference for cues that are often used for explicit judgements of prosody such as distinguishing a question from a statement (Tong et al. 2005, Chien et al. 2019) or identifying emotions from speech (Buchanan et al. 2000, Wildgruber et al. 2002, Mitchell et al. 2003). These cues are mostly, but not exclusively, long and suprasegmental. The left-hemisphere has a preference for cues which are used more often in phonetic and semantic judgments (Tong et al. 2005, Chien et al. 2019). These cues are mostly, but not exclusively, short and segmental. There is ongoing debate over whether lateralisation happens based on the properties of cues themselves or whether the difference is in whether a semantic or prosodic judgement occurs. Task effects and top-

down attentional processes play a crucial role in how a stimulus is evaluated and therefore if and how the processing of that stimulus is lateralised (Wildgruber et al. 2006, Harrington, Haaland and Knight 1998, Geiser et al. 2008, Zatorre et al. 1992). Persons with right-hemisphere damage are more likely to be impaired in their processing of both linguistic and emotional prosody but persons with left-hemisphere damage (if they are impaired in processing of prosody at all) are more likely to be impaired in the processing of linguistic prosody only (Witteman et al. 2011, Friederici 2011, Pell 1998). Linguistic prosody therefore engages a wide cortical network and is a key component in a number of processes that make communication possible. The implications of this are that there are several processing stages might be implicated in impaired prosodic processing. It also means that processing of suprasegmental features may be impaired when making semantic judgements but not prosodic judgements or vice versa.

2.3 Subtypes of PD

This section discusses the theory that multiple subtypes of PD exist. This outline is important to the current study for four reasons. Firstly, it shows that the symptoms of PD are not uniform. From this it can be inferred that people with PD's response to linguistic prosody will not be uniform. This offers an explanation for the mixed results in the literature concerning linguistic prosody in PD. Secondly, the heterogeneity of PD is a continuously developing topic, this outline shows that perception of linguistic prosody (or the perception of speech in general) is so far absent from the ongoing discussion. Finding a reliable marker for linguistic prosody processing is an important goal which would be an important contribution to a field that uses data driven methods. Thirdly, knowing the symptoms that co-occur in PD allows us to predict which people with PD are most likely to present with an impaired perception of prosody and test this prediction. Fourthly, by knowing which symptoms an impairment in prosodic perception occurs with, it allows us to infer shared underlying aetiology.

PD is characterised by the death of the dopaminergic neurons in the substantia nigra within the basal ganglia. The basal ganglia are subcortical cells that mediate, among other things, control of movement. The International Parkinson's and Movement Disorder Society (MDS) set the criteria for a diagnosis of parkinsonism as bradykinesia with a combination of either resting tremor, rigidity or both (Postuma and Berg 2016). These motor symptoms occur when the dopaminergic cells in the substantia nigra begin to die. The substantia nigra innervates the striatum via the dopaminergic nigrostriatal pathway. In addition to the loss of dopaminergic pathways, PD results in the loss of serotonergic and cholinergic pathways both subcortically and cortically. This results in, not only additional motor symptoms, but a myriad of sensory, autonomic and cognitive symptoms. There is ongoing discussion in the literature that the subtypes explored in this section are a result of variations in the extent of the damage to these areas (Sauerbier et al. 2016).

PD is heterogeneous but the extent of the heterogeneity and whether this heterogeneity means there are distinct subtypes is under debate (Porstuma et al. 2016). While the clinical efficacy of subtyping has yet to be established, outlining the common findings is illuminative as it can be inferred that symptoms that occur together may have common underlying causes. Studies commonly identify a spectrum of subtypes that are scaled with *Tremor/Motor Dominant* at one end and a range of categories at the other such as *Non-Tremor Dominant* (Marras and Chaudhuri 2016, Kaasinen et al. 2014*)*; *Diffuse* (Erro et al. 2013, Fereshtehnejad et al. 2015, Mu et al. 2017)*;* and *Postural Instability and Gait Disorder* (PIGD) (Huang et al. 2019, Balestrino et al. 2019, Vervoort et al. 2015, Erro et al. 2019) often with an intermediate category. These categories are derived from large scale cluster analyses on cohorts ranging in size from 73-person (Vervoort et al. 2015) to 1510-person (Ma et al 2015). In these categorisations, motor dominant subtypes have a less severe presentation, fewer non-motor symptoms and a slower progressing disease while the inverse is true for the opposite end of the spectrum. Diffuse PD is associated with more widespread neurological injury and motor dominant more localised (Erro et al. 2013, Fereshtehnejad et al. 2015). Subtypes with less severe symptoms often have more prominent tremor, mild autonomic symptoms, fewer motor complications, and slower disease progression (Fereshtehnejad et al. 2015, Erro et al. 2013, Mu et al. 2017, Ma et al. 2015). This pattern has been found in large scale cluster analyses on cohorts as large as 951 (Mu et al. 2017) and 1510 (Ma et al. 2015). More severe forms of PD are characterised by poorer postural control, decreased coordination, greater cognitive impairment, faster disease progression and often occur in older persons (>75)[1] (Vervoort et al. 2015, Mu et al. 2017, Fereshtehnejad et al. 2015). If impaired perception of linguistic prosody is a cognitive symptom, based on the above characterisation of the disease it would be expected in persons who were older at age of onset and who have more diffuse symptoms.

A number of studies have examined non-motor symptoms only. These studies identify more diverse subtypes that do not fit a sliding scale between two extremes. These studies identify four non-motor phenotypes, cognitive, neuropsychiatric, sleep and autonomic. It is notable that no studies to the author's knowledge directly incorporate symptoms related to either the production or perception speech or prosody into their proposed subtypes. The cognitive phenotype is characterised by severe cognitive impairment that will likely progress into PD with dementia. Persons in the cognitive phenotype are more likely to be older (>72 years of age) (Williams-Gray et al. 2009, Sauerbier et al. 2016, Marras and Chaudhuri 2016). Sleep phenotype is characterised by REM sleep disorder and hallucinations. The autonomic phenotype presents olfactory loss and urinary symptoms and

[1] Older at the time of examination, not necessarily older age at onset.

constipation. Neuropsychiatric subtypes present depression and/or anxiety and shares many symptoms with PIGD subtype such as falls and motor fluctuations. This phenotype also presents cognitive impairment but not as severe as the cognitive phenotype or diffuse forms of the disease (Marras and Chaudhuri 2016, Sauerbier et al. 2016, Tremblay et al. 2013, Brown et al. 2011). Persons in this group are more likely to be younger (Marras and Chaudhuri 2016). Depression and anxiety have been identified as subtypes in an analysis of 513 people with PD (Brown et al. 2011), a meta-analysis of 27 papers (Tremblay et al. 2013) and in subsequent reviews (Marras and Chaudhuri 2016, Sauerbier et al. 2016). Neither speech perception nor prosody are explored in these subtypes. Sensory impairment has been noted in persons with autonomic and PGID symptoms (Muller et al. 2011) but this was in pain sensation not in auditory sensory perception. Braak staging, a measure of the physiology and pathology of pre-symptomatic and post-symptomatic PD, identifies auditory sensory impairment at the latest stages of the disease (Braak et al. 2003), however in non-motor subtypes, limbic pathology has been identified at earlier disease stages (Marras and Chaudhuri 2016). The limbic system is involved in the processing of linguistic prosody (Belyk and Brown 2014) and plays a crucial role in executive functioning (McGough et al. 2018, Herrmann et al. 2019). Impairment in either or both of these processes might result in a primary or secondary impairment in prosodic processing. In the above characterisation of the disease, an impairment in the perception linguistic prosody might be expected in the cognitive or depression/anxiety subtype. It is standard to examine prosody in PD in the absence of dementia as the presence of dementia or dementia like symptoms is confound, especially given that dementia impairs prosodic recognition abilities (Horley et al. (2010)). Therefore it is unlikely that when a study finds a deficit in prosodic recognition in a PD group that this is due to the presence of someone in a severe or cognitive subgroup of PD as these persons would not pass the screening for cognitive impairment that is often used in studies of prosody. This suggests that a deficit in prosodic recognition may be present in other, less severe, subtypes. Depression is also often screened for in studies of prosodic recognition in PD. Gray and Tickle-Degnen (2010) performed a meta-analysis of 34 papers that examined the behavioural response of people with PD to emotion, as expressed through prosody and facial expressions. 17 of these papers tested the effect of depression on the ability of people with PD to recognise emotion. The meta-analysis found no effect for depression. This is at odds with research that has linked severe depression in people without PD to an impaired ability to interpret emotional prosody. This deficit occurs in persons with depression who experience particular impairments in set switching, working memory and executive functioning (Uekermann et al. 2008, Peron et al. 2011, Lima, Garrett and Castro 2013), all symptoms linked with depressed and/or anxiety PD types (Tremblay et al. 2013). Depression, when it occurs with executive dysfunction in PD, may be a result of damage to the dorsal raphe nucleus (Tremblay et al. 2013).

Depression in of itself therefore, may not be an predictor of an impaired ability to interpret prosody but depression when it is one symptom of a number that indicate a depressed/anxious subtype may be a factor. Anxiety is not something generally tested for in studies of PD and prosody so there is no data available to answer if impairments in prosody recognition could be linked to an anxiety subtype. The presence of anxiety (either on its own or with depression) may therefore be a, so far untested, factor in prosodic recognition in PD.

In summary, perception of linguistic prosody is not examined in the literature on the heterogeneity of PD. A cognitive impairment particular to PD and distinct from dementia has been hypothesised by some studies to be the cause of impaired prosodic processing (Breitenstein et al. 2001, Pell and Leonard 2003, Lima et al. 2013). The literature identifies more severe forms of PD that present with more diffuse symptoms. If impaired prosodic processing is caused by a cognitive impairment, such groups may be the ones most likely to present an impairment in linguistic prosody perception. Persons with severe cognitive impairment however are usually, if not always, excluded from studies of prosody in PD. The literature also identifies groups with depression and/or anxiety that present less severe forms of cognitive impairment. These groups present diffuse symptoms such as mild cognitive impairment, postural instability and motor fluctuations but in less severe form. If an impairment in prosody processing is the result of a cognitive impairment particular to PD, this group is another one likely to present impaired prosodic processing. Persons with depression however are usually excluded in studies of prosody and furthermore, depression has been ruled out as a cause of impaired prosodic processing in a number of studies (Gray and Tickle-Degnen 2010, Pell and Leonard 2003, Ariatti, Benuzzi and Nichelli 2008). The presence of anxiety however is not regularly tested for in prosodic studies. It is therefore clear that PD is heterogeneous disease and we should expect to see this reflected in the prosody literature. As for establishing which cluster of symptoms impaired prosodic perception occurs in, this can be speculated on using the existing literature but cannot be firmly established without directly examining linguistic prosody and testing against an exhaustive list of baseline measures.

2.4 Production of Prosody in PD

This section discusses the production of prosody in PD. It outlines that in addition to the motor-speech disorder caused by poor muscle control, there is evidence that there are non-motor and non-dopaminergic processes that exacerbate the motor-speech disorder and impair prosodic production. Impaired prosodic production and perception do not necessarily occur together.

Parkinsonian speech symptoms are given the umbrella term *hypokinetic dysarthria.* Dysarthria occurs in 70-90% of people with PD (Ma, Lau and Thyagarajan 2020). Characteristics of hypokinetic dysarthria

are breathy and harsh voice, uniform pitch, variable speech rate, reduced loudness and stress, and short rushes of speech (D'Alatri et al. 2008, Pinto et al. 2004). The death of dopaminergic pathways results in the loss of fine motor control. This loss of fine motor control extends to reduced articulatory movement which results in a reduced range of fundamental frequency, reduced speech intensity and inconsistent speech rate (Holmes et al. 2000, Rusz et al. 2011). This in turn causes more monotone and quieter speech that is punctuated with frequent pauses. This speech pattern makes it difficult to perceive emotions in the speech of people with PD.

As the disease progresses, people with PD find it increasingly difficult to make their speech intelligible. Harsh voice and reduced loudness make it difficult for words to be communicated and uniform pitch creates a monotone voice that lacks expression. This creates a compounded communication problem in which not only the words themselves are difficult to discern but much of their intended meaning is made unclear. Speech production involves dopaminergic and non-dopaminergic processes, as dopaminergic pathways are at the route of many of the motor symptoms of PD, as the disease progresses and the nigrostriatal pathway breaks down certain patterns of parkinsonian speech, such as cadence and festination, are mirrored in parkinsonian gait and movement (Mekyska et al. 2018, Moreau et al. 2007, Park et al. 2014).

A significant portion of speech production makes use of fine motor control which is controlled by dopaminergic pathways. There is evidence however that impaired production of prosody may not solely be a result of impaired motor control. Ma, Lau and Thyagarajan (2020) identifies a number of studies that identify changes in voice in the prodromal stages of PD. This is prior to widespread damage to the dopaminergic systems (Braak et al. 2003). Rusz et al. (2011) found impaired prosodic production in 60% of persons in the earliest pre-treatment stage of PD. Additionally, impaired prosodic production in PD has been found not to correlate with disease progression or motor impairment (Skodda et al. 2008) suggesting that in addition to inhibited motor control, there are other factors contributing to impaired prosodic production. Treatment options give further indication of distinct or at least interdependent mechanisms resulting in speech disruption with Skodda, Visser and Schlegel 2010, Skodda, Gronheit and Schlegel (2011) finding that, in contrast to reduced severity in motor symptoms, abnormal intonation and intonation rate (integral to prosody) are not improved with dopaminergic treatment. Impairments in the production of prosody have also been linked to the presence of non-motor symptoms and later cognitive decline and conversion to dementia (Rektorova et al. 2016) suggesting impaired production is linked with damage that is not localised to motor and dopaminergic anatomy. Additionally, impaired prosodic production as a result of dysarthria may mask an underlying form of dysprosody. Dysarthria causes Patients with PD to speak quieter. Ho, Bradshaw and Iansek (2000) found that patients overestimate their own loudness. This means that even if

patients were able to correct their quiet speech, they would not know it was necessary to do so. During speech the auditory cortex is supressed, New et al. (2015) found this suppression is impaired in PD which may result in the interrupted feedback. There are therefore non-dopaminergic and non-motor processes interacting with the motor and dopaminergic processes making a complex speech production pathology.

There are treatments that have proven effective in improving prosodic production. Speech Language Therapy, especially high intensity programmes with regular feedback are most effective at improving prosodic production (Gillivan-Murphy, Miller and Carding 2019, Atkinson-Clement, Sadat and Pinto 2015) and provision of high intensity programmes such as LSVT in the NHS increases each year (Parkinson's-UK 2019).

2.5 Perception of Prosody in PD

The following sections discuss the literature on the perception of prosody in people with PD. In comparison to linguistic prosody, there is extensive literature to draw from that shows a likely deficit in the processing of emotional prosody in PD. Literature on the causes of impaired processing of emotional prosody in PD is mixed. This may be due to the heterogeneous nature of the disease. There may even be multiple causes and these may vary from person to person. Processing of emotional prosody is more extensively studied and what is known about this is discussed first. This is balanced against what is known about the processing of linguistic prosody in PD and illustrates why additional studies in linguistic prosody processing in PD are needed.

Literature indicates that people with PD have a heterogeneous response to emotional prosody. A large body of literature identifies an inability to identify emotion from prosody in people with PD (Ariatti et al. 2008, Dara, Monetta and Pell 2008, Schroder et al. 2006, Paulmann and Pell 2010, Benke, Bosch and Andree 1998, Lima et al. 2013) however a not insubstantial minority of studies have found no such inability (Caekebeke et al. 1991b, Clark, Neargarder and Cronin-Golomb 2008, Mitchell and Boucas 2009). Studies therefore have examined if deficits in emotional prosodic perception are the result of additional disease factors. Reviews have identified a general impairment of emotional recognition in PD (Coundouris et al. 2019, Kwan and Whitehill 2011, Gray and Tickle-Degnen 2010). This has been linked to poorer executive dysfunction and working memory in some studies (Gray and Tickle-Degnen 2010, Kwan and Whitehill 2011). Other studies found no link between impaired emotional prosody processing and executive functioning but instead suggest derivation of emotional meaning is impaired due to damage to the basal ganglia and nigrostriatal circuitry that occurs in PD (Dara et al. 2008, Ariatti et al. 2008, Ventura et al. 2012). This converges with evidence of the basal ganglia's involvement in emotional speech processing (Paulmann, Ott and Kotz 2011, Kotz, Schwartze

and Schmidt-Kassow 2009, Paulmann, Pell and Kotz 2008). The sidedness of the motor symptoms in PD is an additional correlate of impaired ability to process emotional prosody. Congruent with evidence for a right-sided preference for non-linguistic functions of prosody (Section 2.2) persons with left-sided motor symptoms (implied right-sided pathology) have been found to be inhibited in recognition of emotion from prosody (Yip et al. 2003, Ventura et al. 2012). The P200 is a component that responds to emotional prosody. Persons with left-sided motor symptoms have shown an increased P200 component in response to emotional prosody (Garrido-Vasquez et al. 2013). In this latter study however, the participants with an altered P200 had no difficulty identifying emotional prosody. Changes in ERP response may therefore predict a later behavioural change. In summary, a deficit in emotional recognition from speech is a symptom that occurs in some people with PD. It is more likely to occur in persons with left-sided motor symptoms and it can occur in the absence of executive or working memory dysfunction.

Impairments in the processing of linguistic prosody in PD are less well documented. Linguistic prosody, even when making use of the same cues as emotional prosody, engages different cortical structures than emotional prosody (Paulmann et al. 2012) (Section 2.2). Convergent with this, in studies reporting inhibited emotional prosody processing, a corresponding inhibition in linguistic prosody is not necessarily found (Ventura et al. 2012). Like emotional prosody, the mixed reports in literature point to a heterogeneous response however deficits in linguistic prosodic processing in PD are less commonly reported or explored. The study of the processing of linguistic prosody is also complicated by the fact that linguistic prosody has multiple functions. Linguistic prosody can be used to stress important information, distinguish a question from a statement, disambiguate garden path sentences and distinguish nouns from verbs. These different functions make use of different cues and interact with different linguistic and semantic processes meaning there are various areas in which a breakdown in processing can occur.

Scott, Caird and Williams (1984) examined the response of 28 people with PD to contrastive stress. Stress in this study was used in two ways; to indicate sarcasm or sincerity; and to resolve the apposition of a sentence.[2] Correct interpretation of the stress in these instances was therefore critical to the correct interpretation of the heard utterances. The study found that people with PD were similar to controls in discriminating pairs of sentences with differing contrastive stress. Their participants with PD however were impaired when asked to comment on how the stress affected the meaning of the sentence. When asked if two sentences with differing stresses had the same or

[2] Example of using prosody to suggest or deny apposition using an example from Scott et al. (1984). *It's me, Alison.* Can be interpreted in two ways. I) *Me* and *Alison* are the same person i.e. they are in apposition. II) *Me* and *Alison* are two different people i.e. they are not in apposition.

different meaning, the PD group were again impaired compared to controls. This early study therefore presented evidence that people with PD are able to detect differences in prosody but are not able interpret the meaning of the prosody or identify that the different prosodies have an effect on the meaning of the sentence.

Blonder, Gur and Gur (1989) assessed the perception of three types of linguistic prosody in 21 people with PD. Again, it was found that PD group performed similarly to controls in discriminating two prosodic structures, however in this study the PD group also performed similarly to controls when asked to explicitly identify statements and questions. The study also tested the perception of compound words; for example, “red coat” and “redcoat”. People with PD in this instance were unable to distinguish the two-word stresses. This paper indicated again that people with PD are able to extract the prosodic cues but were not able to map them to their appropriate meaning in the case of compound words but were able to do so when identifying questions or statements. The reasons for the differing performance may be due to inferring lexical meaning from acoustic cues may be more complex than inferring sentence type. The difference may also be due to difference in cues used to interpret the prosodies. A question is carried by a gradual increase in pitch whereas word stress is carried by a slight elongation and drop in pitch. The study examined if sidedness of PD is a correlate of impaired prosodic perception. They split their PD group into people with PD with left-sided motor symptoms and right-sided motor symptoms. It was found that those with right-sided motor symptoms were more impaired in the stress task. This is in agreement with studies identifying a left-sided preference for short cues and cues conveying semantic meaning (Section 2.2).

A study by Pell (1996) on a smaller cohort of 11 people with PD found discrimination of two different linguistic prosodies to be intact in PD. Unlike in the study of Blonder, Gur and Gur (1989), their PD group were unable to explicitly identify questions, statements or interrogations. A study by Lloyd (1999) on 11 persons with PD reported more results contradicting those reported by Blonder et al (1989). Replicating the red coat/redcoat test, the study found no significant difference in the PD group compared to healthy controls. As this finding was at odds with the previous work, it examined the results at the individual level. They found two of the PD group differed from the other people with PD as well as from each other. One person with PD scored lower in in the red coat/redcoat task and reported that they were unable to hear a difference between the two stresses. The study validated this task by performing the same task written down rather than with audio cues. Those who performed badly on the audio task had an improved performance in the written task, indicating that the inhibition was in processing the prosody in particular. This is one of the few studies to examine and demonstrate a heterogeneric response to linguistic prosody in PD.

As prosody is composed of multiple cues, it may be that the variance in the results is due to people with PD being selectively impaired in which cues they are able to process. This possibility has been explored in pure tone discrimination tasks. Pure tone tasks allow precise modulation of specific acoustic parameters. They also allow the examination of cue processing without the complicating factors of language processing and complex task demands. A study by Harrington, Haaland and Hermanowicz (1998) found that persons with PD were unimpaired when discriminating pure tones of differing frequencies but impaired when discriminating pure tones of differing duration. This is in agreement with the study of emotional prosody by Breitenstein et al. (2001) on 20 people with PD that found that people with PD rely more on pitch cues than durational cues when identifying emotional prosody. These studies suggest an abnormal processing of durational cues which further agrees with literature that suggests that the basal ganglia play an important role in the extraction of temporal cues (Kotz et al. 2009). A study by Troche et al. (2012) on a group of 12 people with PD provides contrary evidence. This study found that persons with PD were able to differentiate pure tones of differing duration but not pure tones that differed slightly in amplitude or frequency. An inability to distinguish differences in amplitude coheres with evidence showing persons with PD have an impairment in judging the loudness of their own voice and the voices of others (both while speaking and when listening to a recording of themselves played back) (Ho et al. 2000, Fox and Ramig 1997, Clark et al. 2014). This impaired self-perception while speaking has been attributed to reduced suppression of the auditory cortex during speech (Arnold et al. 2014). If an additional sensory deficit is present, it would be an exacerbating factor in impaired self-perception as well as causing impairment in the perception of others. Further uncertainty is raised by a study by Dromey and Adams (2000). This study found that persons with PD are able to detect changes in loudness of pure tones. Methodological differences may account for the difference in this instance as the differences in loudness were less subtle than those used in the study by Troche et al (2012).

To summarise, the behavioural studies concerning linguistic prosody and PD present a typically unclear picture. Intact discrimination is most often found (Caekebeke et al. 1991a, Ventura et al. 2012, Scott, Caird and Williams 1984, Lloyd 1999, Pell 1996, Blonder, Gur and Gur 1989). There are however exceptions in discriminating emotional prosody (Pell and Leonard 2003), linguistic prosody (Ariatti et al. 2008) and pure tones of differing frequency (but not duration) (Troche et al. 2012). Explicit identification of the meaning conveyed by linguistic prosody has been found impaired (Blonder et al. 1989, Lloyd 1999, Pell 1996, Scott et al. 1984) but there is disagreement over the type of meaning that is impaired. Namely there is disagreement over whether people with PD can (Blonder et al. 1989) or cannot (Lloyd 1999, Pell 1996) distinguish questions from statements. There is also disagreement over whether people with PD can (Lloyd 1999) or cannot (Blonder et al. 1989) identify meaning from words

with differing contrastive stress. Like emotional prosody, there is likely a heterogeneous response to linguistic prosody. This heterogeneity extends to not just whether linguistic prosody is impaired but the type of linguistic prosody that is impaired. To the author's knowledge, Lloyd (1999) is the only study in linguistic prosody to directly examine the heterogeneous response to linguistic prosodic processing in PD.

Outside of a possible impairment in the processing of certain speech cues, few explanations of the causes of impaired linguistic prosodic perception have been proposed or tested. Troche et al. (2012) suggests that an impairment in linguistic prosody processing occurs in PD because of the amygdala's role in the processing of linguistic prosody in addition to a potential deficit in the control of attentional resources. A deficit of attentional resources in relation to linguistic processing is an avenue worth exploring as data on the P3a component in PD show the assigning of attentional resources to auditory cues is impaired in PD (Lange et al. 2016, Solis-Vivanco et al. 2015, Schomaker et al. 2014). Additionally, some people with PD are impaired in lexical encoding and task learning (Cohn, Moscovitch and Davidson 2010, Vingerhoets, Vermeule and Santens 2005). Such impairments might inhibit performance in novel tasks, especially those making use of auditory cues with complex syntactic, lexical and/or prosodic content. ERPs offer the possibility of exploring the time-course of prosodic perception and marking the point at which impairments occur. They can also show which domain the deficit occurs in (i.e. general processing impairment or an impairment in a specific domain such as linguistic, attentional or prosodic). The following sections examines the literature on ERPs used in the exploration of prosody and PD and how they can be used to shed light on some of the remaining questions in the literature.

How the perception of prosody becomes altered in healthy aging populations provides a cautionary note while also providing complementary data. Orbelo et al (2005) found older persons with a mean age of 72 were impaired compared to younger controls in their ability to identify and discriminate emotional prosody. Like in PD, this was not a universal, and the impairment of identification occurred in approximately one third of their 62-person sample. A later study by Seddoh et al (2020) using a 20-person cohort with a mean age of 76 found older adults performed similarly to younger controls in distinguishing statements from questions as well as in identifying emotions when utterances were composed of sentences with a basic subject-verb-object order. However, in a follow up study with a 14-person cohort with a mean age 75, they found that when using sentences with a more complex syntactic structure (such as the introduction of the introduction of the auxiliary verb "have") the older group performed worse compared to a younger cohort in the identification of emotion from prosody. The study concluded that the older cohort made more use of semantic contextual cues when identifying emotions in the utterances.

Seddoh et al (2018) linked impairments in the perception of prosody in older people to an age-related reduction in dopamine in the amygdala and limbic system. This is startlingly similar to the proposed aetiology of impaired prosodic processing in PD (Belyk and Brown 2014; Troche et al 2012). Also similarly to PD, failure to identify emotion from prosody in older persons, has been linked to possible cognitive decline that is not captured by standard tests of cognition (Goy et al 2018; Lambrecht et al 2012; Orbelo et al 2005). This raises the possibility that people with PD who are impaired in the processing of prosody are experiencing a more pronounced form of an impairment that is found in certain otherwise healthy older persons. McIntosh et al (2015) examined the perception of prosody in PD compared to that of age-matched controls and younger controls. They found that healthy older controls were significantly worse at identifying emotion from prosody than healthy younger controls but that people with PD were significantly worse still. Whether the mechanisms underlying impaired processing of prosody in healthy older persons are the same as those underlying impaired processing of prosody in PD can be examined using EEG markers that mark the processing stages.

2.6 How linguistic prosody can be captured on EEG

Three (not unrelated) ways in which linguistic prosody facilitates the processing of speech are by guiding attention (Wang et al. 2011, Ouyang and Kaiser 2015, Kristensen et al. 2013), building prosodic expectations (Kotz and Paulmann 2007, Paulmann et al. 2012) and by segmenting speech into phrase boundaries (Wagner and Watson 2010, Frazier, Carlson and Clifton 2006, Pannekamp et al. 2005). By manipulating prosody's role in the segmentation of speech, markers for the guiding of attention and for violations of prosodic expectancy can be elicited and the presence or absence of these markers can tell us if and how the processing of prosody is impaired in people with PD. This section reviews the tasks that elicit these markers (dealing first with attention and then with prosodic expectancy), the underlying principles of these tasks, and how the principles of these tasks can be used to study the perception of linguistic prosody.

2.6.1 Linguistic Prosody and Attention Capture

The attentional processes discussed here typically elicit a three-stage cascade of ERPs. These components and the underlying processes that they mark are studied using distraction tasks, 2 or 3-stimulus oddball tasks and switch tasks. In a standard 2-stimulus oddball task the participant is presented with a series of stimuli that contain frequent non-targets and infrequent targets. The participant is instructed to ignore the non-targets and respond in some way to the infrequent targets. A 3-stimulus oddball task takes the same form but a third infrequent, *deviant* stimulus that differs from both the target and non-target is presented. This deviant stimulus (which is otherwise ignored by the participant) elicits the attention capture components of interest. A distraction task is a task that

elicits the attention capture components while the participant is engaged in a primary task while being instructed to ignore any irrelevant (usually auditory) stimuli being presented. The task the participant is otherwise engaged in can be active or passive. A common passive task is to watch a silent film without subtitles (Wang et al. 2005, Carminati et al. 2018, Pakarinen et al. 2014, Light et al. 2007). Active tasks include a range of tasks with varying complexity and difficulty including steering tasks (Scheer et al. 2016), auditory categorisation tasks (Escera et al. 1998), visual categorisation tasks (Muller-Gass et al. 2007), video games (Dyke et al. 2015), or even meditation (Cahn and Polich 2009).

Finally, attention capture components can be elicited in response to tasks that require *task-switching* or *object-switching*. A task-switch is when the participant is instructed to perform a task according to certain rules. During the task a (usually auditory) cue signals that the rules of the task have changed. The task being carried out is often a form of the Wisconsin Card Sorting Task (WCST). In this task participants are instructed sort cards according to one of two rules (an example being to sort cards by shape or colour). After the participant sorts each card, a cue signals whether the next card has to be sorted by the same rule (a repeat cue) or a different rule (a switch cue). Cues that signal a change in rule elicit the ERPs of interest. **Figure 2.1** shows a schematic of the cued WCST.

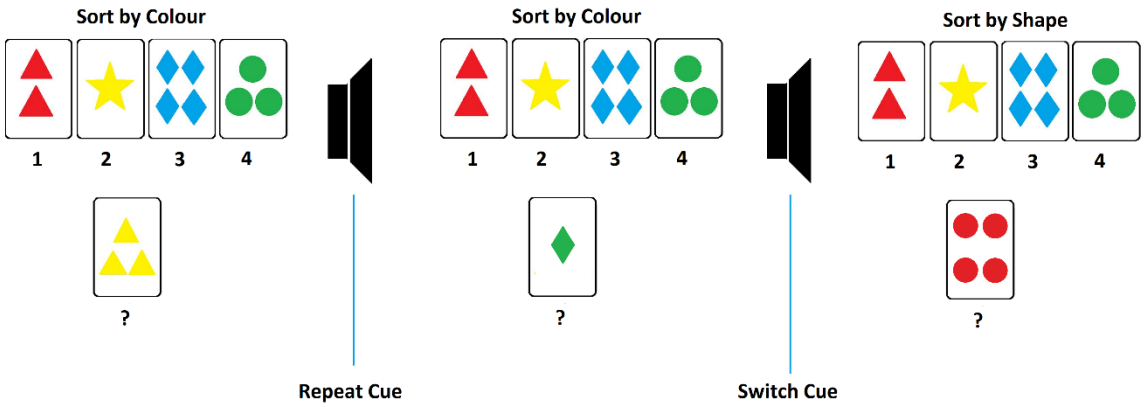

Figure 2.1 Scheme for cued WCST.

This schematic shows three iterations of the cued WCST. In each iteration, the participant is shown four cards, labelled here as cards 1-4. They are also shown a task card, labelled here with a "?". They are instructed to sort the task card by a rule established prior to the commencement of the task. If in this case that rule is colour, in the first iteration, the yellow task card would match with card 2. The participant than hears a repeat-cue that signals that the next task card is to be sorted according to the same rule. This would mean matching the green task card with card 4. The participant then hears a switch-cue that indicates that the next task card should be sorted by a different rule, for example by shape. The third task card featuring circles would then be matched with card 4. The cues used as a repeat or switch cues are often auditory pure tones of two different fundamental frequencies. The ordering of repeated cues and switch cues is randomised. The pure tone that signals the change in task rule elicits the task-switch EEG markers. Figure adapted from https://en.wikipedia.org/wiki/File:Wisconsin_Card_Sorting_Test.jpg.

Task-Switch paradigms have in common that a rule change is signalled by the cue. Object-Switch paradigms, by contrast entail a change in focus from one object to another with no associated rule change. In practice an object-switch entails either a change in an object that is to be recalled (de Vries et al. 2018) or changing of focus from one object to another (Berti 2008, Berti 2016). An example of this is if a participant is shown a grid of coloured objects with instructions to recall one of the colours. An object-switch cue would signal a change in which colour is to be recalled. **Figure 2.2** shows a schematic for an object-study showing the methodology of a study by DeVries et al (2018).

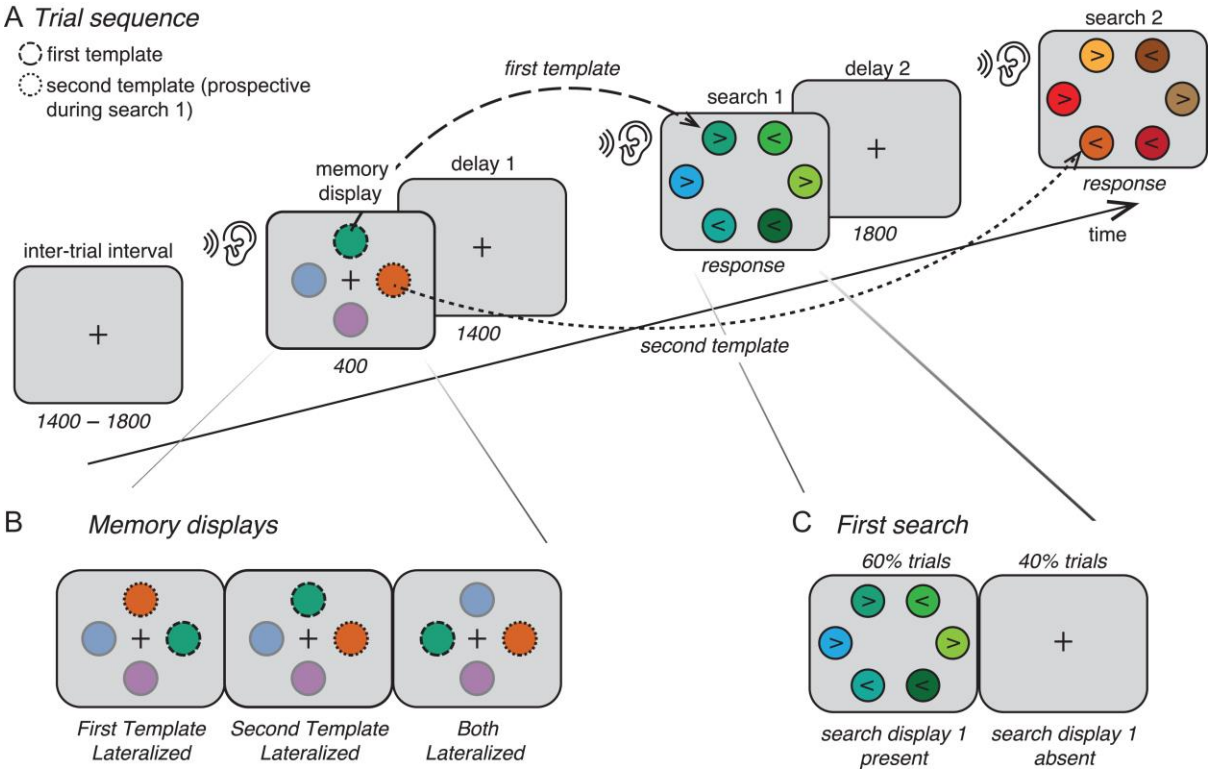

Figure 2.2 Scheme for an object-switch task (De Vries et al 2018).

Object-switch task used in an object-switch study by de Vries et al. (2018). In this task, the participant is shown an array of colours. The border of these colours indicates which should be memorised and in what order they are to be used. The participant is then shown a grid on which they are to identify the first colour and then a grid in which they are to identify the second colour. In 40% of the trials a cue indicates to the participant that they will not be shown only the second grid. This cue in which causes the person to reprioritise the colours in their mind results in frontal delta power activation followed by parietal alpha suppression.

Oddball tasks, distraction tasks and switch tasks each elicit a combination of EEG features associated with the capture and orientation of attention. The occurrence of these features and the processes that they mark can be broken into three stages. In the first stage the N100 and/or mismatch negativity (MMN) occurs. The N100 is a frontal negative component peaking approximately 100ms. The MMN is a frontal negative component peaking at approximately 100-200ms. In the second stage the P3a and/or novelty-P3 (nP3) occurs. The P3a is a frontal positive component peaking at approximately 220-280ms. The nP3 is frontal positive component peaking approximately 360-450ms. When the P3a and nP3 occur together, they are a biphasic wave and are often grouped together as sub-components of a single larger component. In the third stage, the *reorientation negative* (RON) occurs. The RON is a frontal negative that peaks at approximately 450-700ms. Not all three of these stages necessarily occur. Which stages do occur depends on the saliency and importance of the incoming stimulus as well as on the demands of the task being carried out by the participant. Each stage of this process and how these components can be used in the study of linguistic prosody is discussed below.

The first stage of the attention capture process is signalled by an N100 and/or an MMN. The N100 is a component that occurs at the onset of any audio stimulus (Onitsuka, Oribe and Kanba 2013) but its amplitude and latency are affected by the predictability (Schwartze, Farrugia and Kotz 2013, Nelson, Hajcak and Shankman 2015) and salience of a stimulus (Gonsalvez et al. 2007). A distracting stimulus may elicit a prominent N100 instead of the MMN (Berti 2013, Berti, Vossel and Gamer 2017, Escera et al. 1998) or it may elicit an N100 and MMN (Rinne et al. 2006, Berti 2012). It is supposed that the N100 and MMN components mark the initial stages of two parallel streams of attention capture (Berti et al. 2017, Berti 2013, Jaaskelainen et al. 2004, Naatanen, Jacobsen and Winkler 2005, Escera and Corral 2007). According to this theory, *deviant* sounds (those which are different but similar to preceding sounds) elicit an MMN and *novel* sounds an N100 (Rinne et al. 2006, Winkler 2007, Berti 2012). To elicit an N100, the incoming sound should be salient, novel and have no referent (Berti et al. 2017, Berti 2013, Berti 2012, Escera and Corral 2007). Sentence onset words (i.e. those following a prosodic boundary) elicit an N100 (Hahne and Jescheniak 2001) but N100s in response to the onset of words that occur mid-sentence during continuous speech have been found to be reduced (Sanders and Neville 2003) or absent (Connolly and Phillips 1994). Stressed syllables have an increased N100 that is distributed frontally and laterally compared to unstressed syllables which have a medially distributed N100 (Sanders and Neville 2003). The N100 is therefore highly attuned to prosody. The N100 in response to distracting stimuli is most often followed by a biphasic P3a-nP3 that peaks 220-280ms (Berti et al. 2017, Berti 2013, Barry, Steiner and De Blasio 2016) and 360-450ms (Barry et al. 2016). This is in opposition to the MMN which is most often followed by a monophasic P3a.

In the deviant mode of attention capture, the initial stages of the attention capture process are marked by the MMN. The MMN is most often associated with oddball tasks but it is also the starting point in the process of distraction and in response to such a process it is typically followed by the P3a and (in some instances) the RON (Schroger and Wolff 1998b, Schroger, Giard and Wolff 2000, Nikjeh, Lister and Frisch 2009, Jaaskelainen, Schroger and Naatanen 1999, Rinne et al. 2006, Roeber, Widmann and Schroger 2003, Wetzel et al. 2004). The MMN has been elicited to changes in pure tone frequency/duration/intensity (Schroger and Wolff 1998b, Schroger et al. 2000, Berti, Roeber and Schroger 2004, Nikjeh et al. 2009, Jaaskelainen et al. 1999, Rinne et al. 2006, Roeber et al. 2003), emotional and linguistic prosody (Wang et al. 2005, Carminati, Fiori-Duharcourt and Isel 2018) and environmental sounds (Wetzel et al. 2004). The MMN can be elicited while the participant is engaged in a primary task during which they are to ignore the stimuli (Schroger et al. 2000, Sussman et al. 2007, Wang et al. 2005, Carminati et al. 2018, Escera et al. 1998, Escera, Corral and Yago 2002), so is often used as a measure of involuntary attention capture. Stimuli which are sufficient enough to elicit an

MMN are not necessarily sufficient to elicit subsequent attentional processes reflected in the P3a (Schroger et al. 2000, Rinne et al. 2006, Escera et al. 2002, Wang et al. 2005).

The MMN is the result of a dual process of generating a sensory memory and detecting deviances from that memory. By generating a sensory memory, predictions of incoming stimuli can be made and this predictive process streamlines the assignment of attentional resources (Winkler 2007, Justo-Guillen et al. 2019, Sussman 2007). Oddball paradigms are efficacious in eliciting an MMN because the frequent repetition of the standard reinforces the memory trace (Sussman 2007, Sussman et al. 2007). Infrequent prosodic stress patterns on single words and pseudowords elicit an MMN showing a memory trace for prosodic stress (Zora, Schwarz and Heldner 2015, Zora et al. 2016b, Zora, Heldner and Schwarz 2016a). The MMN therefore detects deviance and this deviance can take the form of deviant prosody. Prosody can also be used to highlight or obscure deviance. In both of these cases the MMN is an indirect marker of pre-attentive detection of prosody.

Linguistic prosody has been used to elicit an MMN (Zora et al. 2016b, Zora et al. 2016a, Zora et al. 2015). According to the theory of parallel attention capture streams, prosody has been used in these instances to tap into the deviant stream. Incongruent linguistic prosody is salient and unexpected, it should therefore be possible to use linguistic prosody cues that are sufficiently salient to enter the transient mode of attention capture as well. This could be done in an oddball task, in which case an MMN would also be expected (thus entering both the transient and deviant form of attention capture) or in a distractor or switch task, in which the N100 would be elicited without the MMN (entering solely the transient form of attention capture).

The next stage of attention capture is marked by the P3a and/or the nP3. It will be argued increased frontal delta power is linked with these components and plays a fundamental role in this stage as well. The P3a and/or nP3 have been elicited in response to novel and distracting stimuli (Berti et al. 2017, Berti 2013, Katayama and Polich 1998, Courchesne et al. 1984, Scheer, Bulthoff and Chuang 2016, Dyke et al. 2015, Pakarinen et al. 2014, Cahn and Polich 2009, Light, Swerdlow and Braff 2007, Muller-Gass et al. 2007, Wang et al. 2005, Escera et al. 1998, Rinne et al. 2006, Wambacq and Jerger 2004), cues that signal a task change (Perianez and Barcelo 2009, Prada et al. 2014, Kopp et al. 2006, Hoelig and Berti 2010, Lange et al. 2016) and cues that signal an object change (Frenken and Berti 2018, Berti 2016, Berti 2008).

In a distraction paradigm a participant performs a task while auditory stimuli are played with the intention of distracting the participant. The way in which the distracting stimuli are presented during these tasks is important to the elicitation of the P3a. One method is to present the stimuli in a fashion analogous to a 2-stimulus oddball task (Wang et al. 2005, Carminati et al. 2018, Pakarinen et al. 2014,

Light et al. 2007). In these cases, there are frequent stimuli and infrequent/deviant stimuli - neither stimulus type is a target per se as the participant is instructed to ignore all stimuli, but only the deviant stimuli elicit the P3a. An alternative method is to present three stimuli types in a fashion analogous to the 3-stimulus oddball paradigm (Cahn and Polich 2009, Courchesne et al. 1984), again only the deviant (i.e. the most salient) stimuli elicit a P3a. Using this frequent/infrequent presentation style creates the context in which the deviant stimulus is sufficiently novel and/or distracting to elicit a P3a. This context however is not necessary in paradigms with sufficiently salient distracting stimuli such as unexpected environmental sounds (Dyke et al. 2015).

An early study by Katayama and Polich (1998) captured the importance of context to the elicitation of the P3a. In this study, how the target, non-target and deviant differed from each other was altered. This therefore altered both the difficulty of the task and the salience of the deviant. They found the P3a was only elicited when both the task was difficult (when the target and non-target were similar) and when the deviant was dissimilar from the target. These findings were replicated by Sawaki and Katayama (2006) using visual stimuli. In this task, the deviant stimulus elicited a P300 when the task was easy and the target/deviant distinction was difficult, this was taken as an indication that the participant mistook the deviant for a target. A combination of vigilance on the part of the participant (contrived by task difficulty) and salience on the part of the stimulus (contrived by target/deviant dissimilarity) is therefore key to eliciting the P3a.

The P3a is also affected by task. Increasing task demands in distraction tasks attenuates the P3a (Berti and Schroger 2003, Scheer et al. 2016). Explanations that have been mooted for this are: that there are fewer resources to apportion to the distracting stimuli (Scheer, Bulthoff and Chuang 2016); working memory exerting control over involuntary attention (Berti and Schroger 2003); and reduced vigilance on the part of the participant (Zora, Rudner and Montell Magnusson 2019). In a contrary study, Muller-Gass et al. (2007) found that task difficulty did not affect the P3a amplitude in a ten-person cohort. In this study the participants were instructed to keep track of a moving visual marker. This is in comparison to a study by Scheer et al. (2016) on a 24-person cohort that used a physical demanding steering task. It was found in this cohort that task difficulty did modulate the P3a. Muller-Gass et al. (2007) explained their exceptional result with the supposition that the P3a is at times a strongly automatic process (not attenuated by varying attention) and at times weakly automatic (attenuated by varying attention) and this distinction is governed by the experimental conditions.

In addition to task and context, stimulus type itself is important, sounds used to elicit the P3a include pure tones, environmental sounds and emotional prosody. Pure tones have been found to elicit a smaller P3a than environmental sounds (Scheer et al. 2016). Pure tones that deviate from the target

in ways that make them less salient, such as lowering the intensity have been found not to elicit a P3a (Escera et al. 2002, Rinne et al. 2006). In one instance this was during an active categorisation task and the other a two-stimulus oddball task. In these instances, a lack of saliency combined with sub-optimal context (active distractor task rather than passive distractor task and 2-stimulus oddball rather than 3-stimulus oddball) resulted in the P3a not being elicited. This indicates that when the participant is actively engaged in a task, salience or important information is necessary to demand attention. Generating the salience necessary to elicit a P3a using linguistic prosody is challenging. A number of studies presenting words with deviant linguistic prosody in an oddball fashion found that the deviance only elicited an MMN unless pseudowords were used (Zora, Rudner and Montell Magnusson 2019, Zora, Heldner and Schwarz 2016a, Zora et al. 2016b, Zora, Schwarz and Heldner 2015). One study found that when deviant consonants were highlighted using prosody, this increased the amplitude of the P3a (Wang et al. 2005). In this instance the prosody itself was not the deviant that elicited the P3a. It is also notable that in this study speech sounds, rather than words were used. Deviant changes in linguistic prosody in the form of prosodic tone (not to be confused with a pure tone, see Section 2.2 for definition of tone) in Cantonese do elicit the P3a when presented in an oddball fashion (Zhang and Shao 2018). This deviant prosodic tone conveys a change in semantic meaning in Cantonese so the elicitation of the P3a may be due to the increased functional significance of tone in Cantonese. Emotional prosody, by contrast, elicits a P3a during passive distraction tasks (Carminati et al. 2018, Pakarinen et al. 2014, Charpentier et al. 2018) as well as during two-stimulus oddball tasks (Zora, Rudner and Montell Magnusson 2019, Chen et al. 2016, Yang et al. 2018). Therefore, in terms of stimulus type, the P3a has a preference for highly salient sounds, such as environmental sounds, and sounds that encode meaning (Scheer et al. 2016). When, and if, a P3a is elicited in response to prosody, it indicates that the prosody was detected and that it was salient enough to demand the participant's attention. Importantly, while, deviant emotional prosody elicits an MMN and P3a (Wambacq and Jerger 2004, Carminati et al. 2018, Pakarinen et al. 2014), when presented in an oddball fashion, words intoned with deviant linguistic prosody elicit an MMN only (Zora et al. 2016b, Zora et al. 2016a, Zora et al. 2015) unless pseudowords words (Zora, Heldner and Schwarz 2016, Wang et al. 2005) or deviant prosodic tone is used (Zhang and Shao 2018). This means that small deviances in linguistic prosody presented in this fashion are not salient enough or sufficiently functionally significant to recruit a later attentional response. Stimuli that lack the salience necessary to elicit a P3a require manipulation of the task to increase the vigilance of the participant.

These examples have focused on oddball tasks and distraction tasks. In the latter, the stimuli cause a distracting effect that can often be measured behaviourally. The nP3 and P3a are not however related to distraction per se but to a more general process related to control of attention. This is evidenced

by its occurrence in switch tasks. In a distraction task the stimulus is to be ignored by the participant. In a switch task, the stimulus heard by the participant is relevant to, and necessary for the completion of, the task. Switch tasks can be divided into two types, *object-switch* tasks and *task-switch* tasks. Object-Switch tasks require the participant to hold more than one object in their working memory and reprioritise them when cued to do so by a (visual or auditory) cue. Object-Switch tasks in which P3as are reported require the participant to remember an array of numbers. A cue indicates that an arithmetical operation is to be carried out on one of these numbers. A visual cue then indicates if the next operation is to be carried out on the same number in the grid or a different one. Switch cues in these tasks elicit a P3a (Frenken and Berti 2018, Berti 2016, Berti 2008) and, in one reported case, a RON (Berti 2008). Task-Switch tasks require the participant to perform a primary task in accordance with a certain rule. A (usually auditory) cue signals a change in the rule of the task. Task-Switch tasks often use a variation of the Wisconsin Card Sorting Task (WCST) in which participants are to sort cards according to colour or shape. An auditory cue signals whether the participant is to sort the next card according to the same rule as the previous card or whether the rule has changed. The task-switch cues in these card sorting tasks elicit a P3a (Kopp et al. 2006, Perianez and Barcelo 2009, Lange et al. 2016) or nP3 (Prada et al. 2014). As the P3a is often the focus of these studies, the N100, MMN and RON are usually not examined. Of these studies, one did report an enhanced N100 in response to task-switch cues (Kopp et al. 2006). A study on a 9-person cohort by Hoelig and Berti (2010) reported a full MMN-P3a-RON cascade in response to a task-switch cue. This study had important methodological features that may have been contributed to this response. Hoelig and Berti (2010) presented stimuli in an oddball format in a distraction condition and in a switch condition. In both conditions the participant was to indicate if the pure tone was presented latterly or centrally. In the distraction condition the oddball pure tone was to be treated the same as the standard (i.e. the participant was to indicate if it were presented laterally or centrally). In the task-switch condition they were to indicate if the pitch of the deviant tone was higher or lower than the tone of the previously heard tone (i.e. the oddball tone indicated a change in task rule). The deviant task-switch cue elicited the full MMN-P3a-RON cascade. The deviant mode of attention capture can therefore be entered in a task-switch paradigm. The use of the oddball format confirms that this was a deviant detection and not a transient detection.

The switch paradigms are in some ways an inversion of the distraction paradigms. In the latter, the stimuli are irrelevant, hinder task performance and must be dismissed. In the former, the stimuli are essential to the completion of the task. The same ERPs being elicited in response to paradigms which are at odds raises interesting questions about what the P3a indexes. A process triggered in response to a salient and distracting stimulus is stimulus-driven (bottom-up) and therefore indexes an exogenous attention process. The latter task-switch and object-switching paradigms are governed by

the predetermined rules of the task and therefore task-driven (top-down) and the process triggered is an endogenous attention process. All three task types elicit a P3a. Preceding N100s and MMNs have been reported in task-switch paradigms. RONs have been reported in object and task-switch paradigms. When these ERPs are elicited in response to a distraction, they are often called the *distraction potential* (Escera and Corral 2003) but all of the ERPs that make up the distraction potential can be elicited to task relevant information. In fact, the P3a has been found to be bigger to switching cues than distracting cues, this study had a smaller 9-person sample but used large, 700 trials per condition (Hoelig and Berti 2010). With these diverse tasks with nominally conflicting demands, what exactly the P3a indexes is subject to some discussion. When part of the midpoint of distraction it was thought to index the orientation of attention towards the incoming stimulus. This definition has since been refined but the P3a is still used as a marker for this particular process (See Lange et al. (2016) for an example). A more general theory that encompasses the P3a's role in all these tasks is that it is the top-down control of attention (Barcelo et al. 2006, Hoelig and Berti 2010, Berti 2008, Barry et al. 2016). Related theories include that it is an updating process (be that of WM representations or task goals) (Barcelo et al. 2006), that it has an evaluation or decision-making role (Barry et al. 2016), that it is the evaluation of the contextual novelty of a stimulus (Escera and Corral 2007), and that it is the inhibition of an old task set (Perianez and Barcelo 2009) or old object (Frenken and Berti 2018). The P3a is therefore a component that appears in response to salient cues in tasks that demand the attention of the participant.

The final portion of the attention capture cascade of ERPs consists of the *reorientation negative* (RON). The RON is a frontal negative (450-700ms) typically following the MMN and/or N100 and P3a both as the concluding phase in the process of distraction (Horvath, Winkler and Bendixen 2008, Justo-Guillen et al. 2019) and in switch paradigms (Berti 2008, Hoelig and Berti 2010). In the literature concerning distraction tasks, the RON is commonly supposed to index the reorientation of attention back towards task relevant information following the distracting stimulus (Escera and Corral 2003). This early theory developed from results that indicated that task relevant stimuli do not elicit the RON (Schroger and Wolff 1998a) and because its attenuation being linked to poorer task performance (Mager et al. 2005, Berti, Grunwald and Schroeger 2013, Berti 2013). Like the P3a however, theories as to the exact function of the RON continue to develop (Hoelig and Berti 2010, Justo-Guillen et al. 2019). Hoelig and Berti (2010) found a larger RON to distracting stimuli that contained task-relevant information. From this they hypothesised that RONs can occur in response to task-switch cues. This led to the hypothesis that it is a more general reorientation of attentional resources or selection of an adaptive response (Berti et al. 2013, Hoelig and Berti 2010, Justo-Guillen et al. 2019).

The N100, MMN, P3a, nP3 and RON are the core ERP components indexing attention capture and orientation. How linguistic prosody interacts with these processes has been studied. By presenting words in an oddball paradigm and varying the prosodic stress pattern on these words an MMN-P3a can be elicited (Wang et al. 2005, Zhang and Shao 2018). In these studies the prosodic pattern itself can serve as the deviant that elicits the oddball effect (Zhang and Shao 2018) or it can be used to highlight the deviance (Wang et al. 2005). In the latter case, when deviances are not highlighted using prosodic stress an MMN is elicited but the subsequent P3a is not. This shows the important role linguistic prosody plays in the recruiting of attentional networks. Similar processes have been demonstrated using emotional prosody (Carminati et al. 2018, Pakarinen et al. 2014). These processes have been successfully used to examine impaired prosodic processing in at least one patient group. Congenital amusia is a condition which causes lifelong impairments in pitch processing. A study by Zhang and Shao (2018) on a 24-person cohort found that the MMN in response to changes in tone in Cantonese was present, from which it was inferred that pre-attentive possessing was intact. The P3a however was absent, from which it was inferred that later conscious processing of the pitch was impaired. Eliciting the P3a in this manner is promising but it would not be possible to use this protocol in English as it is not a tone language. The way in which tone encodes semantic meaning in tone languages makes it particularly salient and functionally significant. It is therefore able to recruit both early (MMN) and later (P3a) attentional processes. However, there is no exact analogue of this use of prosody in English. The protocol of Zhang and Shao (2018) therefore demonstrates that the attention ERPs can be used to differentiate successive stages in prosodic processing but it does not provide a method of eliciting these ERPs in response to linguistic prosody in English.

The N100, MMN, P3a, nP3 and RON can be elicited in response to oddball, distraction or switch tasks or a combination of these. Switch tasks are also associated with other ERP components and oscillatory features. These features also index processes related to the capture and the control of attentional resources but these features (so far) have not all been linked together. These features are the switch positive (SP), associated with task-switching; frontal delta power activation, associated with top-down control of attention; and parietal alpha suppression, associated with object switching. These components are all important to the current discussion as it will be argued that linguistic prosody has untapped potential in the examination of these processes.

Task-Switch paradigms elicit an additional ERP response that is not present in distraction paradigms, oddball paradigms and not reported in object-switch tasks. This is a central parietal (Lange et al. 2016, Karayanidis et al. 2010) or left-parietal positive (Astle, Jackson and Swainson 2006, Capizzi et al. 2016) and has been reported to switch cues and peaking 500-1000ms from the cue (Lange et al. 2016, Capizzi et al. 2015). This *switch positive* (SP) is associated with the switch of attention from the old task rule

to the new task rule and is thought to index reconfiguration of the old task set (Capizzi et al. 2016, Lange et al. 2016). This positive has been identified in the WCST (Lange et al. 2016) but also in a diverse number of tasks, from simple tasks requiring discrimination (Astle et al. 2006, Hoelig and Berti 2010, Tarantino, Mazzonetto and Vallesi 2016) to complex tasks requiring lexical access (Capizzi et al. 2016, Capizzi et al. 2015). Larger RTs (Capizzi et al. 2016) and shorter RTs (Karayanidis et al. 2011) have both been linked to increased amplitude in the SP. In reviewing the literature, De Baene and Brass (2014) identify P3bs in older studies that they suspect are actually SPs. As these tasks all entail a change in rule, the SP has been hypothesised to signal activation of the new rule set (Nessler, Friedman and Johnson 2012). The switch that the SP indexes has been generalised, in that it can be elicited to in response to changes in rules governing stimulus domain (verbal/non-verbal/spatial), stimulus quality, response set or a mixture of these. A meta-analysis of 36 studies examining fMRI data confirmed that there are networks common to switching between perceptual features and switching between response features (Kim et al. 2012). The SP has not been elicited to an object-switch. To do so would generalise this switch and would mean that the SP does not index a change in rule per se but a change in endogenous representation(s), whether that representation be a task rule or an object. The SP has not been reported to object-switching but neither has it been examined and found absent. The SP being elicited in response to an object-switch would be consistent with theories that it signals the reconfiguration of stimulus set and preparation for the task (Karayanidis et al. 2011, Karayanidis et al. 2010, Karayanidis and Jamadar 2014b). It is also compatible with the theory that it reflects control of the endogenous task-set (Capizzi et al. 2016). A further generalisation of this theory would be to confirm that this endogenous control of an internal set is not specific to switching the task rules i.e. control of any internal set.

How the SP interacts with the attentional processes indexed by the P3a has been examined in a study with a 35-person PD cohort (35 HCs) (Lange et al. 2016). This study used a WCST and the P3a was used as a marker of orientation of attention to the switch cue and the SP used as a marker for the switch. The PD group as a whole had a reduced P3a compared to HSs but not a reduced SP. Using linear regression, it was found that in individuals with PD having both a reduced P3a and SP predicted worsened performance in the WCST. This was taken to indicate that compensatory strategies can be used when only one domain is impaired. These processes can therefore be individually impaired but have an interdependence that is prerequisite for successful stimulus processing. This is a successful example of using ERPs to simultaneously tease apart these processes and examine their manifestation in PD.

Oddball and switch tasks are associated with oscillatory EEG responses and examining these gives a fuller picture of the processes occurring during these tasks. EEG frequencies are arranged in bands of

varying width. In order of increasing frequency, the frequency bands are named delta (<4Hz), theta (4-7Hz), alpha (8-15Hz), beta (16-31Hz), and gamma (>32Hz). Frequencies also have an associated power (measured in dB) and phase (measured in °). On presentation of a stimulus, the power present in each frequency band changes and the phase of the oscillations may or may not reset. When a change in power is non-phase locked to an event (i.e. when the change of EEG power does *not* occur with a resetting of phase) this is called a change in *induced power*. When a change in power is phase-locked to an event (i.e. when the change of EEG power *does* occur with a resetting of phase) this is called a change in *evoked power*. When deriving ERPs, epochs are averaged together, this attenuates any oscillations that are not phase-locked to the event. Deriving the oscillatory content of an ERP is therefore a method of deriving the phase-locked (evoked) frequencies. Induced potentials are derived by subtracted the evoked power from the total power (Roach and Mathalon 2008).

In a 12-person task-switch study, Prada et al. (2014) found frontal increases in total delta power, in addition to the nP3 to both distractors and to task-switch cues. They found that the delta response to the distractor was evoked (phase locked) in response to the distractor but induced in response to the switch-cue (non-phase locked), a difference they put down to an endogenous response to the switch-cue and an exogenous response to the distractor. Like the P3a and nP3, increased frontal delta oscillations are associated with top-down control of attention (Helfrich et al. 2017, Johnson et al. 2017, Breska and Deouell 2017, Daitch et al. 2013, de Vries et al. 2018). De Vries et al. (2018) carried out an object-switch task examining the oscillatory response as opposed to the EEG response. This study was on a 22-person cohort. 10 were excluded from a larger 32-person cohort for not being sufficiently accurate in the task. This study describes changes of objects in the working memory as *reprioritisations.* In their study, it was shown that working memory reprioritisation is accompanied by frontal delta power increases shortly after the onset of the switch cue which is followed by later parietal alpha suppression at 575-850ms. In their study participants were shown an array of colours, two of which they were tasked with memorising before being asked to identify them in sequence. Infrequently, an audio cue would alert them to ignore the first colour and they would only be asked to identify the second colour. This initiated a change of working memory priority or a switch of attention from one WM representation to another. This resulted in significant increases in total delta power followed by posterior alpha suppression. De Vries et al (2018) suppose that the delta stage is a top-down control of the attention switch rather than the attention switch itself.

Like the nP3, the P300 has an evoked delta component. Evoked delta is associated with decision making and tasks that require a cognitive response. It has been found that the power of evoked delta is inversely correlated with cognitive impairment in persons with schizophrenia, Alzheimer's disease and mild cognitive impairment (Guntekin and Basar 2016). In people with PD evoked delta in response

to a pure tone discrimination task has been found to be reduced but this reduction did not correspond to reduced accuracy in the task (Dushanova, Philipova and Nikolova 2009). If linguistic prosody can be used to elicit evoked delta in persons with PD, it can be used as a marker for the top-down processing of the prosody.

De Vries et al (2018) linked an increase in delta power during switch tasks with top-down control of attention, they linked the switch itself to the later parietal alpha suppression. Parietal suppression of alpha power has been associated with reprioritisation of visual targets in the working memory (de Vries et al. 2018, Myers et al. 2015, Schneider, Mertes and Wascher 2015, Schneider, Mertes and Wascher 2016, van Ede, Niklaus and Nobre 2017) as well as with cues triggering a task-switch (Sauseng et al. 2006, Mansfield, Karayanidis and Cohen 2012, Prada et al. 2014). The explanations forwarded for suppression of alpha in the task-switch tasks have been increased task difficulty and readiness for the next cue rather than due to a switch occurring in the WM. De Vries et al (2018), found frontal delta increases predict this alpha suppression and together they form a linked process in which the frontal delta is the assessing of the incoming stimulus and that the alpha suppression marks the switch itself. Sauseng et al. (2006) reported parietal alpha suppression as well as a P3a in response to a task-switch cue. Alpha suppression in this study was explained as increased task difficulty. In light of these later studies, it may be the case that, rather in response to increased task difficulty, their recorded alpha suppression is due to the switch instruction (with whether it marks the switch itself or other related processes to be established). Prada et al (2014) however found that suppression of alpha to task-switch cues was no different to that of task-repeat cues (cue that indicates the same task rule should apply rather than a new one). Their results suggest that the switch is not the key aspect of the task. Prada et al (2014) report that they assessed only the alpha power occurring contemporaneous to the nP3. De Vries et al (2018) report that alpha suppression that they suppose marks a working memory switch occurs in a later interval. As the study by Prada et al (2014) did not report results for this latter time-window, then it may still be the case that alpha suppression occurs latterly in response to switch cues.

Evidence of alpha power's role in attention capture is also found in distraction tasks which are a handy mirror of switch tasks. In distraction tasks, increases in alpha power are associated with suppression of distracting visual cues (Kelly et al. 2006, Thut et al. 2006, Jensen, Bonnefond and VanRullen 2012, Janssens et al. 2018). It has been shown in a 20-person study that increases in alpha power are most pronounced with an unambiguous distractor (van Diepen et al. 2016). Alpha power has also shown to be inversely proportional with the negative impact a distractor has on behavioural performance (Bonnefond and Jensen 2012). This indicates that alpha increases are a reliable measure of a successfully ignored distractor. Alpha increases and their role in cue inhibition are crucial to speech

processing. In this capacity they play the role of filtering out ambient noise when listening to speech (Strauss, Wostmann and Obleser 2014). Alpha power also increases in contexts where a distractor is expected (Bonnefond and Jensen 2012) indicating that the participant is preparing to ignore the upcoming stimulus. Alpha power increases are therefore an indication of the failure of a stimulus to capture attention or even active inhibition of that attention. Inversely, alpha power decreases are a marker of a stimulus successfully recruiting attentional networks. More specifically, it may indicate the occurrence of a switch occurring within the working memory.

Parietal alpha suppression has not been linked to the SP but both index similar processes. So far alpha suppression has been in response to object switch cues and the SP to task switch cues. Whether it is possible to elicit these processes together and whether the SP can occur in response to object switches are interesting questions. An SP in response to object switching would indicate that the SP is indexes a generalised switch rather than a reconfiguration of the task. Eliciting parietal alpha suppression and the SP together would give a strong indication that they are similar processes.

The above details the ERP and oscillatory markers of attention and orientation as well as the tasks that elicit them. Table 2.1 summarises which each of these component marks. Table 2.2 shows which components have not been elicited under which task conditions.

Table 2.1 The attention related EEG features and what they mark.
The N100 and MMN mark stimulus detection, they therefore have utility as markers for the pre-attentive detection of unusual prosody. The P3a, nP3 and delta activation mark the subsequent top-down processing of a stimulus. They are therefore able to mark if an unusual prosody has been deemed sufficiently relevant to the listener as to warrant additional attentional resources (as opposed to being ignored, which is what the absence of these features would signify). The RON marks the reconfiguration of attentional resources. This marks if a heard stimulus interferes with the completion of the task in such a way as to require a change of attention away from the stimulus and back to the completion of the task. The SP shows a switch between task rules has occurred. This would indicate I) that the prosody has been heard II) that its significance has been understood III) the process of switching has occurred.

	Attention (ERPs)			Attention (Oscillatory)	Switching
EEG Feature	N100 & MMN	P3a/nP3	RON	Delta	SP
What it Marks	Stimulus Detection	Top-Down Response to a Stimulus	Reorientation of attentional resources	Top-down control of attention	Switching between two task rules

Table 2.2 ERP features and the tasks they have been elicited by.
The SP has not been elicited to an object-switch. Alpha suppression has been elicited to object-switches and task-switches but in the latter tasks have been associated with task difficulty rather than switching. An object switch that examines all three stages of the N100-P3a-RON cascade as well as their corresponding evoked oscillations are missing.

Component	Task Type	
	Object-Switch	Task-Switch
P3a	(Frenken and Berti 2018, Berti 2016, Berti 2008)	(Kopp et al. 2006, Perianez and Barcelo 2009, Lange et al. 2016)
SP		(Lange et al. 2016, Karayanidis et al. 2010) or left-parietal positive (Astle et al. 2006, Capizzi et al. 2016)
Δ activation	(de Vries et al. 2018)	(Prada et al. 2014)
α Suppression	(de Vries et al. 2018, Myers et al. 2015, Schneider et al. 2015, Schneider et al. 2016, van Ede et al. 2017)	(Sauseng et al. 2006, Mansfield et al. 2012, Prada et al. 2014)
α Suppression - P3a/nP3		Prada et al (2014)
N1-P3a		(Kopp et al. 2006)
MMN-P3a-RON		(Hoelig and Berti 2010)
P3a-RON	(Berti 2008)	
P3a-SP		(Lange et al. 2016)
Δ activation - nP3		(Prada et al. 2014)
Δ Activation - α suppression	(de Vries et al. 2018)	

In summary, an increase in frontal delta power is associated with top-down control of attention in response to task-switch cues (Prada et al. 2014) and object-switch cues (de Vries et al. 2018). The P3a and nP3 are thought to mark similar control of attention processes in response to task-switch and object-switch cues. This frontal delta has been explicitly linked with the nP3 in a task-switch paradigm. So far, it has not been examined if there is a P3a and/or nP3 accompanied by an increase in delta power in response to an object-switch cue. Showing them in an object-switch paradigm would confirm that delta power and the P3a are both governed by attentional processes that are not specific to task-switching. Likewise, the SP and parietal alpha suppression are thought to index switches of attention. In the case of the SP this is a reconfiguration of task-switching specifically and in the case of alpha the reprioritisation of an object in the visual working memory. Eliciting an SP and examining its oscillatory content in response to an object-switch would indicate that they signal a more generalised switching process. There is therefore a wealth of markers that signpost various points in the attention capture process. Linguistic prosody has been used to examine attention capture in oddball and task-switch paradigms. By using linguistic prosody in an object switch task, it can be determined if these tasks are governed by the same generalised processes. Doing so would also provide various markers for the processing of linguistic prosody. The N100 as a marker of pre-attentive sensory detection. The P3a and delta as the assigning of the appropriate attentional resources to the prosody (and therefore a marker that the heard prosody was deemed significant by the listener). The RON and alpha suppression as a marker of flexibly responding to the new information. Combining this with a behavioural task will be able show if any changes in these EEG markers prefigure behavioural changes (should there be no behavioural changes) or can be linked to behavioural changes (should there be EEG and behavioural changes). There is precedent for using these markers to mark prosodic processing (Wang et al. 2005, Zhang and Shao 2018) but they do not index explicitly prosodic processes. In this sense they are proxy markers. If there are no changes in the markers but a change in behavioural response this may be due to a specific prosodic impairment not flagged by the markers. There are prosody specific markers than can and have been used and these are discussed in the following section.

2.6.1.1 The Attention Components in PD

The attention components have been examined in PD by a number of studies. Studies making use of auditory oddball tasks to elicit an N100 frequently report that the amplitude of this component does not differ between controls and people with PD (Annanmaki et al., 2017; Yilmaz et al., 2017; Philipova et al., 2006; Smolnik et al., 2002; Pirtošek et al., 2001; Jiang et al., 2000; Tsuchiya et al., 2000; Karayanidis et al., 1995). One exception, using a standard oddball task, found that their 29-person PD cohort elicited an N100 with an increased amplitude compared to that of their age-matched healthy controls (Tanaka et al., 2000). An N100 amplitude comparable to that of controls, is congruent with theories that bottom-up processing is largely preserved in PD (Dirnberger and Jahanshahi 2013).

While the amplitude of the N100 is often preserved, prolonged N100 latencies in people with PD have been reported and these prolonged latencies linked to people with PD who have additional impairments in working memory (Annanmaki et al. 2017). This link is unsurprising. Attention capture is dependent on the context a stimulus is delivered in. In the case of oddball tasks, the context is the preceding stimuli and the task instructions. The significance of targets or distractors in an oddball task is derived from how their acoustic features differ from the stimuli heard previously. Working memory therefore plays an important role in this. In the case of incongruent prosody, the incongruence occurs within the same stimulus therefore no implicit comparison is being made with previously heard stimuli. This may mean that the N100, as it is elicited by prosody may not be as sensitive to changes in working memory capacity but this remains untested.

The P3a, which is mediated by top-down processes, is altered in PD. The amplitude of the P3a reduces with increased disease stage and this reduction is not affected by dopaminergic medication, this reduction however does not necessarily correspond to an impaired behavioural response (Solis-Vivanco et al. 2011, Solis-Vivanco et al. 2015). A reduced or absent P3a in people with moderate to advanced PD may therefore prefigure a symptomatic change or people with PD may be employing compensatory strategies when completing tasks in which a P3a is normally elicited. This complements the study by Lange et al. (2016) (Section 2.6.1) that showed that a behavioural impairment only occurs in the WCST when both the SP and P3a are absent. With these considerations, any study using the P3a to examine prosody in PD would have to control for disease stage when examining if the changes to attention indexed by the P3a can be linked to changes in how people with PD perceive prosody. The link between the P3a and the SP presents an opportunity to examine if the same compensatory strategy observed in the WCST is also observed during the processing of prosody.

There are fewer studies examining the RON in PD. It has been shown that the RON is present but reduced in people with PD. The amplitude however (unlike that of the P3a) is modulated by the use

of dopaminergic medication (Solis-Vivanco et al. (2011)). This makes the RON a particularly useful marker in people with PD who may have a reduced or absent P3a as the attention reorientation processes as marked by the RON can still be examined in this group.

2.6.2 Linguistic prosody and the building of expectations

This section details a second method of eliciting EEG markers in response to the processing of linguistic prosody. Prosody is used to build predictions that facilitate rapid speech processing and by subverting this process a family of related components can be elicited (Astesano, Besson and Alter 2004, Eckstein and Friederici 2005, Paulmann et al. 2012). These components are the *prosodic expectancy positives* (PEPs) and the *right-anterior negative* (RAN). These components flag the reanalysis of prosody in response to unexpected changes. These components therefore directly mark a prosodic process rather than attentional processes that are ancillary to the processing of prosody proper.

A positive component in response to prosodic reanalysis was first observed in a 16-person study by Astesano et al (2004). This study examined the EEG response to unexpected linguistic prosody by cross-splicing statements and questions to create stimuli that began intoned as statements and ended intoned as questions. Participants listened to the audio during two different tasks. One task asked in which they were asked to answer if the prosody of the utterance they heard was congruous or incongruous and one task in which they were to answer if the semantics of the utterance they heard was congruous or incongruous. The prosodic task elicited a centroparietal positive component peaking approximately 800ms from the splicing point which they named the P800. This component was deemed to mark the additional processing which had been triggered by the prosodic incongruity. The positive did not appear when semantics were the task focus. This was taken to mean that semantic processing superseded prosodic processing in this instance.

A number of studies subsequently found this positive ERP component in response to rapid changes in emotional prosody and named it the *Prosodic Expectancy Positive* (PEP) (Paulmann et al. 2012, Paulmann et al. 2008, Paulmann and Kotz 2008, Kotz and Paulmann 2007). In response to emotional prosody, this component can be elicited when prosody is not the task focus and appears with a shorter latency of 420ms (Kotz and Paulmann 2007, Paulmann et al. 2012). This emotional PEP has been used to examine dysprosody in 12 persons with left-sided basal ganglia lesions (Paulmann et al. 2008). In this study the participants were shown to be unable to identify emotion from prosody in a behavioural task. In an EEG recording a PEP was elicited in the group demonstrating that rapid deviance detection was intact. The PEP was therefore used to infer that inhibited prosodic perception in that group must have been due to later processes such as evaluating the emotional content of the stimuli.

A 20-person study by Paulmann et al. (2012) directly compared the PEP in response to linguistic prosody violations and emotional prosody violations. The violations of linguistic prosody took the form of statements that rapidly changed to become questions. Violations of emotional prosody took the form of rapid changes from one emotion to another. A third condition examined a combination of linguistic and emotional violations with a rapid change from a statement spoken with one emotion to a question spoken with a different emotion. Two task conditions were used, a task which focused linguistic prosody in which the participants were asked if the sentence they heard was intoned as a statement or a question and a task which focused emotional prosody in which the participants were asked if the sentence they heard was intoned neutrally or with emotion. The linguistic violation in both tasks elicited a parietal PEP peaking after 620ms. This differs in both location and latency from the frontal P800 reported in Astesano et al (2004). This positive in response to sudden changes in linguistic prosody was also present when emotion was the task focus whereas the P800 did not appear when semantics were the task focus. The emotion task draws attention away from the linguistic prosody but nevertheless does draw the participants' attention to the prosody. This task demand may have been sufficient to cause the PEP to be elicited when linguistic prosody was not the task focus. Additionally, the use of highly salient emotional violations may have primed the participants to engage with the prosody, regardless of whether the incongruity was emotional or linguistic. Rapid changes in emotional prosody elicited a frontal PEP that peaked 470ms after the change. Rapid changes of emotional and linguistic prosody elicited a PEP that covered the scalp which peaked 170ms. Emotional and linguistic prosody therefore combine for more rapid analysis. Paulmann et al. (2012) supposed that the PEP reflects the point that semantic and prosodic expectancy diverge. The PEP is therefore a tool which has utility in marking prosodic perception and identifying the processing stage impaired. This principle has been demonstrated in a study examining emotional prosody in people with basal ganglia lesions. A 12-person study by Paulmann et al. (2008) found that the PEP is preserved in people with basal ganglia lesions who have a behavioural impairment in identifying prosody. From this it was inferred that this behavioural response was not due to impaired processing of prosody but due to a particular executive dysfunction. The utility of the PEP for examining emotional prosody in patient populations has been proven but its utility in the study of linguistic prosody in pathological populations remains untested. It has not been demonstrated that the PEP to linguistic violations can be elicited without the participant being engaged in a task that asks them to identify prosody in some way. If this task demand is necessary for the PEP to be elicited than its use in patient populations who may not be able to identify prosody is limited. The PEP's utility as a marker for linguistic prosodic processing in patient populations is therefore yet to be established.

Eliciting the PEP in response to linguistic prosody made use of declarations that rapidly became interrogations using cross-splicing. Eckstein and Friederici (2005) used splicing to create an alternative linguistic prosodic incongruity in a 24-person study. Utterances use IPBs to indicate when a sentence (or the utterance itself) has concluded. This takes the form of a drop in pitch and an elongation on the final word. The IPB acts as a vocal full stop. When an utterance concludes without an IPB, it conveys that the speaker has not finished speaking and the listener expects the utterance to continue. Eckstein and Friederici (2005) used splicing to alter the IPB in two ways creating two incongruous prosodic conditions. In the first incongruous condition the pitch contour was altered on the final word to create the false expectancy that more is about to be said. In the second incongruous condition an additional IPB was added to the penultimate word while retaining the IPB on the final word. This created the impression that the utterance finished twice. Participants in this study listened to these utterances and were asked whether the sentences had incongruous grammar. Their attention therefore was not drawn explicitly to the prosody (i.e. the participants were not asked to comment on the prosody itself). The first incongruity resulted in a right anterior negative component (RAN) followed by a positive that they identified as a P600 (a component typically elicited in response to syntactic incongruities). Using the IPB in this way may have created a more salient incongruency than that of Astesano et al. (2004) therefore resulting in an EEG response (in this case a RAN) when prosody was not the task focus. Alternatively, the processes reflected by the RAN may be more sensitive to unexpected changes in prosodic profile than those indexed by the PEP. Creating a vocal ellipsis using prosody therefore results in a dual syntactic (reflected by the P600) and prosodic (reflected by the RAN) revaluation process even in when the participant's focus is not on the prosody being listened to. Violations of syntax that typically elicit a P600 are grammatical disagreement ("*The girl **walk** home*"), category errors ("*The boy **drove** the school*"), and garden path sentences ("*Whenever John walks the dog is chasing him."* (Pauker et al. 2011)). As these syntactic violations do not occur in the study of Eckstein and Friederici (2005), a subsequent study by Paulmann et al. (2012), based on their previous work on the PEP (Kotz and Paulmann 2007, Paulmann et al. 2008, Paulmann et al. 2011, Paulmann et al. 2012), raised the possibility that the P600 elicited in response to this form of expectancy violation may actually be a PEP. The positive elicited in Eckstein and Friederici (2005) shares a topography and latency with the PEP identified in the study of Paulmann, Jessen and Kotz (2012). The RAN being a marker of reanalysis that is specifically linked to the IPB was confirmed in a study by Honbolygo et al. (2016). This study elicited a RAN with an alternative manipulation of the IPB. In this methodology the IPB is removed mid-sentence creating grammatical ambiguities that are not resolved until the sentence concludes. This creates a similar false expectancy. Like the PEP, the RAN is supposed to reflect a rapid and automatic re-evaluation process triggered by the unexpected prosodic profile. This study also elicited

a positive that they identified as P600. This study used embedded clauses to create a local syntactic ambiguity that had to be resolved by the participant. This use of syntax in this way is a common way to elicit a P600 (Osterhout and Holcomb 1993, Osterhout, Holcomb and Swinney 1994, Itzhak et al. 2010, Steinhauer et al. 2010, Hwang and Steinhauer 2011, Pauker et al. 2011). The RAN has not been used in patient groups and has only been elicited in two studies to the author's knowledge. It being elicited when prosody is not the task focus and it reflecting a specifically a prosodic (as opposed to syntactic or semantic) re-evaluation process makes it a promising and understudied component that can potentially act as a marker for and provide answers about the cause of impaired prosodic perception in patient groups. Furthermore, the reanalysis process that the incongruous use of the IPB triggers may elicit a PEP as well. This use of IPBs may then provide two components that explicitly mark prosodic processing and can be used in patient groups.

2.6.2.1 The Prosody Components and PD

The PEP and RAN have not been studied in PD. The PEP has been successfully utilised in the study of prosody in people with basal ganglia lesions as a result of various types of stroke (Paulmann et al (2008)). This shows its utility in the study of populations with injury to the basal ganglia such as those with Parkinson's disease.

2.7 Rationale

This chapter has reviewed wide-ranging literature regarding PD, namely: the processing of prosody; the ways in which the impairments in the processing of prosody manifest in PD; and how prosodic processing can be studied using EEG in healthy and PD populations.

The review showed that:

- EEG and fMRI reveal that emotional prosody and linguistic prosody engage different areas of the brain. Literature most often identifies a right-lateralisation of emotional prosody whereas there is no consensus on how, or if, linguistic prosody is lateralised. How linguistic prosody is lateralised may depend on what is being conveyed by the prosody, for example intonation or tone. This sensitivity to what is being conveyed makes the lateralisation of linguistic prosody heavily task dependent. The location and saliency of EEG markers also varies between emotional and linguistic prosody, with the PEP having a shorter latency and more parietal location in response to emotional prosody and a longer latency and more frontal location in response to linguistic prosody.
- The processing of prosody is impaired in PD. Impairments in the processing of emotional prosody are more commonly reported and more widely studied. Studies examining the processing of emotional prosody have demonstrated the efficacy of using EEG markers to assess the cause of impaired processing in patient populations. In PD, impairments in the processing of emotional prosody have been linked to a more generalised emotional deficit in PD. Impairments in the processing of linguistic prosody in PD are less commonly reported but studies have reported impairments in distinguishing statements from questions and in distinguishing the meaning conveyed by different forms of contrastive stress. One study identified that the impairments in the processing of linguistic prosody occurred in only a subset of their cohort. Although there are few studies eliciting EEG markers in response to linguistic prosody, EEG markers have not yet been used to study the processing of linguistic prosody in PD.
- A number of large-cohort studies have identified potential PD subtypes. Most commonly, studies identify less severe forms of the disease that present with mainly motor symptoms and more severe forms of the disease that present with a range of autonomic and cognitive symptoms. Studies focusing on non-motor symptoms only have identified less severe forms of PD which nonetheless present with cognitive impairment. Notably, the presence of anxiety and/or depression has been linked with cognitive impairment in PD, this cognitive impairment is less severe than that present in the most diffuse and debilitating forms of the disease. Given

that PD is heterogeneous, it stands to reason that people with PD will have a heterogeneous response to prosody. This is borne out by the mixed results in the literature examining how people with PD process linguistic prosody.

- The processing of prosody is multi-staged and EEG can be used to differentiate these stages. Specifically, EEG markers can be, and have been, used to: identify pre-attentive signal extraction; assigning of attentional resources to a salient prosody; and automatic reanalysis of an unexpected prosody. The presence or absence of these components combined with a behavioural impairment can be used to make inferences about the cause of that impairment. This use of EEG markers has precedent in the literature in studies examining the cause of impaired processing of emotional prosody in people with PD and people with basal-ganglia lesions.

Despite this wealth of knowledge concerning the processing of linguistic prosody in PD and the ways in which EEG markers can be used to examine it, there are still important gaps in the literature. More specifically:

- The cause of impaired processing of linguistic prosody in PD is uncertain.
- There are various PD subtypes but it is not known whether an impairment in the processing of prosody can be linked to any particular subtype or comorbidity.
- Impaired processing of prosody does not occur in all people with PD but the prevalence with which it does occur is not known.
- It is not known if the full range of components that mark the orientation of attention in response to a stimulus (MMN/N100, P3a, delta and RON) can be elicited in response to linguistic prosody in healthy persons in a non-tone language. Deviant prosodic tone can elicit an MMN and P3a in Cantonese and studies have elicited the MMN in response to linguistic prosody in a number of non-tone languages but have only been able to elicit the P3a in response to linguistic prosody in non-tone languages using pseudowords.
- The efficacy of using the full range of attentional components to examine impaired processing of linguistic prosody in patient groups has not been tested.
- The efficacy of using the prosodic expectancy markers, the RAN and PEP, to examine impaired processing of linguistic prosody in patient groups has not been tested.

Addressing these gaps in the literature is important because:

- Determining the cause of impaired processing of linguistic prosody is the first step towards identifying a means of treating it.
- Studies that can only elicit the MMN or the N100 are only able to examine the earliest stage of prosodic processing. The MMN is a marker for pre-attentive deviance detection, an explicit evaluation of the prosody does not have to occur for deviance detection to occur. The P3a marks the assignment of attentional resources to a stimulus that has been deemed important enough to warrant it. For this (optional) processing to occur, an evaluative judgement of the prosody is necessary. The occurrence of the P3a and the latter attentional markers can be used to infer that an evaluation of the prosody has occurred.
- The RAN and PEP mark a rapid prosodic reanalysis process. If these components can be elicited in people with PD in response to linguistic prosody, they can be used to directly determine if prosodic analysis is intact or absent. If they are found to be present in a group (or individual) that has a behavioural impairment in identifying or discriminating prosody, it would reveal that this impairment is not due to an impairment in processing prosody per se but due to a secondary (most likely cognitive) impairment. The exact nature of this secondary impairment can then be determined in future studies.
- Knowing if impaired processing of linguistic prosody can be linked to a subtype of PD is important for a number of reasons. If impaired processing of prosody is linked to a particular subtype it would aid future studies of prosody in PD as they will no longer be examining if the symptom occurs in PD as a whole and they will no longer be carrying out analyses on groups that might be heterogeneous. This information may also give some indication of the cause of the symptom, as symptoms that are found to cluster may have a shared physiology. If impaired processing of prosody can be linked to a specific subtype it might also serve as a reliable marker for that subtype that is quicker and easier to assess than the other symptoms of that subtype.
- While the prevalence of impaired processing of prosody is not known, the number of people who are affected by a symptom with a potentially devastating impact on quality of life is also not known.

In order to address these issues, the aim of this study was to design and test a protocol that elicits EEG markers that can be used to study the processing of linguistic prosody in people with PD.

2.7.1 Objectives

1) Design a protocol that is able to elicit EEG markers that can be used to segment the different stages of processing of linguistic prosody for the purposes of identifying which stages may be impaired in people with PD.
2) Validate the protocol by running it on a large group of healthy older persons.
3) Check the protocol's efficacy by running it on individuals with PD

2.7.2 Research Questions

1) Does the healthy senior (HS) cohort show the full range of attention capture and orientation markers in response to the linguistic prosody?
2) Does the HS cohort show the full range of prosodic reanalysis markers in response to the linguistic prosody?
3) Can the case studies provide preliminary indications of the suitability of the study for use on people with PD?

Chapter 3

Methodology

3 Methodology

This study was granted favourable opinion by NHS REC 16/WS/0052 on the 20th April 2016. The letter of favourable opinion can be viewed in Appendix 1.

3.1 Introduction

The current study was concerned with eliciting EEG markers for the processing of linguistic prosody and collecting behavioural data to support the interpretation of these markers. For this purpose, a study with one EEG task and two behavioural tasks was designed and implemented. The function of these markers is to serve as a tool for examining the perception of linguistic prosody in Parkinson's disease. This study therefore reports results from three groups: a pilot cohort, composed of younger participants; a healthy senior (HS) cohort, composed of participants aged 59 and older; and a two people with Parkinson's disease, presented here as case studies. The HS cohort serves as a proof of concept of the method and case studies serve to give initial data on the suitability of the method in examining linguistic prosody in Parkinson's disease.

The EEG portion of the study was based on the methodology of Eckstein and Friederici (2005) which used IPBs to elicit a right-anterior negative as well as a late positive component that may be a P600 or PEP. IPBs consist of a drop in pitch on and elongation of the final word followed by a gap and resetting of pitch and intensity. This acts as a vocal full stop. The task was adapted to prompt the elicitation of additional attentional components that can be used in the examination of the processing of linguistic prosody: the N1-P3a-RON; the SP; and evoked delta. There were two incongruent prosody conditions used in this study, one with no IPBs, named IPB-0 and one with two IPBs named IPB-2. The study aimed to use the IPB-0 condition to elicit the RAN and PEP and the IPB-2 condition to elicit the attentional components. The study of Eckstein and Friederici (2005) also elicited an N400 in response to a double IPB, this may or may not be affected by the use of a probe task in the current study.

Having a sentence that terminates without an IPB creates a false expectancy which elicits a RAN and may elicit a PEP. In addition to this, the current study aimed to use the IPB-2 to prompt an object-switch in the verbal working memory. To achieve this, the EEG portion of the study used a probe task in which the participant was asked to remember the final word that they heard and answer yes/no if a word displayed on screen matched this word. An IPB on the penultimate word signalled to the listener that this was the final word. This prompted them to remember that word for the purposes of completing the probe task. They then heard the final word which prompted a surprise response and a change of attention from the penultimate word to the final word. By combining this unexpected prosody with the demands of a probe task, the study aimed to contrive an effect salient enough to elicit an object-switch and elicit the attention EEG components. Figure 3.1 illustrates this principle.

Figure 3.1 Using 2 IPBs to prompt an object-switch.

An example sentence is shown. IPBs are indicated by #. In the IPB-2 condition the participant will hear a sentence with two IPBs. In this example, the first IPB occurs on the word *bakes* and the second on the word *cakes*. The probe task asks the participant to memorise the final word of the heard sentence. It is predicted that the participant will memorise the word *bakes* in order to complete the probe task. The participant will then hear the word *cakes* which prompts a switch of their focus away from *bakes* and towards *cakes.*

This use of prosody to prompt an object-switch is novel. Prompting the EEG markers associated with object-switching has the dual purpose of eliciting components that can be used to mark the stages of processing linguistic prosody and examine if this mode of switching elicits an SP.

3.2 Participants

Three cohorts were recruited for this study. The first cohort was, an 8-person pilot cohort consisting of eight right-handed males aged 22-30 and was used to establish that the protocol could successfully elicit the desired response. The results of the pilot cohort also provided a pertinent comparison with the older cohort who were all aged 59 and above. As this group were originally intended to yield pilot data only, data gathering was ended once it was established that the EEG had produced the desired result.

The second cohort was a healthy senior (HS) 36-person cohort consisting of persons aged 59 and older without depression or dementia. The results from this cohort were used to examine if the protocol could successfully elicit the desired response in healthy older persons. They also served as a healthy comparator to the PD case studies. At 36 people, the results were considered robust enough to finish data collection within the time constraints of the project.

The third cohort consisted of two persons with PD. The results from the participants in this cohort were examined as case studies rather than as a group. H&YI-III is a broad pool, people at different stages of PD were included as a means to gather preliminary data examining if the current protocol can be used to examine the prosody in the various stages of PD as prosodic impairment is not always reported to correlate with disease progression. The study ran into difficulty recruiting within the time period of the project which resulted in a low number of participants with PD. Five persons with PD were recruited, of whom, three had to be excluded. As the project had achieved its aim of developing the protocol, it was determined that two participants were sufficient to serve as preliminary case studies.

All participants were recruited from within an hour's travelling distance from Glasgow and all participants spoke English as their first language. While all participants were from the UK and lived in Glasgow and the surrounding areas, not all were originally from Glasgow and the UK has many distinct accents. *Unfamiliar* regional accents have been found to have an impact on early (but not late) EEG components (Goslin et al (2012)). While not everyone who took part in the study was from Glasgow, it was assumed that living in the area they were familiar with the accent and so the impact on their EEG would be minimal.

3.2.1 Inclusion and Exclusion Criteria - Pilot

The pilot cohort were recruited based on the inclusion and exclusion criteria listed here.

Inclusion Criteria

1) Provided informed consent
2) English as a first language.
3) Right-handed.
4) Sufficiently accurate vision (or corrected) to view the words displayed on the monitor.
5) Sufficiently accurate hearing to hear the sentence material without the use of a hearing aid.
6) Does not have a history of speech problems.
7) Is not currently depressed or being treated for depression

Exclusion Criteria

1) Has PD or any other neurological problems that impact speech and language production and perception such as such as stroke Huntington's disease, schizophrenia, epilepsy or dementia.
2) Has suffered a severe head trauma or has undergone neurosurgery.
3) Has a cochlear implant.
4) Has a pacemaker, implantable defibrillator or any other implantable electronic device.
5) Has a known allergy to skin preparation paste or has particularly sensitive skin.

3.2.2 Inclusion and Exclusion Criteria – HS Cohort

The HS cohort were recruited on the basis of the inclusion and exclusion criteria listed here. Suitability was confirmed by the study through the use of the ACE-III and GDS-30. Hearing and vision status were self-reported by the participants but example trials of the Discrimination Task and Identification Task were carried out to ensure participants were able to hear the stimuli and to understand the tasks.

Inclusion Criteria

1) Provided informed consent
2) English as a first language
3) Right-handed
4) Sufficiently accurate vision (or corrected) to view the words displayed on the monitor.
5) Sufficiently accurate hearing to hear the sentence material without the use of a hearing aid
6) Less than 80 years old [later removed in a non-substantial amendment]
7) Is not currently depressed or being treated for depression

Exclusion Criteria

1) Has PD or any other neurological problems that impact speech and language production and perception such as such as stroke Huntington's disease, schizophrenia, epilepsy or dementia.
2) Has suffered a severe head trauma or has undergone neurosurgery
3) Has a cochlear implant
4) Has a pacemaker, implantable defibrillator or any other implantable electronic device.
5) Has a known allergy to skin preparation paste or has particularly sensitive skin
6) Taking part in a study that involves use of treatment that may affect their performance or study outcome

3.2.3 Inclusion and Exclusion Criteria – PD Case Studies

Persons with PD were recruited on the basis of the inclusion and exclusion criteria listed here. Suitability was confirmed by the study through the use of the ACE-III and GDS-30. Hearing and vision were not formally examined by the study but example trials of the Discrimination Task and Identification Task were carried out to ensure participants were able to hear the stimuli and to understand the tasks.

Inclusion Criteria

1) Provided informed consent
2) Hemispheric idiopathic Parkinson's disease with a typical onset age
3) Within H&Y stages I-III
4) English as a first language
5) Right-handed
6) Sufficiently accurate vision (or corrected) to view the words displayed on the monitor.
7) Sufficiently accurate hearing to hear the sentence material without the use of a hearing aid
8) Less than 80 years old [later removed in a non-substantial amendment]
9) Is not currently depressed or being treated for depression
10) Other than PD, has no neurological problems that impact speech and language production and perception such as such as stroke, Huntington's disease, schizophrenia, epilepsy or dementia.

Exclusion Criteria

1) Has suffered a severe head trauma or has undergone neurosurgery
2) Has a cochlear implant
3) Has a pacemaker, implantable defibrillator or any other implantable electronic device.
4) Has been treated using deep brain stimulation (DBS)
5) Has a known allergy to skin preparation paste or has particularly sensitive skin
6) Taking part in a study that involves use of treatment that may affect their performance or study outcome

3.2.4 Recruiting Process – Pilot

The pilot cohort were recruited from the Department of Biomedical Engineering at the University of Strathclyde. People were approached and asked if they would like to take part. Participants self-reported if they met the inclusion/exclusion criteria.

3.2.5 Recruiting and Screening Process – HS Cohort

The HS cohort were recruited from the Centre for Lifelong Learning at the University of Strathclyde. Adverts were posted by the department and persons who wished to take part were contacted by phone or email.

Those who wished to take part underwent additional screening. Participants self-reported that they met the inclusion/exclusion criteria, including that they were right-handed and had no neurological impairments. Depression and neurological impairment were excluding factors. These were tested using the Geriatric Depression Scale 30 (GDS-30) and the Addenbrooke's Cognitive Evaluation Version 3 (ACE-III). The GDS-30 is a 30-question questionnaire filled out by the participant and scored by the research team. The questionnaire is designed to capture depression in older adults. Each question is a Yes/No question and scores either one or zero. Persons with a score of 10 or above (indicating mild depression) were excluded. One HS was not able to take part on this basis. Participants were sent the GDS-30 which they had the option to complete prior to or following their arrival.

The ACE-III is a test administered by an examiner in which the participant answers a series of questions and completes a series of tasks. This is designed to capture dementia. A score of 88/89 or lower is indicative of mild cognitive impairment. A score of 75/76 or lower is indicative of dementia. The ACE-III was administered and scored by a trained speech and language therapist. Participants with a score of 88 or lower were excluded from the study. No HSs were excluded on this basis.

3.2.6 Recruiting and Screening Process – PD Case Studies

Patients were recruited from the Speech and Language Therapy Department of the Queen Elizabeth University Hospital in Glasgow and from the Centre for Lifelong Learning at the University of Strathclyde.

Patients recruited through the NHS were first approached by their consultant who introduced the study. The consultant approached patients based on the inclusion/exclusion criteria and approached only those who were expected to pass screening. Those interested in taking part were introduced to the author who explained the study and gave them the Participant Information Sheet. Those who wished to take part then contacted the study's author. One patient contacted the study through the Centre for Lifelong Learning at the University of Strathclyde. All patients who wished to take part discussed the study with the research team to insure they were able to give full informed consent which they could withdraw at any time.

Those who contacted the study through the NHS had been deemed to meet the inclusion/exclusion criteria through their consultant but confirmed this in person through self-report. The participant who approached through the Centre for Lifelong Learning confirmed through self-report that they met the inclusion/exclusion criteria.

Depression and neurological impairment were excluding factors. These were tested using the Geriatric Depression Scale 30 (GDS-30) and the Addenbrooke's Cognitive Evaluation Version 3 (ACE-III). The GDS-30 is a 30-question questionnaire filled out by the participant and scored by the research team. The questionnaire is designed to capture depression in older adults. Each question is a Yes/No question and scores either one or zero. Persons with a score of 10 or above (indicating mild depression) were excluded. One person with PD was excluded on this basis. Participants were sent the GDS-30 which they had the option to complete prior to or following their arrival.

The ACE-III was administered and scored by a trained speech and language therapist. Participants with a score of 88 or lower were excluded from the study. Two persons with PD were excluded on this basis and their GPs informed of their score.

3.2.7 Background Details – PD Case Studies

The background information collected for each case study are listed here.

Background Information

1) Handedness
2) Hoehn and Yahr Stage
3) Intelligibility
4) Sidedness of motor symptoms
5) Time since diagnosis

Hoehn and Yahr stage was provided by the participants' healthcare team. As not all consultants used the UPDRS, it was decided to settle for the Hoehn and Yahr staging as a broad but adequate marker of disease progression.

To rate intelligibility one minute of the participant in conversation was recorded. Three trained speech and language therapists ranked the persons intelligibility according to the scale shown in Table 3.1. In addition to this the SLTs were asked to note the presence or absence of breathiness or hoarseness of voice, mono-pitch, reduced loudness, inconsistent or inappropriate rate of speech, initiation problems, inappropriate pauses between speech, or other symptoms.

Handedness, sidedness of motor symptoms, and time since diagnosis were provided by self-report.

Table 3.1 Intelligibility Rating Scale (Dobinson 2007)

This is the 9-point scale used to rate the intelligibility of the PD case studies. Rating is a 9-point scale with a score of 9 being indicating no impairment and a score of 1 indicating that the speaker cannot make themselves understood. The 9-point scale is subdivided into 5 categories. n.b. a score of 8 indicates that the person is still fully intelligible, albeit with additional effort required on the part of the listener.

Intelligibility	Effort	Rating
Able to fully understand what the person was telling you	Easy	9
	Pay a little attention	8
Able to fully understand what the person was telling you but had to take extra care in listening	Listen carefully	7
	Concentrate hard	6
Able to understand part of what the person was telling you	Nearly all (over 75%)	5
	Most (over 50%)	4
	Not much	3
Able to understand some individual words but unable to understand what the person was telling you		2
Able to understand nothing at all		1

3.2.8 Pilot Cohort Details

Eight right-handed males aged 22-30 took part in the pilot. All spoke English as a first language.

3.2.9 HS Cohort Details

36 participants in the HS cohort took part in the study, their details are shown in **Table 3.2**.

Table 3.2 HS Cohort Individual Details

The details of each of the participants are shown. Each participant is given an arbitrary number 1-36. Sex is shown as self-reported male (m) or female (f). ACE-III score out of 100 is shown. GDS-30 score out of 30 is shown. There are ten more females than there are males. All participants had scores that indicated no depression, dementia or mild cognitive impairment. The lowest, median and highest value for age, ACE-III and GDS-30 are shown at the bottom of their respective columns.

Control Number	*Sex*	*Age*	*ACE-III (/100)*	*GDS (/30)*	*Control Number*	*Sex*	*Age*	*ACE-III (/100)*	*GDS (/30)*
1	m	59	96	4	*29*	f	74	94	0
2	f	76	94	5	*20*	m	71	92	3
3	f	68	92	0	*21*	f	69	95	4
4	f	77	98	7	*22*	f	63	93	0
5	f	73	97	1	*23*	f	68	97	4
6	f	67	95	5	*24*	m	70	98	2
7	f	69	98	8	*25*	f	67	99	1
8	m	66	93	1	*26*	f	63	100	0
9	f	69	96	3	*27*	f	68	94	2
10	m	70	96	2	*28*	f	69	98	0
11	m	69	100	0	*29*	m	62	98	2
12	m	62	100	1	*30*	f	62	99	2
13	f	69	98	0	*31*	f	70	99	2
14	f	68	95	0	*32*	f	64	99	0
15	m	69	99	4	*33*	m	65	97	0
16	m	61	94	0	*34*	f	61	97	4
17	m	78	91	5	*35*	m	71	96	0
18	f	62	99	2	*36*	f	64	96	0

Total	Youngest Median Oldest	Lowest Median Highest	Lowest Median Highest
m-13 f--23	59 68 78	91 97 100	0 2 8

The ACE-III and GDS-30 scores of the HS cohort are presented in histograms in Figure 3.2 and Figure 3.3. The scores of the two participants with PD are shown in the same figures and are discussed in Section 3.2.10.

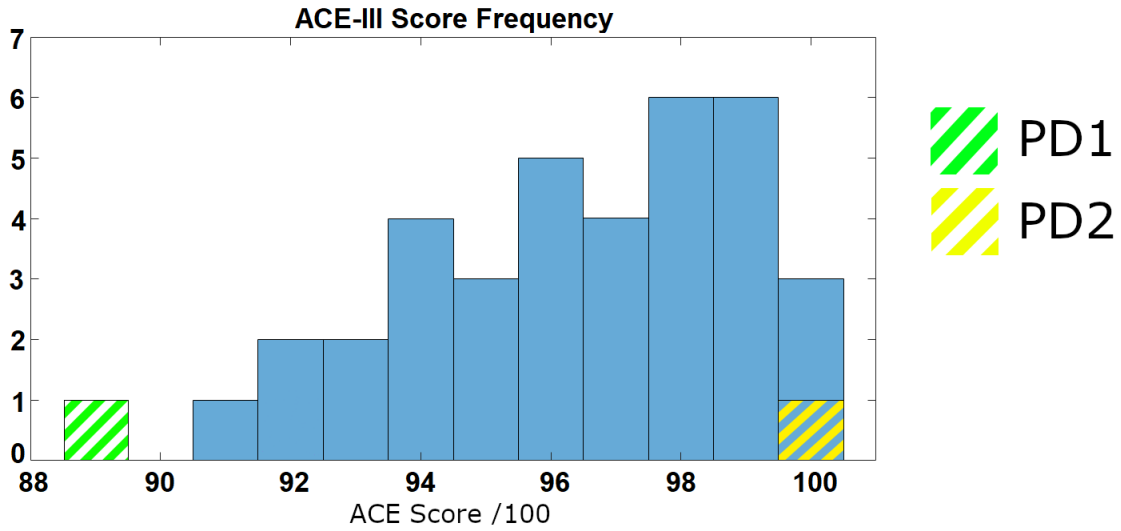

Figure 3.2 Histogram of ACE-III scores.

The score (out of 100) of the HS cohort is shown in blue. All participants scored over the required 88; median=97; StdDev=2.46. The data skew rightwards toward the top score. Overlaid are the patient results. PD1 (shown in green) scored 89 and PD2 (shown in yellow) scored 100. PD1 scored the lowest of all participants. All participants scored above the required 88 indicating no participants had dementia, dementia-like symptoms, or mild cognitive impairment.

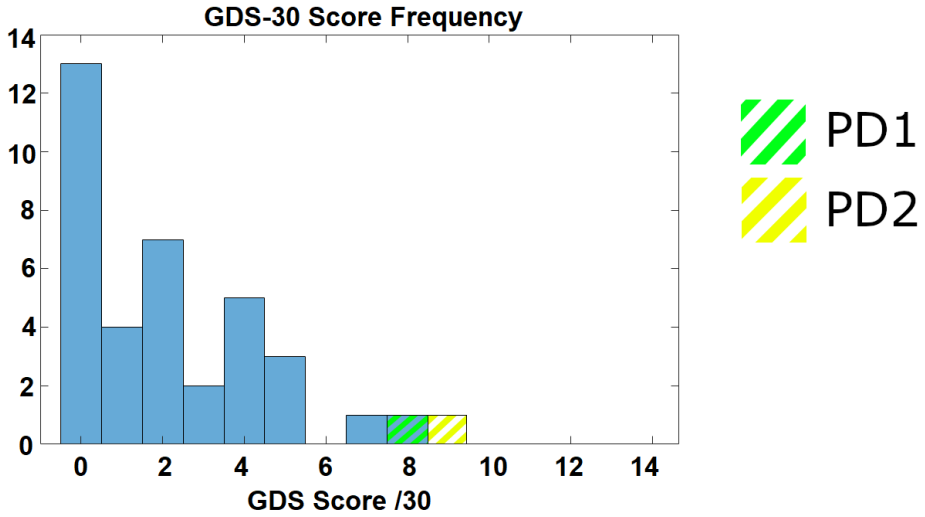

Figure 3.3 Histogram of GDS-30 Scores

The score (out of 30) of the HS cohort is shown in blue; median=2 StdDev=2.6. A score of <10 indicates no depression. 20>Score>9 indicates mild depression. The HS data are skewed leftward towards a score of 0. PD1 (shown in green) had a score of 8 indicating no depression. PD2 (shown in yellow) had a score of 9 indicating no depression.

3.2.10 PD Case Study Details

Two people with PD took part in their details are presented here. The details are presented in a table for each participant and are then elaborated on in order to give a profile of each participant.

3.2.10.1 PD1

PD1 was aged 81 at the time of recording and H&YIII. Their details are shown in Table 3.3

Table 3.3 Details of PD1.

The details of PD1 are shown. PD1 was male and H&YIII. They had intelligibility scores indicating they can be understood and were on Rasagiline and Sinemet which are both dopaminergic treatments.

	PD1		
Sex	Male		
Age	81		
Handedness	Right		
Hoehn & Yahr	Stage 3		
Time Since Diagnosis	21 Months		
Sidedness of Motor Symptoms (self-reported)	Weakness in right arm, left leg shakes		
GDS-30	8		
ACE-III	89		
Intelligibility	8	8	7
Medication	Rasagiline, Sinemet, Macrogol, Aspirin, Nicorandil, Simvastatin, Finasteride, Tamasulosin hydrochloride		

At 81 years old, PD1 was the oldest participant who took part in the study.

H&YIII is a moderately advanced PD stage. PD1 had ratings of 7 and 8 in intelligibility which indicates that all three SLTs who assessed their speech were able to fully understand this participant but that the SLT who rated a 7 had to listen more carefully than the others. This indicates that PD1 only had minorly reduced intelligibility at the time of recording.

PD1 reported that it had been 21 months since his diagnosis at the time of recording. This combined with his stage being H&YIII indicates that his PD was diagnosed late or that it has progressed rapidly (Zhao et al. 2010).

PD1 was on medication targeting constipation which is a common autonomic symptom of PD.

PD1 was on dopaminergic medications Rasagiline and Sinemet. The dosage of these medications is not known so the strength of impact that they had cannot be accurately established. The impact these medications may have on PD1's results are considered in the Discussion (Section 4.4).

PD1's ACE-30 score as it compared with the HS group is shown in Figure 3.2. PD1 scored 89, this is the lowest score of any participant who took part and the lowest score allowed by the study protocol.

The GDS-30 score as it compared with the HS group is shown in Figure 3.3. PD1's score of 8 is outside 2 standard deviations from the median of the HS group but is the same as one other member of the HS group and not the highest in the study overall. This score, albeit high, does not indicate the presence of depression. PD1 was not on medications used to target depression or symptoms of depression.

3.2.10.2 PD2

PD2 was aged 76 at the time of recording and H&YI. Their details are shown in Table 3.4.

Table 3.4 Details of the PD2.

The details of PD2 are shown. PD2 was male and H&YI. They were ranked 9 in intelligibility by two SLTs, the highest ranking, indicating they were intelligible. They were not on any medications at the time of recording.

	PD2		
Sex	Male		
Age	76		
Handedness	Right		
Hoehn & Yahr	Stage 1		
Time Since Diagnosis	9 months (noticed tremor 11 months prior)		
Sidedness of Motor Symptoms (self-reported)	Tremor in left arm		
GDS-30	9		
ACE-III	100		
Intelligibility	9	9	8
Medication	None		

PD2 was at H&YI, the earliest stage of the PD when taking part. PD2 was also not on any medication and was ranked fully intelligible by 2/3 SLTs who assessed their speech.

PD2's ACE-III score as it compared with the HS group is shown in Figure 3.2. PD2's ACE-III score was the highest possible. This was higher than the median of the HS group which was 97 and just outside one standard deviation of that median.

PD2's GDS-30 score as it compared with the HS group is shown in Figure 3.3. PD2 had the highest score in the GDS-30 of anyone who took part. Their score however still indicated that they did not have minor or major depression.

3.3 Materials

3.3.1 Sentences

The current study consisted of an EEG task and two behavioural tasks. The EEG recording used 150 audio stimuli. The two behavioural tasks used a subset of these stimuli. The EEG task had one congruent condition with 40 stimuli, two incongruent conditions with 40 stimuli each, and two filler conditions with ten stimuli each. The behavioural tasks had one congruent condition and two incongruent conditions. The congruent condition and both incongruent conditions consisted of forty sentences with identical semantics (but with three different prosodic structures). These sentences were controlled for number of words, number of syllables, and stress pattern. This ensured that the prosody within each sentence condition was uniform and any prosodic effects were controlled for. An example of one of the sentences is below:

Martin knows that his sister bakes cakes

The first word of each sentence was a person's name. Each name was used once per forty sentences. The number of names traditionally perceived as male and traditionally perceived as female were balanced i.e. 20 male names and 20 female names were used. Each sentence ended in a verb-noun pair. The verb in each case was ambitransitive (e.g. "bakes"). This means the verb could function as a transitive or an intransitive verb which means each sentence was syntactically correct with or without an object (the final noun). This ensured that any incongruences arose only as a result of the prosody and not due to errors in sentence semantics or syntax. Ten verb-noun pairs were used. The subject of the subordinate clause was either mother, father, sister or brother, with each being used ten times. Table 3.4 shows each of the sentences that made up the congruent and incongruent conditions.

Table 3.4 Bank of Sentences used to make the congruent and incongruent conditions in the EEG and behavioural tasks.

There are 40 unique sentences. Each is formed using 40 unique names (20 male and 20 female). Each sentence has a subordinate clause, the object of which is either “brother”, “father”, “sister”, or “mother”. There are 10 verb-noun pairs.

Name (n=40)	Main Verb (n=1)	Subject of Subordinate Clause (n=4)	Verb-Noun Pair of Subordinate Clause (n=10)
Ewan	knows that	his brother	bakes cakes
Brendan	knows that	his father	bakes cakes
Rachael	knows that	her mother	bakes cakes
Kirsty	knows that	her sister	bakes cakes
Stuart	knows that	his brother	cooks dinner
Lewis	knows that	his father	cooks dinner
Amy	knows that	her mother	cooks dinner
Sophie	knows that	her sister	cooks dinner
Merel	knows that	her brother	drives lorries
Eva	knows that	her father	drives lorries
Richard	knows that	his mother	drives lorries
Simon	knows that	his sister	drives lorries
Fraser	knows that	his brother	eats apples
Russell	knows that	his father	eats apples
Becky	knows that	her mother	eats apples
Lucy	knows that	her sister	eats apples
Vhairi	knows that	her brother	paints fences
Nicole	knows that	her father	paints fences
Peter	knows that	his mother	paints fences
Stephen	knows that	his sister	paints fences
Karen	knows that	her brother	reads papers
Alice	knows that	her father	reads papers
Andrew	knows that	her mother	reads papers
Alan	knows that	his sister	reads papers
Charlotte	knows that	her brother	rents houses
Hannah	knows that	her father	rents houses
Michael	knows that	his mother	rents houses
Martin	knows that	his sister	rents houses
Heather	knows that	her brother	runs bistros
Sarah	knows that	her father	runs bistros
Gary	knows that	his mother	runs bistros
Graeme	knows that	his sister	runs bistros
Patrick	knows that	his brother	saves vouchers
Jamie	knows that	his father	saves vouchers
Morgan	knows that	her mother	saves vouchers
Helen	knows that	her sister	saves vouchers
Calum	knows that	his brother	writes journals

Sandy	knows that	his father	writes journals
Ashleigh	knows that	her mother	writes journals
Laura	knows that	her sister	writes journals

There were two filler conditions. As the length of the sentences in **Table 3.4** are all identical, filler sentences of different length were included in the EEG task to ensure the listener could not predict the end of the sentence based on the length of the utterance. There were therefore two filler conditions, one that was shorter than the other conditions, *Filler-Short* and one that was longer, *Filler-Long*. No EEG analysis was performed on these sentences. The short and long filler conditions were adapted from ten sentences chosen from the bank of forty sentences shown in **Table 3.4**. For the short filler condition, the final noun was removed to produce sentences of the following format:

Martin knows that his sister bakes

To produce the filler-long condition an additional clause added to produce sentences of the format below:

Stephen knows that his sister paints fences and cuts grass

There were ten sentences in each of the filler conditions.

3.3.2 Recordings

The above sentences were recorded with different IPB structures. In the congruent condition the utterance was spoken with a neutral affect with an IPB following the final word. This was called the *IPB-1* condition due to the presence of a single IPB. There were two incongruent conditions, one with no IPB and one with two IPBs, these were called *IPB-0* and *IPB-2* respectively. In the IPB-0 condition there was no IPB on the final word. This gave the impression to the listener that the utterance was going to continue, an effect akin to an auditory ellipsis. In the IPB-2 condition there was an IPB on both the penultimate and ultimate word. The IPB on the penultimate word gave the impression that the utterance had ended. The listener then heard the unexpected final word. In both the Filler-Long and Filler-Short conditions the prosody was produced with a neutral affect and there was an IPB on the final word. This created two congruent conditions that differ in length from the IPB-1 congruent condition.

Table 3.5 The prosody used in each condition.

is used to denote the presence of an IPB. In the congruent IPB-1 condition this falls at the end of the sentence. In the incongruent IPB-0 condition there is no IPB. In the incongruent IPB-2 condition there are two. In the two filler conditions the IPB falls at the end. Both filler conditions have congruent prosody. The number of trials in each condition in the EEG task is also shown. There are ten trials in the filler conditions and forty in each of the rest.

Condition	Example	No Trials
IPB-1 (Congruent)	Martin knows that his sister bakes cakes**#**	40
IPB-0 (Incongruent)	Martin knows that his sister bakes cakes	40
IPB-2 (Incongruent)	Martin knows that his sister bakes**#** cakes**#**	40
Filler-Short (Congruent)	Martin knows that his sister bakes**#**	10
Filler-Long (Congruent)	Stephen knows that his sister paints fences and cuts grass**#**	10

Sentences were recorded on an Edirol R-09HR voice recorder. Unlike in similar studies, no cross-splicing was used in the production of the stimuli. An SLT was coached on the desired prosodic structure and spoke each condition. No manipulation of the prosody was made after the recording. The SLT spoke in a west of Scotland accent. The SLT produced stimuli of five different conditions; three congruent and two incongruent. The IPB-2 condition was altered using Praat to ensure a 0.25s gap between the end of the penultimate word and the beginning of the final word. This ensured there was always a consistent gap between the penultimate and ultimate word in this condition. The IPB-0 condition terminates in a high boundary tone (a rising intonation). It was found to be too difficult to produce stimuli with no IPB and no rising intonation that was salient enough to be captured on the EEG without artificially manipulating the pitch. This rising intonation was settled on after piloting various intonations and splicing methods. Example f_0 contours on the critical word(s) for each condition are shown in **Figures 3.4a-e**. All 140 sentences were used in the EEG Task. The sentences used in the behavioural tasks are selected from this bank of sentences (See Sections 3.3.4 & 3.3.5).

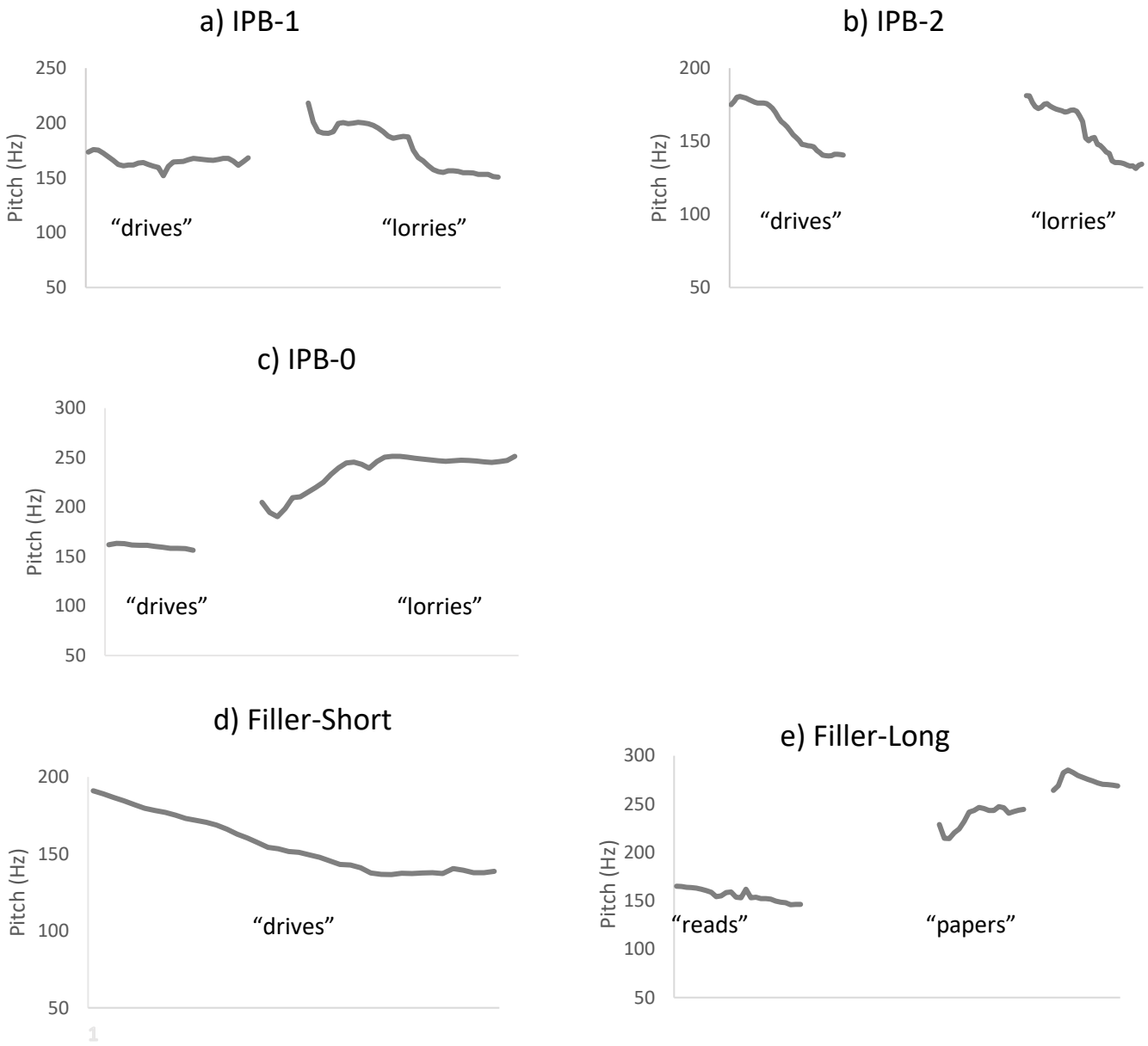

Figure 3.4a-e Example f_0 contour for each condition.

Example of the f_0 contour on the final two words in the 1-IPB (congruent), 2-IPB (incongruent), and 0-IPB (incongruent). Also shown is the f_0 contour on the corresponding word(s) in the Filler-Short and Filler-Long conditions (both congruent). 3.3a-3.3c each shows the same two words being spoken *drive* and *lorries.* 3.3d shows only the word *drive* being spoken. 3.3d shows the words *paints fences* being spoken. The drop in pitch can be seen on the word *lorries* in both the 1-IPB and 2-IPB conditions. There is no drop in pitch on the word *lorries* in the 0-IPB condition and no drop on the word *fences* in the Filler-Long condition. A drop on pitch can be seen on the word *drives* in the 2-IPB condition and the Filler-Short condition. In the 0-IPB condition and the Filler-Long condition a rise in intonation can be seen on the words *drives*/*reads* and *lorries*/*papers* respectively. The IPB-0, IPB-1, IPB-2, and Filler-Short conditions terminate at the final word shown on the graphs whereas the Filler-Long condition continues.

3.3.3 Stimulus Preparation

ERPs are time-locked to an event. Studies examining detection of prosodic deviance often use cross-splicing, with the point at which the stimuli are spliced being a handy event onset point. As the stimuli used in the current study were not cross-spliced, there was no splicing point at which to epoch the sentences from. The sentences were instead epoched from the point at which the final word occurred. As each utterance occurred as a single event when presented during the EEG, it was not possible to timestamp the EEG at the onset of the final word. Instead the EEG was timestamped at the onset of the audio. To make it possible to epoch each event, the sentences of the IPB-1, IPB-2 and IPB-0 conditions were adjusted to ensure the onset of the final word always occurred 2.95s following the onset of audio file. Having the final word always occur at 2.95s allows the epoch to be extracted 2.95s following the timestamp which occurred at the onset of the audio file. This adjustment was performed by inserting silences of varying length at the beginning of each audio file using PRAAT v6.1.16. This method means that the epochs were out of sync prior to the onset of the final word but in sync at the crucial moment just prior to the onset of the unexpected prosody. Natural speech varies in duration and the longer that speech lasts the more varied the differences between each stimulus will be so it would not be practicable (nor necessary) to produce natural sounding speech samples that were in sync for the length of a whole utterance as it was not necessary to analyse the EEG prior to the onset of the final word. Figure 3.5 is a diagram of how this effect was achieved.

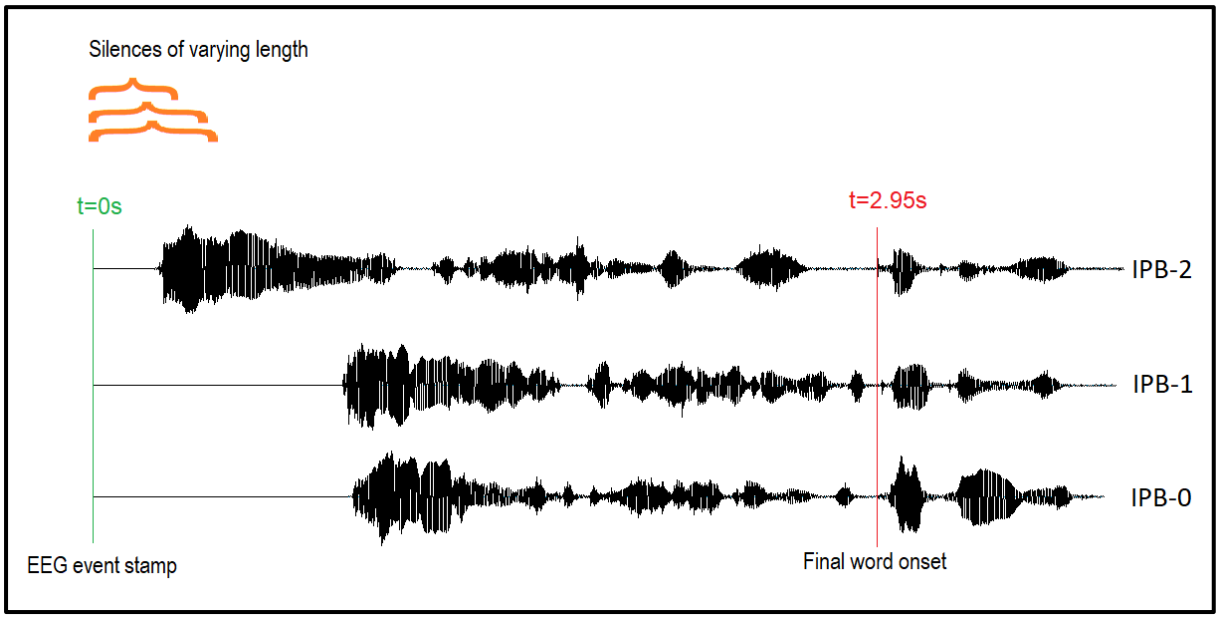

Figure 3.5 A diagram of example speech samples in the IPB-2, IPB-1 and IPB-0 conditions.

A green line shows where the EEG is time-stamped at a time of 0s. The silences of varying length at the beginning of each stimulus can be seen. The final word always occurs at t=2.95s. The EEG of each trial from 2.95s onwards (i.e. from the onset of the final word) is therefore in sync. There is always in 0.25s silence prior to the onset of the final word in the IPB-2 condition. This is due to the presence of the first IPB prior to the onset of the final word.

3.3.4 Discrimination Task

In the discrimination task participants heard pairs of semantically identical sentences that may or may not have had identical prosody. The participant was asked to answer if the pair of sentences they heard had the same or different intonation. The sentences used in this task were a subset of the IPB-1, IPB-0 and IPB-2 conditions described in **Section 3.3.1**. 30 pairs of sentences were used in the discrimination task. Half of these pairs (15) matched and half did not match and each combination of conditions played an equal amount of times.

Table 3.6 Sentence pairs used in the Discrimination Task.

There were six combinations of pairs with 5 pairs in each combination. Overall there were 15 matching pairs and 15 unmatching pairs. All pair combinations were represented. Matching combinations are highlighted in green and mismatching pairs highlighted in red.

Pair Combination	No. of each pair
IPB-1 & IPB-1	5
IPB-2 & IPB-2	5
IPB-0 & IPB-0	5
IPB-1 & IPB-2	5
IPB-1 & IPB-0	5
IPB-0 & IPB-2	5

3.3.5 Identification Task

A subset of 15 sentences from those described in **Section 3.3.1** were used in the Identification Task**.** Five each are taken from IPB-0, IPB-1, and IPB-2 groups. Each participant therefore identified 15 prosodies. 5 were congruent and 10 were incongruent.

3.4 Procedure

Each stage of the procedure is outlined in this section. Participants were given the option to spread the procedure over two visits (the behavioural tasks in one day and the identification tasks in the other) but none chose to. The whole procedure took between 90-120 minutes for all participants. Participants were introduced to the study and the inclusion/exclusion criteria were discussed with them prior to their arrival. All inclusion/exclusion criteria were self-reported but the presence of depression and dementia-like symptoms confirmed using the GDS-30 and ACE-III. The ACE-III was carried out by a trained SLT. Those who were excluded due to their score in these tests discussed their results with the SLT and were advised to discuss their results with their GP and took no further part in the study. The experiment was carried out in a spacious ground floor lab. The lab was not soundproofed but quiet and free from distractions and testing carried out when adjacent rooms were not in use. All experiments occurred between 9am and 5pm.

3.4.1 Discrimination Task

The Discrimination Task was run on a PC using E-Prime. The participant sat approximately 1m in front of a 19" Dell LCD monitor and Logitech Z200 speakers. The volume and position of the speakers were marked for consistency between subjects. The participant responded using an E-Prime RB-40 serial response box which was placed on their lap and the PC running the experiment saved their responses and response times. The participant was instructed that they would hear pairs of sentences that would either be spoken with the same intonation or with a different intonation. Example sentences from each condition were played so the participant was aware of what to listen for. Participants were then asked if they could hear and understand the stimuli and that they understood the task based on what the instructions they had been given and the example sentences they had been played. When the experiment began an audio recording of two sentences was played back to back and the participant had to answer yes/no on the response box whether the two sentences were said in the same way. The participant also had the option of pressing a button that repeated the sentence pairs. Once they had answered the next sentence played. They had as long as they needed to answer and were encouraged to answer in their own time. The experiment was entirely auditory, nothing was displayed on the computer monitor. Each participant's response, response time and number of repeats were logged. Each participant was played thirty sentence pairs played in a random order. Half of the pairs played matched and half did not. Each correct answer was totalled for a maximum possible score of 30.

3.4.2 Identification Task

The Identification Task was run on a PC using E-Prime. The participant sat approximately 1m in front of a 19" Dell LCD monitor and Logitech Z200 speakers. The volume and position of the speakers were marked for consistency between subjects. The participant responded using an E-Prime RB-40 serial response box which was placed on their lap and the PC running the experiment saved their responses and response times. Prior to the commencement of this task the participants were played example sentences to familiarise themselves with each condition. It was explained to the participant that they would hear sentences spoken in a "usual" and "neutral" manner. Example sentences from each condition were played which was considered "usual" and which were considered "unusual" were discussed with the participant. It was explained that they should use one button on their response box to identify "usual" sounding sentences and another to identify "unusual" sounding sentences. The participants were therefore to press one button on the response box when they heard a sentence from the IPB-1 condition (usual) and another when they heard a sentence either from the IPB-0 or IPB-2 conditions (unusual). They were also given the option of pressing a third button to hear the audio again. Participants were then asked if they could hear and understand the stimuli and that they understood the task based on what the instructions they had been given and the example sentences they had been played. When the experiment began they were played one sentence and once they had answered the next sentence played. They had as long as they needed to answer and encouraged to answer in their own time. The experiment was entirely auditory, nothing was displayed on the computer monitor. Each participant's response, response time and number of repeats were logged. Each participant was played 15 sentences in a random order. Each participant was played the same sentences but in a different order. Five sentences from each condition were played. There were therefore 5 congruent and 10 incongruent sentences played. Each correct answer was totalled for a maximum possible score of 15.

3.4.3 Speech Recording

Connected speech was recorded from each participant with PD. This was recorded on an Edirol R-09HR voice recorder. During the setup of the EEG a conversation between the experimenter and the participant was recorded to capture spontaneous speech. A sample of this conversation was given to three SLTs who assessed the intelligibility of the participant.

3.4.4 EEG Procedure

A 20-electrode montage based on the 10-20 system was used with electrodes at F7, F3, Fz, F4, F8, Fc5, FCz, FC6, C3, Cz, C4, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8. The ear was used as a reference and PCz used as ground. The EEG was connected using NeuroScan Synamps2 System using a 128-electrode Easy Cap and recorded using Curry Neuroimaging Suite 7.0.8 XSB (Compumedics, Australia) with a sampling frequency of 2kHz. The impedance was monitored and kept below 5kΩ. Time stamps were sent to Curry by E-Prime v2.0 (Psychology Software Tools, Inc., Pittsburgh, PA, USA) stimulus presentation software via a serial cable.

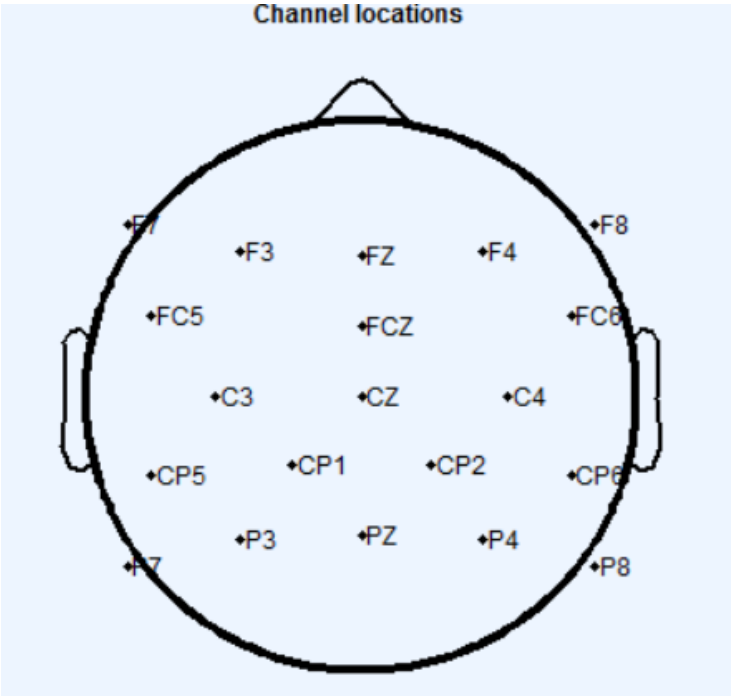

Figure 3.6 EEG Montage

Figure showing the electrodes used and their location on the scalp. The montage covers the frontal, central, and parietal regions of the scalp.

The EEG task was run on a PC using E-Prime. The participant sat approximately 1m in front of a 19" Dell LCD monitor and Logitech Z200 speakers. The volume and position of the speakers were marked for consistency between subjects. Speakers were used to better replicate a natural speech environment, this follows the example of previous studies that have elicited the RAN and PEP (Paulmann, Jessen and Kotz 2012, Eckstein and Friederici 2005). An E-Prime RB-40 serial response box

was placed on their lap. The participant responded using the response box and the PC running the experiment saved their responses and response times. A second PC recorded the EEG using Curry Neuroimaging Suite 7.0.8 XSB. The experiment and EEG were monitored in real time. The PC running the experiment sent timestamps to the PC recording the EEG.

The cap was placed on the participant's head. NuPrep Skin Prepping Paste (Weaver and Company, USA) was applied to clear the scalp of excess skin, reduce impedance and create a stable interface between the skin and the electrodes. Electro-Gel (ECI) was applied to increase the conductivity between the electrodes and the skin. The setup of the EEG took between 10 and 15-minutes. **Figure 3.7** shows this experimental setup.

Once the experiment was setup, initial examples from one of the experiment blocks were played to establish if the participant could hear the stimuli and that they understood the task.

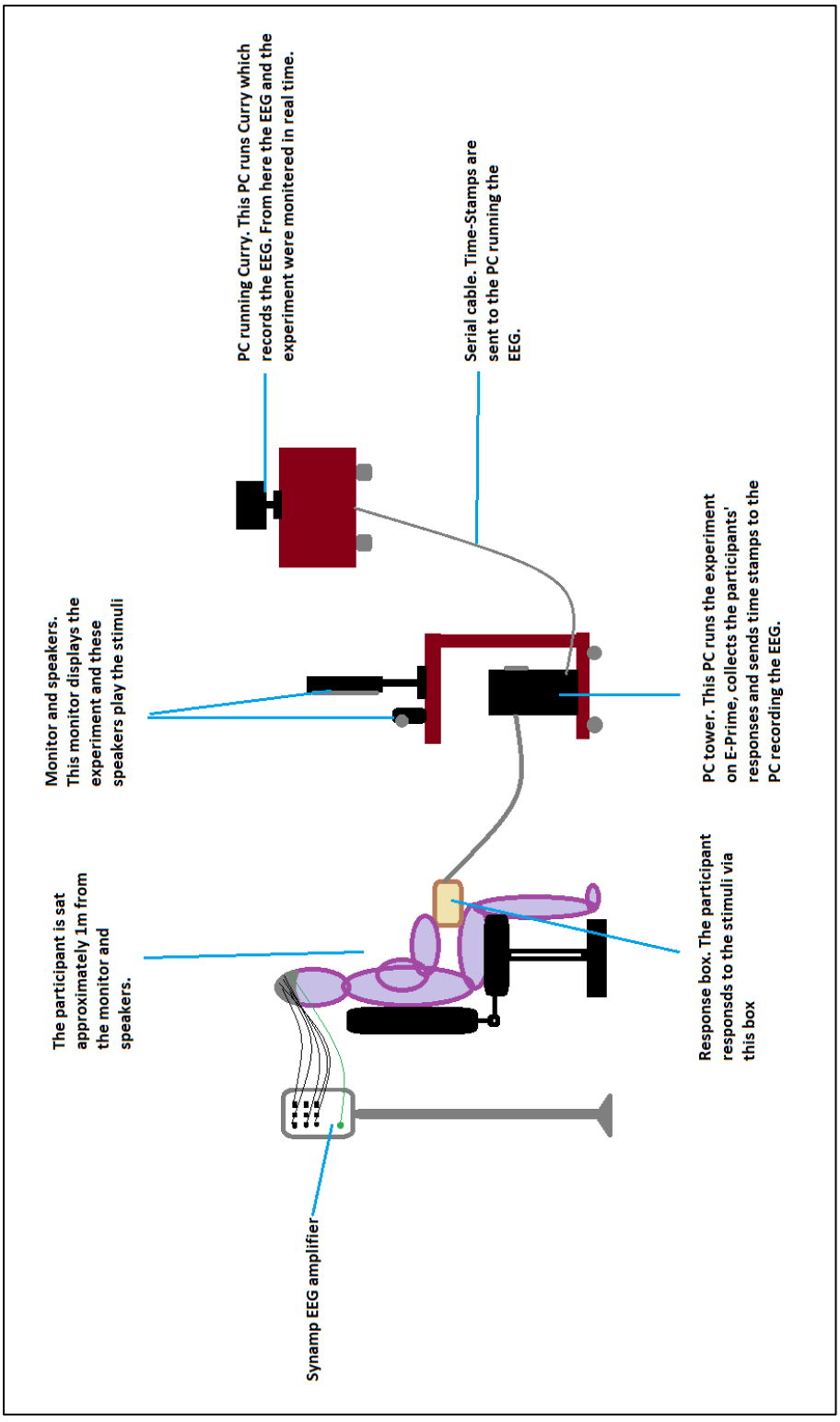

Figure 3.7 EEG setup with participant.

The participant sat approximately 1m from the monitor that displayed the experiment and the speakers that played the stimuli. EEG was recorded from the scalp and sent via the Synamps2 amplifier to a second PC from where it was monitored in real time by the experimenter. The participant responded using a response box resting on their leg or on cushion (whatever their preference). The responses were saved in the PC running the experiment. The PC running the experiment sent timestamps to the PC recording the EEG.

The participant was instructed that a cross would appear on screen and that while this was on screen they should try to keep their gaze on it without blinking and they should also not swallow, clench their teeth, or move their arms or feet. They were told that while the cross was on screen they would hear a sentence. After the sentence has played a word would display on screen and they should answer yes/no using the response box whether the displayed word matched the last word they heard in the audio. There was no time limit for them to answer and they were told to take as long as they needed. The EEG aimed to capture natural speech processing as fully as possible. For this reason, no time pressure was applied to the participants. This served a second purpose of not unduly stressing or pressuring any participants which may prompt incorrect answers. As the EEG was captured prior to the point at which the participant was shown the probe word and thus tasked with answering, having a time pressure on this task was deemed to have minimal impact on the elicited EEG but a possible negative impact on participant experience and performance. As the recording was not analysed at the point at which the participant was considering their answer, the participants were told they could take this time to blink or swallow. 0.2s prior to the onset of each audio file (the onset of the initial word varies according to the length of the initial silence) the monitor displayed a crosshair to ready the participant and to provide a focus to minimise eye movements. At the onset of the crosshair the event stamp was sent to Curry Neuroimaging Suite 7.0.8 XSB (Compumedics, Australia) and the audio file initiates. The final word played at 2.95s after this point. 4.05s after the final word was played the probe word appeared on screen. This ensured a 4.05s epoch during which the participant had processed the audio but was not required to move, was not tasked with any further instructions and had not yet seen the probe word. The participant then had as long as necessary to answer yes or no to the probe word. After the participant answered there was an interval of either 2s or 2.5s during which the screen was blank. For half of the trials the interval was 2.5s and for the other half it was 2s but the order was random. Following this interval the crosshair reappeared and the cycle began again.

The probe word matched the final heard word in 52% of the trials. The participant was instructed to use their left and right index finger to answer (one for each answer). This balanced the use of the left and right hemispheres of the brain and avoided the use of thumbs which produce a larger EEG motor effect. Which answer corresponded to the left finger and which answer corresponded to the right finger was the same for all participants. Except for the first stimulus played, the stimuli were played in a random order using the E-Prime shuffle function. The first utterance was always the Filler-Short condition to ensure the participant would expect sentences of varying length. The participant had as long as they needed to answer the yes/no question and were told they can effectively pause the EEG by delaying answering if they needed to rest or blink. They were instructed to minimise movements, particularly blinking, swallowing or shuffling their feet while the cross is on screen and the EEG was

monitored in real time for excessive artefacts. The EEG was split into four parts lasting approximately 6-8 minutes. Figure 3.8 shows what the monitor displayed throughout the experiment and how long for.

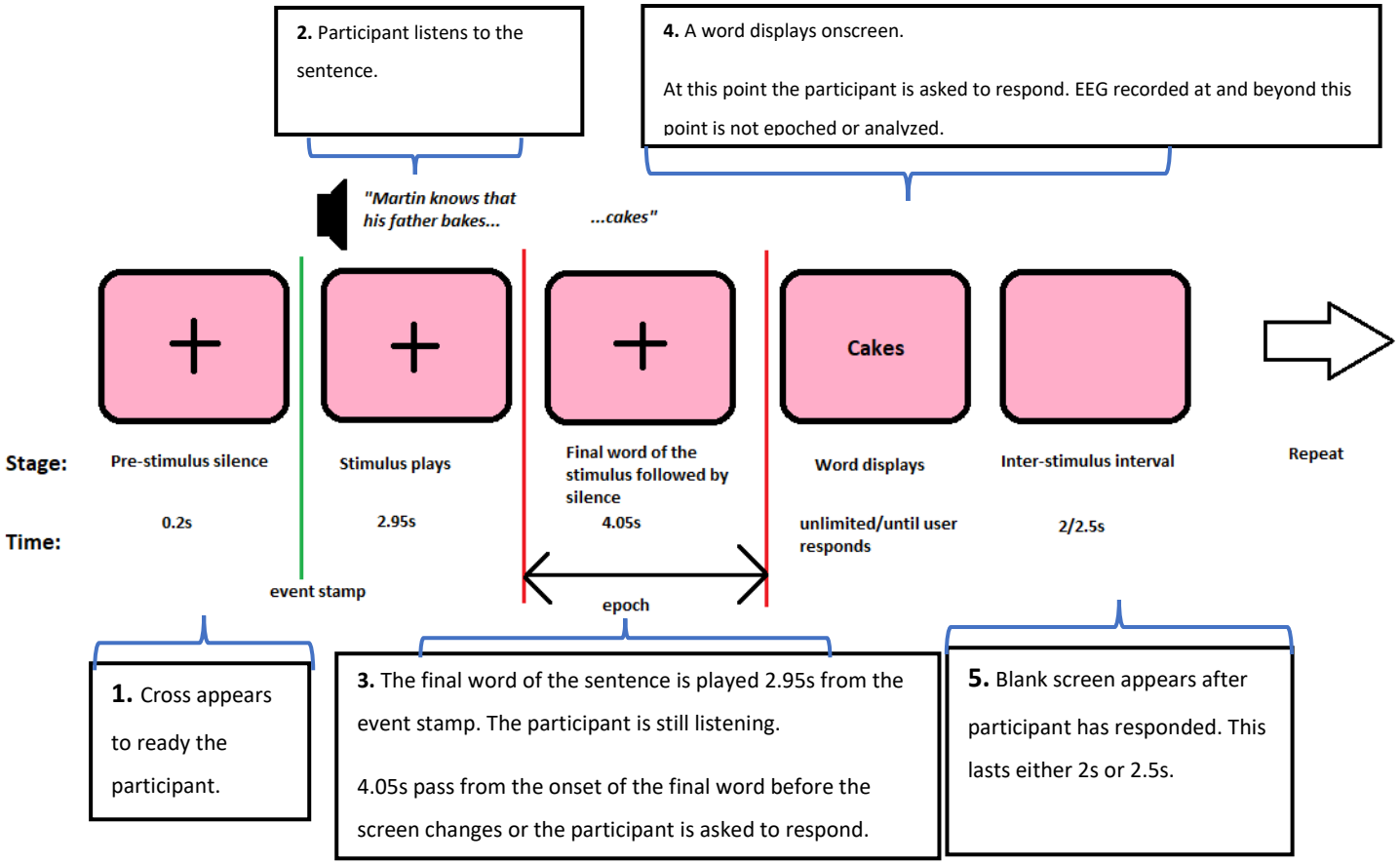

Figure 3.8 Timeline of what the participant will see and hear.

The event stamp is sent at the commencement of the audio file. The audio file is synced so the final word always commences at 2.95s. The epoch is therefore 2.95s following the event stamp. There is always a 4.05s gap between the commencement of the final word and the probe word appearing on screen.

The intention of the Probe Task was to implicitly draw the participants' attention to the final word of the sentence. The participant was not therefore being explicitly asked about the prosody during this task but the participant would implicitly use the prosody (as is natural in conversation) to deduce when the final word occurred. The use of this particular task instruction was anticipated to result in an object-switch in the IPB-2 condition. In the IPB-2 condition, the first IPB would indicate to the participant that the penultimate word was the final word. The task instructed the participant to memorise the final word for the purposes of completing the Probe Task. In cases where the prosody was guiding the participants' attention they would memorise the penultimate word. When they then heard the final word they would forget the penultimate word in favour of the final word. If prosody does guide the participants' attention in this fashion, it was predicted that the components associated with an object-switch would occur (N1-P3a-RON, delta power activation, and perhaps an SP). If the participant does not hear the unusual prosody or cannot decode the IPB, these components would be absent.

3.4.5 Procedure Summary

The procedure is summarised in Table 3.7.

Table 3.7 Table Summarising the full procedure. Full procedure is detailed here. The procedure is divided into screening, behavioural tasks and EEG. The approximate length of time taken for each procedure is shown.

Part	Screening		Behavioural		EEG				
Task	GDS-30 (scoring)	ACE-30 (Carrying out an scoring)	Discrimination Task (Explanation and carrying out)	Identification Task (Explanation and carrying out)	EEG Setup	EEG Part 1	EEG Part 2	EEG Part 3	EEG Part 4
Approximate time taken (minutes)	5	15	10	10	10-15	10	10	10	10

3.5 Pre-Processing and Analysis

This section details the methodology of the EEG pre-processing and analysis. Sections 3.5.1 and 3.5.2 outline the theory of Monte Carlo Simulations and of Clustering as a form of multiple comparison correction. Section 3.5.3 outlines the calculation used to derive a corrected alpha value that accounts for the variability in the statistical model used in the current study. Section 3.5.4 outlines how the time-windows used for analysis in the current study were empirically derived. The remainder of this section outlines the process of pre-processing and analysing the collected data. All analyses in the time and frequency domains were carried out using Monte Carlo simulation with 10,000 permutations.

3.5.1 Theory of Monte Carlo Simulations

The current study made use of Monte Carlo (MC) simulations of permutation tests to carry out analyses. A permutation test is a non-parametric test which have a long history of use in biological studies. The assumptions that underpin MC permutation tests make them particularly suited to the analysis of EEG data as they are easier to control in comparison to those that underpin equivalent parametric tests (such as ANOVA/MANOVA) which are often violated in biological studies. The process of a permutation test and its associated assumptions are outlined below.

In a permutation test, a test statistic is derived for the observed data. This statistic can be any statistic deemed appropriate to the data being tested. In the present study two incongruent conditions were separately compared to a congruent condition. As this means that in each case two groups of data were being compared, a t-statistic was derived. There are therefore two groups containing a certain number of values in each permutation test deriving a t-statistic. Firstly, the t-statistic comparing these two sets of observed data is derived and this is denoted u_0. The data are then shuffled randomly between the two groups to create two groups of the same size but containing a new configuration of the data (i.e. a new permutation). The test statistic is then derived for this new permutation, this new statistic is *simulated statistics* and is denoted as u_s. The data are then reshuffled and a new test statistic derived for the new permutation. This is repeated until all possible permutations of the data have been exhausted. The distribution of these test statistics is the permutation distribution. The statistic derived from the observed data, u_0 is compared against all the statistics in the permutation distribution and a p-value is derived using **Equation 3.1**

.

$$p = \frac{B}{N}$$

Equation 3.1 – The derivation of a p-value in a permutation test.

B – the number of test statistics higher than the observed statistics

N – the number of permutations

p - the probability of the observed test statistic occurred by chance

Equation 3.1 calculates the probability that the observed u_0 occurred by chance and is denoted by the p-value. The p-value is then compared with α to indicate if the p-value is significant.

The null hypothesis of a permutation test supposes that if there is no difference between the two groups being tested then each permutation of the two groups has as much chance of occurring than the rest. Therefore, under the null hypothesis, the observed test statistic is as likely to have occurred as a test statistic derived from any permutation. Should it prove to be the case that the observed data are at the unlikely tail of the permutation distribution (i.e. the p-value is smaller than α) then the null hypothesis can be rejected.

$$H_0 : p \geq \alpha$$

Equation 3.2 The null hypothesis

If the probability of the observed data (p) occurring is greater than α then the null hypothesis (H_0) holds.

Permutation tests are free from the assumptions about population and data inherent to parametric tests that often invalidate them in biological studies. Assumptions constraining parametric tests that are important to the current study are normality, noise distribution, population sampling and low sample sizes (Giacalone et al. 2018, Giancristofaro and Brombin 2014). All of these are difficult to control for in an EEG study, particularly small-scale ones that cannot control for population by recruiting countrywide or internationally. By contrast, the assumptions underpinning a permutation test are under the tester's control in an EEG study. The primary assumption underpinning a permutation test is exchangeability (Maris and Oostenveld 2007, Manly 1991, P 2018, Giancristofaro and Brombin 2014). In order for the permutation to be valid, the data must be exchangeable i.e. a permutation distribution can only be constructed if altering the permutations does not alter the probability distribution (Maris and Oostenveld 2007, Manly 1991, P 2018, Giancristofaro and Brombin 2014). In practice, this means the samples being measured have to be independent. In the present case, when doing a between-trials analysis independence means there are no additive or dampening effect of the EEG or any cross-contamination between trials. A dampening effect would be if the

patient were fatigued towards the end of the study, making the effect of the component less salient in later trials. This can be controlled for by allowing sufficient breaks and monitoring the test in real time to ensure the participant is comfortable. Cross-contamination can be avoided by using appropriate interstimulus intervals. Independence between trials can also be reinforced by shuffling the stimuli. In a between-subjects test, the subjects themselves have to be independent of each other. Therefore, the advantage of the exchangeability assumption over the assumptions inherent to a parametric test is that, with careful planning of the study, independence is within the control of the tester. An added advantage is that many of the precautions ensuring exchangeability are good EEG practice regardless.

In reality it is usually not practical or necessary to enumerate all possible permutations of u. A Monte Carlo simulation enumerates a sample of all possible permutations. This gives an estimated p-value than can be compared against alpha. This estimated value is denoted $\hat{p}$. As the p-value found at a full enumeration of all estimates is often hypothetical, it is often denoted p_∞. MC simulations have the advantage of having the same power as the equivalent parametric test, if the assumptions restricting the parametric test are true (Manly 1991). When these assumptions (which are difficult to control) are violated, it performs better than equivalent parametric tests. Additionally it also performs better than the Wilcoxon Signed Ranked for tested non-normal distributions (Manly 1991). Monte Carlo simulations have their own important caveats. Most importantly is the uncertainty of $\hat{p}$, as $\hat{p}$ is an estimate. Phipson and Smyth (2010) criticise the frequency with which $\hat{p}$ is reported without error estimates and suggests that this increases the chances of making a Type I error, a chance that is compounded when many tests are performed. This error can be satisfactorily accounted for by correcting α.

To demonstrate how this uncertainty can be calculated and accounted for, let t_0 be the t-statistic of the observed data. In a Monte Carlo simulation, a set number (N) permutations of the observed data are generated. A t-statistic for each of these permutations is calculated. Let these be called simulated statistics (t_s). There are therefore N number of simulated statistics and one additional statistic for the original observed data i.e. there are N+1 t-statistics generated in a Monte Carlo simulation. To determine significance, t_0 is compared against all values of t_s. In a single sided test, if t_0 is larger than a certain proportion of the simulated t-statistics then the null hypothesis (H_0) that any observations in the data are due to chance can be rejected with an α level of certainty. In a double-sided test, the observed statistic can be significant if it is either higher or lower than a proportion of the simulated statistics. The proportion of simulated statistics greater than the observed statistic that are permissible is determined by α. For any chosen value of α, the number of simulated statistics permissible above t_0 will be denoted by m; which can be calculated as:

$$m = \alpha(N+1)$$

Equation 3.3 – The proportion of permissible test statistics (m) allowable above the observed statistic for a given number of permutations (N) (Manly 1991).

In a parametric t-test, if $p < \alpha$ then the null hypothesis can be rejected by a degree of certainty determined by α. In a permutation test, the p-value is the probability that the observed statistic is less than a simulated statistic chosen at random. If an infinite number of permutations were to be carried out, $p < \alpha$ would give an accurate and desirable benchmark for significance. The number of permutations that can be carried out is denoted by the binomial coefficient of the observed data. This is often too high to practicably simulate which is why MC simulations are used. MC simulations can be used because it is not necessary to permute to impossibly high levels as the variation in $\hat{p}$ and the certainty by which the null hypothesis can be rejected can be calculated.

In a permutation test, the level of certainty with which you can reject the null hypothesis is affected by the number of permutations. The probability of being able to reject the null hypothesis for a given value of α is:

$$P = \sum_{r=0}^{m-1} \binom{N}{r} * p^r (1-p)^{N-r}$$

Equation 3.4 – The power of a Monte Carlo test (Manly 1991).

P – The probability from 0 to 1 of being able to reject H_0. This in itself is the sum of the probabilities that there are no simulated statistics greater than the observed statistics up until the permissible number of observed statistics.

r – the (hypothetical) number of simulated statistics greater than the observed statistics

N – the number of permutations produced

p – the p-value of the test

$\binom{N}{r}$ – the binomial coefficient of the data; i.e. the maximum possible permutations of the data

Equation 3.4 shows the certainty with which the null hypothesis can be rejected at varying levels of alpha, given a certain number of permutations. This equation shows that when the p-value differs greatly from alpha, not many permutations are required before the certainty with which you can reject or accept the null hypothesis tends towards 0 or 1. If increasing numbers of permutations are carried out, the closer to 1 or 0 this value gets (never reaching exactly 1 or 0). It can be concluded that increasing N will therefore increase the accuracy of the permutation test but with diminishing returns after a certain point. This is why full enumerations are not necessary and do not improve the power of the analysis. The above is true for when p̂ is not close to alpha. It is not true in borderline cases.

Figure 3.9 shows the calculated probability of being able to reject or accept the null hypothesis for α=0.05 for five example p-values of 0.08, 0.051, 0.05, 0.049, and 0.008.

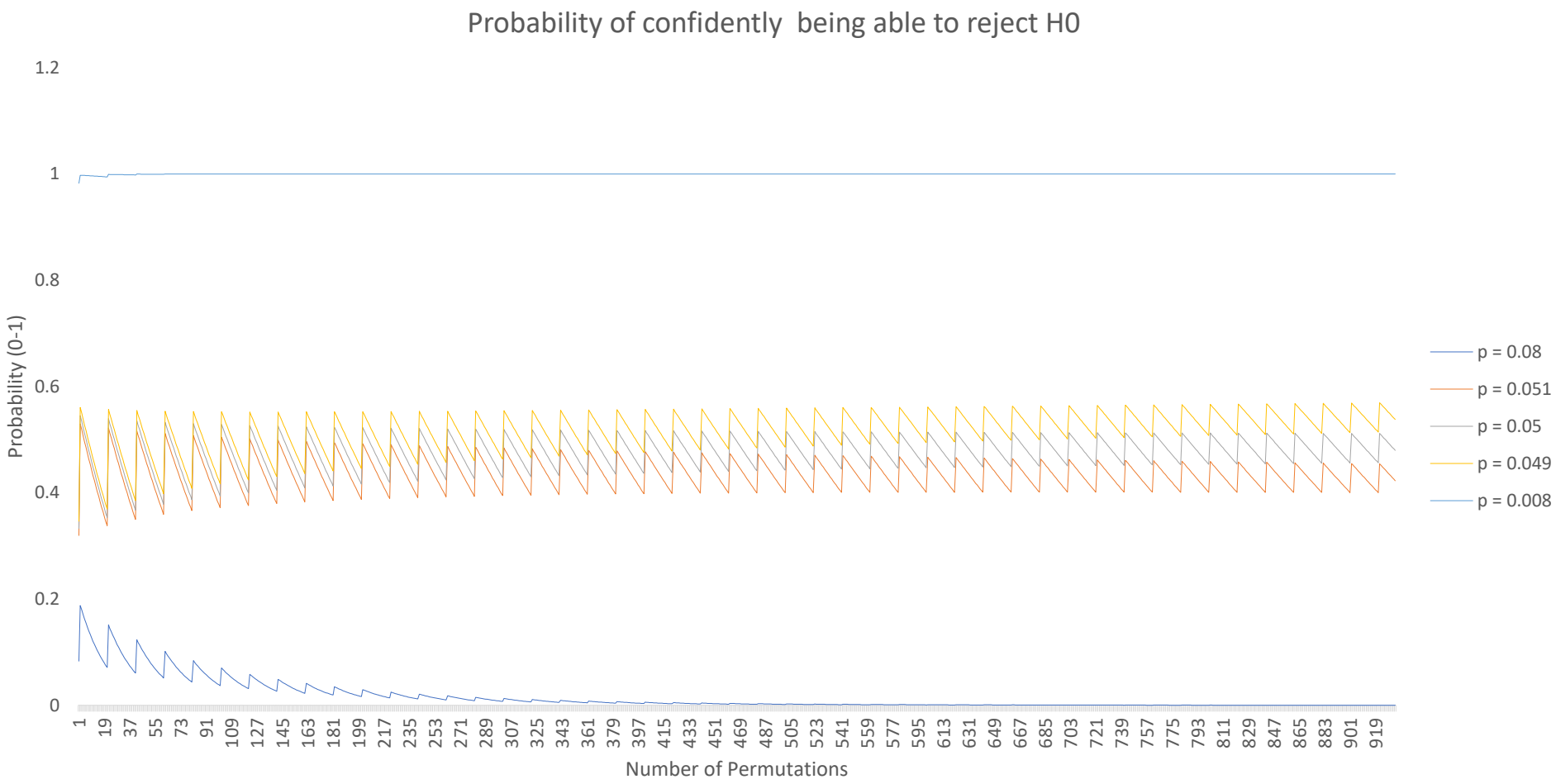

Figure 3.9 The probability of being able to reject H_0 for 5 given p-values at an increasing number of permutations.

For the low p-value of 0.008, the probability tends towards 1 at approximately 500 permutations. For the high value of p=0.08, the probability tends towards 0 at approximately 250 permutations. At the borderline values, both below and above alpha, the probability begins at approximately 0.5 and remains at 0.5 no matter how many permutations are carried out.

When p=0.008, H_0 can be rejected with a high degree of confidence (at alpha=0.05) for values of N as low as approximately 500. When p=0.08 H0 can be accepted with a high degree of confidence (at α=0.05) after values as low as approximately 250. In all three borderline cases, there is about 50% confidence of being able to reject or fail to reject H_0. This means at values of p̂ close to alpha, if the test is repeated it is as likely to return a significant p̂ as it is to return an insignificant p̂. Therefore, little more is known about the data than prior to having done the test and no increased number of permutations will improve this situation. This uncertainty is due to the fact that the calculated p-value will vary by some amount if a permutation test is repeated. This variation can be calculated. For a calculated p-value, 99% of all possible p-values will fall within the following boundaries:

$$p \pm 2.58 * \sqrt{\frac{p * (1-p)}{N}}$$

Equation 3.5 – The error in the estimated p-value (Manly 1991).

p – the p-value of the test

N – the number of permutations

Equation 3.5 shows that the variance in p is a function of the number of permutations carried out. The variations decrease with a higher number of permutations. The decreasing variance in p is illustrated in **Figure 3.10** which shows the variance in the borderline case of p = 0.049 for an increasing number of permutations.

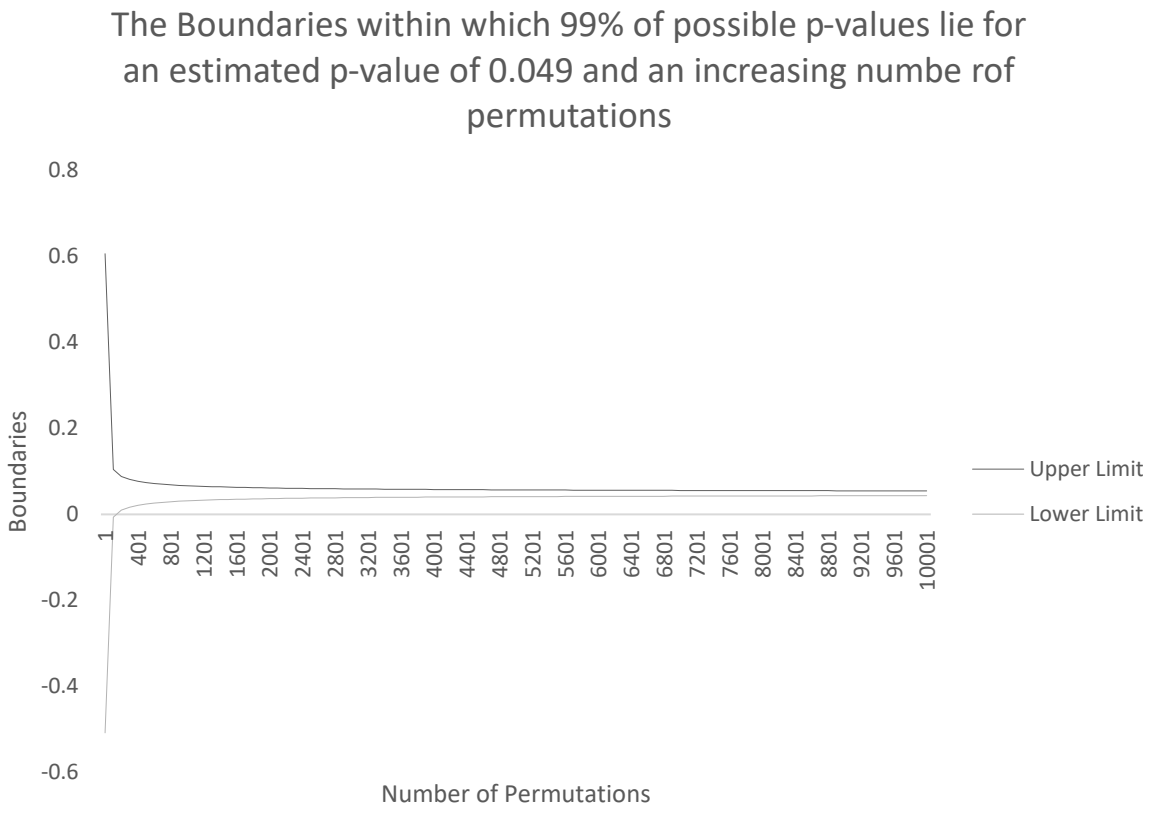

Figure 3.10 The Boundaries within which 99% of possible p-values lie for an estimated p-value of 0.049 and an increasing number of permutations.

99% of possible p-values fit between the upper limit line and the lower limit line. The space between these lines (the variance) decrease with increasing permutations.

Figure 3.10 shows that increasing the number of permutations does indeed decrease the uncertainty with which you can reject H_0 but the values at 10001 permutations demand closer inspection. At p=0.049 and N=10001, the upper and lower bounds of 99% of p-values are 0.054569 and 0.043431 respectively. This means if you repeat the test 100 times you can reasonably expect to return a p-value ≥α 50% of the time. Essentially demonstrating by other means the principle of **Equation 3.4** and showing that a p-value of the nominally significant value of 0.049 reveals very little about the data. As this variance can be calculated a corrected alpha value is easy to calculate (See Section 3.5.1).

3.5.2 Theory of Clustering for Multiple Comparison Correction

EEG montages necessitate analysis at multiple electrode sites and at multiple time periods. An alpha of 5% allows you to reject the null hypothesis with a 95% certainty. This means, that when performing one test there is a 5% chance of making a Type I error. If dozens (or 100+) electrodes are analysed individually then the chances of making a Type I error increases. This is called the Familywise Error

and the likelihood of making this error is the Family Wise Error Rate (FWER). In the current study 20 electrodes are used, analysing these individually with a 5% alpha, the FWER can be calculated as follows:

$$FWER \leq 1 - (1 - \alpha)^n$$

$$FWER \leq 64\%$$

Equation 3.6– Equation for FWER.

The likelihood of making a Type I error when carrying out multiple hypothesis tests.

n - Number of hypothesis tests carried out.

The current study uses a 20-electrode montage so the FWER ≤ 64%.

Therefore, using a 20-electrode montage, at each time interval analysed there is 64% that one Type I error has been made. This can be reduced using Multiple Comparison Correction (MCC). A common and intuitive method is Bonferroni correction. Bonferroni correction entails dividing alpha by the number of observations (i.e. 20, one for each electrode). When using dense montages Bonferroni is stiflingly conservative which increases the chances of making a Type II error. A less conservative method is Holm-Bonferroni in which the returned t-statistics are ranked. The lowest p-value is compared against the alpha/n. It is then excluded therefore the second lowest can be compared with alpha/n-1 and so forth until the results are no longer significant. In this form of MCC, only the most significant values in the data are Bonferroni corrected. Maris and Oostenveld (2007) developed a clustering method of multiple-comparison correction that is tailored specifically for EEG studies. It has been in turn been adapted from the method of Bullmore et al. (1999) which was specifically developed for use in MRI studies. This method extends the theory of Monte Carlo Simulations to the special domain by clustering neighbouring electrodes.

The clustering is performed as follows:

I) Test statistics are determined at each electrode (in this case derived using MC simulations)

II) All electrodes with test-statistics that are larger than a chosen threshold are clustered. This clustering is done both spatially and temporally. Temporal clustering is done with adjacent time windows and spatial clustering with neighbouring electrodes (in a two-sided study, this gives you negative and positive clusters).

III) The tests within each cluster are summed to derive the cluster statistic.

IV) The clusters are then permuted to derive a probability distribution which the non-permuted cluster is compared against.

This type of multiple comparison correction is underpinned by assumptions particular to EEG (and MEG) studies. If the global H0 is true i.e. H_0 is true at all electrodes, the probability distribution is equal at all electrodes. In an EEG setup, physiological responses are what cause H_0 to become violated. Such a physiological response would be present at all sensors. Therefore (to some extent) H_0 becomes broken at all sensors. Clustering treats the montage as one object so there are no longer multiple comparisons. The FWER may be increased by carrying out clustering a large number of tests. Since it has been developed, clustering has become established in published literature (the study has been cited 2691 times as of June 2020). Clustering is particularly suited to dense montages. The current study uses a 20-electrode montage which is not dense. Clustering and Bonferroni correction are used individually and the results compared.

3.5.3 Derivation of Alpha in the Current Study

Monte Carlo simulations return an estimated p-value. This p-value has an uncertainty which means the returned p-value will vary by some amount if the test is repeated. This means that when a p-value is close to the alpha value, whether the test returns a significant result is matter of chance. In the current study this uncertainty is eliminated by using a corrected alpha value. This alpha is derived by calculating the upper and lower bounds of the uncertainty of estimated p-values for 10,000 permutations. In the current uses a 5% certainty prior to MCC. The highest estimated p-value at which 99% of calculated p-values are under 0.05 is calculated. This serves as the corrected alpha value. As the test is two-sided this is divided by two. **Equation 3.5** calculates the upper and lower bounds within which 99% of returned p-values will fall. This means that for p-values close to 0.05 repeating the test may change the outcome (Section 3.5.1). The upper and lower bounds of ever decreasing p-values for a Monte Carlo simulation with 10,000 permutations were calculated and shown in Figure 3.11.

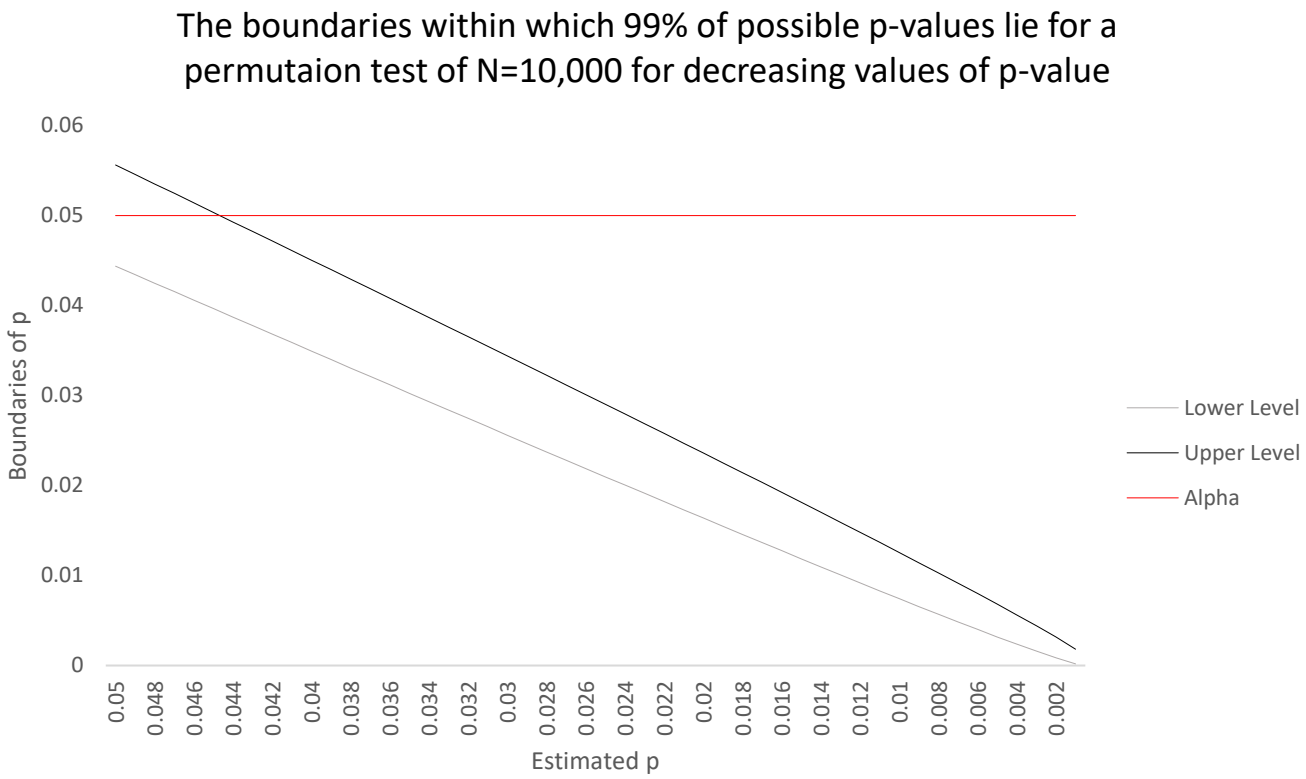

Figure 3.11 The boundaries within which 99% of possible p-values lie for a permutation test of N=10,000 for decreasing p-values.

Estimated p-values are plotted in the x-axis and the uncertainty of these values on the y-axis. The upper and lower bounds of estimated p-values are shown in black and grey respectively. From the graph it can be observed that for a returned p-value of 0.046, if the simulation were repeated there is a <99% chance that a non-significant value will be returned. This means that a value of 0.046 cannot reliably deemed significant for an alpha value of 0.05.

Based on **Equation 3.5**, at p=0.044, 99% of all possible p-values when the test is repeated will fall below 0.049, giving a high degree of certainty that H_0 can be rejected. If using an alpha of 0.01 then at p=0.007 99% of all p-values fall below 0.009.

The current study is a two-sided test, it is therefore appropriate to examine values at which p is safely below 0.025. Dividing 0.044 by 2 gives a value of 0.022. Using **Equation 3.5** however returns a value of 0.021. An appropriate alpha value for a two-sided MC simulation with 10,000 permutations is therefore 0.021. This alpha value is used in the current study (prior to MCC) to give a 5% certainty.

This alpha value is valid with 10k permutations. Increasing the number of permutations would allow us to approach values closer to 0.025. This would be at huge computational cost to salvage cases with very low statistical significance. Given the use of MCC in this study, this was deemed unnecessary as marginally significant results would be filtered out regardless. This was confirmed empirically by

examining some of the HS dataset using 100k permutations. In all examples tested, the same results were returned but with a huge increase in analysis time.

3.5.4 EEG Pre-Processing

The EEG was recorded in four parts, so each part was merged prior to pre-processing. The EEG were filtered from 0.1-50Hz using Curry Neuroimaging Suite 7.0.8 XSB (Compumedics, Australia). Using MATLAB v2015 (Natick, Massachusetts: The MathWorks Inc), the EEG were re-referenced to a common average. Epochs of the three conditions were extracted from -1000-5800ms around the timestamp. A ±50µV threshold was applied to the epochs to remove large artefacts. The epochs were then scanned visually for further artefacts. Participants had been instructed to blink and swallow prior to recording to aid with this identification. 8 participants with an excessive number of artefacts were removed from the EEG analysis completely. Detrending was applied to epochs that showed drift. Min-Max normalisation was then applied to the epochs.

Table 3.8 The outcome of the artefact rejection.

These figures do not include the 9 participants who had all of their trials rejected. The number of trials removed from the group as a whole is shown as well as the mean removed from each remaining participant.

	IPB-1	IPB-2	IPB-0
Total Trials	1120	1120	1120
Trials Removed Total	696	730	670
Trials Removed Mean	25	26	24
Trials Remaining Total	424	390	450
Trials Remaining Mean	15	14	16

3.5.5 Derivation of the Temporal Resolution of the Analyses

Analysis in the time-domain was carried out by dividing the epoch into overlapping time-windows. For group analyses, the average amplitude of the EEG in each time-window in the IPB-1 condition was separately tested against the average amplitude in the IPB-2 condition and IPB-0 condition in a 10k permutation MC simulation deriving independent t-statistics. The size of the overlapping time window was derived empirically by examining the results of different sized time-windows. The epoch in each instance was 1.6s from the onset of the final word. Six sizes of time-windows were tested and these are shown in **Table 3.9**. This method of analysis was used to avoid a-priori assumptions about the location or latency of any of the components the study sought to elicit.

Table 3.9 Table showing the tested interval sizes.

The least precise window size tested was 9 windows of 250ms. Each window was positioned 200ms apart, therefore they overlapped by 50ms. The smallest time window examined was 25ms wide with an overlap of 15ms which resulted in 108 windows in total.

Iteration	Size of Intervals (ms)	Window Shift (ms)	Final Interval (ms)	Total Number of Time-Windows
1	250	200	1600-1850	9
2	200	150	1650-1850	12
3	150	100	1600-1750	17
4	100	80	1600-1700	21
5	50	30	1590-1640	54
6	25	15	1605-1630	108

To perform the temporal resolution analysis, the epoch was divided into overlapping windows of equal size. Within those windows the average amplitude of each participant in the congruent condition was compared with the average amplitude of each participant in the incongruent condition. A dependent t-statistic was derived at each interval. 10,000 permutations were then simulated and a dependent t-statistic derived for each one, at each electrode. The dependent variable was the amplitude of the EEG and the independent variable were the conditions, IPB-1, IPB-2 and IPB-0. These t-statistics are clustered with their neighbours and positive and negative clusters (if any) were derived. From these a cluster-level $\hat{p}$ was derived to determine significance. The process was then repeated for the next temporal window.

After each window in the epoch was analysed, the window sizes were reduced and the process repeated.

The process was carried out twice. Once comparing IPB-1 with IPB-0 and once comparing IPB-1 with IPB-2. A total of 442 windows were therefore analysed.

The test was two-sided so an alpha of 0.021 was chosen.

The binomial coefficient of the data is as follows:

$^{56}C_{28}$ =7.6487e+15

There was therefore a 1/7.6487e+15 probability that any one permutation was drawn. It is therefore unlikely that there were repeats increasing the error margins of the p estimate, even with 10000 permutations.

From this it was seen that 100ms and 50ms time-windows were sufficient to show all EEG features. It was also seen that 25ms time-windows increased the chance of noise in the data returning an erroneous significant result. Reducing the time window to that size therefore reduced the accuracy of the data. To be conservative a time-window of 50ms was used in all time-domain analyses.

3.5.6 Multiple Comparison Correction

For each p-value derived two forms of MCC are separately carried out, Bonferroni correction and clustering. The current study used a 20-electrode montage. When applying Bonferroni correction, $\alpha=0.021/20$. Only $p<0.00105$ are therefore considered significant when using Bonferroni correction.

The process of clustering is as follows:

V) MC simulations are carried out at each electrode.

VI) All electrodes with test-statistics that are larger or smaller than the threshold set by $\alpha=0.021$ are clustered with their neighbours.

VII) The tests within each cluster are summed to derive the cluster statistic. This cluster statistic is compared with $\alpha=0.021$ and this determines the significance of the cluster.

Which electrodes were neighbours was determined by their proximity. The neighbours are shown in **Figure 3.12**.

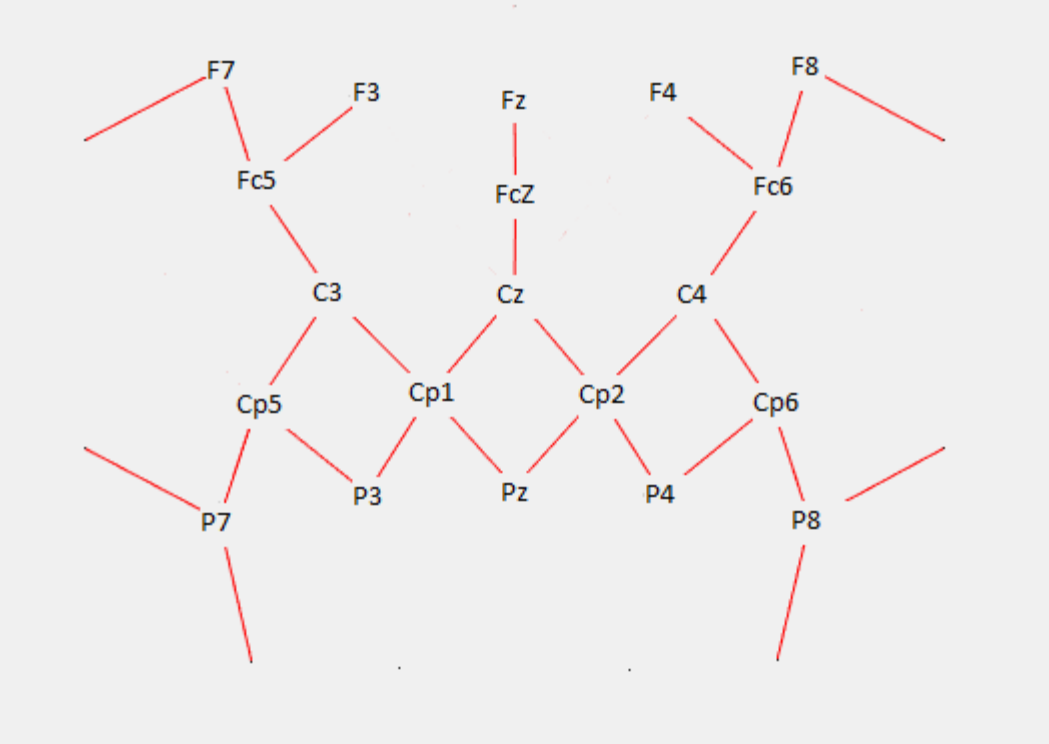

Figure 3.12 Montage showing the neighbouring electrodes.

The red lines indicate which electrodes are deemed to be neighbouring. Due to the montage not being dense, there are a number of adjacent electrodes that do not directly neighbour, for example F7 and F3. These however are able to cluster through an intermediary, in their case Fc5. So while F7 and F3 are unable to form a cluster on their own, they can form an anterior-left cluster.

Figure 3.12 shows the neighbours used in all subsequent cluster analyses.

3.5.7 Time-Domain Analysis - Group

Significant ERP features in the Pilot and HS cohort were identified in the same way. In the Pilot cohort there were 8 participants used in the analysis and in the HS cohort there were 28 participants. The pre-processed epochs of each participant were grouped by condition (IPB-1, IPB-2 or IPB-0) and averaged. These averages were divided into 50ms windows that overlapped by 30ms. The average amplitudes of the EEG within these windows were the dependent variables. The condition was the dependent variable. The IPB-1 condition, as the congruent condition, was separately tested against the IPB-2 condition and IPB-0 condition. In the HS cohort there was therefore 28 average amplitudes for each time window for each condition and at each electrode. The epoch was divided into 55 time-windows (including a pre-stimulus time-window) of 50ms length. There were 20 electrodes. Comparing the IPB-1 and the IPB-2 condition, for each test carried out, there were 28 dependent variables and two independent variables. At each time window a 10,000 permutation MC simulation deriving two-sided independent t-values was carried out 20 times (once per electrode). Clustering and Bonferroni correction were carried out separately for comparison. This process was carried out 55 times (once for each time window) and this identified the ERP features. The exact same process was carried out testing the IPB-1 against the IPB-0 condition.

3.5.8 Frequency-Domain Analysis - Group

The grand averages were convolved using a Hanning window. The Hanning window was 1s wide to allow a resolution of 1Hz. A 100ms baseline was taken from the 100ms prior to the onset of the crosshair (artefact rejection was carried out on the baseline). The EEG was analysed in windows corresponding to each of the EEG bands delta through to gamma. Bordering frequencies (for example 4Hz which borders theta and delta) were not analysed to avoid artefacts from neighbouring frequency bands. Beta and gamma were split into three equally sized overlapping bands. The frequency bands used in the analysis of the group are shown in Table 3.11. Within each of these bands the epoch was divided into 21 100ms time-windows that overlap by 80ms. In each of these time-windows a 10,000 permutation MC simulation deriving independent t-statistics was carried out and Bonferroni and cluster MCC carried out separately. The simulation was therefore carried out in 21 time-windows at 20 electrodes in each of the 9 frequency bands.

Table 3.10 Frequency windows used in the analysis and their corresponding EEG bands.

Band	Bounds of the Frequency Analysis
Delta	1-3Hz
Delta	1-2Hz
Delta	2-3Hz
Theta	5-6Hz
Alpha	9-14Hz
Lower-Beta	17-22Hz
Mid-Beta	21-26Hz
Upper-Beta	25-30Hz
Lower-Gamma	33-38Hz
Mid-Gamma	38-43Hz
Upper-Gamma	44-48Hz

3.5.9 Male-Female Analysis

The HS group were checked for interaction by sex. The group was divided into a male group and female group. The groups were first examined separately using a 10,000 MC simulation deriving independent t-tests for each condition using 50ms time-windows. The interaction of sex was examined using a mixed-between-within subject 2x2 factorial design. The layout of this design is shown in **Table 3.12**. There were 17 participants in the female group and 10 in the male group.

Table 3.11 The layout of the 2x2 factorial design.

In this design (1,1) is subtracted from (1,2) and (2,1) is subtracted from (2,2). This is carried out twice, separately comparing IPB-1 with IPB-2 and comparing IPB-1 with IPB-0.

		Factor	
		IPB-1	IPB-2/IPB-0
Level	Female	(1,1)	(1,2)
	Male	(2,1)	(2,2)

In the factorial study the IPB-1 condition is subtracted from the IPB-0 and IPB-2 conditions. Male and Female groups are then tested against each other in a 10,000 MC simulation deriving independent t-statistics with cluster MCC.

This forms the group of tests shown in **Table 3.11**.

Table 3.12 The two factorial designs being carried out for the male-female analysis.

In iteration 1 Female IPB-1 is subtracted from Female IPB-2. Male IPB-1 is subtracted from male IPB-2. They are then compared in a Monte Carlo simulation deriving independent t-tests. The process is repeated in iteration 2 but with IPB-0 in place of IPB-2.

Condition	Group	Group	Test
IPB-2	Female IPB-2 – Female IPB-1	Male IPB-2 – Male IPB-1	Independent t-test
IPB-0	Female IPB-0 – Female IPB-1	Male IPB-0 – Male IPB-1	Independent t-test

3.5.10 Individual Analyses

Between-Trial analyses were carried out on eight individuals in the HS group (chosen for their high number of artefact-free trials) and on each of the PD case studies. The power of the MC simulation is limited by the number of artefact-free trials available. Participants on which analyses were carried out were determined by the number of artefact free trials each participant had. Low trial numbers reduce the validity of the MC simulation in two important ways. The $\hat{p}$ that can be reached in a permutation test is limited by the number of permutations that are available. S5 had 4 trials in the IPB-1 condition and 6 trials in the IPB-2 condition. The binomial coefficient of this is 210. With this number of permutations, the minimum p-value that can be reached is 0.004762. In a two-sided test, there is not enough data to find any significance in S5's data. This was the only subject for which the minimum p-value is greater than 0.021 but there were other borderline cases in which significance could only be reached in the most favourable of circumstances or with caveats that invalidate the test.

S2, S5, S9, S18 and S19 had binomial coefficients of less than 10,000 in the IPB-2 condition. S2 and S5 had binomial coefficients of less than 10,000 in the IPB-0 condition. It is computationally possible to fully enumerate these subjects to derive a p-value that is not an estimate. With fewer permutations the power of the test is reduced but this is not the most important implication. An MC simulation is not able to fully enumerate all permutations accurately. S5 (for example) had a binomial coefficient of 210 in the IPB-2 condition. If 210 permutations are used, there is a $1/210^{210}$ chance that all permutations are fully enumerated with no repeats. Each repeat reduces the accuracy of the simulation. Each repeat that produces a t-value higher than the observed t-value weighs the test away from significance and the inverse is true for simulated t-values less than the observed statistic. In the case of 10,000 permutations, it is likely that all possible permutations have been enumerated. In this case though there are at least 9790 repeats, each reducing the accuracy of the estimated p-value. Constructing an algorithm capable of fully enumerating these participants would be of little value.

The number of artefact-free trials of each participant in the HS group is shown in **Table 3.14**. The participants on which MC simulations were carried out are highlighted in green. **Table 3.15** shows the number of artefact free trials for each of the PD case studies. Analyses are carried out on all three participants with PD.

Table 3.13 The number of artefact free trials per participant in the HS group.

The trials used for analyses are highlighted in green. HS3 is only analysed in the IPB-2 condition and S13 is only analysed in the IPB-0 condition.

HS	IPB-1	IPB-2	IPB-0
1	19	29	26
2	8	5	4
3	14	21	15
4	13	12	12
5	4	6	15
6	18	15	19
7	18	15	11
8	15	10	15
9	8	8	12
10	25	20	20
11	30	27	26
12	22	17	22
13	13	15	24
14	9	10	7
15	21	17	24
16	10	11	7
17	18	19	14
18	6	8	11
19	9	5	9
20	16	7	15
21	20	26	22
22	7	8	12
23	12	10	8
24	22	18	28
25	13	16	17
26	16	12	12
27	14	13	12
28	14	10	15

Table 3.14 The number of free trials per PD case study.

PD2 only has 13 free trials in the IPB-1 condition which reduces the likelihood of finding significant results for PD2.

	IPB-1	IPB-2	IPB-0
PD1	13	20	22
PD2	27	31	33

Analyses on individuals in the time-domain were carried out in a manner similar to that of the group as a whole (Section 3.5.4) but deriving dependent instead of independent t-statistics. For each participant, each artefact free trial was grouped into each condition (IPB-1, IPB-2 and IPB-0). Each trial was divided into 55 50ms time-windows that overlapped by 15ms. Dependent t-statistics were derived in each time-window and at each electrode. Bonferroni and clustering were separately carried out. Due to having different numbers of artefact free trials, each participant had a different number of independent variables which are listed in **Table 3.14**.

Table 3.15 No. of independent variables for each t-test carried out on each HS's data.

IPB-1-IPB-2		IPB-1-IPB-0	
Participant	No. of independent variables	Participant	No. of independent variables
S1	48, t(46)	S1	45, t(43)
S3	35, t(33)	S10	45, t(43)
S10	45, t(43)	S11	56, t(54)
S11	57, t(55)	S12	44, t(42)
S12	39, t(37)	S13	37, t(35)
S15	38, t(36)	S15	45, t(43)
S21	46, t(44)	S21	42, t(44)
S24	40, t(38)	S24	50, t(48)

Table 3.16 No. of independent variables for each t-test carried out on each PD's data.

IPB-1-IPB-2		IPB-1-IPB-0	
Participant	No. of independent variables	Participant	No. of independent variables
PD1	33, t(31)	PD1	35, t(33)
PD2	58, t(56)	PD2	60, t(58)

Frequency transforms were carried out on individuals in the same manner as carried out on the group. Each person's EEG is convolved using a Hanning window. The Hanning window was 1s wide to allow a resolution of 1Hz. A 100ms baseline was taken from the 100ms prior to the onset of the crosshair (artefact rejection was carried out on the baseline).

Analysis carried out on individuals found fewer significant changes in frequency power when wide frequency bands were analysed. Analysis was therefore carried out in 1Hz wide bands covering delta (1-2Hz, 2-3Hz, 3-4Hz) and alpha bands (9-10Hz, 10-11Hz, 11-12Hz, 12-13Hz, 13-14Hz). Within each of these bands the epoch was divided into 21 100ms time-windows that overlap by 80ms. In each of these time-windows a 10,000 permutation MC simulation deriving dependent t-statistics was carried out and Bonferroni and cluster MCC carried out separately. The simulation was therefore carried out in 21 time-windows at 20 electrodes in each of the 8 frequency bands.

3.5.11 Pilot

Piloting revealed indications of a RAN, a PEP-like positive, and a P3a. From this it was deemed that no further adjustments were necessary to the EEG protocol. As the participant characteristics of the pilot cohort (young adults) were distinct from the main study group (older adults) and could thus serve as an important comparison to the older HS cohort, it was decided that the pilot results would be integrated into the overall set of results for this thesis. The pilot results are therefore reported fully in Chapter 4.

Chapter 4

Results

4 Results

Results are presented in the current section. The Pilot results are presented first to show the response in a younger cohort. Following this the IPB-2 condition is presented. This is the condition which aimed to elicit an object switch and the attention capture components, N100, P3a, RAN, delta activation and SP. The results of analyses on the HS cohort are shown first. Between-Trial analyses on three HS individuals are then presented. These are examples of an exemplary individual response, a middling individual response and an individual response different to that of the group as a whole. The IPB-0 condition is then presented. This is the condition that aimed to use a false prosodic expectancy to a PEP and RAN. One exemplary response is presented in this condition as an outlier. Finally, the case studies are presented. All ERPs in this section are shown without smoothing.

4.1 Pilot Results

The current section presents the results of the Pilot cohort, first in the IPB-2 condition and then in the IPB-0 condition. The data consist of 8 subjects with a total of 134 trials in the IPB-1 condition; 144 trials in the IPB-0 condition; and 130 in the IPB-2 condition. The Pilot cohort did not do the Identification Task or the Discrimination Task as the cohort originally took part to determine if the EEG Task elicited the desired components. Presented are results of 10,000 Permutation Monte Carlo Simulations deriving independent t-statistics. Analyses in the time domain are carried out using 50ms time-windows with a 20ms overlap. Analyses in the frequency-domain are carried out using 100ms time-windows with a 50ms overlap. The pilot cohort were used to test the efficacy of the EEG task in eliciting the desired components so they did not take part in the Discrimination or Identification Task.

4.1.1 IPB-2 Pilot

10k MC simulations t(14), p<0.021 with clustering and Bonferroni MCC failed to reveal an N100 or RON. Both forms of MCC did reveal a salient P3a. **Figure 4.1** shows electrodes and intervals at which there is a significant result with Bonferroni correction. These show a distinct-P3a like waveform.

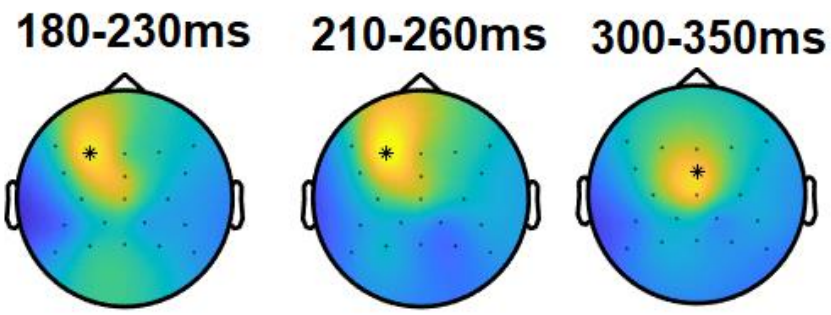

Figure 4.1 Intervals in which there is a significant ERP response following Bonferroni MCC in the Pilot Cohort in the IPB-2 Condition.
Electrodes and intervals in which there is a significant result are highlighted with asterisks. There are 2 overlapping 50ms intervals ranging from 180-260ms. There is an additional interval 300-350ms. These show a salient positive component at F3 and FCz. This indicates the presence of a component that is topographically and temporally congruent with a P3a.

While Bonferroni MCC revealed the areas at which the P3a is most salient, Cluster MCC reveals the wider topography of the component and shows the front-central topography characteristic of the P3a. This is shown in **Figure 4.2**.

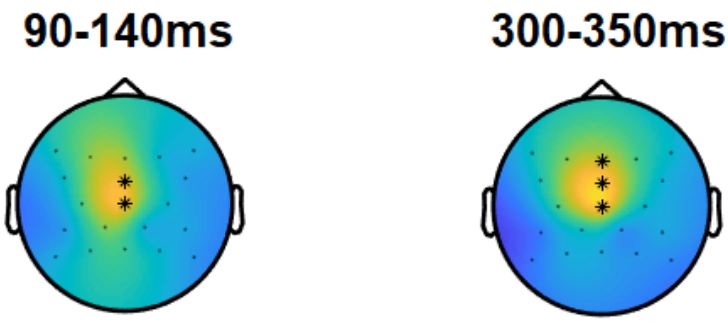

Figure 4.2 Intervals in which there is a significant ERP response following Cluster MCC in the Pilot Cohort in the IPB-2 Condition.
Electrodes and intervals in which there is a significant result are highlighted with asterisks. There are is a 90-140ms interval followed by a 300-350ms window. These reveal a front-central P3a component at Cz, FCz and Fz.

The shape of this component at electrode FCz is shown in **Figure 4.3**.

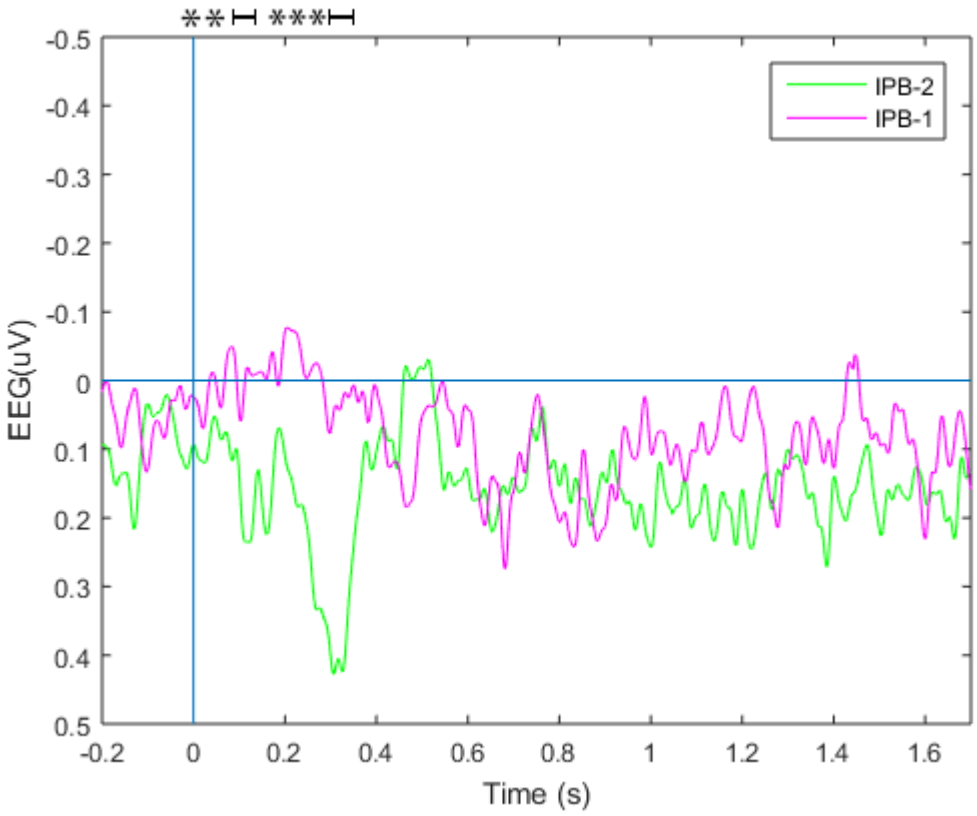

Figure 4.3 ERP of the Pilot Cohort in the IPB-2 condition at FCz with significant differences highlighted.
ERP plot at the FCz electrode. The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The significant intervals are highlighted. Double asterisks highlight the intervals that are significant with Bonferroni MCC and triple-asterisks highlight the intervals that are significant with both Cluster MCC and Bonferroni MCC. A salient P3a is visible within the 210-350ms interval. Bonferroni MCC captures the peak of this waveform 300-350ms. The P3a is preceded by a lesser positive component in the 90-140ms interval.

The frequency decomposition at each electrode was analysed using 10k MC simulations. The frequency decomposition at FCz, where the P3a is most salient, is shown with significant differences highlighted are shown in **Figure 4.4**.

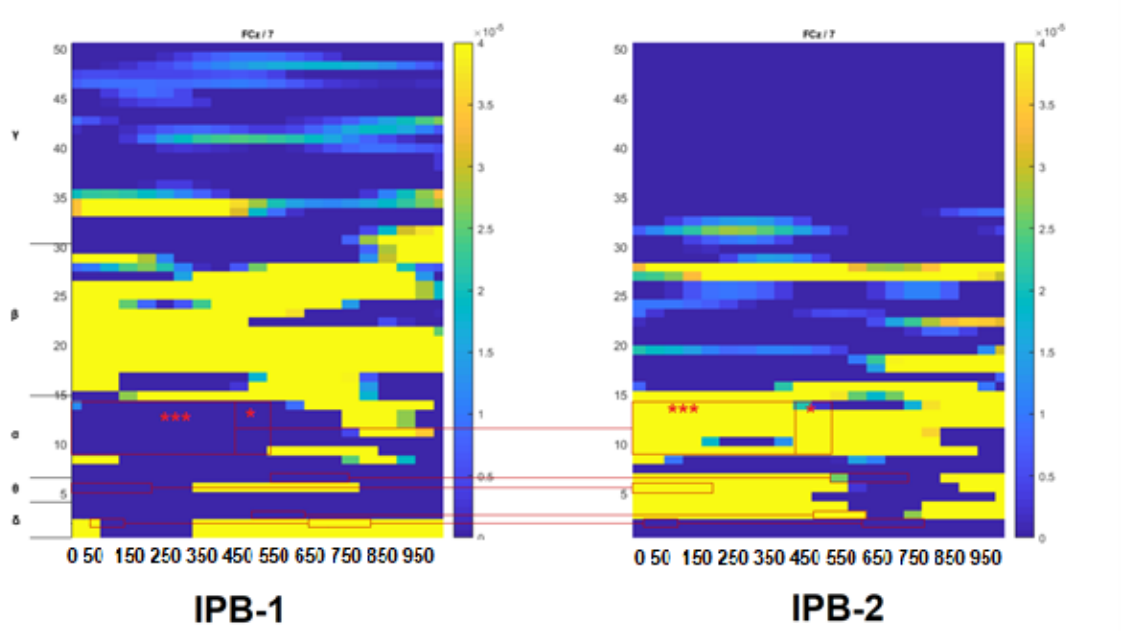

Figure 4.4 Frequency decomposition at channel FCz in IPB-2 condition
The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-2 condition. Highlighted are significant differences in the two conditions. A single asterisk indicates areas of cluster significance. A double asterisk indicates areas on Bonferroni significance. A triple asterisk indicates overlapping areas of Bonferroni and cluster significance. A cluster significant increase in alpha power occurs prior to and during the P3a at 0-500ms. A Bonferroni significant alpha occurs 0-400ms. A Bonferroni decrease in delta (2Hz) occurs 650-750ms. A cluster decrease in delta (2Hz) occurs 600-700ms. No MCC increases in theta occur prior to and after the P300 at 0-150ms (6Hz) and 500-700ms (7Hz).

There is an increase in alpha power overlapping the P3a. The expected increase in delta power is absent.

4.1.2 IPB-0 Pilot

Results of 10K MC simulations t(14), p<0.021 with clustering and Bonferroni MCC revealed a RAN and PEP component. These are presented separately below.

The RAN is composed of a negative cluster composed at F4, F8 and FC6 in the interval 360-410ms and at F4 and FC6 450-500ms. The negative cluster at F4 and FC6 reoccurs at 840-890ms and 900-950ms. From 870-920ms there is a negative cluster Fz and CPz. There are negative Bonferroni significances 360-410ms: F8 and FC6. 390-440ms: FC6. 450-500ms: F4 and FC6. 480-530ms: FC6. 540-590ms: FC6. 630-680ms: Fz 780-830ms: Fz. 810-860ms: F4 and Fz. 840-890ms: F4, FC6 and Fz. 870-920ms: F4 and Fz. 930-980ms: FC6.

Both waveforms are visible with Bonferroni MCC as can be seen in Figure 4.5.

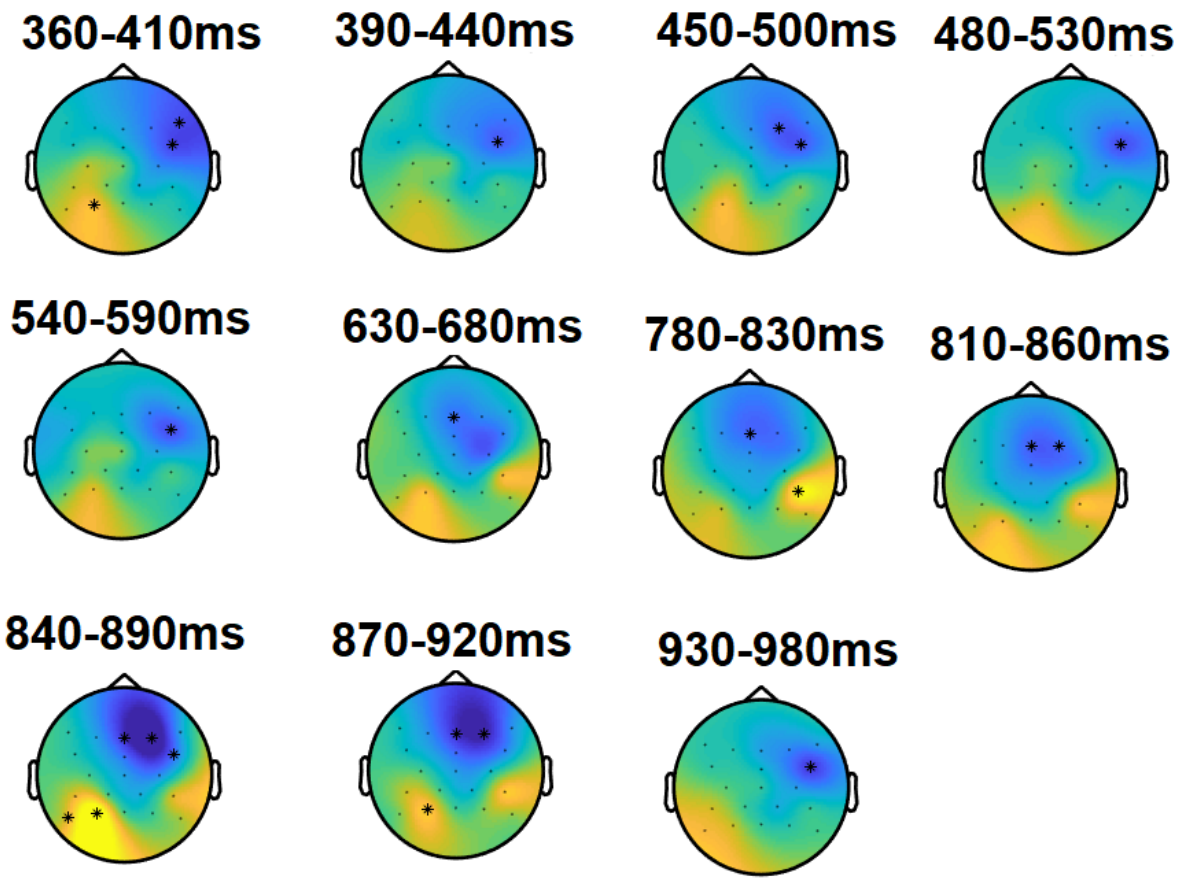

Figure 4.5 Intervals in which there is a significant ERP response following Bonferroni MCC in the Pilot Cohort in the IPB-0 condition.
Electrodes and intervals in which there is a significant result are highlighted with asterisks. There is a RAN component 360-980ms. This moves between the right-anterior electrodes Fz, F4, F8,and FC6.

The RAN as it appears with Cluster MCC is shown in Figure 4.6.

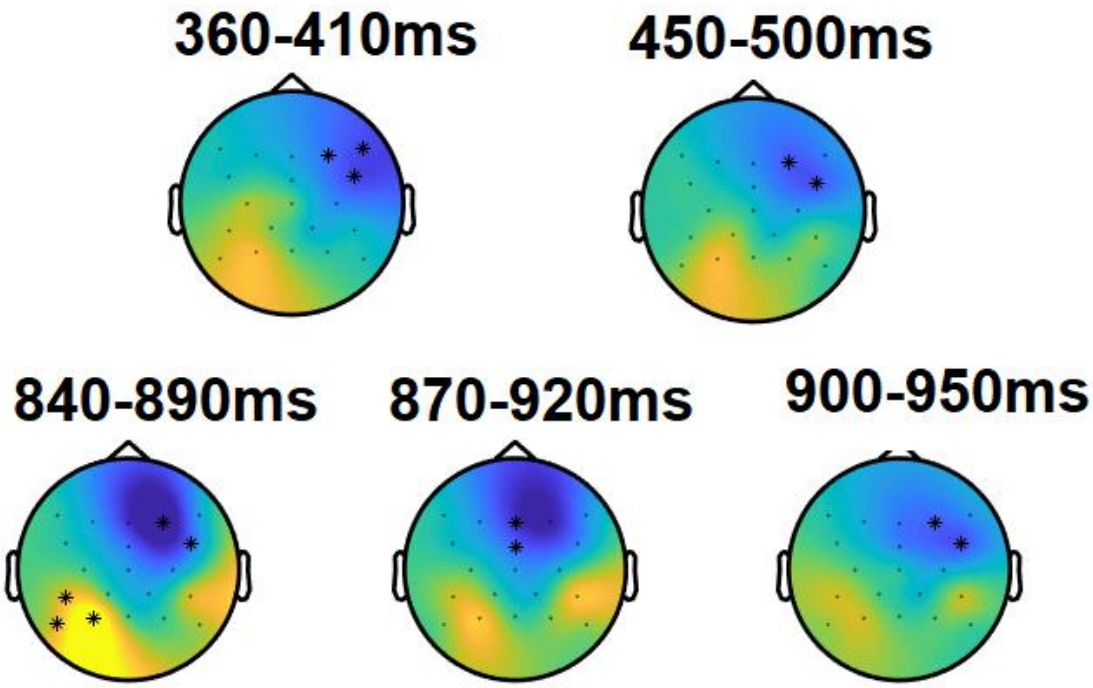

Figure 4.6 Intervals in which there is a significant ERP response following Cluster MCC in the Pilot Cohort in the IPB-0 condition.
Electrodes with a significant response are highlighted with asterisks. A RAN cluster occurs 360-500ms and 840-950ms.

Two RAN clusters at 360-410ms and 840-950ms are visible.

The ERP of this component as it appears at F4 is shown in Figure 4.7.

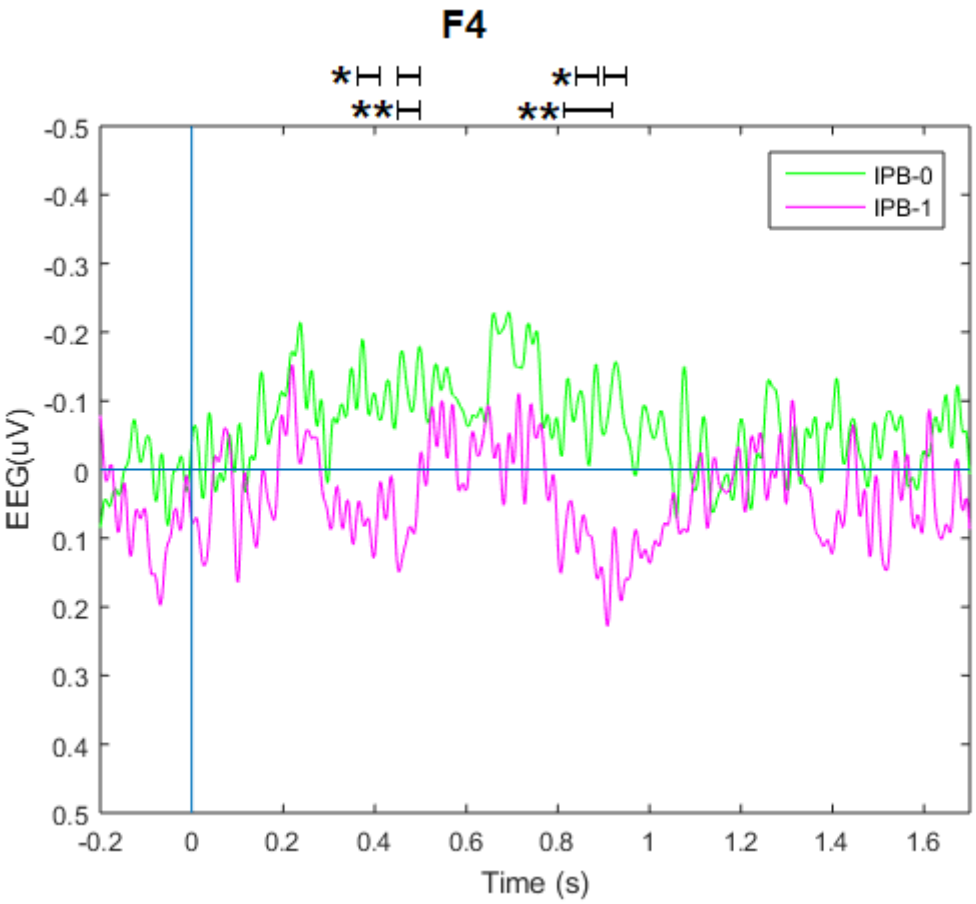

Figure 4.7 ERP of the Pilot Cohort in the IPB-0 condition at F4 with significant differences highlighted.
ERP plot at the F4 electrode. The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. The significant intervals are highlighted. Single asterisks highlight intervals that are significant with Cluster MCC. Double asterisks highlight the intervals that are significant with Bonferroni MCC. The double RAN can be seen 360-500ms and 840-950ms.

The frequency composition of this component as it appears at F4 is shown in Figure 4.8.

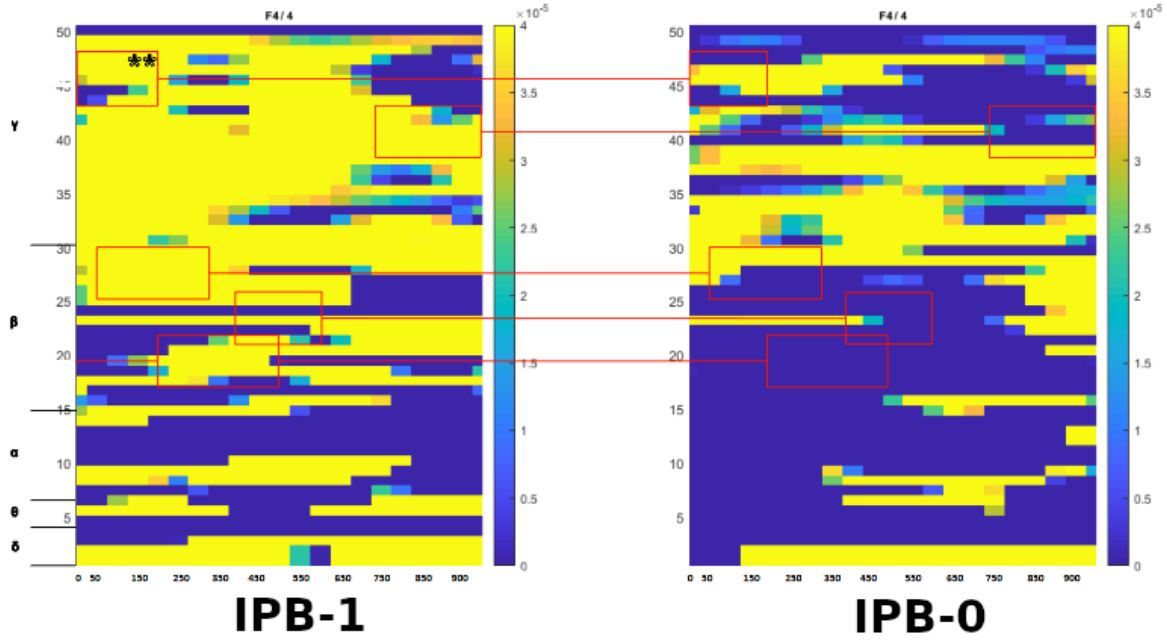

Figure 4.8 Changes in frequency power at F4 in the IPB-0 condition in the pilot cohort.
The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-0 condition. Highlighted are significant differences in the two conditions. The double asterisk indicates areas of Bonferroni significance. There is a significant drop in gamma power (43-48Hz) prior to the onset of the initial negative component. There are drops in beta power during the initial negative components (17-22Hz). These drops are also recorded at electrode F8.

The PEP component is composed of an early parietal positive cluster that occurs 330-380ms at CP5, P3 and P7. Positive clusters appear parentally 780-830ms P4 and P8. Cp5, P3 and P7 840-890ms. Cp5 and P3 870-920ms. Cp5, P3 and P7 930-980ms. There are positive Bonferroni significances 90-140ms: P3. 360-410ms: P3. 600-650ms: CP6. 660-710ms P3. 690-740ms: P3&CP6. 720-770ms: P3. 780-830ms: CP6. 840-890ms: P7 and P3. 870-920ms: P3. 1050-1100ms: CP6. 1560-1610ms: CP6.

The PEP as it appears with cluster MCC is shown in Figure 4.9.

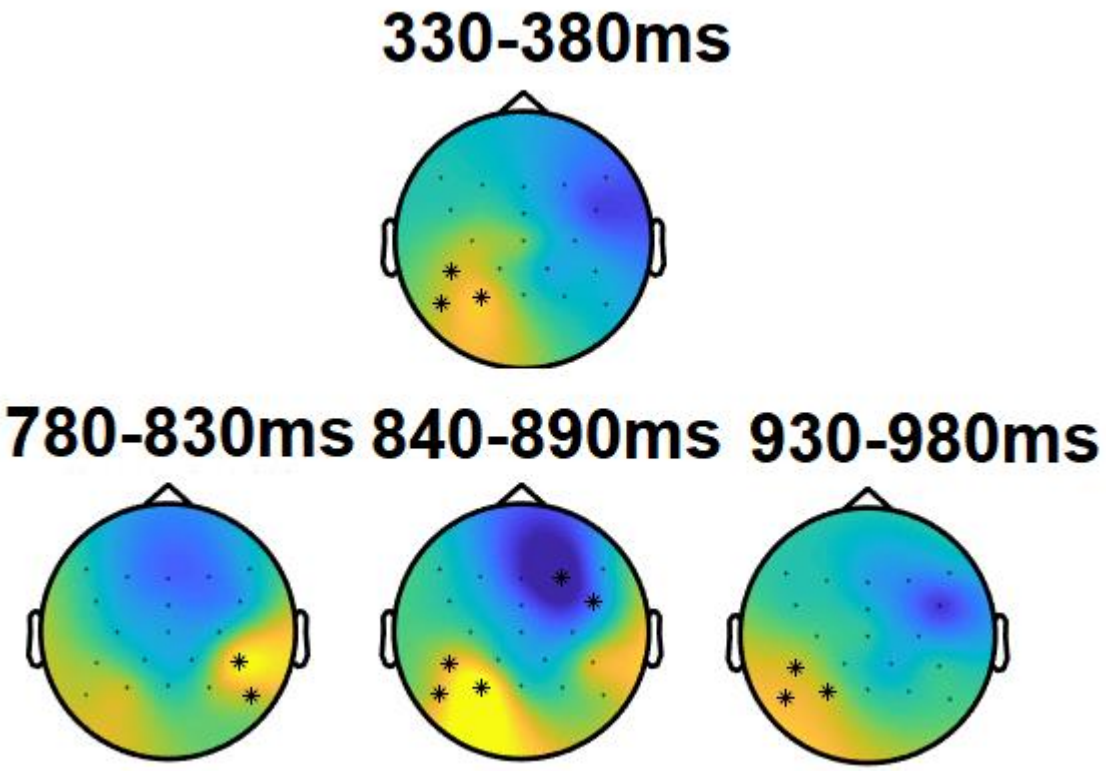

Figure 4.9 Intervals in which there is a significant ERP response following Cluster MCC in the Pilot Cohort in the IPB-0 condition.
Electrodes with a significant response are highlighted with asterisks. A PEP cluster occurs 3330-380ms and 780-980ms.

The peaks with Bonferroni significance are shown in Figure 4.10.

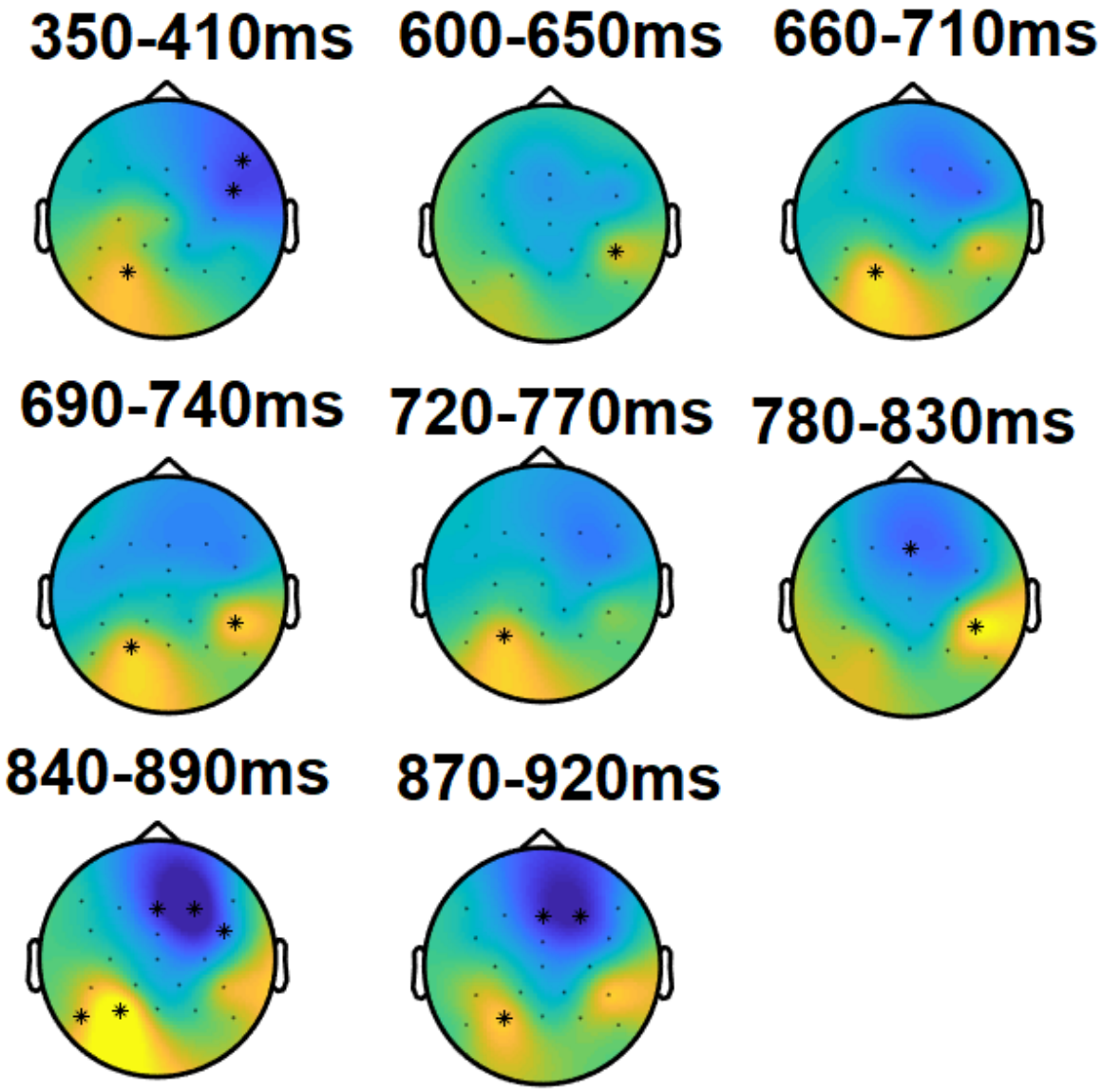

Figure 4.10 Intervals in which there is a significant ERP response following Bonferroni MCC in the Pilot Cohort in the IPB-0 condition.
Electrodes with a significant response are highlighted with asterisks. A PEP cluster occurs 350-410ms and 600-920ms.

The ERP of this component as it appears at electrode P7 is shown in Figure 4.11.

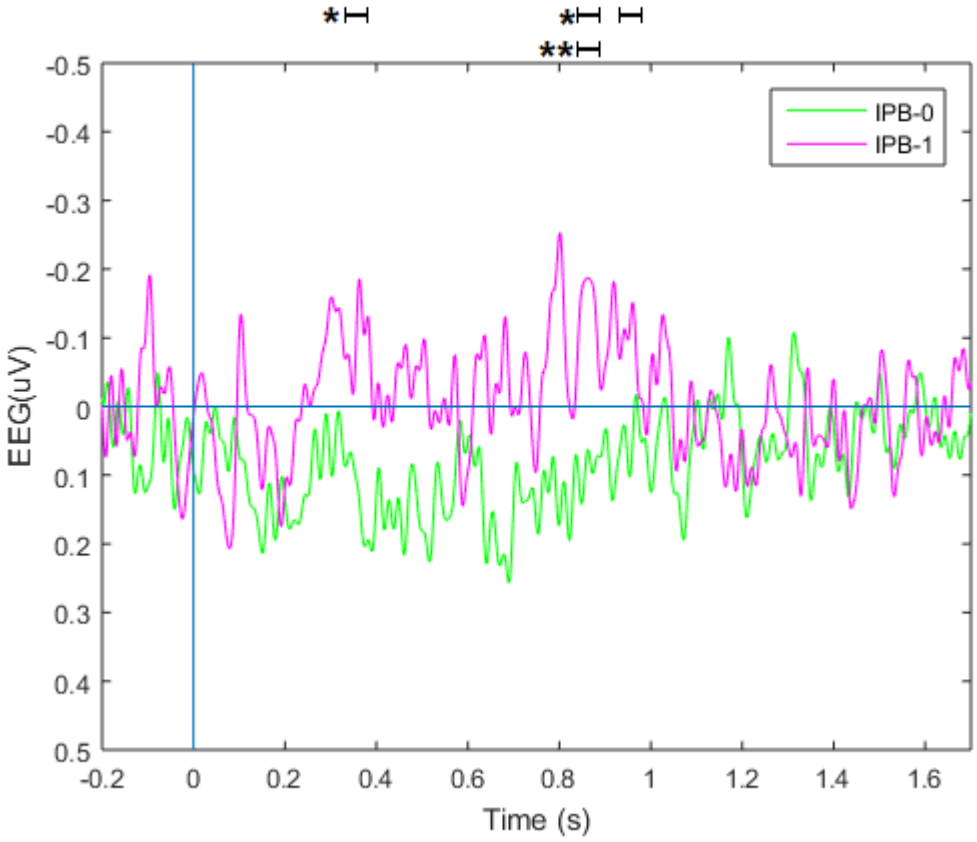

Figure 4.11 ERP of the PEP at P7 with the interval of significance with MCC highlighted.
The IPB-0 condition is shown in green and the IPB-1 condition is shown in purple. Highlighted are areas of significant difference. Single asterisks indicate areas with cluster MCC. Double asterisks indicate areas of Bonferroni MCC. The two intervals of the PEP can be seen 330-380ms and 690-920ms

Figure 4.12 shows the frequency decomposition of this component at P7.

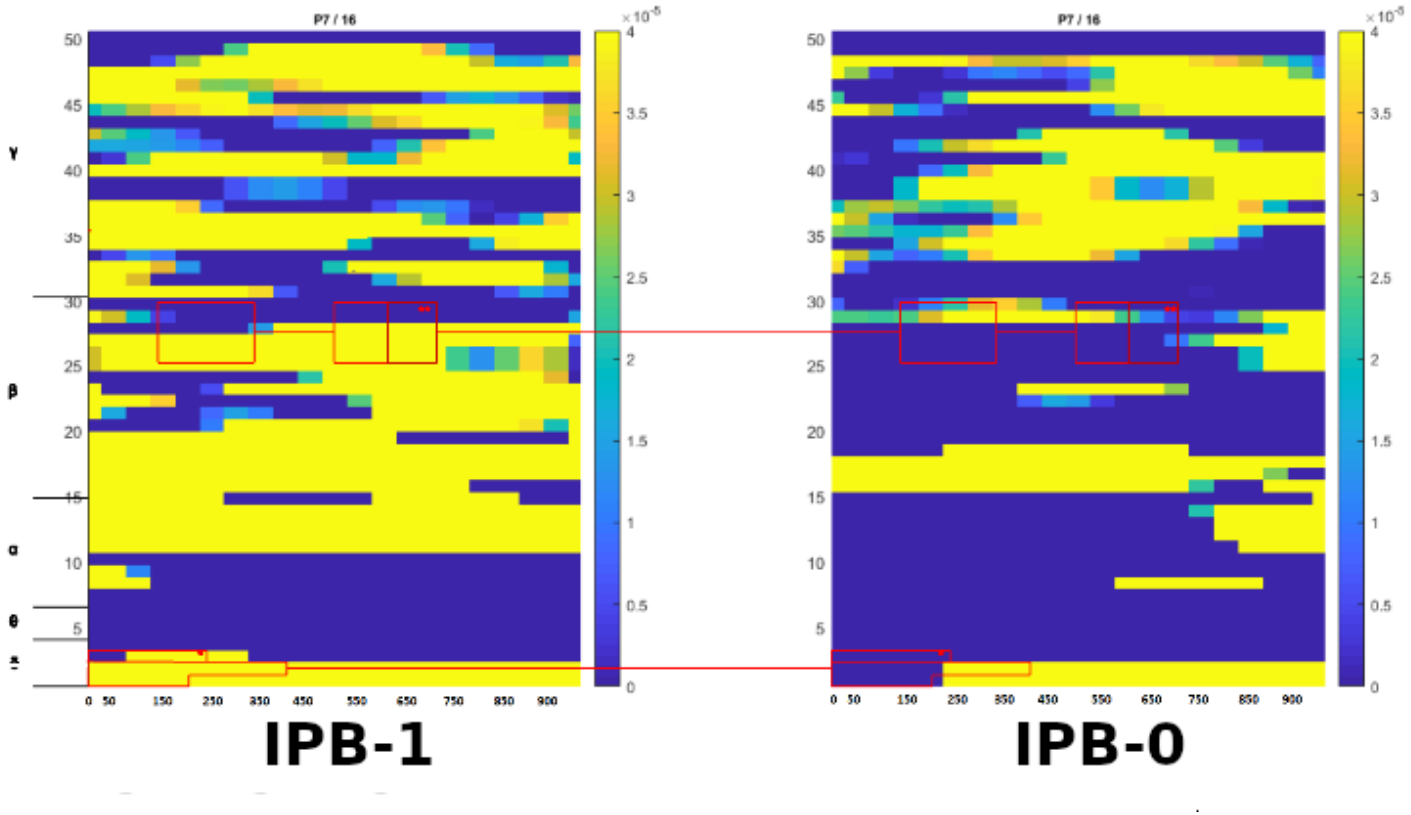

Figure 4.12 Changes in evoked power at P7 in the pilot cohort in the IPB-0 condition.
The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-0 condition. Highlighted are significant differences in the two conditions. The double asterisk indicates areas of Bonferroni significance. The single asterisk indicates areas of cluster significance. There is a drop in upper-beta power 25-30Hz.

Clustering and Bonferroni correction both return strong evidence of a RAN and PEP-like component in the IPB-0 condition. The Bonferroni response is unusually long-lasting which may be due to the low number of participants meaning localised changes have a more pronounced effect on the data. The RAN and PEP occur with drops in beta and gamma power. The oscillatory content of the RAN and PEP have not been reported in literature so this aptness of this frequency response could not be verified.

4.1.3 Pilot Summary

Clustering and Bonferroni correction both return strong evidence of a RAN and PEP-like component in the IPB-0 condition. These ERPs occur with drops in beta and gamma power. The oscillatory content of the RAN and PEP have not been reported in literature so this aptness of this frequency response could not be verified.

Clustering and Bonferroni correction both return strong evidence of a P3a. The other attentional components are absent. The P3a occurs with increases in alpha power. There are no significant frontal delta activations or parietal alpha suppression. These and the other attentional components may only be visible in larger groups.

The presence of a RAN and P3a were taken as sufficient enough evidence to begin testing in larger groups.

4.1.4 IPB-2 HS Cohort

The HS cohort built on the preliminary work of the Pilot but recruiting a larger cohort of persons aged 59 and older. The IPB-2 condition aimed to elicit an N100, P3a, RON and delta as markers for successive stages in the processing of incongruent linguistic prosody in this cohort. In addition, the IPB-2 condition was used to examine if the switch in attention prompted by the double prosodic boundary in the IPB-2 condition could elicit an SP; a component commonly used as a marker for task-switching. Each component is examined in turn in both the temporal and frequency domains.

4.1.4.1 N100

The current section shows the results of the analyses indicating the presence of an N100 component. A t(54) 10k MC simulation comparing IPB-1 with IPB-2 at 20 electrodes was carried out at 55 time intervals. This section shows the results within the -50-200ms interval. Shown first are results with Cluster MCC followed by the results with Bonferroni MCC. The ERP is then shown with significant intervals highlighted. Finally, the interaction of sex is shown. There was no significant evoked frequency response.

Figure 4.13 shows all significant results following clustering at a threshold of α=0.021 within the time interval in which the N100 was expected to occur.

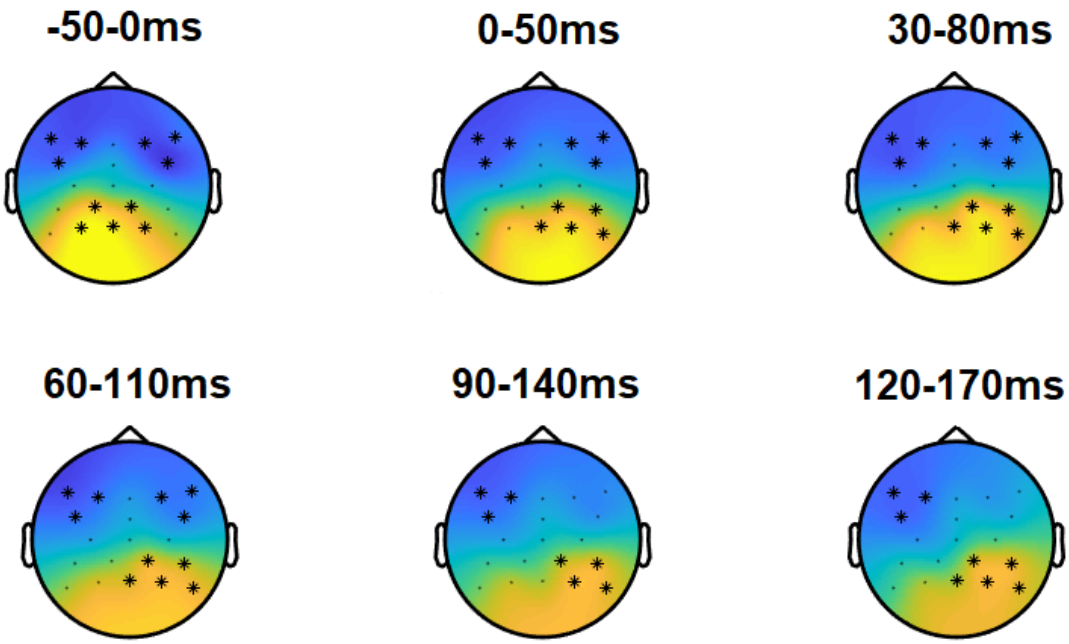

Figure 4.13 Intervals in which there is a significant ERP response in the N100 time-window following cluster MCC in the HS cohort in the IPB-2 condition.
Electrodes with significant effects are highlighted with asterisks. There are 6 overlapping 50ms intervals ranging from -50-170ms. Following 170ms there is no significant effect prior to the occurrence of the P3a at 270ms. From prior to the onset of the final word (word onset is 0ms) until 110ms there is a bilateral anterior negative component. From 90-170ms there is left anterior negative component. There is a central parietal positive component -50-170ms.

Figure 4.14 shows all the significant results within the N100 time period following Bonferroni MCC, all significant results shown are p<0.00105.

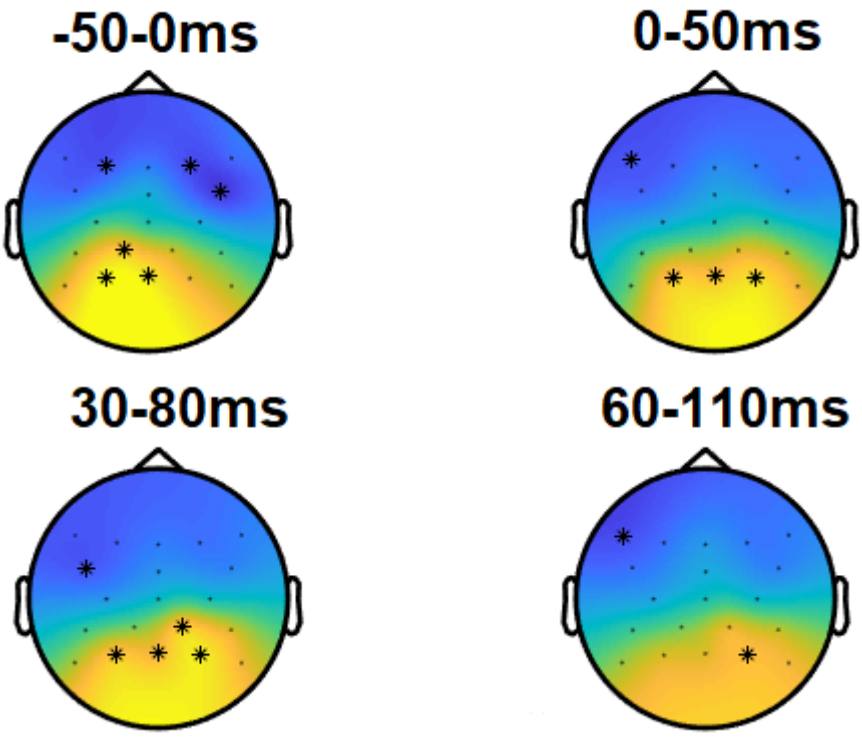

Figure 4.14 Intervals in which there is a significant ERP response on the N100 time-window following Bonferroni MCC in the HS cohort in the IPB-2 condition.
Electrodes with significant effects are highlighted with asterisks. There are 4 overlapping 50ms intervals ranging from -50-110ms. Following 110ms there are no significant effects prior to the occurrence of the P3a at 240ms. There are negative bilateral peaks in each of the four intervals. There are central parietal positive peaks -50-110ms.

Analysis within the N100 interval identified a component that occurs prior to the onset of the final word in the -50-0ms interval. Anything occurring prior to 0ms has a pre-stimulus origin so cannot be an N100. There are bilateral frontal negative components occurring 0-170ms. This is within the location and time-period at which an N100 was expected to occur.

In addition to the attentional components there is a parietal positive component -50-170ms present with both forms of MCC. This resembles a closure positive shift (CPS) in response to the IPB on the penultimate word.

Figures 4.15 shows the ERPs at F7. This shows the frontal negative component at the location at which it is most salient.

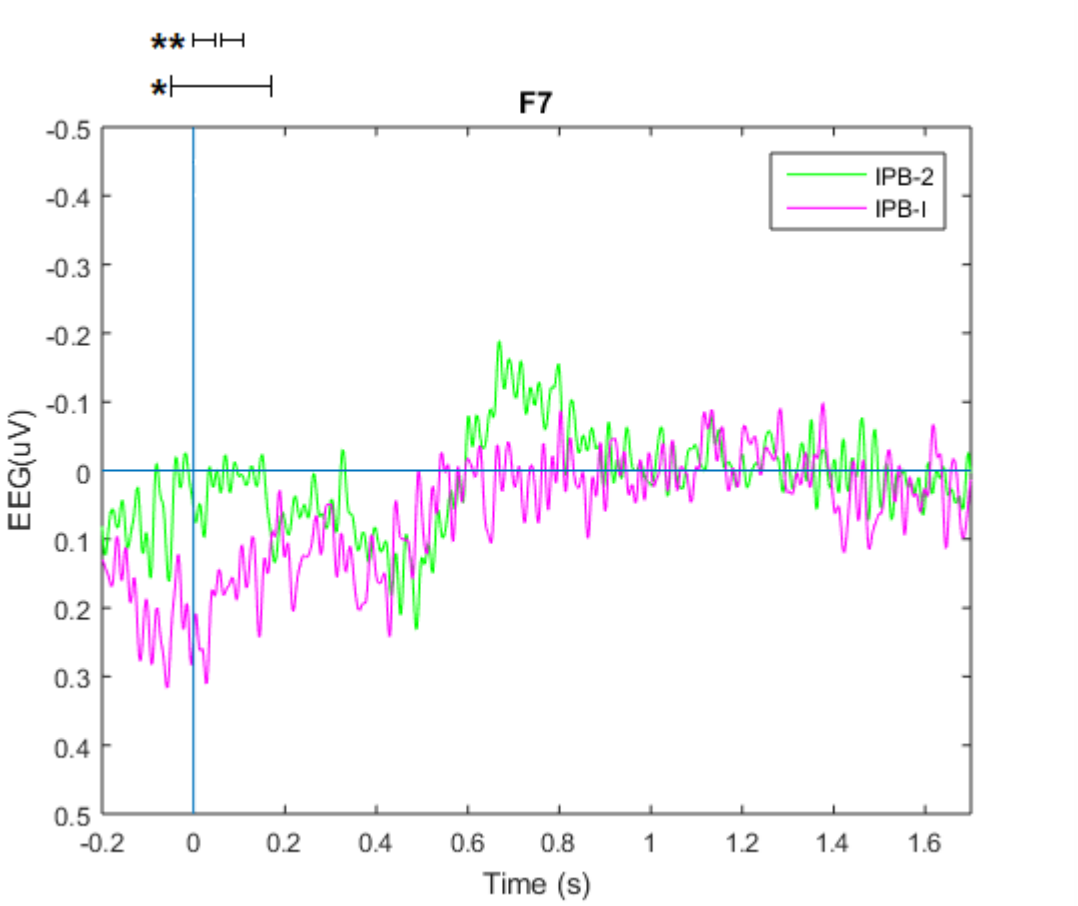

Figure 4.15 ERP plot at the F7 electrode in IPB-2 condition in the HS cohort.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The significant intervals within the -50-170ms interval are highlighted. A single asterisk indicates intervals that are significant with cluster MCC and a double asterisk highlights the intervals with Bonferroni MCC. The pre-stimulus component is visible in the negative interval. The Bonferroni significances at 0-50ms and 60-110ms are highlighted.

Testing for interactions by sex found interaction within the N100 time window. **Figure 4.16** shows this interaction with cluster MCC.

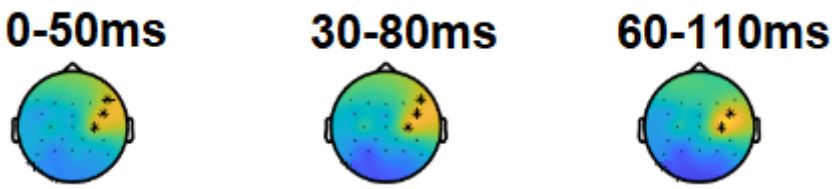

Figure 4.16 IPB-2 mxf interaction in the HS cohort in the interval of the N100.
How the male group differs from the female group is shown. Clustering is used in identifying interactions. Electrodes at which a significant effect occurs are highlighted using asterisks. A significant red area is an area where the male group is significantly more positive than the female group. There is an interaction by sex within the N100 time period. The male group has a significantly more positive effect in right anteriorly from 0-110ms.

The male group showed a similar effect in the left anterior but differed significantly from the female group right-anteriorly. The N100 effect may be weaker right-anteriorly for males in the HS cohort.

There was no significant anterior evoked frequency component within the N100 time-window. There is therefore a salient negative component in the N100 time-window. This overlaps with a negative component occurring prior to the onset of the final word.

4.1.4.2 P3a

The current section shows the results of the analyses indicating the presence of an P3a component. A t(54) 10k MC simulation comparing IPB-1 with IPB-2 at 20 electrodes was carried out at 55 time intervals. This section shows the results within the 240-410ms interval. Shown first are results with Cluster MCC followed by the results with Bonferroni MCC. The ERP is then shown with significant intervals highlighted. The corresponding evoked delta response is shown with Cluster and Bonferroni MCC. There was no significant interaction with sex in the P3a time window.

Figure 4.17 shows the results in the P3a time-window with Cluster MCC and **Figure 4.10** shows the result with Bonferroni MCC.

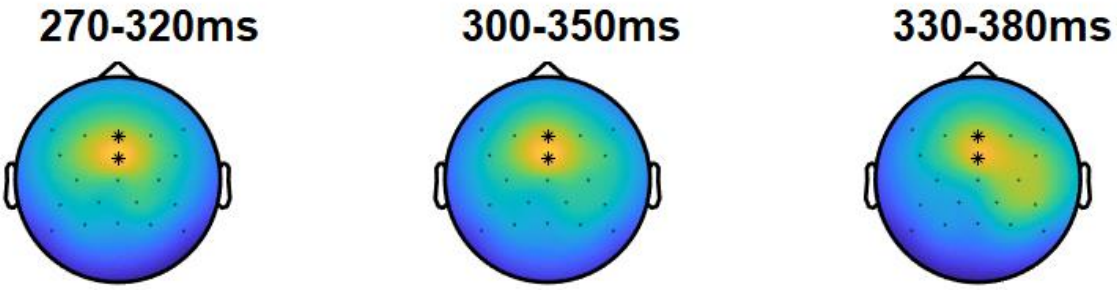

Figure 4.17 Intervals in which there is a significant ERP response in the P3a time-window following cluster MCC in the HS cohort.
Electrodes with significant effects are highlighted with asterisks. There are 3 overlapping 50ms intervals ranging from 270-380ms. Following 380ms there is no significant effect prior to the occurrence of the RON and SP at 630ms. There is a positive component present at Fz and FCz in all three time-windows. This frontal and central positive is characteristic of a P3a.

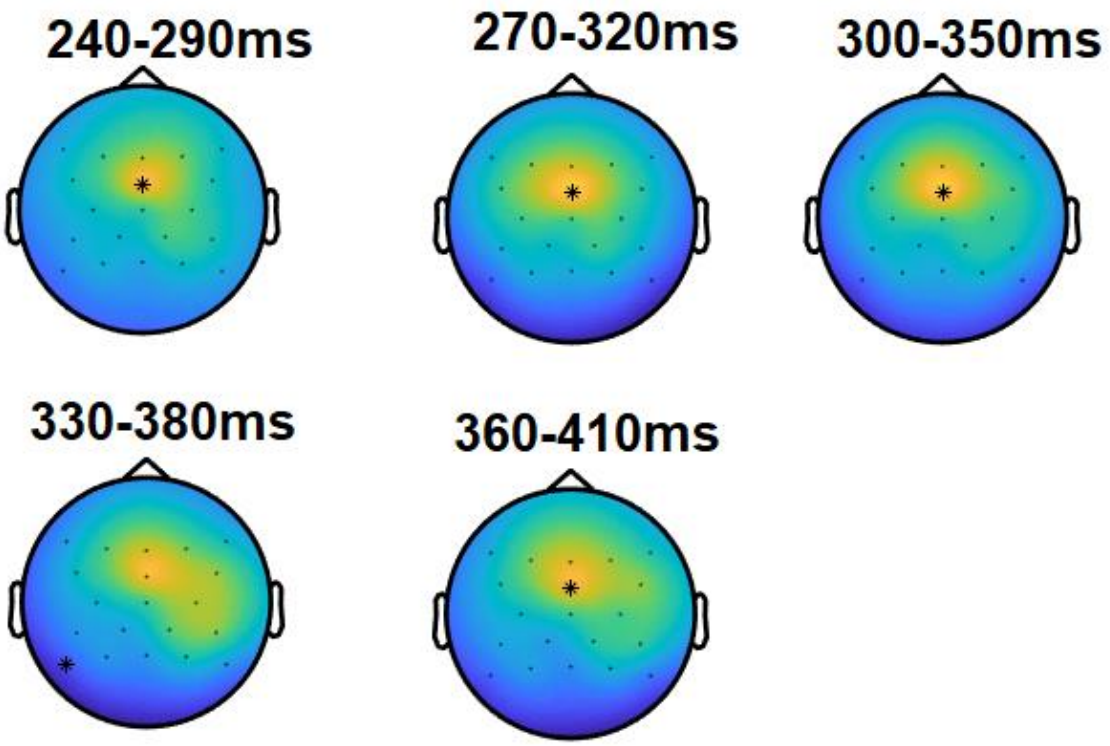

Figure 4.18 Intervals in which there is a significant ERP response in the P3a time-window following Bonferroni MCC in the HS cohort.
Electrodes with significant effects are highlighted with asterisks. There are 5 overlapping 50ms intervals ranging from 270-410ms. There is a positive component 240-350ms and 360-410ms. This is indicative of a salient and long-lasting P3a response.

The shape of the P3a response at FCz is shown **Figure 4.19**

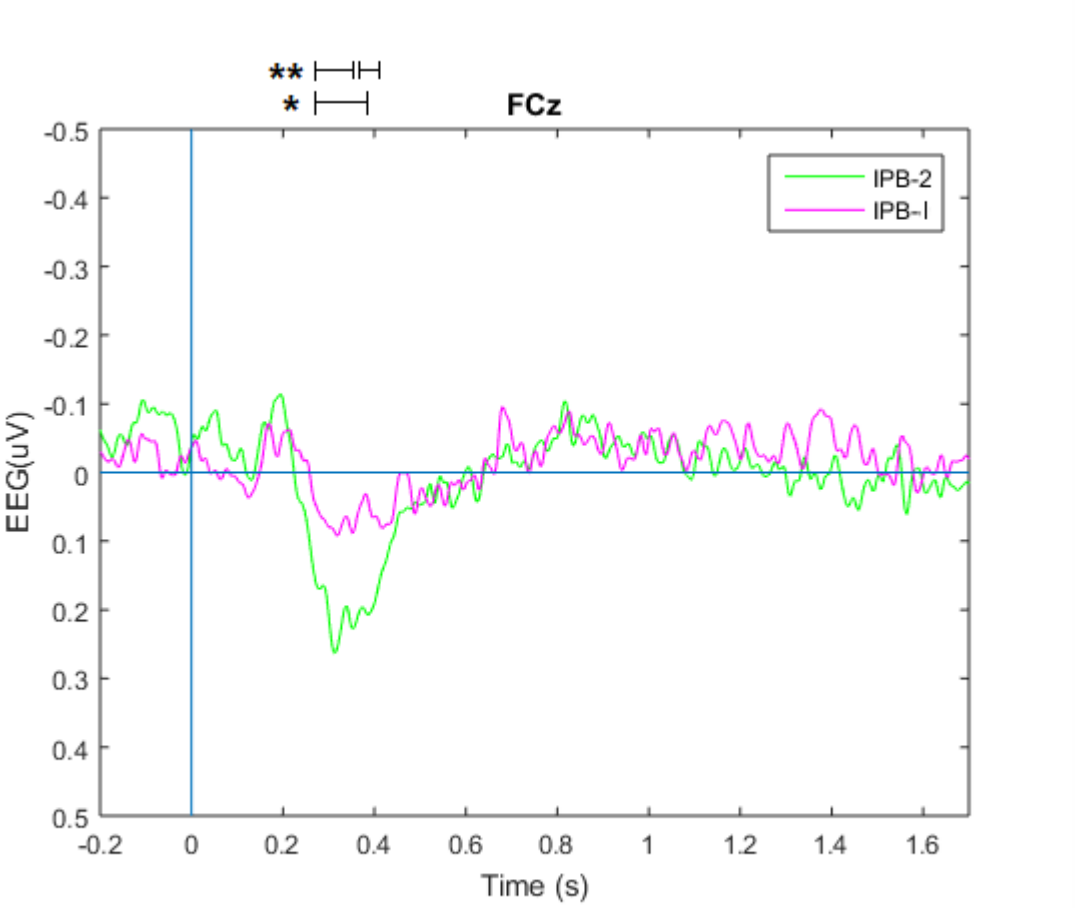

Figure 4.19 ERP plot at the FCz electrode of the HS cohort in the IPB-2 condition.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The significant intervals within the 240-410ms interval are highlighted. A single asterisk indicates intervals that are significant with cluster MCC and a double asterisk highlights the intervals with Bonferroni MCC. A prominent P3a is visible within the 240-410ms interval.

Analysis within the P3a interval found a widespread evoked delta response occurring prior to and following the P3a. Figure 4.20 shows the topography of this response and the time-windows in which it occurred.

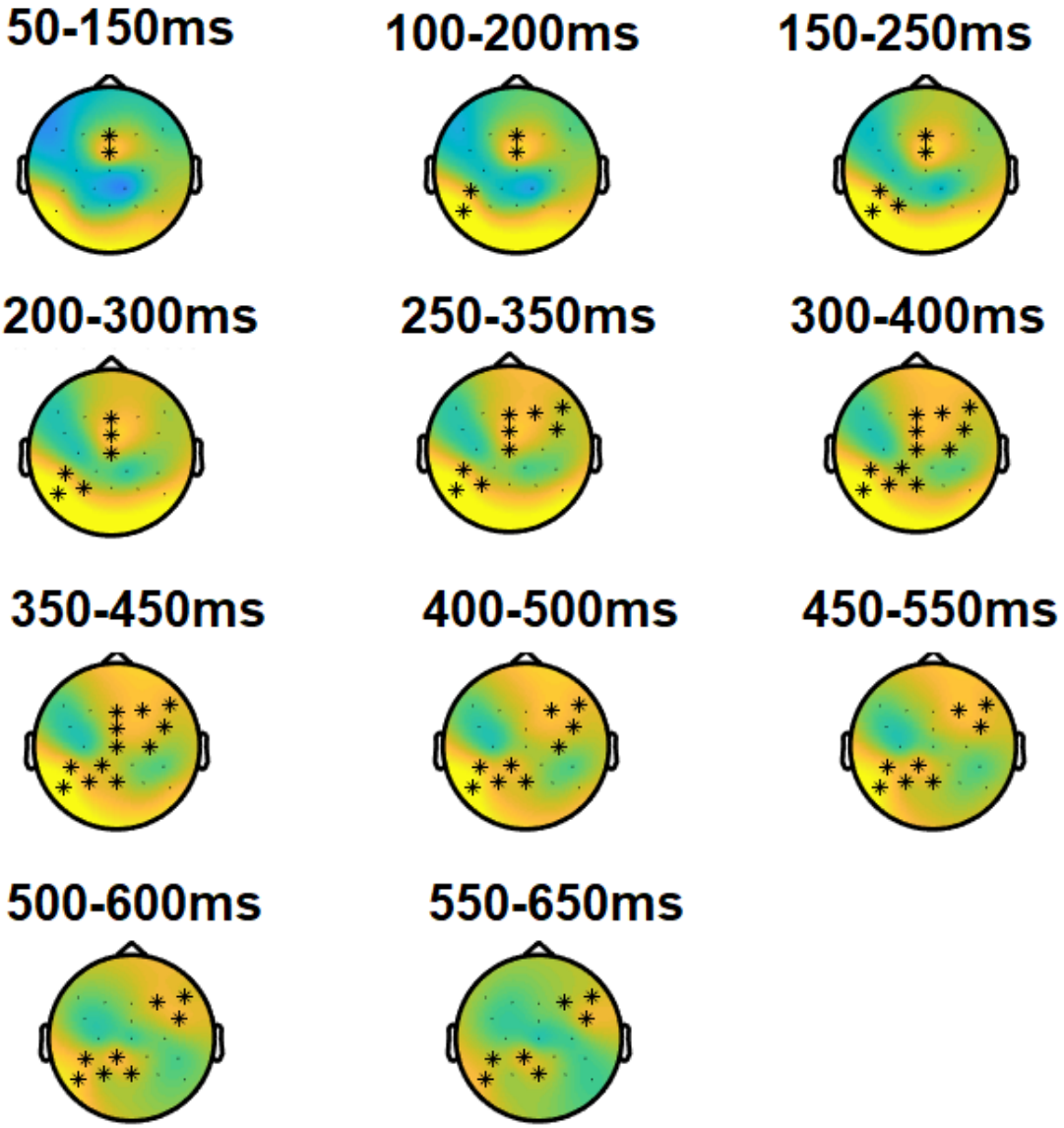

Figure 4.20 Significant changes in 2-3Hz frequency band (delta power) in the IPB-2 condition in the HS cohort with Cluster MCC.
Significant evoked delta occurs 50-650ms. This increase begins 50ms post-final word onset at Fz and FCz; the two electrodes with the most prominent P3a. At 100ms P7 and CP5 join. These electrodes overlay the left-angular gyrus. At 250ms the right-anterior is recruited.

Figure 4.21 shows the same delta response with Bonferroni MCC.

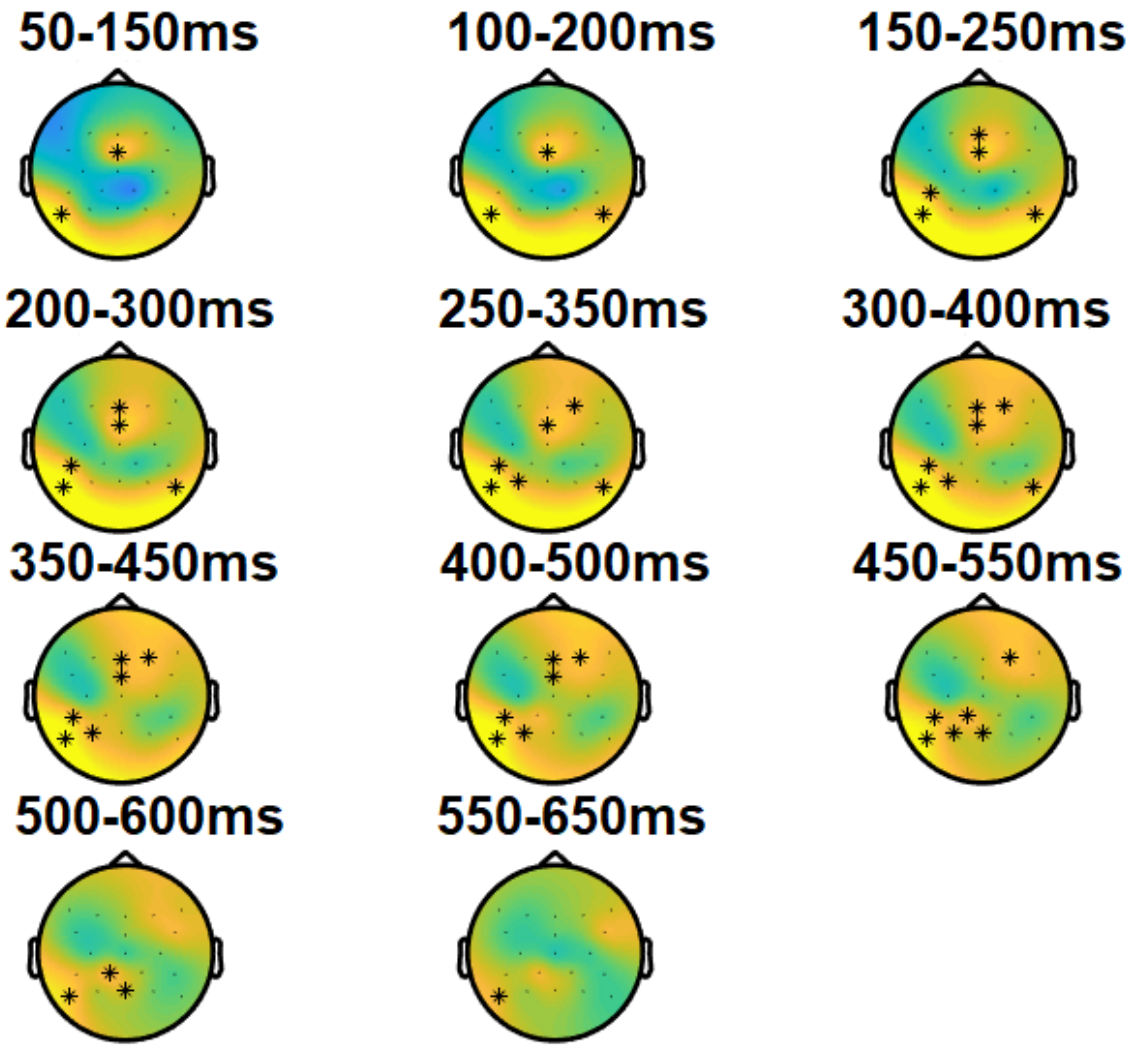

Figure 4.21 Significant changes in 2-3Hz frequency band (delta power) in the IPB-2 condition with Bonferroni MCC. Significant evoked delta occurs 50-650ms. This increase begins 50ms post-final word onset at FCz; this is the electrode at which the P3a is most salient. In addition to the electrodes associated with the P3a, there are significant increases in delta power parietally throughout the 50-650ms interval shown.

The topography of the evoked delta power initially overlays the P3a. The remainder of the evoked delta does not correspond with any visible ERP components. This evoked delta occurs right-anteriorly and left-parietally. The former region is associated with the decoding of prosodic aspects of speech and the latter with the processing of lexical access. The time-frequency breakdown at electrode Fz is shown in **Figure 4.22**. The extent of the increase in delta power can be seen. Where this increase in delta power is significant with cluster MCC is highlighted.

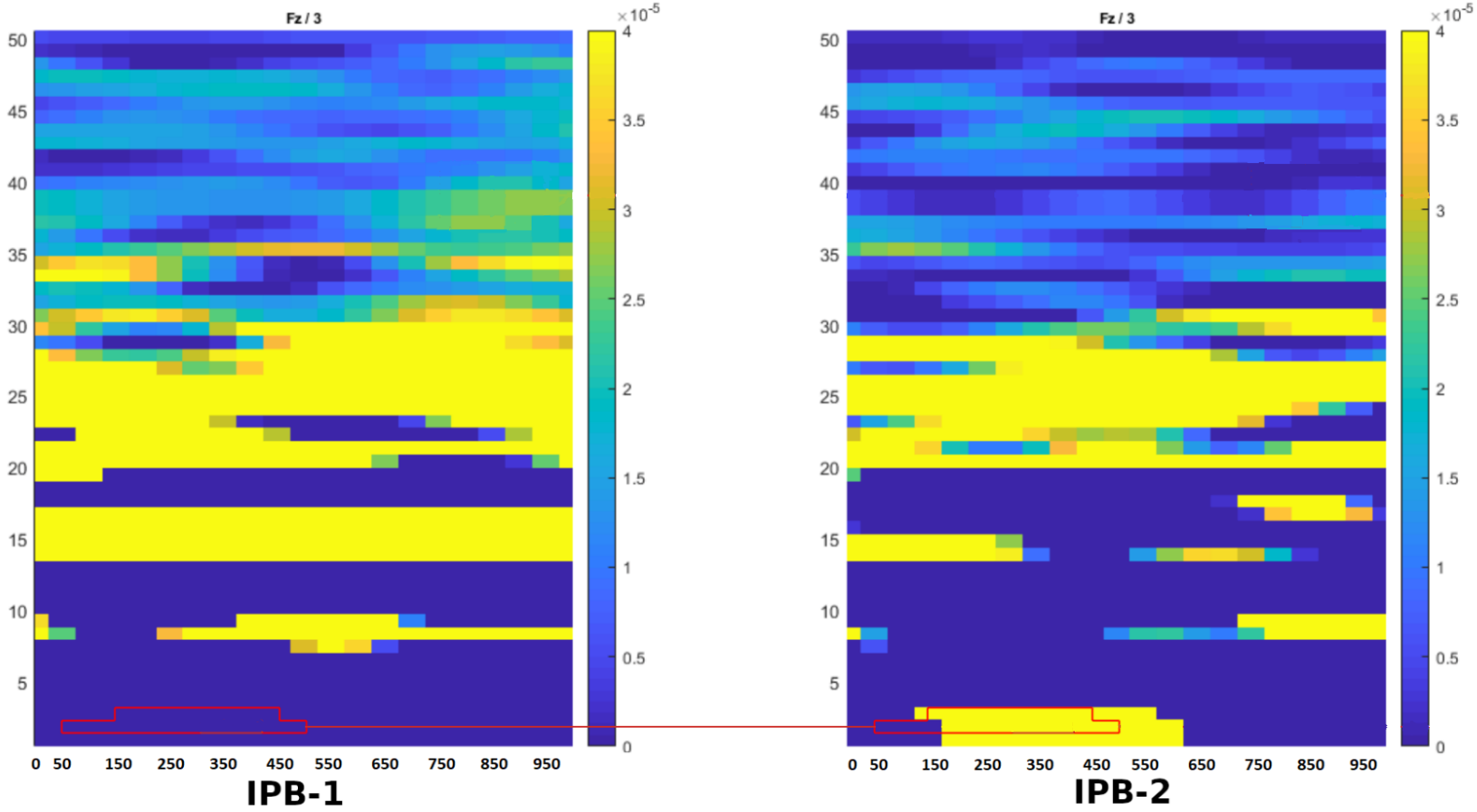

Figure 4.22 Frequency decomposition at Fz in the IPB-2 condition in the HS cohort.

The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-2 condition. t=0 is the onset of the final word. Highlighted are significant differences in the two conditions with Cluster MCC. There is significant evoked delta in the 2-4Hz range 150-450ms.

How this delta power corresponds to the P3a response is shown in **Figure 4.23.**

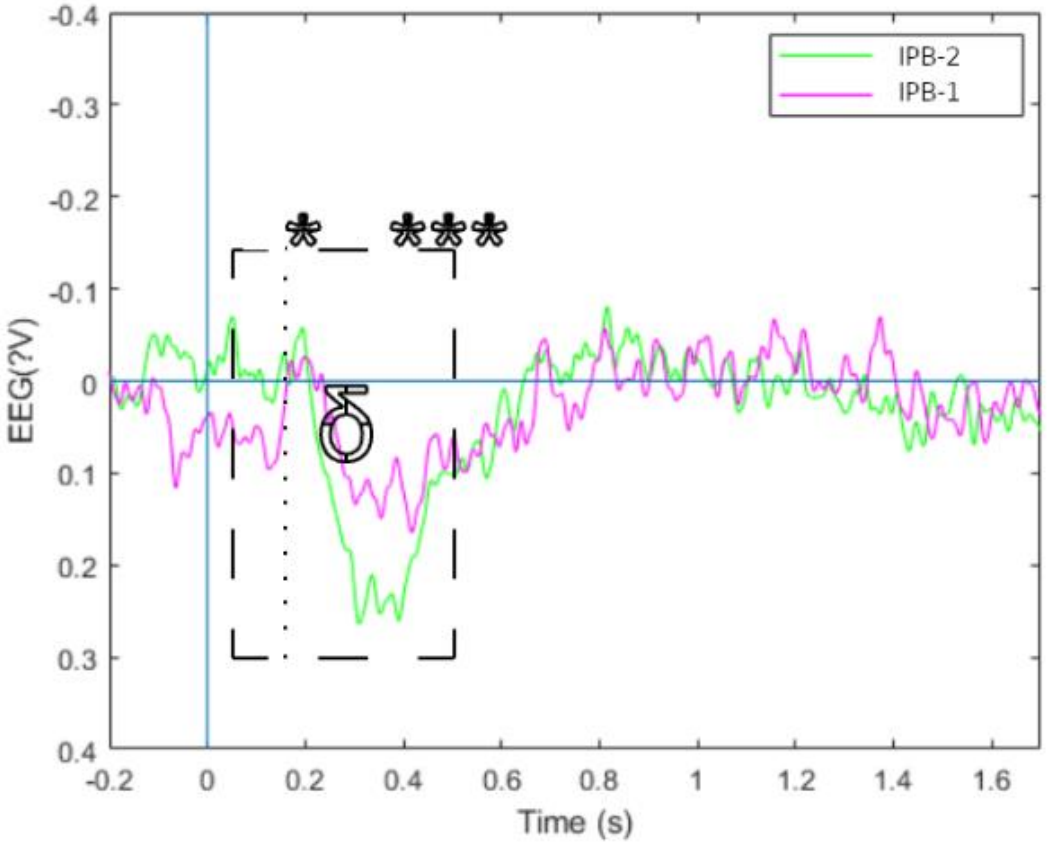

Figure 4.23 ERP of the P3a at Fz with intervals of significant evoked power in the 2-3Hz range highlighted. The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The single asterisk indicates time periods of significance with cluster MCC (50-150ms). The triple asterisk indicates overlapping areas of both cluster and Bonferroni significance (100-450ms). These changes in delta power are overlay the P3a.

There is a salient P3a response in the HS cohort in response to the IPB-2 condition. This is evidenced by the significant response found anteriorly and centrally in the 240-410ms time window. The P3a also overlaps with a significant increase in evoked delta power.

4.1.4.3 RON

The latter stage of the response the IPB-2 condition aimed to elicit is the RON. There was no effect in the RON interval significant enough to be present following Bonferroni MCC. Cluster MCC revealed a right-anterior waveform 630-680ms and left-anterior waveform 660-710ms. These are shown in **Figure 4.24**.

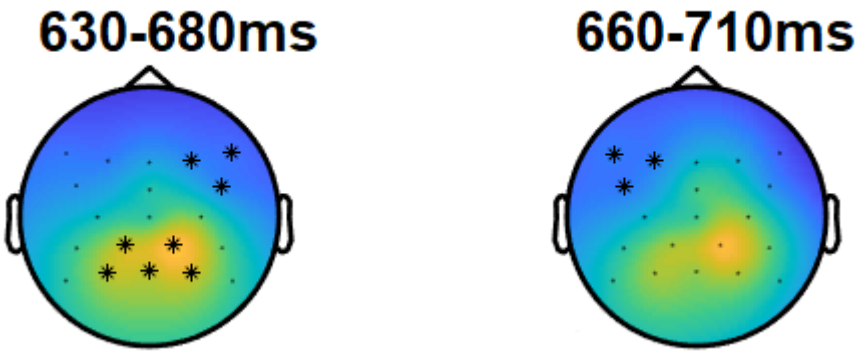

Figure 4.24 Intervals in which there is a significant ERP response following Cluster MCC in the RON interval in the HS cohort.
Electrodes with a significant response are highlighted with asterisks. 2 overlapping 50ms intervals ranging from 630-710ms are shown. There is a right-anterior negative component in the initial 630-680ms interval and a left-anterior negative in the later 660-710ms interval.

This waveform is shown as an ERP at electrodes F7 in **Figure 4.25**.

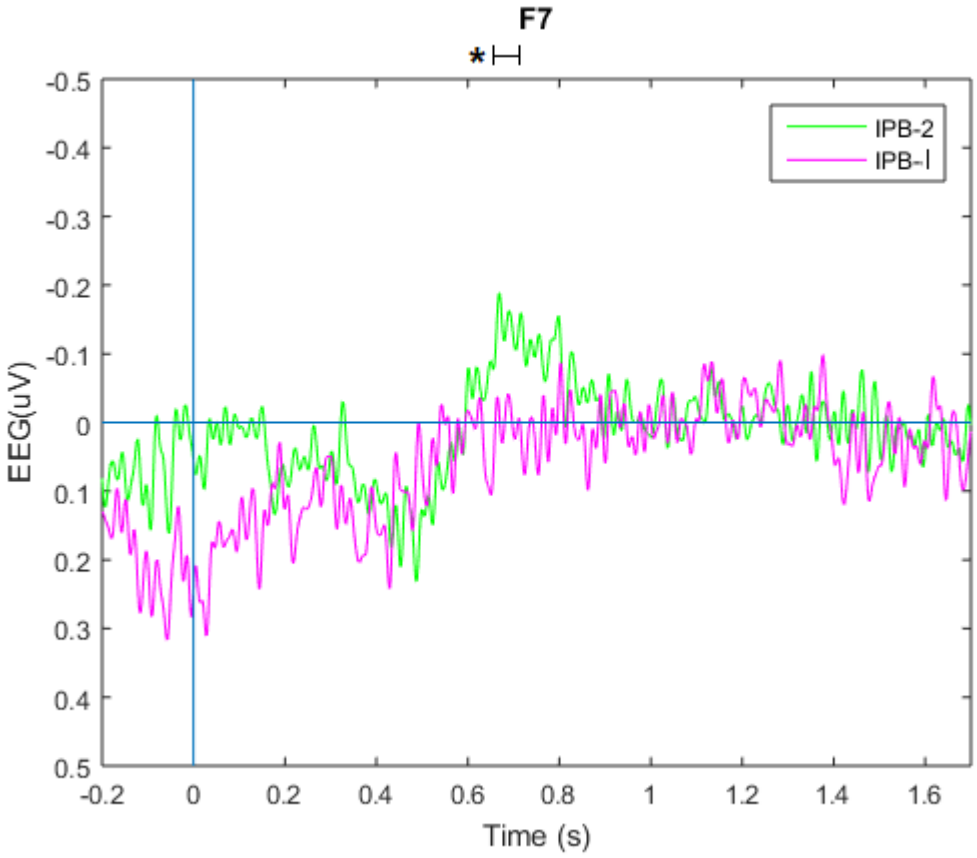

Figure 4.25 ERP of the RON at F7 with the interval of significance with MCC highlighted.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The single asterisk indicates the time period of significance with cluster MCC (660-710ms). The N100 is also visible.

4.1.4.4 SP

The shift-positive is visible 630-800ms with both Cluster MCC and Bonferroni MCC. These are shown in Figure 4.26 and Figure 4.27.

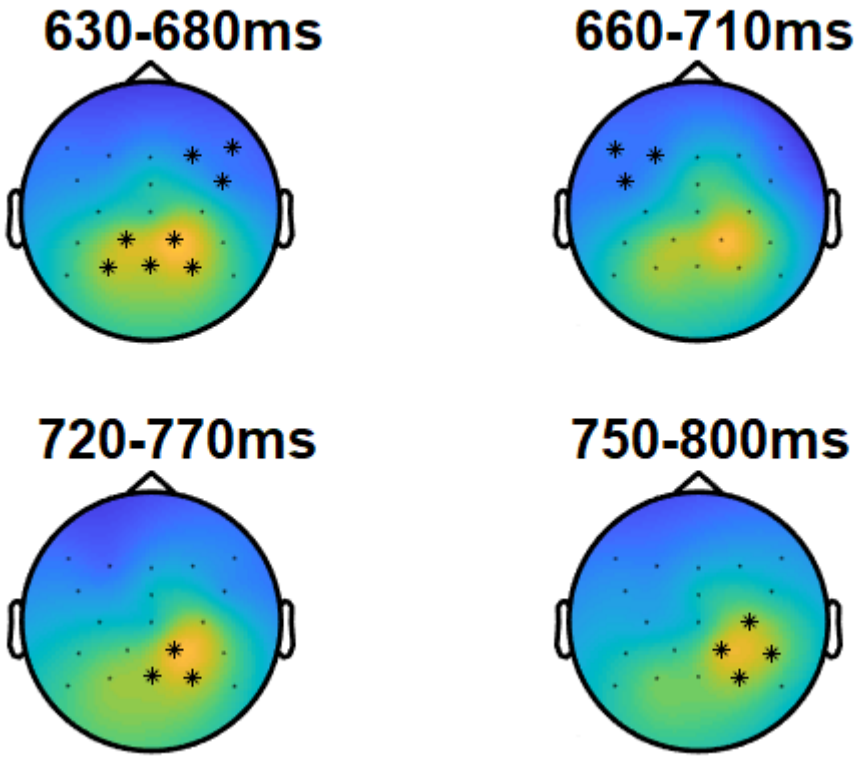

Figure 4.26 Intervals in which there is a significant ERP response following Cluster MCC.
Electrodes with a significant response are highlighted with asterisks. 4 overlapping 50ms intervals ranging from 630-800ms are shown. There is a centre-parietal positive component in the initial 630-680ms interval and in the later 720-800ms interval.

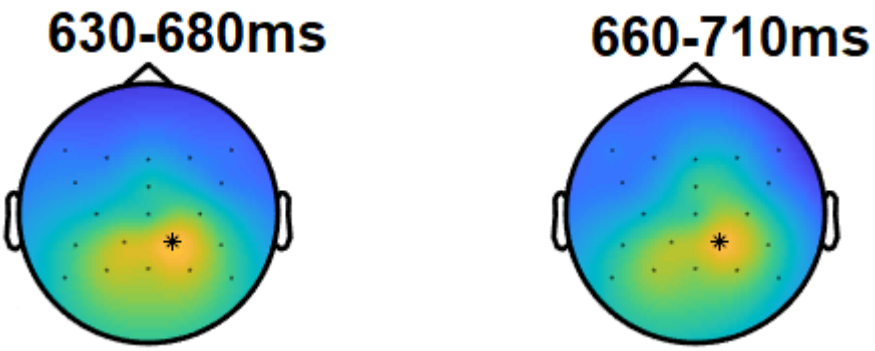

Figure 4.27 Intervals in which there is a significant ERP response following Bonferroni MCC.
Electrodes with significant effects are highlighted with asterisks. There are 2 overlapping 50ms intervals ranging from 630-710ms. The centre-parietal component peaks at electrode CP2 in this time window.

CP2, the electrode at which the SP is most salient is shown in **Figure 4.29**.

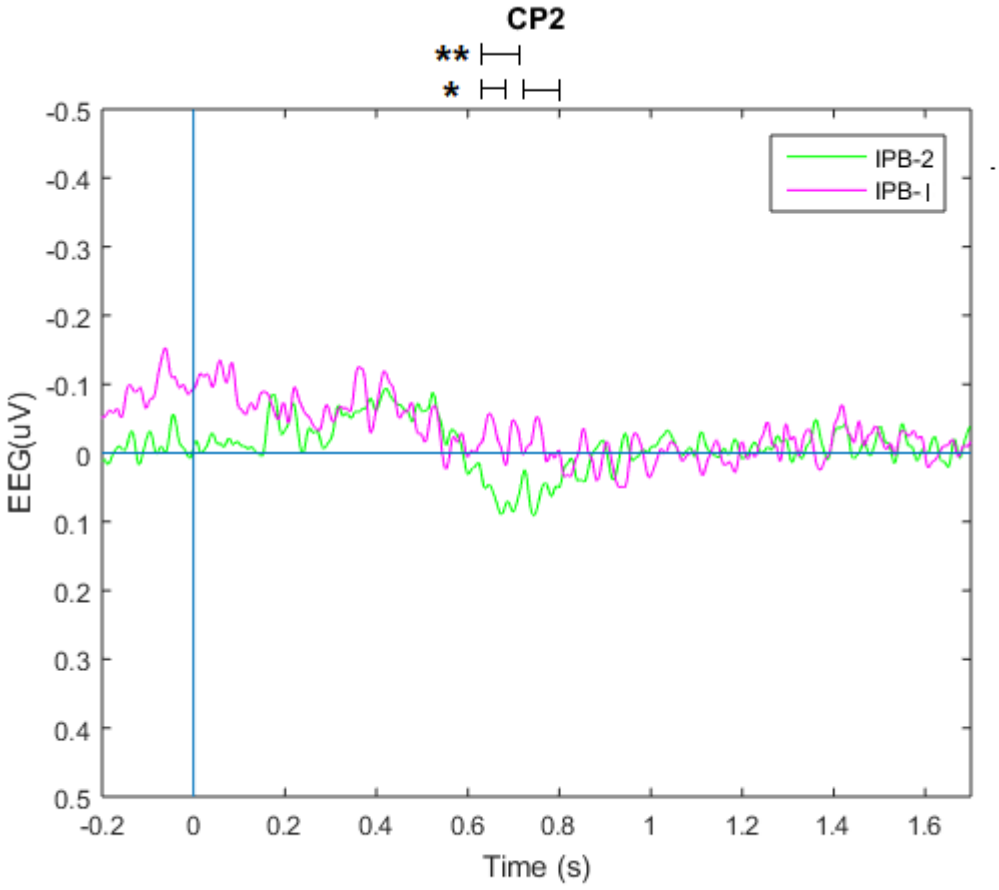

Figure 4.28 ERP plot at the CP2 electrode.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The significant intervals with MCC are highlighted. A single asterisk indicates intervals that are significant with cluster MCC (630-680ms & 720-800ms) and a double asterisk highlights the intervals with Bonferroni MCC (630-710m).

An interaction by sex was found in the SP time-window.

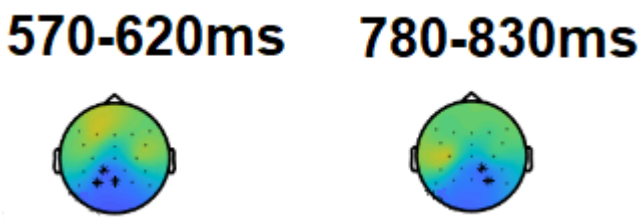

Figure 4.29 IPB-2 mxf interaction in the HS cohort in the interval of the SP.
How the male group differs from the female group is shown. Clustering is used in identifying interactions. Electrodes at which a significant effect occurs are highlighted using asterisks. A significant red area is an area where the male group is significantly more positive than the female group. The male group is significantly less positive in the peripheral time windows suggesting the SP in this group is less long-lasting than in the female group.

An evoked frequency response was found to overlap the SP in both the alpha and gamma frequency bands. The alpha response was apparent with both Cluster MCC and Bonferroni MCC. The gamma response was more weakly significant and only visible without MCC. The drop in alpha is shown in Figure 4.30 and Figure 4.31.

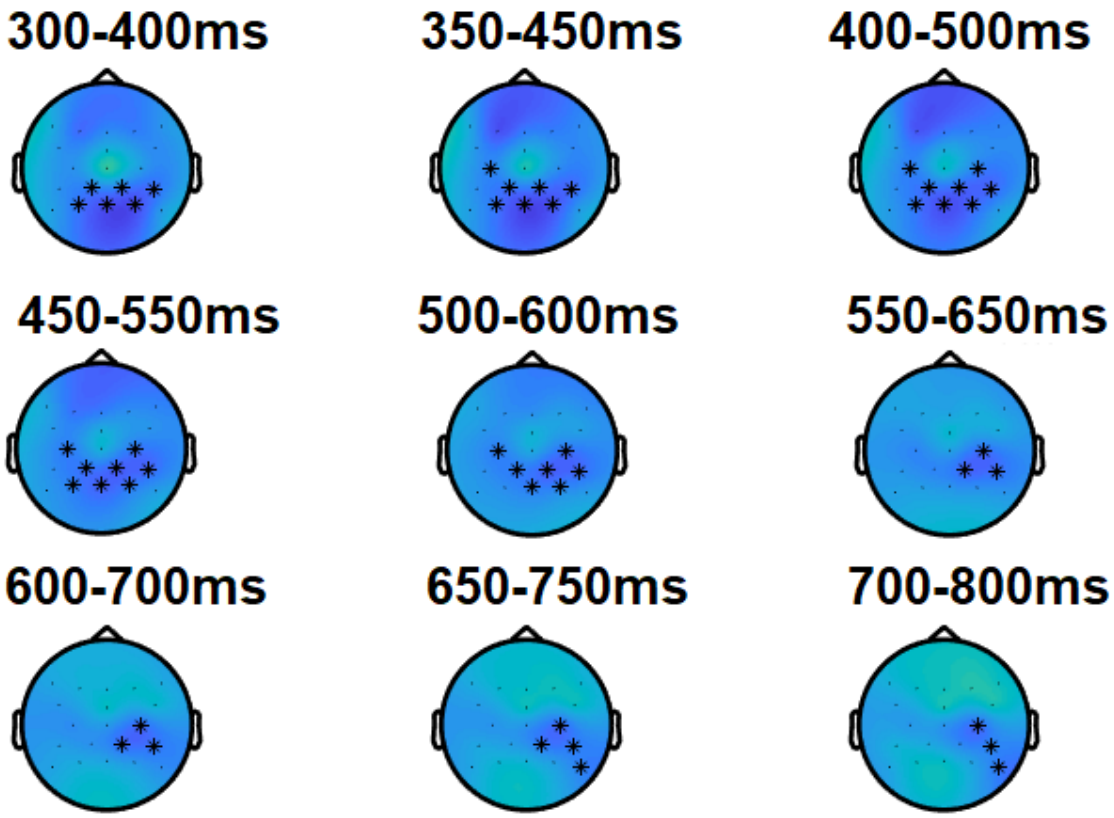

Figure 4.30 Significant changes in 9-14Hz frequency band (alpha power) in the IPB-2 condition with Cluster MCC.

Significant reductions in evoked alpha occur 300-800ms. This reduction begins 300ms post-final word onset centre-parietally; the region in which the SP was most salient.

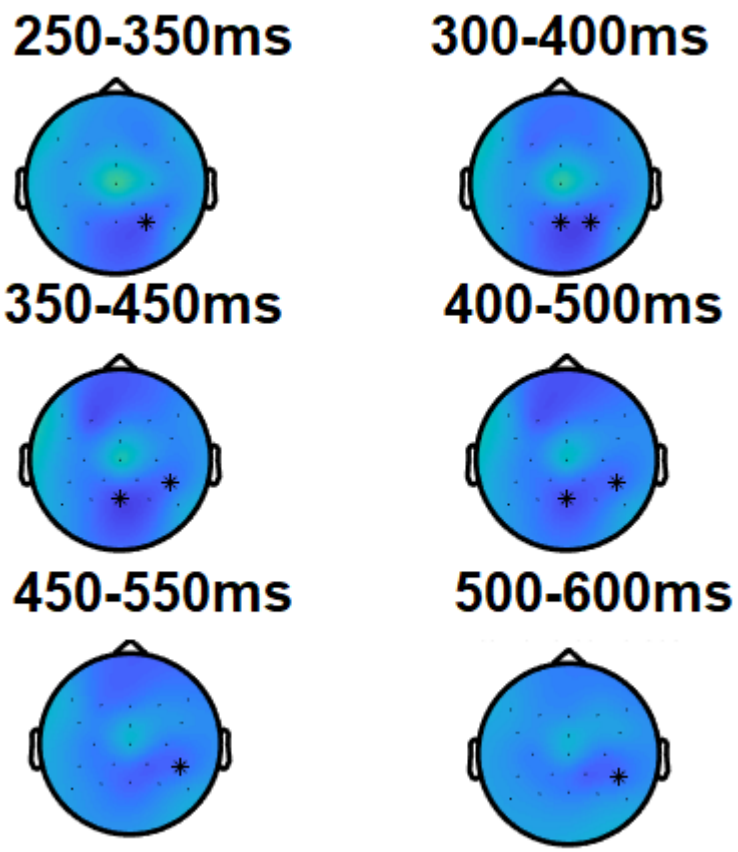

Figure 4.31 Significant changes in 9-14Hz frequency band (alpha power) in the IPB-2 condition with Bonferroni MCC.
Significant reductions in evoked alpha occur 250-600ms. Bonferroni peaks occur at three centre-parietal electrodes Pz,P4 and CP6.These are all electrodes at which the SP was significant with SP but at earlier intervals.

There is a drop in alpha in the central parietal region. This is the region in which the SP occurs. The drop in alpha however, begins prior to the onset of the SP. The alpha response begins as early as the 250-350ms time window, in comparison to the SP which begins latterly at 630-680ms.

The more weakly significant drop in gamma power occurs in the same interval as the SP, beginning at 650-750ms. This is shown in Figure 4.32.

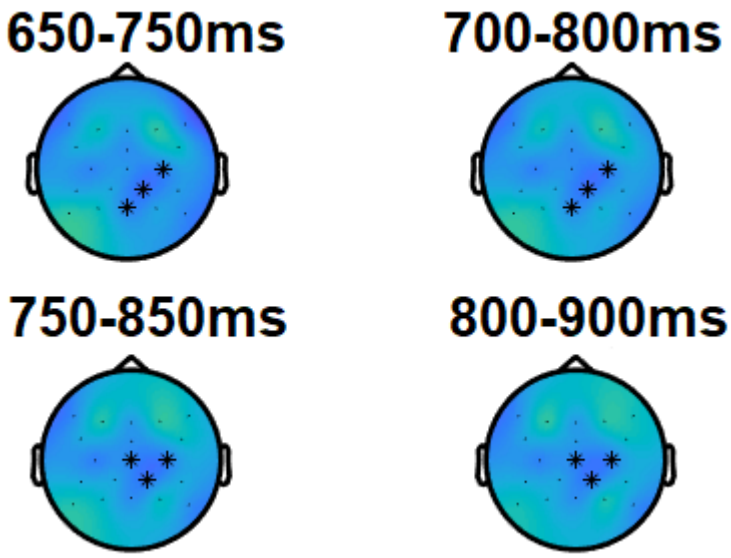

Figure 4.32 Significant changes in 33-38Hz frequency band (lower gamma power) in the IPB-2 condition without MCC.
There is a centre-parietal drop in gamma powewr 650-900ms.

Significant reductions in evoked gamma occur 650-900ms. None of these reductions occur with MCC. Reductions are centre-parietal and occur at electrodes and in time-periods at which the SP was most salient.

The full frequency breakdown as it occurs at CP2 is shown in Figure 4.33.

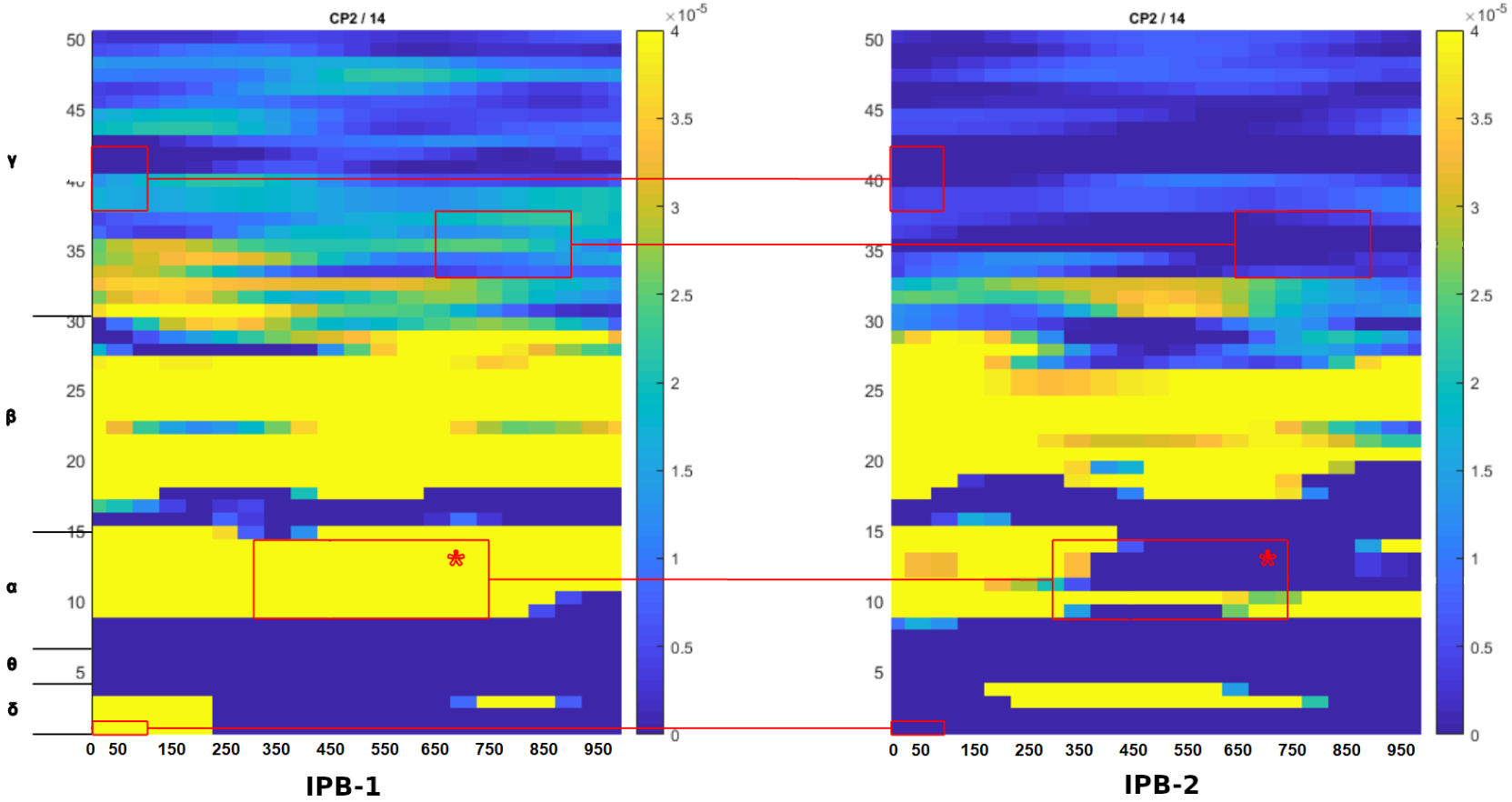

Figure 4.33 Frequency decomposition at CP2 in the IPB-2 condition in the HS cohort.
The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-2 condition. t=0 is the onset of the final word. Red boxes highlight significant differences in the two conditions. Red boxes with an asterisk show areas at which the differences are significant with cluster MCC. There is a salient reduction in alpha power 300-750ms. There is also a reduction in lower-gamma power 650-900ms.

How these changes in frequency compared with the component itself is shown in Figure 4.34 and Figure 4.35.

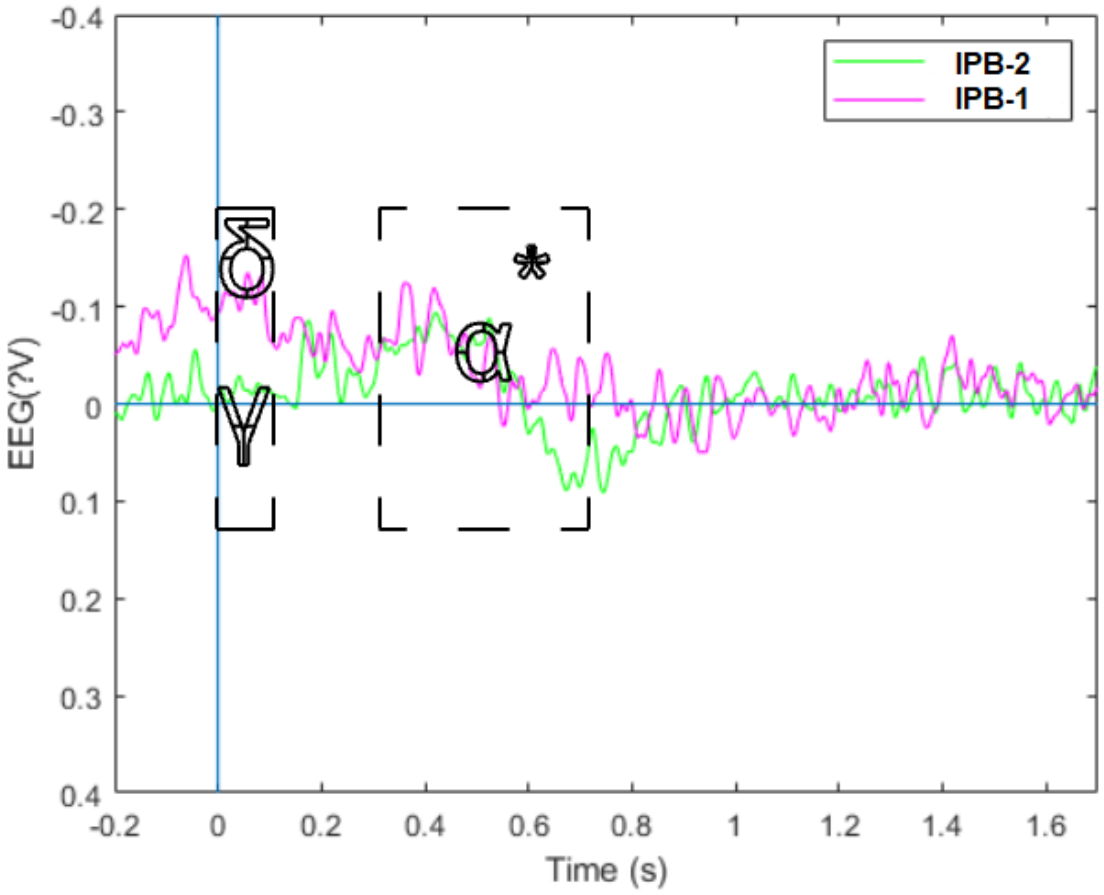

Figure 4.34 ERP of the SP at CP2 with intervals of significant reductions evoked alpha power with cluster MCC highlighted.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The drop in alpha power occurs prior to and overlays the initial phase of the SP. Also shown are early changes in evoked delta and gamma which overlay the early positive component.

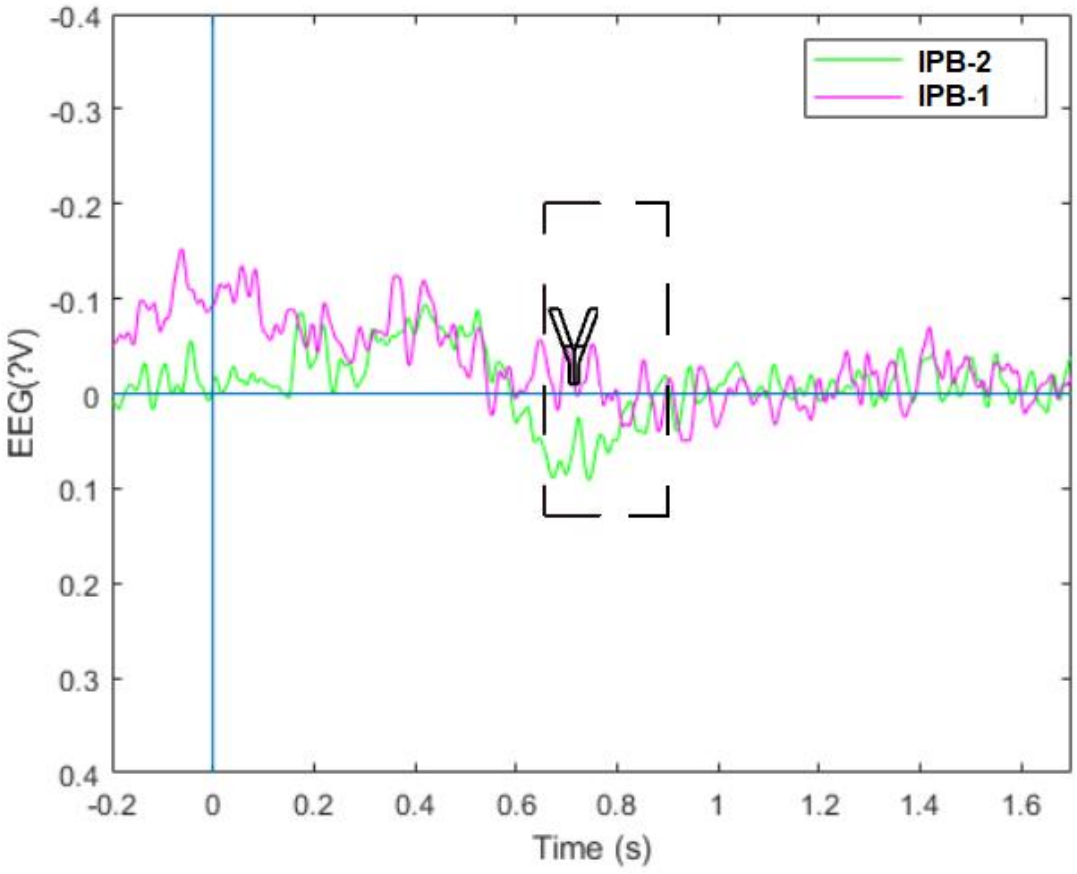

Figure 4.35 ERP of the SP at CP2 with intervals of significant reductions evoked lower gamma power with no MCC highlighted.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The drop in lower gamma power overlays the SP.

There is therefore a highly significant SP occurring 630-800ms. Partially overlapping this are significant drops in alpha power and weakly significant drops in gamma power.

4.1.4.5 N400

Ancillary to the principal findings of the current study is the occurrence of a possible N400. With cluster MCC, there is no apparent N400 in the IPB-2 condition in the HS cohort. With Bonferroni MCC, there is a highly salient negative peak at P7. This is the appropriate time-period for an N400 but too localised. Prior to MCC, the analysis indicates the presence of a significant negative at P8.

The result with Bonferroni MCC is shown in Figure 4.36. The strongly significant waveform at P7 is shown in Figure 4.37 and the weakly significant waveform is shown in Figure 4.38.

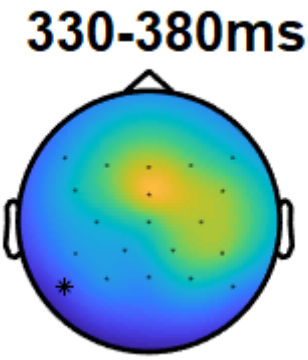

Figure 4.36 Interval in which there is a significant ERP response in the N400 time window following Bonferroni MCC.
Electrodes with significant effects are highlighted with asterisks. There is a 50ms interval in which there is a salient N400 response at P7.

The ERP at P7 is shown in Figure 4.37 with the area of Bonferroni significance highlighted.

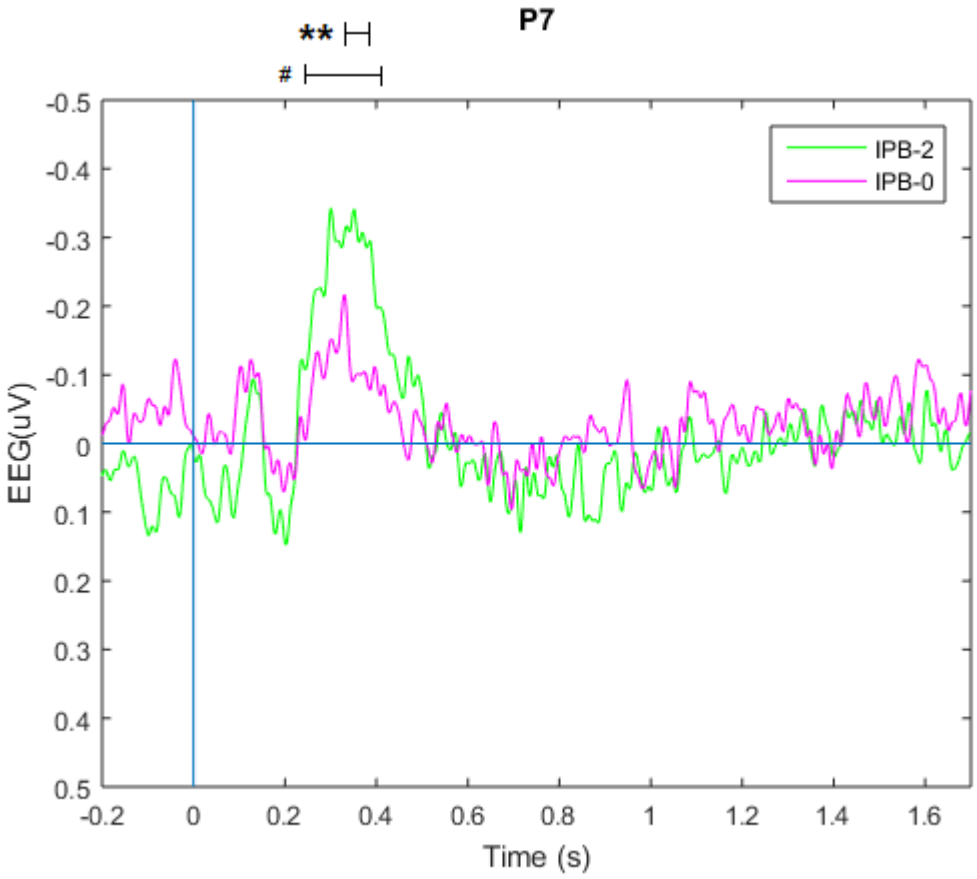

Figure 4.37 ERP plot at the P7 electrode in the IPB-2 condition.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The significant interval in which the significance with Bonferroni MCC occurs is highlighted with a double asterisk. Intervals in which there is a significant response without MCC are highlighted with a #. There is a salient negative component, the peak of which is captured with Bonferroni MCC.

The less powerfully significant negative at P8 is shown in Figure 4.38.

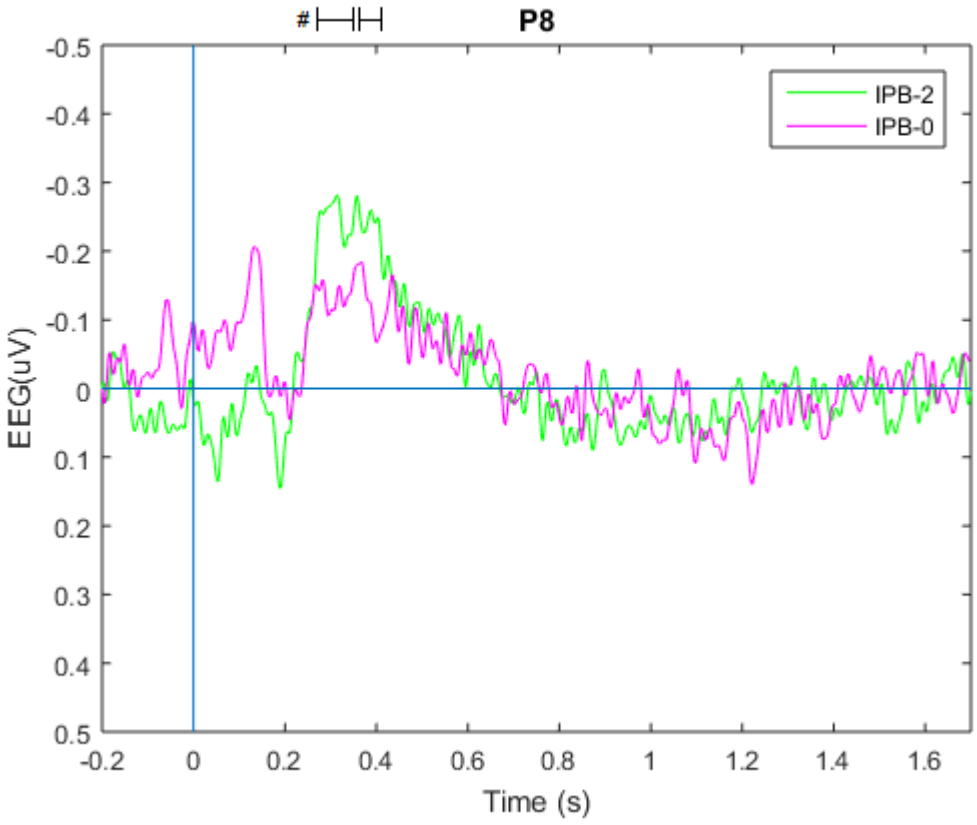

Figure 4.38 ERP plot at the P8 electrode in the IPB-2 condition.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. Intervals in which there is a significant response without MCC are highlighted with a #. There is a salient negative component which does not reach Bonferroni significance.

As these two responses are isolated at the periphery of the non-dense montage it would not be possible to capture them with Cluster MCC. The peak at P8 is not strong enough to be captured by the conservative Bonferroni MCC. This unusual split component may still be an N400 that is obscured by the occurrence of other central parietal ERP activity.

4.1.5 Summary

The HS group the IPB-2 condition elicited a clear P3a. This is visible frontally 270-380ms at electrodes Fz and Fcz with clustering and with Bonferroni correction. In addition to this, significant frontal negatives are strong evidence of a pronounced N100. There are however significant frontal negatives in the pre-final word onset interval. This means that either the frontal negative component is not in response to the onset of the final word or that the N100 overlaps with another negative component. Between 630-710ms there is a frontal negative which is evidence of a RON. Taken together there is evidence of an N1-P3a-RON cascade. Such a cascade is indicative a transient attention capture process occurring due to the incongruent prosody. The P3a alone is evidence of this but the P3a often occurs with both an N100 and RON when an unexpected and salient cue occurs. Additionally, there are frontal increases in delta power and an SP. These processes in combination with the P3a are indicative of an attention switch having occurred. Specifically, an object-switch in the verbal WM. SPs are commonly reported in response to task-switches but have not been reported in response to object-switches to the author's knowledge. The SP and parietal alpha suppression are topographically similar with both occurring at the midline centre-parietal and parietal electrodes. Alpha suppression has a shorter and is more long lasting being significant 300-800ms. The SP overlaps the latter portion of this at 630-800ms. The delta power occurs front-right and parietal-left. Front-Right lateralisation is associated with the decoding of prosody. In sum, the protocol has elicited the EEG features associated with attention capture in a group of older persons.

An N400 occurs at the periphery of the montage. This is visible at P7 with Bonferroni correction and visible at P8 $p<0.021$. An N400 is a response to the syntax in the IPB-2 condition and has been reported to this prosodic construction previously. That it only occurs at the periphery of the montage suggests that it has been obscured by the processes that are occurring as a result of the task demands.

A parietal positive component occurs prior to the onset of the final word and continues until 170ms. This has the topography and latency of a CPS in response to the IPB on the penultimate word.

4.1.6 Individuals

To examine if the protocol is sensitive enough to elicit these components in individuals, individual participants were examined in a between-trial study. The results from two persons are presented here. These are contrasting results, presented as an example of a model result and of an example of a participant who did not elicit the anticipated response.

4.1.6.1 S10

S10 was a female participant with 25 trials in the IPB-1 condition and 20 trials in the IPB-2 condition. t(43) MC simulation with 10k permutations was carried out. This participant shows strong indications of a P3a, N400, SP and RON using both Bonferroni and cluster MCC. The P3a as it appears with cluster and Bonferroni MCC is shown in Figure 4.39.

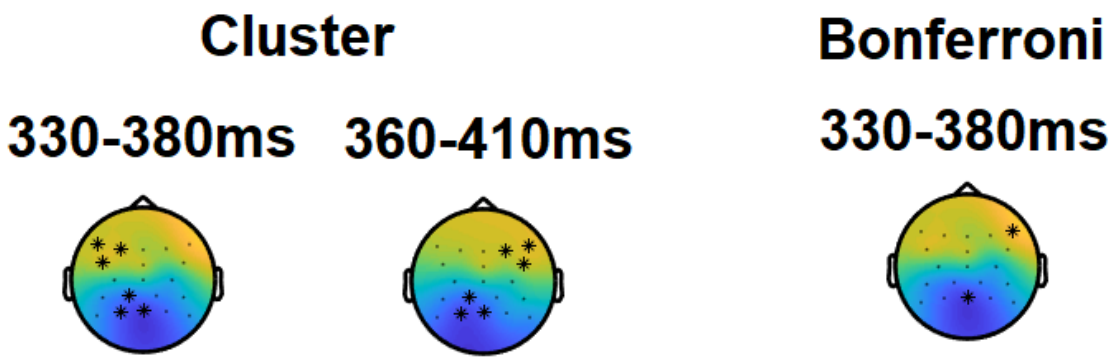

Figure 4.39 Significant differences with cluster and Bonferroni MCC in S10 in the IPB-2 condition in the P3a latency.

On the left are the results following cluster MCC and on the right are result following Bonferroni correction ($p<0.00105$). There are clusters indicative of a front central P3a 330-410ms.

In S10, this P3a response was elicited with corresponding evoked delta power. Analysis of the 2-3Hz delta band show many similarities to the group as a whole. When clustering and Bonferroni MCC are used there are localised increases in delta power 150-700ms at Fz, Fcz and Cz. When no MCC is used the pattern of delta power activation is topographically similar to the group as a whole. This is shown in Figure 4.40.

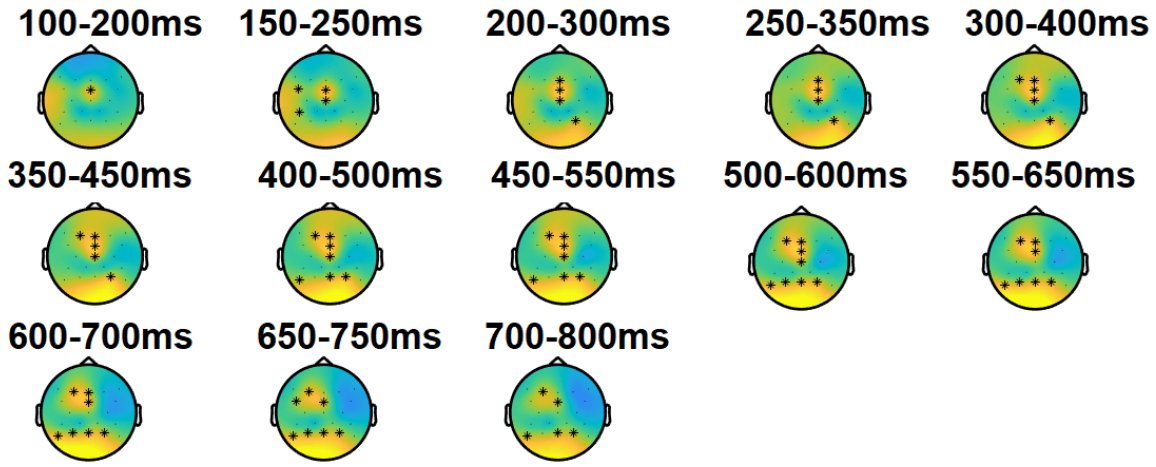

Figure 4.39 Weakly significant (p<0.021) changes in evoked frequency in the 2-3Hz band in the IPB-2 condition without MCC in S10.
There are increases in delta power 100-700ms. These begin front central before spreading parietally p<0.021.

This delta response mirrors that of the HS group overall. The breakdown of the frequency response at Fz is shown in Figure 4.41.

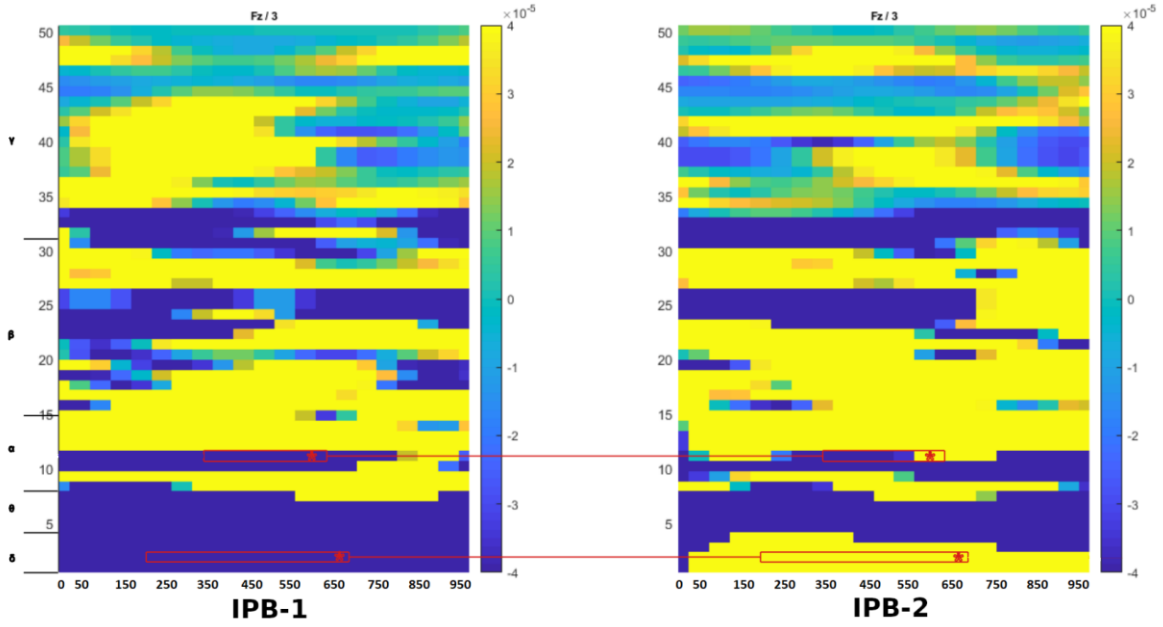

Figure 4.40 Time frequency decomposition of S10 at Fz in the IPB-2 condition.

The left plot shows the frequency power in the IPB-1 condition and the right plot shows the frequency power in the IPB-2 condition. Highlighted are significant differences in the two conditions. The single asterisk indicates areas of significance with cluster MCC. There are significant increases in delta with MMC are 200-700ms. The delta increases overlap with the P3a.

The analysis also revealed evidence of a RON and SP in S10. The former is visible with cluster MCC only and the later is visible with both cluster and Bonferroni MCC. These are shown in Figure 4.42.

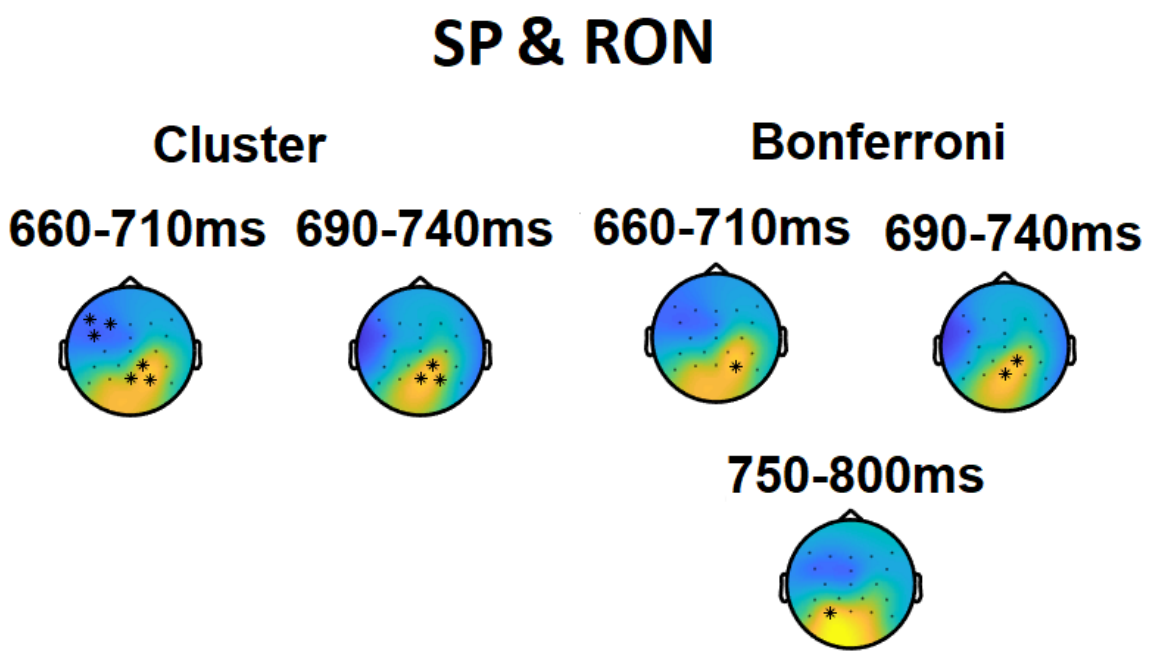

Figure 4.41 Significant differences with cluster and Bonferroni MCC in S10 in the IPB-2 condition in the RON and SP latency.
On the left are the results following cluster MCC and on the right are result following Bonferroni correction ($p<0.00105$). There are clusters indicative of a RON 660-710ms and an SP 660-740ms. Bonferroni MCC shows a peak in the SP 660-740ms and 750-800ms.

In contrast to the HS group as a whole, S10 showed a salient N400 response.

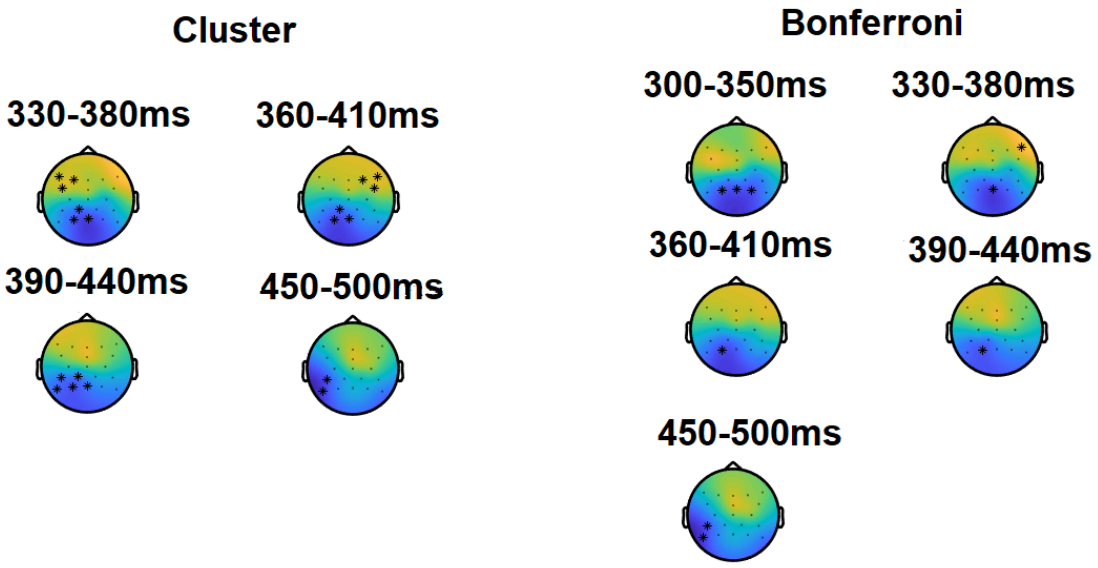

Figure 4.42 Significant differences with cluster and Bonferroni MCC in S10 in the IPB-2 condition in the N400 latency.
On the left are the results following cluster MCC and on the right are result following Bonferroni correction ($p<0.00105$). There are clusters indicative of an N400 330-500ms. Bonferroni MCC shows a peak in the N400 300-500ms.

S10 has a more widespread N400 response than the group as a whole with the significant cluster taking in P7, P3, Pz, CP5 and CP1 at its largest extent. The P3a is also more widespread than the group as a whole, appearing right-anteriorly and left-anteriorly as opposed to being localised in the centre. The SP is significant with clustering and Bonferroni correction ($p<0.00105$). The N100 and CPS are absent. In addition to the identified components, there are late positive and negative components 900-1040ms. The group as a whole also had unidentified late positive and negative components.

4.1.6.2 S12

S12 was a male participant with 22 trials in the IPB-1 condition and 17 trials in the IPB-2 condition. A 10k MC simulation t(37), $p<0.021$ with clustering and Bonferroni MCC found no significant changes in the IPB-2 condition. In addition to this they were the only participant to have no increases in delta at the 2Hz band. S12 has no increases in delta power above their baseline in either the IPB-1 or IPB-2 condition. There were no deviant scores in the Probe Task in the HS group (Figure 4.56). ERP and oscillations do not necessarily correlate with performance in the EEG or prosody task.

4.1.6.3 Individual Summary

It is possible to elicit the attention components at the subject level. Analyses were unable to reveal alpha suppression in any of the individual subjects. Of those analysed, only one participant showed no evidence of any of the components. Given this response, it is possible to view components in a case study basis in the PD group. As the components are less likely to appear at the subject level, their absence in the current study cannot be used to infer anything. Their presence however would give a preliminary indication of how these components link to an ability to perceive prosody as indicated by performance in the discrimination and ID tasks.

4.1.7 Attention Components Summary

The HS group showed the P3a and RON attention related ERP components. There was also evidence of an enhanced N100 but this is overlapped with a pre-stimulus component. In addition to the attentional ERPs there is also an SP. There is also an isolated N400. This is an indication of set-shifting. In the frequency domain there was widespread delta activation and parietal alpha suppression. This study has therefore shown these components in response to prosody and to object-switching in the verbal working memory. At the individual level all of these components were visible in some of the individuals with the exception of alpha suppression. The protocol was therefore sensitive enough to elicit these components in some individuals but not others.

4.2 HS IPB-0 Condition - Prosody Domain Components

4.2.1 HS Group Analysis

The IPB-0 condition sought to elicit a RAN and PEP. In the IPB-0 condition 10k MC simulation t(56,2) show no RAN or PEP with or without MCC. In the absence of any topographic maps with significant results the ERPs at the electrodes at which the RAN and PEP were expected to be elicited are shown. The similarity between the two conditions is particularly stark.

4.2.1.1 RAN

The protocol aimed to elicit the RAN at F4, F8 and/or FC6. These electrodes are shown in Figure 4.43, Figure 4.44 and Figure 4.45 respectively.

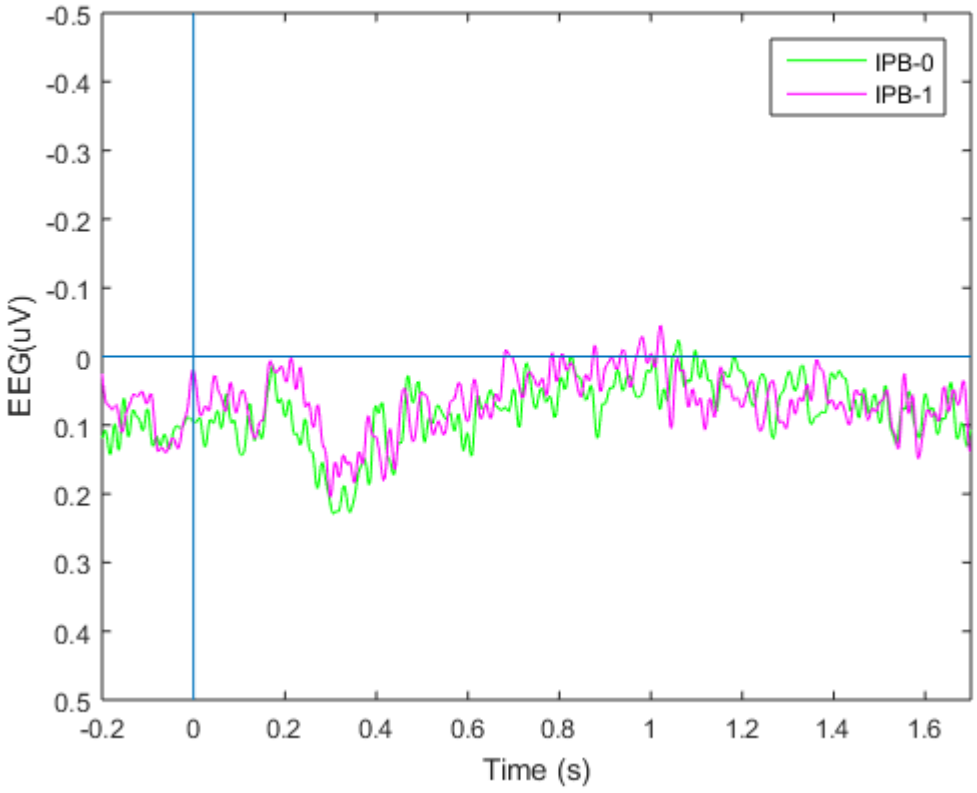

Figure 4.43 ERP plot at the F4 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no RAN and that there is little difference between the two conditions overall.

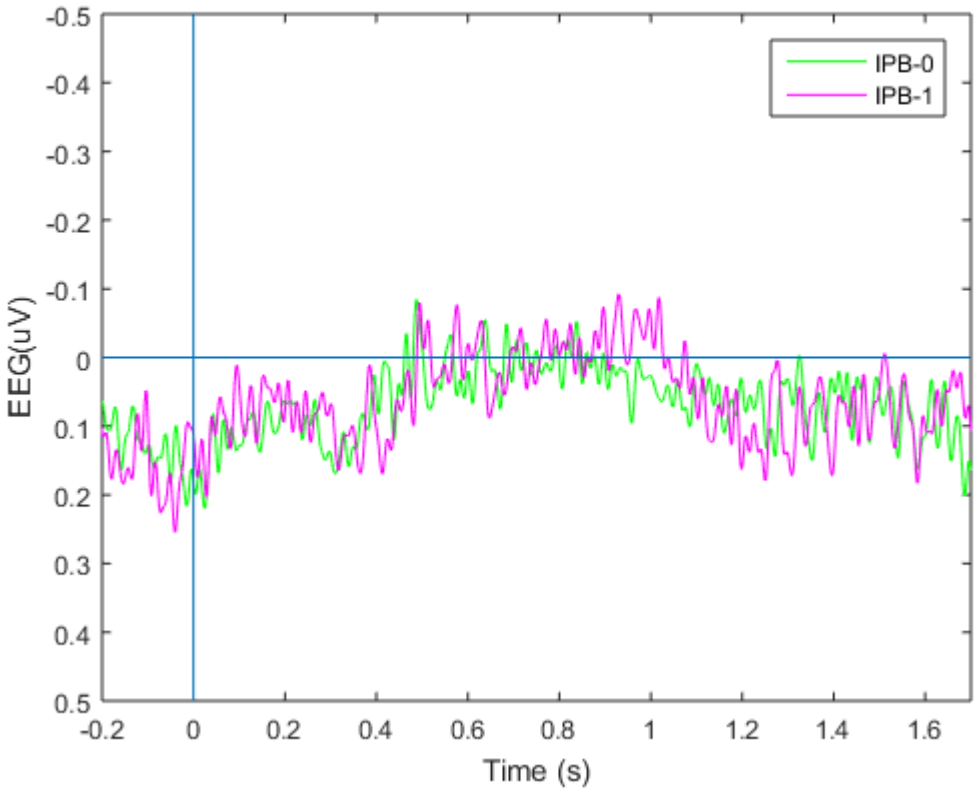

Figure 4.44 ERP plot at the F8 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no RAN and that there is little difference between the two conditions overall.

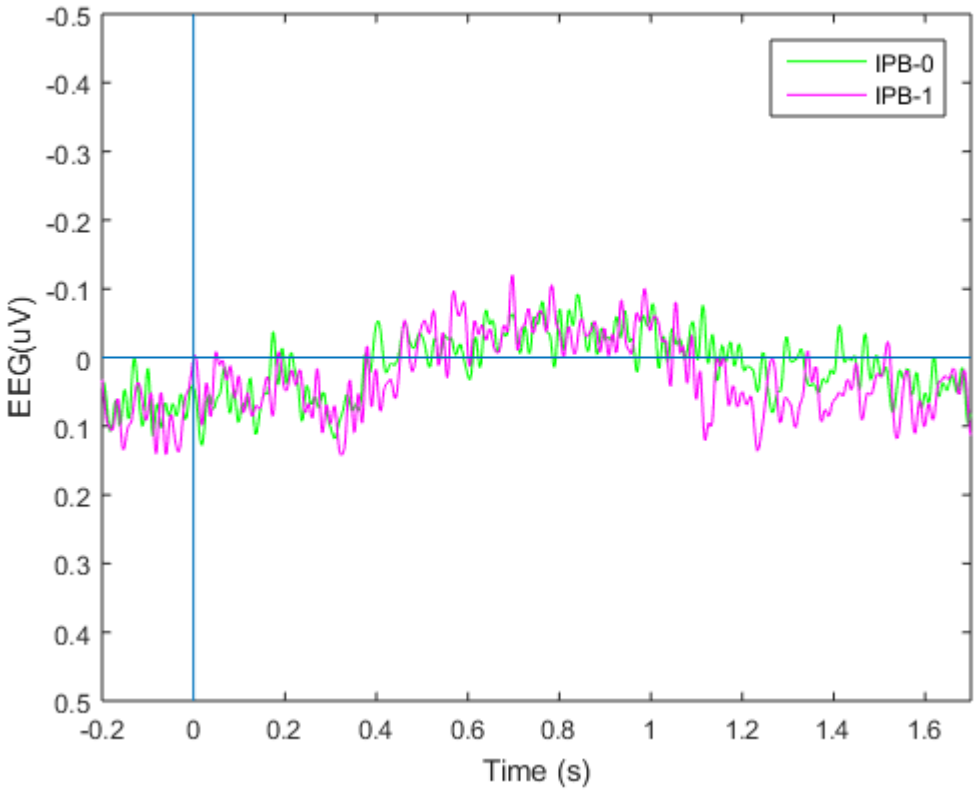

Figure 4.45 ERP plot at the FC6 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no RAN and that there is little difference between the two conditions overall.

It is clear that the current protocol was unable to elicit a RAN in the HS cohort.

4.2.1.2 PEP

The protocol aimed to elicit a PEP parietally. In the pilot cohort the PEP was most salient at the peripheral and centre-parietal electrodes. The ERP response at electrodes P7, CP1, CP2 and P8 are shown in Figure 4.46, Figure 4.47, Figure 4.48 and Figure 4.49 respectively.

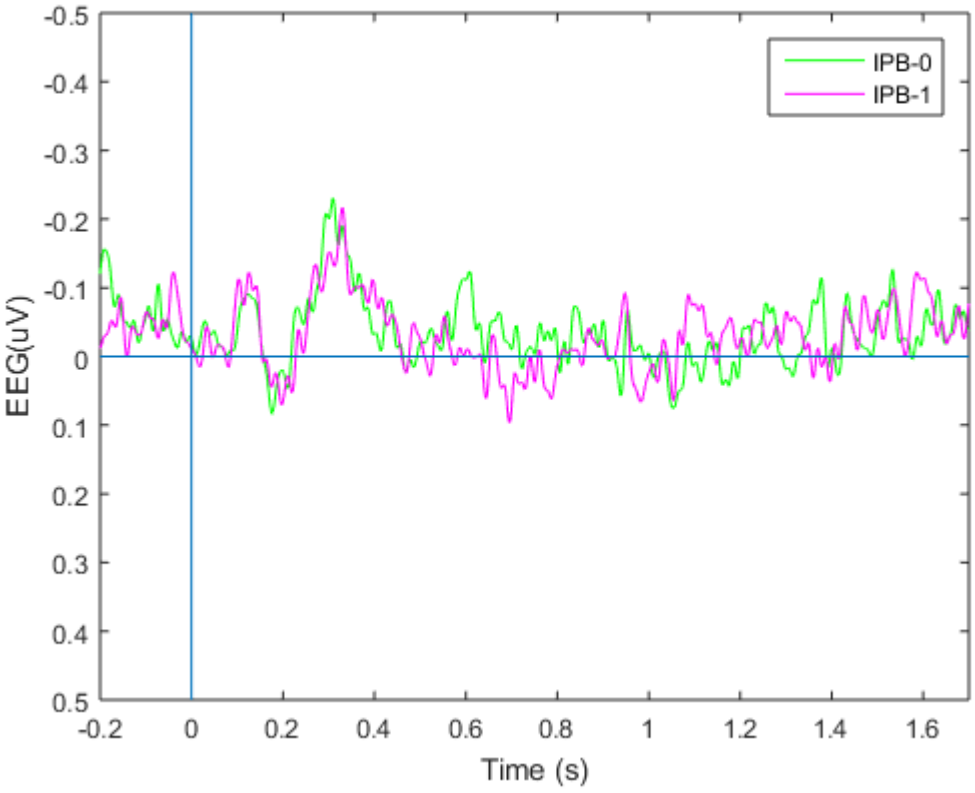

Figure 4.46 ERP plot at the P7 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no PEP and that there is little difference between the two conditions overall.

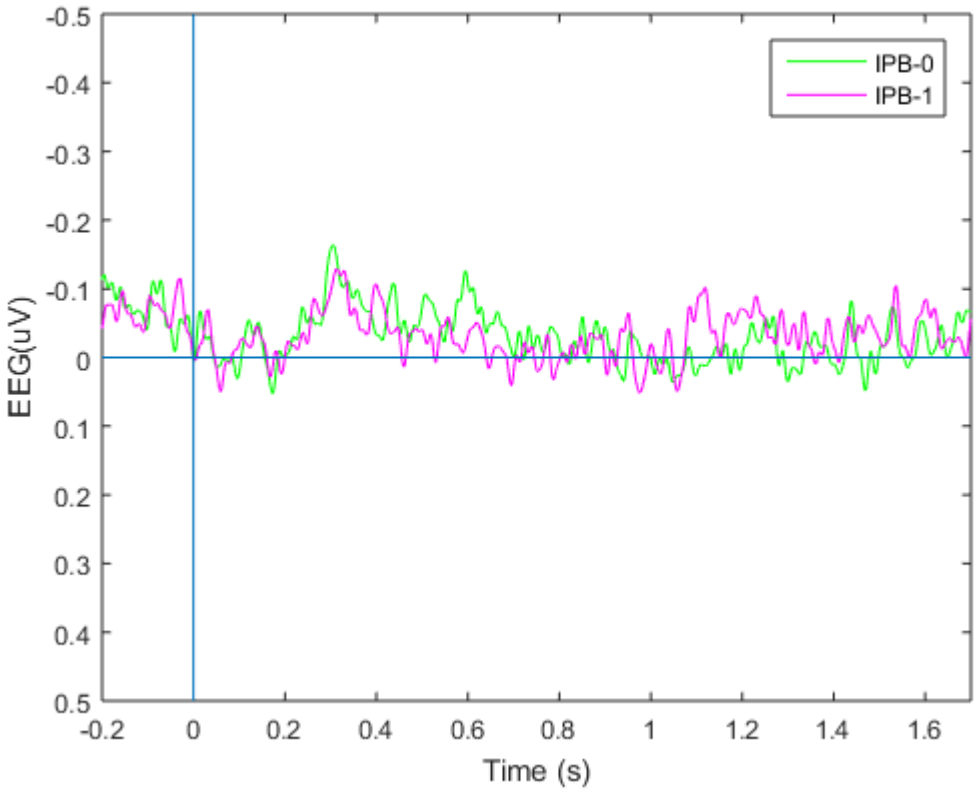

Figure 4.47 ERP plot at the CP5 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no PEP and that there is little difference between the two conditions overall.

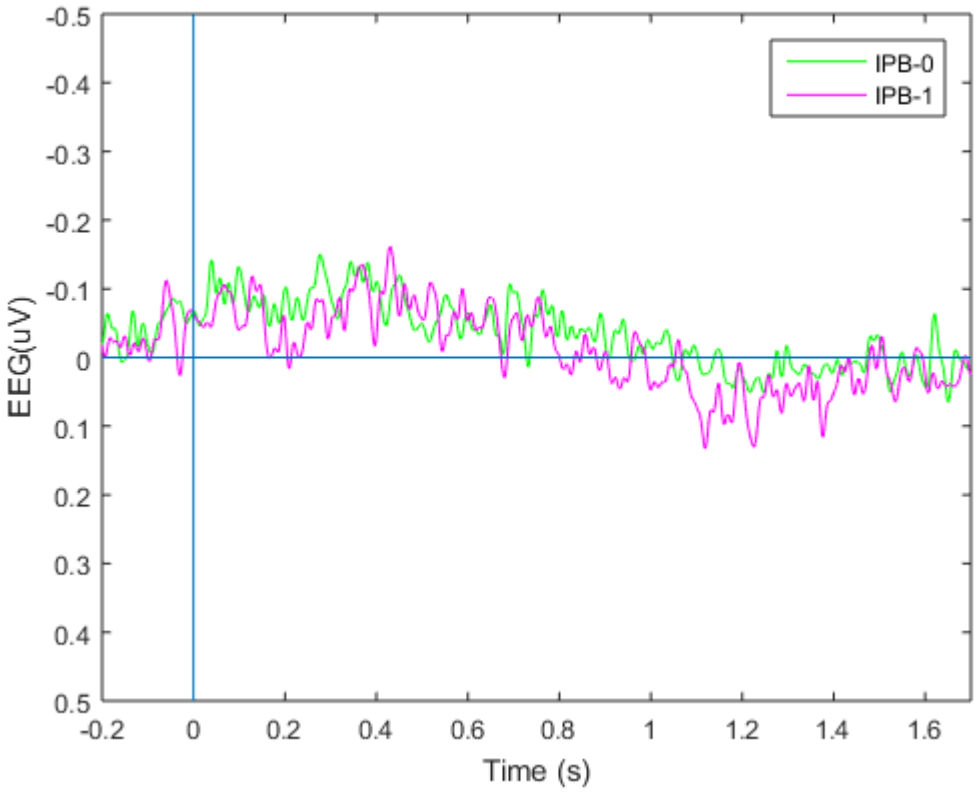

Figure 4.48 ERP plot at the CP6 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no PEP and that there is little difference between the two conditions overall.

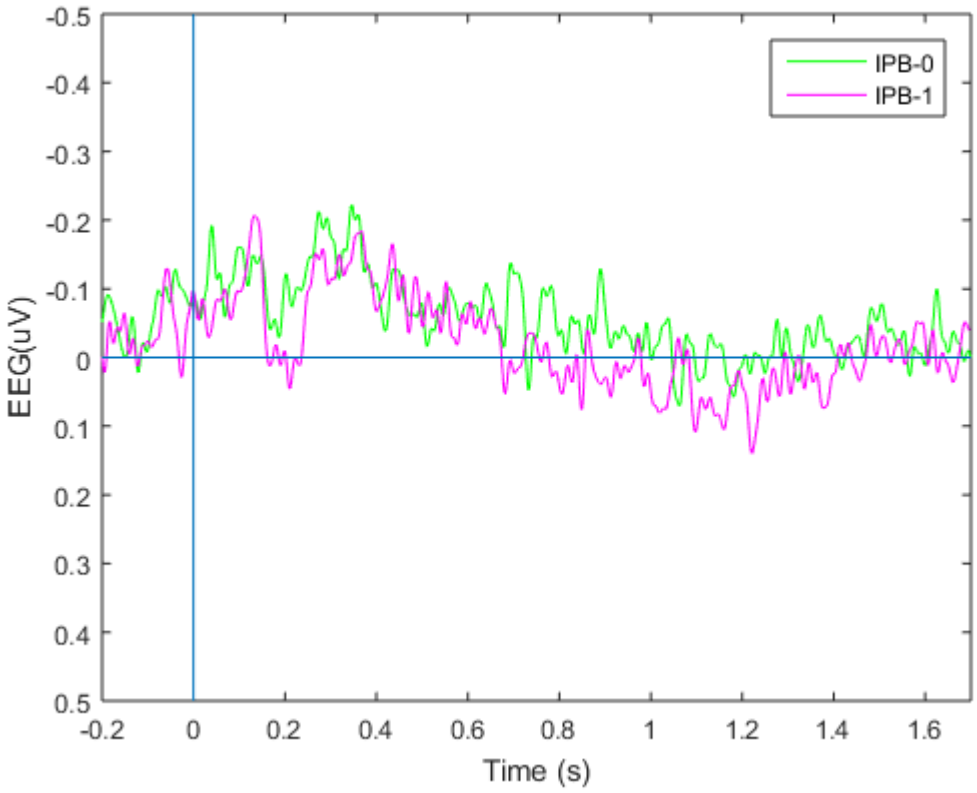

Figure 4.49 ERP plot at the P8 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant difference between the two conditions. It is apparent there is no PEP and that there is little difference between the two conditions overall.

It is apparent that there is no PEP in the HS group in the IPB-0 condition.

4.2.1.3 Frequency Response

The protocol failed to elicit the RAN or PEP in the HS group. The strongest response in the IPB-0 condition was a change in evoked frequency 4-5Hz frequency band (borderline delta/theta) and 5-7Hz (theta) frequency band. These were present with cluster MCC and are shown in Figure 4.51 and Figure 4.52.

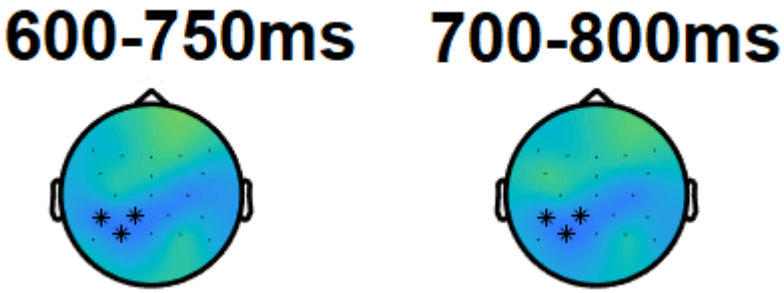

Figure 4.50 Changes in the IPB-0 condition in the HS group in the 4-5Hz frequency band with clustering
There is a drop in the 4-5Hz frequency band at electrodes CP5, CP1 and P3. These overlay the left-angular gyrus.

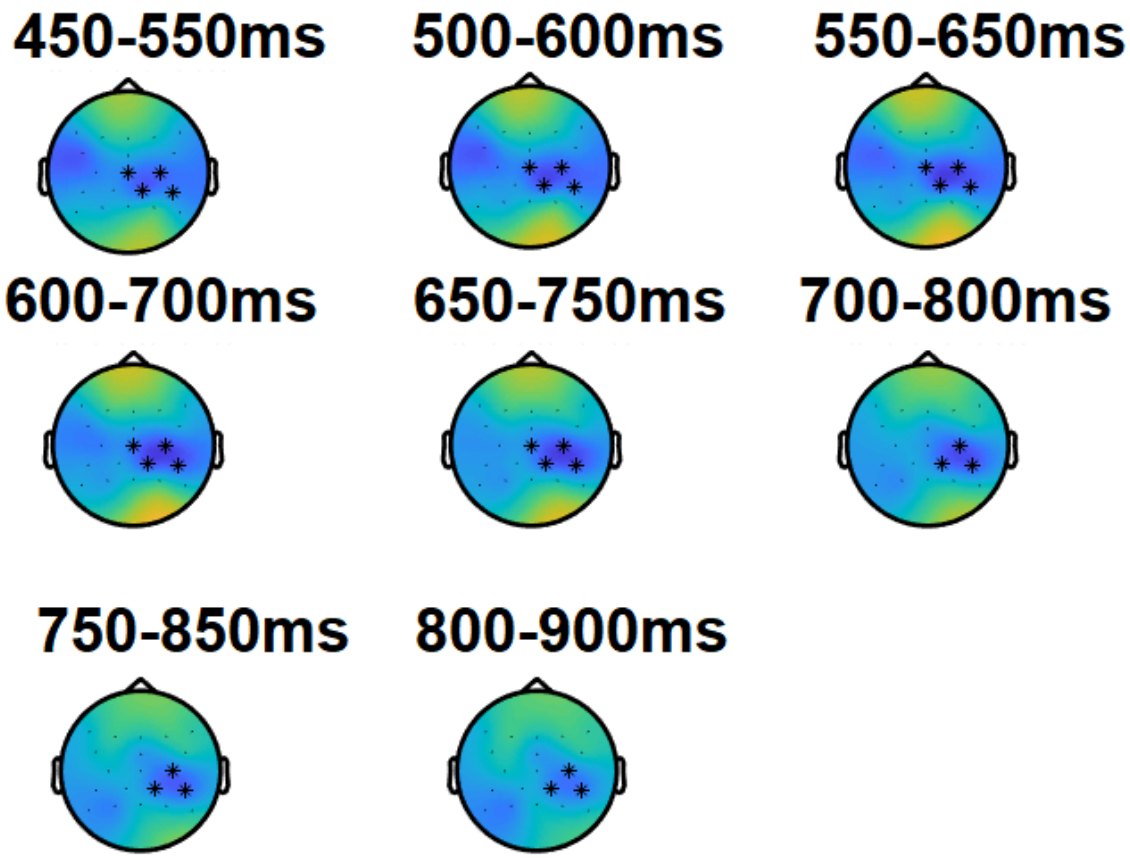

Figure 4.51 Changes in the 5-6Hz (lower-theta) frequency band with clustering
There is a drop in theta frequency power at Cz, C4, CP2 and CP6 450-900ms.

The HS cohort differed from the pilot cohort in both the time and frequency domains. The predicted RAN and PEP were not elicited. The RAN may not be an appropriate component to use in older participants. Individuals

4.2.2 Individual Response

Between-Trial analyses on the HS group revealed that, one participant did elicit a RAN in response to the IPB-0 condition.

4.2.2.1 S21

S21 was a female participant aged 68 at the time of the recording. They had 20 artefact-free trials in the IPB-1 condition and 22 in the IPB-0 condition t(42). The RAN component with cluster and Bonferroni MCC is shown in Figure 4.54.

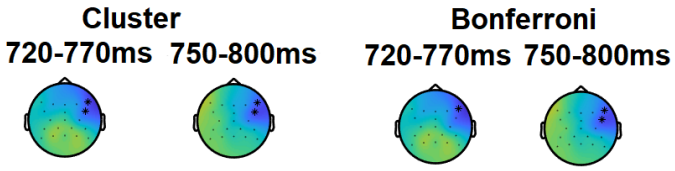

Figure 4.52 S21's significant response in the IPB-0 condition with cluster and Bonferroni correction.
A strongly significant (p<0.00105) RAN is present at F8 750-800ms and FC6 720-770ms There is also a RAN present with cluster MCC 720-800ms.
There are indications of a right-anterior component 720-800ms.

The ERP response at F8, FC6 and (the non-significant) F4 are shown in Figure 4.55, Figure 4.56 and Figure 4.57.

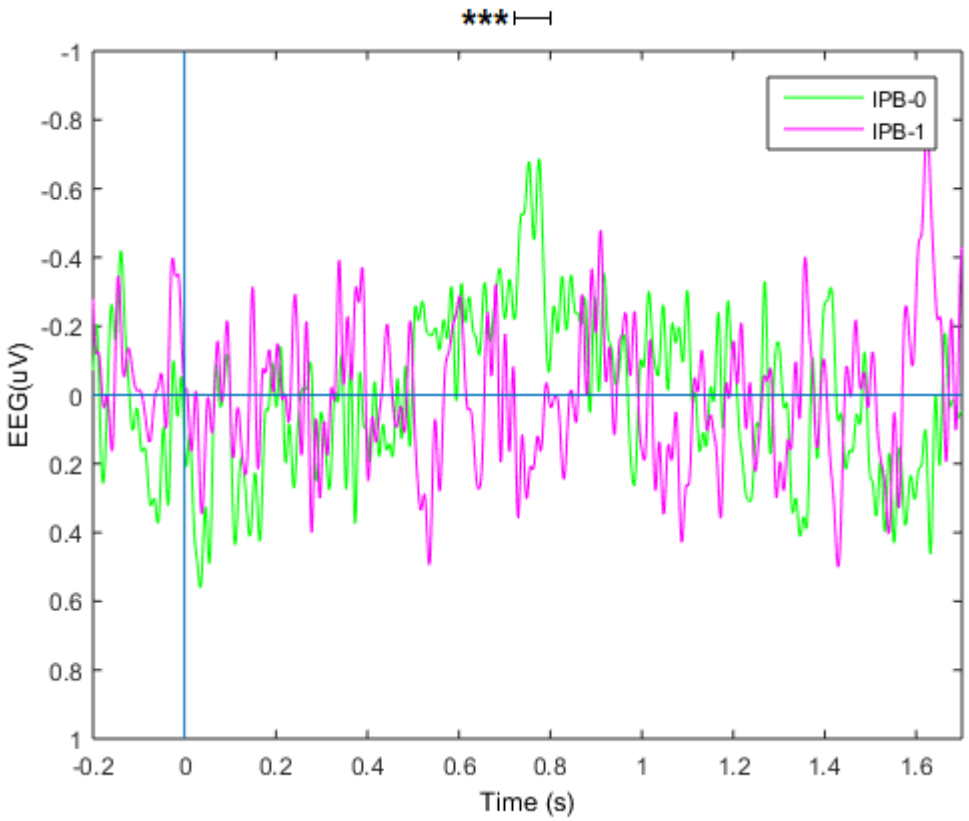

Figure 4.53 S21's ERP plot at the F8 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. The interval in which there is a significant ERP response with both Bonferroni and cluster MCC is marked with a triple asterisk. The peak of the RAN is visible 720-800ms.

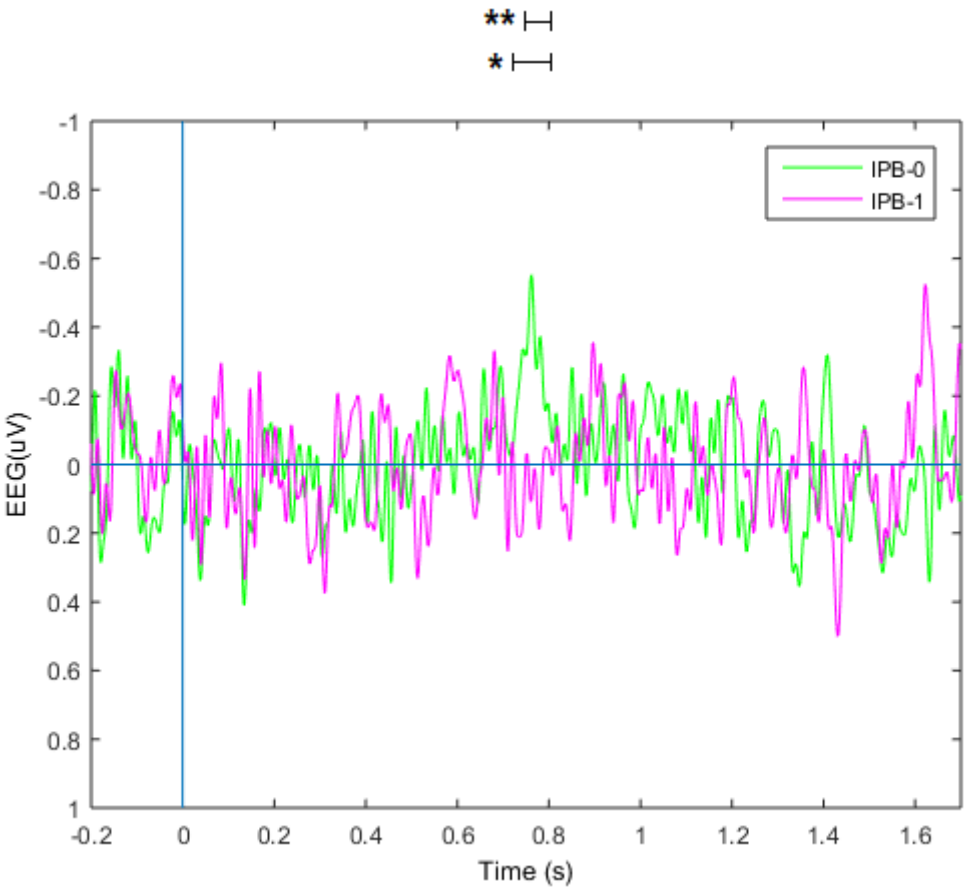

Figure 4.54 ERP plot at the Fc6 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. The interval in which there is a significant ERP response with Bonferroni MCC is marked with a double asterisk. The interval in which there is a significant ERP response with cluster MCC is marked with a single asterisk. The peak of the RAN is visible 720-800ms.

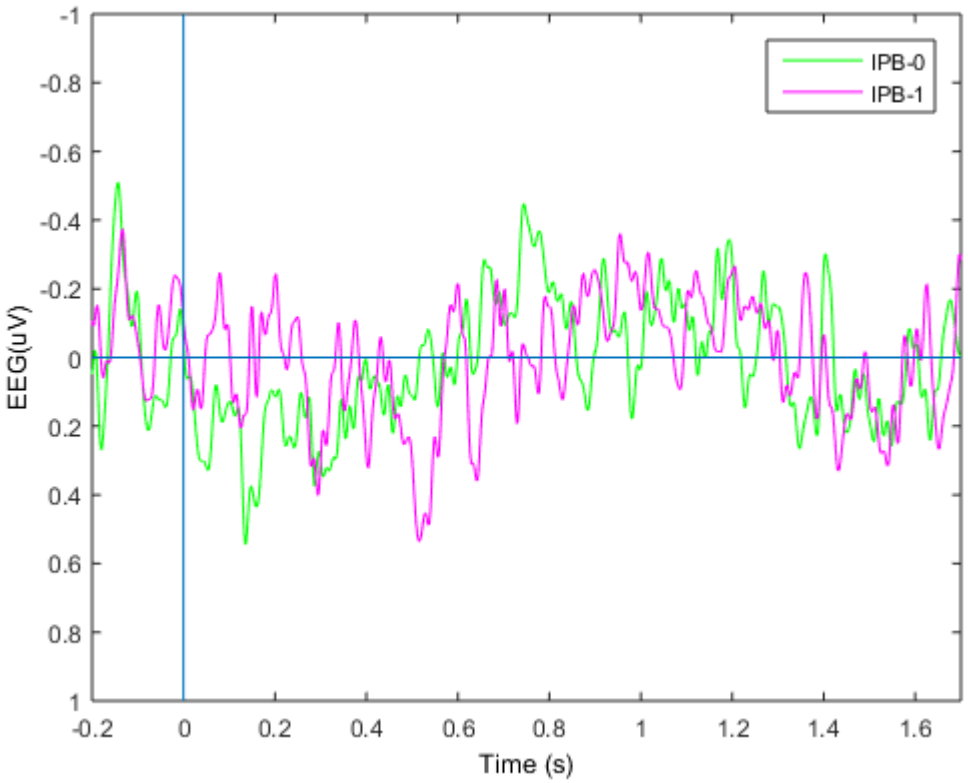

Figure 4.55 ERP plot at the F4 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. There are no intervals in which there is a significant response with MCC. A weak peak that may be the periphery of the RAN is visible between 700-800ms.

The RAN in S21 did not have a significant evoked frequency response. There were no significant changes frequency power at any band at the right anterior electrodes F8, F4 and FC6. There was a weakly significant drop in theta power ($p<0.021$) 300-400ms at FCz and Cz. There was a weakly significant ($p<0.021$) drop in upper-beta power (25-30Hz) 50-150ms Upper-beta at C4. This participant differs from the rest of the HS group as a whole.

4.2.3 Prosody Components Summary

The protocol failed to elicit a RAN or PEP in the HS group. Between-Trial analyses revealed one participant elicited a RAN.

4.3 Behavioural Results

In this section the results of the Probe Task, Discrimination Task and Identification Task are presented. The HS cohort are presented with the results of the two participants with PD. The EEG response of the participants with PD are presented separately in Section 4.4.

4.3.1 Probe Task

During the EEG, participants were asked to listen for the final word of each presented sentence. They were then shown a word and asked to answer if this word matched the last word of the sentence they just heard. This task intentionally does not require the participant to assess the prosodic content of what they have heard. The score frequencies in this task are shown in Figures 4.56a and 4.56b. The maximum score has a rightward skew towards the maximum score of 140. The response times (RTs) have a leftward skew towards shorter response times. The results of PD1 and PD2 are overlaid on the HS results.

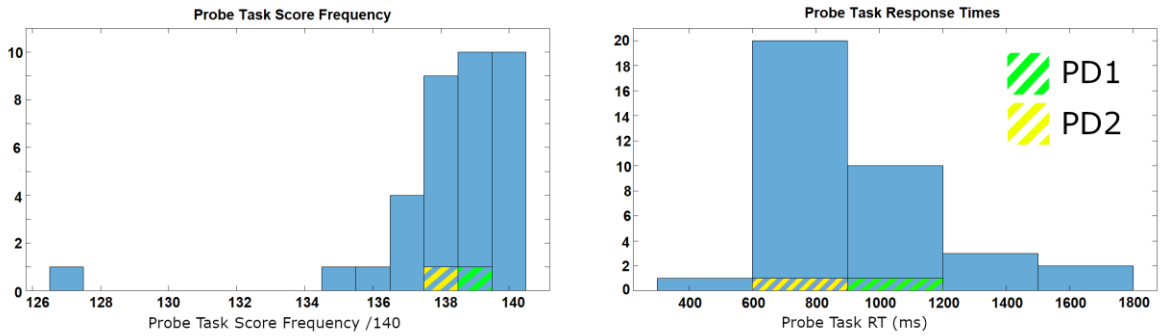

Figure 4.56a&b Histogram of Probe Task scores and response times.

The Probe Task scores are skewed toward the top score of 140; median=139; StdDev=2.3. 10 HSs scored 140/140. PD1 made one error, scoring 139. PD2 made two errors, scoring 138. The median RT in the HS group was 848.98ms with a StdDev=271.54. PD1 had a mean response time of 1124.99ms. PD2 had a mean response time of 794.74ms. Both participants with PD had scores and RTs comparable to the HS group

4.3.2 Discrimination Task

In the discrimination task participants answered if the prosody of two consecutively presented voice stimuli were the same or different. The histogram of these results and the response times are shown in Figures 4.57a and 4.57b. The maximum score in the discrimination task was 30. The score has a rightward skew towards the maximum score and the RTs have a normal distribution about the median score. The results of each of both of the PD case studies are overlaid.

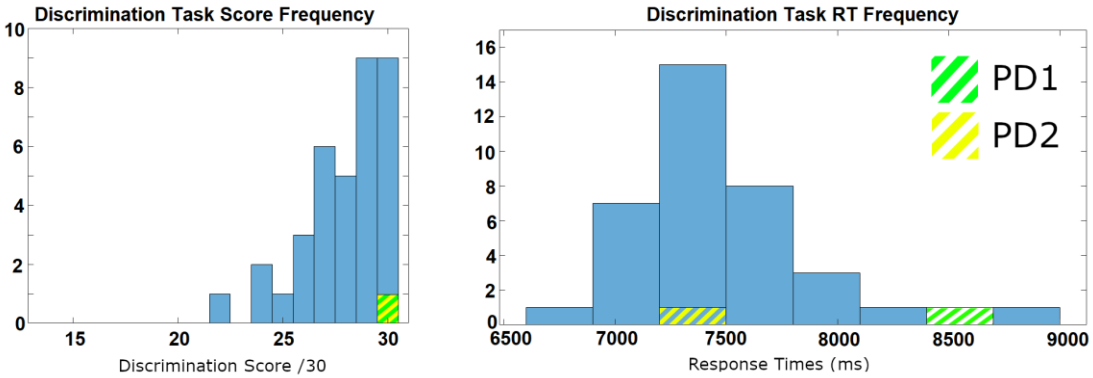

Figure 4.57a 4.57b Discrimination Task score frequency and response times

HS discrimination scores are shown in Figure 4.57a. The mean response times of each participant are shown in Figure 4.57b. The discrimination scores are skewed toward the top score of 30; median=28; StdDev=1.98. 9 HSs and PD1 and PD2 scored 30/30. Response times are more normally distributed; RT Median=7393ms; RT StdDev=369.38. PD1 had a mean response time of 8471ms. PD2 had a mean response time of 7490ms.

PD1 and PD2 both scored 30/30. PD2 had mean RTs within one standard deviation of the median. PD1 had RTs outside two standard deviations from the median.

4.3.3 Identification Task

In the Identification Task participants were asked to answer if the prosody they heard sounded unusual. There was a maximum score of 15 and the HS group results skew rightward to this score. The score of each HS and the average response times are shown in Figures 4.58a and 4.58b. The PD case study scores and response times are overlaid.

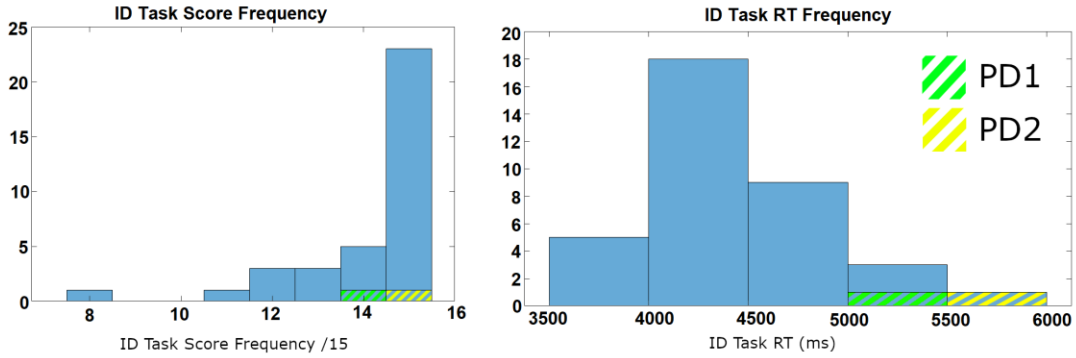

Figure 4.58 & 58b Identification task score frequency and response times.

HS ID scores are shown in Figure 4.58a. The mean response times of each participant are shown in Figure 4.58b. The ID scores are skewed toward the top score of 15; median=15; StdDev=1.51. 23 HSs and PD2 scored 15/15. PD1 scored 14. Response times are more normally distributed; RT Median=4363ms; RT StdDev=458.8. PD1 had a mean response time of 4593ms. PD2 had a mean response time of 5943ms.

PD1 scored 15 and PD2 made one mistake which is within 1 standard deviation of the median. PD1 had RTs within 1 standard deviation of the median. PD2 was just outside one standard deviation and well within two. The pattern in RTs in not consistent between this task and the discrimination task. Response times in this task were 59% of that of the discrimination task indicating the participants found this task easier.

4.4 Case Study – PD1

In this section the EEG results from PD1 in both conditions are presented. PD1 was a male aged 81. PD1 had the most advanced disease stage (H&YIII) and the lowest ACE-III score. He scored similarly to controls in the discrimination task (30/30) and identification task (14/15).

4.4.1 IPB-2

In PD1, results from 10k MC simulations t(31), p<0.021 found no significant changes with cluster and Bonferroni MCC in the IPB-2 condition.

PD1 did show a weakly significant (p<0.021) increase in frontal delta power localised to Fcz 200-450ms.

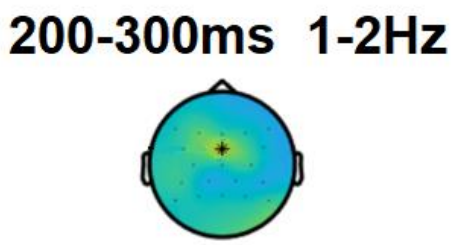

Figure 4.59 The frequency response of PD1 in the IPB-2 condition in the 1-2Hz bandwidth

There was an increase in delta power 200-450ms without MCC. The change in delta had the latency and location of where the P3a was expected.

The ERP at this electrode is shown in Figure 4.66.

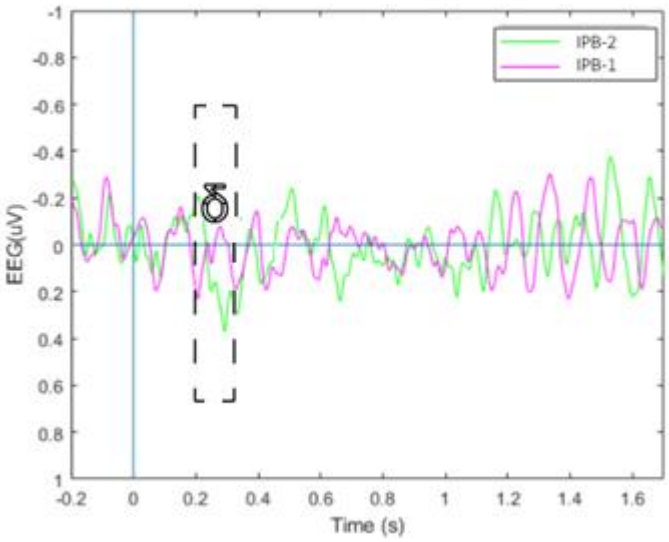

Figure 4.60 PD1's ERP at FCz in the IPB-2 condition with intervals of significant increases in evoked delts power with no MCC highlighted.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. A waveform with the appearance of an attenuated P3a is visible 200-300ms, this however failed to reach significance. The increase in delta power is shown 200-300ms.

In the IPB-2 condition, changes in delta power are only at one electrode and the P3a is absent.

4.4.1.1 IPB-0

The results of 10k MC simulations t(33), p<0.021 for the IPB-0 condition in IPB-0 revealed a weakly significant (p<0.021) anterior negative 800-850ms at F4.

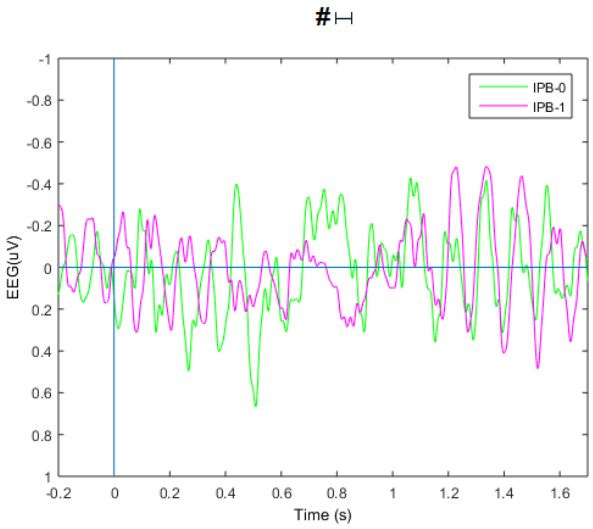

Figure 4.61 PD1's ERP plot at the F4 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. The area of weakly significant difference is highlighted with a hash symbol 800-850ms. The RAN-like negative is visible at wider area but differs most strongly with the IPB-1 condition in the significant interval. There is visible noise in the IPB-1 condition following 1.2s.

This is a weakly significant and localised response. The response at F8, and FC6 are shown in Figure 4.62 and Figure 4.63. This is no significant ERP response at these electrodes but these are electrodes of interest due to the significant response at F4.

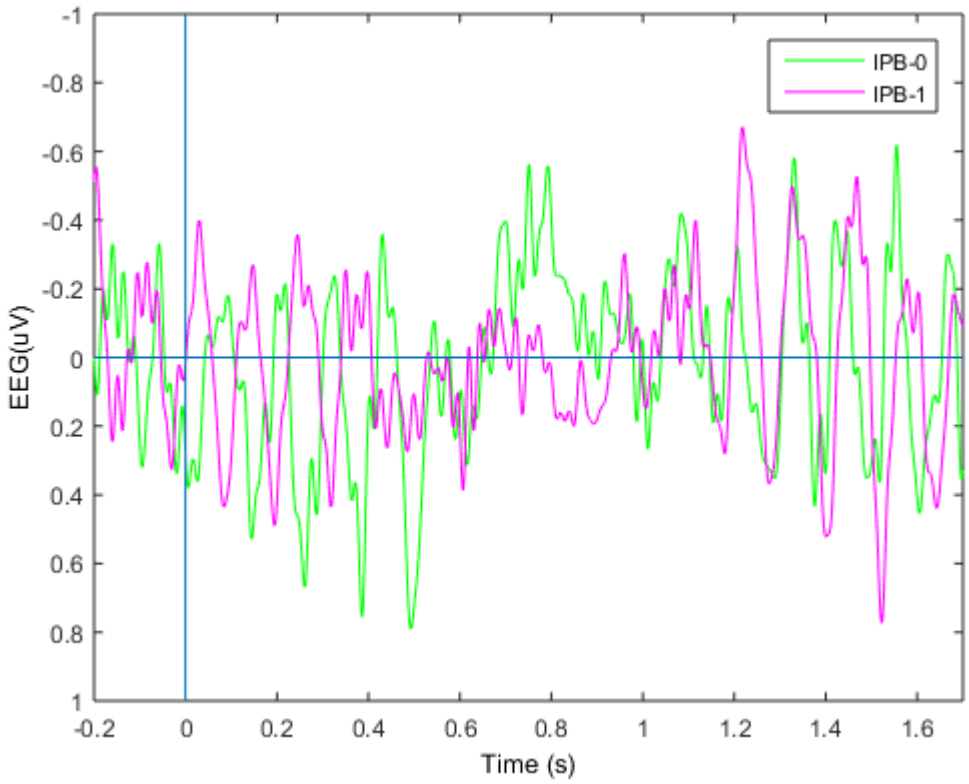

Figure 4.62 PD1's ERP plot at the F8 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. A non-significant negative component is visible 500-900ms. The cyclical response in both conditions prior to 400ms and after 1200ms are indications of noise which make this participant's data difficult to interpret.

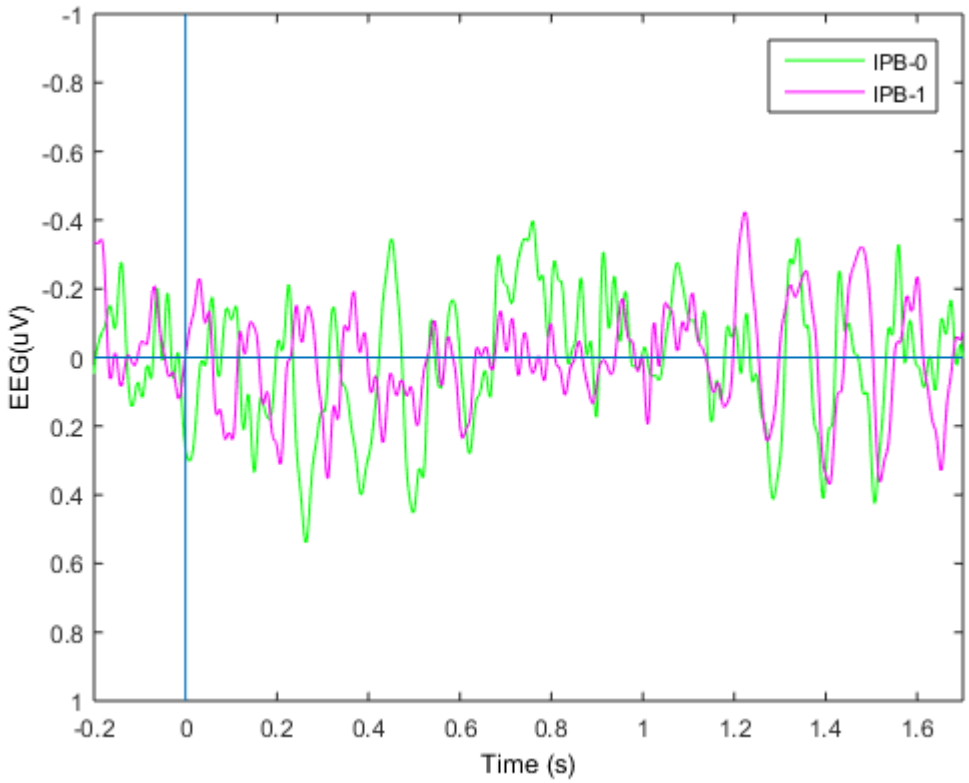

Figure 4.63 PD1's ERP plot at the Fc6 electrode in the IPB-0 condition.
The IPB-0 condition is shown in green and the IPB-1 condition shown in purple. A non-significant negative component is visible 600-800ms. The cyclical response in both conditions after 1200ms are indications of noise which make this participant's data difficult to interpret.

PD1 shows very weak indications of a RAN-like response. The quality of their data overall is poor, making any interpretations tentative.

4.4.2 Summary

PD1 shows none of the ERP components associated with the IPB-2 condition. They have a localised increase in delta power. This may be due to the frequency response being easier to differentiate from noise in the data. In addition, there are weak indications of a RAN-like response in this participant.

4.5 Case Study – PD2

PD2 was male aged 76 at the time of recording. They were the earliest staged of all the patients (H&Y I) and were not on dopaminergic medication at the time of recording. They scored a 100% ACE-III and 100% in the ID task and identification task. In the IPB-2 condition they showed a significant N400, a central P300 and weakly significant SP and RON. In the IPB-0 condition they have no significant ERPs, this is similar to the HS group as a whole.

4.5.1 IPB-2

4.5.1.1 P3a

Results of 10k MC simulations t(56), p<0.021 with cluster and Bonferroni correction indicated the presence of a P3a. This is shown in Figure 4.64.

Figure 4.64 PD2 cluster and Bonferroni significances in the IPB-2 condition in the P3a latency.

There was centre-parietal right P3a 330-410ms with cluster and Bonferroni MCC.

The ERP of this component at Cz is shown in Figure 4.65.

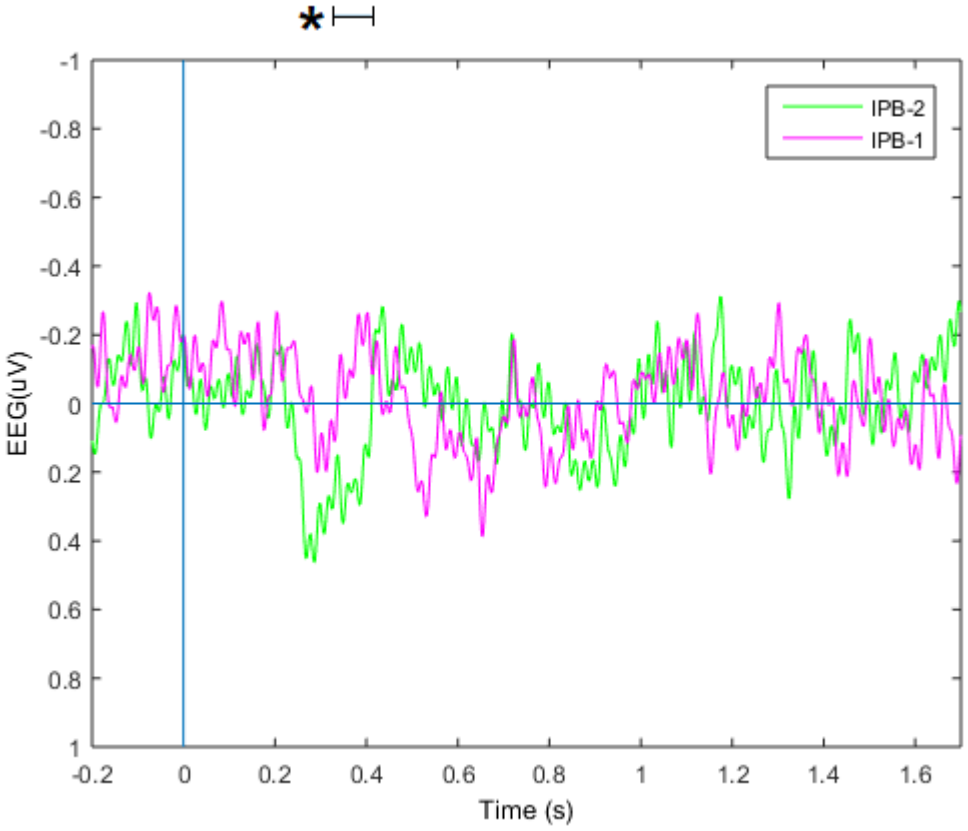

Figure 4.65 PD2's ERP plot at the Cz electrode in the IPB-2 condition.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The 330-410ms interval of cluster significance is marked with a single asterisk. A P3a is visible within this interval.

Concurrent with the P3a was an increase in delta power (1-3Hz) without MCC 200-400ms at the Fcz electrode. The topography of this localised response is shown in Figure 4.66. How this cimpares with the ERP response at FCz is shown in Figure 4.67.

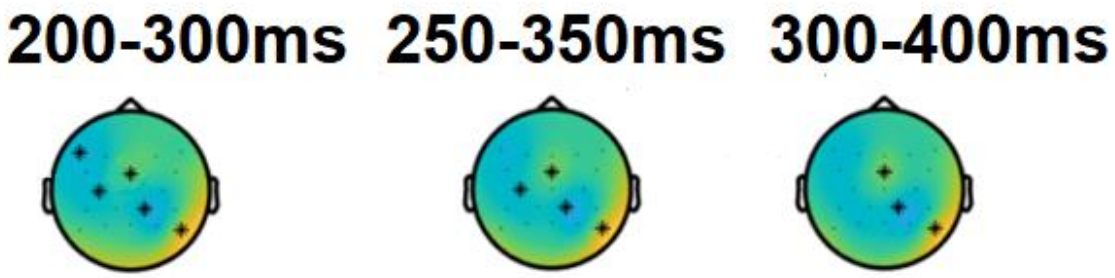

Figure 4.66 Change of evoked power in the 1-300Hz frequency band in PD2 in response to the IPB-2 condition.
There is a significant increase in delta power without MCC at FCz 200-400ms. This is localised and is concurrent with drops in delta power at C3 and CP2.

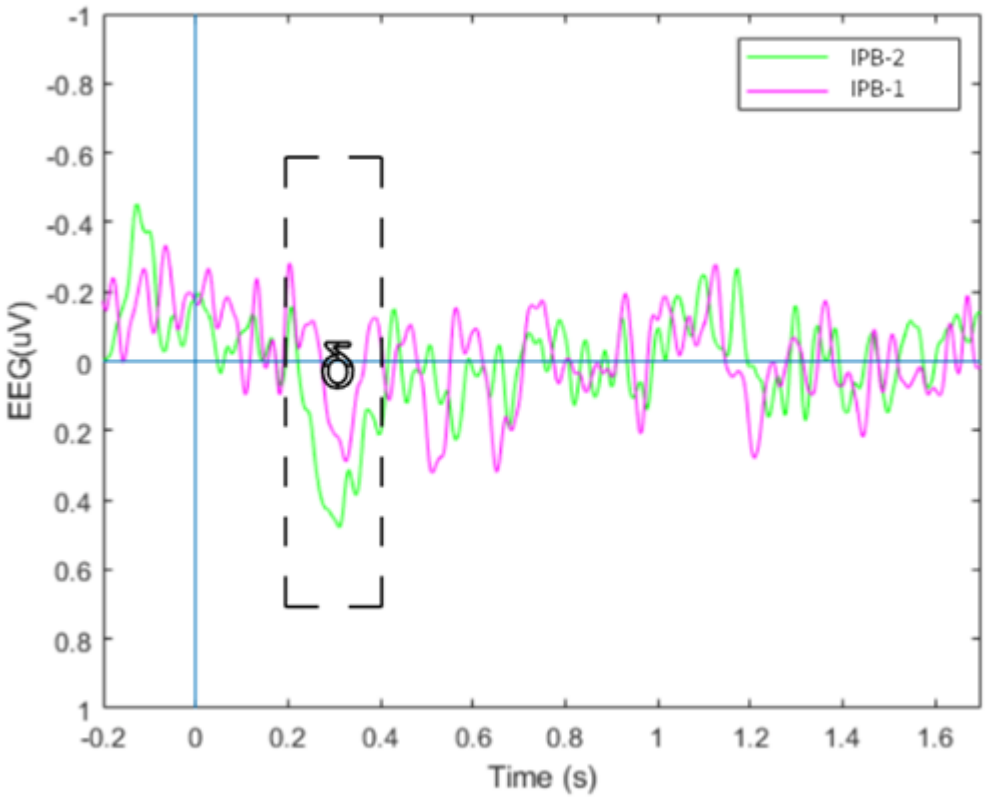

Figure 4.67 PD2's ERP at FCz in the IPB-2 condition with intervals of significant increases in evoked delta power with no MCC highlighted.
The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The 200-400ms of delta increase without MCC significance is marked. A P3a is visible within this interval but it should be noted that this did not reach significance in the analysis.

4.5.1.2 N400

Cluster and Bonferroni MCC also showed indications of an N400 which are shown in Figure 4.68.

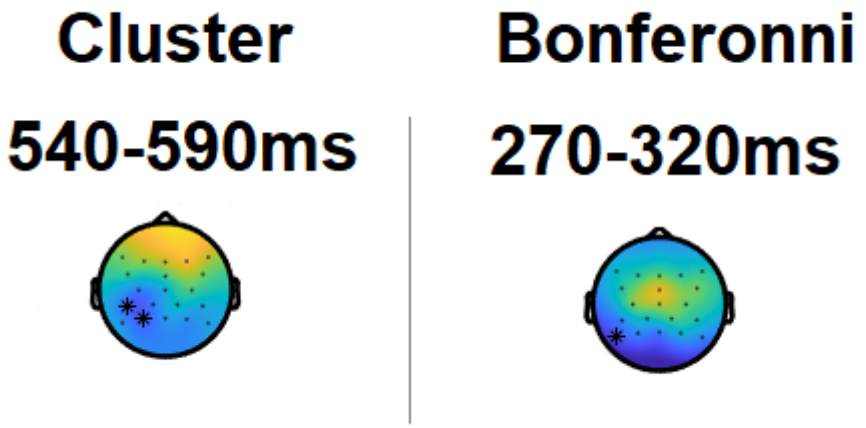

Figure 4.68 PD2 cluster and Bonferroni significances in the IPB-2 condition in the N400 latency.
There is a left-parietal negative cluster 540-590ms and a Bonferroni peak 270-320ms.

The N400 is left-lateralised which is similar to the HS group which also had a more pronounced leftward N400. The ERP as it appears at P7 is shown in Figure 4.69.

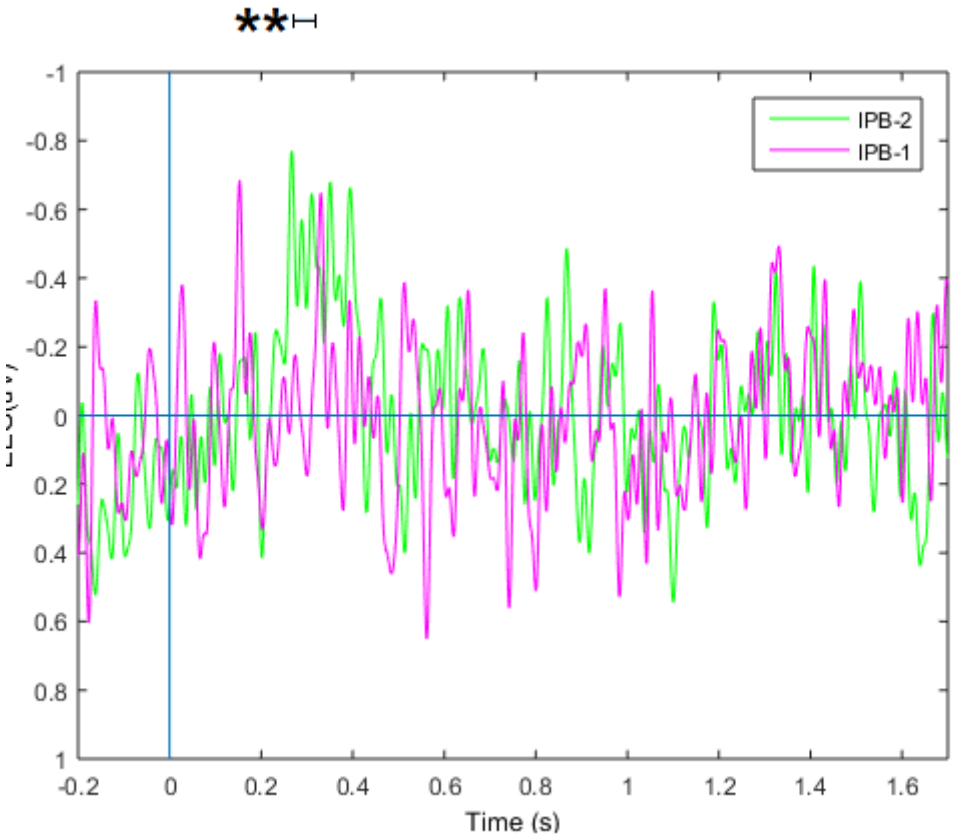

Figure 4.69 PD2's ERP plot at the P7 electrode in the IPB-2 condition.

The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The 270-320ms interval of Bonferroni significance is marked with a double asterisk. The ERP response at this electrode is noisy and difficult to discern. There is a negative peak in the IPB-2 condition 300-400ms, this is behind a spike in the IPB-1 condition at approximately 320ms.

The N400 is hidden behind a noisier response but the clustering of the response makes it unlikely that this is an artefact in the data.

4.5.1.3 Switch-Positive

Without MCC there were indications of a SP 840-890ms at CP1, CP2, P3 and P7. This response is shown in Figure 4.70. The ERP of this response at P7 is shown in Figure 4.71.

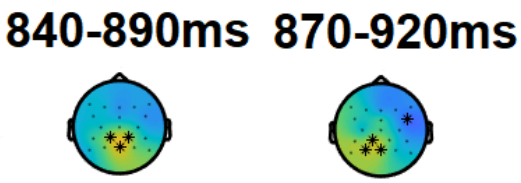

Figure 4.70 PD2's weakly significant components in the IPB-2 condition

Weakly significant ($p<0.021$) SP and RON components are visible 840-920ms.

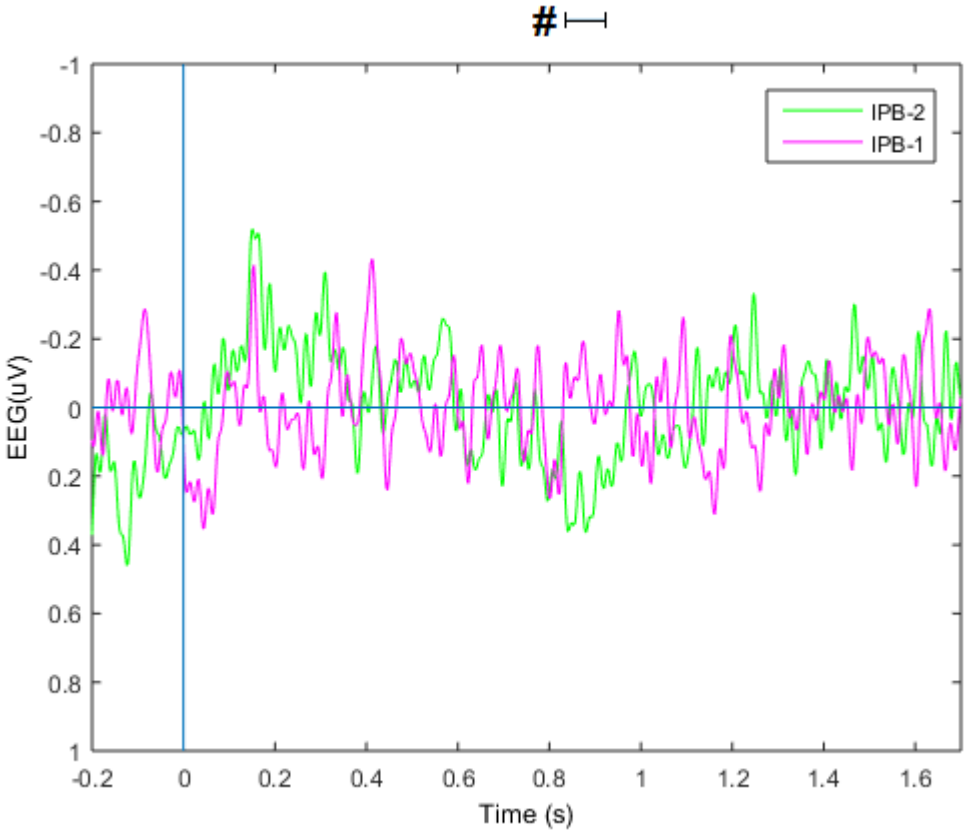

Figure 4.71 PD2's ERP plot at the Pz electrode in the IPB-2 condition.

The IPB-2 condition is shown in green and the IPB-1 condition shown in purple. The 840-920ms interval of significance without MCC is marked with a hash. A positive component can be seen in this interval.

PD2 elicited an increase in delta power at FCz, an N400, and a possible P3a. They also showed indications of a weakly significant SP and RON.

4.5.2 IPB-0

In the IPB-0 condition, results of 10k MC simulations t(58) returned no significances with cluster nor Bonferroni correction. There were no components in the IPB-0 condition indicating that PD2 did not have a significant response to the IPB-0 condition. This is similar to the HS group as a whole. Due to this negative result, there are no topographies or ERPs to show.

Chapter 5

Discussion

5 Discussion

The aim of the current study was to design and implement a protocol suitable for studying impaired processing of linguistic prosody in people with PD. To fulfil this aim, a study was designed, tested on a Pilot cohort, implemented with a 36-person HS cohort, and preliminary data gathered on two people with PD. To establish if the study successfully met this aim the current section discusses these results by answering the research questions laid out in Section 2.7.2. Firstly, the discussion examines whether the current protocol was successfully able to elicit the attention orientation components and the prosody expectancy components in response to linguistic prosody in healthy older persons. The discussion then examines both of the PD case studies and discusses their results in the context of the findings of the HS cohort. Finally, the discussion examines the Probe Task, and whether the use of linguistic prosody combined with the probe task can answer questions about the guiding and control of attention.

5.1 Does the HS cohort show the full range of attention capture and orientation markers in response to the linguistic prosody?

The current protocol made use of transitory attention capture processes to elicit the attention orientation EEG components in the IPB-2 condition. These components are the N100, P3a, RON, and delta activation. The current section discusses each of these features and their occurrence in the HS cohort in turn.

The IPB-2 condition elicited two early frontal negative clusters; front left at (-50-170ms) and front right (-50-110ms) (Figures 4.13 & 4.14). Unfortunately, anything occurring prior to 0ms has a pre-stimulus origin so cannot be an N100, however the pre-stimulus component may overlap with an N100. To establish if this is the case, it is necessary to identify the cause of the pre-stimulus negative. In the IPB-2 condition, the IPB on the penultimate word tells the listener that this is the final word. The task tells the listener to memorise this final word. The participant therefore treats this word as a target. Targets elicit P3bs (Sawaki and Katayama 2006, Katayama and Polich 1998). Frequently, P3bs are preceded by an N200 in an N200-P300 complex. This combination is often elicited in paradigms that require response inhibition on the part of the participant (Boucard et al. 2012, Laurent et al. 2001, Ramautar, Kok and Ridderinkhof 2006), as well as in working memory tasks (Covey et al. 2018, Covey, Shucard and Shucard 2019), and in paradigms with conflicting stimuli that require a conflict monitoring response from the participant (Azizian et al. 2006). In the current study the participant is expected to identify the penultimate word as a target due to the IPB. As the task requires a delayed response, the participant also inhibits any response to this target until they are cued by the probe word. Functionally therefore, an N200 (although not wanted) can be expected. Topographically, these clusters also match the N200. Between the offset of the penultimate word and the onset of the final word there is a 250ms gap. -50ms (i.e. 200ms after the offset of the final word) is therefore within the latency at which an N200 would be expected to peak. This is an unfortunate confound as the N100 is expected to peak 80-120ms. These components would therefore overlap almost exactly. Regardless, there is reason to believe that an N100 occurs in this time-window. 0ms is the onset of the final word, this word follows an IPB, it therefore has the same prosodic structure as a sentence onset word. Sentence onset words elicit an N100 (Hahne and Jescheniak 2001) as do those that are made salient using prosodic stress (Gonsalvez et al. 2007, Sanders and Neville 2003). Words with prosodic stress have anterior and lateral N100 as opposed to unstressed which have medial (Sanders and Neville 2003). The final word was unexpected and salient due to the prosody, the task demands and the use of filler stimuli. To elicit an N100, the incoming sound should be salient, novel and have no referent (Berti, Vossel and Gamer 2017, Berti 2013, Berti 2012, Escera and Corral 2007). Topographically, the clusters were anterior-left and anterior-right which is the topography expected of an N100 elicited to words that are stressed

using prosody. There is therefore likely an N100 but due to the occurrence of overlapping components, the presence or absence of N100-like components in patient groups using this protocol should be interpreted cautiously.

Early frontal negative clusters may also be indications of the occurrence of an MMN, it is necessary therefore to rule out the occurrence of an MMN. Many of the stimulus features and responses to these features that make an N100 likely are shared by the MMN. Namely, an attention capture process was occurring (Escera and Corral 2007), and a memory updating process was occurring (Justo-Guillen et al. 2019). The stimuli used in the current study fulfilled criteria that have been sufficient enough to elicit a MMN in literature; namely, the stimuli were salient (Berti, Roeber and Schroger 2004) and delivered in an unpredictable manner (Yabe et al. 1997). Furthermore there is precedent in the literature for using incongruous prosody to contrive this salience and unpredictability (Zora et al. 2016b, Zora, Heldner and Schwarz 2016a). However the MMN is a front-central component that peaks approximately 100-250ms post-stimulus onset (Winkler 2007, Escera and Corral 2007, Justo-Guillen et al. 2019). The anterior negative elicited by the current protocol was an anterior bilateral component with no central clusters that was too early to be an MMN. Functionally, the current stimuli were not presented in an oddball fashion. Each stimulus was presented with equal frequency so there was no memory trace from which to detect a violation from and if there was, an MMN would also be expected in the IPB-0 condition but there was no early frontal negative in that condition. There was therefore an early frontal negative in the N100 latency that did not match the latency or function of the MMN. There was therefore likely no MMN.

The P3a occurred 270-380ms and 270-350ms with cluster and Bonferroni correction respectively. This was a highly salient component that was significant with both forms of MCC. The P3a is known to peak 220-280ms (Berti et al. 2017, Berti 2013, Barry, Steiner and De Blasio 2016), this corresponds with the current results. There was no nP3 which is a later and more parietal component peaking approximately 360-450ms (Barry et al. 2016). The presence of a P3a in the absence of an MMN is evidence of the transient mode of attention capture having occurred. Cluster and Bonferroni MCC showed a clear and salient P3a. The P3a is related to both the N100 and the MMN. The N100, when elicited in response to transient cues is often followed by a biphasic P3a and nP3 lasting approximately 250-350ms (peaking 247ms) and 220-320ms (peaking 235ms) respectively (Barry et al. 2016, Escera and Corral 2007, Escera et al. 1998, Berti et al. 2017, Berti, Grunwald and Schroeger 2013). The MMN is elicited in response to deviant cues and is followed only by the initial P3a (Munka and Berti 2006, Escera et al. 1998, Berti et al. 2013, Berti 2008). The current study showed no MMN and a possible N100 followed by a P3a, indicating transient detection but this, unusually, was not followed by an nP3. A study by Berti (2017) showed that when the interstimulus interval is in transient detection trials is ≤1s in

younger participants and ≤0.5s in older participants, the N100 was still elicited but was followed only by the early P3a. In the IPB-2 condition the participant was focused on the penultimate word due to the prosodic boundary. They then refocused on the ultimate word. Both words were essentially two cues and the length of time between the two words equivalent to an interstimulus interval. The length of time between the ultimate and penultimate word was always 250ms. This is a short interval and falls below the 500ms required to elicit only the P3a and not the nP3. There was therefore a highly salient P3a component which was topographically and temporally congruent with the P3a in literature. There was no nP3 component and this too aligns with what is known about how the N100, P3a and nP3 respond to rapid stimuli. There is therefore strong evidence that the P3a occurred in the HS cohort.

The absence of the nP3 can also reveal information about how the linguistic prosody was processed by the cohort. A study by Berti (2013) argued that the N100 stream of attention capture is more efficient than the MMN stream of attention capture. The nP3 has been shown to be linked to the physical *orientation reflex*, this response was therefore absent in the HS cohort. This may have been due to the streamlined processing of continuous streams of speech. As discussed in Section 2.6.1, the attention ERP components can be elicited in response to a distracting stimulus or to switch cues. The interstimulus interval study by Berti et al. (2017), in which it was shown that only the early P3a is elicited to rapidly presented stimuli, was an oddball task using rare novel stimuli as deviants. The deviance in that study is detected due to bottom-up salience detection therefore the P3a elicited in that study is governed by exogenous attentional processes. This was therefore a distraction study. The current study made use of IPBs in a manner similar to the studies of Honbolygo et al. (2016) and Eckstein and Friederici (2005). These studies did not report P3as. The occurrence of the P3a in the current study must therefore be a result of the difference in task demands which result in changed top-down processes i.e. endogenous attentional processes. Furthermore, the IPB-2 condition caused the participant to focus on the penultimate then ultimate word. This is an object-switch, something governed by endogenous attentional processes (Frenken and Berti 2018). This shows the ISI effect occurs in switch paradigms as well as distraction paradigms. This indicates that the processes marked by the nP3 and P3a do not differ when elicited by distracting or informative stimuli.

The next component the current study sought to elicit was the RON. The current study found an anterior negative 630-720ms (Figures 4.24 & 4.25). This latency and topography is consistent with a RON which is commonly found anteriorly 450-700ms (Justo-Guillen et al. 2019). The RON is often described as indexing the reorientation of attention back to the relevant aspects of a task following distraction (Justo-Guillen et al. 2019). This definition stipulates that the RON only appears in response to stimuli that are not task relevant. This early theory developed from results that indicated that task

relevant stimuli do not elicit the RON (Schroger and Wolff 1998) and its attenuation being linked to poorer task performance (Mager et al. 2005, Berti et al. 2013, Berti 2013). The RON however has been elicited in cues signalling object-switches (Berti 2008) and task-switches (Hoelig and Berti 2010) i.e. cues essential to completion of the task. The RON can therefore be elicited to task relevant switch cues when presented as infrequent deviant in an otherwise regular sequence of stimuli. The current study does not have an oddball style. In the IPB-2 condition the participant memorises the penultimate word before they hear the final word. In this sense the IPB-2 condition resembled a distraction paradigm in which an unexpected/transient cue is heard. Transient cues elicit an N100, P3a and RON in the absence of an MMN. When listening to an utterance, irrelevant and ambient noise is filtered out. Entering the transient mode of attention capture (signalled by the N100-P3a-RON in the current instance) signals that a stimulus has overcome this internal filtering (Berti 2013). Correa-Jaraba et al. (2016) found that novel, unexpected stimuli elicit larger RONs than those presented in an oddball fashion. Surprise and salience are therefore stimulus features that are important to eliciting the RON. In the IPB-2 condition the participant focuses on the penultimate word before hearing the final word. Under these circumstances the final word may be treated as a (transient) distraction in the first instance. This is congruent with the theories that the RON reflects allocation of attention to relevant information (regardless of whether it is new information or old information that has been distracted from (Hoelig and Berti 2010)) or the selection of an adaptive response (Berti 2013). Attenuation would result in poor task performance under these definitions as well. This therefore holds true in the absence of an oddball presentation, as long as that information is surprising and salient or presented as a distraction. The RON-like negative in the current paradigm occurred 630-710ms. This is in the latter period in averages cited in reviews and the RON is frequently reported as occurring prior to this (Justo-Guillen et al. 2019). The latency of the RON is heavily age-dependent (Correa-Jaraba et al. 2016, Mager et al. 2005, Tusch et al. 2017). Correa-Jaraba et al. (2016) reports that the RON peaks at 650ms in participants 65 and above which corresponds neatly with the current study's result.

Finally, the current study sought to elicit evoked delta which has been linked to switch tasks and to the P3b and nP3. The current study elicited clusters of delta 50-650ms. This delta activation can be linked to the occurrence of the P3a and to the task demands. Prada et al. (2014) made a direct link between the nP3 and delta activation in response to a task-change. de Vries et al. (2018) found frontal delta activation in response to an object-switch. P3as have been elicited in response to object-switches (Frenken and Berti 2018, Berti 2016, Berti 2008). The P3a and delta activation have therefore been elicited separately in response to object-switch cues. The current study showed a P3a 270-380ms at electrodes Fz and FCz (See Figure 4.17), with this being most salient at FCz (Figure 4.18). The current study also showed a cluster of delta activation at Fz and FCz 50-450ms (with more widespread

activation continuing to 650ms) (Figure 4.4.20). The delta activation therefore prefigured and then overlapped (temporally and topographically) the P3a (See Figure 4.23 for an ERP representation with the delta activation overlaid). There are a number of studies that elicit a P3a to object-switches (as well as to task-switch cues and surprising cues). These studies show the P3a is expected (Berti et al. 2017, Berti 2016, Hoelig and Berti 2010, Berti 2008). The P3a is thought to index the top-down control of attention towards an incoming stimulus (Barcelo et al. 2006, Hoelig and Berti 2010, Berti 2008, Barry et al. 2016), as is delta activation (Helfrich et al. 2017, Johnson et al. 2017, Breska and Deouell 2017, Daitch et al. 2013, de Vries et al. 2018). The occurrence of both in the current study made the link between the two processes explicit.

There are some interesting differences in the delta activation of the current study and in the task-switch paradigm of Prada et al. (2014). The delta activation elicited by Prada et al. (2014) peaked centrally and parietally 300-400ms. This has a later latency than the current study (although there is temporal overlap) as well topographically different to the current study that showed frontal delta activation. Prada et al (2104) elicited the nP3 rather than the P3a. There are methodological differences that account for this difference in components. In the protocol of Prada et al. (2014), there was always a cue prior to the target and 50% of the time this was a switch cue. There was also an interstimulus interval 800-1500ms. So while the sequence of their switch and repeat cues was random, the occurrence of *a* cue was regular (i.e. there was a cue 100% of the time). The P3a is associated with cues that are salient, unpredictable (Berti et al. 2017, Berti 2013, Berti 2012, Escera and Corral 2007) and have a short ISI (Berti et al. 2017). Due to the task demands of the current study and the use of misleading prosody that occurred p=0.29 (as well as filler conditions that exacerbated this unpredictability), the occurrence of the final word is surprising. Furthermore, the length between the penultimate and ultimate word was 250ms, essentially a short ISI. These methodological decisions are what caused a P3a rather than nP3 to be elicited. The P3a has a shorter latency and more anterior location than the nP3, it is interesting that the delta activation mimics this. The surprise element may account for the quicker recruitment of delta power; delta activation indexes the recruitment of attentional resources and it stands to reason that surprising stimuli demand a quick response. This hypothesis complements the data showing recruitment of the shorter latency transient attention pathway (Section 2.6.1).

In addition to these components alpha power suppression occurred 300-800ms in the HS group (Figure 4.30). Alpha power is linked to attention, with increased alpha power indicating a stimulus has been ignored or the response towards it inhibited (Kelly et al. 2006, Thut et al. 2006, Jensen, Bonnefond and VanRullen 2012, Janssens et al. 2018). Conversely, reduced alpha indexes increased task difficulty and has been elicited to object switches (de Vries et al. 2018) and task switches (Sauseng et al. 2006,

Mansfield, Karayanidis and Cohen 2012, Prada et al. 2014). Studies examining alpha most frequently examine total power or induced power. The current study indicates that there is a corresponding evoked suppression of alpha power in response to a salient and surprising prosodic cue.

A number of studies have elicited the MMN in response to linguistic prosody in a various languages. These used single words presented in an oddball presentation. The stress on these words varied infrequently which elicited an MMN (Zora, Rudner and Montell Magnusson 2019, Zora et al. 2016b, Zora et al. 2016a, Zora, Schwarz and Heldner 2015). These studies did not elicit a P3a or RON. As the MMN only marks deviance detection at the earliest stage it cannot be used to infer that the prosody has been fully processed. The P3a occurs when a stimulus has been deemed significant enough to elicit it. If elicited in response to prosody it can be inferred that that the prosodic structure has been deemed significant. A study by Wang et al. (2005) did use prosodic stress to elicit an MMN and P3a in an oddball paradigm but in this study the prosody itself was not the deviance that elicited the P3a. In this study the deviant was an infequent change in consenant which was highlighted using prosodic stress, which was not in of itself incongruous. A study by Zhang and Shao (2018) elicited the MMN and P3a in Cantonese. This was in response to incongruent tone, a feature not present in English. The occurrence of the P3a, delta and RON in the current study can be used to infer that the prosody or the final word has been deemed functionally significant to the listener. The current protocol therefore successfully elicited the latter attention orientation components in a way that has not been previously done to the author's knowledge and these can be used to mark the processing of prosody.

In summary, the current study successfully elicited a clear and salient P3a, RON and evoked delta in the HS cohort. The combination of the unexpected prosody combined with task demands that caused the participant to switch their attention from the penultimate to the ultimate word caused a switch in attention that elicited the P3a, RON and evoked delta. There is evidence that an N100 also occurred but as this overlapped with a pre-stimulus effect, its occurrence or absence in patient groups must be interpreted cautiously.

5.1.1 The N400

The study of Eckstein and Friederici (2005) elicited an N400 in repsonse to a double IPB. This component occurs in response to incongruous syntax. This component is not one of the attentional components targeted by the current study but if it were to occur then it too would be a useful proxy marker for intact prosodic perception. The N400 is therefore discussed in this section.

The HS group elicited an N400-like at P7 330-380ms (Figure 4.36), this is only over a 50ms time-window but this is the time-window in which it is significant with Bonferroni MCC so it is likely only capturing the peak of a larger component. There is also a weakly significant (P<0.021, no MCC) N400 at P8 (Figure 4.38). The N400 therefore appears to only occur at the peripheral parietal electrodes. This side-lining of the N400 can be interpreted in two ways. The first is that the linguistic repair processes that the N400 indexes have been superseded by the task demands of the Probe Task. The second is that there are other components occurring in the same time window that overlap with and therefore cancel out the N400. The latter would be the case if the participant identifying the penultimate word as a target results in a P3b in the time-window shared by the N400. Such an overlap would obscure the component. The appearance of the component in the HS group, however marginalised is evidence that a syntactic repair process is occurring as a result of the prosody. The N400 can therefore be used as a marker in the individuals in which it appears but it is more difficult to make confident inferences based on its absence in any individuals. The N400 was visible in S10 (Figure 4.42) and PD2 (Figure 4.68). The N400 can therefore tell us that a syntactic repair process as a result of the incongruous prosody did occur in PD2. This is congruent with his behavioural results (Figures 4.57 & 4.58) which showed they were unimpaired in their interpretation of prosody.

The N400 has been found to be present in people with PD, albeit sometimes at a later latency (Dissanayaka et al. 2017, Angwin et al. 2017, Friederici et al. 2003). Of the people with PD who took part in the current study, only PD2 (H&YI) showed an N400. It is notable that the N400 is highly diminished in the HS group so its absence in the PD group does not signal a group difference. The effect of the task demands and the possibility of other components overlapping the N400 means its elicitation in the current protocol does not make it a good candidate as a marker for prosodic perception. However future work examining the N400's relationship to prosody could explore whether ancillary language processes are carried out when they are not necessary for the completion of the task or whether these processes are subordinate to attentional or prosodic processes.

5.2 Does the HS cohort show the full range of prosodic reanalysis markers in response to the linguistic prosody?

The current study sought to elicit a RAN and PEP in the HS cohort in the IPB-0 condition. There was no indication of either of these components occurring in the group with or without MMC. There are three factors which may explain the absent RAN in the HS group. I) Differences in task; II) Differences in stimuli used; III) Differences in age. Each of these are discussed in turn.

The RAN was targeted in particular due to its insensitivity to task effects (Honbolygo et al. 2016, Eckstein and Friederici 2005). This was particularly important in the study of prosody. A component was needed in which the participant would not have to answer a question about prosody to complete the task. The Probe Task was a working memory task. In some circumstances a working memory task may be sufficiently engaging for incongruent prosody to be ignored. However this is not likely to be the case in the current study. The task asked the participant to listen for the final word and the prosody of the sentence conveys to the listener which word is the final word. It is therefore necessary for the participant to listen to the prosody in order complete the task, this makes them more likely to detect the incongruency. It may be the case that this group ignores the prosody completely and listens only for the final word. This would require listening to the sentence but ignoring its prosody and using instead the absence of any more words as the cue that the utterance has ended. The presence however of the attentional components in response to the IPB-2 condition is strong evidence that the participants did not listen to the sentences in this unusual and cognitively costly manner. Further evidence of the use of prosody to complete the task is the presence of the RAN in the Pilot cohort (Figure 4.5 & 4.6). The task demands may have affected the older cohort differently from the younger cohort but this is an age effect rather than a task effect. The PEP in response to linguistic prosody is task sensitive. It has been shown to be absent when a task asking participants to identify incongruous semantics was used (Astesano, Besson and Alter 2004). However the PEP in response to linguistic prosody was elicited in a study when in which participants were asked to evaluate the emotional content of prosody (in this study the utterance had a linguistic prosody violation spoken with an emotional prosody) (Paulmann, Jessen and Kotz 2012). In this latter example, the participant is still explicitly asked to assess the prosody which may be enough to draw their attention to the non-emotional aspects of that utterance's prosody. The task used in the current study was designed to implicitly draw the attention of the listener to the prosody in a similar manner. In the case of the older HS cohort this has not worked. There may be a task effect that older participants are more sensitive to. This can be confirmed with a study examining multiple tasks in older and younger participants.

An alternative possibility is that the stimuli used in the current study are not able to elicit a RAN or PEP. For this to be true, they would have to be sufficiently different from the stimuli used by Eckstein and Friederici (2005). The current study aimed to produce a RAN through the use of sentences with an absent IPB. The study of Eckstein and Friederici (2005) cross-spliced German sentences to create an incongruent prosody. The sentences used in that study ended in verb-noun pair. A resetting of the pitch contour on the final noun created the false expectancy of an additional incoming word. Where this differs from the current study is that in the IPB-0 condition there is a rise in pitch on the final word but in the study of Eckstein and Friederici (2005) the pitch rises and then falls. So, while a false expectancy is created in both studies, two different uses of pitch are used to achieve it. German has grammatical features that aided in the cross-splicing of sentences. In German, a statement that has only one clause has the same word order as English, namely, verb-noun (or verb-object) i.e. "bakes cakes". This verb-noun word order is inverted ("cakes bakes") in German when the verb and noun are part of a subordinate clause. This feature, not present in English, facilitated the cross-splicing of prosodies to produce natural sounding (but incongruent) stimuli. The use of a rising intonation spoken by a trained SLT was used to insure the IPB-0 condition was both salient and natural. To prime the participants expectancies two filler conditions were used Filler-Short and Filler-Long, one of which contained this rising intonation followed by a clause (See Figure 3.4e). If the rising intonation resulted in the participant interpreting the stimulus as a question, there would be no semantic and prosodic divergence and therefore no RAN. Is this the most likely scenario? There is sparse information on ERP differences in declarative or interrogative intent in the ERP literature. Two studies showed MMNs when interrogative/declarative intent is presented in an oddball paradigm (Leitman et al. 2009, Borras-Comes et al. 2012). The IPB-0 condition is not rare enough to be a typical deviant. There is little to indicate in the literature that a simple statement or simple question produce different ERPs but little to rule it out either. An alternative approach to determine the likelihood of this scenario is to look at the semantics of the stimuli. The sentences used are not semantically formed as a question (Bailey 2010). Prosody can be used to form *declarative questions* in English in instances in which a question word order is not used (Bailey 2010). Declarative questions express doubt on the part of the speaker and invite contradiction from the listener who is assumed to be more knowledgeable (Brown, Karen and Kenworthy 2015). The sentences were identified as incongruous by the participants with a median score of 100%. This suggests that the participants did not interpret the prosodic structure of the IPB-0 condition to be a question. Only a post-EEG questionnaire however would have been able to address this question explicitly. Another question this raises is whether a declarative question elicits a PEP at the point when the prosody diverges from that expected by the semantics. Sudden changes from neutral to interrogative have been shown to elicit a PEP (Paulmann et al. 2012, Astesano et al.

2004, Kotz and Paulmann 2007) due to this divergence. These previous studies differ from the current one in that cross-splicing was used to achieve the effect. The EEG probe task did not require the participant to make explicit judgement of the prosody. It may be argued that such a task makes it less likely for a component such as the PEP to be elicited. However it has been found that tasks that not only do not require explicit judgements of prosody but that actively distract from the prosody do not cause an attenuated PEP in response to both linguistic and emotional prosody (Paulmann et al. 2012, Astesano et al. 2004, Kotz and Paulmann 2007). The task in the present study was intended to draw the attention to the prosody implicitly so, if the utterance was interpreted as a question, a PEP should be expected. While the stimulus affect may be sufficient enough not to elicit a RAN, in the absence of other effects, an incongruous rise in intonation should have elicited a PEP. The differences in stimuli may be the reason a RAN was not elicited but is less likely to be the reason a PEP was not elicited. Data gathering on the participant's interpretation will be necessary in future studies.

Finally, a major difference between the current study and previous studies eliciting the RAN (Eckstein and Friederici 2005, Honbolygo et al. 2016) was the age of the participants. The RAN is present in the pilot cohort (aged 22-30). The median age of the HS cohort was 68. The older controls did not elicit a RAN-like response. Studies have reported that persons over 60 experience a non-sensory decline in their ability to interpret prosody including the ability to identify questions (Mitchell, Kingston and Boucas 2011, Mitchell 2007). If prosodic processing were interrupted in the latter stages (such is a non-sensory interruption) this may translate to an absent late-latency component such as the RAN. Prosodic and semantic integration indexed by N400 has shown to be reduced in older participants (Steinhauer et al. 2010, Faustmann et al. 2007). The PEP has been examined in stroke survivors, these participants had an average age of 49 and emotional prosody was used (Paulmann, Pell and Kotz 2008). The median age of the HS cohort was 19 years older than the mean age of the stroke study. The age of the youngest HS was also 10 years older than the mean age of the stroke cohort. There may then be age-related decline in persons over 60 which may or may not be particular to the RAN and the linguistic prosody PEP. Older participants have been shown as more likely to judge ambiguous prosody as congruous compared to younger participants (Steinhauer et al. 2010). This change in perception would result in participant being less likely to interpret prosody as incongruent. The absent RAN indicates that this difference in perception occurs as early as 500ms from the onset of the anomaly. This is not 500ms from the absent IPB as the ERP is measured from the onset of the final word. There therefore may be a pre-symptomatic change in sensitivity due to age that is shown by the absent RAN and PEP. Studies examining changes in how healthy older adults interpret emotional prosody have failed to link to age-related hearing loss or narrow it down to an impairment in a particular cognitive domain (Schorer et al 2020; Dupuis and Pichora-Fuller 2015; Mitchell 2007). If

there were changes in how prosody was interpreted in the HS cohort due to age-related changes in cognition in this group a RAN and PEP would likely still be present as rapid prosodic reanalysis processes would still be intact. The difference in that case would be seen in the explicit prosodic judgements made in the behavioural tasks. The absent RAN and PEP therefore support the theory that this difference is not due to a change in cognition. Schorer et al (2020) found evidence that differences in how older persons interpret prosody may be due to how they use contextual cues, particularly semantics and syntax. The IPB-0 condition is an unusual prosodic structure. As this structure is not signposted in anyway by the syntax of the stimuli used (an example of this would be using angry syntax to accompany angry prosody) it may be the case that it was less salient to the HS cohort and therefore not salient enough to elicit a convincing EEG response. The findings of the current study therefore fit with what is currently known about how healthy older persons interpret prosody. The HS group with a median accuracy of 100% deemed IPB-0 incongruous in the behavioural task (Figure 4.58). There may be a lessening of sensitivity to prosodic affect in older persons. The current study therefore provides evidence of an age-related change to prosodic sensitivity that makes the RAN unsuitable for use in older persons with PD. A more comprehensive study into the age effect on the RAN and PEP with a larger young adult cohort is necessary to confirm this finding. It would be of particular interest to view the difference in the emotional-PEP and linguistic-PEP as the former is more salient and functionally important. This would determine if this age-related change in sensitivity occurs only to linguistic prosody or if it also occurs in response to emotional prosody.

In summary, the current study failed to elicit a RAN or a PEP. This may have revealed an age effect to these components which needs to be confirmed with a larger young cohort.

5.3 Case Studies

5.3.1 PD1

There are multiple factors that are necessary to consider when examining PD1's results. PD1 was the oldest participant and had the lowest ACE-30 score of all the participants who took part. In addition to this, he had moderately advanced PD, being at H&YIII, and was on dopaminergic medication (but their dose and status are not known) at the time of recording. PD1's results in the behavioural tasks and their EEG response are discussed with these factors considered.

5.3.1.1 Probe Task

The current protocol is designed to examine the perception of prosody in PD. A fundamental design criteria was an EEG task that people with PD who may or may not be able to understand prosody have no difficulty completing.

PD1 scored 139/140 in the probe task. This is the same as the median response of the HS group. This indicates that this participant did not find the task difficult and that their H&Y stage, age and ACE-30 score did not cause them to perform differently in the task from people without PD. This is promising initial data on the suitability of the EEG task for use with people with PD with complicating factors.

5.3.1.2 Discrimination and ID Tasks

The Discrimination Task and ID Task sought to assess participants' ability to discriminate and identify prosodic structures. The former of these tasks does not require explicit decoding of the prosody while the latter does. This is an important distinction with literature most often finding an impairment in one of these processes does not always result in an impairment in the other (Caekebeke et al. 1991, Ventura et al. 2012, Scott, Caird and Williams 1984, Lloyd 1999, Pell 1996, Blonder, Gur and Gur 1989). PD1 scored 30/30 in the Discrimination Task (two above the median of 28) and 14/15 (one below the median of 15) in the ID task. PD1 therefore showed no difficulty in discriminating or identifying linguistic prosody.

PD1 scored the lowest in the ACE-30 of all participants who took part. Impaired perception of *emotional* prosody has been linked to reduced working memory, executive dysfunction and mild cognitive impairment (Gray and Tickle-Degnen 2010, Kwan and Whitehill 2011, Benke, Bosch and Andree 1998). In this instance, a lower ACE-30 score did not result in a lower score in the recognition of linguistic prosody.

PD1 was H&YIII at the time of the study. Being at a moderately advanced stage of PD and not having an impaired ability to discriminate or identify prosody fits with what is known about the non-linear progression of non-motor symptoms in PD (Halliday et al. 2008, Erro et al. 2013, Tremblay et al. 2013).

5.3.1.3 IPB-2

Analysis failed to find a significant P3a in PD1. This is consistent with previous studies that have shown absent or reduced P3as and nP3s in people with PD (Hirata et al. 2002, Solis-Vivanco et al. 2011, Solis-Vivanco et al. 2015, Tsuchiya, Yamaguchi and Kobayashi 2000). A study by Solis-Vivanco et al. (2015) examined the P3a in persons with PD in H&Y stages 1, 2 and 3 found that reduction of the P3a predicts disease stage independently of other factors such as use of dopaminergic medication and presence of cognitive impairments (as measured by the Mini-Mental State Exam). That analysis failed to find a significant P3a in PD1 therefore fits with what is known about the P3a and people with PD.

In addition to PD, age has been shown to reduce the amplitude of the P3a in participants aged up to 73 years old (Pontifex, Hillman and Polich 2009, Brush et al. 2020, Cona et al. 2013). This is therefore a second factor contributing to a reduced P3a response.

An attenuated P3a has been found *not* to be linked with poorer performance in cognitive tasks (Lange et al. 2016, Porcaro et al. 2019). (This is in contrast to the P3b, which has been linked to poorer cognitive outcomes in otherwise healthy older people (Porcaro et al. 2019) and in people with schizophrenia (Kruiper et al. 2019). A reduced P3a in PD1 did not impact their score in the EEG Probe Task nor in their score in the either of the prosody tasks (Figures 4.57 & 4.58). The absence of the P3a therefore did not translate to poorer behavioural performance in this instance which is in agreement with previous research into the P3a and task performance. As the P3a amplitude correlates with PD progression, PD stage has to be controlled for in future work examining the P3a response to incongruent prosody.

There was weakly significant ($p<0.021$, no MCC) delta activation 200-450ms at FCz in PD1 (Figure 4.59 & 4.60). Evoked delta activation has been linked to the P300 and the nP3. Its presence in this study indicates that it also makes up the oscillatory component of the P3a. Its presence in PD1 is a possible indication that it may be easier to capture in instances in which the P3a has been attenuated or is absent. As the P3a and delta activation reflect similar processes, delta activation may be an additional measure of preserved attention capture responses in participants whose PD has moderately progressed.

5.3.1.4 IPB-0

PD1 was one of the few older participants to show indications of a RAN component ($p<0.021$, no MCC) (Figure 4.61). The presence of the RAN in PD1 can serve to indicate that prosodic reanalysis was preserved in this participant. This is an interesting occurrence as PD1 was at H&Y stage 3 and was using dopaminergic medication. This is the first study to attempt to elicit a RAN in participants with PD. This result however is somewhat overshadowed by the findings in the HS group that age affects the production of the RAN. So, while the presence of moderately advanced PD was not a barrier to eliciting this component in this instance, the value of this finding is limited by the more substantial age effect found in the HS group.

5.3.1.5 Summary

Three important considerations when examining the results of PD1 were: moderate disease stage, their use of dopaminergic medication and their score in the ACE-30. This participant scored comparably to the HS group in the Probe Task. This shows that he did not have difficulty in the EEG task. This participant scored comparably to the HS group in the discrimination and identification of linguistic prosody. This suggests that in this instance, these factors did not impede their prosodic recognition ability.

PD1 had an absent P3a which agrees with literature that finds the P3a diminishes with disease progression. A promising result from this case study is that when the P3a is diminished, it may be detectable in the frequency domain. This gives an additional mode of enquiry for future studies in instances when the time domain data may be difficult to read due to noise or particularly attenuated..

The most surprising result is a weakly significant RAN in this participant. The RAN was absent in the HS group, indicating an age effect of this component. The presence of the RAN in PD1's results suggests that age is a more important influence on the RAN than PD as the combination of both did not serve to inhibit its production.

5.3.2 PD2

PD2 was at H&Y stage 1, was not on medication and scored 100 in the ACE-30. They therefore provide in interesting comparator to PD1 who, by contrast, had more confounding factors complicating the interpretation of their data.

5.3.2.1 Probe Task

PD2 scored 138/140 in the probe task. This is one below the median response of the HS group. This indicates that this participant did not find the task difficult and did not perform differently in the task from people without PD and of a similar age. This is promising data that people with PD are able to perform the EEG task.

5.3.2.2 Discrimination and ID Task

PD2 scored 30/30 in the Discrimination Task (two above the median of 28 in the HS cohort) and 15/15 (the median of the HS cohort) in the ID task. PD2 therefore showed no difficulty in discriminating or identifying linguistic prosody. This indicates that he understood the task instructions and was able to discriminate and understand the linguistic prosody.

PD1 self-reported that their motor symptoms were mainly left-sided. The relationship between sidedness of motor symptoms and impairments in linguistic prosodic perception are not clear. Ventura et al. (2012) examined prosodic perception in people with right-sided and left-sided motor symptoms. They found that people with left-sided motor symptoms are more likely to have an impairment in the recognition of emotional prosody but not in discriminating linguistic prosody. This is therefore in agreement with PD1's results. The right-hemisphere has been linked to the ability to distinguishing statements from questions (Tong et al. 2005, Chien et al. 2019). Interpretation of IPBs differs from this form of prosodic judgment. PB1's results show that, in this instance, left-sided motor symptoms (implied right-hemisphere pathology) did not result in an impairment in recognising incongruous IPBs. It is therefore worth examining if these two forms of prosodic recognition are indeed distinct in future work. One of the few studies to examine linguistic prosody and sidedness found persons with right-sided motor symptoms had difficulty distinguishing different forms of prosodic stress (Blonder et al. 1989). It is therefore an open question whether people with right-sided motor symptoms are also more likely to have an impairment in interpreting IPBs. The results from this case study give an early indication that the current protocol is an appropriate method of examining this.

This participant is an example of someone at the earliest stages of PD not showing indications of an impairment in the processing of linguistic prosody. Future work examining the discrimination and identification of linguistic prosody in more people in the earliest stages of PD will be able to determine if there is heterogeneity in the response from the earliest disease stage.

5.3.2.3 IPB-2

PD2 elicited a P3a with Bonferroni and cluster MCC. In addition to this, they showed indications of a more weakly significant increase in evoked delta power, a RON and an SP. This suggests an attentional response similar to that of the HS group. This is preliminary data that these responses can be elicited in people with PD at H&Y stage 1 and that these components can therefore be examined in people with PD with a prosodic impairment.

It should be noted that this study used relatively few trials. It is therefore expected that examining individuals would return more weakly significant results due to fewer trials being averaged resulting in a smaller signal to noise ratio. Examining larger cohort would more confidently capture the desired components.

5.3.2.4 IPB-0

PD2 showed no indication of a RAN or PEP. Given the age-effect in the HS cohort this is result was expected and is more evidence that the RAN may not be a suitable component to examine prosody in older persons.

5.3.2.5 Summary

PD2 provides promising data that both the behavioural and EEG portions of the study work for people with early-stage PD. In the case of the EEG components, it is possible to extract high quality data and the sought-after components even at the individual level.

5.3.3 Can the case studies provide preliminary indications on the suitability of the study for use on people with PD?

The case studies give two examples of the EEG task being appropriate for someone at an earlier (H&YI) and more moderate (H&YIII) stage of PD. An important concern when answering this question is whether the study had an EEG task that was both able to elicit the anticipated EEG components while not being difficult to learn and carry out by people with PD. Examining the components elicited by PD2 can yield some insights on how the task was carried out by this person. PD2 showed a weakly significant SP without MCC. The presence of an SP reveals that an object switch was occurring in the IPB-2 condition. People with PD are frequently reported to be mentally inflexible and score poorly in the WCST (Dirnberger and Jahanshahi 2013). The two participants with PD did not have trouble with the particular object-switch occurring in the IPB-2 condition as their Probe Task scores were 139 and 138 out of 140. A review by Dirnberger and Jahanshahi (2013) examining executive functioning in PD hypothesised that people with PD do not have trouble with switching their attention, so much as complex task planning that requires top-down mediation. The current study made use of a Probe Task to increase the functional significance of the prosody and make it more salient to the listener. This

was necessary for the linguistic prosody to elicit the full range of ERPs but came with the risk of added task difficulty. PD1 who was at H&YIII had no difficulty in the Probe Task. This evidence that the current study managed to balance the prosodic salience and task difficulty and is likely suitable for use in people with early to mid-stage PD as a means to examine the processing of linguistic prosody.

All components were attenuated in the case studies. This was expected due to the nature of ERPs as individuals have fewer trials than groups as a whole. PD1 however showed the most attenuated response to the IPB-2 condition and this is congruent with literature that reports that attentional components are diminished both in older people and in people with more moderately advanced PD. The presence of evoked delta in this participant is an indication that an attenuated P3a did occur. This means that if this protocol is to be used in people with PD H&YIII, the use of a larger group may still capture it. That the P3a was captured in PD2 is a demonstration that the prosodic effect in the current protocol is salient enough to elicit the desired attention reorientation response so is therefore a useful tool in marking the processing of linguistic prosody in people with PD. This study also demonstrated the value of capturing the oscillatory content of the P3a. Significant delta activation was found in PD1 who had an attenuated or absent P3a. The study therefore provides a useful additional marker for people with PD who may have a diminished P3a response or data with a poor signal to noise ratio.

While the case studies are too few in number to make any inferences about the population of people with PD as a whole, there is nothing in their response to either the behavioural tasks or the EEG tasks that raises any concerns about the suitability of the study for use in people in PD. That the study was able to elicit meaningful components at an individual level using few trials is promising preliminary data that the study will yield important insights if carried out on a large cohort of people with PD.

5.4 Linguistic prosody as a tool to examine the attention capture processes

The current study elicited the attention components using a novel paradigm. This combination of linguistic prosody and attention switching revealed new information concerning how attention is captured and orientated. What the current results reveal about object-switching in the visual working memory is discussed.

5.4.1 Object-Switching, Task-Switching and The Switch Positive

The current study sought to prompt an object-switch by combining the incongruent prosody in the IPB-2 condition with the demands of the Probe Task. Through this it was possible to examine if object-switches are able to elicit an SP. The current study elicited a parietal positive 630-710ms (Figures 4.26 & 4.27) consistent with an SP, which is elicited parietally 400-600ms (Wong et al. 2018, Karayanidis and Jamadar 2014a). The current study has in common with studies that elicit the SP that an endogenous representation was altered in response to a cue. The current study differed from the literature in that, until now, the SP has only been elicited in response to cues signalling a rule change. In the current study there was a switch between two objects in the verbal working memory but the rules of the task remain unchanged. Current theories as to what the SP indexes are: reconfiguration of the stimulus-set (Karayanidis et al. 2011, Karayanidis et al. 2010); preparation in anticipation of the target (Karayanidis and Jamadar 2014b); and endogenous control of a task set (Capizzi et al. 2016). The SP in the current study occurred in the late end of commonly reported latencies. A review by Karayanidis (2014) identifies an early SP and a late SP peaking approximately 400ms and 600ms respectively. The hypothesise that the early SP marks disengagement from the old task set (something absent in the current study as there is no old task to disengage with). They hypothesise that the later SP marks preparation in anticipation of a target following the switch cue (a process likely to occur in the current study as the participant is preparing for the probe word following the surprise final word). An SP in the current study would be consistent with the theory that it indexes preparation. It is also consistent with the theory that it indexes endogenous control, however this theory would have to be generalised to include endogenous control of any internal set and not solely task-sets and stimulus-sets. Switches of attention have been generalised in an fMRI study which found changes in task-set, response-set and perceptual-set activated the same cortical networks (Kim et al. 2012). Eliciting an SP in response to a change in object representation suggests that this too makes use of the same switching processes. If the positive elicited in the current study is not an SP, then the parietal positive must be indexing a separate process that occurs contemporaneous to the object-switch. Parietal positives that occur in this time window are the P600 and P3b. The possibility of these ERPs occurring is discussed below.

The P600 is a central-parietal positive typically peaking after 500ms (Molinaro, Barber and Carreiras 2011). The P600 is classically elicited to syntactic rule violations (Frenck-Mestre et al. 2008, Molinaro et al. 2008, de Resende, Mota and Seuren 2019) and ambiguities created by garden path sentences (Osterhout and Holcomb 1992, Friederici 1995, Osterhout et al. 1994, Friederici and Mecklinger 1996). It has however been elicited to non-syntactic violations (Faustmann et al. 2005, Kolk et al. 2003) and violations that are entirely non-linguistic (Nunez-Pena and Honrubia-Serrano 2004). This has led to competing theories as to whether the P600 indexes a linguistic process (Friederici 2011) or domain-general attentional process (Sassenhagen and Fiebach 2019). In the former theory the P600 signals linguistic ambiguities being reattended (Kolk et al. 2003) or the mapping of syntactic information or in cases where semantics have elicited it, the integration syntactic and semantic features (Friederici 2011). The latter theory posits that the unifying feature is salience of the event and the P600 is in fact a P3b, delayed due to the additional complexity of linguistic processes compared to simple stimuli used in oddball paradigms (Sassenhagen and Fiebach 2019). The parietal positive is in a typical location and time for the P600 (Friederici 2011, Molinaro et al. 2011). The IPB-2 condition uses the prosodic boundary to create parsing difficulty that requires reanalysis. This IPB-2 condition is based on an incongruous prosody used in the study of Eckstein and Friederici (2005). In their study, the incongruous prosody with a double IPB (the condition most similar to the IPB-2 condition) did not elicit a P600 (n.b. this study does report a P600 but in the condition in which the IPB is absent (similar to the IPB-0 condition)). It has been suggested that grammatical structure violations elicit a repair process and garden path sentences elicit a reanalysis process (Friederici 2011). Reanalysis processes elicit a frontal P600 and repair processes elicit a parietal P600 (Friederici 2011). The distinction in these processes is not always clear and whether or not a P600 occurs can be dependant on the subjective interpretation of the participants (Osterhout and Mobley 1995). The IPB-2 condition required repairing of the utterance but not in the way typical of repair-P600s. In the IPB-2 condition the sentence was grammatically correct. It can therefore be argued either that a revaluation process occurred on delivery of the final word; or a repair process occurred in the form of attaching the noun to the verb. The parietal positive elicited in the current study more closely resembles the topography of a repair process (Friederici 2011) suggesting that if this were a P600, the participants repaired, rather than reassessed the utterance. A repair/reanalysis did not necessarily occur at all as such a process is not essential to the completion of the task. Literature on task demands on the P600 show that the P600 is reduced (Verhees et al. 2015) or absent (Schacht et al. 2014, Hahne and Friederici 2002) when performing a primary task that draws attention away from syntax. In a study eliciting the P600, Schacht et al (2014) used a probe task similar to the current study in which participants had to answer if a word displayed subsequent to the uttered sentence occurred in that sentence. The

syntactic errors in this study were not formed by prosody or speech effects. The probe aspect of this task differs from the current study in that it was not necessarily the final word that was being probed so the participant is focused on remembering the whole utterance and not just the final word. The probe task of Schacht et al (2014) resulted in an attenuated N400 and an absent P600. There is therefore evidence that primary tasks, and probe tasks in particular, result in attenuated or absent P600s. Furthermore, we know from the presence of the P3a and from the task setup that domain-general attentional processes are occurring, we cannot for certain say that syntactic reanalysis processes are occurring as these are not essential to a successful outcome in the task. Results from individual participants give crucial evidence that this is not a P600. The P600 has been found to require 20-30 participants to be reliably elicited (Yano et al. 2019) as opposed to the SP which can be elicited, not only in healthy individuals, but in individuals with PD (Lange et al. 2016). The current data showed the late parietal positive component in a number of individuals. S10 showed positive parietal cluster 690-710ms and positive Bonferroni significances 600-710ms (Figure 4.41). PD2 showed weakly significant parietal positives 840-890ms ($p<0.021$, no MCC) (Figure 4.70). This suggests the late positive parietal component, unlike the P600, is visible in individuals at a low number of trials. The P600 is also further attenuated by PD (Friederici et al. 2003) decreasing the likelihood that it would be visible in individuals with PD.

There is no obvious P3b in our data, it is necessary to ask if our data showed a delayed P3b rather than an SP. The oscillatory content in our data strongly suggests the presence of a P3a-P3b but not necessarily in the SP latency window. Evoked delta was present initially front-central and front-right before extending to parietal left up until 650ms. Increases in delta are associated with the P3b (Guntekin and Basar 2016), peaking and subsiding with the latter in unison. The increase in delta oscillations in the current study mirrors that of the P3a, it then extends parietally into the latter 300-650ms time window which is where a P3b might be expected. The increase in delta power ceases at 650ms. The SP occurs subsequent to this in the 630-800ms time window, making it less likely to be a P3b or an attention allocation process. The RON occurs in the same time window as the SP. If this were a P3b, the process of assigning of attentional resources to the incoming stimulus co-occurs with the (usually subsequent) process of utilising these resources to attend to the stimulus. No such clash occurs if this is an SP. If a P3b does occur it likely overlaps with the N400 (as the delta activation suggests) which would be an explanation for the N400 only occurring at the periphery (strongly ($p<0.021/20$ at electrode P7 and weakly at electrode P8 ($p<0.021$, no MCC)).

Finally, the case studies also showed that the parietal positive behaved in a way consistent with what is known about the SP. People with PD are often reported as having poor mental flexibility which manifests itself as impaired performance in the WCST. If the EEG in the current study constitutes a

switch in attention, then people with PD may find it difficult. In the Probe Task PD1 and PD2 scored 139/140 and 138/140 respectively (Figure 4.56). This shows the participants had no difficulty in the task. Lange et al. (2016) examined the P3a and SP in people with PD while carrying out a WCST. They found that participants were only unable to answer correctly in the WCST when both the P3a and SP were absent. PD2 shows a P3a (Figure 4.64 & 4.65) and a weakly significant SP 840-890ms ($p<0.021$, no MCC) (Figure 4.70). The SP may therefore be signalling successful endogenous control of the memorised word in response to the incongruous prosody. In this small sample the P3a and SP pairing are therefore responding in a way that is consistent with literature on people with PD. PD1 is a counter example in which the SP and P3a were absent but the participant performed similarly to the HS group in the probe task. PD1 elicited no ERPs in the IPB-2 condition. It is difficult to infer that an absence of ERPs in their case is an absence of underlying processes or that the EEG data is poor. This cannot be proven either way though with one sample. The presence of evoked delta suggests a present but attenuated P3a. It is likely that the noisy data combined with a P3a that was attenuated due to disease stage combined meaning no significant P3a was found. Alternatively, it is possible to complete the probe task without a switch of attention occurring if the participant ignores the prosody. Not responding to the incongruent prosody would be another reason for all of the ERPs being absent in the IPB-2 condition. PD1 was 81 at the time of recording, they are therefore the oldest of all in the cohort which would have the twin effect of dampening the ERPs generally (Cona et al. 2013) and dampening their response to prosody (Ben-David et al. 2019). It is therefore more likely in their case that the absence of ERPs is due to the poor quality of their EEG data.

There is therefore a parietal positive functionally and topographically consistent with a switch positive. This is evidence that the SP indexes a generalised switching process rather than a task-switch in particular. Given the wide variety of switch responses that have elicited the SP, this is not huge adaptation of the current theory of the SP but it is a significant one. It is known that the SP responds to changes in the cue-target interval (Karayanidis and Jamadar 2014b). Future work using cued object-switches to determine if the cue-target interval has an analogous effect on the object-switch SP and the task-switch SP can substantiate the current study's finding. The current study therefore provides evidence of a common task-switch and object-switch mechanism but requires confirmation with future work.

5.4.2 Verbal Working Memory and Visual Working Memory

The current study used incongruous linguistic prosody to direct the attention between two words. This resulted in EEG components associated with a switch in attention. These were the P3a (Figures 4.17 & 4.18), delta activation (Figure 4.20 & 4.21) and alpha suppression (Figure 4.30). The elicitation of these components allows us to examine the EEG signatures and processes that are common to switching of attention between visual WM representations and switching attention between verbal WM representations.

The current study elicited a P3a (270-380ms) (Figures 4.17 and 4.18) which is a correlate of object-switching (Frenken and Berti 2018, Berti 2016, Berti 2008) as well as task switching (Kopp et al. 2006, Perianez and Barcelo 2009, Lange et al. 2016). The object-switches that have elicited a P3a involve the processing visually presented numbers (Frenken and Berti 2018, Berti 2016, Berti 2008). This study extends the elicitation of the P3a to a cue signalling an object-switch in the verbal WM. This is not a surprising result as the P3a (along with the N100 and RON) is a correlate of top-down control of attention (Barcelo et al. 2006, Hoelig and Berti 2010, Berti 2008, Barry et al. 2016) not attention switching per se. Furthermore, the P3a (and N100 and RON) are most commonly elicited in distraction tasks using auditory cues (Section 2.6.1). Studies using task-switch cues have also already shown that the switching of attention that the P3a marks is not limited the visual domain. Task-Switches may involve the configuration of stimulus-sets and/or response set mappings (Hsieh and Wu 2011), neither of which involve the manipulation of endogenous visual representations. The P3a has therefore been elicited to cues signalling an object-switch in the visual WM and cues signalling a switch in task. The current study ties these together by eliciting a P3a in response to surprising prosody that signals a change of object in the verbal WM. This tells us that the P3a in the current study is playing a role in filtering and processing of exogenous stimuli rather than the direct control of endogenous representations.

The current study elicited frontal evoked delta activation 50-650ms (Figure 4.20 & 4.21) and alpha suppression 300-600ms (Figure 4.30). Increases in total, as well as evoked, delta power, have been shown to be top-down control of attention (Helfrich et al. 2017, Johnson et al. 2017, Breska and Deouell 2017, Daitch et al. 2013, de Vries et al. 2018). Alpha suppression has been elicited in studies involving object-switching (de Vries et al. 2018, Myers et al. 2015, Schneider et al. 2015, Schneider et al. 2016, van Ede et al. 2017) and task-switching (Sauseng et al. 2006, Mansfield et al. 2012, Prada et al. 2014). The combination of induced frontal delta (-75-1025ms) and parietal alpha suppression (peaking approximately 600-700ms) have been elicited in response to an object-switch in the visual WM (de Vries et al. 2018, Helfrich et al. 2017). This study and a later review that elaborated on them theorised that this oscillatory pattern of frontal delta activation followed by parietal alpha suppression

indexes control of specifically visual WM representations (de Vries, Slagter and Olivers 2020). In particular, that review proposes that this activation pattern signals the reprioritisation of the "current [visual WM] representation" and the "prospective [visual WM] representation." In a supplementary analysis de Vries et al. (2018) calculate that changes in induced power make up the significant contribution to their change in total power. The current study shows that a corresponding evoked delta and alpha response occur in response to a cues signalling an object-switch. The current study differs from de Vries et al. (2018) in a number of key ways. In the current study the memorised stimuli are auditory therefore cannot be stored as visual WM representations. Furthermore, there is no prospective representation that is being reprioritised; the listener hears one word then abandons it in favour of another. There are a number of studies pointing to delta activation and alpha suppression being generalised rather than particular to the control of visual objects. Delta activation consistently occurs in response to (oddball) targets as well as informative and/or salient cues (Basar-Eroglu et al. 2001, Demiralp et al. 2001a, Demiralp et al. 2001b, Prada et al. 2014). Parietal alpha suppression occurs in anticipation of expected auditory stimuli and the strength of suppression correlates with efficient behavioural processing of these cues (Mazaheri et al. 2010). Parietal alpha suppression has also been reported previously with the P300 in response to task-switch cues (Sauseng et al. 2006). There are also many studies showing the role of increased alpha power in filtering auditory distractions (Kelly et al. 2006, Thut et al. 2006, Jensen, Bonnefond and VanRullen 2012, Janssens et al. 2018). There are therefore ample studies showing alpha suppression in response to processed auditory stimuli and alpha activation in response to successfully ignored stimuli. The current results showed an evoked alpha suppression occurring in response to the same triggers. Given the frequency with which these oscillatory features have been elicited (separately) to studies examining the control and orientation of attention, as well as delta activation's close relationship with the P3 family of components, there is strong evidence that the P3a, delta activation and alpha suppression elicited in the current study index a reprioritisation process similar to those that occur in response to visual stimuli and that the delta activation indexes top-down control of attention, and alpha suppression indexes a filtering and reprioritisation process.

Chapter 6

Conclusions

6 Conclusions

6.1 Did the study fulfil its aim?

The current study aimed to elicit the attention orientation and prosody reanalysis component in response to linguistic prosody. To do this, a protocol was designed that combined incongruent prosodic structures and task demands in a novel way. In the case of the attention capture components this aim was successful. The P3a, RON and delta activation were convincingly elicited in the HS group. This was done while the participants listened to utterances with incongruent linguistic prosody. Studies of linguistic prosody so far have elicited the P3a in response to linguistic prosody using pseudowords, deviant tone in Cantonese and deviant consonants that have been highlighted using prosodic stress. All of these studies made use of single words presented in an oddball fashion. The current study dispensed with the oddball presentation and used utterances consisting of complete sentences. To make the linguistic prosody salient enough to elicit the latter attentional components it was necessary to increase the functional significance of the prosodic structure using the task demands. This is commonly done by asking participants to explicitly identify prosodic structures. The current study opted against this strategy as participants who are not able to identify prosodic structures would not be able to take part in the study. Instead, a Probe Task that specifically asked the participants to memorise the final word of the utterance was used. This served a dual purpose. The end of the utterance was signalled by the IPB. The participants would then be implicitly interpreting the prosody to listen to the end of the utterance. Secondly, in the IPB-2 condition, participants would falsely identify the penultimate word as the word necessary to complete the Probe Task. When the participant heard the final word, this initiated a switch in attention, a process that is made visible on the EEG by the attention capture components. It was through this novel task design that the P3a, RON and delta were successfully elicited. This protocol was designed to be inclusive of patients who are not able to explicitly identify prosody. PD1 and PD2 show preliminary data that people at the earliest stage of PD (H&YI) and more moderate stage (H&YIII) of PD are able to complete this task.

In the case of the prosody components the RAN and PEP, the current study was not successful in eliciting these components in older persons. This was in contrast to the Pilot cohort that showed a RAN and PEP with clustering and Bonferroni MCC. The Pilot cohort was smaller but the effect, $p<0.00105$ was large for both the RAN and PEP. The current protocol not eliciting the prosody components in the HS cohort has revealed an age effect. This age effect may mean that the components themselves are absent in older persons or it may mean that older participants interpreted the particular prosodic structure used in the IPB-0 condition differently from the younger Pilot cohort and so the processes that the RAN and PEP mark were not triggered. This effect can be fully described

in future work by testing different task conditions and different prosodic structures in younger and older people.

In summary, the aim of the study was partially met in that the attentional components were elicited in the HS group. Eliciting these components provides an EEG tool for studying the causes of impaired linguistic prosody that has so far been absent from the literature. The study failed in its aim to elicit the prosody components in response to linguistic prosody in older people but in doing so revealed an age effect. This too is an important finding as it means these components may be unsuitable for use in patient groups of comparable age to the HS cohort. This unfortunately includes many people with PD.

6.2 Summary of Findings and Their Functional Significance

This section summarises the current protocol's novel findings and their implications for future work in PD and prosody.

By using linguistic prosody to create a false expectancy, the current study elicited a RAN and PEP in the younger and smaller (n=8, 22-30yrs) pilot cohort but no such response in the larger older cohort (n=36, 59-78yrs). This indicates a possible age effect in the RAN and PEP components. This is clinically significant in the study of the perception of prosody in people with PD as it means these particular components are not useful in the study of prosody in persons above 59 years old. This rules-out a large part of the PD population. These components may still be useful for people with PD who are younger than 59. This result has now also raised the question of whether the PEP that occurs in response to emotional prosody is also absent in older persons. There is therefore possibly an important age-effect, which if confirmed, has important implications for the study of prosody in older persons with PD and in older persons generally. However, these components can still be of use in the study of prosody in clinical populations that have documented impairments in prosodic perception and a larger number of younger persons such as autism and schizophrenia.

The current study found a P3a in response to an object switch in the verbal WM. The P3a has been elicited to prosodic cues and task-switches but not to a prosodic cue signalling an object-switch in the verbal WM. This confirms the P3a's role in attention capture. In addition to this, the current study elicited an increase in evoked delta that overlapped temporally and topographically with the P3a. Delta activation has been linked to the nP3 and the P3b but never the P3a. This links the delta activation with all the components of the P300 family. Eliciting these together in healthy persons revealed an advantage to their use with people with PD. Evoked delta, which indexes top-down control of attention was elicited in two persons with PD at H&Y I and III. Prosodic processing can therefore be measured using this study in early to moderate PD. Moreover, this response was detectible (albeit with weak significance) in one participant who did not have a P3a (PD1). Delta activation may therefore be a more sensitive marker of the orientation of attention towards incongruent or salient prosody than the ERPs.

The incongruent prosody of the IPB-2 condition combined with the task demands of the Probe Task elicited a switch-positive (SP) component. The SP is a component consistently elicited in response to task-switch cues. These cues signal a change in rule. Using the current protocol, an SP was elicited in response to an object-switch with no change in rule. The SP is therefore not specific to the reconfiguration of rule sets. The parietal positive overlaps temporally and topographically with alpha suppression has been elicited to both task-switches and object-switches. Alternatively, object-

switches elicit a parietal positive functionally and temporally similar to the SP that has not before been documented. The SP was elicited by PD2 ($p<0.021$, Figure 4.70). PD2 also elicited a P3a-like response ($p<0.00105$, Figure 4.64 & 4.65). The interaction of the P3a and SP (as correlates of initial attentional and later orientation responses) has been studied in PD (Lange et al. 2016). The interaction was used in a WCST study to examine compensatory strategies in those who had an impairment in either one of these responses. Only participants who had neither an SP nor P3a were unable to complete the task-switch required by the WCST. By eliciting these components in response to a simpler object-switch, these compensatory strategies can be examined in people with PD when performing a less onerous task. These components can therefore be used as markers of mental inflexibility in response to prosody.

The salient linguistic prosody used in the current study elicited a RON. The RON has traditionally been linked to reorientation of attention back to the task following a distraction but more recent studies suggest the RON is a general reorientation of attention based on protocols that have elicited it in response to task-relevant stimuli. The current study elicited the RON to an unexpected task relevant cue. This is in agreement with more recent theories of the RON's purpose. The RON has been studied in PD and responds to dopaminergic treatment (Solis-Vivanco et al. 2011, Kahkonen et al. 2002). It also signals an essential part of orientation of attention. There is opportunity to use the RON as it was elicited in this study to examine how the orientation of attention in PD interacts with prosody and whether this response is affected by dopamine treatment. Furthermore, with the elicitation of the SP, there is opportunity to study how orientation of attention towards task relevant aspects of the stimulus and reconfiguration of the internal set interact in PD, for example can the task be completed with one or both of these impaired?

The results on the healthy cohort showed that parietal alpha suppression marks the later stage processing of prosody. This alpha suppression was not detected using any between-trial analyses. Alpha suppression therefore marks the processing of stimulus that is deemed relevant in healthy persons but is only detectable using the current protocol at the group level. Its utility in studying prosody in PD or the ways in which PD affects this marker remains untested as not enough persons with PD took part in the study to perform a group level analysis. Any future work using this protocol on a large cohort will show if PD affects the latter integration process shown by this marker.

In summary, the current study provides a control database that can be used to examine prosodic perception and attention switching in older pathological populations. The study has proven the utility of eliciting the attentional components (N100, RON, SP) in the examination of prosody. The EEG task is in four parts which together take less than an hour. This is important as older persons and persons

with PD may become fatigued in long-lasting EEG recordings. The method presented here has demonstrated its utility in capturing markers for the processing of linguistic prosody in pathological and healthy populations. This is an important step as linguistic prosody is understudied in both the ERP literature and PD literature.

6.3 Limitations

The findings of the current study are limited by factors related to how the data were collected, the tasks used and to the number of participants recruited. These factors limited the number of inferences which it was possible to make with the data. These limitations are detailed here.

6.3.1 Data Collection

The experiences of this study have highlighted ways in which the data collection used in the current study can be developed in future work. Speech and language ERPs are affected by the subjective response of the participant. The participants should have been interviewed following the EEG to evaluate their interpretation of the stimuli and to examine if it was consistent across participants. This limitation affects the IPB-0 condition more than the IPB-2 condition. The HS cohort responded differently from the Pilot cohort to the IPB-0 condition. This reveals a possible age effect but this effect may be due to a difference in how each group interpreted the rising intonation in the IPB-0 condition rather than a difference in how each group processes prosody. If the difference between groups is one of interpretation, this is still significant as it is still an age effect and it reveals that cultural differences that may be present in different age groups need to be accounted for in future work. It should still be noted that the IPB-0 condition was deemed incongruous by the HS group in the behavioural task. The incongruency in the IPB-2 condition was salient enough to elicit an attentional response in both groups and in the participants with PD. Had this not been the case however a post EEG interview would have revealed why. So while this limitation did not affect the result of the IPB-2 condition, an interview would have served as a contingency.

Another development that can widen the scope of future findings concerning prosody in PD is in how the PD demographics are collected. Much of the demographic data collected in the current study was self-reported. Studies have reported a sidedness effect in how people with PD interpret emotional prosody. The study wrongly anticipated that participants with PD would be able to accurately self-report the sidedness of their symptoms so did not request permission to be given this information by a clinician. The study was unable to examine if an impairment in the processing of linguistic prosody could be linked to sidedness of symptoms because the information provided by the participants was not definitive whereas information provided by a clinician would be. This limitation fortunately did not extend to the presence or absence of depression as, while the GDS-30 is filled in by the participant, it is an evaluative tool that is efficacious in identifying depression in older persons.

Another limitation was the self-reporting of hearing ability. It was confirmed that the participants were able to respond to the tasks prior to them undertaking the behavioural and EEG task. Small changes in hearing ability however may impact the EEG response. The N100 component, which indexes pre-

attentive signal extraction, would be particularly sensitive to this. If future work were to use the absence of an EEG component to infer the underlying cause of impaired prosodic processing, quantification of each participant's hearing ability would strengthen this conclusion.

The study did not collect information on medication dosage. One person who took part was on dopaminergic medication and analysis of their data failed to find a P3a. Dopaminergic medication has been documented to have an effect on both the P3a and RON. Without information on dosage however it is impossible to examine the strength of impact his medication may have had on his EEG response. Dosage information will be vital in any future work implementing this study on full-sized PD cohort.

The H&Y scale gives a very limited overview of a someone with PD. The UPDRS would have given a more comprehensive understanding of the disease presentation of each case study. This would have allowed further exploration of how impairments or lack of impairments in prosody link with other disease features and how this fits with current literature on heterogeneity in PD.

The ACE-30 is a test for dementia and dementia-like symptoms. If impaired prosodic processing is a result of a cognitive impairment, it may be the case that the particular cognitive impairments revealed by the ACE-30 are not the ones that cause impaired prosodic processing. For example, it has been noted that the ACE-30 inadequately tests for executive dysfunction (Brown et al. 2019). The ACE-30 therefore is adequate to exclude dementia but future work can implement a fuller battery of cognitive testing which would more precisely interrogate various cognitive domains.

There were a high number or trials excluded due to artefacts. This was due to the experience of the investigator who was not practiced at spotting these in real time. The high number of artefacts meant that analyses carried out on individuals often failed to reach significance using MCC. In the IPD-2 condition the impact on the HS group as whole was F low as all ERPs of interest were elicited with either Bonferroni MCC, Cluster MCC or both. This was able to inform the results from individuals. It is possible that an increased number of trials would have found a PEP or RAN in the HS group. Given that these were found in the Pilot cohort this still indicates a reduced effect in the older participants but a larger number of trials would be able to more confidently establish that the components are completely absent.

6.3.2 Task

The effects found in the current study were large enough to be confidently to confidently address the aims of the current study however small adaptations to the task would be able to extend the remit of some of the findings.

Firstly, the behavioural tasks and EEG were carried out once per participant. Carrying these out multiple times would have revealed how consistent the effects were and, in the case of the participants with PD, whether they were affected by medication cycle. Analysis did not find a significant P3a in PD1. There was however a non-significant P3a visible in their ERP and they did have evoked delta power. It is not known if repeating the EEG would elicit the P3a or other attentional components – either due to a change in medication status or simply as a result of obtaining a recording with a higher signal to noise ratio.

The current study was designed with an unusually low number of EEG trials. This was both a benefit and a drawback. Each condition only had 40 trials which is particularly low in EEG studies. This was done so the EEG would be short which would make it easier for people with PD to participate. EEG studies typically use short auditory stimuli so these can be repeated multiple times without excessively increasing the overall time of the EEG. The utterances used in the current study were much longer than typical EEG stimuli so a compromise was necessary. This compromise in many ways paid off as, even using this lean methodology, many features were identified in both the group that were present with two kinds of MCC, the conservative Bonferroni correction and less conservative clustering. However, there was an important and significant disadvantage to this approach which is in the huge loss of data. This disadvantage is particularly apparent in the huge amounts of data rejected in the HS group. The HS group consisted of 36 persons. Of these, 28 had EEG data clean enough for use in the group analysis and only 8 of these had EEG clean enough to use in a between-trial analysis. If this study were scaled up this would be a huge amount of lost data. PD1's EEG was particularly noisy and this also may have been due to the number of their epochs rejected in pre-processing due to the presence of artefacts (27/40 rejected in the IPB-0 condition). Due to this noise, it is difficult to conclude if the limited ERP response in PD1 was due to an attenuated ERP response as a result of the PD, poor signal to noise ratio as a result of a low number of trials or a combination of both. If the number of stimuli were doubled this would increase the signal to noise ratio of the collected data but an extra hour of recording may be an undue burden on the participants, especially those with PD. This burden could be ameliorated by splitting the EEG recording over two days.

The current study found an SP. This is the first study to identify an SP in the absence of a rule change. This finding would be made more robust with a direct comparison of a change of rule and a change of

object. This was not done as this finding was ancillary to the overall aims of the study. The SP however was present in the group and a number of individuals with Bonferroni significance which is a promising result as the SP may prove to be a marker for object-switching in general and object-switching in response to linguistic prosody.

6.3.3 Participants

The results concerning PD in this study are limited by the fact they are only based on two case studies so cannot be generalised. In the absence of a large cohort it cannot be known whether these results are representative or outliers. Despite this, the case studies do still provide information of important clinical value and, most importantly, they were able to demonstrate that the study can be used in persons with PD and can identify attentional components in them.

The use of case studies limits the ERP study in other ways. The current study made inferences about how each person with PD processed the prosody based on the presence or absence of a number of components. If two groups of comparable size were used, the degree of difference in ERPs could be measured. This means that if a component were present in one group, it may be attenuated or amplified in another group. Group analyses would have revealed degrees of change in ERPs rather than just their presence or absence. So while the case studies are not equipped to detect these more subtle changes, a large scale cohort using the same protocol would be. The current study showed absent P3a in a person at H&Y stage 3. This is expected as this component become attenuated as PD progresses. A larger cohort may have found the P3a but reduced compared to people at earlier stages of PD and compared to the HS cohort. Detecting an attenuated P3a would allow for this component to be used in the study of prosody in moderate PD as long as the disease stage was controlled for.

The current study presented evidence for an age effect on the RAN and PEP. This result was unexpected so relies on the comparatively smaller (n=8) pilot cohort. A more balanced study is necessary to test this effect directly. This result, if it is confirmed however, is of great clinical importance so it is an important preliminary finding. A repeat of the current study in various cohorts of increasing age would confirm this difference and establish the age at which it occurs. To fully explore the reasons for the difference, utterances with prosodic structures of varying salience should be used, as should a post-EEG questionnaire querying how the utterances were interpreted. Such a questionnaire would establish if there were differences in how the prosody was interpreted in the older and younger participants which would support the discussion on the cause of the age-related difference that was found. It would also allow them give feedback on the ease or difficulty of the task which would support improving and streamlining the protocol.

6.4 Future Work

The current protocol was carried out in the course of an EngD. There were therefore constraints on time and resources. This means that, while the current study reports a number of important findings, the scope of some those findings is limited in some respects. They do however lay the groundwork for promising future work.

6.4.1 Current Protocol

Based on the outcome of this study, the next step is to implement the protocol using a large cohort of people with early-stage (H&YI-II) PD without comorbidities such as depression or mild cognitive impairment. The method would be updated address the limitations detailed in Section 6.3. These updates would include the collection of UPDRS data, hearing examinations and post-study questionnaire for each participant. The protocol would aim to answer the following questions:

- Do people with PD in the earliest stages of PD have a heterogeneous response to prosody?
- How do the EEG components in people with PD who *do not* have an impairment in their interpretation of prosody compare with the HS cohort?
- How do the EEG components in people with PD who *do* have an impairment in their perception of prosody compare with the those with PD who do not?

If the attentional components are comparable in persons with PD who are and are not impaired in their ability to respond to prosody in behavioural tasks, it would confirm that, not only was the prosody detected but that it was deemed significant enough to assign attentional resources to it in both groups. This would indicate an impairment, not in the processing of prosody per se but in a later cognitive impairment (for example, an impairment executive functioning that makes responding to or learning the tasks demands difficult). Such a marker can therefore be used to explore theories that (some) persons with PD have a specific set of cognitive impairments that may not be detectable by examinations that test for dementia such as the ACE-III.

Following a successful implementation on a large PD cohort, there would be scope to expand the study to include other populations who have reported impairments in the processing of prosody such as schizophrenia. The current study could be used to examine the sensory and attentional response to prosody in these groups. If younger patient groups elicit the RAN and PEP, the current protocol could also directly test prosodic reanalysis in these patient groups.

6.4.2 Examining the age effect

The current study indicated the presence of a possible age effect on the RAN and PEP. This was based on the results from a small (n=8) cohort or people aged 22-30. This can be confirmed by retesting the protocol on a larger younger cohort. Additionally, different age ranges can be tested to reveal the age which at which this effect occurs. Questionnaires can be added to examine if, in addition to the markers, prosodic interpretation is affected by age. As the presence of the RAN and PEP are likely affected by the salience of the prosodic deviance, this should be controlled to examine if only less salient deviances are affected by age. The task can also be altered to examine how attention and age interact. The current study examined the PEP in response to linguistic prosody. A study examining age should include the PEP in response to emotional prosody to examine if there is an analogous effect age effect on the emotional prosody PEP. The questions answered by such work are of particular significance in the study of speech perception in PD. If the interpretation of prosody is affected by age, it is crucial that this is accounted for in studies examining the perception of prosody in PD. Any changes in ERP may be a result of age and not the presence of PD. More importantly, if these components are absent altogether in older people, they would not be suitable for use in older patient groups. If it were found that the stimuli that elicit these components have to be particularly salient to elicit them in older people, then this would be an important methodological consideration in future studies. This age effect is not just important to work concerning people with PD but also to work concerning stroke survivors, who are another patient group who are typically older and in which impairments in the processing of prosody have been reported.

6.5 Conclusion

The current study presents a protocol that is able to mark pre-attentive detection of deviant linguistic prosody (N100), attention and orientation towards that deviant linguistic prosody (P3a and delta), and reorientation as a result of that linguistic prosody (RON). It provides a database of 36 healthy persons aged 59 and above which can be used as control data in a study of attention capture and orientation, and perception of prosody in patient groups. The case studies do not show any indication that the study is unsuitable for use in people with both early (H&YI) and moderate (H&YIII) PD. The current study elicited attentional markers, in people with PD. This is the first time that these attentional components have been elicited in response to linguistic prosody in people with PD to the author's knowledge. The methodology presented here provides a means of examining these components in people with PD.

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Appendix 1 NHS REC - Favourable Opinion

WoSRES
West of Scotland Research Ethics Service

NHS
Greater Glasgow and Clyde

West of Scotland REC 3
West of Scotland Research Ethics Service
West Glasgow Ambulatory Care Hospital
(former Royal Hospital for Sick Children Yorkhill)
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Dear Dr Lakany

Study title:	**Developing A Means of Examining and Diagnosing Deficits in Prosodic Perception in People With Parkinson's Disease**
REC reference:	**16/WS/0052**
Protocol number:	**UEC15/43**
IRAS project ID:	**162954**

Thank you for responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered in correspondence by a Sub-Committee of the REC. A list of the Sub-Committee members is attached.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mrs Liz Jamieson, wosrec3@ggc.scot.nhs.uk.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to

the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Poster advertising for controls]	2	22 March 2016
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Indemnity 1]	1	01 August 2015
GP/consultant information sheets or letters [Letter to GP]	2	22 March 2016
Letters of invitation to participant [Invitation Letter]	3	22 March 2016
Other [Sponsor Indemnity 2]	1	01 August 2015
Other [Sponsor Indemnity 3]	1	01 August 2015
Other [No Opinion Letter from Leicester Central]		10 February 2016
Other [Response to No Opinion Letter]		16 February 2016
Other [PIS Control]	1	22 March 2016
Other [Consent Form Controls]	2	22 March 2016
Other [Response to REC]	1	22 March 2016
Participant consent form [Consent Form PD]	2	22 March 2016
Participant information sheet (PIS) [PD Patients]	3	03 March 2016
REC Application Form [REC_Form_28012016]		28 January 2016

Research protocol or project proposal [Protocol]	1	25 January 2016
Summary CV for Chief Investigator (CI) [CV - Heba Lakany]	1	25 January 2016
Summary CV for student [CV Student]	1	26 January 2016
Summary CV for supervisor (student research) [CV Anja Lowit]	1	07 December 2015

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality- assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

16/WS/0052	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Liz Jamieson

Liz Jamieson
REC Manager
On behalf of Eoin MacGillivray, Vice Chair

Enclosures: List of names and professions of members who were involved in the review
"After ethical review – guidance for researchers"
Copy to: Helen Baigrie, University of Strathclyde

West of Scotland REC 3

Sub-Committee of the REC meeting held between 1st and 22nd April 2016

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Anne-Louise Cunnington	Consultant Geriatrician	Yes	
Mr Eoin MacGillivray	Retired Dentist - Vice Chair	Yes	
Mr Robert Paterson	Retired Lecturer - Lay Plus Member	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Liz Jamieson	REC Manager