PROFILING NEUROPHYSIOLOGICAL ASSESSMENT (P300) ON INDIVIDUALS WITH APHASIA AT PRE-THERAPY PERIOD

Sreerenthu S Viswan

18SLP034

A Dissertation Submitted in Part Fulfilment of Degree of

Master of Science (Speech-Language Pathology)

University of Mysore, Mysuru

ALL INDIA INSTITUTE OF SPEECH AND HEARING

MANASAGANGOTHRI,

MYSURU – 570006

JULY, 2020

CERTIFICATE

This is to certify that this dissertation entitled **"Profiling neurophysiological assessment (P300) on individuals with aphasia at pre-therapy period"** is a bonafide work submitted in part fulfilment for degree of Master of Science (Speech-Language Pathology) of the student Registration Number: 18SLP034. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Dr. M. Pushpavathi

Director

All India Institute of Speech and Hearing

Manasagangothri, Mysuru- 570006

Mysuru,

July, 2020

CERTIFICATE

This is to certify that this dissertation entitled **"Profiling neurophysiological assessment (P300) on individuals with aphasia at pre-therapy period"** is a bonafide work submitted in part fulfilment for degree of Master of Science (Speech-Language Pathology) of the student Registration Number: 18SLP034. This has been carried out under my supervision and guidance. It is also been certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Dr. Hema N

Guide

Assistant Professor in Speech Sciences

Department of Speech-Language Sciences

All India Institute of Speech and Hearing

Manasagangothri, Mysuru- 570006

Mysuru,

July, 2020

DECLARATION

This is to certify that this dissertation entitled **"Profiling neurophysiological assessment (P300) on individuals with aphasia at pre-therapy period"** is the result of my own study under the guidance of Dr. Hema N, Assistant Professor in Speech Sciences, Department of Speech-Language Sciences, All India Institute of Speech and Hearing, Manasagangothri, Mysuru, and has not been submitted earlier to any other university for the award of any other Diploma or Degree.

Mysuru, **Registration No. 18SLP034**

July, 2020

This Dissertation

is

Dedicated

to my

FAMILY,

FRIENDS,

and my GUIDE

ACKNOWLEDGEMENT

I must say that this dissertation would not have been completed without the help of a lot of people. Firstly, I thank Almighty for his abundant grace on me. Whatever I am today and whatever I have achieved till now is definitely by the grace of God.

I thank our beloved director Dr. M Pushpavathi, for providing us this platform. Thank you, ma'am.

I thank my guide, Dr. Hema N, for the constant support and guidance throughout this process. Ma'am, the way you helped and supported me means a lot to me. Thank you, ma'am, for making me a good researcher.

Thank you, Jesnu sir, for helping me with the instrument as well as the software for analysis. Thank you, sir, for your time and the efforts that you took for us. Without your guidance, this journey would not have been this easier.

I thank all the staff of AIISH for all the motivation and guidance and for making me a good learner and a better professional. Especially thanking, Yeshoda ma'am, Sreedevi ma'am, Jayashree ma'am, Swapna ma'am, Sangeetha ma'am, Rajasudhakar sir, Jayakumar sir, Priya ma'am, Abhishek sir, and Yeshomathi ma'am. I thank Gopishankar sir, Preethi ma'am, Geetha ma'am, Deepa ma'am, Prathima ma'am, Pradeep sir, Aruna ma'am, and Seema ma'am for helping me with the practical aspects in clinics.

Thank you, my dissertation partner, Prasanna for motivating me and for helping me throughout this journey.

I especially thank Nadeer, Siva, and Binu for helping me with the participants. Whenever I disturbed you guys with something or the other, you always helped me. Thank you, guys.

I thank my Achan and Amma for being my support system. My dear parents, I know without your blessings and prayers, I would not have reached here. I am so blessed to have you as my parents and, I am proud to be your daughter. Thank you, my dear sister (Chippi) for being there with me, for encouraging me, for supporting me, and for everything. You are such a wonderful gift to me. I would also like to thank my family and well-wishers for all the blessings and prayers.

I thank all my teachers, right from my school days to my college days for all the blessings and prayers. Thank you all for guiding me, inspiring me, and for helping me grow and learn. Thank you, Rasitha ma'am, Dhanya ma'am, Jabir sir, Rahmath ma'am, Lisha ma'am, and Neethu ma'am.

I thank all my friends who helped me in one way or the other, for the completion of this dissertation from the bottom of my heart. I feel blessed to have you all as my friends.

A special thanks to all my hostel friends for making this hostel lockdown a memorable one. Amidst this pandemic, sitting with the dissertation was a bit stressful, but you guys helped me a lot.

Thank you, all my batchmates, "BRAINIACS", for all the wonderful memories.

I thank all my seniors and juniors, my friends and every one who directly or indirectly helped me to complete this dissertation.

TABLE OF CONTENTS

List of Tables

List of Figures

Chapter I

Introduction

Measurement of event-related potentials (ERPs) are based on electroencephalogram (EEG) signals associated with specific stimuli or impulse presentation. The processes in the brain are recorded using this technique with a precision of milliseconds (Gaudreault et al., 2013). ERPs are thus a specific type of EEG and are perceived as a subset of evoked potentials (Casey, 2010). The electrical response for each stimulus will be added across the repeated presentations, and the measures are then amplified, summated, and averaged (Kuperberg, 2008). This reduces artifacts of electrical activity that typically co-occurs with the activity in response to the intentional stimulation. Event-related potentials (ERPs) are an objective parameter that reflects the cognitive functions, and they are called cerebral responses which are associated with psychological events (Grover et al., 2012; Tanriverdi, 2009). ERPs are not affected by educational and cultural influences and could be a useful, non-invasive means for the cognitive process exploration (Lai et al., 2010).

ERP events can be measured for any type of somatosensory, olfactory, visual, or auditory stimulation.The evoked potentials are categorized into exogenous potentials and endogeneous potentials. The endogeneous potentials (N100, P200, and N200; early waves reaching the peak approximately within the first 100-200 milliseconds after stimulus) are also termed as sensory potentials as they are greatly affected by stimulus physical features, like, intensity and frequency (Kuperberg, 2008). The ERPs occurring later are categorized as endogenous potential or cognitive potentials (P300), which reflect only cognitive abilities. These ERPs are sensitive to alternations in the mental state of the subject which reflect the meaning of the

stimulus (Kuperberg, 2008; Sur & Sinha, 2009). Thus, P300 assess the information processing ability and the waveforms are characterized according to latency and amplitude (Sur & Sinha, 2009).

In particular to visual or auditory stimulation, the related cognitive component, which is related to attention and memory processes is the P300 ERP component (Grover et al., 2012). This evoked potential is the measure of endogenous cognitive process that is directed attention and the context-specific updating of working memory (Turetsky, 2007). The task involves appreciation or identification or recognition of infrequent stimuli in an array of frequent stimuli. Hence, this can be used for the assessment of attention and working memory. P300 is recordable from various cortical and subcortical positions and it has a maximum amplitude in the central-parietal regions in the midline. Large foci of P300-generating cerebral tissue tend to be found in the hippocampus, superior temporal sulcus, prefrontal ventrolateral cortex, and, possibly, intraparietal sulcus (Halgren et al., 1998; Kiss et al., 1989; Smith et al., 1990).

The P300 potential has two components, namely P3a and P3b. The P3a component has its maximum amplitude in the frontal region, and the P3b has the maximum amplitude in the parietal-central region. The P3a peak can be triggered by passive attention, whereas P3b requires active attention. In other words, P3b is elicited during target stimulus processing, and it is a task-relevant potential. Depending on the focus of the study, a sensory stimulus (often auditory in the realm of aphasiology) is presented repeatedly. Even other sensory stimuli are found to elicit a P300 response like the auditory stimulus, but the commonly used one is the auditory modality. The descending order of clinical use of the stimuli is: auditory, visual,

somatosensory, olfactory, or even taste stimulation (Polich & Pitzer, 1999). Since studies tend to evaluate language processing and attention in language disorders, they rely on the auditory stimulus.

When an infrequent tone is presented along with a series of frequent tones (oddball paradigm), in the absence of a task, it can yield a peak with short peak latency and maximum amplitude over the central and parietal regions, which is the P3a. Whereas, P3b is a task-relevant potential. Hence, when the ERP researchers mention the P300 waveform, they mean the P3b component. The P300 is easily observable, and it mirrors the attention and working memory processing (Polich, 2007). P300 can be quantified using two variables, which are latency and amplitude. Latency is related to information processing time, and amplitude is related to the attentional level (Rossini et al., 2007). It is reported by Polich (2000) that, the amplitude of P300 is the measure of activity occurring in the central nervous system, that happens in response to the production of stimulus memory representations and that is proportional to the number of attentional resources allocated to a particular task. If the latency of the P300 is prolonged, it means that the person is taking more time for processing information, and if the amplitude is less, it means that the person has an attentional deficit.

A review article by Nieuwenhuis et al. (2005), stated that the P300 component is associated with decision-making. Zhang et al. (2013) carried out a study on six healthy females. For obtaining behavioral measures participants were asked to play a monetary gambling game by pressing the letters "F" or "J" on a conventional computer for gambling. Behavioral data (the frequency of strategy switching and the risk ratio) were obtained using the E-prime software. Then the event-related potentials

were also recorded. The P300 component was larger following wins and after strategy switching. According to them, the changes in the decision-making process across the subsequent trials were related to the amplitude of the P300 (fronto-central P3a) and found that P300 is related to the decision-making process in normal individuals.

The usual task used for recording P300 is the oddball paradigm which generally evaluates the classic P300 (P3b). The tasks given to the subjects were either with auditory or visual stimuli. In the auditory oddball paradigm, stimuli at different frequencies were presented, whereas, in a visual oddball paradigm, different figures were used (Jiang et al., 2015; Tsolaki, 2015). Oddball paradigms using syllables could be used to investigate the brain activation changes, during aphasia rehabilitation, as these paradigms using Norwegian (native language) syllables are related to speech sound processing (Becker &Reinvang, 2007a).

A systematic review was done from January 2011 to January 2017 in a review article by Pavarini et al. (2018) on the P300 assessment. The P300 amplitude varied from 2.2 µV to 18.5 µV and the values of latency from 320 ms to 484 ms in healthy elderly subjects. Majority of the studies focussed on neurotypicals, persons with Dementia, and other clinical conditions. In the Indian context, the psychometric properties of aphasia therapy on individuals with aphasia can be objectively commented or evaluated by assessing the P300 potential.

1.1 ERP- P300 in Adult Language Disorders

The P300 potential is seen to be affected in different conditions, in which there are problems with cognition, memory, or attention. There are many studies that state about the P300 amplitude and latency in conditions like, Alzheimer's Disease, Aphasia, Schizophrenia, Hypothyroidism, and other conditions in which there is

cognitive impairment or attentional deficit. Therefore, the cognitive functions in elderly subjects, including those with dementia, were evaluated.

The photographs of babies crying or smiling were shown to assess the visual event-related potential (P300). P300 was measured using this visual oddball paradigm, and the amplitude and latency were analyzed. It was found that the group with Dementia of the Alzheimer's type had significantly longer latencies and significantly smaller amplitudes when compared to that of the healthy group (Asaumi et al., 2014). The deterioration of language, memory, and executive functions seen in individuals with Alzheimer's disease can be seen as a reflection in the P300 measures. The latency of P300 reflects impaired attention and cognition, which is associated with Alzheimer's disease (Bae et al., 2012). Thus, P300 is considered a biomarker for the detection of Dementia.

A study was also done to quantitatively analyze the cognitive skills of individuals having mild to severe hypothyroidism using P300. P300 was measured during thyroid insufficiency and in the 1st and 6th month of euthyroidism. Both mild and severe hypothyroid patients had prolonged P300 latencies when compared to controls. It was found out that, after the first month of euthyroidism, there was a notable decrease in the P300 latencies in the overt hypothyroid patients and there was no change in the latency values in the subsequent 6 months. But the latency of the group with mild thyroidism normalized at the 6th month of euthyroidism. This finding indicates that there are a variety of clinical outcomes of distinct thyroid insufficiency states on the human brain (Tütüncü et al., 2004), which can be indirectly measured through P300.

Regarding stroke patients, another study was done. Stroke patients with and without depression were also compared with a control group to find out the discrepancies in their P300. It was found that the post-stroke patients had higher P300 latencies and lower P300 amplitudes when compared with the control group and the no depression groups (Zhang et al., 2019). In patients with aphasia, it was seen that they have difficulty in detecting and recognizing different phonemes from each other, and that is why they have a problem in word recognition and comprehension.

Individuals with aphasia having mild or moderate auditory comprehension deficits and individuals with aphasia having severe or very severe auditory comprehension deficits were also compared during an active auditory discrimination task. It was found that there were no remarkable differences between a healthy control group, and the two aphasia groups, in terms of P300 amplitude. This finding was related to the simple behavioral task, and because the frequent and infrequent stimuli differed in more than one feature, that is the place of articulation and voicing (Becker & Reinvang, 2007b).

Seventeen patients who were right-handed and diagnosed as having global aphasia post left-hemisphere stroke were studied. Once in a month, at the same time of the day after having breakfast, the recording of P300 was done. The infrequent stimuli were a 1 kHz tone, and the frequent stimuli were 0. 5 kHz. Apart from ERP recordings, neuropsychological and clinical assessment, CT scan, and routine blood evaluation were carried out for all patients. The language skills were assessed using the Aachen Test. Particularly two subtests were assessed: i) Token test and ii) Comprehension. The participants were also undergoing language rehabilitation. In the beginning, 7 patients showed P300 responses. Over time, all the participants exhibited

the P300, except for 1 participant. The language test was administered after 6 months. The participants with global aphasia who exhibited a P300 during the evaluation for the first month showed better improvement in their comprehension when compared to those who haven't exhibited it initially. The early presence of P300 post-stroke is a positive sign indicating progressive recovery of comprehension. The latency of the P300 waveform became longer throughout the observation window. Patients showing improvement in language comprehension who had earlier shown P300 indicates that passive P300 can be used to monitor the recovery in global aphasia (Nolfe et al., 2006).

In a standard rehabilitation program, eight individuals with aphasia, in the age range of 18 – 66 years received 8 – 12 hours of speech-language therapy per week. The recording of the P300 potential was done at admission (90 days post-injury) and discharge (mean 208 days). They were asked to press a button whenever they heard /ta/ syllable which was presented along with /ba/ syllable. It was found that there was an increase in the amplitude of the P300 waveform, as well as an improvement in its latency for individuals with aphasia at the time of discharge (Becker & Reinvang, 2007a). Thus, the studies using the event-related potentials (ERPs) which are based on the oddball-paradigm, to a greater extent helps to characterize, evaluate, and monitor, the phonological problems and auditory comprehension deficits in patients with aphasia. It was found that to monitor the patterns of recovery in the early stages of aphasia and follow up long-term periods, the P300 potential is a good non-invasive measure (Aerts et al., 2015).

1.2 Need for the Study

Even though the data collected through behavioral measures provide useful information regarding the language deficits in individuals with aphasia, techniques which use event-related potentials (ERP-P300) directly assess the neurological functioning without solely depending on the behavioral measures since the majority of aphasia population have hemiplegia. ERP being a non-invasive assessment, may provide information regarding the role of the right hemisphere in language comprehension in those who have damaged the left hemisphere. If the tasks for recording the potentials are designed differentially to involve the hemispheres (example: use of syllables presented through auditory mode involves left hemisphere, use of designs presented through visual mode involves right hemisphere) and if it involves a non-differentiating or neutral task (example: picture image/orthographic word matched to implied meaning or designs matched with abstract meaning), it will provide much information about interhemispheric processing in persons with aphasia. Hence, ERPs can also be used to study the cortical level of language representation (Selinger, 1989).

Among the various event-related potentials, the most likely used one is the N400 and P300 concerning the linguistic task of appreciating semantic incongruence event, which is found to be a sensitive marker for assessing the effects of therapy. It is because these potentials are easy to acquire with minimum involvement of the participants' consciousness and voluntary responses.These neurophysiological assessments can be used to explore and monitor the plasticity patterns and therapy-related differences in brain recovery (Aerts et al., 2015). Therefore, examining the event-related potential is another method of studying plasticity.

The P300 can be used as a prognostic tool for long term monitoring in rehabilitation medicine and used as an alternative to neuropsychological methods involving behavioral responses from the participants (with motor issues) during the assessment processes of individuals' cognitive skills. It is reported in a study that as the early presence of P300 predicts the fast recovery of comprehension in patients with global aphasia, this potential is useful in post-stroke aphasia clinical evaluation. The presence of unstable P300 in individuals with global aphasia over time indicates cognitive failures in attention and discrimination (Nolfe et al., 2006). Thus, the additional advantage of ERPs is that they can be used to assess the cognitive processes of individuals, who are unable to give motor or verbal response (Becker & Reinvang, 2007b).

ERP studies on effects of therapy on language functions and underlying neuronal circuits are rare. The outcome of such studies demonstrates the positive effects of treatments by portraying increased amplitudes of P300 (Aerts et al., 2015). Therefore, there is a need to monitor the individuals with aphasia and note their progress during their course of speech-language rehabilitation using neurophysiological assessment (P300) along with or without the routine behavioral language assessment. Hence, the present study was planned to carry out a P300 assessment on individuals with aphasia and profile the P300 assessment of individuals showing the presence of the P300 component in comparison with the absence of the P300 component.

1.3 Aim of the Study

The study aims to conduct a neurophysiological assessment (Event-Related Potential-P300) in individuals with aphasia at their pre-therapy period.

1.4 Objective

1) To measure the amplitude and latency values of ERP-P300 using auditory stimuli (speech stimuli) in individuals with aphasia at their pre-therapy period (< 5 sessions).
2) To profile the P300 assessment of individuals with aphasia showing the presence of a P300 component in comparison of individuals with aphasia with absent P300 component.

Chapter II

Review of Literature

Electrophysiological evaluation is carried out to identify the physiology of the structures. Event-related potentials are being recently used to look into the brain functions more effectively. Auditory-evoked potentials (AEPs) or event-related potentials (ERPs) are responses obtained from the brain in response to some stimuli that is presented. The ERPs reflect the events that are happening in the human brain in response to the stimulus presented. There are two types of ERPs depending on the mechanism of the generation of responses. They are exogenous and endogenous potentials. Exogenous potentials are Auditory Brainstem Responses (ABR), Middle Latency Responses (MLR), N100, T-complex, etc., whereas potentials like P300, N400, P600, and, Contingent Negative Variations (CNV) are endogenous potentials. P300 is an ERP which is related to one's attention and memory.

2.1 P300 Event-Related Potential

P300 is a positive potential occurring at around 300 milliseconds post the onset of the stimulus. It was first reported by Sutton et al in 1965. This particular potential can be elicited by presenting two stimuli in such a way that one is occurring around 80% of the time and the other one is occurring only 20%. Once the person can identify that the two stimuli that were presented are different, the positive peak is obtained at around 300 milliseconds after the onset of the stimulus.

P300 amplitude is assumed to measure brain activity that is needed to retain working memory when the stimulus environment's mental model, i.e., context is updated (Donchin et al., 1986). The P300 amplitude is also proportional to the amount of attention allocated on a given task (Kramer & Strayer, 1988) and has been linked

with superior memory performance (Fabiani et al., 1990). Therefore, P300 amplitude can be seen as a measure of CNS activity that represents the processing of input information as it is integrated into the stimulus memory representations and the setting in which the stimulus occurs. Hence, the variations in the amplitude of the P300 reflect the quality with which the incoming information is processed. In evaluating P300 amplitude, inter-stimulus interval (ISI) and the interval between successive target stimuli interact with likelihood: when the ISI is 6s or longer, the likelihood of stimulation decreases considerably (Polich, 1990 a, b). Squires et al. (1976) reported that when there was a successive repetition of the stimuli, there was a reduction in the P300 amplitude. The amplitude of P300 is also influenced by expectations produced by the sequence of stimuli occurring before the eliciting stimulus.

The latency of the P300 waveform is considered as a measure of stimulus classification speed (Polich, 1987). P300 latency indicates the time needed for processing the stimulus or it indicates the speed of stimulus classification. The latency of P300 is not related to the process of response selection. The latency is also independent of the behavioral reaction time (Duncan-Johnson, 1981; Kutas et al., 1977; McCarthy & Donchin, 1981). The P300 latency is a responsive temporal measure of the neural activity that underlies the attention allocation processes and immediate memory. Furthermore, in normal subjects, P300 latency is negatively correlated with mental activity, with shorter latencies associated with superior cognitive output (Polich et al., 1983, 1990b). The neuropsychological measures better associated with P300 latency are those that determine how rapidly subjects can assign and retain attention resources. This correlation is also confirmed by findings showing that P300 latency increases as the cognitive capacity of dementing disease decreases

(Squires et al., 1979) and in both normal and clinical populations, P300 latency is directly associated with cognitive capacity.

2.2 Components of P300

P300 potential has two components, P3a and P3b. The maximum amplitude of P3a is in the frontal region and the maximum amplitude of P3b is in the parietal central region. Passive attention triggers P3a peak and active attention results in P3b. In other words, P3b is elicited during target stimulus processing, and it is a task-relevant potential. When the ERP researchers mention the P300 waveform, they mean the P3b component (Polich, 2007).

2.3 Generators of P300

Numerous investigations have been carried out to identify the generator sites of the P300 waveform. Understanding the P300 generating sites is as important as information concerning the P300 generator sites, as it provides insight into the various cognitive processes underlying them. It has been found out through various neuroimaging methods that the brain areas involved in the generation of P300 are complex as they have simultaneous activation of multiple sites which are overlapping. Using an oddball paradigm an infrequent tone is presented along with frequent tones without a task and it produces a positive wave with a central or parietal maximum amplitude distribution. This component is the "P3a" and it is distinguished from the task-relevant "P3b". In about 10 – 15% of normal young adults P3a can be readily observed from an auditory oddball task (Polich, 1988). This indicates that the generation of subcomponents varies across individuals.

Even though appreciable progress has been made in identifying the neural generators of P300 in the last 25 years, it is not imprecisely delineated. P300 is

recordable from various cortical and subcortical positions. Large foci of P300-generating cerebral tissue tend to be found in the hippocampus, superior temporal sulcus, prefrontal ventrolateral cortex, and, possibly, intraparietal sulcus (Halgren et al., 1995, 1998; Kiss et al., 1989; Smith et al., 1990).

Patients with frontal lobe lesions showed a decrease in amplitude of P3a, while the same patients had a higher parietal amplitude for P3b. Consequently, integrity of frontal lobe is essential for generating P3a (Knight, 1984; Knight et al., 1995). Patients with frontal lobe lesions showed the decreased amplitude of P3a while those having focal hippocampal lesions also showed reduced amplitude of P3a from novel distractors but normal components of P3b from targets (Knight, 1996). Initial hippocampal formation studies using depth electrodes in humans indicated that at least some portion of the P300 (P3b) is produced in the medial temporal lobe (Halgren et al., 1980). Evidence indicates that, given that part of this complex subcortical and cortical brain system remains intact, there is still the capacity to generate P300 (Nieuwenhuis et al., 2005).

2.4 Variables Affecting P300

Many variables affect the latency as well as the amplitude of the P300 waveform. They include the stimulus-related parameters, and the subject-related parameters respectively.

2.4.1 Stimulus Related Parameters

The various stimulus-related parameters like the stimulus intensity, stimulus probability, whether the task is active or passive, and the sound environment in which the testing is carried out affects the measurement of P300 potential. In an auditory oddball paradigm, the intensities of the stimulus were manipulated from 15 to 65 dB

to investigate its effect on P300 potential and it was found that intensity variations affected the P300 latency, but not amplitude (Papanicolaou et al, 1985). Vesco et al., (1993) found that there was a reduction in the amplitude along with longer peak latencies when low-intensity stimuli were presented.

The P300 response is optimally evoked in an oddball test paradigm by erratic, infrequent acoustic stimuli randomly presented with a likelihood of 15 to 20 percent. The typically recommended probability for target stimuli in P300 measurement is 80 percent for standard & 20 percent for deviant stimuli. A reduction in the stimulus target probability resulted in an increase in the amplitude and lengthening of peak latency, which was more evident in simple tasks than complex tasks (Polich, 2003).

This potential can be elicited by either active or passive tasks. In an active task, the subject has to pay attention to the stimulus and respond, whereas, in passive mode, he or she is asked to selectively attend to the target stimuli. In a study carried out by Bennington and Polich (1999), they compared the effect of an active and passive task for auditory as well as visual stimuli on P300. They found out that the P300 amplitude was larger in the active condition (raising finger) than the passive condition (daydreaming) and it was more for auditory stimuli when compared to visual stimuli. The latency of P300 was shorter for auditory stimuli than the visual stimuli condition. In a study, Kemal-Arikan et al., (1999) found that distinct differences in the P300 response occurs when the recordings were carried out with the stimulus presented in silent environment versus in background noise. The P300 is also influenced by the nature of the background sound. Amplitude reduced directly as a function of SNR when P300 was recorded with standard versus deviant stimuli presented in competing noise.

2.4.2 Subject Related Factors

The subject-related factors like the subject's attention, state (whether he is sleepy or alert), motivation, memory, and whether he or she has consumed any drugs also have an impact on the potential. Any brain disorder affecting the primary cognitive operations of attention allocations and memory, will influence the P300 measures by increasing the latency or reducing the amplitude (Polich, 2000). When the stimuli are ignored or when the attention is drifted away, the stimuli which usually elicits a P300 fail to do so (Hillyard et al., 1973). Polich (1987) reported that P300 latency was longer and greater when the subject silently counted the target signal than when the subject pressed a thumb button.

The presence of a P300 waveform varies with the stages of sleep. According to Cote (2002), when P300 was recorded with Fz electrode sites, P300 was absent in stage I and stage II. In rapid eye movement sleep (REM sleep) – stage V, where the brain is active similar to the awakened state, P300 was obtained. The subject's motivation also affects the P300 response. In a study, Johnson (1989) found that a greater P300 is generated by adding monetary value to correct target signal recognition. When motivating instructions were given, a greater amplitude of P300 was obtained than neutral ones.

Caffeine was proven to increase the amplitude of P300 as it led to an increase in a CNS activity and eradicated the distinction in latency of P300 between tired and rested subjects that was evident in placebo circumstances. Research on the impact of acute ethanol consumption on P300 disclosed a change in the P300 neural generator to an inferior brain position (Lukas et al., 1990). The decline in P300 amplitude owing

to alcohol intake was significant across the right hemisphere compared to that of the left hemisphere (Porjesz & Begleiter, 1981).

Memory patches for target signals are necessary as a yardstick for great representation. Stimuli which were distinguished are more likely to be tracked down and produced greater P300 components during encoding than those which were not remembered. Indeed, the P300 magnitude was affected by the rehearsal method, so the amplitude of the elements was greater than those which were consequently remembered if the respondents used rote instead of semantic strategies (Fabiani et al., 1986).

The relationship between P300 and long-term memory is investigated by Johnson et al. (1985). In their study, the subjects were given a list of target words, named the Study Series, which were to be memorized. These words were later examined for recognition by presenting them alongside new distracting words. Upon termination of these behavioral tasks, P300 was recorded using target stimuli alone. The findings of the study disclosed large P300 amplitude for target words, in particular, in its initial presentation and shorter latency for those target words that were memorized by the participants in the behavioral task. Thus, there is a clinical relevance of P300 with the cognitive process called memory. However, the methodological issues related to P300 measurement with and without a behavioral task is still a questionable issue in certain clinical population associated with or without motor issues.

2.5 Applications of P300 Potential on Clinical Populations (Example: Adult Language Disorders)

The P300 event-related potential has several applications. It can be used to assess the cognitive function, and the amplitude and latency of P300 in the normal population is not as same as that in the disordered conditions. In patients with brain damage, this particular potential is said to be affected.

The foremost review is a systematic review carried out by Pavarini et al. (2018), in which P300 was assessed as a tool for cognitive assessment in healthy aging. 26 studies that involved 940 participants were identified and all the studies reported that age influenced cognitive processing. One study reported that there was a decrease in the P300 amplitude as the age advances (van Dinteren et al., 2014). Another review article reported that an increase in latency as well as a decrease in the P300 amplitude was found as age advances. In this review study, 26 articles were selected and in those articles, 50% used visual mode of stimulus presentation, and 50% used auditory mode of stimulus presentation. In the articles that were selected 53.8% used P300 to identify whether age affected cognitive processing. P300 was used to compare the electrophysiological findings between cognitively impaired participants and healthy subjects in 19.2% of studies and it was used to monitor the effects of therapy in 15.4% of studies. Half of the articles selected showed that cognitive processing was influenced by age. According to Kuba et al. (2012) the latency of P300 rises by around 2 ms per year, as the amplitude reduces linearly in older people. The reviewed articles also showed that the latency values were ranging from 320 ms to 484 ms and the P300 amplitude values were ranging from 2.2μV to 18.5μV (Pavarini et al., 2018) for neuro-typical individuals.

The deficits in cognitive processing in different clinical groups are reflected by a prolonged latency of P300 or a decreased amplitude or total absence of the potential. The reduction of the amplitude of P300 was initially recorded 35 years ago and it is repeatedly replicated (Duncan et al., 2009). This result may be associated with observed frontal-temporal atrophy seen in many schizophrenic patients and their persistent attention deficit (Nuechterlein et al., 2006). Further study found that the amplitude of P300 was reduced in schizophrenia patients, but the differences were desirable for auditory but not visual stimuli (Duncan et al., 1987a).

The cognitive functions of people with Dementia were also evaluated in different studies using event-related potentials like P300. In a study carried out by Asaumi et al. (2014), 48 elderly subjects were included. Visual oddball paradigm was used where the photographs of babies crying or smiling were shown to assess the event-related potential (P300). The subjects were divided into the Dementia with Alzheimer's disease group, intermediate group (neither Alzheimer's disease nor healthy control group), and the healthy group. The event-related potential was recorded at Fz, Cz, Pz, and Oz positions, using Ag/AgCl electrodes, as given by the International 10-20 system, with the reference electrodes connected at the mastoids. The target stimuli were a crying or a smiling face and the non-target stimuli were a neutral face. The duration of the stimulus was 200 ms and the probability of the target stimuli was 20%. The subjects were asked to look at the baby's face on the screen and they were asked to push a button whenever they encountered the target stimuli. P300 was measured using the visual oddball paradigm, and the amplitude and latency were analyzed. It was found that the group with Dementia of the Alzheimer's type had significantly longer latencies and significantly smaller amplitudes when compared to that of the healthy group. They reported that the P300 amplitude became smaller and

the P300 latency became longer in Alzheimer's disease patients, implying that Alzheimer's disease patients allocate a smaller amount of attention resources (Asaumi et al., 2014). Even though the P300 wave is a useful psychophysiological measure that is reflecting the cognitive functioning, the association between P300 indices and neuropsychological test measures in patients with Alzheimer's disease (AD) remains uncertain.

Hence, Bae et al. in 2012 conducted a study on thirty-one patients with Alzheimer's disease and thirty-one healthy controls. The two groups were age and education level matched. When the patients with Alzheimer's disease were compared with the normal group it was found that Alzheimer's disease patients showed significantly reduced P300 amplitude, but there was no significant difference in P300 latency between the two groups. The results suggest that the P300 potential is sensitive to the declination of executive functions, memory, and language which is seen in Alzheimer's disease patients. P300 can also be used as a biomarker for impaired neuropsychological function in patients with Alzheimer’s disease.

P300 amplitude is noted to be less in people with alcoholism, and not as a result of the brain's deleterious effects of alcohol.Upon abstinence, many of the characteristic clinical and electrographic signs of alcohol dependency then return to normal; nevertheless, the reduction of the P300 amplitude persists. Studies have reiterated the utility of a decrease in P300 amplitude as a possible endophenotypic marker, indicating that the degree of reduction in P300 found in alcoholics was strongly associated with the number of alcohol-dependent individuals within the family (Duncan et al., 2009).

P300 is also been used to investigate the brain-injury survivors. In a study done by Duncan et al. (2005), 11 head injury survivors were selected as participants and the control group included 8 men who matched the brain injury survivors based on their age, handedness, and educational level. To elicit the event-related potentials, visual as well as auditory stimuli were used. The letters 'H' and 'S' were used as the visual stimuli and the high (1500Hz) and low (600Hz) were used as the auditory stimuli. It was found that the P300 waveform was significantly delayed in the brain injury survivors when compared to the healthy controls. The pattern of differences in latency indicates that the slower responses found in survivors were not due to receiving delayed feedback, but to taking longer to differentiate and categorize stimuli, and to choose and execute a response. A significant effect of head trauma tends to be the slowing down of auditory processes of the higher-order, believed to be the result of damage in the information processing system at several loci.The more prominent results seen on auditory than on visual tasks indicate that trauma may be more susceptible to the brain system that supports auditory processing than visual processing.

In another study, the patients who were having Hashimoto’s thyroiditis and overt hypothyroidism were the participants enrolled in the study protocol. Among them, 13 patients with overt hypothyroidism and twenty-four patients with mild thyroid failure were the participants included in the study. The P300 event-related potentials recording was carried out by the same clinician three times. The first recording was carried out at the beginning of the study, i.e., when the participants were having thyroid insufficiency and the second one was done after the establishment of euthyroidism (normalized plasma T_3, T_4, and TSH values) with levothyroxine supplementation. To evaluate the stability of the P300 the third evaluation was carried

out at least 6 months after the establishment of euthyroidism. As 4 participants in the severe thyroid failure group and six participants in the mild thyroid failure group didn't want to go for a third recording, the recording was not done for them. The third recording was carried out on the remaining 9 severe hypothyroid participants and 18 subclinical hypothyroid participants. The healthy control group comprised of volunteers from the hospital set-up where the study was being carried out.

The auditory oddball paradigm was used to record the P00 potential. Two tones of 1000 Hz and 8000 Hz were the stimuli that were used. The infrequent stimuli were 8000 Hz which constituted 20% of the stimuli and the frequent stimuli were 1000 Hz which constituted 80% of the stimuli. The participants were asked to count the infrequent stimuli which were randomly presented in a series along with the frequent stimuli. Recording of the potential was done using silver electrodes placed on scalp sites Fz, Cz, and Pz (International 10-20 system). In the severe hypothyroid group, the TSH values, as well as the P300 latencies, were significantly higher than the moderate hypothyroid group at the beginning of the analysis. A reduction was seen in the P300 latencies in the first month of euthyroidism in the severe hypothyroid group and they did not show any significant change afterward. Contrastively, there was an increase in the P300 latency seen in the subclinical group in the first month after reaching euthyroidism. It was noticed that overt hypothyroidism showed a pronounced delay in the P300 wave that normalized after establishing euthyroidism.While hypothyroidism indicated prolonged latency of P300, the recovery time of this potential was different in different groups of participants (Tütüncü et al., 2004).

Apart from the above-mentioned adult language disorders, the present study focuses more on individuals with aphasia. However, there is also review related to

Event-related potentials like P300 being used in patients with aphasia. Event-related potentials (ERPs) have shown great potential in characterizing, evaluating, and monitoring language abilities in individuals with aphasia.

2.6 Applications of P300 Potential on Clinical Populations (Example: Persons with Aphasia)

Unexpectedly, the number of ERP studies measuring the effects of therapy on persons with aphasia and the reorganization of their neuronal circuits are very less in number. The outcome is nevertheless encouraging, showing positive results of extensive, impairment-based care in the form of greater P300 amplitudes in response to meaningful words. (Pulvermuller et al., 2005). From the studies, it was found out that the neurophysiological changes were strongly linked with the improved performance of behavioral language. Besides, despite the intact behavioral performance, ERPs may also shed light on potential defects in neuronal processing (Becker & Reinvang, 2007b). ERPs can provide a complimentary resource for diagnostic and therapeutic assessment of patients with aphasia, and facilitate clinical observations to also be related to neurological findings. This could not only help clinical practice but also increase understanding of the neurophysiological processes involved in language processing and their evolution after stroke (Kim &Tomaino, 2008). Until now, the literature has not provided a long-term analysis of the linguistic abilities of individuals with aphasia during their initiation of therapeutic behavioral interventions in association with the neurophysiological assessment trends.

Becker and Reinvang (2007a) studied the changes in brain activity related to speech and tone processing during aphasia rehabilitation. The participants were eight patients with aphasia and they underwent a standard rehabilitation program. The

program comprised of 8 to 12 hours of speech and language therapy per week and it was one to one therapy. The patients were in the age range of 18-66 years (3 men and 5 women). All subjects were assessed in 2 sessions, that is, at admission (mean 90 days after injury) and at discharge or shortly after (mean 208 days). The event-related potentials were obtained using 3 different paradigms; tone discrimination paradigm (passive), a syllable discrimination paradigm (passive), syllable discrimination, and identification paradigm (active).

The speech stimuli were the Norwegian syllables /ba:/ and /ta:/. For the unattended paradigm, the patients were asked not to attend to the stimuli, instead just go through a magazine, and for the attended paradigm, they were asked to attend to the stimuli and to push a button in response to the target stimuli as fast as possible. It was found that all patients were able to differentiate the speech sounds and identify the target syllable /ta:/ except for one person (patient 5) who was only able to perform the task in the second session. When both the investigations were compared, it was seen that there was a significant increase in the amplitudes of both P3 and N2 components at the ipsilesional frontal electrode site. Nevertheless, a change in the hemispherical distribution of amplitudes of the N2 component was seen. This suggests that the bilateral organization of the brain takes place during aphasia rehabilitation and that future ERP-rehabilitation research of aphasia should concentrate on ipsilesional frontal areas. There is also a need to profile the findings at the initiation of aphasia therapy.

The same authors conducted another study in which they investigated syllable detection in patients with aphasia having processing deficits by event-related potentials. In this study, 20 patients with aphasia were recruited for rehabilitation and

11 control subjects were the non-brain damaged patients of the hospital and the hospital staff. All participants were identified to be right-handed, except for two individuals with severe aphasia and one individual with moderate aphasia. The comprehension of the participants was assessed using the Norwegian basic Aphasia Assessment (NGA) (Reinvang, 1985) and the Token test (De Renzi & Faglioni, 1978). From the medical charts of the patients, the etiology and lesion locations were retrieved.

Based on the comprehension of the individuals with aphasia they were divided into two groups: a group comprising of patients with aphasia having mild or moderate impairment in auditory comprehension (moderate aphasia group) and another group comprising of patients with aphasia having severe or very severe impairment in auditory comprehension (severe aphasia group). Both groups did not differ significantly from each other as well as from the control group in terms of their age, sex, time post-injury, or years of education. The stimuli presented were the syllable detection paradigm. The frequent or the standard syllable was /ba:/ and the infrequent or the target syllable was /ta:/. A total of 205 syllables were presented binaurally through headphones at around 80 dB SPL, and among these were 30 target syllables. The participants sat comfortably in a sitting chair or their wheelchair and were told to push a button with their chosen hand's index finger when they heard the target syllable /ta:/ as soon as possible.

The waveforms of standard syllable /ba:/ were analyzed for the N1 component and the waveforms of the target syllable /ta:/ were analyzed for N1 and the P300 component. All the patients with aphasia except for 3 patients with severe auditory comprehension deficit detected all the 30 target syllables. In the controls, the P3

portion was observed as the typical large positivity with a maximum parietal peak at 436 ms. In the moderate aphasia category, a much earlier maximum was observed. P300 was slightly attenuated in the severe aphasia category and it peaked over the frontal midline. Nevertheless, no major differences in mean amplitudes or latencies between groups were found in the P300 component. It indicates that there was no severe impairment in the detection of the target syllable. The lack of a difference between the two groups of patients with aphasia contrasts with the previous studies on P300. This might be due to the large difference between the two syllables selected for the study and also the simplicity of the task (Becker & Reinvang, 2007a). Hence, while selecting the stimulus for the study, the information provided in this particular study was considered. The advantage of this particular study is that they divided the patients with aphasia into two groups based on their impairment in auditory comprehension and then the event-related potentials were compared. Well, stimuli used were syllables that don't need much of language processing ability in the task.

With reference to the aphasia rehabilitation period, Nolfe et al. (2006) studied seventeen right-handed patients with lesions in the left hemisphere and with global aphasia. The study aimed at obtaining the percentage of patients who are having the P300 potential at the beginning of rehabilitation; to identify whether there is any improvement in the potential during the time of rehabilitation; and to identify the correlation between electrophysiological alterations and global aphasia recovery. All the participants were males and their mean age was 65 years. The mean interval between the onset of the stroke and the first recorded P300 was 12.9 days.

The severity of the stroke at the onset was assessed using the Scandinavian Stroke Group ("Multicentre trial of hemodilution in ischemic stroke--background and

study protocol. Scandinavian Stroke Study Group.", 1985). The control group comprised 20 age-matched individuals and all the participants had normal hearing. Ag/AgCl electrodes were used for recording the potential. Potentials were recorded once a month after breakfast at the same time of the day. The stimuli used were high pitch (1000 Hz) target stimuli and low pitch (500 Hz) standard stimuli. To assess the language impairment, Aachen Test – validated for the Italian population (Luzzatti et al., 1987) was used. The two subitems which are token test and comprehension were assessed. All the patients were enrolled in a rehabilitation plan for 6 months. For treating their language impairment, Schuell's aphasia therapy was applied.

In the recordings done at the beginning of rehabilitation, seven patients (41%) showed the P300 responses in the right hemisphere. When the patients were compared with the controls it was found that patients showed an increase in the latency which was significant. Only one among the 17 global aphasic patients did not show the response in 6 months and for only one patient the response was stable over time. The Token test and comprehension sub-items were assessed at the baseline and after 3 months and 6 months. It was observed that the global aphasic patients who were having a P300 potential in the first month obtained better prognosis in their comprehension and the patients who lacked the P300 potential at the beginning showed the same score in their comprehension. Hence, the early appearance of P300 after stroke was a good indication of recovery in comprehension.

Till now only a few studies have focused on using neurophysiological assessments to assess the effect of therapeutic intervention on persons with aphasia. The prognosis of persons with aphasia can be assessed using the event-related potential P300. From the above-mentioned studies, it is understood that ERPs are a

useful method that can be utilized for identifying the individual activation patterns relevant to recovery in aphasia rehabilitation.

Chapter III

Method

The study aimed to to conduct a neurophysiological assessment (Event-Related Potential-P300) in individuals with aphasia (IWA) at their pre-therapy period. The objectives of the study were, to measure the amplitude and latency values of ERP-P300 using auditory stimuli (speech stimuli) in IWA at their pre-therapy period and to profile the P300 assessment of IWA showing the presence of a P300 component in comparison with IWA showing absent P300 component.

3.1 Participants

A total of 3 individuals with Broca's aphasia (non-fluent type) were selected based on the availability of cases in the Department of Clinical Services, All India Institute of Speech Hearing, Mysore. These participants had a diagnosis of 'Aphasia' by the Neurologists and the Speech-Language Pathologists after the administration of Western Aphasia Battery-K (Chengappa & Kumar, 2008). These individuals had just initiated their speech and language therapy and had attended less than five sessions before recruiting them for the present study. This period was noted as a pre-therapy period. The demographic details of all the participants of the clinical group are as follows in Table 3.1.

Table 3.1

Demographic Details of Participants Included in the Study

Sl No.	Participants	Age	Gender	Educational Status	Aphasia type	WAB scores				AQ scores	Neuro-imaging findings	Languages known
						SS	N	R	AVC			
1.	A	25yrs	M	Secondary Education	Global Aphasia	0	0	0	1.2	2.4	MRI: 27.08.19; Acute onset of aphasia and right sided weakness CT SCAN without contrast: 05.09.19: Ill defined hypodensities in left peri-rolandic cortex and temporo occipital cortex- sub acute infarcts.	Kannada, English
2.	B	65yrs	M	Nil	Broca's Aphasia	0	0	0	8.5	17	Hyperacute infarct involving frontal operculum and posterior frontal regions	Konkani, Kannada, English & Hindi
3.	C	28yrs 11 months	M	Not mentioned Occupation: Fertilizing Manager (Agricultural dept.)	Global Aphasia (Resolving to Broca's Aphasia) Re-Evaluation:18.12.19 Broca's Aphasia	0 0	0.4 0	0.2 0	3.35 4.4	7.9 8.8	Left fronto-parieto-temporal lobe chronic infarct with gliosis	Kannada, English, Hindi, Telugu, Tamil.

The individuals with aphasia (participants) who had just initiated their speech-language therapy followed special inclusionary criteria and the same are listed below;

- The post morbid duration was six months or above.
- Handedness was checked using Edinburgh handedness inventory - Revised (Williams, 2010), and the three individuals with similar (left) handedness (after the post morbid condition) only were considered for the present study.
- Aphasia quotients were falling below 93.8 on the administration of Western Aphasia Battery – Kannada version (WAB-K) (Chengappa & Kumar, 2008).
- Individuals with aphasia were monolingual or bilingual, and the languages known by the individuals were noted down.
- They had no complaint about any otological problems or ototoxicity. To identify any such issues, a detailed general case history was taken.
- Individuals with aphasia underwent a routine audiological evaluation before participating in the study. Air conduction thresholds were less than or equal to 30 dBHL in both the ears on Pure Tone Audiometry. (Clinical audiometer-Madsen OB922, (Version 2.64) with TDH 39 earphones enclosed in MX-41/AR supra oral ear cushions used to estimate the air-conduction thresholds, and Radio Ear B-71 bone vibrator).
- Individuals with aphasia had no other associated clinically significant neurologic disorders other than stroke. Participants, if taking any sedatives and memory dietary supplements, were asked to suspend them for 72 hours before testing.

- Individuals with aphasia had no associated neurogenic speech disorders like apraxia or dysarthria, and if present, the same was noted during the evaluation processes.

3.2 Research Design

The present study was of single subject design, wherein profiling of neurophysiological assessments (ERP measurement of P300) of individuals with aphasia at their pre-therapy period was carried out.

3.3 Data Collection Procedure- Electrophysiological Experimental Paradigm

3.3.1 Testing Environment

The recording was carried out in a sound-attenuated and electrically shielded room, where the noise levels were within permissible limits (American National Standards Institute, 1999). For the same, the recording room of the Department of Speech-Language Sciences was used.

3.3.2 Instrumentation

The following instrument was used to record the stimuli and collect data.

1. Net Station 5 Electrical Geodesic Inc. (EGI) Geodesic EEG Software (version 5.4.2) instrument was used to record Event-Related Potential (ERP) (128 Channels).
2. The recorded stimuli which were scaled and RMS normalized were used to obtain the evoked potentials, viz., P300.

3.3.3 Stimuli

The E-prime software version 2.0.8.90 (Psychology Software Tools, Inc., Sharpsburg, PA, USA) on a Hewlett Packard Z240 Tower Workstation (Intel Core i5at 3.20 GHz and 8.00 GB RAM) running Windows 7 Pro was used for the

preparation as well as the presentation of the stimulus. The EGI equipment supports two machines for carrying out the experiment. The Net Station software records multiple tracks of the stimulus along with the EEG data. Another computer generates and presents the stimuli, and it sends simple triggering or complex stimulus identification information to Net Station software. The speech stimuli used for testing were syllables /ḍa/ and /ga/, where the frequent one was /da/ and the infrequent one (target) was /ga/. These audio stimuli were presented from an audiospeaker centred 85 cm above the participant connected to a Creative SB X-Fi audio card. Speech sounds were presented free field at 70 dBSPL, measured by a Sound Level Meter (SLM). The interstimulus interval was 2000 ms. A total of 250 sweeps was presented. Participants were instructed to listen to the stimuli. The response to the task depended on the capability of the participants. A 700 msec time window was used, and analysis was based on the numerical values of the latencies (ms) and amplitudes (μV). P300 identified as a positive deflection after the N1-P2-N2 complex was considered as responses for further analysis.

3.3.4 Recording

3.3.4.1 Planning. The participants arrived at the recording room with freshly washed (not wet) hair and did not use any hair products (for example, gels or hair spray) when they came for recording. Before the participant arrived, the electrolyte solution was prepared, and the necessary items like measuring tape, pipettes, syringes, and three clean towels were kept ready.

3.3.4.2 Preparing the Electrolyte Formulation. As per the Electrical Geodesic Inc. (EGI) recommendation, HydroCel Saline (Potassium Chloride electrolyte

solution) was used for standard recordings. Following are the steps that were followed.

1. 10 cc (2 teaspoons) of powdered potassium chloride (KCl) was added into the rinse/electrolyte bucket.

2. 1 litre of warm distilled water was added to it.

3. 5 cc (1 teaspoon) of Johnson's Baby Shampoo was added to it.

4. The ingredients were stirred vigorously until the KCl is completely dissolved.

5. The solution was kept for 5 minutes.

3.3.4.3 Head Measurement. The head measurement was found out before applying the Geodesic Sensor Net to the subject's head. The head circumference was measured by running the tape along the side of the head, above the ear, toward the back and 2.5 cm above the external occipital protuberance (Inion), around the other side and above the other ear, and back to glabella. One end of measurement tape was placed on the glabella, and the other end was placed on the Inion, and the midpoint was marked. Similarly, the midpoint between the pre-auricular joints were marked. The point at which these two intersect is the vertex point, otherwise called Cz in the international 10-20 system (Silverman, 1963). The Net of the appropriate adult size was selected based on the measurement obtained. Marking the vertex was as follows:

1. The subject was asked to hold one end of the measuring tape to the nasion.
2. The tape was run over the top of the head until it reached Inion, and the midpoint was located. The midpoint was marked using a marker on the subject's head.
3. The distance between the pre-auricular points were measured by extending the measuring tape across the top of the head. The midpoint was located,

and it was marked on the head. The intersection point of these two lines gave the location of the vertex.

3.3.4.4 Net Application. The Net was soaked in the electrolyte solution (as it has sponge inserts), and was safely applied on the participant's head in such a way that the Cz electrode came on the vertex marked on the head. The participants were asked to remove earrings, glasses, and hair ties as it would become uncomfortable for them. The sensor net can be applied in less than 10 minutes without scalp abrasion, recording paste or gel, as the high-density geodesic sensor networks and related high-impedance amplifiers have been developed to accept impedance values of up to 100KΩ.

3.3.4.4.1 ***Soaking the Net in the Electrolye.*** The net was not soaked for a longer time, and care was taken so that the connectors not get wet.

1. The sensor end of the Net was dipped into the "electrolyte" bucket.
2. The sensors of the Net was dipped in electrolytes for at least 5 minutes to ensure adequate wetting of the sponges.
3. A towel was given to the participants to catch the electrolyte drips.
4. A towel was draped over the participant's shoulders.
5. The Net was lifted vertically out of the electrolyte bucket and was held in the same position, such that the excess electrolyte drip back into the container.

Then the Net was placed on the participant's head in such a way that the electrode mentioned as Cz was coming on the vertex. It had to be ensured that all the electrodes were placed correctly on the scalp of the participant. The chin strap was moved underneath the participant's chin and was secured using the cord lock. Participants were asked to rest on the chair and to remain awake throughout the

procedure. It was ensured that the interelectrode impedance was ≤ 50KOhms prior to testing. If the impedance was more, the electrolyte solution was put on the sponge on the electrodes.

The electrodes FCz and AFz were regarded as reference and ground, respectively during the online recording. Vertical (VEOG) and horizontal electroocculograms (HEOG), two additional electrodes, were used to monitor the eye movements. Particularly, VEOG was positioned at the right side of the right eye (Channels 8, 126, 25, 127), and HEOG was positioned below the left eye (Channels 125 and 128). Impedances for all electrodes were kept below 50 KΩ, during the whole task.

The ERPs that were used to record was P300. P300 was recorded as per the guidelines provided by Duncan et al. (2009). Few of the important guidelines that were considered in the present study are:

1. Use of oddball paradigm (passive paradigm, participants would only concentrate on stimuli without responses (Pokorny et al., 2013) - as it elicits robust P300 and reveals how the brain discriminates stimuli and process probability.
2. A minimum of 36 or more artefact-free trials with correction for ocular contributions.
3. The elicitor stimulus was delivered binaurally through speakers at 70 dB SPL. In order to elicit P300, the oddball paradigm was used. The summary of the protocol for recording is shown in Table 3.2.

Table 3.2

Summary of the Protocol for Recording P300.

Stimulus Parameters	**Details**	
Stimuli	Frequent	Infrequent
	/ḍa/	/ga/
Frequent to infrequent ratio	4 to 1 (80:20)	
Ear	Binaural	
Transducer	Speaker	
Intensity	70 dB SPL	
Inter-stimulus-interval	2000 ms	
Total number of sweeps	250	
Acquisition Parameters		
Filters	0.1 Hz -30 Hz	
Electrode	Cap electrode	
Montage	Hydrocel GSN 128 1.0	

3.4 Data Analysis Procedure- Response Analysis

Artifacts were automatically detected and manually verified for exclusion from additional analysis (bad channel >200 microvolts, eye blinks >140 microvolts, and eye movement >100 microvolts). For marking a channel bad, 50% or greater bad segments were used as the criteria for every channel; for marking a segment bad, greater than 20 bad channels were used as a criterion for every segment.

Bad channels (fluctuations over 200 μV) were spherical spline interpolated from nearby electrodes. Data were baseline-corrected using a 100 ms window prior to

the onset of all stimuli. Data were re-referenced from vertex recording to an average mastoid reference.

All artifact-free segments after processing were averaged by condition to produce a single event-related potential waveform for each condition for all participants and it was exported for plotting and statistical analysis. For analysis, the P300 was defined to be the most positive peak between 300 and 700 ms following stimulus onset.

The obtained raw electroencephalogram (EEG) file from the Net Station Acquisition Program was subjected to preprocessing using the Net Station Tools program and further analysis was carried out using the EEGLAB toolbox within the MATLAB software (The Mathworks Inc., MA).

3.4.1 Segmentation

The obtained continuous raw EEG data had to be segmented first. For this purpose, the Net Station Tools program was utilized. Initially, a segmentation tool was created using this program to segment the raw EEG data file. This segmentation tool was named "Speech segmentation". Within the speech segmentation tool, the parameters were set in such a way that, segments containing the stimuli /da/ and segments containing the stimuli /ga/ were segmented. Each segment consisted of 100ms duration before the presentation of the stimulus and 1500ms after the presentation of the stimulus. Thus, each stimulus was segmented in 250 segments (200 segments of frequent stimuli /da/ and 50 segments of infrequent stimuli /ga/).

3.4.2 File Export

Following the process of segmentation, the files had to be converted to Net Station Simple Binary format (.raw) to carry out further analysis using MATLAB. For

this purpose, the Net Station Tools program was utilized. A file conversion tool was created to convert the segmented files into the ".raw" format. This was executed for the speech EEG files to obtain converted files in the ".raw" format.

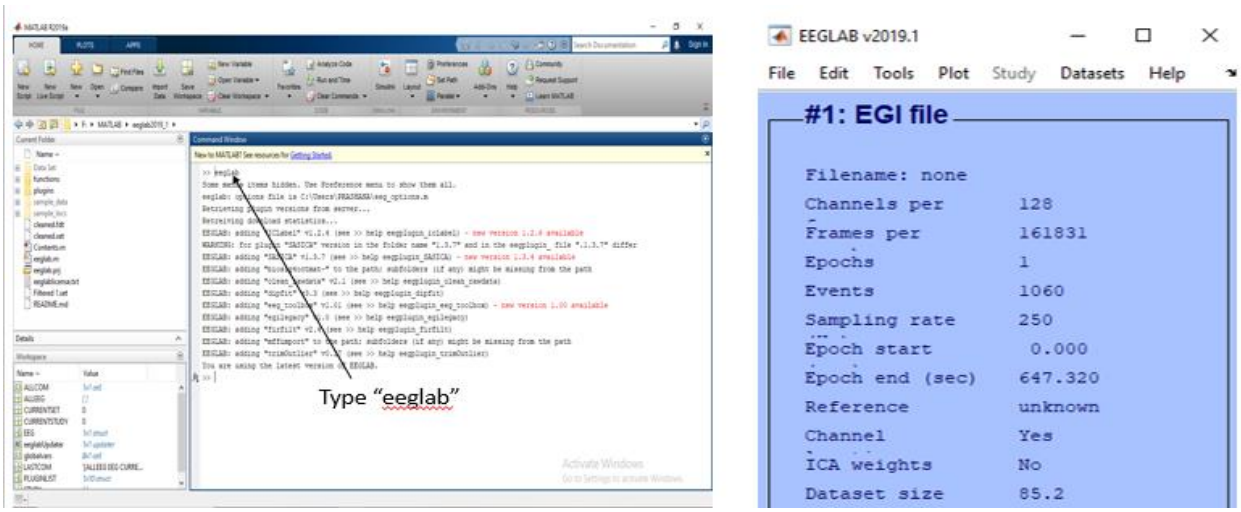
3.4.3 Processing in MATLAB

EEGLAB plugin (Swartz Center for Computational Neuroscience, CA)which is an interactive MATLAB toolbox for processing continuous and event-related EEG was used for further analysis. Further analysis in MATLAB was carried out according to Makoto's preprocessing pipeline (https://sccn.ucsd.edu/wiki/Makoto%27s_preprocessing_pipeline). The steps of processing in MATLAB are as follows:

Step 1: MATLAB was opened and the EEGLAB toolbox was loaded into MATLAB by typing "eeglab" as shown in Figure 3.1.

Figure 3.1

Steps for Loading EEGLAB Toolbox to the Software

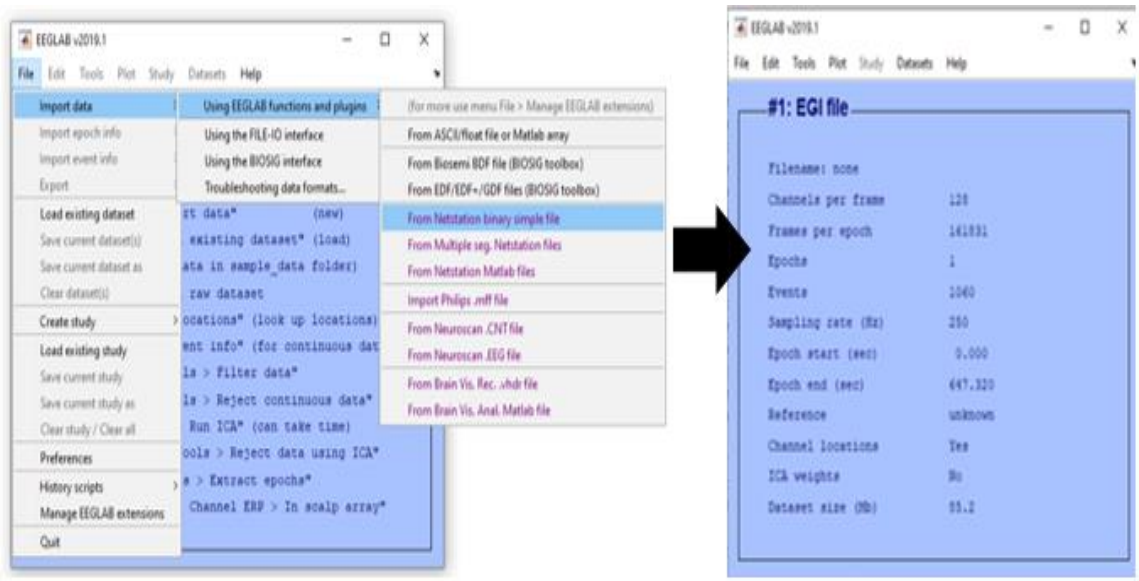


Step 2: Importing the binary EGI data file was done for initiating the analysis process as shown in Figure 3.2.

File > Import Data > Using EEGLAB functions and plugins > From Netstation binary sample file > Select the raw data > Ok

Figure 3.2

Steps to be followed for Importing the Data



Step 3: Importing channel locations (Geodesic Sensor Net Hydrocel 128) was done to plot the EEG scalp maps either in 2-D or 3-D template and for approximating data source locations, the EEGLAB dataset must, therefore, hold information on the scalp locations of the recording electrodes.The channel location was imported and was applied as shown in Figures3.3 and 3.4.

Edit > Channel Locations > Read Locations > Sample locs – GSN Hydrocel 128 > Autodetect – Ok > Opt Head Centre > Autodetect > Ok

Figure 3.3

Steps to Import the Channel Location

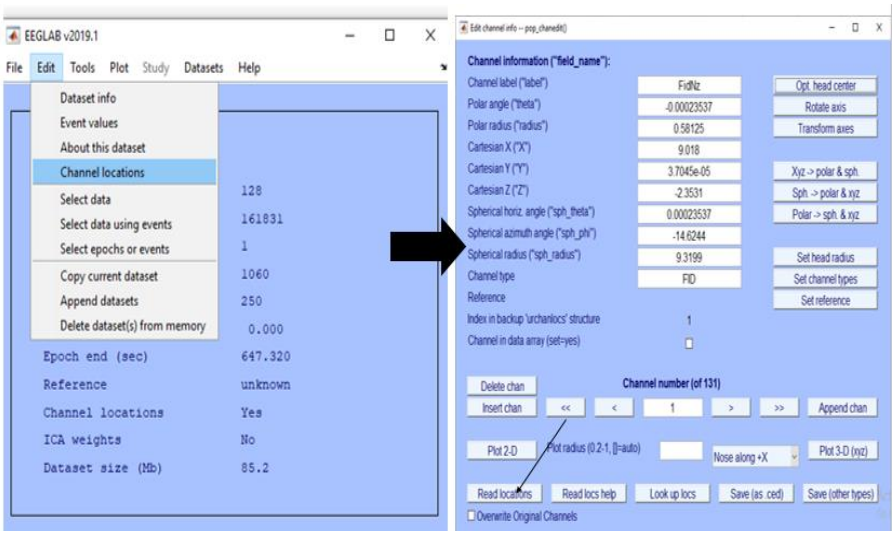
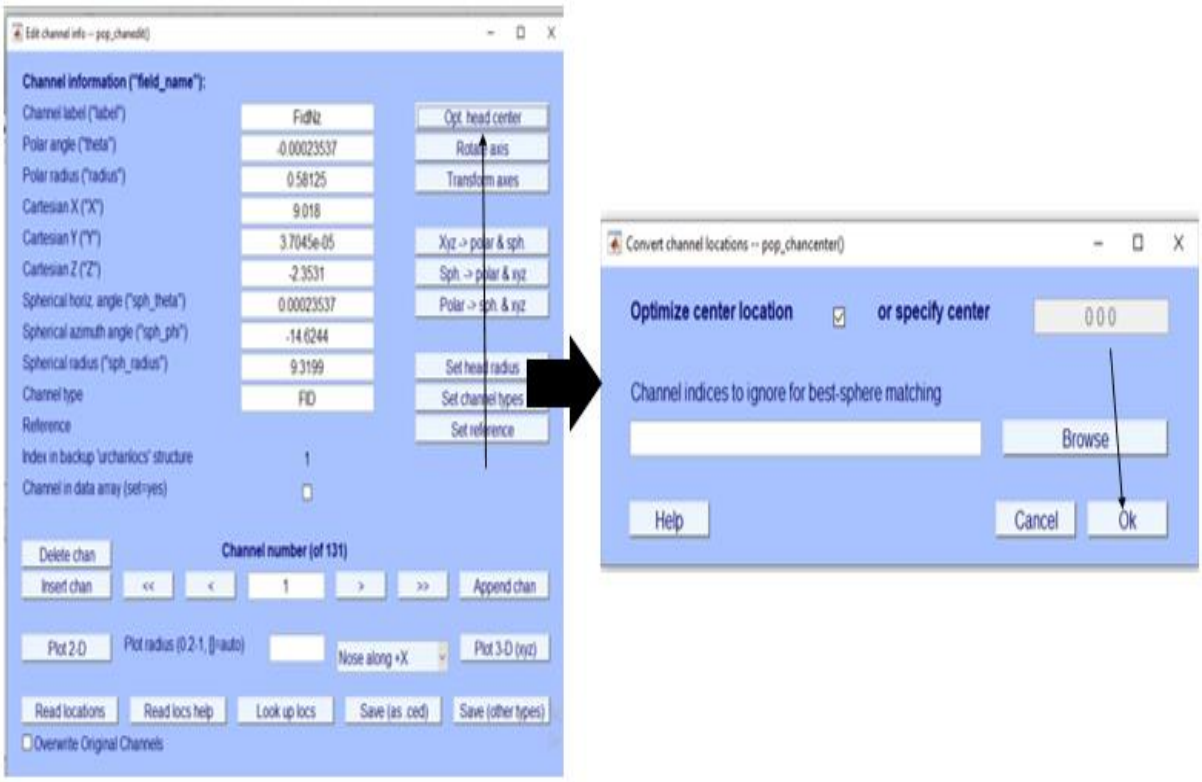


Figure 3.4

Steps to Apply the Channel Location

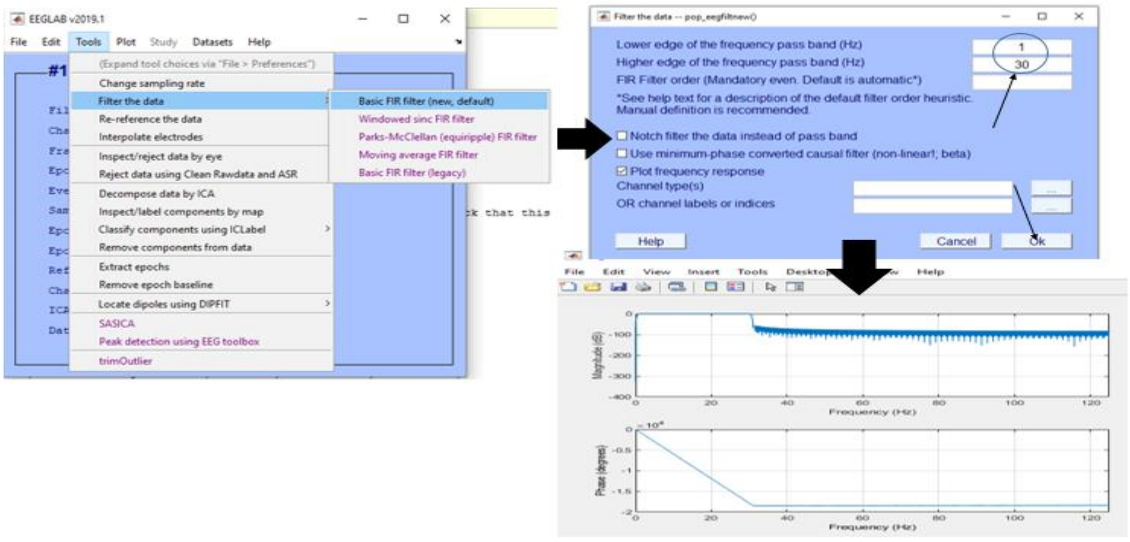


Step 4: Data was then subjected to Finite Impulse Response (FIR) Filtering with a bandpass of 0.1 Hz to 30 Hz as shown in Figure 3.5. It was strongly suggested that continuous EEG data be filtered before epoch or artifact removal, even though epoch data may even be filtered with this function (each epoch being filtered separately). Continuous data filtering mitigates the emergence of filtering artifacts at epoch boundary and the data set is saved.

Tools > Filter the data > Basic FIR Filtering > Set Lower and Higher edge of the frequency pass band as 0.1 Hz and 30 Hz respectively > Ok

Figure 3.5

The Steps to follow for Filtering the Data



Step 5: Initially, the entire EEG data file was screened via scrolling manually through channel activities for bad channels and visual artifacts. These were removed manually. Following this, a clean raw data EEGlab plugin was applied for controlled objective rejection criteria as shown in Figure 3.6.

Tools > Clean the data using clean raw data and ASR. Figure 3.7 shows the rejected data in red colour and the retained data in blue colour.

Figure 3.6

The Steps followed for Cleaning the Data

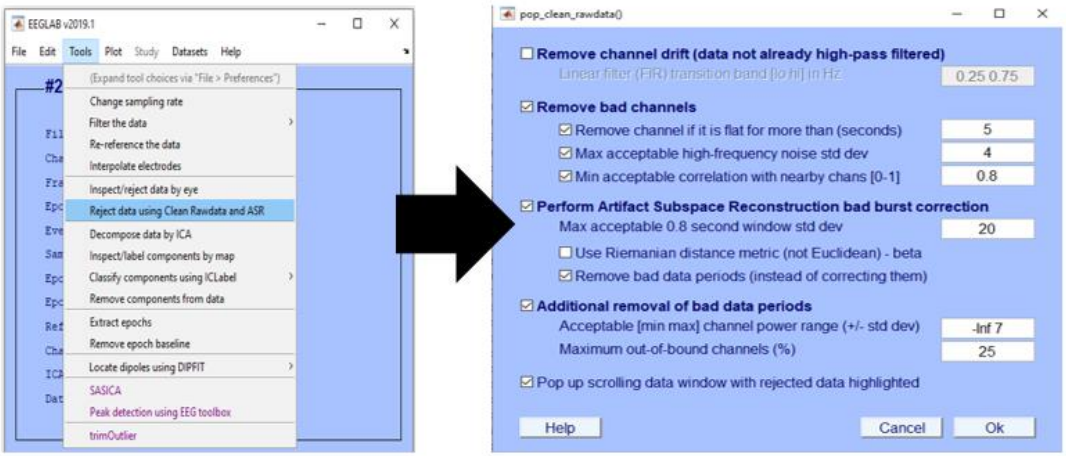
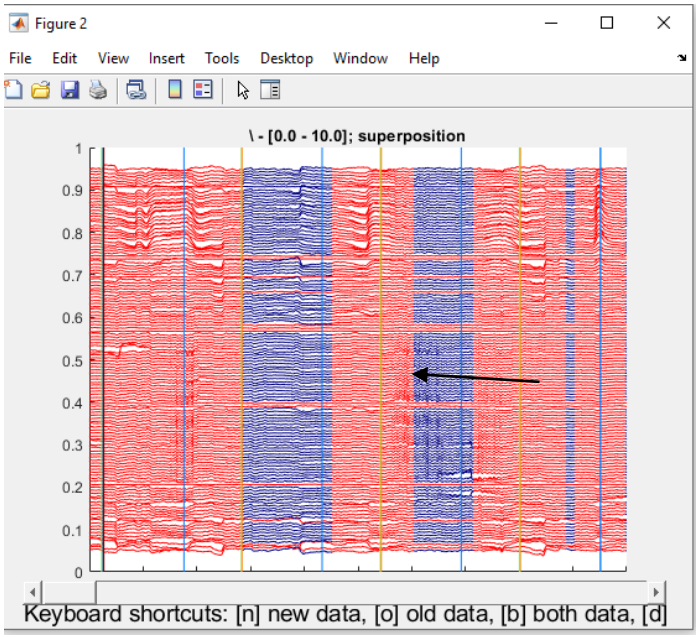


Figure 3.7

The Window with the Rejected and Retained Data



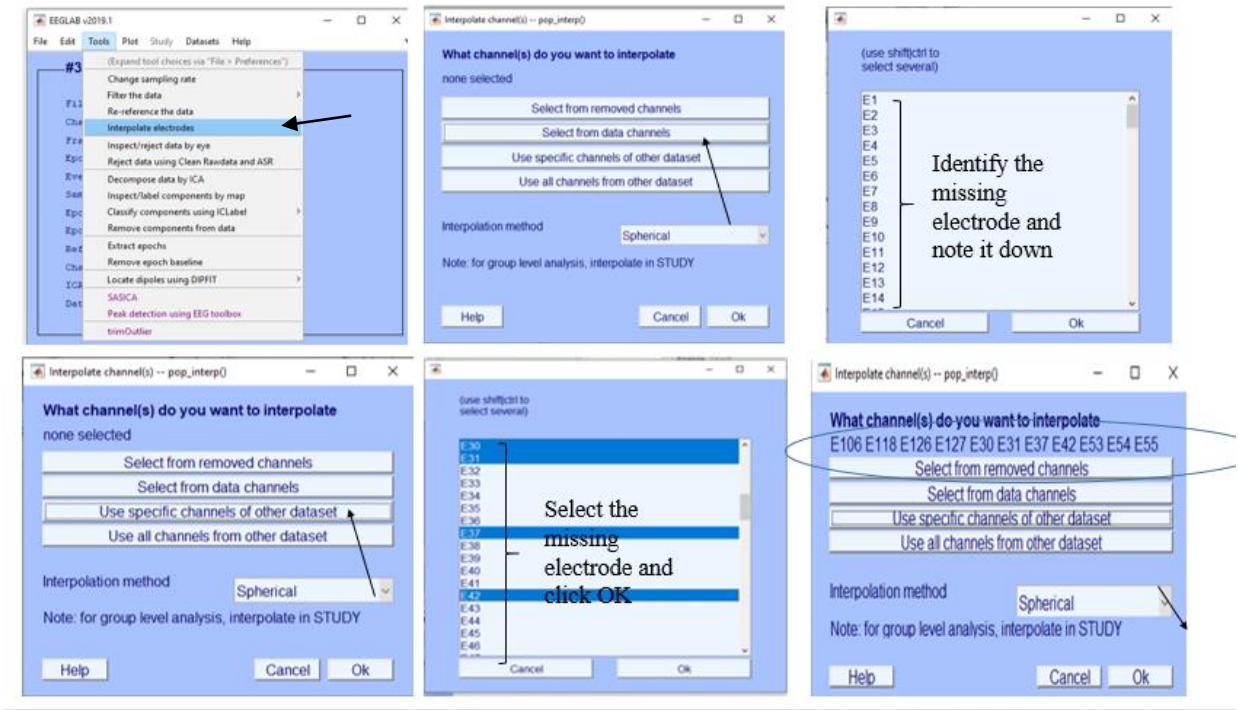
Step 6: Interpolation of all of the channels removed was carried out to reduce potential bias in the next average reference stage. For instance, if 128 channels exist and 20 channels are recognized as bad and rejected, but only from the right

hemisphere, then the number of channels in the left vs. the right hemisphere is 64 vs. 44, with a mean bias towards the left hemisphere. To prevent such events, the channels were interpolated. In this procedure, when the cleaned data is processed, the researcher will note the missing rejected data as well as the channels selected in the filtered data set, and the dataset was saved as shown in Figure 3.8.

Tools > Interpolate electrodes > Select from data channels – Note down the channels that are removed > Use specific channels of other data set > Dataset Index – Give the number of Filtered Dataset > Select the removed electrodes > Ok

Figure 3.8

The Steps followed for Interpolating the Electrodes



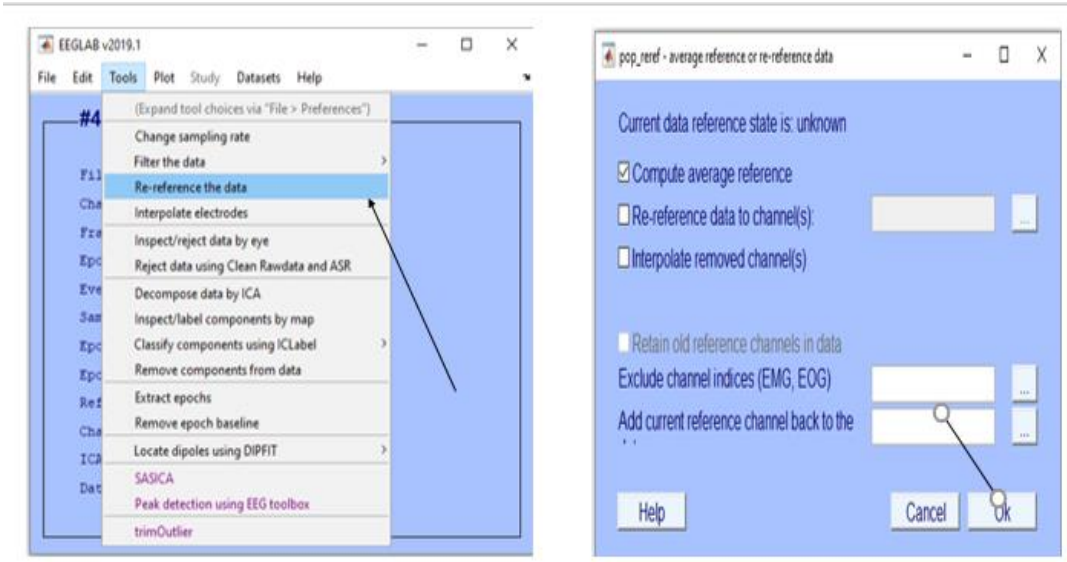
Step 7: The data were re-referenced to the average reference because when the EEG is produced on a cortex with a dipolar current distribution and without external sources, there are at all times the very same number of positive and negative potential changes due to the retention of the charge. Therefore, scalp topography should be null. By re-

reference to average channel values, we presume that there is (really) no generation of charges that are monopolar sources and sinks, and also the average reference is often very helpful in suppressing line noise.

Tools > Re-reference the Data > Compute average reference > Ok as shown in Figure 3.9.

Figure 3.9

The Steps followed for Re-referencing the Data



Step 8: Independent Component Analysis (ICA) was conducted. The decomposition of data by ICA (including PCA) includes a linear change of base from data gathered by single scalp channels to a spatially transformed "virtual channel" premise. In other words, rather than collecting simultaneously recorded single-channel data records, the data is processed into a collection of simultaneously recorded spatial filter outputs applicable to all multi-channel data, and 64 components with maximum channel activity representation were derived and components were classified using the IC label.

Tools > Decompose data by ICA > Commandline option – ‘pca’, 64 > Ok (as shown in Figure 3.10) and the components were classified by following these steps: Tools > Classify Components > View extended component properties > Component indices to plot – 1:64 (as shown in Figure 3.11)

Figure 3.10

The Steps followed for Decomposing the Data and the Components obtained after Following the Steps

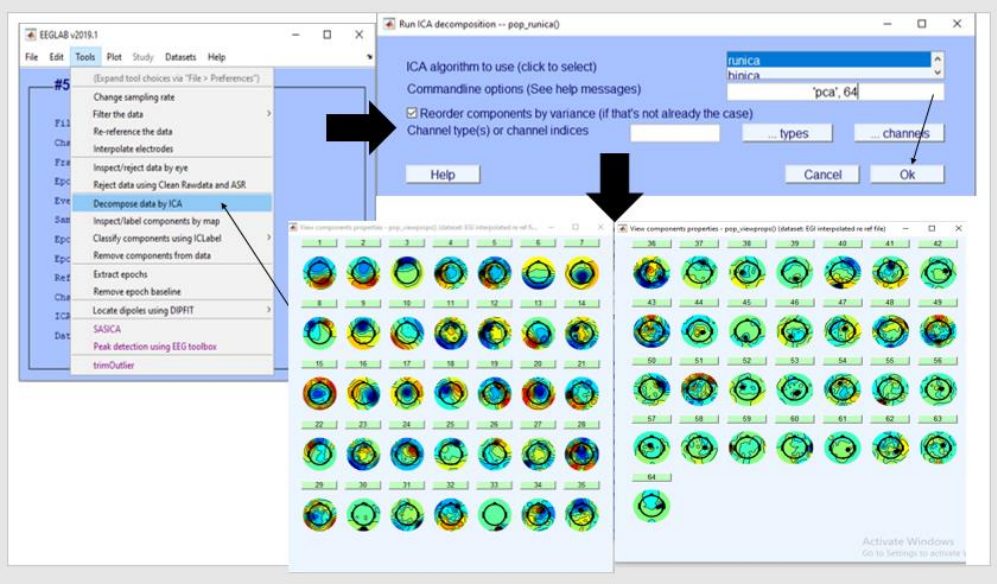


Figure 3.11

The Steps followed for Classifying the Components

Step 9: SASICA plugin was applied to perform the automatic detection of artifactual components - The methods include 1). Autocorrelation, which identifies noisy elements with weak autocorrelation (usually muscular artifacts). 2). Focal components identify components that are too focal and are therefore unlikely to match neural activity (usually the wrong channel or muscle artifacts). 3). Signal-to - noise ratio, works by detecting components with a weak signal-to-noise ratio among both arbitrary baselines as well as interest time windows. After applying the plugin another window pops up showing the artefacts in red colour which makes it easier to remove the unwanted components as shown in Figure 3.13.

Tools > SASICA > Autocorrelation – Enable; Focal components – Enable; Correlation with other channel(s) – Enable; Adjust selection – Enable > Compute (as shown in Figure 3.12)

Figure 3.12

The Steps followed for Applying the Plugin

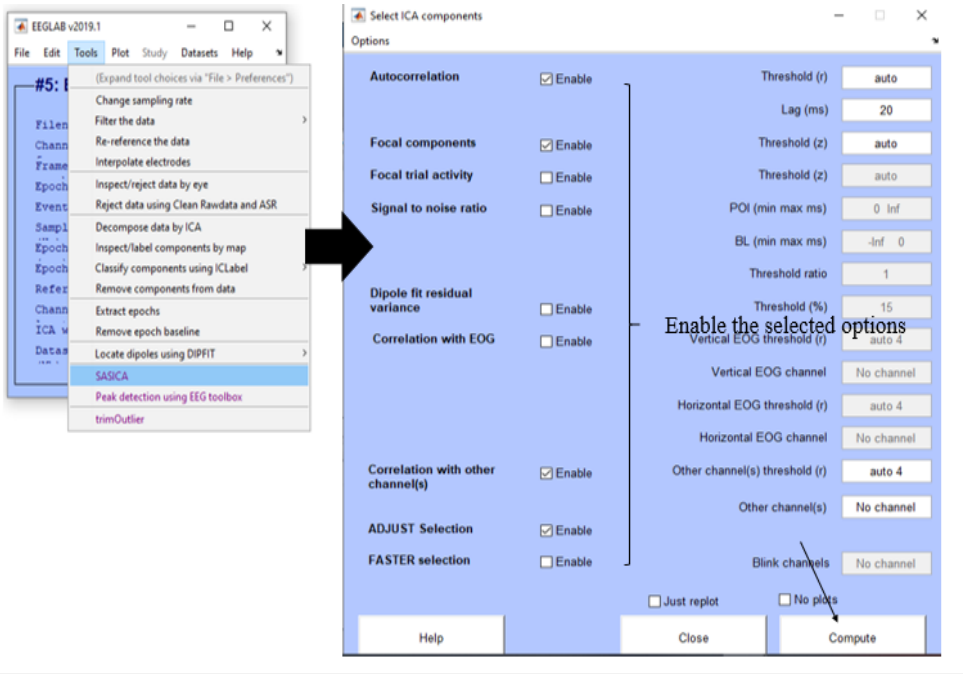
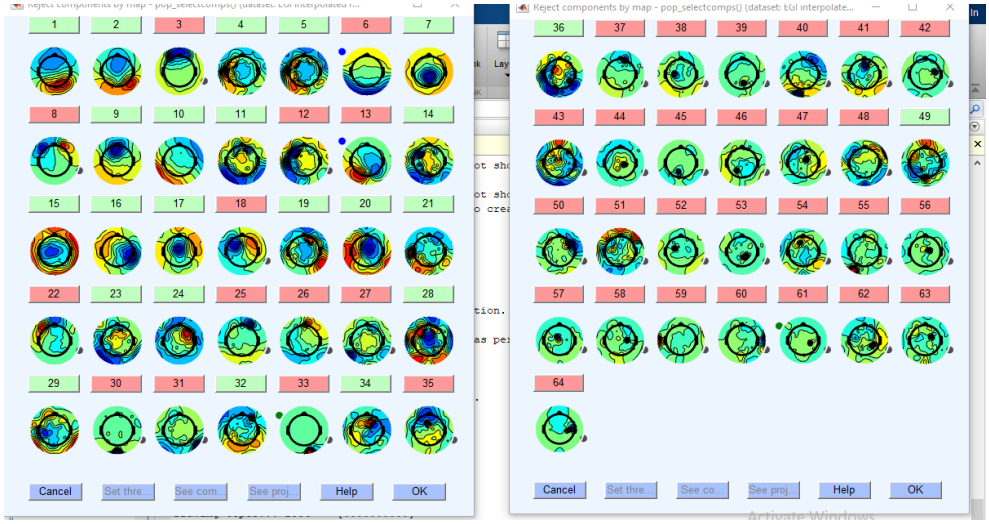


Figure 3.13

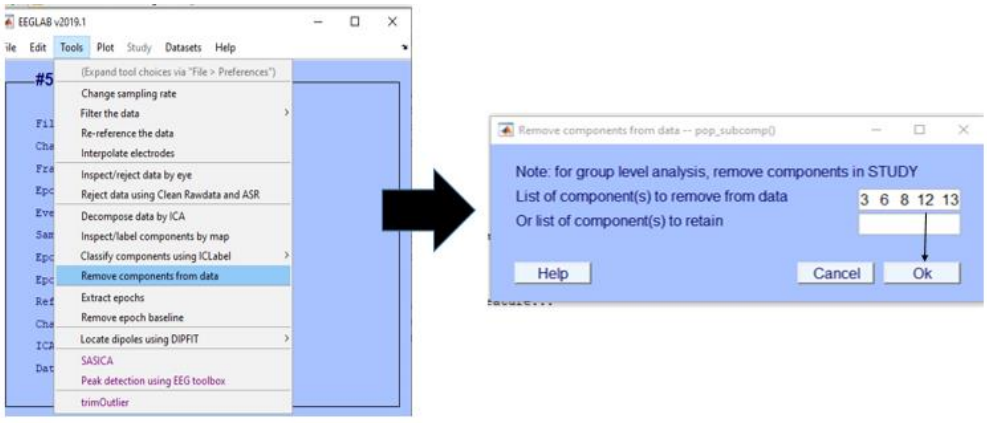
The Components with Artefacts in Red Colour



Step 10: Independent Components (ICs) with eye-related or muscle-related components were removed, and ICs with activities of interest from the Brain (confirmed with the presence of dipoles and ERP waves) were selected as shown in Figure3.14. Tools > Remove components from data > OK > Accept > Save as a new file. After removing the unwanted components, the dataset was saved to extract epochs from this dataset.

Figure 3.14

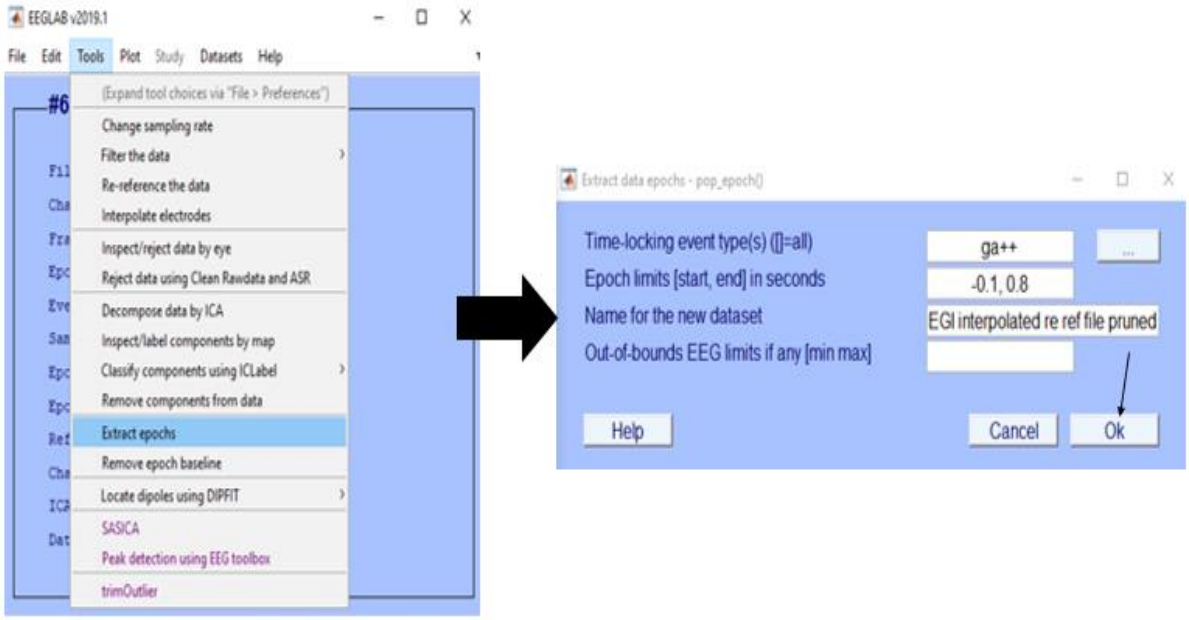
Steps followed for Removing Unwanted Components



Step 11: Epochs were extracted from the retained ICs with the epoch limit of 0.1 seconds before the stimulus onset and 0.8 seconds after the stimulus onset for both the frequent and the infrequent events. The steps followed were as shown in Figure3.15. Tools > Extract Epochs > Time locking event type – Select the event (for example: ga) – Epoch limit – Mention as "-0.1 0.8" – Ok

Figure 3.15

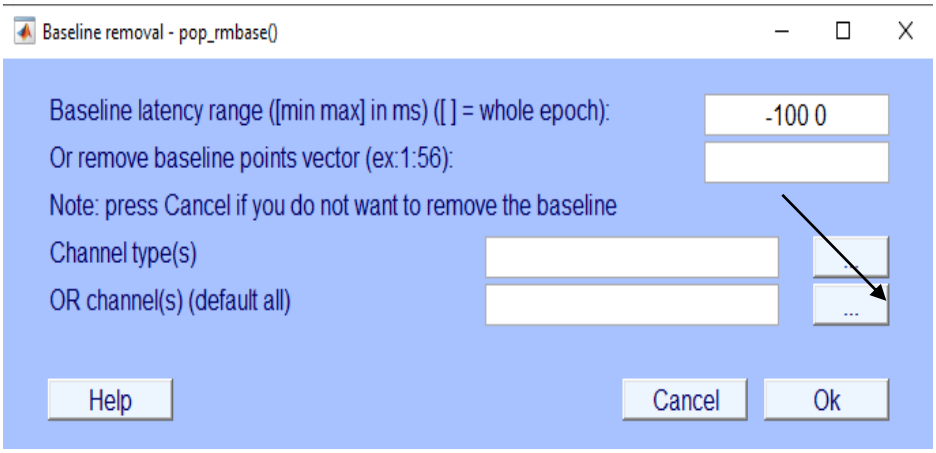
Steps followed for Extracting the Epochs



Step 12: Baseline correction was carried out with a latency range of 100ms, where Baseline correction is a common method used during the analysis of event-related potentials, to account for irrelevant differences in the signal baseline. It is applied to an epoch data set by specifying a sub-window, where the mean value of the signal in that window is subtracted from the whole signal (by channel or component). The Figure 3.16 shows the baseline correction being applied.

Figure 3.16

The Window that Pops up after Step 11



Step 12: ERP image was plotted. The waveform of the P300 potential as well as the topographical representation was plotted.The Figure 3.17 shows the steps that were followed for plotting the ERPs and Figure 3.18 shows the P300 potential.

Plot > Sum/Compare comp. ERPs. > Datasets to average – Give the dataset numbers– Ok

Figure 3.17

The Steps followed for Plotting the ERP

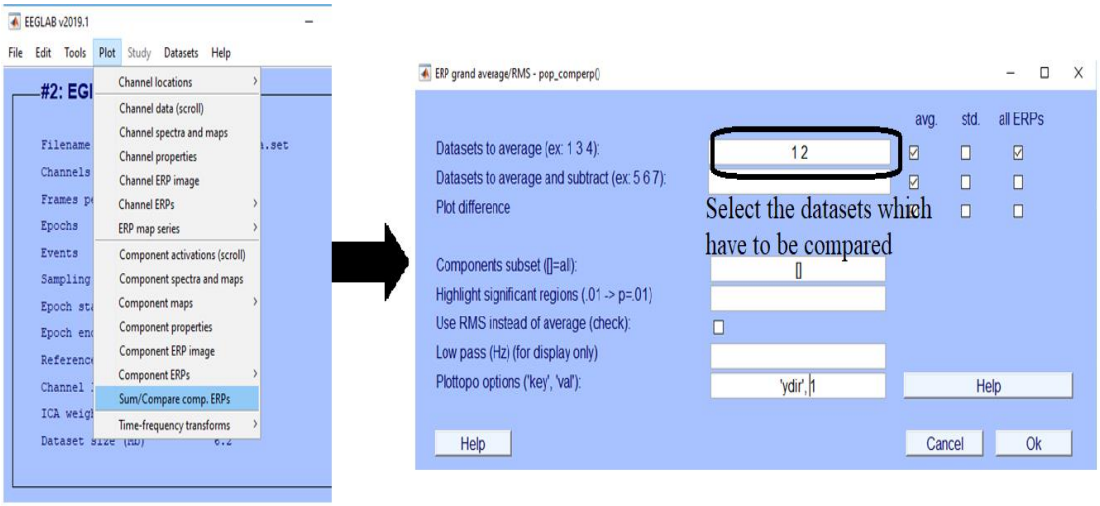
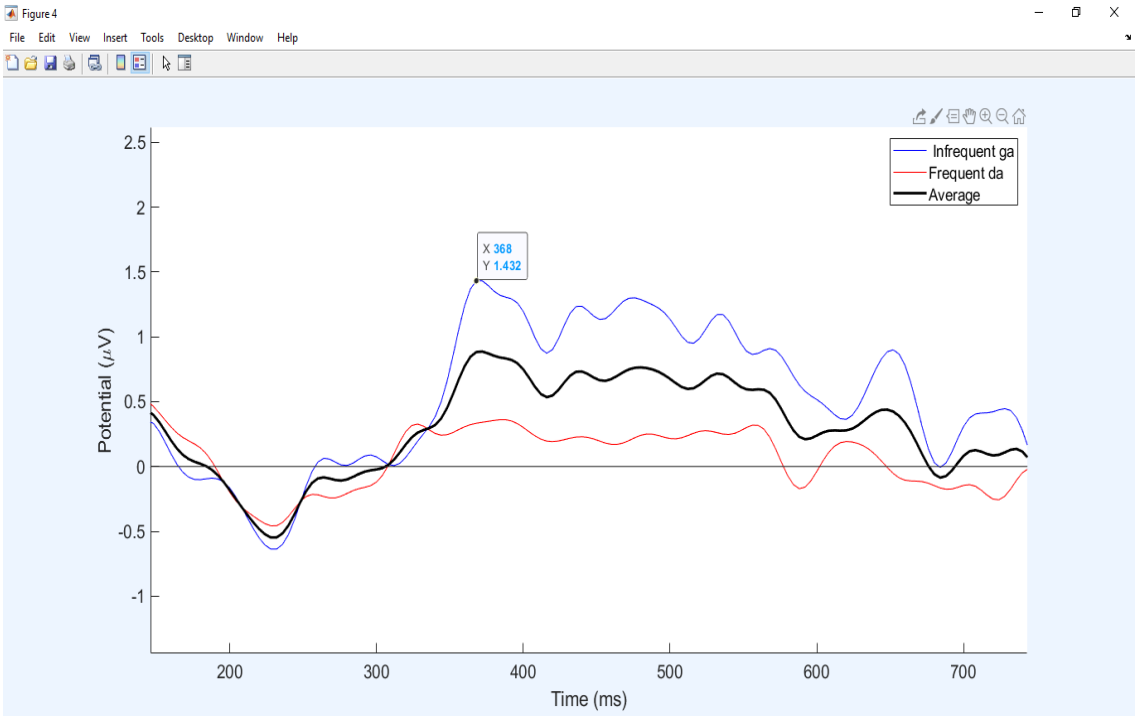


Figure 3.18

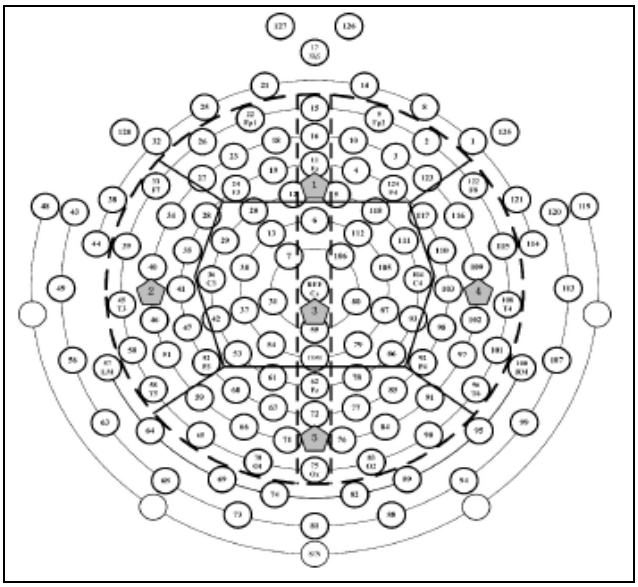
The Event Related Potential P300 obtained after the Analysis



Thus, the P300 responses were identified in each participant for the oddball paradigms, and it was analyzed to obtain the peak amplitude and latency. The average waves which were recorded for the target, as well as non-target stimuli, were compared. As the responses from different electrode sites were to be compared, the method mentioned by Bian et al., (2014), was used. In his study, he mentioned that electrodes should be focussed on during the analysis and he divided the electrodes on the sensor net into different regions to ease the analysis procedure as shown in Figure 3.19.

Figure 3.19

Electrode Distribution of 128 Channel Geodesic Sensor Net with Reference to Bian et al., (2014).



To detect the EEG power in different areas of the brain, it was divided into five regions: namely, frontal (F), left temporal (LT), central (C), right temporal (RT), and posterior (P). The vertical line in the middle separates the regions into right and left hemispheres (Bian et al., 2014). The grey colour electrodes, which are in the outermost belt of electrodes of the sensor-net (19 channels - E43, E48, E49, E56, E63, E68, E73, E81, E88, E94, E99, E107, E113, E119, E120, E125, E126, E127, and E128) were not considered for analysis as they tend to show residual muscle artefacts (Calbi et al., 2019). For analysis, the frontal electrode sites, central electrode sites, midline electrodes, posterior electrode sites, and the left and the right-side electrodes were considered. Apart from these, topographical analysis at the cortical level was also carried out.

Chapter IV

Results

The primary aim of the study was to profile the neurophysiological assessment (P300) of individuals with aphasia. i.e., Participant-A, Participant-B, and Participant-C, by checking for the presence or absence of P300 components through the analysis of waveforms in the particular electrode sites and commenting on the corresponding brain activation (active brain source configuration) of these individuals through topographical representation. Since the study comprised of only three participants, statistical analysis was not carried out. The results are organized under the following headings:

- **P300 Represented in the Recorded Waveform of Individuals with Aphasia**
- **Topographical Representation of P300 in Individuals with Aphasia**

4.1 P300 Represented in the Recorded Waveform of Individuals with Aphasia

To obtain the waveform representing the P300 response, the analysis was carried out incorporating the electrodes (Appendix A) at different brain areas off line using Net station 4.5 software (Electrical Geodesics) and the corresponding amplitude and latency were noted. The interested electrodes were selected to detect EEG power in different regions and inter-/intra regions, the brain was divided into five regions: Frontal (F), Left Temporal (LT), Central (C), Right Temporal (RT), and Posterior (P). For the aim of the present study, the analysis was further divided and named under the following sub-headings (1). Posterior electrode site (Colour code - Orange- Appendix A), (2). Central electrode site (Colour code-Purple- Appendix A), (3). Midline electrode (Marked as a dotted line), (4). Frontal electrode Sites (Colour code-Pink-

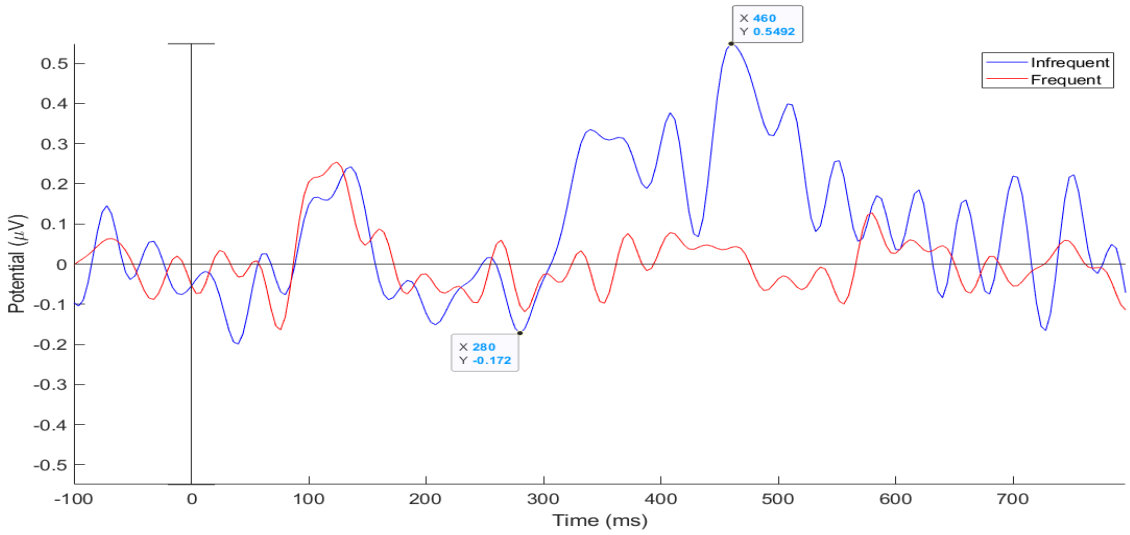
Appendix A), (5). Left electrode site (Portion towards left side from the midline) and (6). Right electrode site (Portion towards right side from the midline). (7). Average.

Out of the three participants who participated in the study, the P300 potential was present in only 'Participant A'. Participant B and Participant C did not exhibit the P300 potential. Hence the P300 representation with reference to latency and amplitude at various electrode sites of 'Participants A' only is profiled in detail under the following sub-headings.

4.1.1 Posterior Electrode Sites

Figure 4.1

Waveforms with P300 Responses for Posterior Electrode Regions of 'Participant A'

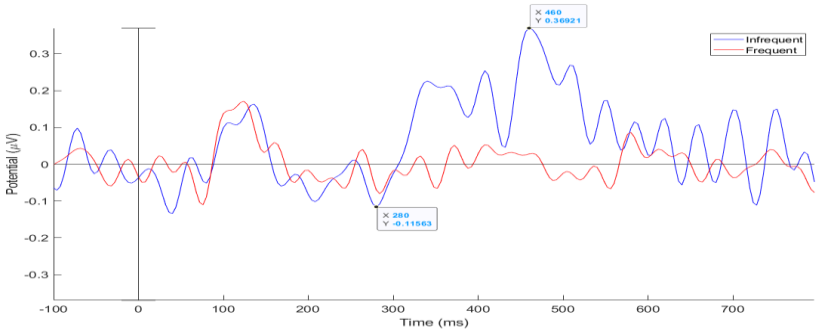


With reference to the brain region, the posterior region is one of the best noted in comparison with all other electrode sites. Figure 4.1 shows the responses from the electrode sites in this posterior region. The latency of the P300 potential is 460 ms and it has an amplitude of 0.549 μV.

4.1.2 Central Electrode Sites

Figure 4.2

Waveforms with P300 Responses for the Central Electrode Sites of 'Participant A'

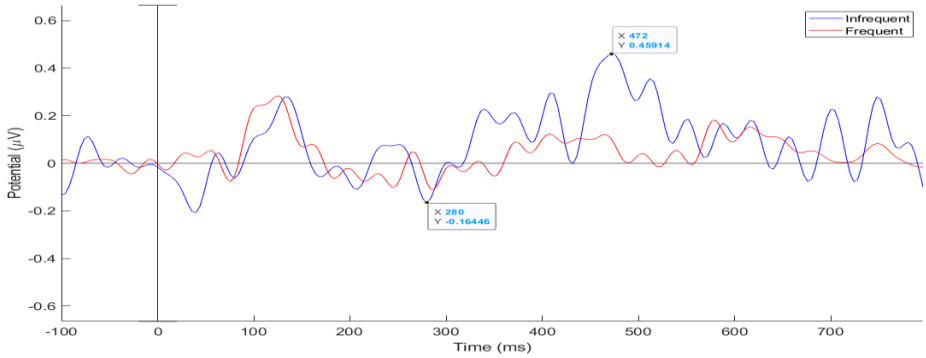


The responses from these electrodes were grouped as the central region. Figure 4.2 shows the P300 potential with an amplitude of 0.369 μV and a latency of 460 ms.

4.1.3 Midline Electrode Sites

Figure 4.3

Waveforms with P300 Responses for the Midline Electrodes Sites of 'Participant A'

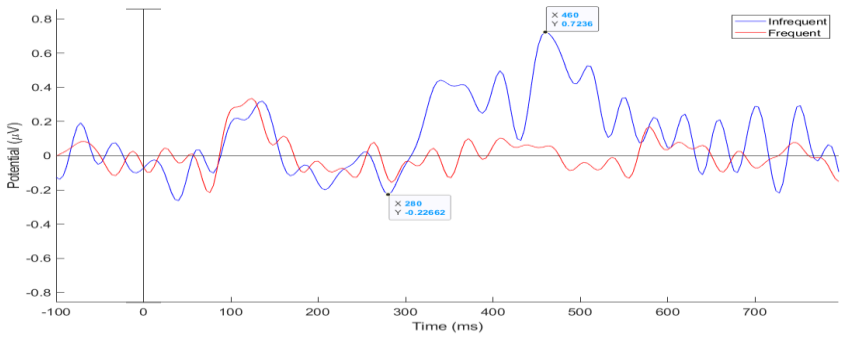


The responses from the midline electrodes were also analyzed and the corresponding waveform is shown in Figure 4.3. The P300 potential has an amplitude of 0.459 μV and a latency of 472 ms.

4.1.4 Frontal electrode Sites

Figure 4.4

Waveforms with P300 Responses for Frontal Region Sites of 'Participant A'

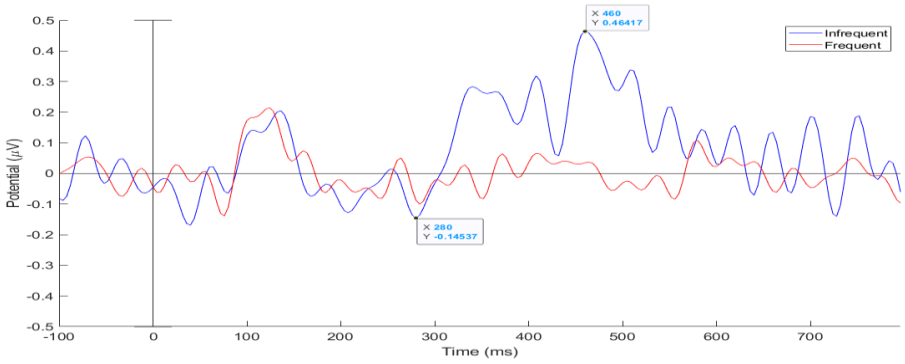


The responses from the electrode sites of the frontal region are shown in Figure 4.4. The latency of the P300 potential is 460 ms and it has an amplitude of 0.723 μV.

4.1.5 Left Electrode Sites

Figure 4.5

Waveforms with P300 Responses for Electrodes of the Left side Region of the Brain of Participant A

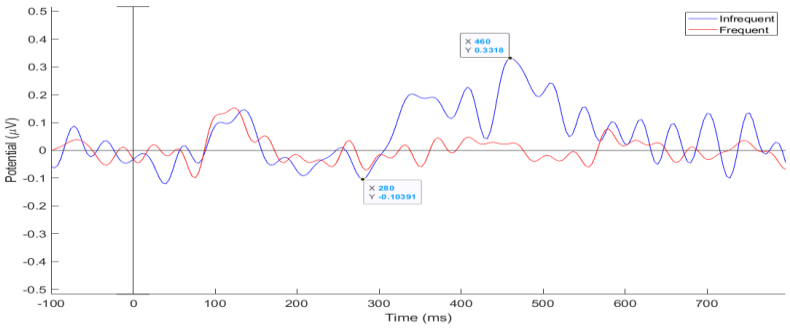


The responses picked up by the electrodes on the left side of the brain were grouped as left electrode sites. Figure 4.5 represents a latency of 460 ms and an amplitude of 0.464 μV of the P300 potential.

4.1.6 Right Electrode Sites

Figure 4.6

Waveforms with P300 Responses for the Electrodes of the Right side Region of the Brain of ParticipantA

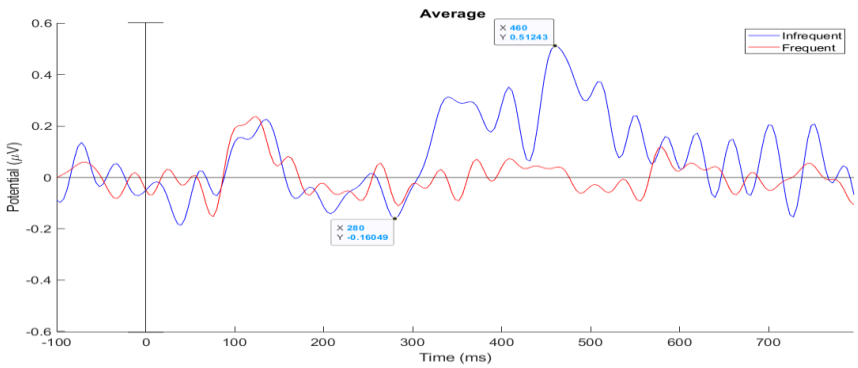


Similar to the left electrode site, the right electrode sites were also studied. The responses from the electrodes on the right side are shown in Figure 4.6. The P300 potential has an amplitude of 0.331 μV and a latency of 460 ms.

4.1.7 Average

Figure 4.7

Waveforms with P300 Response Averaged for the Speech Stimuli at all Electrode Sites of Participant A



The grand average from all the electrode sites is shown in Figure 4.7. The P300 potential has a peak latency at 460 ms and an amplitude of 0.512 µV.

Figure 4.8

Waveforms showing the Average Responses for Participant B

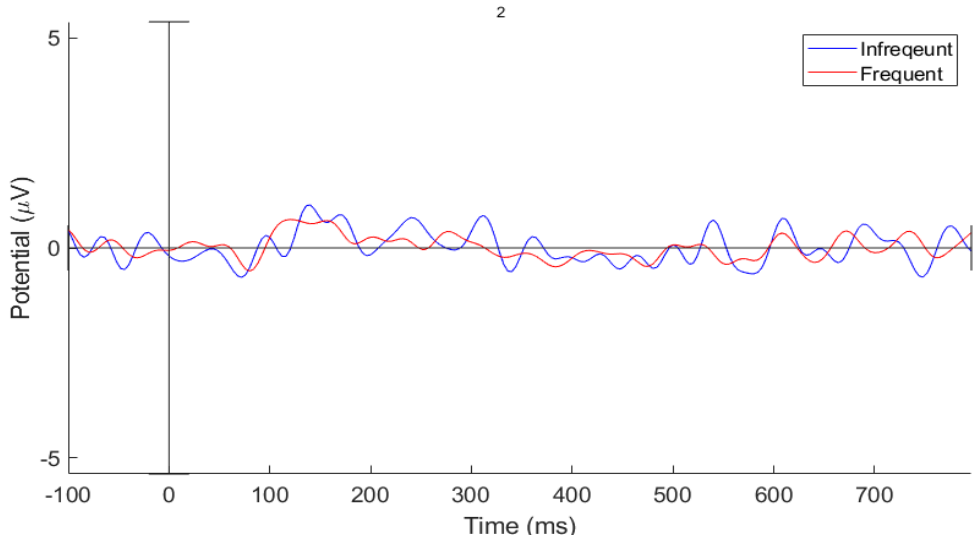
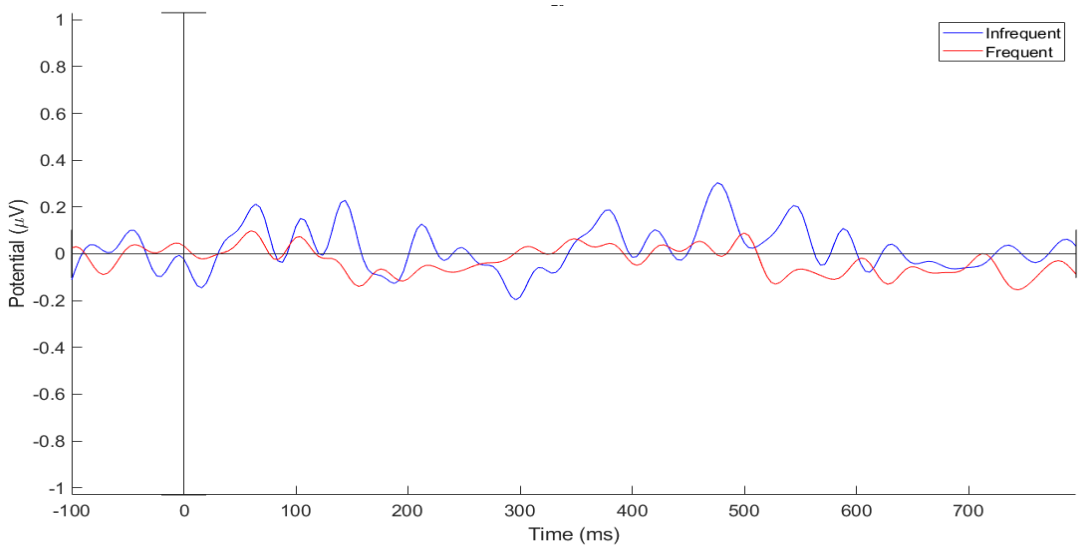


Figure 4.9

Waveforms showing the Average Responses for Participant C



The P300 potential of Participants B and C are as shown in Figure 4.8 and 4.9.

The P300 potential was found to be absent in all of the electrode sites for 'Participant B' and 'Participant C' for the auditory stimuli that were presented.

To summarize, the P300 responses of the 'Participant A'with reference to different electrode sites, the amplitude, and the latency value is tabulated in Table 4.1. From the table, it is observed that the latency is relatively prolonged for the 'Midline' electrode site in comparison with the other electrode sites. With reference to amplitude, the amplitude is highest for 'Frontal' followed by the 'Posterior' electrode site. Figure 4.10 and Figure 4.11 represent the latency and amplitude value separately for each electrode sites of Participant A.

Table 4.1

Overview of the Latency and Amplitude of the P300 Potential of 'Participant A'

Electrode Sites	Latency (ms)	Amplitude (μV)
Posterior	460	0.549
Central	460	0.369
Midline	**472**	0.459
Frontal	460	***0.723***
Left	460	0.464
Right	460	0.331
Average	460	0.512

Figure 4.10

Graphical Representation of the Latencies across Different Electrode Sites

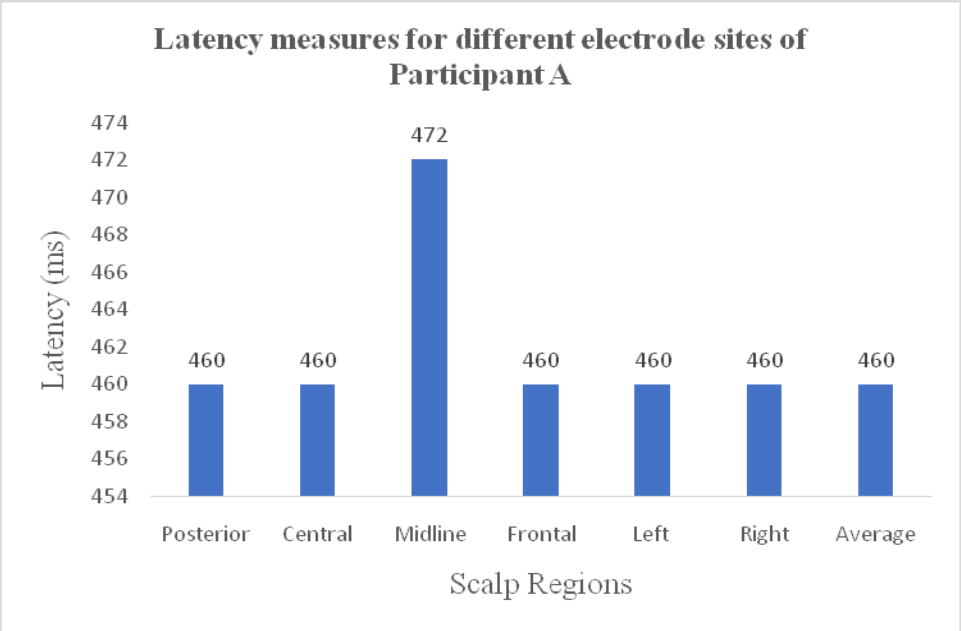
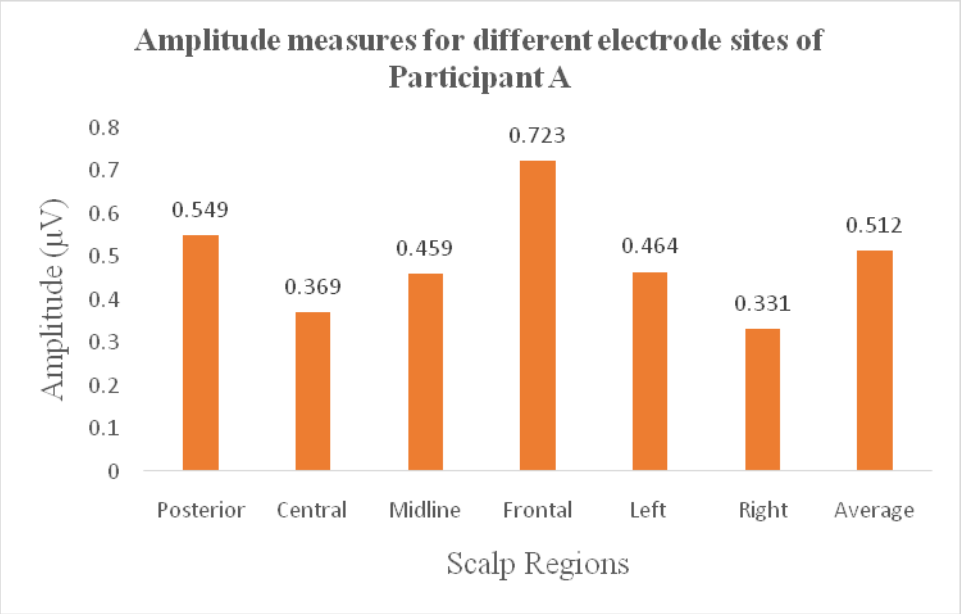


Figure 4.11

Graphical Representation of the Amplitude Values across Different Electrode Sites



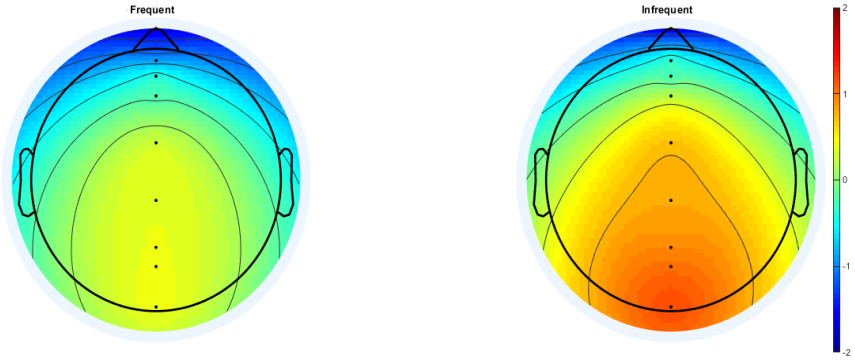
4.2 Topographical Representation of P300 in Individuals with Aphasia

The topographical distributions of the mean amplitude and latency for the frequent and infrequent stimuli were studied for 'Participant A' who showed the presence of P300 potential (peak latency and amplitude) in comparison with 'Participant B & C' who did not show the presence of P300.

Topography distributions of the P300 potential of 'Participant A' at the peak latency is represented in Figure 3.1.

Figure 4.12

Comparison of Activation at Peak for Participant A



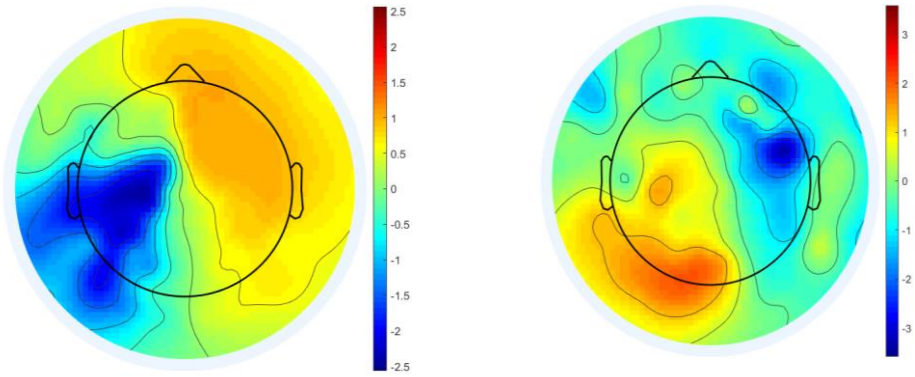
*Note.*The brain activation for the frequent and the infrequent stimuli are shown in the figure. The darker red shades in the posterior aspect of the brain indicatesbrain activation in response to the stimuli.

Figure 4.12 shows the comparison of brain activation for the frequent and the infrequent stimuli at the peak latency. The darker shades for the infrequent one shows the brain activity for the infrequent stimuli at posterior electrode site to a greater extent than the other electrode sites. There is comparatively no brain activation seen for the frequent stimuli. The brain activation is seen in the form of scattered responses from the scalp regions of Participant A.

When the topographical representation of Participant A was compared with Participant B and C, it was relatively very dissimilar as shown in Figure 4.13. The brain activation from all the electrode sites for both Participant B and Participant C have been averaged in the figure shown below. Participant B shows minimal brain activity on the right hemisphere region and some regions of the frontal electrode sites of the left hemisphere, where as Participant C shows minimal amount of brain activity on the posterior aspect of the left hemisphere even though the P300 potential is absent. The minimum responses seen in the scalp regions of participant B and C are scattered responses from the brain.

Figure 4.13

Comparison of the Activation for all the Electrodes of 'Participant B' and 'Participant C'



Participant B Participant C

Note. The darker red shades shows greater brain activation and the blue shades shows no activation

Chapter V

Discussion

The present study aimed to measure the amplitude and latency values of ERP-P300 using auditory stimuli (speech stimuli) in individuals with aphasia at their pre-therapy period (<5 sessions) and to profile the P300 assessment of individuals with aphasia. The analysis of the obtained data showed that only one among the three participants exhibited the P300 potential. An attempt has been made to justify the findings and to derive appropriate implications.

This discussion is organized into the following sub-headings:

- P300 Potential and Topography in Participant A
- P300 Potential and Topography in Participant B
- P300 Potential and Topography in Participant C
- P300 Potential with respect to the Amplitude and Latency in Individuals with Aphasia and the Topographic Representation

5.1 P300 Potential and Topography in Participant A

The analysis was carried out for the three participants and, it was found out that only 'Participant A' exhibited the P300 potential. The analysis was carried out in detail for Participant A to identify whether there are any changes in the waveform in terms of its amplitude and latency concerning the different electrode sites, namely, frontal, midline, central, posterior, left and right electrode regions.

Participant A was diagnosed as having Global Aphasia after the evaluation and was observed to be showing significant improvement in WAB – K results at the time of pre-therapy evaluation. MRI findings showed ill-defined hypodensities in the left

peri-rolandic cortex and temporo-occipital cortex- subacute infarcts. The scores of Spontaneous Speech (SS), Auditory Verbal Comprehension (AVC), Repetition (R), and Naming (N), were improving at the time of pre-therapy evaluation.The possible reason for this improved score on WAB- R could be the speech stimulation during the post morbid duration. With reference to the P300 assessment, the participant was giving attention to the stimulus on observation during the recording and was not getting distracted. The normative values for the P300 amplitude varied from 2.2 μV to 18.5 μV in healthy elderly subjects (Pavarini et al., 2018). For normal healthy adults, the amplitude values of P300 range from 1.7 μV to 20 μV (Reis & Iório, 2007). However, the amplitude value for the P300 potential in Participant A was found to be reduced when compared to neuro-typical. This finding correlates to the review by Hagoort et al. (1996), suggesting people diagnosed with left-hemispheric lesion and aphasia showed reduced P300 amplitudes in a semantic-processing task when compared to controls. The present study involved only an auditory stimulus with no linguistic load.

With reference to cognitive functions after stroke, Nolfe et al. (2006) concluded that P300 potential is an indicative assessment of the retained elementary cognitive function after a stroke affecting areas relevant for language production and processing. Participant A has retained elementary cognitive function as noted from the presence of the P300 potential. It has been suggested that the medial temporal lobe and the integrity of the temporoparietal junction play a role in modulating or even creating the P300 amplitude (Knight & Scabini, 1998; Picton, 1992; Polich, 2007). In persons with aphasia (global aphasia), significant infarct in the temporal lobe and temporoparietal junctions could have contributed to reduced amplitude.

When the different electrode sites were analyzed, the amplitude values were found to be varying from one region to another, with the highest amplitude in the frontal electrode sites. The descending order of the amplitude is: Frontal > Posterior > Grand average > Left > Midline > Central > Right. Some authors reported that young adults showed maximum amplitude at the parietal regions (Saliasi et al., 2013). According to Becker and Reinvang (2007b), some possible reasons for the amplitude reduction are, that, the electrophysiological changes observed might not be due to the language functions, but due to the impairment only in the acoustic processing.

Also, the amplitude attenuations may only be unspecific manifestations of brain lesion and lesion size that are not particularly linked to aphasia/the site of lesion in aphasia. Reduction in the amplitude when measured from electrodes in different locations, has a complex relationship with the underlying brain activity. Lesion effects such as atrophy, gliosis, or edema can influence the registration of activity from nearby generators (Korpelainen et al., 2000).

The latency of the P300 potential varied from 320ms to 484ms in healthy elderly subjects (Pavarini et al., 2018). The P300 latency ranges between 250 and 350ms for adults, according to Kraus et al. (1995). Didoné et al. (2016), reported that the minimum and maximum latency values were 247.5ms and 362.5ms, respectively, for participants in the age range of 18 -59 years when tone burst stimuli was used. In the present study, for Participant A the latency values were found to be prolonged and latency values were found to be constant across all sites of the electrode except the midline electrodes. In the literature, according to Rossini et al. (2007), the latency of the P300 potential is related to the information processing time. Such findings can be correlated with the present study since the constant values across the majority of the

electrode site indicate that the time taken to process the stimuli remains the same. The latency value varied only when the response was obtained from the midline electrodes. The possible explanation for the presence of the P300 event-related potential can be that most of the regions of frontal, parietal, and temporal lobe were collectively involved in information processing. Equal participation and collective involvement of all the lobes are required for information processing and hence this might have contributed to the same latency value in the case of Participant A. To support some from the review, the P300 potential was observed to be present in a person with an ischemic lesion in the left hemisphere involving the caudate nucleus, the anterior tip of the superior temporal lobe, the insula and the parietal lobe (Aerts et al., 2015).

The P300 potential has a maximum amplitude in the central-parietal regions in the midline. Large foci of P300-generating cerebral tissue tend to be found in the hippocampus, superior temporal sulcus, prefrontal ventrolateral cortex, and, possibly, intraparietal sulcus (Halgren et al., 1998; Kiss et al., 1989; Smith et al., 1990).The lesion site and the size of the lesion at sub-cortical structures could have a different impact on the P300 potential generated as the activity from nearby generators, which could be possible in global aphasia. Another factor that could have attributed for the presence of the potential can be the attentional allocation to the stimuli.

The event-related potential P300 is a potential that is related to the attention and the memory processes (Grover et al., 2012) and it requires active attention from the participant (Polich & Pitzer, 1999). The participant paying attention to the stimulus will increase the chances of the potential being present. Another possibility for the presence of the P300 potential may be the discrimination ability of the

individual. In a study by Becker and Reinvang (2007a), wherein individuals with moderate and severe aphasia were able to detect the target syllables among the standard syllables.They reported that the P300 did not significantly differ in the aphasic groups, indicating no severe impairments in target recognition and it implies that the individuals with aphasia were able to identify the target syllables behaviourally. But the electrophysiological variables were significantly attenuated in the stimulus discrimination in some of the individuals with aphasia. This indicates that the response was based on the acoustic features and not based on linguistic analysis. This can be applied to only those studies using stimulus as syllables that do not have any association with linguistic expression or comprehension. Thus, the acoustic variable of discrimination ability has played a major role to elicit a P300 response.

To summarize, the activation of peak latency in the topographical representation of P300 for Participant A showed the presence of brain activation for the infrequent stimulus at the posterior regions of the brain. There is a centroparietal generator for auditory as well as visual P300 for individuals in the age range of 16 – 65 years (Sangal & Sangal, 1996). Similarly, Smith et al. (1990) reported parieto-temporal generators for auditory P300.

The brain activation seen in the case of Participant A was in the form of scattered responses from the scalp regions instead of centralised activation. The activation was absent for the frequent stimulus, which indicates that the brain has perceived the stimuli as being different, whereas, in the neuro-typicals the topographical representation for the P300 potential was found to be having centralised activation (Pfefferbaum et al., 1984; Picton & Hillyard, 1974).

5.2 P300 Potential and Topography in Participant B

Participant B belonged to the geriatric population, and, was diagnosed as having Broca's aphasia. He had very poor scores in spontaneous speech, naming, and repetition, whereas better auditory verbal comprehension scores on the administration of WAB-R. The MRI findings showed hyperacute infarct involving left frontal operculum and posterior frontal region, indicating that the lesion was localized to the frontal region. But even though the other regions were not affected, the potential was found to be absent.

A possible reason might be the participant's attention allocated to the stimuli that were presented, was very poor to elicit a P300 response. Studies have stated that P300 is a potential that depends on the attention of the participant (Grover et al., 2012; Polich & Pitzer, 1999; Turetsky, 2007). For attentional allocation, the thalamus and the fronto-parietal network (Shomstein et al., 2012) were said to play a major role. In Participant B, the lesion was localized to the frontal region.

Despite the good comprehension scores, the potential was found to be absent. Becker and Reinvang (2007b) studied the individuals with aphasia having mild or moderate auditory comprehension deficits and severe auditory comprehension deficits and both the groups didn't show any changes in the P300 potential in terms of its amplitude. But the absence of the potential is contradicting another study by Nolfe et al. (2006), as their study reported that early presence of P300 post-stroke is a positive sign of recovery of comprehension.

The age of the participant may be also acting on the presence of event-related potential. Pavarini et al. (2018) have stated in their review article that there is a

reduction in the amplitude of the potential and an increase in the latency of the potential in the healthy elderly population. Stenklev and Laukli (2004) gave a possible explanation that the participant's age could also be a factor to result in reduced amplitude and prolonged latency. They reported that the presence of P300 is reported in only 52 percent of individuals over the age of 60.

To summarize, the P300 potential was found to be absent, but there was minimal amount of brain activity present on the right hemisphere regions, and, some parts of the frontal electrode sites of the left hemisphere in the topographical representation of Participant B. Responses from the scalp regions were not in the form of centralised activation rather it was scattered.

5.3 P300 Potential and Topography in Participant C

Participant C was diagnosed as having Global aphasia, but he was resolving into Broca's aphasia. He showed very poor scores in spontaneous speech, poor scores in naming and repetition, and an average score in auditory-verbal comprehension. MRI findings showed Left fronto-parieto-temporal lobe chronic infarct with gliosis, indicating diffuse lesion. The absence of the event-related potential can be due to the presence of a diffuse lesion. Lesion involving the sites responsible for the potential might have caused the absence of the potential.The major areas contributing to the P300 potential are the hippocampus, superior temporal sulcus, prefrontal ventrolateral cortex, and, possibly, intraparietal sulcus (Halgren et al., 1995, 1998; Kiss et al., 1989; Smith et al., 1990). Since all these areas are most affected in the case of Participant C, that might have led to the absence of the potential.Despite attending to the stimulus, the potential was found to be absent in Participant C. Participant C exhibited minimal amount of brain activity on the posterior aspect of the left

hemisphere in response to the speech stimuli that was presented, even though the P300 potential is absent.

5.4 P300 Potential with respect to the Amplitude and Latency in Individuals with Aphasia and the Topographic Representation

The findings from the present study indicate that the event-related potential P300 is participant specific and cannot be attributed to the type of aphasia, attention of the participant, or size and the extent of the lesion, solely. Any of these factors can affect the presence of the P300 potential and it depends on the participant's individual factors.These individual factors could be the age of the participants that affects the presence of the P300 potential. Pavarini et al. (2018) has reported that the amplitude of the P300 potential decreases and the amplitude increases in healthy elderly individuals.In one of the participants, despite better auditory comprehension scores, the potential was found to be absent. Here the individual participants factor and its relationship between deficits in auditory and speech sound processing and the language function in aphasia participants remains unclear.

A study (Becker & Reinvang, 2007) reported that the participants with mild or moderate and severe auditory comprehension deficits were able to successfully detect the syllables that were used as the stimulus. Another factor that might have potentially influenced the result in the case of Participant B could be the psychological status of the person for example: depression. However, their general health condition would have been documented as an inclusionary criteria or in brief the psychological status could have been assessed by the professional in the present study, and this could be the further directions for further studies. Since, the prolonged P300 latencies were found to be related to post-stroke depression and post-stroke depression was found to

affect the long-latency ERPs (Korpelainen et al., 2000). Even though education and cognitive tests didn't show any relationship to the electrophysiological results, it is a factor which is said to influence the age-related P300 results (Raggi et al., 2013).

Another study reported better latency and amplitude values for participants without subjective memory complaints when compared to those with memory complaints (Smart et al., 2014). Post-stroke patients with depression were reported to have greater latencies and reduced amplitudes when compared to stroke patients without depression (Zhang et al., 2013). To summarize, the event-related potential P300 can be affected by several factors and it is participant specific.

Chapter VI

Summary and Conclusion

Event-related potentials (ERPs) is an objective parameter which reflects the cognitive functions, and they are called as cerebral responses which are associated with psychological events (Grover et al., 2012; Tanriverdi, 2009). In particular, the related cognitive component, which is related to attention and memory processes is the P300 ERP component (Grover et al., 2012). This evoked potential is the measure of endogenous cognitive process, i.e., directed attention and the context-specific updating of working memory (Turetsky, 2007). Hence, this can be used for the assessment of attention and working memory. The neurophysiological assessment has also been used as an alternative for behavioral responses, as it doesn't always require a response from the participant. ERPs can also be used to monitor the effects of therapeutic intervention on individuals with aphasia.

Stroke patients with and without depression were compared with a control group to find out the discrepancies in their P300. It was found that the post-stroke patients with depression had higher P300 latencies and lower P300 amplitudes when compared with the control group and the no depression groups (Zhang et al., 2013). In patients with aphasia, it was seen that they have difficulty in detecting and recognizing different phonemes from each other, and that is why they have a problem in word recognition and comprehension. Thus, the studies using the event-related potentials (ERPs) which are based on the oddball-paradigm, to a greater extent helps to characterize, evaluate, and monitor, the phonological problems and auditory comprehension deficits in patients with aphasia. It was found that in order to monitor

the patterns of recovery in early stages of aphasia and follow up periods which are long-term, the P300 potential is a good non-invasive measure (Aerts et al., 2015).

The present study aimed to conduct a neurophysiological assessment (Event-Related Potential-P300) in individuals with aphasia at their pre-therapy period. The objectives of the study were, to measure the amplitude and latency values of ERP-P300 using auditory stimuli (speech stimuli) in individuals with aphasia at their pre-therapy period and to profile the P300 assessment of individuals with aphasia showing the presence of a P300 component in comparison of individuals with aphasia with absent P300 component.

A total of three participants were included in the study with non-fluent type of aphasia after they met the inclusionary criteria and the neurophysiological assessment (P300) was carried using an oddball paradigm. The stimuli used for recording were the syllables /da/ and /ga/, wherein /da/ was frequent and /ga/ was infrequent one. The participant was instructed to just pay attention to the stimuli that were being presented. Net Station 5 Electrical Geodesic Inc. (EGI) Geodesic EEG Software (version 5.4.2) instrument was used to record Event-Related Potential (ERP) (128 Channels) and the recording was done in a sound-attenuated and electrically shielded room, where the noise levels were within permissible limits (American National Standards Institute, 1999). P300 was recorded as per the guidelines provided by Duncan et al. (2009). Analysis of the obtained data was carried out using the MATLAB software.

The results are organized under two headings, P300 represented in the recorded waveform of individuals with aphasia and topographical representation of P300 in individuals with aphasia. Out of the three participants who participated in the

study, the P300 potential was present in only Participant A. Participant B and Participant C did not exhibit the P300 potential. Hence the P300 representation with reference to latency and amplitude at various electrode sites of Participants A was only profiled in detail. It was observed that the latency was relatively prolonged for the midline electrode site in comparison with the other electrode sites. With reference to amplitude, the amplitude was highest for frontal followed by the posterior electrode site.

The topographical distributions of the mean amplitude and latency for the frequent and infrequent stimuli were studied for Participant A who showed the presence of P300 potential (peak latency and amplitude) in comparison with Participant B and C, who did not show the presence of P300, where the increased brain activity for the infrequent stimuli at posterior electrode site was found to be greater than the other electrode sites, whereas no brain activation was seen for the frequent stimuli. The other electrode site regions had scattered activation for Participant A, B, and C, all being the clinical population, possible reason for this results were illustrated by Hagoort et al. (1996), whereas the present study involved only an auditory stimulus with no linguistic load. With reference to cognitive functions after stroke, Nolfe et al. (2006) concluded individuals with aphasia retain elementary cognitive function as noted from the presence of the P300 potential.

It has been suggested that the medial temporal lobe and the integrity of the temporoparietal junction play a role in modulating or even creating the P300 amplitude (Knight & Scabini, 1998; Picton, 1992; Polich, 2007). In persons with aphasia (global aphasia), significant infarct in the temporal lobe and temporoparietal junctions could have contributed to reduced amplitude.

According to Becker and Reinvang (2007b), some possible reasons for this amplitude reduction are, that, the electrophysiological changes observed might not be due to the language functions, but due to the impairment only in the acoustic processing. The amplitude attenuations may only be unspecific manifestations of brain lesion and lesion size that are not particularly linked to aphasia/the site of lesion in aphasia.

Participant A's latency values were found to be constant across all sites of the electrode except the midline electrodes. In the literature, according to Rossini (2007), latency of the P300 potential is related to the information processing time. Such findings can be correlated with the present study, since the constant values across the majority of the electrode site indicate that the time taken to process the stimuli remains the same. The latency value varied only when the response was obtained from the midline electrodes. Equal participation and collective involvement of all the lobes are required for information processing and hence this might have contributed to the same latency value in the case of Participant A and not in case of other participants. The lesion site and the size of the lesion at sub-cortical structures could have a different impact on the P300 potential generated as the activity from nearby generators, which could be possible in global aphasia. Another factor that could have contributed for the presence of the potential can be the attentional allocation to the stimuli. Another possibility for the presence of the P300 potential may be the discrimination ability of the individual and the acoustic variable of discrimination ability has played a major role to elicit a P300 response.

The topographical representation of the Participant A showed brain activity in the posterior aspect of the brain and the responses were scattered instead of

centralised activation. One possible reason for the reduced brain activation seen in case of Participant A may be because of either the lesion present in the brain or the attention allocated to the stimuli.

The other contributing reasons to support the findings of Participant B, and C, would be the factors listed in previous paragraph along with these following additional factors. The age of the participant may be also acting on the presence of event-related potential. Pavarini et al. (2018) have stated in their review article that there is a reduction in the amplitude of the potential and an increase in the latency of the potential in the healthy elderly population.The major areas contributing to the P300 potential are the hippocampus, superior temporal sulcus, prefrontal ventrolateral cortex, and, possibly, intraparietal sulcus (Halgren et al., 1995, 1998; Kiss et al., 1989; Smith et al., 1990). Since all these areas are most affected in the case of Participant C, that might have led to the absence of the potential.The topographical representation of Participants B and C did not show any significant brain activation as the P300 potential was absent. Minimal amount of activity was seen scattered across the frontal regions of Participant B, which may be because of the attention allocated to the stimuli.These findings suggest that event-related potential, P300 is participant specific and can be dependent on many factors like the type of aphasia, size and the extent of the lesion, language function, the age of the participants, post-stroke depression (Korpelainen et al., 2000).

6.1 Implications

One particularly interesting clinical use of ERPs in the diagnosis and treatment of aphasia would be measuring the language comprehension function. Comprehension abilities of patients are not always easy to assess and an additional approach is

required beyond clinical tests. The findings of the study highlighted the individual differences in the P300 potential when a neurophysiological assessment was carried out. This is a single subject design wherein the findings obtained for each of the participants were separately discussed. As the study comprised only a small number of participants, the findings cannot be generalized. In the future, studies can be carried out with a greater number of participants to identify the effect of different factors on the P300 potential. Studies that compare the effects of different types of stimuli can be carried out to find out its effect on the P300 potential. Effect of speech and language therapy on individuals with aphasia can be carried out using event-related potential P300.

6.2 Limitations with Future Directions

The present study focussed on individuals with aphasia during their pre-therapy period. Post-therapy analysis, if carried out could have shown the effects of speech and language therapy on the P300 potential. Analysis of the responses obtained from the ipsilesional and contralesional areas of the frontal lobe was not compared. The study included only a smaller number of participants; hence the findings cannot be generalized. A comparison of the ipsilesional and contra-lesional responses from the frontal electrode sites has shown that the P300 potential was better at the ipsilesional frontal site (Becker &Reinvang, 2007). This comparison can be carried out in studies using event-related potential P300 in the future. The present study did not consider the post-stroke depression as a factor. Studies have shown that post-stroke depression can affect P300 potential.

References

Aerts, A., Van Mierlo, P., Hartsuiker, R. J., Santens, P., & De Letter, M. (2015). Neurophysiological sensitivity for impaired phonological processing in the acute stage of aphasia. *Brain and Language, 149*, 84 96. https://doi.org/10.1016/j.bandl.2015.07.001

American National Standards Institute. (1999). *Maximum Permissible Ambient Noise Levels for Audiometric Test Rooms*(ANSI S3.1-1999)

Asaumi, Y., Morita, K., Nakashima, Y., Muraoka, A., & Uchimura, N. (2014). Evaluation of P300 components for emotion-loaded visual event-related potential in elderly subjects, including those with dementia. *Psychiatry and Clinical Neurosciences, 68*(7), 558-567. https://doi.org/10.1111/pcn.12162

Bae, K., Lee, M., & Lee, S. (2012). Neuropsychological correlates of P300 in patients with Alzheimer's disease. *International Journal of Psychophysiology, 85*(3), 390-391. https://doi.org/10.1016/j.ijpsycho.2012.07.077

Becker, F., & Reinvang, I. (2007). Event-related potentials indicate Bi-hemispherical changes in speech sound processing during aphasia rehabilitation. *Journal of Rehabilitation Medicine, 39*(8), 658-661. https://doi.org/10.2340/16501977-0112

Becker, F., & Reinvang, I. (2007). Successful syllable detection in aphasia despite processing impairments as revealed by event-related potentials. *Behavioral and Brain Functions, 3*(1). https://doi.org/doi:10.1186/1744-9081-3-6

Bennington, J. Y., & Polich, J. (1999). Comparison of P300 from passive and active tasks for auditory and visual stimuli. *International Journal of Psychophysiology*, *34*(2), 171-177. https://doi.org/10.1016/s0167-8760(99)00070-7

Bian, Z., Li, Q., Wang, L., Lu, C., Yin, S., & Li, X. (2014). Relative power and coherence of EEG series are related to amnestic mild cognitive impairment in diabetes. *Frontiers in Aging Neuroscience*, *6*. https://doi.org/10.3389/fnagi.2014.00011

Calbi, M., Siri, F., Heimann, K., Barratt, D., Gallese, V., Kolesnikov, A., &Umiltà, M. A. (2019). How context influences the interpretation of facial expressions: A source localization high-density EEG study on the "Kuleshov effect". *Scientific Reports*, *9*(1). https://doi.org/10.1038/s41598-018-37786-y

Casey, D. A. (2010). Event-related potentials and the diagnosis of Alzheimer's disease— the COGNISION™ system. *US Neurology*, *06*(02), 34. https://doi.org/10.17925/usn.2010.06.02.34

Cote, K. A. (2002). Probing awareness during sleep with the auditory odd-ball paradigm. *International Journal of Psychophysiology*, *46*(3), 227-241. https://doi.org/10.1016/s0167-8760(02)00114-9

Chengappa, S. K., & Kumar, R. (2008). Normative & Clinical Data on the Kannada Version of Western Aphasia Battery (WAB-K). *Language in India*, *8*(6).

De Renzi, E., & Faglioni, P. (1978). Normative data and screening power of a shortened version of the token test. *Cortex*, *14*(1), 41-49. https://doi.org/10.1016/s0010-9452(78)80006-9

Didoné, D. D., Garcia, M. V., Oppitz, S. J., Silva, T. F., Santos, S. N., Bruno, R. S., Filha, V. A., & Cóser, P. L. (2016). Auditory evoked potential P300 in adults: Reference values. *Einstein (São Paulo), 14*(2), 208-212. https://doi.org/10.1590/s1679-45082016ao3586

Donchin, E., Karis, D., Bashore, T. R., Coles, M. G., Gratton, G., 1986. Cognitive psychophysiology and human information processing. In: Coles, M.G.H., Donchin, E., Porges, Ž. S.W. Eds. , Psychophysiology: Systems, Processes, and Applications. The Guilford Press, New York, pp. 244-267.

Duncan-Johnson, C. C. (1981). Young Psychophysiologist award address, 1980. *Psychophysiology, 18*(3), 207-215. https://doi.org/10.1111/j.1469-8986.1981.tb03020.x

Duncan, C. C., Morihisa, J. M., Fawcett, R. W., & Kirch, D. G. (1987a) P300 in schizophrenia: state or traitmarker? *Psychopharmacology Bulletin*, *23*,497–501.https://doi.org/10.1016/s0140-6736(99)00261-5

Duncan, C., Kosmidis, M., & Mirsky, A. (2005). Closed head injury-related information processing deficits: An event-related potential analysis. *International Journal of Psychophysiology*, *58*(2-3), 133-157.https://doi.org/10.1016/j.ijpsycho.2005.05.011

Duncan, C., Barry, R., Connolly, J., Fischer, C., Michie, P., Näätänen, R., Polich, J., Reinvang, I., & Van Petten, C. (2009). Event-related potentials in clinical research: Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clinical Neurophysiology*, *120*(11), 1883-1908. https://doi.org/10.1016/j.clinph.2009.07.045

Fabiani, M., Karis, D., &Donchin, E. (1986). P300 and recall in an incidental memory paradigm. *Psychophysiology*, *23*(3), 298-308. https://doi.org/10.1111/j.1469-8986.1986.tb00636.x

Fabiani, M., Karis, D., &Donchin, E. (1990). Effects of mnemonic strategy manipulation in a von Restorff paradigm. *Electroencephalography and Clinical Neurophysiology*, *75*(1-2), 22-35. https://doi.org/10.1016/0013-4694(90)90149-e

Gao, M., Yun, X., Zhang, H., Guo, H., Wang, K., Niu, X., &Qiao, Y. (2016). Efficacy of telerehabilitation mode on memory disorders. *Chinese Journal of Rehabilitation Theory and Practice*, *22*(5), 518-522.http://www.cjrtponline.com/EN/10.3969/j.issn.1006-9771.2016.05.007

Gaudreault, P., Gagnon, J., Montplaisir, J., Vendette, M., Postuma, R. B., Gagnon, K., & Gosselin, N. (2013). Abnormal occipital event-related potentials in Parkinson's disease with concomitant REM sleep behavior disorder. *Parkinsonism & Related Disorders*, *19*(2), 212-217. https://doi.org/10.1016/j.parkreldis.2012.10.006

Grover, S., Chetri, D., Sood, A., Das, C., & Nehra, R. (2012). P300 latency and neurocognitive functioning in recently diagnosed human immunodeficiency virus patients. *Indian Journal of Psychological Medicine*, *34*(4), 376. https://doi.org/10.4103/0253-7176.108225

Hagoort, P., Brown, C. M., &Swaab, T. Y. (1996). Lexical—semantic event–related potential effects in patients with left hemisphere lesions and aphasia, and

patients with right hemisphere lesions without aphasia. *Brain*, *119*(2), 627-649. https://doi.org/10.1093/brain/119.2.627

Halgren, E., Baudena, P., Clarke, J. M., Heit, G., Marinkovic, K., Devaux, B., Vignal, J., &Biraben, A. (1995). Intracerebral potentials to rare target and distractor auditory and visual stimuli. II. Medial, lateral and posterior temporal lobe. *Electroencephalography and Clinical Neurophysiology*, *94*(4), 229-250. https://doi.org/10.1016/0013-4694(95)98475-n

Halgren, E., Marinkovic, K., &Chauvel, P. (1998). Generators of the late cognitive potentials in auditory and visual oddball tasks. *Electroencephalography and Clinical Neurophysiology*, *106*(2), 156-164. https://doi.org/10.1016/s0013-4694(97)00119-3

Halgren, E., Squires, N., Wilson, C., Rohrbaugh, J., Babb, T., & Crandall, P. (1980). Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. *Science*, *210*(4471), 803-805. https://doi.org/10.1126/science.7434000

Hillyard, S. A., Hink, R. F., Schwent, V. L., &Picton, T. W. (1973). Electrical signs of selective attention in the human brain. *Science*, *182*(4108), 177-180. https://doi.org/10.1126/science.182.4108.177

Jiang, S., Qu, C., Wang, F., Liu, Y., Qiao, Z., Qiu, X., Yang, X., & Yang, Y. (2015). Using event-related potential P300 as an electrophysiological marker for differential diagnosis and to predict the progression of mild cognitive impairment: A meta-analysis. *Neurological Sciences*, *36*(7), 1105-1112. https://doi.org/10.1007/s10072-015-2099-z

Johnson, R. (1989). Developmental evidence for modality-dependent P300 generators: A normative study. *Psychophysiology*, *26*(6), 651-667. https://doi.org/10.1111/j.1469-8986.1989.tb03167.x

Johnson, R., Pfefferbaum, A., &Kopell, B. S. (1985). P300 and long-term memory: Latency predicts recognition performance. *Psychophysiology*, *22*(5), 497-507. https://doi.org/10.1111/j.1469-8986.1985.tb01639.x

Kemal Arikan, M., Devrim, M., Oran, Ö., Inan, S., Elhih, M., &Demiralp, T. (1999). Music effects on event-related potentials of humans on the basis of cultural environment. *Neuroscience Letters*, *268*(1), 21-24. https://doi.org/10.1016/s0304-3940(99)00372-9

Kim, M., &Tomaino, C. M. (2008). Protocol evaluation for effective music therapy for persons with Nonfluent aphasia. *Topics in Stroke Rehabilitation*, *15*(6), 555-569. https://doi.org/10.1310/tsr1506-555

Kiss, I., Dashieff, R. M., &Lordeon, P. (1989). A Parietooccipital generator for P300: Evidence from human intracranial recordings. *International Journal of Neuroscience*, *49*(1-2), 133-139. https://doi.org/10.3109/00207458909087048

Knight, R. T. (1984). Decreased response to novel stimuli after prefrontal lesions in man. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *59*(1), 9-20. https://doi.org/10.1016/0168-5597(84)90016-9

Knight, R. T., Grabowecky, M., &Scabini, D. (1995). Role of human prefrontal cortex in attention control. *Advances in Neurology*, *66*, 21–34.

Knight, R. T. (1996). Contribution of human hippocampal region to novelty detection. *Nature*, *383*(6597), 256-259. https://doi.org/10.1038/383256a0

Knight, R. T., &Scabini, D. (1998). Anatomic bases of event-related potentials and their relationship to novelty detection in humans. *Journal of Clinical Neurophysiology*, *15*(1), 3-13. https://doi.org/10.1097/00004691-199801000-00003

Korpelainen, J. T., Kauhanen, M. L., Tolonen, U., Brusin, E., Mononen, H., Hiltunen, P., Sotaniemi, K. A., Suominen, K., & Myllyla, V. V. (2000). Auditory P300 event related potential in minor ischemic stroke. *Acta Neurologica Scandinavica*, *101*(3), 202-208. https://doi.org/10.1034/j.1600-0404.2000.101003202.x

Kramer, A. F., & Strayer, D. L. (1988). Assessing the development of automatic processing: An application of dual-task and event-related brain potential methodologies. *Biological Psychology*, *26*(1-3), 231-267. https://doi.org/10.1016/0301-0511(88)90022-1

Kraus, N., McGee, T. (1994). *Auditory event-related potentials. In: Hand book of clinical audiology*. Williams and Wilkins; pp. 406–426.

Kuba, M., Kremláček, J., Langrová, J., Kubová, Z., Szanyi, J., &Vít, F. (2012). Aging effect in pattern, motion and cognitive visual evoked potentials. *Vision Research*, *62*, 9-16.

Kuperberg, G.R. (2008). Electroencephalography, event-related potentials, and magnetoencephalography. In: D.D. Dougherty, S.L. Rauch & J.F. Rosenbaum

(Eds.) *Essentials of Neuroimaging for Clinical Practice*. pp.117 – 127, American Psychiatric Publishing, Inc.

Kutas, M., McCarthy, G., & Donchin, E. (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. *Science*, *197*(4305), 792-795. https://doi.org/10.1126/science.887923

Lai, C., Lin, R., Liou, L., & Liu, C. (2010). The role of event-related potentials in cognitive decline in Alzheimer's disease. *Clinical Neurophysiology*, *121*(2), 194-199. https://doi.org/10.1016/j.clinph.2009.11.001

Lukas, S. E., Mendelson, J. H., Kouri, E., Bolduc, M., & Amass, L. (1990). Ethanol-induced alterations in EEG Alpha activity and apparent source of the auditory P300 evoked response potential. *Alcohol*, *7*(5), 471-477. https://doi.org/10.1016/0741-8329(90)90034-a

Luzzatti, C., Willmes, K., Bislacchi, P, et al. (1987). L'AachenerAphasie Test (AAT). II. Proprieta` psicometrichedellaversioneitaliana. *Archivio di psicologia, neurologia e psichiatria,48*, 480–519.

McCarthy, G., & Donchin, E. (1981). A metric for thought: A comparison of P300 latency and reaction time. *Science*, *211*(4477), 77-80. https://doi.org/10.1126/science.7444452

Multicenter trial of hemodilution in ischemic stroke--background and study protocol. Scandinavian Stroke Study Group. (1985). *Stroke*, *16*(5), 885-890. https://doi.org/ 10.1161/01.str.16.5.885

Nieuwenhuis, S., Aston-Jones, G., & Cohen, J. D. (2005). Decision making, the P3, and the locus coeruleus--norepinephrine system. *Psychological Bulletin*, *131*(4), 510-532. https://doi.org/10.1037/0033-2909.131.4.510

Nolfe, G., Cobianchi, A., Mossuto-Agatiello, L., & Giaquinto, S. (2006). The role of P300 in the recovery of post-stroke global aphasia. *European Journal of Neurology*, *13*(4), 377-384. https://doi.org/10.1111/j.1468-1331.2006.01237.x

Nuechterlein, K. H., Pashler, H. E., & Subotnik, K. L. (2006). Translating basic attentional paradigms to schizophrenia research: Reconsidering the nature of the deficits. *Development and Psychopathology*, *18*(03). https://doi.org/10.1017/s095457940606041x

Papanicolaou, A. C., Loring, D. W., Raz, N., & Eisenberg, H. M. (1985). Relationship between stimulus intensity and the P300. *Psychophysiology*, *22*(3), 326-329. https://doi.org/10.1111/j.1469-8986.1985.tb01608.x

Pavarini, S. C., Brigola, A. G., Luchesi, B. M., Souza, É. N., Rossetti, E. S., Fraga, F. J., Guarisco, L. P., Terassi, M., Oliveira, N. A., Hortense, P., Pedroso, R. V., & Ottaviani, A. C. (2018). On the use of the P300 as a tool for cognitive processing assessment in healthy aging: A review. *Dementia & Neuropsychologia*, *12*(1), 1-11. https://doi.org/10.1590/1980-57642018dn12-010001

Pfefferbaum, A., Ford, J. M., Wenegrat, B. G., Roth, W. T., & Kopell, B. S. (1984). Clinical application of the P3 component of event-related potentials. I. Normal aging. *Electroencephalography and Clinical*

Neurophysiology/Evoked Potentials Section, *59*(2), 85-103. https://doi.org/10.1016/0168-5597(84)90026-1

Picton, T. W. (1992). The P300 wave of the human event-related potential. *Journal of Clinical Neurophysiology*, *9*(4), 456-479. https://doi.org/10.1097/00004691-199210000-00002

Pokorny, C., Klobassa, D. S., Pichler, G., Erlbeck, H., Real, R. G., Kübler, A., Lesenfants, D., Habbal, D., Noirhomme, Q., Risetti, M., Mattia, D., & Müller-Putz, G. R. (2013). undefined. *Artificial Intelligence in Medicine*, *59*(2), 81-90. https://doi.org/10.1016/j.artmed.2013.07.003

Polich, J. (1987). Task difficulty, probability, and inter-stimulus interval as determinants of P300 from auditory stimuli. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *68*(4), 311-320. https://doi.org/10.1016/0168-5597(87)90052-9

Polich, J. (1988). undefined. *Journal of Clinical Neurophysiology*, *5*(3), 287-294. https://doi.org/10.1097/00004691-198807000-00004

Polich, J. (1990). undefined. *International Journal of Psychophysiology*, *10*(2), 163-170. https://doi.org/10.1016/0167-8760(90)90030-h

Polich, J., Howard, L., & Starr, A. (1983). P300 latency correlates with digit span. *Psychophysiology*, *20*(6), 665-669. https://doi.org/10.1111/j.1469-8986.1983.tb00936.x

Polich, J., Ladish, C., & Burns, T. (1990). undefined. *International Journal of Psychophysiology*, *9*(3), 237-248. https://doi.org/10.1016/0167-8760(90)90056-j

Polich, J., & Pitzer, A. (1999). P300 in early Alzheimer's disease: Oddball task difficulty and modality effects. In: Comi, G., Lucking, C.H., Kimura, J., Rossini, R.M. _Eds.., *Clinical Neurophysiology: From Receptors to Perception,* EEG Supplement. Elsevier, pp. 281- 287.

Polich, J. (2000). P300 as a clinical assay: Rationale, evaluation, and findings. *International Journal of Psychophysiology*, *38*(1), 3-19. https://doi.org/10.1016/s0167-8760(00)00127-6

Polich, J. (2003). Overview of P3a and P3b. In J. Polich (Eds). *Detection of change: event-related potential and fMRI findings.* Boston, MA: Kluwer

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*(10), 2128-2148. https://doi.org/10.1016/j.clinph.2007.04.019

Porjesz, B., & Begleiter, H. (1981). Human evoked brain potentials and alcohol. *Alcoholism: Clinical and Experimental Research, 5,* 304-317.

Pulvermüller, F., Hauk, O., Zohsel, K., Neininger, B., & Mohr, B. (2005). Therapy-related reorganization of language in both hemispheres of patients with chronic aphasia. *NeuroImage, 28*(2), 481-489. https://doi.org/10.1016/j.neuroimage.2005.06.038

Raggi, A., Tasca, D., Rundo, F., & Ferri, R. (2013). Stability of auditory discrimination and novelty processing in physiological aging. *Behavioural Neurology*, *27*(2), 193-200. https://doi.org/10.1155/2013/462462

Reinvang, I. (1985). *Aphasia and brain organization*. Springer Science & Business Media.

Reis, A., & Iório, M. (2007). P300 emsujeitos com perdaauditiva. *Pró-FonoRevista De AtualizaçãoCientífica*, *19*(1), 113-122. https://doi.org/10.1590/S0104-56872007000100013

Rossini, P. M., Rossi, S., Babiloni, C., & Polich, J. (2007). Clinical neurophysiology of aging brain: From normal aging to neurodegeneration. *Progress in Neurobiology*, *83*(6), 375-400. https://doi.org/10.1016/j.pneurobio.2007.07.010

Saliasi, E., Geerligs, L., Lorist, M. M., & Maurits, N. M. (2013). The relationship between P3 amplitude and working memory performance differs in young and older adults. *PLoS ONE*, *8*(5), e63701. https://doi.org/10.1371/journal.pone.0063701

Sangal, R. B., & Sangal, J. M. (1996). undefined. *Clinical Electroencephalography*, *27*(3), 145-150. https://doi.org/10.1177/155005949602700307

Selinger, M. (1989). undefined. *Brain and Language*, *36*(3), 377-390. https://doi.org/10.1016/0093-934x(89)90074-6

Silverman, D. (1963). The rationale and history of the 10-20 system of the international Federation. *American Journal of EEG Technology, 3*(1), 17-22. https://doi.org/10.1080/00029238.1963.11080602

Shomstein, S., Kravitz, D. J., & Behrmann, M. (2012). Attentional control: Temporal relationships within the fronto-parietal network. *Neuropsychologia, 50*(6), 1202-1210. https://doi.org/10.1016/j.neuropsychologia.2012.02.009

Smart, C. M., Segalowitz, S. J., Mulligan, B. P., & MacDonald, S. W. (2014). Attention capacity and self-report of subjective cognitive decline: A p3 erp study. *Biological Psychology, 103,* 144-151. https://doi.org/10.1016/j.biopsycho.2014.08.016

Sokolik, M., Baudena, P., Musolino, A., Liegeois-Chauvel, C., et al. (1990). The intracranial topography of the P3 event-related potential elicited duringauditory oddball. *Electroencephalography and Clinical Neurophysiology, 76,* 235–248.

Squires, K., Wickens, C., Squires, N., & Donchin, E. (1976). The effect of stimulus sequence on the waveform of the cortical event-related potential. *Science,* 193(4258), 1142-1146. https://doi.org/10.1126/science.959831

Squires, N. K., Galbraith, G., Aine, C. (1979). Event-related potential assessment of sensory and cognitive deficits in the mentally retarded. In: Lehmann, D., Callaway, E. _Eds.., Human Evoked Potentials: Applications and Problems. Plenum Press.

Stenklev, N. C., & Laukli, E. (2004). Cortical cognitive potentials in elderly persons. *Journal of the American Academy of Audiology*, *15*(6), 401-413. https://doi.org/10.3766/jaaa.15.6.2

Sur, S., & Sinha, V. (2009). Event-related potential: An overview. *Industrial Psychiatry Journal*, *18*(1), 70. https://doi.org/10.4103/0972-6748.57865

Tanriverdi, F., Yapislar, H., Karaca, Z., Unluhizarci, K., Suer, C., & Kelestimur, F. (2009). Evaluation of cognitive performance by using P300 auditory event related potentials (ERPs) in patients with growth hormone (GH) deficiency and acromegaly. *Growth Hormone & IGF Research*, *19*(1), 24-30. https://doi.org/10.1016/j.ghir.2008.05.002

Tsolaki, A., Kosmidou, V., Hadjileontiadis, L., Kompatsiaris, I. (., & Tsolaki, M. (2015). Brain source localization of MMN, P300 and N400: Aging and gender differences. *Brain Research*, *1603*, 32-49. https://doi.org/10.1016/j.brainres.2014.10.004

Turetsky, B. I., Calkins, M. E., Light, G. A., Olincy, A., Radant, A. D., & Swerdlow, N. R. (2006). Neurophysiological Endophenotypes of schizophrenia: The viability of selected candidate measures. *Schizophrenia Bulletin*, *33*(1), 69-94. https://doi.org/10.1093/schbul/sbl060

Tütüncü, N. B., Karataş, M., & Sözay, S. (2004). Prolonged P300 latency in thyroid failure: A paradox. P300 latency recovers later in mild hypothyroidism than in severe hypothyroidism. *Thyroid*, *14*(8), 622-627. https://doi.org/10.1089/1050725041692837

Van Dinteren, R., Arns, M., Jongsma, M. L., & Kessels, R. P. (2014). P300 development across the lifespan: A systematic review and meta-analysis. *PLoS ONE*, *9*(2), e87347. https://doi.org/10.1371/journal.pone.0087347

Vesco, K. K., Bone, R. C., Ryan, J. C., & Polich, J. (1993). P300 in young and elderly subjects: Auditory frequency and intensity effects. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *88*(4), 302-308. https://doi.org/10.1016/0168-5597(93)90054-s

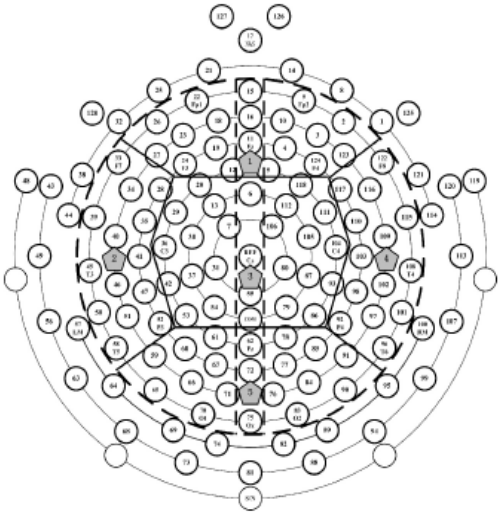
Williams, S. M. (2010). A major revision of the Edinburgh Handedness Inventory. *Colchester, Essex, United Kingdom*.

Zhang, D., Gu, R., Wu, T., Broster, L. S., Luo, Yi., Jiang, Y., Luo, Y. (2013). An electrophysiological index of changes in risk decision-making strategies. *Neuropsychologia, 51,* 1397 – 1407.

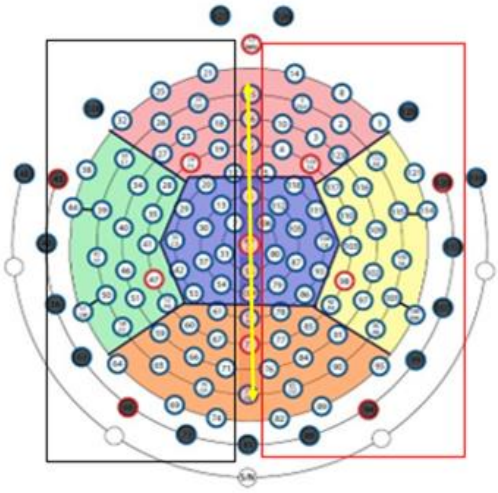
Zhang, H., Li, H., Li, R., Xu, G., & Li, Z. (2019). Therapeutic effect of gradual attention training on language function in patients with post-stroke aphasia: A pilot study. *Clinical Rehabilitation*, *33*(11), 1767-1774. https://doi.org/10.1177/0269215519864715

Appendix A

Electrode Selection to form specific sites



Electrode distribution of 128 channel Geodesic sensor net with reference to Bian et al., (2014).



Colour coded electrode distribution for the convenience of ERP analysis

	Frontal (F)
	Central (C)
	Midline (M)
	Posterior (P)
	LeftHemisphere
	RightHemisphere
	LeftTemporal
	Right Temporal

The interested electrodes were selected to detect EEG power in different regions and inter-/intra regions, the brain was divided into five regions: frontal (F), left temporal (LT), central (C), right temporal (RT), and posterior (P).

Frontal: E32, E25, E21, E14, E18, E1, E26, E22, E15, E9, E2, E27, E23, E18, E16, E10, E3, E123, E24, E19, E11, E4, E124, E12 & E5;

Central: E6, E7, E13, E20, E29, E30, E31, E36, E37, E42, E53, E54, E55, E79, E80, E86, E87, E93, E104, E105, E106, E111, E112 & E118;

Posterior: E61, E62, E78, E60, E67, E72, E77, E85, E59, E66, E71, E76, E84, E91, E65, E70, E75, E83, E90, E64, E69, E74, E82, E89, and E95;

Midline: E17, E15, E11, E6, E55, E62, E72 and E75;

Right: E14, E8, E1, E121, E114, E100, E95, E89, E82, E83, E90, E96, E101, E108, E115, E122, E2, E9, E10, E3, E123, E116, E109, E102, E97, E91, E84, E76, E77, E85, E92, E98, E103, E110, E117, E124, E4, E5, E118, E111, E104, E93, E86, E78, E79, E87, E105, E112, E106, and E80;

Left: E21, E25, E32, E38, E44, E57, E64, E69, E74, E70, E65, E58, E50, E45, E39, E33, E26, E22, E18, E23, E27, E34, E40, E46, E51, E59, E66, E71, E60, E52, E47, E41, E35, E28, E24, E19, E12, E20, E29, E36, E42, E53, E61, E54, E37, E30, E13, E7 and E31;

Average: Average from all the electrode sites.