Design, Construction and Analysis of an Alternative Stroke Rehabilitation Device based on the Principles of Neuroplasticity

by

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Thesis presented in partial fulfilment of the requirements for the degree of Master of Engineering (Mechatronic) in the Faculty of Engineering at Stellenbosch University

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Declaration

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Date: . . . . .December 2016

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Abstract

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The use of robotics in post-stroke patient rehabilitation and research has increased substantially during the last two decades. However, it has also led to important social and economic concerns, as the number of patients in developing countries that can afford the expensive outpatient rehabilitation, and therefore be treated, are limited. Not much is known about alternative low-cost rehabilitation devices. The motivation behind this thesis is to eventually address two of the most prominent limiting complications in stroke recovery programs, which are the time available for patient engagement, and the cost for outpatient rehabilitation. It presents the experimental design, construction, and analysis of a prototype stroke rehabilitation device, based on the principles of sensory stimulation therapy and neuroplasticity. The main objective of this project was to come to the conclusion whether it is possible to sense different electrobiological potentials in the brain during discrete events, from the constructed wearable sensory feedback device. The device is experimentally tested through the implementation of a case-control observational Event-Related Potential (ERP) study on healthy test subjects. The experimental results demonstrate the detection of cognitive and sensory-motor brain activity in response to, and in anticipation of, a somatic sensation. Electroencephalography (EEG) data is analyzed and decomposed to replicate three different ERPs, namely the P_{200} exogenous-sensory and -visual component, and the P_{300} endogenous component. The statistical analysis results indicate that a definite correlation is found between the Visual vs. P_{200} (F = 1.274, p = 0.28535) and the P_{200} vs. P_{300} (F = 64.253; p < 0.001) components when compared to previous ERP studies. The present evidence supports the use of

mechanical-assisted therapy and indicates that potentially cost saving alternative rehabilitation techniques are possible in their use of providing sensory feedback, and recording and analyzing EEG feedback.

Uittreksel

Ontwerp, Vervaardiging en Analise van 'n Alternatiewe Beroerte-Rehabilitasie Toestel, gebaseer op die Beginsels van Neuroplastisiteit

("Design, Construction and Analysis of an Alternative Stroke Rehabilitation Device based on the Principles of Neuroplasticity")

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Die gebruik van robotika in die rehabilitasie en navorsing van pasiënte na beroerte het gedurende die afgelope twee dekades aansienlik toegeneem. Dit het egter ook gelei tot sekere nadelige sosiale en ekonomiese gevolge, aangesien die aantal pasiënte wat die duur buitepasiënt-rehabilitasie kan bekostig, en dus in effek behandel kan word, afneem. Buitendien is daar min inligting bekend oor alternatiewe laekoste-rehabilitasietoestelle. Die motivering van hierdie tesis is om uiteindelik twee van die mees prominente komplikasies in beroerte herstellingsprogramme, naamlik die tyd wat beskikbaar is vir pasiënt behandeling en die koste verbonde aan buitepasiënt-rehabilitasie, aan te spreek. Hierdie tesis handel oor die proefondervindelike toetsing, ontwikkeling en analisering van 'n lae-koste beroerte-rehabilitasietoestel prototipe, wat op die beginsels van sensoriese stimulasie terapie en neuroplastisiteit berus. Die hoofoogmerk van hierdie projek was om tot gevolgtrekking te kom of dit moontlik is om verskillende elektrobiologiese potensiale wat deur die ontwikkelde draagbare toestel gelewer word, in die brein op te tel tydens diskrete aktiwiteite. Proefondervindelike toetsing op gesonde individue het deur middel van die implementering van 'n geval-gekontroleerde observerende *Respons-Verwante Potensiaal* (RVP) studie plaasgevind. Die proefondervindelike resultate toon dat kognitiewe en sensories-motoriese breinaktiwiteit opgetel word in reaksie op, en in afwagting van 'n somatiese sensasie. Elektro-ensefalografie (EEG) data is ontleed en voorgestel as drie verskillende RVP's, naamlik die P_{200}-eksogene-sensoriese

en -Visuele komponent, en die P_{300}-endogene komponent. Die statistiese ont-leding van die resultate dui aan dat 'n definitiewe korrelasie gevind is tus-sen die Visuele- teenoor P_{200}-komponent (F = 1,274; p = 0,28535) en die P_{200}- teenoor P_{300}-komponent (F = 64,253; p < 0.001), in vergelyking met vo-rige soortgelyke RVP-studies. Die huidige bewyse ondersteun die gebruik van meganiese-bystand terapiemetodes en dui aan dat potensiele kostebesparing rehabilitasie-tegnieke moontlik is in die gebruik van verskaffing van sensoriese terugvoer, EEG-terugvoer opnames en ontleding.

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Last but not the least, I would like to thank my family and friends, for their emotional support and enthusiasm.

Dedications

This thesis is dedicated to all stroke victims - with good care and rehabilitation, there is life after stroke...

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Nomenclature

Abbreviations and Acronyms

ADC   Analog-to-Digital Converters

ADL   activities of daily living

API   Application Programming Interface

ATP   Adenosine Triphosphate

BCI   Brain-Computer Interface

BERG Biomedical Engineering Research Group

BSI   Brain Symmetry Index

CIMT Constraint-induced movement therapy

CNS   Central Nervous System

COM   Component Object Model

CSV   Comma Separated Values

CT   Brain Computed

CTA   Computed Tomography Angiogram

DC   Direct Current

ECG   Electrocardiogram

EDF   European Data Format

EEG   Electroencephalography

ERP   Event-Related Potential

FCU   *flexor carpi ulnaris*

FDA   Food & Drug Administration

FDP   *flexor digitorum profundus*

NOMENCLATURE

FFT   Fast Fourier Transform

GUI   Graphical User Interface

HCI   Human Computer Interaction

ICA   Independent Component Analysis

LEDs Light Emitting Diodes

LSB   Least Significant Bit

MCA Middle Cerebral Artery

MRI   Magnetic Resonance Imaging

NFB   Neurofeedback

NIPMO National Intellectual Property Management Office

NMDA N-Methyl-D-aspartate

OSR   Omitted Stimulus-Response

PCB   Printed Circuit Board

RVP   *Respons-Verwante Potensiaal*

SMR   Sensorimotor Rhythm

SSH   Secure Shell

SST   sensory stimulation therapy

tDCS Transcranial Direct-Current Stimulation

TMS   Transcranial Magnetic Stimulation

tPA   Tissue Plasminogen Activator

TTO   Technology Transfer Office

USART Universal Synchronous/Asynchronous Receiver/Transmitter

USB   Universal Series Bus

WHO World Health Organization

NOMENCLATURE

Symbols

α	Alpha brain wave frequency	[Hz]
β	Beta brain wave frequency	[Hz]
δ	Delta brain wave frequency	[Hz]
$\mathscr{F}$	Fourier Transform function	[-]
μ_A	population mean in treatment Group A	[-]
μ_B	population mean in treatment Group B	[-]
ω	discrete-time, symmetrical window function	[-]
σ^2	population variance (SD)	[-]
θ	Theta brain wave frequency	[Hz]
a	conventional multiplier for alpha $= 0.05$	[-]
AF_3	left frontal electrode	[-]
AF_4	right frontal electrode	[-]
b	conventional multiplier for power $= 0.80$	[-]
C_p	capacity at a one-ampere discharge rate	[A·h]
hav	Haversine Function	[-]
I	discharge current	[A]
k	Peukert constant	[-]
k	Sample number in the time domain	[Samples]
N	width of a discrete-time, symmetrical window function	[Samples]
n	frequency over the sampling period	[Hz]
n_S	the sample size in each of the groups	[-]
P_z	parietal midline electrode	[-]
P_{200}	Positive potential deflection at 200 ms	[ms]
P_{300}	Positive potential deflection at 300 ms	[ms]
t	discharge time	[h]
T_7	left temporal electrode	[-]
T_8	right temporal electrode	[-]

Glossary

Arduino is an open-source electronics platform based on easy-to-use hardware and software. 45

active transfer is the process by which energy (in the form of Adenosine Triphosphate (ATP)) in the cell is used to transport molecules across a membrane. 12

auditory system is a body system that is responsible for the sense of hearing. 24

basal ganglia is a group of structures linked to the thalamus in the base of the brain and involved in the coordination of movement. 15

baud rate is the number of pulses per second in electronic communication. 102

brain hemorrhage is a type of stroke caused by an artery in the brain bursting and causing localized bleeding in the surrounding tissue. 17

central sulcus is a fold in the cerebral cortex in the brain. It separates the parietal lobe from the frontal lobe and the primary motor cortex from the primary somatosensory cortex. 17

cognition is the mental action of acquiring knowledge and understanding through thought, experience, and the senses. 94

COM port is the interface to a device which communicates through serial commands. 101

contralesional describes the half of a patient's brain or body away from the site of an injured organ. 20

cortical pyramidal cells are types of neurons found in areas of the brain. They are the primary excitation units of the prefrontal cortex and the corticospinal tract. 33

dorsal portion means situated on or toward the upper side of the body. 14

GLOSSARY

embolus is a particle that moves about in our blood vessels. 17

endocytosis is a process where particles that are too large to pass through biological membranes, are taken into cells. 12

enzymes are biological molecules (proteins) that act as catalysts and help complex reactions occur in your body. 12

exocytosis is the process by which a variety of substances leave a cell. 12

ganglion is a nerve cell cluster or a group of nerve cell bodies located in the autonomic nervous system. 13

hemiparesis is the weakness of the entire left or right side of the body. 15

hemiplegia is paralysis of one side of the body. 17

internal capsules are white matter structures situated in each of the cerebral hemispheres of the brain. 15

interstitial space is the fluid-filled areas that surround the cells of a given tissue. 27

ischemia is an inadequate blood supply to an organ or part of the body, especially the heart muscles. 17

lymphatic drainage is a type of gentle massage which is intended to encourage the natural drainage of the lymph, which carries waste products away from the tissues back toward the heart. 27

microprocessor is an electronic component that is used by a computer / controller to do its work. 4

neuroendicrine disorders are disorders that affect the interaction between the nervous system and the endocrine system. 17

neurologic sequelae are medical conditions associated with damaged neurons resulting from a previous disease, injury or other trauma. 17

neuroplasticity is the ability of the brain to repair itself. 30

paediatric is the branch of medicine that deals with the medical care of infants, children, and adolescents, and the age limit usually ranges from birth up to 18 years of age. 1

physiatrist is a medical doctor who specializes in physical medicine, rehabilitation, and pain medicine. 81

GLOSSARY

postsynaptic neuron is the nerve cell on the receiving end of an electrical impulse from a neighboring cell. 12

pseudounipolar neuron is a kind of sensory neuron in the peripheral nervous system. 13

sensorimotor (of nerves or their actions) having or involving both sensory and motor functions or pathways. 10

sensory modality is one aspect of a stimulus or what we perceive after a stimulus. 31

somatosensory system is a complex system of nerve cells that respond to changes to the surface or internal state of the body. 27

subarachnoid space is the area between protective membranes that cover the brain. 18

synaptic cleft is a microscopic gap between neurons. 12

synergies are the interactions of elements that, when combined, produce a total effect that is greater than the sum of the individual elements. 75

terminal bouton is the somewhat enlarged, often club-shaped ending by which axons make synaptic contacts with other nerve cells. 12

thrombus is a blood clot that forms in a vessel and remains there. 17

visuospatial deficits are deficiencies in the visual perception of the spatial relationships of objects. 25

weighted decision matrix is a quantitative technique used to rank the multidimensional options of an option set. 43

Chapter 1

Introduction

1.1 Background

Statistics obtained from the World Health Organization (WHO), show that 15 million people suffer a stroke worldwide each year (World Health Organization, 2002). Of these, 5 million people die and another 5 million are permanently disabled, requiring post-stroke rehabilitation ranging from neurorehabilitation and physiotherapy to medical treatment for movement therapy. As reported by the Internet Stroke Center, nearly three-quarters of all strokes occur in people over the age of 65 (Internet Stroke Center, 2015). According to the National Stroke Association, paediatric strokes affect only about 6 out of 100,000 children, though it is the leading cause of child death in the United States as of 2014 (National Stroke Association, 2015). Furthermore, it contributed to 51% of deaths in South Africa in 2013 (Statistics South Africa, 2013). Evidently, stroke has a large impact on the society, and methods to improve its treatment and prevention need to be thoroughly addressed.

After someone has suffered a stroke, the first step is to seek medical care as soon as possible. Hence, the so-called 'stroke sequence' is initiated to provide rapid assessment and treatment to minimize disability. At the hospital, a doctor will examine the individual and run tests to confirm the diagnosis and determine whether the stroke was caused by clots (ischemic stroke) or from bleeding in the brain (hemorrhagic stroke). This is usually done by means of a Brain Computed Tomography (CT) scan, blood tests and an Electrocardiogram (ECG). After the results have been produced, choices for therapy methods commence, depending on the type of stroke. With a diagnosis of ischemic stroke, fibrinolytic therapy is usually considered. This type of therapy works by dissolving clots which are obstructing blood flow to the brain. In contrast, a diagnosis of brain hemorrhage results in the consultation of a neurologist or neurosurgeon. On both accounts, patients will be then be admitted to a stroke unit or intensive care unit (Jaimison, 2016).

From experimental studies, it is evident that within hours after a stroke, regenerative mechanisms are activated and develop along with cellular demise

as part of the brain recovery phase (Cheng *et al.*, 2007). According to Jenkins and Merzenich (1987) and Masiero and Carraro (2008), the well-known capacity of the central nervous system to adapt its structural organization after a stroke is mainly influenced by sensory input, experience, and learning. It is therefore very important to start with different techniques that use these inputs to encourage methods of healing as soon as possible, in order to optimally benefit the adaptation phase. What thus follow after admittance to a medical unit, are a series of patient rehabilitation and therapeutic methods, including the medical management of stroke, physiotherapy, and neurorehabilitation programs. These stroke rehabilitation programs, which typically start in the hospital and continue through the recovery process, are essential to regaining functioning after a stroke. Modern stroke rehabilitation techniques focus primarily on treating the patient in order to provide compensation for any physical deficit resulting from a motor stroke. As a result, stroke rehabilitation requires different levels of interaction with physiotherapists, as some patients may have difficulty moving their facial muscles or limbs (Foulkes *et al.*, 1988). Professional physiotherapists, therefore, need a certain level of knowledge, skills, and aptitude to treat problems with joints, muscles, and nerves by using physical techniques that encourage healing.

1.2   Motivation

The motivation behind this thesis is to eventually address two of the most prominent limiting complications in stroke recovery programs, which are the time available for patient engagement, and the cost for outpatient rehabilitation. According to Maciejasz *et al.* (2014), the existing shortage of therapists and caregivers assisting physically disabled individuals at home is expected to increase and become a serious problem in the near future. The population of stroke patients needing physical rehabilitation is also constantly increasing, which requires an increase of available therapists. Due to economical reasons, the duration of primary rehabilitation for patients who have suffered a stroke is decreasing (Richards *et al.*, 2008). Even with the adequate amount of physical care and training, patients deriving benefit from rehabilitation services will not always receive medical aid and cover from federal programs, as health care programs only assist some comprehensive outpatient rehabilitation facilities, and for certain patient eligibility (like blindness, old age, and disabilities) (Rees, 1997). Results of a study conducted by Rhoda *et al.* (2009) revealed that there is a lack of therapy services to provide rehabilitation to stroke patients at Community Health Centres (CHCs) in the Western Cape, South Africa. Their findings of the process of rehabilitation indicated that the frequency of physiotherapy, occupational therapy, and speech therapy, as well as the number of hours of physiotherapy, were low.

According to Godwin *et al.* (2011), the average cost for outpatient stroke rehabilitation services and medications after the first year post inpatient re-

habilitation discharge amounted to USD 17,081. The corresponding average yearly cost of medication was USD 5,392, while the average cost of yearly rehabilitation service utilization was USD 11,689. Typically, in a South African environment, stroke patients undergo the so-called 'gross motor skills' therapy, which are skills that require whole body movement and involve the large (core stabilizing) muscles of the body to perform everyday functions. For acute stroke cases, post-stroke rehabilitation amounts to more or less R 450.00 for 30-45 minute sessions and, following discharge, the same amount for 60 min sessions (Aucamp, 2016).

Two factors influenced by these aforementioned complications are life expectancy and other diseases in the elderly population. Life expectancy continues to increase, and it is accompanied by the prevalence of both moderate and severe motor disabilities in the elderly population (Nordin *et al.*, 2014). As a countermeasure, clinical studies and evaluations have been conducted on technically advanced devices, with the sole purpose of assisting in physical rehabilitation. Hillman (2004) states that such devices for movement therapy are relatively novel methods for stroke rehabilitation, with increased availability, although not all devices have been confirmed to target specific subject groups (Patton *et al.*, 2008). An additional complication is that because these devices are so technically advanced, their production costs increase, rendering them too expensive and too difficult to repair in many developing countries, such as South Africa, which need new, low-cost medical technology that can be manufactured locally. According to an opening address at the Global Forum on Medical Devices by Dr Margaret Chan, Director-General of the World Health Organization, worldwide, annual government expenditure on health ranges from well over USD 7,000 per person to less than USD 10. These low levels of expenditure on health help explain why many medical devices are considered luxuries (Chan, 2010).

Keeping these complications in mind, certain aims and objectives were established to not only eventually improve the regenerative mechanisms of stroke patients, but also to decrease the costs involved in rehabilitation.

1.3   Aims

The overall goal was to apply methods similar to current neuro- and physical rehabilitation in the field of sensory stroke rehabilitation. This was done by proposing a mechanical sensory feedback rehabilitation prototype that may be used to rehabilitate stroke patients, in addition to the rehabilitation they normally receive post-stroke.

The aims of this project were as follow:

1. Design and manufacture a potentially low-cost wearable prototype, that uses different methods to supply sensory feedback to the wearer. These

methods should be similar to those used during neurorehabilitation and physical therapy sessions for patients with ischemic stroke.

2. Test the feasibility of the prototype by obtaining electrobiological measurements of healthy subjects through an observational study, and comparing those results with previous studies.

1.4   Objectives

Specific steps were taken to achieve the aims and focussed on dividing this project into two main phases: the concept design phase, and the experimental phase. The objectives for both phases were as follow:

1. Researching and understanding the biology of neural control and strokes, and gaining sufficient behavioral and physiological knowledge to decide which parameters were necessary for the design and experimental phases.

2. The mechanical design and construction of a wearable prototype - this prototype should be worn by the user and should provide different types of sensory feedback to which the user should be able to react.

3. The design, construction, and testing of the electronics required for the feedback of the prototype.

4. Acquiring a commercially available device that can record, process and relay electrobiological measurements.

5. Conducting an observational study in order to deduce whether any feedback provided by the prototype can be picked up and analyzed via biosignals, by the acquired device.

6. The design, construction, and implementation of a microprocessor that will, in turn, analyze the electrical signals generated by the acquired device.

7. The implementation of a serial port communication channel between the microprocessor of the prototype and a personal computer.

8. The incorporation of a computer program that communicates with the microprocessor of the prototype in order to track its feedback and decisions.

9. Practical demonstration of the feasibility of the device using adequate healthy test subjects.

10. Compiling a full project report and user manual for the device.

11. Conducting a clinical trial study in order to evaluate possible neuroplasticity through the use of rehabilitation and recorded EEG data, ERP analysis and Functional Motor Assessments of adequate post-stroke test subjects.

12. Evaluate the prototype's ability to possibly decrease patient-time engagement, while increasing the rehabilitation session duration of individual stroke subjects.

1.5   Problem Statement

In summary, by combining the background, motivation, and aims, the problems this project wishes to address are based on the diagram illustrated by Figure 1.1. From this diagram, it can be seen that a generic stroke process flow would entail the initial brain injury, rehabilitation therapeutics, and stroke recovery. However, a discontinuity arises in this flow, in societies in which the aforementioned limitations play a significant role. The research problem and -question propose to add a solution that merges the treatment and recovery phases.
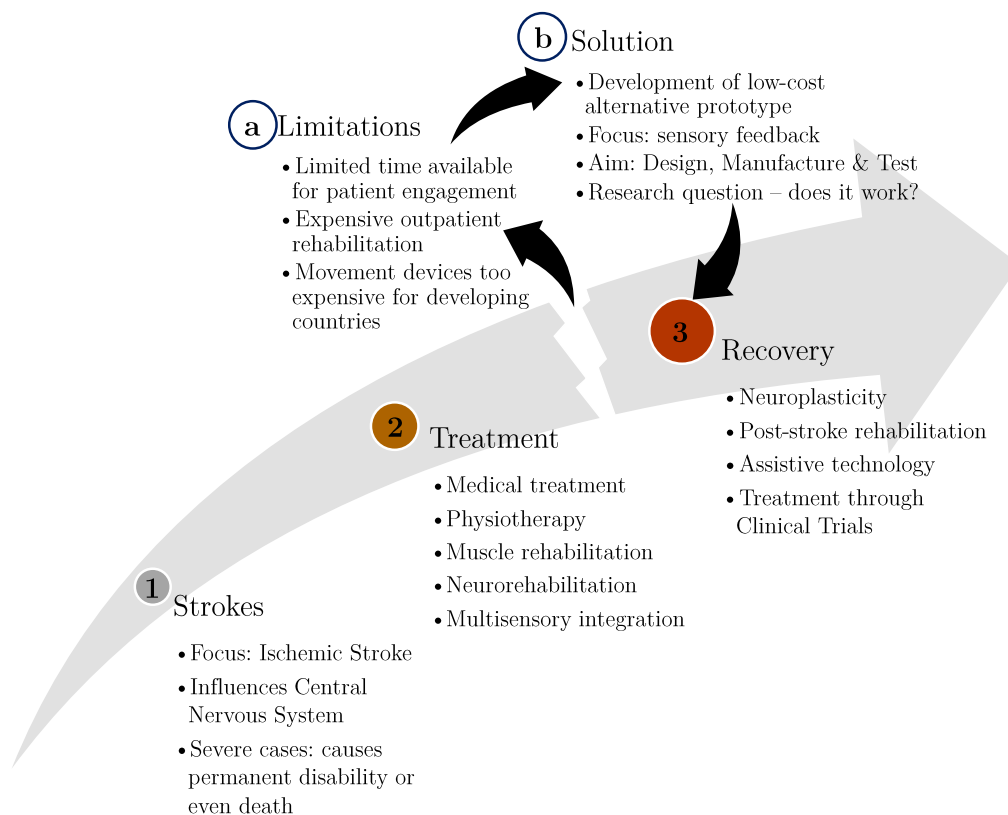
Figure 1.1: Problem Statement diagram

By combining the specified aims and the methods to achieve them, a primary research question was set up in order to illustrate what the research eventually aimed to answer: *Would it be possible to sense Event-Related Po-*

tentials (using EEG) in the brain during discrete stimuli, from a constructed wearable sensory feedback device?

The scope of the study does not extend to a consideration of the influence of the prototype on the recovery period of stroke patients, because of the lack of time and resources. Furthermore, it is not a production-ready prototype. However, the research and discussion involve the concept of neuroplasticity and its evaluation in stroke victims as part of future recommendations. As discussed in the Literature Review, most previous work in the area of stroke rehabilitation has concentrated on mechanical assisting devices and the utilization of virtual environments to improve motor functionality. On this occasion, however, attention is directed at presenting a prototype that focuses more on providing input to the peripheral nervous system (that connects the Central Nervous System (CNS) to the limbs), rather than to the strengthening of the muscles.

This thesis is presented in partial fulfilment of the requirements for the degree of Master of Engineering (Mechatronic) in the Faculty of Engineering at Stellenbosch and is aimed at the application of Biomedical Engineering. It stems from a proposal by the principle investigator.

1.6   Thesis Outline

The thesis will, amongst others, describe in detail all of the following:

Chapter Two: A literature study is conducted on the principle of human neural networks, and how it correlates with the anatomy of stroke patients, their side effects and methods of treatment via different electrobiological techniques. This is then followed by conducted research on current stroke rehabilitation designs, medical applications, and clinical studies. Research gaps are identified, and approaches to filling these gaps are proposed.

Chapter Three: This chapter commences the design section. Engineering specifications and design parameters for concept theory, generation, selection, and manufacturing are set. The prototype hardware and control designs are explained.

Chapter Four: This chapter introduces the experimental procedures of this project, and focuses on an observational study. Analytical explanations for the procedure and methodology of investigations and experiments are summarized. The subjects, materials, and methods used to obtain experimental data through the study, are discussed in detail.

Chapter Five: The results obtained from the observational study are summarized. Statistical analysis is performed on valid results. Statistical impact of the results and comparisons to previous studies are discussed.

Data analysis includes a descriptive summary of EEG preprocessing techniques and data extraction using *EEGLAB*.

Chapter Six: A discussion of the obtained results is given. Results are compared with that of previous literature and their medical relevance is discussed. The future impact of the project is also discussed in detail. It contains information of a proposed clinical trial on stroke patients and its methodology. It also includes descriptions of the stroke patient selection criteria. Furthermore, related theory and calculations necessary for the data analysis of a clinical trial are discussed.

Chapter Seven: A final conclusion at the end contains notes and summaries of the aims of this project. The contribution of this project to the field of Biomedical Engineering is discussed. Recommendations are made with regards to improvements of this project. The conclusion will also be corroborated in the central chapters described above.

Chapter 2

Literature Review

2.1   Background

This section includes an in-depth literature review that was done in order to accumulate enough information on which to base the rest of the project activities. Some of the contents involve outlining philosophical or even methodological principles which underpin what was done during this project. In order to have a better idea of the overall approach that was followed to know which principles and topics for discussion to include in the literature review, special focus was placed on the research question and what information it contains. From it, the following keywords were highlighted:

"sense...in the brain; electrobiological potentials": Here, attention will be focussed on the occurrence of action potentials in the brain and body. The study of these potentials is called Electrophysiology. Although various methods exist to obtain such information from the body, the research will focus more on the measurement of Electroencephalography (EEG)- and Event-Related Potential (ERP)-data, and how EEG is analyzed and presented in the form of ERPs.

"discrete stimuli": Discrete stimuli or events of a measurement are presented as a discrete sequence of events in time. Each event occurs at a particular instant in time and marks a change of state in the measurement. This means the literature review will include information about measuring such events, especially during clinical trials. Further elaboration will be done on ERPs.

"constructed; wearable; device": This relayed that a (wearable) prototype needed to be constructed, which meant that information should be retrieved from literature about similar concepts and devices used for the purpose of stroke rehabilitation, including the methods mentioned in Chapter 1.5.

2. LITERATURE REVIEW

"sensory feedback": This is feedback provided within the sensory systems of the body, where information from sensory receptors is returned along the afferent pathways of the nervous system. This meant a thorough literature study should be done on the Central Nervous System of the brain, how neurons work in order to relay sensory information and how they are influenced by strokes in general.

Figure 2.1 illustrates the structure of the literature review that followed after consideration of the research question.
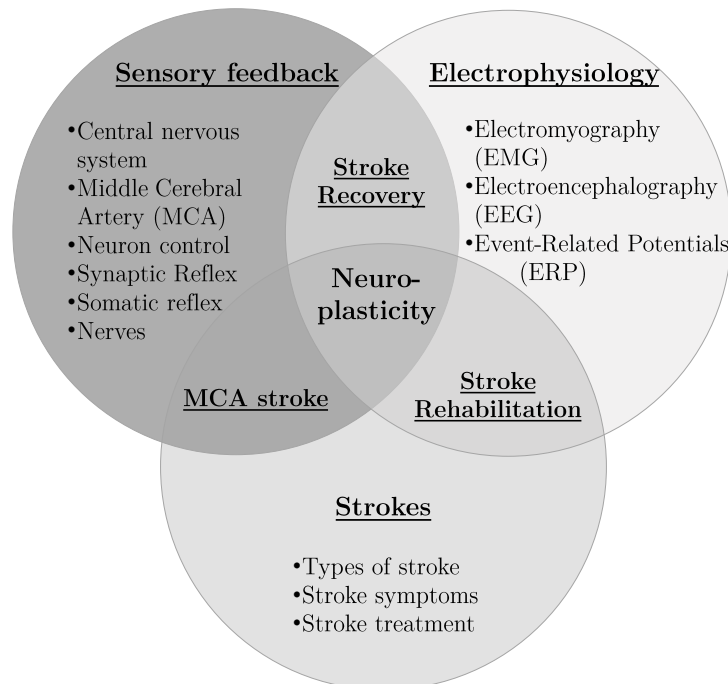
Figure 2.1: A Venn Diagram showing the relevant sections that were included or mentioned in the literature review process

As mentioned in Chapter 1.5, the possible influence of the prototype on the recovery period of stroke patients would also be necessary to discuss, as future recommendations that could have certain medical relevance, can be made. For an understanding of the recovery of stroke patients, information on the principle of the causes and consequences of strokes, as well as the treatment thereof, was done as part of the initial research phase. Finally, the concept of neuroplasticity (brain changeability), how it correlates with a Middle Cerebral Artery (MCA) stroke, its rehabilitation and recovery, and certain experimental features that should be present during the facilitation thereof, are addressed.

2.2   Sensory Feedback

The mention of sensory feedback is of great significance to the literature review, as this is part of both the first aim and one of the objectives of this project. Sensory feedback, which ultimately comprises different types of feedback presented to the body, includes auditory-, visual- and haptic information (feedback in the form of vibration). The Central Nervous System (CNS) is an organ system of the body that receives and processes this type of information from all parts of the body. The nervous system is made up of the brain and spinal cord, and contains a network of specialized cells called neurons. Neurons time and coordinate all the impulses of the brain by transmitting signals into different areas of the body through the spinal cord.

The uppermost region of the CNS in humans is called the cerebrum. All conscious thought originates in the cerebrum and can influence the subconscious functions of the lower regions of the brain. Other than the fact that it controls all voluntary action, the cerebrum also has control over movement, sensory processing, and learning and memory. These cortical areas receive blood supply from the main cerebral arteries, like the anterior cerebral, middle cerebral and posterior cerebral arteries. Amongst others, the following important functions and parts of the body are necessary for sensory feedback to be relayed efficiently from the body part to the brain: sensory receptors and nerves in the human body (to pick up and relay a signal), the neurons (communication cells), the synaptic- and somatic reflex systems (to integrate the nerves and the brain) and the arteries and portions of the motor cortex (the part of the brain that controls reaction and movement).

2.2.1   Sensory Receptors

Receptors in the human body respond to many different sensorimotor stimuli and can be classified by location, rate of adaptation, morphology or adequate stimulus (the amount and type of energy required for the stimulation of a specific receptor) (Purves *et al.*, 2001). One of these receptors, called a Mechanoreceptor, responds to a wide array of external and internal stimuli, such as touch, pressure, movement, and vibration.

Neural impulses that control the execution of movement by the skeletal muscles are generated when a body part is stimulated. These neural impulses are generated by the primary motor cortex and are transferred via a network of nerves in the body. Normally, when a person's hand or arm is touched, an electrical signal passes to the spinal cord and up to the brain, where it turns on the cells in the map that make the body part feel touched (Doidge, 2008). In addition, signals generated from the left motor cortex, cross over to the right side of the body's mid-line, and vice versa. All the body parts usually influenced by a stroke (the shoulder, upper- and lower arm, wrist and the associated muscles and nerves) are represented in the primary motor cortex.

The ulnar nerve (Figure 2.2) is one of the three main nerves in the arm. It comes from the medial cord of the brachial plexus (C8-T1) - this is a network of nerves that extend from the spinal cord through the neck, over the first rib, and into the armpit (Goel *et al.*, 2014). Beyond the elbow, the ulnar nerve travels under muscles on the inside of the forearm and into the hand on the side of the palm with the little finger. Two of the muscle groups the ulnar nerve innervates, are the forearm and wrist muscles. In the forearm, the ulnar nerve supplies the *flexor carpi ulnaris* (FCU) and the medial half of the *flexor digitorum profundus* (FDP).
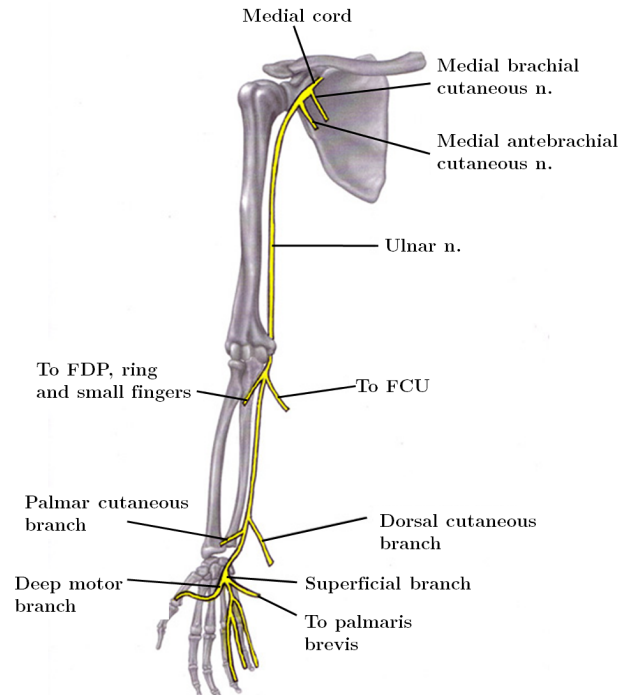
Figure 2.2: The nerve structure containing the medial- and ulnar nerves (Hart, 2015)

2.2.2 Neuron Control

The neural impulses will not be able to relay information via the nerves without the existence of neurons. A neuron is an electrically excitable cell that processes and communicates information throughout the brain and body using electrical and chemical signals. These signals can be inhibitory (a synaptic potential that makes a neuron less likely to generate an action potential) or excitatory (a synaptic potential that makes a neuron more likely to generate an action potential). The main idea of inhibitory / excitatory neurons is that they are responsible for behavior, based on predetermined signals received from the brain. The types of neurons are, therefore:

Sensory / afferent neurons: Conduct impulses to the CNS

Motor / efferent neurons: Conduct impulses away from the CNS

Association / interneurons: Connect sensory and motor neurons with one another and connect different parts of CNS with each other.

2.2.3   The Synaptic Reflex System

During the stimulation of the different sensory areas of the body, neurons communicate through a connection called a synapse. The general synapse shown in Figure 2.3 is the connection between two neurons and is important when a nerve message (action potential) needs to be passed on from one neuron to another. Two neurons are usually separated by a thin cleft and the message therefore needs to be transmitted - for this to happen, the electrical signal must be converted to a chemical signal.
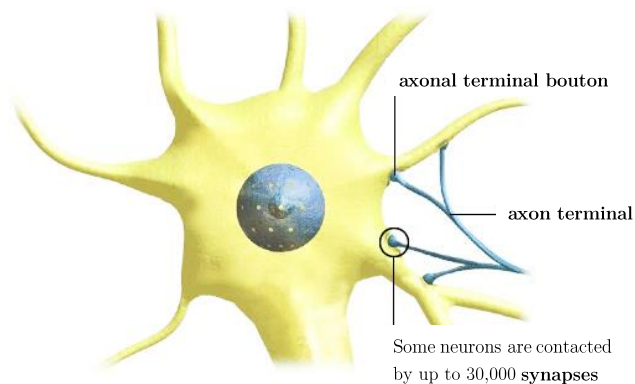
Figure 2.3: A Synapse (TheHumanBody, 2007)

Firstly, a nerve signal will reach the terminal bouton. This causes Ca^{2+} (unbound calcium) channels to open. The Ca^{2+} acts as a 'messenger' that activates the vesicles (small organelles within a cell) with a transmitter to release their neurotransmitter into the synaptic cleft by means of exocytosis. The neurotransmitters are contained in a synaptic vesicle.

As shown in Figure 2.4, the neurotransmitter molecules then diffuse across the synaptic cleft where they prepare to bind with receptor sites on the postsynaptic neuron to influence the electrical response in the postsynaptic neuron. The moment these molecules come into contact with the receptors of the postsynaptic neuron, an electric signal is generated. Next, the Na^+ (sodium ion) channels on the receptor membrane open and depolarization occurs on the membrane, causing an action potential to happen (which in turn is prompting the conduction / energy transfer). When the signal has finished transferring, the neurotransmitters are destroyed by means of enzymes inserted into the cleft area, active transfer or endocytosis (Marieb, 2012).
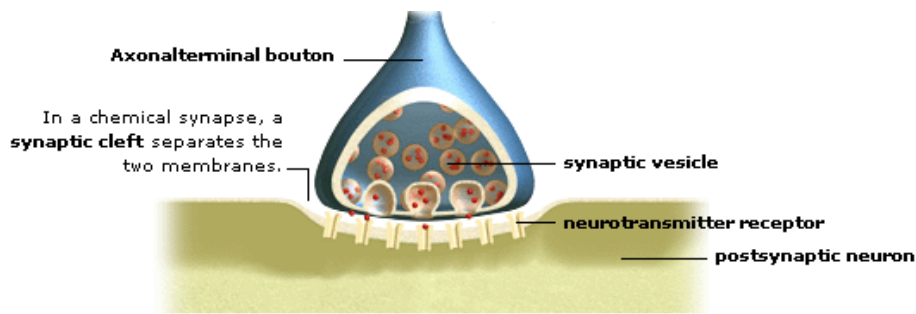
Figure 2.4: A Synapse - detailed view (TheHumanBody, 2007)

2.2.4   The Somatic Reflex System

The reflex system is responsible for the contractions of human muscle. A reflex always comprises five subdivisions:

- Receptor
- Afferent path
- Integration area
- Efferent path
- Effector

As a muscle contraction is caused by a somatic reflex, the receptors originate from the surface (soma) of the human body and hence refer to all the possible sensory inputs a human can perceive, such as sight, touch, smell, and sound. The afferent path (Figure 2.5) is always a single sensory neuron that enters the spinal cord at the posterior (back) side. It is classified as a pseudounipolar neuron and the cell body thereof is situated outside the CNS in a structure called a ganglion.

Since this is a spinal reflex, the integration area is the spine which is part of the CNS. The efferent path shown in Figure 2.6 is always one single motor neuron that leaves the spine at the front (anterior). The effector that is influenced by the motor neuron is the skeletal muscle, which is the only effector a human can consciously control (Marieb, 2012).

The functioning of the somatic reflex is quite simple. An example is shown in Figure 2.7. A stimulus, like pain, is picked up by a pain receptor in your finger. From there on it is relayed by an afferent neuron to the spine where it synapses directly or via an interneuron with an afferent neuron. This afferent neuron relays the action potential caused by this connection to the effector, which is the skeletal muscle. The muscle contracts and your finger is reflexively pulled away from the object that has caused the pain - hence you have executed a decision-making event for movement.
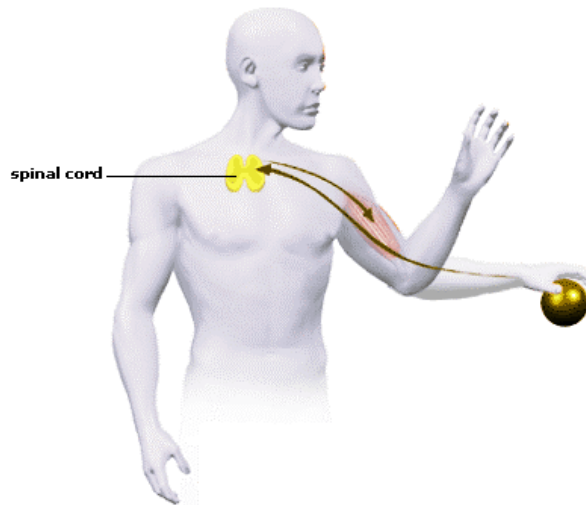
Figure 2.5: Afferent path of the Reflex System (The-HumanBody, 2007)
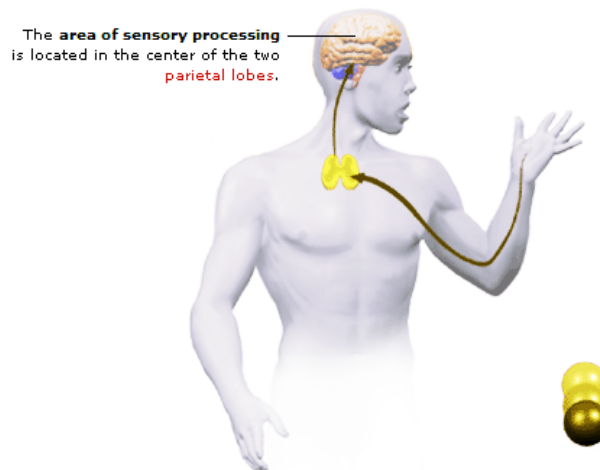
Figure 2.6: The Efferent path causes a reaction in the skeletal muscle (TheHumanBody, 2007)

2.2.5 The Primary Motor Cortex

During a decision-making event for movement, the brain activates a certain area in order to process and execute the movement. This area is also called a 'brain map'. One of the main brain maps involved in motor function is called the primary motor cortex (Figure 2.8). It is located in the dorsal portion of the frontal lobe and runs alongside the precentral gyrus. The motor cortex functions through the partial blood supply of the MCA, together with the supplementary motor area (which controls sequential movements) and the posterior parietal cortex (which produces planned movements).

The MCA furthermore supplies blood to most of the outer convex brain

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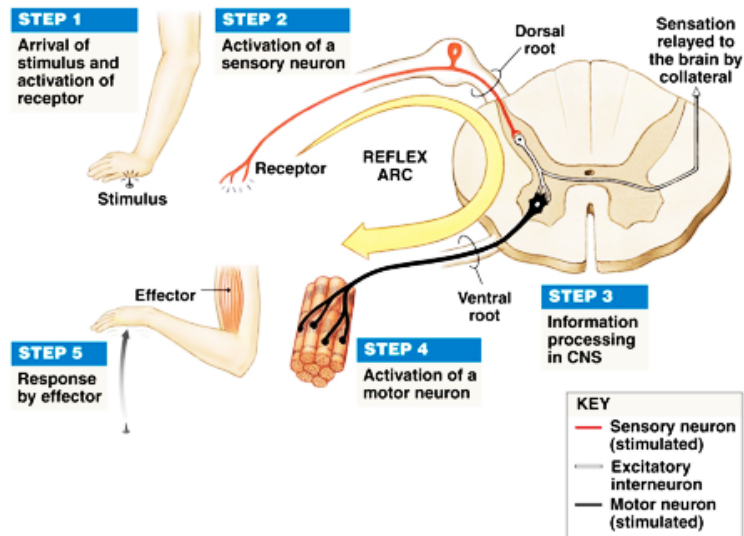
Figure 2.7: The Somatic Reflex System (Marieb, 2012)

(A) **Lateral View**
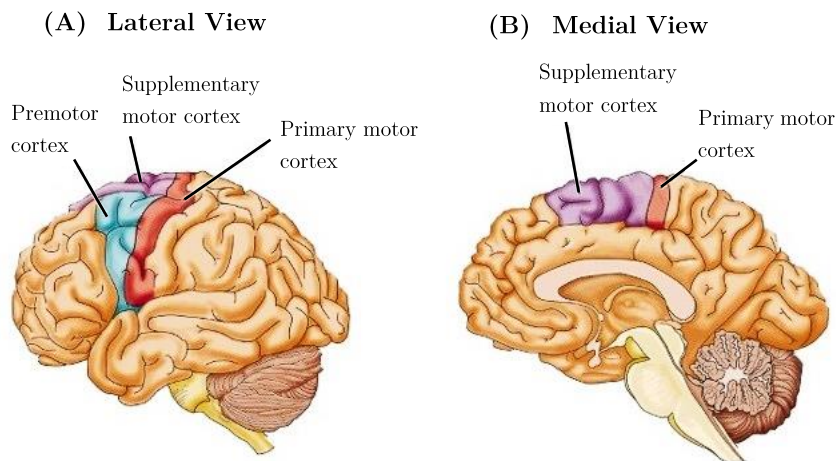
(B) **Medial View**

Figure 2.8: The lateral and medial views of the brain, showing the primary motor cortex (Clinic, 2015)

surface (cortex), nearly all the basal ganglia, and the posterior and anterior internal capsules (Slater *et al.*, 2016). Failure of blood supply to any of these regions leads to a pure motor stroke or the occurrence of hemiparesis.

According to Krayenbühl *et al.* (1982), the MCA can be classified into four parts, or so-called segments (M1-M4). The MCA supplies blood to the lateral aspects of three of the four brain lobes, shown in Figure 2.9. These lobes are the frontal lobe, which is responsible for thought, language, emotions and voluntary movements, the temporal lobe, which recognizes and interprets sounds, and helps to form new memories, and finally the parietal lobe, which is responsible for the perception and interpretation of the sense of touch (Moore *et al.*, 2013). Figure 2.9 also shows the major branches of the middle cerebral

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artery. The internal carotid, anterior cerebral, and anterior communicating arteries, the optic chiasm, the internal capsule, and the temporal lobe of the brain are shown for orientation purposes.
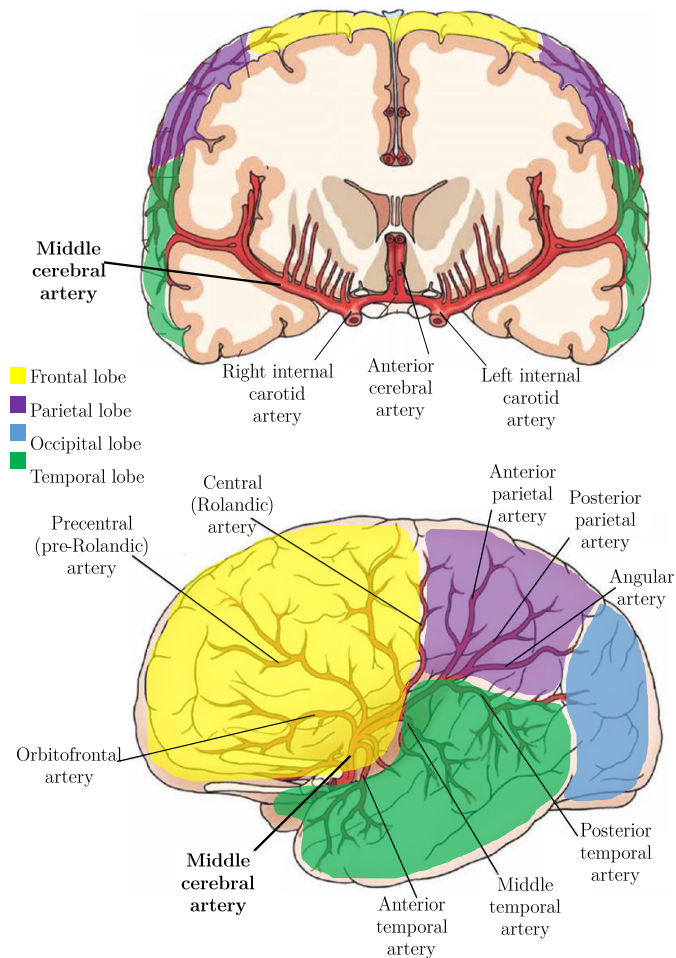
Figure 2.9: Top: Branches of the middle cerebral artery. Bottom: Positions of the frontal, temporal and parietal lobes (Nguyen, 2014)

The MCA arises from the major arteries of the head and neck. Each person has a left and a right internal carotid artery, and these arteries divide the brain into the anterior cerebral artery and the middle cerebral artery (Kandel *et al.*, 2000). From there, the MCA continues into the lateral sulcus where it then branches and projects to many parts of the lateral cerebral cortex. It also supplies blood to the anterior temporal lobes (lobes responsible for the formation of explicit long-term memory) and the insular cortices. The insular cortices are believed to be involved in consciousness and play a role in diverse functions usually linked to emotion or the regulation of the body's homeostasis (Mufson *et al.*, 1981). Visual and sensory feedback play a very important role in the rehabilitation of stroke victims. The MCA supplies a portion of the lateral surface of the parietal lobe, which controls the regions of these senses.

Being one of the four major lobes of the cerebral cortex, the parietal lobe is positioned above the occipital lobe and behind the frontal lobe and central sulcus. It has a sensational and perceptional region, as well as a region concerned with integrating sensory input, primarily with the visual system. According to Kandel *et al.* (2000), individuals with damage to the synapses and neurons of their parietal lobes often show striking deficits, such as abnormalities in body image and spatial relations.

2.3 General Strokes

Now that an adequate understanding as been established about the sensory feedback system of the body, the focus shifts to how these information processing systems and parts of the body and brain are influenced by strokes. The types of strokes that can occur, their symptoms, and methods of treatment were all necessary to research in order to know at which level of detail a sensory feedback device should be designed. Questions like how the sensory system is influenced by different types of strokes, how the brain picks up signals received from the senses, and how this processing of information differs due to a stroke, were essential to answer.

2.3.1 Types of strokes

Any stroke is characterized by a sudden loss of function of a part of the brain. This loss is a result of either a loss of circulation, or perfusion, to a specific part of the brain (ischemia), or due to brain hemorrhage. This causes certain areas of the brain influenced by the stroke to not function as it is supposed to, which can result in paralysis of one or more limbs, usually on the opposite side of the body (hemiplegia). Another side effect is the result in loss of speech or loss of vision to one side of the field of vision. Areas of dead tissue resulting from a pure motor stroke may cause diverse neurologic sequelae, including a number of neurophysiological processes that, in rare cases, can lead to the development of neurodegenerative and neuroendicrine disorders (Adibhatla and Hatcher, 2007), (Adibhatla and Hatcher, 2008). These disorders then cause the loss of the neuronal circuitries that support cognitive and sensory-motor functions (Lee *et al.*, 2015).

According to the American Heart Association (2015), 87% of strokes are ischemic in nature, meaning they are caused by a restriction of blood flow to the brain, and commonly result from an arterial obstruction by a thrombus (coronal blood clot) shown in Figure 2.10 or embolus (any detached, travelling intra-vascular mass that travels in the bloodstream). This causes the brain to be deprived of any oxygen and other nutrients after which it suffers damage as a result of an injury. This injury is triggered by an alpha-amino acid called glutamate, which is used in the biosynthesis of proteins. Due to the starvation of oxygen, certain neurons release an excessive amount of glutamate onto

nearby neurons. In turn, these neurons become overexcited and overloaded in calcium, after which they die. The excess in calcium also triggers the release of macromolecular biological catalysts called enzymes, which catalyze the destruction of the brain cells.
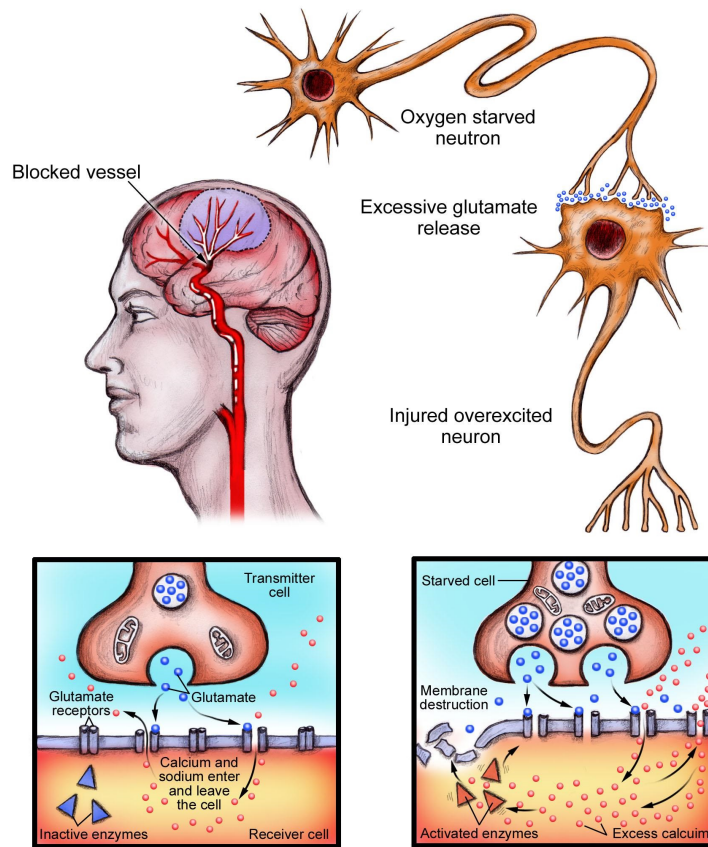
Figure 2.10: Ischemic Stroke - Formation of a coronal clot and glutamate transfer (Internet Stroke Center, 2015)

The other type of stroke is called a hemorrhagic stroke. Contributing to 13% of all strokes, this stroke is caused by the rupture or leak of a blood vessel either within the primary brain tissue or subarachnoid space (Thom *et al.*, 2006). Since the MCA comprises the larger part of the brain, it is the most common site of the first and most common type - an ischemic stroke. One of the most efficient ways to obtain data regarding the type of stroke a patient has, and to have a prognosis of the stroke, is to first determine the severity of the stroke through diagnosis and how quickly medical care can be given.

2.3.2 Stroke Diagnosis

A stroke, and its severity, is diagnosed based on the patient's signs and symptoms, medical history, a physical exam, and test results. These test results are usually accompanied with the results of a type of scan that is conducted on

the patient's body and brain. These scans include, but are not limited to, the following:

Brain Computed Tomography: A Brain Computed (CT) Tomography scan, is a scan that uses X-Rays to take detailed pictures of structures inside of the body and brain. This test is often done right after a stroke has occurred and can show bleeding in the brain or damage to the brain cells from a stroke.

Magnetic Resonance Imaging: According to Gibbons (2013), Magnetic Resonance Imaging (MRI) uses magnets and radio waves to create pictures of the organs and structures in the body. This test is alternative to a Brain CT scan and can detect changes in brain tissue and damage to brain cells from a stroke, although it is usually more expensive.

Computed Tomography Angiogram: A Computed Tomography Angiogram (CTA) can help diagnose and evaluate the large blood vessels in the brain by using an injection of an iodine-rich contrast material. Because an arterial obstruction caused by a thrombus influences the state of the blood vessels, these tests may give a radiologist more information about the site of a blood clot and the flow of blood through the brain.

Carotid Ultrasound: The carotid arteries are major blood vessels in the neck that supply blood to the brain, neck, and face. The carotid ultrasound scan is usually accompanied by Doppler ultrasound - a special test that shows the speed and direction of blood moving through the blood vessels.

The optimal reduction of risk factors is paramount in the prevention and management of an MCA Stroke. After the results of a scan has been analyzed, patients are then immediately admitted to a stroke care unit to minimize the damages inflicted by stroke side-effects.

2.3.3   Side-Effects of an MCA Stroke

Several symptoms affect the patient and can cause more than just physical damage. In addition to the weakened muscle on the left or right hemisphere of the body, the following are defined as general symptoms a patient may encounter after an MCA Stroke:

- Spasticity
- Pain in the patient's limbs and shoulders
- Shoulder subluxation
- Depression
- Urinary incontinence - the inability to control bladder movements

- Urinary tract infection

- Fecal incontinence - the inability to control bowel movements

2.3.3.1   Hemispatial Neglect

Although an MCA stroke may not always be the cause of a sensory loss in the limbs of a patient, a challenging condition known as hemispatial neglect may occur. In basic terms, a patient will tend to 'neglect' the side of the body that is influenced by the stroke. Neglect may also extend or be confined to personal space, with patients failing to acknowledge their own contralesional body parts in daily life. Moreover, some patients fail to use their contralesional limbs even if they have little or no weakness - the so-called "motor neglect". This does not only affect the behavior and movement capabilities of a patient, but also discourages any exercise the patient may have with the affected limbs. This is a condition that needs to be avoided at all costs.

2.3.3.2   Motor Neglect

Motor neglect occurs in association with hemispatial neglect, and is more a neuropsychological condition than a physical deficit. Laplane and Degos coined the term motor neglect, giving this definition "*Absent or low use of spontaneous contralesional limb (lower and / or higher), despite preserved motor skills ... not explained by weakness or lack of sensitivity, it improves with the verbal suggestion*" (Laplane and Degos, 1983). This condition is more generally found in patients that have had a stroke, but with no weakness in their contralesional arm or leg. Specifically, patients that are verbally encouraged to use the limb with motor neglect have relatively normal movement. In contrast, the same patients have difficulty to perform the same movement spontaneously. The observation here is that the signals that are being sent out by the brain are intact, but the means in which the reflex is activated, may not always cause a successful response.

It can be argued that the language processing functions, which are carried out in the cerebral cortex, are managed in a different area than the one used for processing psychological commands, so what a patient hears and thinks are processed differently (Geary and Huffman, 2002). Ultimately, a way to overcome this is to target specific stimuli that successfully eliminates the side-effects of motor neglect by bypassing the non-responsive synapses and finding a way to encourage spontaneous movement without the need for verbal influence.

Another deficit that is related to motor neglect, which was worth researching, is a self-awareness deficit called "Anosognosia". This condition causes a person suffering from a disability to seem unaware of the existence of his or her disability. It typically results from physiological damage to the parietal lobe and higher level neurocognitive areas (Vallar and Ronchi, 2006). An example of a higher level neurocognitive process is the integration of sensory

information and the somatosensory system, like spatial or bodily representations. Anosognosia is similar to motor neglect in the sense that it is thought to be caused by these neurocognitive processes, rather than the sensory loss due to brain damage. Here it is again important to observe the relation between physiological- versus physical damage.

2.4 Rehabilitation Methods

Stroke rehabilitation is an important part of recovery after stroke and consists of a variety of pharmaceutical- and physical techniques that encourage healing. As with many diseases or disabilities, drug treatments are also one of the rehabilitation methods used to treat stroke victims. This section will summarize existing relevant methods of rehabilitation, and will briefly discuss current designs and applications of stroke rehabilitation devices and the methods they use. In the literature study conclusion, it will also be noted where these methods fall short, and their limitations, in order to focus on which factors to try and solve throughout the design and experimentation processes that follow.

2.4.1 Physiotherapy

Since the stroke process described in Figure 2.10 occurs via glutamate receptors, including N-Methyl-D-aspartate (NMDA) receptors, scientists believe that damage can be stopped through the use of agents that block these receptors. There exist many different antiplatelet medicines and blood thinners that can be used to treat ischemic strokes. One of the well-known treatments for acute ischemic stroke is the use of a protein called Tissue Plasminogen Activator (tPA). This drug treatment has been approved by the United States Food & Drug Administration (FDA) and is given via intravenous therapy (U.S. Department Health and Human Services, 2015). This type of medical therapy infuses the tPA directly into the vein (usually via a drip chamber) and works by dissolving any blood clots in the affected veins. This then causes the blood flow to improve to the affected part of the brain that was initially deprived of blood flow.

Another form of medical treatment entails invasive treatment. This involves a surgeon inserting a small mechanical device (called a mechanical thrombectomy device) into the vein of the affected area in the brain. The device then traps the blood clot that has formed and is either pulled out by the surgeon, or kept at the affected area to dissolve the clot using tPA. The improvement in medical advances increases the survival rates of stroke patients. There are also, however, certain side effects caused by the excess use or the sudden disuse of medical treatments. According to Drugs.com (2014), medicines like *Baclofen* and *Lioresal* have side effects that include high fever, changes in mental status and muscle stiffness and spasms. These spasms may then result in further complications in the conditions of the stroke patients,

due to the stroke already contributing to spasticity. Finally, unlike ischemic strokes, hemorrhagic strokes can not be treated with antiplatelet medicines or blood thinners, since these medicines can make bleeding worse.

After medical treatment, such as surgery and drugs have been prescribed and administered, stroke patients are then usually allocated to physiotherapists, who then manage the training and rehabilitation of motor skills and muscles. Physiotherapists are important key factors in post-stroke rehabilitation, as they are one of the first rehabilitation options to be considered immediately after stroke. Physiotherapists work both independently and in a team in the health sector. They help patients of all ages to overcome dysfunctions and recover from illness or injury.

The comprehensive health care of physiotherapists to the stroke community focuses on prevention, cure, and rehabilitation and usually requires different levels of correspondence with their patients. In addition to techniques such as taping, electrotherapy, and hydrotherapy, the most effective techniques are manual techniques (e.g. massage, mobilization, and manipulation), exercise therapy, and movement analysis and retraining. These techniques are repeated constantly until fully functional recovery is reached. Physiotherapists usually attend to the patients in either a rehabilitation unit in the hospital, a sub-acute care unit, a rehabilitation hospital with individualized inpatient therapy or during home therapy. It has been found that stroke patients managed in a stroke unit in the acute stage have better outcomes (Trialists Collaboration, Stroke Unit, 2007).

According to a study conducted by De Wit *et al.* (2005), rehabilitation sessions are considered optimal and accurate when patients spend on average 2 hours in therapy daily. This accuracy is sometimes hard to achieve, as specifically in the Western Cape, findings of the process of stroke rehabilitation indicate that the frequency of physiotherapy, occupational therapy and speech therapy as well as the number of hours of physiotherapy, is low (Rhoda *et al.*, 2009). This lack of intensity was shown to be partly linked to a lack of accessibility to the centres. Together with physiotherapy, other therapy options for post-stroke rehabilitation include occupational therapy, speech-language pathology, audiology, and neurorehabilitation.

2.4.2 Neurorehabilitation

Recent reports by Nordin *et al.* (2014) and Riener *et al.* (2005) indicate that improved, low-cost, and alternative solutions are constantly being considered, with a special focus on neurorehabilitation. This rehabilitation refers to a type of therapy where sensors or electrodes are attached to the body of the patient that relay electrobiological measurements shown on a computer screen. The aim of neurorehabilitation is to aid recovery from a nervous system injury, e.g. a stroke, and to minimize any functional alterations resulting from it.

Real-time neurorehabilitation, such as cognitive rehabilitation, focuses on the prevention, diagnosis, and treatment of strokes and other diseases of the

brain and spinal cord. Usually, a neurologist is present during this rehabilitation, but it can also be conducted by rehabilitation nurses, physical therapists and neuropsychologists, depending on the severity of the stroke. Neurofeedback (NFB) brain wave training based on the principle of brain plasticity is a well-known method for cognitive rehabilitation (Cho *et al.*, 2015). It refers to a type of therapy where sensors or electrodes are attached to the body of the patient, that relay feedback shown on a computer screen. During a common neurofeedback training session, a physiotherapist will interact with a patient using different feedback examples. This is usually accompanied by experiments containing virtual reality. One such study revealed that haptic control is a useful therapeutic option in rehabilitation featuring virtual reality interaction (Afzal *et al.*, 2015). As with visual and vibrotactile biofeedback, kinesthetic haptic feedback was used to assist in postural control, and to achieve balance control. The results showed that kinesthetic haptic feedback can be delivered via a commercially available haptic device and can enhance the balance stability of both young healthy subjects and stroke patients.

Sometimes the underlying sessions use the patient's auditory system to condition the various stages of concentration and relaxation processes in the brain. The purpose of the training is to adjust brain waves within a specific range. Different parts of our brains reflect different frequencies, depending on the mental activity and what we're doing. Brain waves occur in four main states. Each of the major brain states has an electrical frequency range that is associated with it, and is given in Hertz (Hz). It is divided into the following bands delineating slow, moderate and fast waves:

Beta (β): Normal waking state of consciousness, cognitive tasks, alertness, decision-making, and focused mental activity (14-30 Hz)

Alpha (α): Resting state, daydreaming, wakefulness with eyes closed (8-13.9 Hz)

Theta (θ): Meditation, creativity, insight, learning and memory (4-7.9 Hz)

Delta (δ): Meditation, dreamless sleep, external awareness, source of empathy, healing and regeneration (0.1-3.9 Hz)

As an example, as we fall asleep, we move from the beta state, through alpha, and theta to delta. When we wake up, the process is reversed. The sleep brain waves have the additional function of self-regulation that enables us to produce appropriate brainwaves for given situations. Ideally, a patient would like to experience a large amount of slow alpha and theta waves in an act of daily living (ADL). This is usually associated with relaxation and the production of *serotonin* (a monoamine neurotransmitter), endorphins and many Sensorimotor Rhythm (SMR)- and beta-1-waves, which promote concentration. On the other hand, if an association of excessive adrenaline is required, very few fast high beta waves need to be experienced.

Eventually, the optimum brainwave adjustment improves the level of awakening and affects various functional elements of the patient. For example, the

beta wave improves concentration and reaction time when activated with a brain wave in the corresponding frequency interval. Through beta wave activation, NFB training aims to improve cerebral function by enabling patients to activate this brain wave by reinforcing or suppressing certain frequencies based on visual and auditory feedback (Cortoos *et al.*, 2006), (Sokhadze *et al.*, 2008). Previous research has shown that NFB is effective in improving cognitive functions, including visual perception, memory, and concentration in patients with brain injuries, such as traumatic brain injury or stroke (Egner *et al.*, 2004), (Scott *et al.*, 2005). However, research on cognitive rehabilitation through NFB on existing stroke patients has been limited to single case studies, and sufficient studies on its effectiveness and clinical usability have not yet been conducted.

2.4.3 Rehabilitation Methods and Devices

After having obtained a solid information base about the different methods of rehabilitation, the design and applications of current medical devices used for the rehabilitation of post-stroke patients, were researched. These designs aim to rehabilitate and monitor stroke patients, with the goal to reduce the recovery period of their cognitive and sensory-motor functions through the repetitive rehabilitation of motor activities and decision-making events.

2.4.3.1 Prismatic Adaptation

As mentioned previously, a general symptom that affects a stroke patient is hemispatial neglect. Prismatic adaptation (or Prism adaptation) is one of the techniques used to treat patients with hemispatial neglect. It has always been used as a tool to investigate perceptual- and motor-control and adaptation for over a century (Held and Hein, 1958), (von Helmholtz and Southall, 2005). Prismatic adaptation is used as a rehabilitation technique when a patient has visuospatial deficits. These deficits cause a patient's frame of visual attention to be much smaller and thus the sensory and motor systems need adaptation.

During prism adaptation, an individual wears the special prismatic goggles (Figure 2.11) that are made of prism wedges. These wedges displace the visual field perceived by the patient in a lateral or vertical direction. The task for the patient is then to identify visual targets by pointing at them, i.e. to engage in a perceptual-motor task. This rehabilitation technique exists as a means to alleviate cognitive deficits of patients with brain damage, and can also lead to cerebral plasticity, as explained by Crottaz-Herbette *et al.* In their study, they investigated in humans how far other types of functions known to involve the parietal cortex are influenced by a brief exposure to prismatic adaptation (Crottaz-Herbette *et al.*, 2014).

Although the aims of this project do not focus on patients with visuospatial deficits, this rehabilitation technique provides insight on the influence of repetitive practice that results in changes in the human motor cortex.
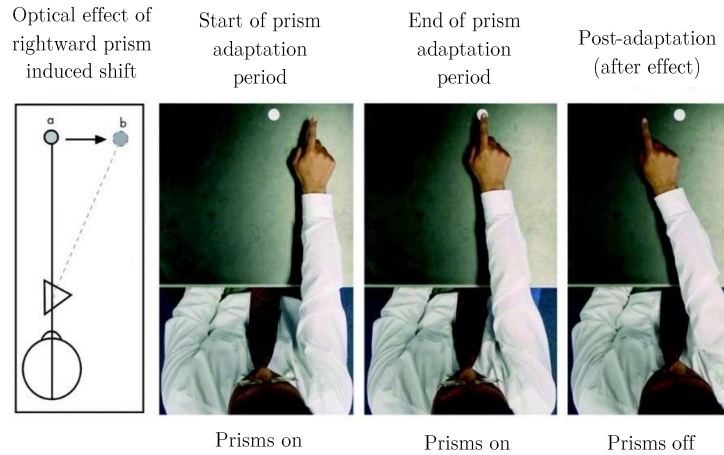
Figure 2.11: The effect of Prismatic Adaptation (Parton *et al.*, 2004)

2.4.3.2   Electrical and Magnetic Stimulation

Two stimulation types used in current applications are electrical pulse stimulation and magnetic stimulation. Galvanic Vestibular Stimulation is one example of an electrical stimulation and is another type of rehabilitation method that is used to treat stroke victims. This stimulation focuses on maintaining the patient's balance through electrical stimulation in the vestibular area of the ear.

Transcranial Magnetic Stimulation (TMS) is also a common stroke rehabilitation technique. The use of a magnetic field generator that is placed above a patient's head, causes small electric currents in the region of the brain beneath the coil. The electric currents then stimulate small regions in the brain. However, this method is more effective when used diagnostically, which means the connection between the brain and the muscles can be measured after a patient has had a stroke, in order to evaluate damage from the stroke.

Another electrical stimulation method is a form of neurostimulation called Transcranial Direct-Current Stimulation (tDCS) and works in much the same way as TMS. Instead of a magnetic coil, electrodes are placed on the scalp of the patient, and emit a constant, low current to the brain. According to an online article by Tom Feilden, tests have shown that the use of tDCS can increase cognitive performance on a variety of tasks, depending on the area of the brain being stimulated (Feilden, 2012). *Bioness*® *Inc.* (Santa Clarita, California) is an open-source company devoted to developing and manufacturing medical devices that can be worn by stroke patients. One of their medical devices is the *H200* Wireless Hand Rehabilitation System shown in Figure 2.12. This USD 6,800.00 system's advanced technology delivers low-level electrical stimulation to activate the nerves that control the muscles in the hand and forearm, thereby helping the patient to regain freedom and independence (Hausdorf and Ring, 2006).

The system applies electrical stimulation in a precise sequence, which then

Figure 2.12: The *H200* Wireless Hand Rehabilitation System (Hausdorf and Ring, 2006)

activates the muscles. This helps the muscles relearn to respond to signals for movement.

2.4.3.3   Constraint-Induced Therapy

Constraint-induced movement therapy (CIMT) is a form of rehabilitation therapy that improves upper extremity function in stroke and other central nervous system damaged victims by increasing the use of their affected upper limb (American Heart Association, 2015). For example, if patients who have suffered from an MCA stroke has difficulty moving their right arm, then their left arm is seen as the 'unaffected limb'. This limb is restrained, and is combined with the intensive use of the opposite limb, or the 'affected limb'. One of the restraint types used for a patient undergoing CIMT uses a bandage or cast on the unaffected limb, which reinforces the use of the affected limb during training exercises. Even though the effects of constraint-induced movement therapy have been found to improve movements of everyday functional tasks, there are still limitations to its applications, due to the high cost of resources needed to conduct CIMT treatment protocol (Viana and Teasell, 2012).

2.4.3.4   Mechanical Support

Some physiotherapists use shoulder taping as a method to treat shoulder pains in patients with acute stroke. An example of this method is a definitive rehabilitative taping technique called the Kinesio® Taping method (Kinesio USA Corporation Ltd, Albuquerque, U.S.A.) shown in Figure 2.13. It is designed to facilitate the body's natural healing process while providing support and stability to muscles and joints. Furthermore, it surpasses the general restrictions involved with taping techniques, owing to the fact that it does not limit the body's range of motion in any direction. It also provides extended soft tissue manipulation to prolong the benefits of manual therapy administered within the clinical setting.

By targeting different receptors within the somatosensory system, *Kinesio Tex Tape* alleviates pain and facilitates lymphatic drainage by microscopically lifting the skin. This lifting effect forms convolutions in the skin, thus increas-

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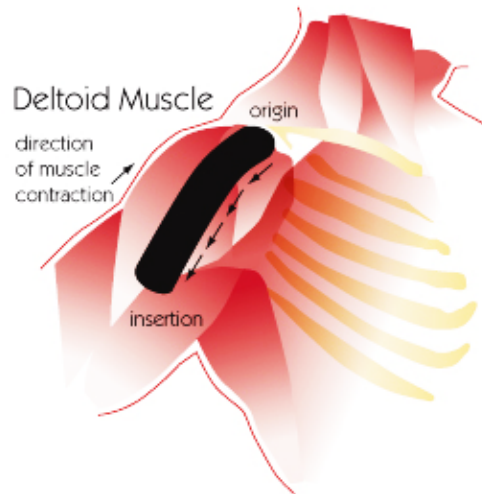
Figure 2.13: The *Kinesio* Taping Method (Kase, 2015)

ing interstitial space and allowing for a decrease in inflammation of the affected areas.

Saebo® (Charlotte, U.S.A.) is another company doing much the same work as *Bioness Inc. Saebo*'s pioneering treatment principles are based on the latest advances in neurorehabilitation research documenting the brain's ability to achieve neural changes through mass practice and task oriented arm training (Saebo, 2014). The only difference is that, instead of using electrical stimulations, the *Saebo* products are all mechanically operated. One of their products specially designed for post-traumatic brain injury patients, is the *SaeboFlex*© device shown in Figure 2.14. Individuals that have suffered from neurological impairments use the *SaeboFlex* hand rehabilitation device by wearing it like a glove. The cost of the device is about USD 1,690.00.
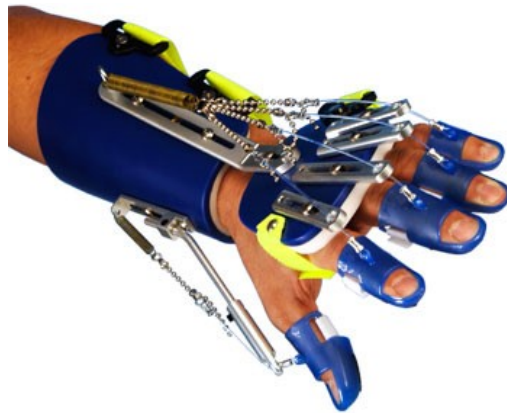
Figure 2.14: The *SaeboFlex* Hand Rehabilitation Device (Saebo, 2014)

During an interview with a post traumatic brain injury patient that has had experience with *Saebo*, Gerhardus Verster, he confirmed that one of the side effects that affect him the most during his rehabilitation, is spasticity (Verster, 2015). He explained that he has continuous difficulty extending his arm due to the fact that the spasticity that he experiences, affects the ventral side of his arms. This side allows the patient to extend and contract the arm using the muscles on the inner side. The *SaeboFlex* device, therefore, forces the arm to extend, which in turn prevents the patient to close his/her arm and fingers due to the mechanical spring tension. This allows the wrist and fingers to be mechanically extended in preparation for any functional activities the user wishes to perform and also causes the re-opening of the hand to release an object that has been picked up.

2.4.4   Neuroplasticity

The latest neurorehabilitation studies show that the concept of neuroplasticity can be applied effectively to the rehabilitation regimen of brain-injured patients, leading to improved outcomes and enhanced functional abilities (Dobkin and Dorsch, 2013), (Dimyan and Cohen, 2011), (Belda-Lois *et al.*, 2011). Neuroplasticity is the process in which the brain's neural synapses and pathways are altered as an effect of changes in the patient environment, behavior, and neural conditioning.

2.4.4.1   Overview

The concept of neuroplasticity is better to understand by comparing it to an electrical system, for example, your home electrical system, where an electrical wire flows from the electrical panel (the source) to the television (the load). If that wire is damaged, which evidently means if it has an infinite internal resistance, the television won't work, as the current that is supposed to flow through the wire's interior is interrupted. Since the current won't flow, this means that the electrons that are supposed to be carried through the current from the source to the load are 'blocked'. Now, if another wire is found to be connected to the same load in parallel with the first wire, and it has less or no damage at all, chances are that the current would eventually find a way to flow through the second wire. This means that other electrons that are not used by other loads in the household, would find a way through the second wire and eventually power the television as effectively as the first wire.

This is the same routine described by the concept of neuroplasticity. Similarly, in order for new knowledge to be retained in memory, or for specific changes in movement or coordination to be recorded, changes in the brain representing the new knowledge must occur. This means that in the event of brain injury, the remaining functions of a person's limbs (the load) will be maximized through compensation by the stronger synaptic connections in the brain (the source). The weaker synaptic contacts are therefore eliminated

through synaptic pruning, and the connections that are then used regularly are strengthened. This new use for neurons is also important for their preservation. The reason for this is due to a process called apoptosis. Apoptosis is a process of programmed cell death that occurs in multicellular organisms (Green, 2011). An example is evident during the development of a human embryo where the cells between the digits of the human hands and feet undergo apoptosis in order for the separation of the fingers and toes to take place. The neurons of the cells become damaged and die. This means that the neurons must have a purpose in order to survive. Neurons that have a purpose have more experience, and more experience leads to stronger connections. The weak connections are seen as ineffective connections and are therefore 'pruned'.

2.4.4.2 Clinical Use

According to Dr. Caroline Leaf, a cognitive neuroscientist with a Ph.D. in Communication Pathology specializing in Neuropsychology, the hypothesis that repetitive steps and exercises established as a supply of input to your sensorimotor system can result in physical changes in the structure of your brain, is indeed possible. She has conducted several experiments involving the treatment of patients with brain injuries and strokes. In her book, *Switch on your Brain*, she has also mentioned the notion of brain malleability and that a brain and its brain cells can grow constantly by deep intellectual thinking (Leaf, 2013).

Neuroplasticity is equivalent to sensory substitution, which means to transform the characteristics of one sensory modality into stimuli of another sensory modality (Renier and De Volder, 2005). This notion was supported by Paul Bach-y-Rita, an American neuroscientist whose most notable work was in the field of neuroplasticity in 1969. Bach-y-Rita demonstrated first successful signs of this concept when he tested the 'sight' of blind patients by letting them sit on a chair containing a bank of 400 vibrating plates. These plates were set to vibrate in connection with an image on a camera that was placed behind the chair. Reportedly, the pattern in which the simulation occurred caused the blind patients to 'see' the image in their mind's eye. Bach-y-Rita suggested this was an example of neuroplasticity, as he believed the signals sent to the brain from the skin via touch were being processed in the visual cortex, because of the way the patients interpreted the information (Bach-y Rita, 1967).

2.4.4.3 Sensory stimulation therapy

When considering the methods used by physiotherapy, neurorehabilitation and cognitive rehabilitation, a perfect combination of the above, results in another experimental therapy, called sensory stimulation therapy (SST). The aim of this type of therapy is to utilize neural plasticity mechanisms to aid in the recovery of somatosensory function after stroke or cognitive ageing. According to Gopnik *et al.* (1999), by the time an infant is two or three years old, the

number of synapses in the brain is approximately 15,000 synapses per neuron. This amount is about twice that of the average adult brain, which is a result of cognitive ageing. As we age, old connections are deleted through a process called synaptic pruning. Studies have also shown that neurons in a particular system in the brain will not function properly if the input to that particular neural system is eliminated (Biad, 2014). It has been suggested that age-related cognitive decline is due in part not to neuronal death but to synaptic alterations (Hof and Morrison, 2004). Thus, the goal of SST is to reduce these factors via rapid stimulation of nerves in a section of skin to drive neuronal changes in the participant. SST takes advantage of the effect of neuroplasticity and the senses are presented with simple stimulation to cause changes inside the brain.

2.5 Previous studies

Before any medical device can be clinically tested and deemed as a respected medical grade device, certain studies, experiments and validity tests need to be performed. This also requires the approval of FDA's policy of accepting scientifically valid clinical data from clinical studies in support of premarket submissions for devices (U.S. Department Health and Human Services, 2015). Hence, clinical studies are conducted in order to produce certain statistics and solutions for medical-related studies. This section summarizes some methods and techniques used during the administering of such studies.

2.5.1 Electroencephalography

2.5.1.1 EEG Background

During stroke-related clinical studies, some of the techniques used to relay electrobiological feedback to the doctor are done by measuring the electrical activity of the brain of a patient. The technique for evaluating and recording this electrical activity is called Electroencephalography, or EEG. This technique may be used as a means of monitoring the progress for stroke patient recovery, and is also used during experiments involving stroke rehabilitation on different areas of the brain.

During an EEG experimental procedure, electrodes are put into contact with the patient's scalp. These electrodes detect tiny complex signals resulting from postsynaptic potentials of cortical pyramidal cells in the brain. These charges are amplified and appear as a graph on a computer screen or as a recording that may be printed out on paper (Figure 2.15). According to Hopkins (2015), an EEG can be used to detect abnormalities in brain waves, or in the electrical activity of the brain. This makes EEG recording one of the most efficient ways to obtain information about some patients with brain diseases, including stroke.
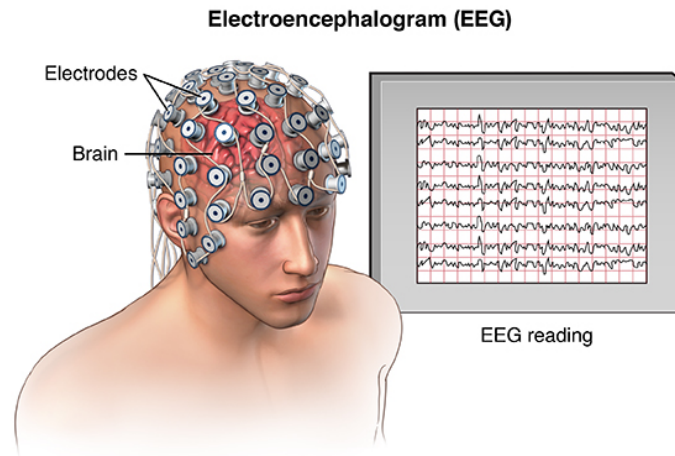
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Figure 2.15: Reading EEG activity (Hopkins, 2015)

EEG can also be used to illustrate multisensory integration, also known as multimodal integration, which is the process by which inputs from the different sensory modalities (sight, sound, touch, smell, self-motion, and taste) are bound together by the nervous system. Such a study is called a Multimodal EEG study. Multisensory integration also deals with how different sensory modalities interact with one another and alter each other's processing (Landini *et al.*, 2005). Movement or reaction is established by sensation, perception, and cognition. During integration, a visual or auditory sensation is transferred as a perception, which is then recognized by the brain in a specific brain map (cognition). This is then followed by the desired reaction or movement strategy. One of the methods to distinguish between the different sensory modalities or stimuli is to study the occurrence of event-related potentials.

2.5.1.2   Emotiv©

Emotiv Systems is an Australian electronics innovation company that develops technologies to evolve Human Computer Interaction (HCI). According to *Emotiv* co-founder, Tan Le, the majority of our functional brain is distributed over the outer surface layer of the brain. In order to increase the area that is available for mental capacity, a highly folded cortical system exists on the brain's surface. As a result, in order to interpret surface electrical impulses on the surface area of the scalp, localization of specific locations is important to achieve, since this cortical folding presents a significant challenge for interpretation. Each individual's surface is folded differently, so even though a signal may come from the same functional part of the brain, by the time the structure has been folded, its physical location is very different between individuals (Breen and Le, 2007). The best way to approach this scenario in order to read EEG signals with ease, as well as analyze EEG data, is to research a product that can map EEG signals efficiently.

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The EEG headset that was sourced for the present study, the *Emotiv Insight*, was developed in 2015 and has not been used for clinical purposes or previous research yet, though its predecessor, the *Emotiv EPOC*, has proven to be adequate in its use for tracking brain activity (Taylor and Schmidt, 2012). The *Insight* shown in Figure 2.16 is a sleek, 5-channel, wireless headset that allows the optimization of brain fitness and performance, and measures and monitors cognitive health and well-being. The five channels record activity from five brain surface locations based on the 10-20 system shown in Figure 2.17 (an internationally recognized method to describe and apply the location of scalp electrodes): AF_3, AF_4, T_7, T_8 and P_z. The letters F, T and P stand for frontal, temporal, and parietal lobes, respectively. Even numbers (4 and 8) refer to electrode positions on the right hemisphere, whereas odd numbers (3 and 7) refer to those on the left hemisphere. A z (zero) refers to an electrode placed on the midline of the scalp.

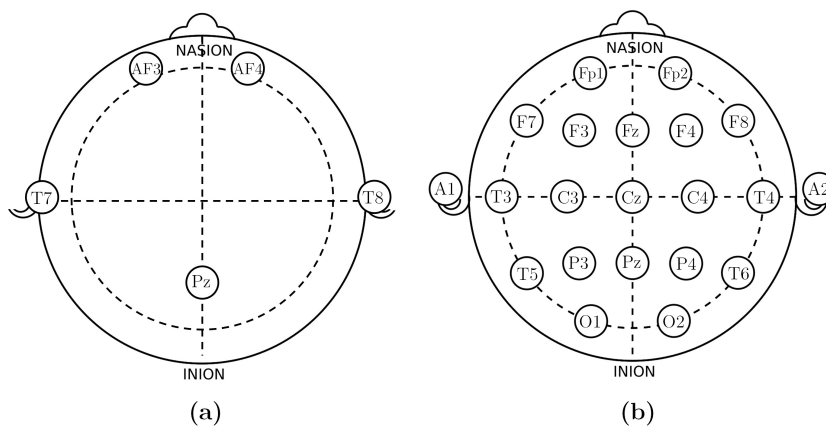**Figure 2.16:** The *Emotiv Insight* EEG headset (Emotiv.com, 2016)

Figure 2.17: (a) The five channel locations of the *Emotiv Insight* created in *EEGLAB*, compared to (b) the 10-20 system locations (Husain *et al.*, 1999)

2.5.2 Event-Related Potentials

2.5.2.1 Background

As far as 1929, a German psychiatrist, Hans Berger, has demonstrated the possibility of recording the electrical activity of the brain by placing electrodes on the scalp surface of the patient (Fabiani *et al.*, 2000). More recent research has shifted its focus towards time-locked electrical potentials to sensory, motor, or cognitive events called event-related brain potentials, or ERPs.

In order to detect the required motor activity and decision-making events from patients, EEG data can be used to pinpoint ERPs. According to Ekanayake (2010), ERPs reflect brain activity from a pooled synchronous activity of a large population of neurons that occurs in preparation for or in response to discrete events. This activity causes local current flows which can then be measured by EEG electrodes and characterized as action potentials (voltage measurements) that occur in different areas of the scalp of the subject. ERP-events can be external or internal to a subject. The external sensory categorization for ERPs is called exogenous, where the potential starts within the first 100 milliseconds of the stimulus. These potentials' characteristics are largely dependent on the physical properties of the external stimulus. In contrast, the internal cognitive categorization called endogenous ERPs link not to the physical attributes of a stimulus, but to a subject's evaluation and reaction to it (Jones, 1988).

2.5.2.2 Medical Relevance

ERP-related research has impacted our understanding of normal cognitive processes (including language) and thus has great potential for investigating their disruption by different brain diseases. A recent neuropsychology study conducted by Kutas *et al.* (2012) has shown that under the appropriate experimental conditions, different aspects of the ERP waveform can be analyzed to determine whether and when certain neural/mental operations take place, both with typical (healthy) and compromised brains. The precision of ERPs as a real-time index of cortical neural activity makes them an apt tool for identifying when, and how, the information processing stream is in various neuropsychological disorders (Kutas *et al.*, 2012). Furthermore, ERPs from neuropsychological patients can serve a localizing function (Handy, 2005). Since ERPs can be elicited even without any overt response requirement, they are particularly suitable for work with communicatively impaired individuals, for example, those with aphasia, motor deficits, or stroke (Pinhas *et al.*, 2014).

2.5.2.3 Paradigms

During typical ERP experiments, ERP patterns are linked to perceptual, cognitive, and affective processes in subjects through the use of paradigms (different patterns or examples). Perhaps the most well-known ERP paradigm is

the "oddball" paradigm, whereby presentations of sequences of repetitive audio or visual stimuli are interrupted by a deviant stimulus (Wronka *et al.*, 2008). ERP measurements, called events, consist of different characteristic voltage displacements, either in the positive (P) or negative (N) voltage. Displacements having fixed latencies are then categorized according to their deflection direction and latency, for example, the P_{100}- and N_{200}-events are so named because they are positive and negative electrical potentials that peak at 100 ms and 200 ms respectively after a stimulus onset (Sur *et al.*, 2009), (Key *et al.*, 2005). Most researchers focus on the robust positive potentials variously called P_3 or P_{300} and P_2 or P_{200}. They are large and reliable potentials elicited by various processing and sensory categorization progresses. Although there is no consensus on exactly which cognitive operation (e.g., working memory updating, event categorization) these events index, much is known about their behavior in the oddball paradigm. By the studies of Duncan-Johnson and Donchin (1982) and Kok (2001), it has been proven particularly useful for investigating the timing of stimulus-evaluation processes (vs. response-related processes), event categorization, and attentional allocation in dual-task situations, amongst others.

Evidence from the works of Evans and Federmeier (2007) indicates that the P_{200}-event may reflect general neural processes that occur when a visual or another sensory input is compared with an internal representation or expectation in memory, and that manipulations of sensory stimuli can be used to modulate the characteristics of the P_{200}-event. The P_{300}-event is considered to be associated with the evaluation and classification of different stimuli and reflects the anticipation or absence of an anticipated stimulus event (Polich, 2007). From the studies of Duncan Duncan-Johnson (1977), Duncan-Johnson and Donchin (1982) and Squires Squires *et al.* (1976), discriminating the target from the standard stimulus produces a robust P_{300} that increases in amplitude as the target's global and local sequence probability decrease. This component appears at the moment when the stimulus is expected and is a typical endogenous component. This is supported by Chen *et al.* (2014), who has shown that the P_{300} component can be elicited using an active or passive oddball paradigm. Active P_{300} requires a person's intentional response, whereas passive P_{300} does not require an intentional response, which means the P_{300} component can be characterized as either an exogenous or endogenous ERP.

2.5.2.4 Component Characteristics

According to an Omitted Stimulus-Response (OSR) study conducted by Busse and Woldorff (2003), responses linked to visual and haptic sensory categorizations consist of an early posterior negative wave (180-280 ms) followed by larger anterior positive waves (>200 ms).

The P_{200}-component has a latency (delay between stimulus and response) varying between 150 and 275 ms after the onset of some external stimulus and is evoked as part of the normal response to visual or external stimuli

(Evans and Federmeier, 2007). The amplitude and latency may be affected by exogenous factors, such as repeated stimuli.

With regards to its amplitude and latency, P_{300} occurs as a positive deflection in the voltage (usually 2-5 μV) with a latency range of 250-400 milliseconds after the onset of a stimulus, although the range in amplitude can vary depending on subject characteristics, stimulus modality and task conditions Fabiani *et al.* (2000), Makeig *et al.* (2004), Sur *et al.* (2009). P_{200}-waveforms are usually located around the centro-frontal and the parieto-occipital regions and P_{300} is typically measured by placing electrodes covering the regions of F_z, C_z, and P_z in the standard 10-20 system (Leeman, 2008), (Teplan, 2002).

2.5.3   Power Spectral Techniques

According to Roomali *et al.* (2014), power spectral density techniques can be used to distinguish between stroke subjects and healthy test subjects. The power spectrum of a time series describes the distribution of power into frequency components composing that signal and can be used to compare the activity in the two hemispheres of stroke patients. Multiple cortical areas of the human brain motor system interact coherently in the low-frequency range (<0.1 Hz), even in the absence of explicit tasks (Bajaj *et al.*, 2015). Following stroke, cortical interactions are functionally disturbed.

Since it is argued that a stroke patient has less functional capabilities than someone without a stroke background, their power spectra would then reveal a different frequency distribution. Furthermore, it is speculated that the power spectra would also show an improvement in spectral density after about three months of rehabilitation (Giaquinto *et al.*, 1994). For example, stroke patients who have had a left stroke would show an asymmetric power distribution with regards to the right hemisphere. By using this approach, patients with left middle cerebral artery (L-MCA) lesions were hypothesized to show significantly lower power spectrum analysis values compared with all other localizations on the right side, and vice versa. Power spectra have also been used as a method of comparison between control- and experimental groups in the acute (≤ 10 days post-stroke), subchronic (11-35 days post-stroke) and chronic (>60 days post-stroke) phases of the stroke (Leamy *et al.*, 2014).

As a measure for the amount of ischemic damage, the Brain Symmetry Index (BSI) of stroke patients can be calculated. This index was recently introduced for monitoring possible brain ischemia in carotid surgery (van Putten *et al.*, 2004). This measure is defined as the mean of the absolute value of the difference in mean hemispheric power in the frequency range from 1 to 25 Hz. The lower bound for the BSI is zero (perfect symmetry for all channels), whereas for the upper bound BSI equals 1, which, according to van Putten *et al.* (2004), implies maximal asymmetry. From a quantitative continuous electroencephalography study by the same author, it was also proven that EEG data can be quantified using a measure for symmetry in patients with acute ischemic hemispheric stroke.

2.5.4   Stroke Recovery Evaluation

Stroke severities are usually diagnosed by means of a head CT-scan or brain MRI. This is done as soon as possible after the onset of the stroke, as knowledge of its location and distribution increases the diagnostic yield and results in a better understanding of the lesion pattern. A Computed Tomography Angiogram (mentioned in Chapter 2.3.2) is usually done during this stage, as it can clearly show a blocked artery that is responsible for the infarct. To evaluate the recovery and physical changes in the brain area damaged by a stroke, follow-up scans are conducted. These scans are then compared to previous scans to indicate any recovery in the specific region.

Another method to determine the degree of functional lesions of the brain is via computer EEG measurements. EEG data of stroke patients can be recorded during rehabilitation to compare to existing studies, control groups or previous EEG data. According to a study conducted by Kozelkin and Kuznetsov (2004), local changes of EEG-pattern prevail in patients with acute ischemic cerebral hemisphere stroke. They have also shown that background EEG is the most representative technique to reflect the bioelectric activity of the brain. These techniques enable the assessment of the plasticity and reactivity processes of the brain. It can also be used during Brain-Computer Interface (BCI) tests to evaluate and compare the efficacy and accuracy of training with both stroke-affected and healthy participants.

2.6   Conclusion

The conducted literature study provided a thorough understanding of the specific environment of this project, which includes insight about sensory feedback, MCA strokes, how it affects a patient's physical and mental state, and how it can be prevented or treated. However, certain limitations were identified in the methods and solutions provided for stroke rehabilitation. Table 2.1 shows the limitations identified within the literature. These gaps are not necessarily novel, though they still assist with the specifications of the design and functioning of the prototype during concept generation.

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Table 2.1: The identified research gaps

Section Heading	Research Gaps
Physiotherapy	• Personal care from therapists incur additional expenses • Medical aid institutes do not cover certain costs relating to outpatient rehabilitation • The time the physiotherapists have available for each patient, is compromised by the above • The frequency of physiotherapy and other therapy methods is low • Finally, there exists a lack of accessibility to the centres
Neurorehabilitaion	• In spite of its importance, it unfortunately has certain inclusion criteria for patients, with regards to their cognitive processing and understanding • As mentioned in Chapter 2.3.3, some conditions cause stroke victims to seem unaware of the existence of their disability. This can result in the person not being able to entirely benefit from cognitive neurorehabilitation • In studies involving clinical trials, some patients have the inability to perform or give informed consent due to severe language or cognitive impairment
Current Applications	• High-cost resources are needed to conduct certain treatment protocol • Some methods, like Taping and *SaeboFlex*, only influence the muscle groups and strengthening thereof, and do not focus on the actual nervous system responsible for muscle movement • A limitation of electrical stimulation devices is that they cause involuntary contractions of the patient's muscles during treatment. The neural pathways to the brain are not completely reinforced, as the brain, especially the motor cortex, has little control over these contractions (Springer, 2004) • Where low-level electrical stimulation is indeed used, such devices costs up to USD 6,800.00 (roughly ZAR 93,874.00)

2.6.1   Research Approach

These limitations result in the pursuit of additional rehabilitation methods, that are either less expensive, or do not require much attention from a therapist. It is aimed to provide a solution to the lack of services of therapists, as well as the patients' inability to access the stroke rehabilitation centers. The development of a device that can be used before and/or during rehabilitation programs, and has an ease of use that allows it to be used at home without the constant guidance or presence of a therapist will be one such solution.

From the sensory feedback- and EEG literature (Chapters 2.2.1 and 2.5.1), it is now known that the prototype planned to be constructed should emit some kind of feedback during rehabilitation, and that this feedback can be monitored via EEG sensing. The feedback should be a stimulus that can be picked up by the receptors of the wearer, and recognized by the brain. Furthermore, from Chapter 2.3.3 (Motor neglect), it was learned that certain stimuli should be targeted that do not require a patient to make his/her own decisions during rehabilitation, but rather to follow visual, haptic or auditory feedback command. From the ERP literature (Chapter 2.5.2), it is also known that feedback should require different types of responses from the subject, and that feedback should occur at a frequent rate as characteristic to a paradigm of an ERP experiment.

This frequency of stimuli is supported by the neuroplasticity and sensory stimulation therapy sections (Chapter 2.4.4), which provide insight on the influence of repetitive practice that results in changes in the human motor cortex. It is also clear that by applying technologies such as EEG sensing, in combination with the repetitive steps and exercises of alternative rehabilitation programs, stroke patients may eventually learn to use undamaged neurons to enhance the neural repair process and reinforce the necessary neural pathways and synapses in a much faster way, than when no intervention has taken place.

The question remains whether it is indeed possible to pick up different electrobiological potentials in the brain during discrete events, relayed by one or different types of sensory feedback of a constructed device.

Chapter 3

Concept Design

With the information gleaned as described in Chapter 2 (especially the research solution), the design parameters for the concept of the prototype had to be set up. This set of parameters served as a guide through the design process and any generated concept had to adhere to it, as it was set up by taking the principle investigator's requirements into account. The project supervisors were also consulted on a weekly basis to ensure the adherence to engineering requirements, as well as for any general advice.

3.1   Required Facilities

This research project was done as part of the Biomedical Engineering Research Group (BERG), Faculty of Engineering, Stellenbosch University. The manufacture of the conceptual design and the observational study was done in the BERG laboratory. Apart from the laboratory space, the following tools were available to BERG and were used for the manufacturing and analysis of the concept:

3-D Printer: The different concepts (discussed in Appendix B) were deemed too expensive to construct, and therefore a *Makerbot Replicator II 3-D printer* (MakerBot® Industries, Brooklyn, U.S.A.) was used on a regular basis to print different samples. Concepts that were printed were tested thoroughly and evaluated according to the engineering requirements (Table 3.1).

Soldering Equipment: The feedback device and integration circuit consist largely of electronic circuits. Electronic components obtained from Mantech®, Netram® Technologies and Microrobotics® were soldered and tested using soldering equipment from the BERG laboratory.

Computer: In order to design, evaluate and program the final concept, the BERG office computer was used. The principle investigator's laptop was used during the training sessions at the medical clinics and Faculty of Engineering.

Mathematical Software: *MATLAB*® (MathWorks, Massachusetts, U.S.A.) was used in order to stream and process the raw electrobiological data. Power spectra were also generated using built-in functions, and *EEGLAB*.

EEGLAB©**:** This interactive *MATLAB* toolbox for processing continuous and event-related EEG data by incorporating independent component analysis (ICA), time/frequency analysis, artifact rejection, and event-related statistics, was used to generate 2-D and 3-D topographic arrangements of EEG data.

Data Acquisition Software: The *Emotiv* (Emotiv, San Francisco, U.S.A.) software pertaining to the EEG headset was used in order to generate algorithms used for the feedback training. Extensions of this software, the *Emotiv Xavier* Testbench and *Emokey* (Emotiv Systems, Sydney, Australia), were also used to capture real-time raw EEG data and send serial data.

Arduino®**:** This software was the main source for programming the *ATmega32U4* (Atmel, California, US) microcontroller used to drive the vibration motors and Light Emitting Diodes (LEDs), which is part of the planned haptic- and visual feedback system of the rehabilitation device.

3.2 Concept Theory

This concept theory is necessary to understand before different concepts could be generated as part of the selection phase. Though the aim to obtain electrobiological measurements of healthy subjects rests, the concept should still adhere to the characteristics of a stroke rehabilitation device. Hence, the concept was created with the side effects and treatment of an MCA stroke in mind. In a general case, stroke patients that have had a left MCA stroke have a weakness on their right side, and vice versa. During an interview with Deborah Calitz, a registered physiotherapist in Cape Town, it was confirmed that a sensory feedback nature of a rehabilitation device should act as a stimulus in order to commence the working of the somatic reflex system of the wearer (Calitz, 2015). For example, if a patient that wears the device has had a left MCA stroke, a particular side effect is that the patient has difficulty moving his/her right arm due to the neuropsychological condition known as hemispatial neglect (explained in Chapter 2.3.3). This condition causes the patient's brain to be unable to process and perceive the 'existence' of the right arm, therefore being unable to move the arm consciously.

A possible way the patient could then move his/her arm, is when some kind of external sensory input is received in order to simulate the stimulus or touch normally perceived by the brain. The proposed device (which is worn on the same arm) should then simulate this stimulus via sensory feedback, which rests on the theory that the brain will then be constantly 'reminded'

of the arm's existence. In turn, this could allow the patient to move his/her arm accordingly to some degree without assistance, and will also cause sensory feedback during a normal therapy rehabilitation session.

Figure 3.1 shows the theory of how the proposed rehabilitation device is planned to influence the nervous system of the wearer. A sensation, ①, is received when the sensory receptors on the arm are activated. This sensation is relayed through the ulnar- and medial nerves, ②, to the spinal cord, ③. In the brain, ④, the neural signal is organized and interpreted. This sensation is projected back to the apparent source through ②. For movement to be executed, the primary motor cortex, ⑤, generates the signal that controls the movement of the arm through the medial nerve, which activates the arm muscles. The gray line, ⑥ is a representation of a nerve that cannot relay this signals due to damaged neural pathways of the brain after stroke. The green line, ⑦, is proposed to be a functional nerve after strengthening of the neural pathways and synapses in the motor cortex occurs as a result of stroke rehabilitation.
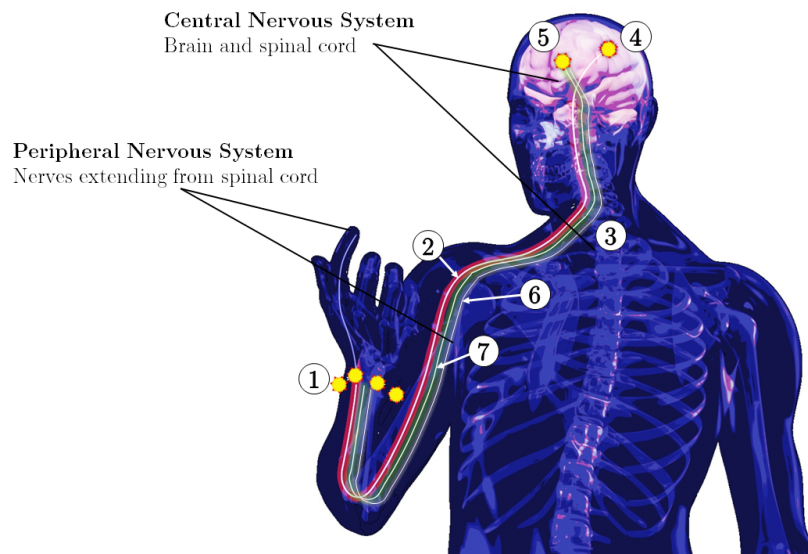
Figure 3.1: The theory behind the concept of the rehabilitation device. Figure adapted by author from (Zimmerman, 2012)

3.3   Concept Generation

An alteration of Pugh's method was used to generate, evaluate and finalize the concepts for the rehabilitation device prototype (Shafer *et al.*, 1976). Pugh's method is a quantitative technique used to rank the multi-dimensional options of an option set. Each specification was accompanied by a relative importance percentage and each concept needed to conform to the mechanical guidelines displayed in Table 3.1.

Table 3.1: Weighted Matrix for Mechanical Guidelines

Engineering Specifications	Importance
The device should be built as a wearable system with actual sensors	10%
The device should be able to deliver some stimulus on the lower arm of the patient	35%
A vibration motor must be included in the design of the concept	30%
An EEG sensor should be included to measure brain activity	30%
The EEG sensor should be able to measure muscle/limb movement (on the lower arm of the patient) and transfer the measurements wireless to a computer	5%
The device should use this transferred data from the EEG device to give sensory feedback to the wearer based on predetermined rules	5%
The controller must be a small *ATmega32U4* controller with only the necessary additions like a small battery with high power and a small Printed Circuit Board (PCB)	2%
Serial communication of the device with the operator should be enabled with the use of a standard USB to serial converter or RS232RF wireless or Bluetooth system	3%

3.4   Concept Selection

This section is concerned with the stage where different rehabilitation device concepts were generated before the final design was chosen. Throughout the development of each concept, an iterative process where each concept was evaluated against the provided engineering specifications using a weighted decision matrix, was followed. The advantages and disadvantages of each concept were identified and the gained information was used to help improve the next concept by excluding evident design and experimentation errors. The concept selection stage underwent five phases, representing five main concepts and concept alterations, and resulted in a final concept (Concept E) that satisfied all of the applicable engineering specifications. The selection processes, with the necessary information of all concepts, are shown in Appendix B - Concept Development. Figure 3.2 illustrates a hardware high-level diagram that includes all the necessary subsystems of the final design.

3. CONCEPT DESIGN

The mechanical design (using *CAD* and *Solidworks Professional® 2014*) of the layout and the integration of the circuits with the sensors, described in the next section were finalized to be ready for ordering and manufacturing.
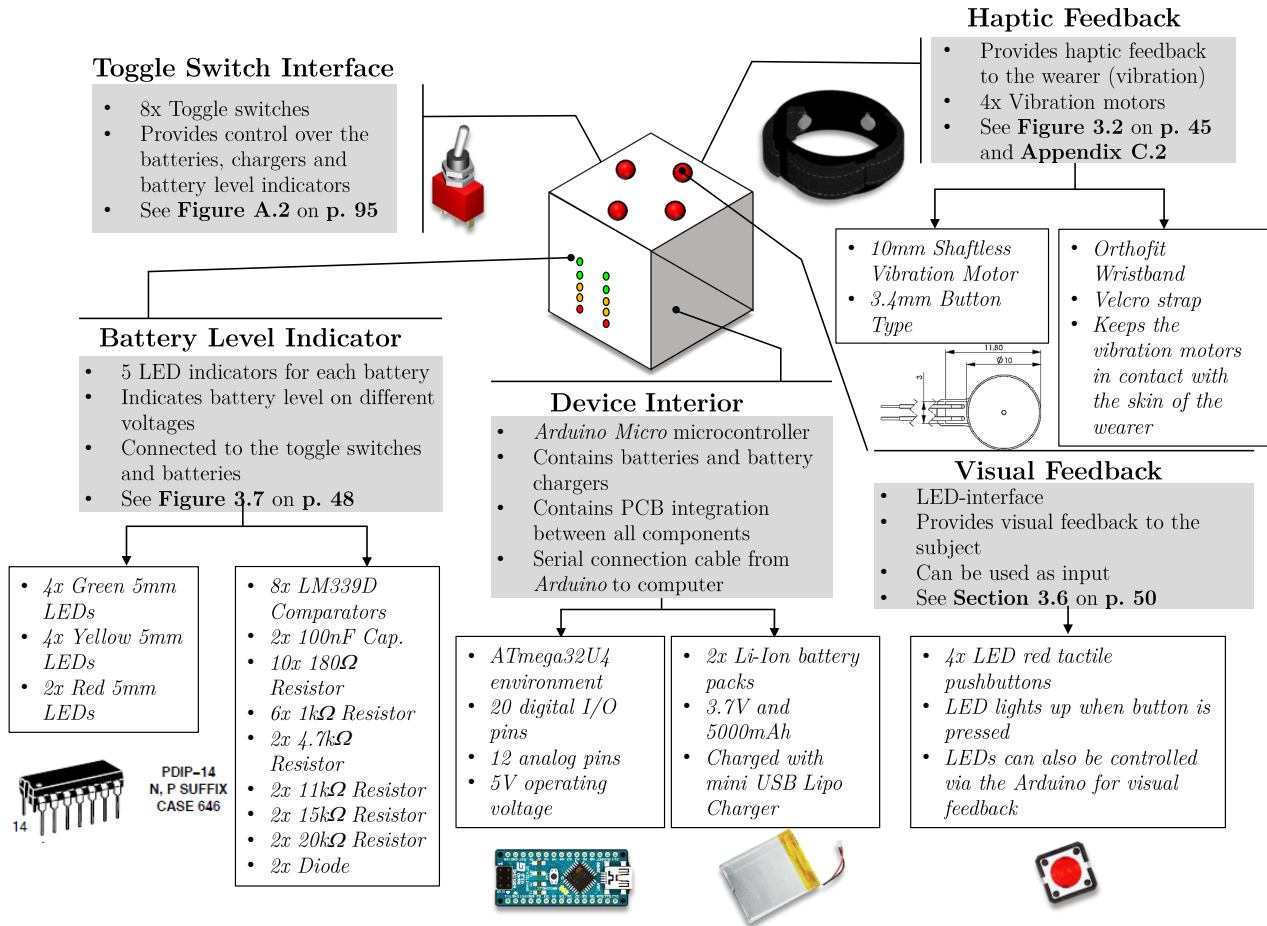

Figure 3.2: Hardware High-Level Diagram showing all the physical sub-systems of the device

3.5   Design and Hardware Selection

The physical design of the system took place first, incorporating components for every separate function contained in the concept. Controllers and sensors had to be chosen, a mechanism for the feedback device had to be finalized, components had to be researched and calculations had to be made to determine the correct components to choose. Calculations for the interface sensors, as well as the specific battery requirements, were necessary.

Several hardware selections were researched to determine the most cost effective components to use. Table 3.2 includes the list of components, with the total cost of each.

Table 3.2: Final Hardware Expenses

Component	Quantity	Distributor	Cost
Arduino Micro Controller	1	Micro Robotics	R 269.00
Orthofit Wrist Band	1	Orthofit	R 41.00
Vibration motors	4	Netram	R 287.80
Polymer Lithium Ion Battery	2	Micro Robotics	R 570.00
Resistors, capacitors, etc.	n.a.	Netram	R 100.00
USB LiPo charger	2	Communica	R 390.00
PCB Board Construction	1	Trax	R 758.66
Breadboard Mini Blue	1	Netram	R 54.95
Breadboard Self Adhesive	1	Netram	R 74.95
LED Tactile Button Red	4	Netram	R 119.80
USB Cable mini	1	Netram	R 29.95
USB Cable micro	1	Netram	R 29.95
Emotiv Insight EEG Headset	1	Emotiv	R 9,637.14
TOTAL	**n.a.**	**n.a.**	**R 12,483.00**

3.5.1   Controller - *Arduino Micro Rev3*

During the design phase of the device, it was essential to keep in mind that the device needed to be low-cost. Therefore it was chosen to look for the smallest possible *ATmega32U4* microcontroller, which will still serve its purpose concerning the number of analog and digital inputs and outputs that were required for the number of sensors. This component served the need introduced in one of the objectives described in Chapter 1.4. The *Arduino Micro* (one of the smallest *Arduino* microcontrollers), was the chosen microcontroller board.

It has 20 digital input/output pins (of which 7 can be used as PWM outputs). This controller was chosen, as it has enough pins to support all the different sensors and motors. It is similar to the *Arduino Nano*, but it has more available pins. Furthermore, the *ATmega32U4* Application Programming Interface (API) has a user-friendly software and was easier to use in the design and programming of the device.

3.5.2   *Orthofit* Wristband

One of the components of the rehabilitation device, the haptic feedback component, required a way to be attached to the limb of the patient. The product acquired for this use was an *Orthofit* Wristband, which was fitted on the patient's lower arm. This band contains the vibration motors, and will be

connected to the controller by means of standard insulated copper wires. A secondary function for this wristband is that it also provides comfortable support to the wrist for sprains, strains, and stress injuries. It can therefore also contribute to the relief of spastic strains in the arm of the patient.

3.5.3   Vibration Motors

As mentioned in the research approach section from Chapter 2.6, it was necessary to incorporate sensors that provide feedback during its operation which stimulates the wearer intermittently via haptic, visual or auditory feedback. The vibration motors shown in Figure 3.3 are ideal for haptic feedback, as it simulates the sensory input of a vibration or 'touch' received from an external source.

Figure 3.3: The motors used as vibratory feedback (MicroRobotics, 2014)

All moving parts of the motor (that cause the vibration) are protected within the motor housing. It has an adhesive backing, making it easy to assemble at the back of the *Orthofit* wristband, and it also has reinforced connection wires, which can be extended in order to place on any part of the limb. Four of these motors were incorporated in the prototype.

3.5.4   Batteries and Charger

It was necessary to power the device once all components had been assembled. The best way to decide which batteries to use was to determine the power that the components would possibly draw and use those calculations to determine the voltage and current requirements of the batteries. The datasheets of the separate components and sensors were used to determine the required voltages and currents for the necessary components. They are summarized in Table 3.3. The necessary datasheets can be viewed in Appendix C.

The process in choosing the correct battery was difficult to complete, as the batteries were either too big or too expensive. Eventually, Peukert's Law

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Table 3.3: Maximum sustainable voltages and currents

Component	Voltage	Current
Arduino Micro	$7 - 12$V	Provides $40 - 50$mA per pin
Vibration Motor	$2.5 - 3.8$V	Rated current: $75 - 80$mA
EMG sensor module	3.5V	n.a.
SD Module	$2.5 - 3.8$V	Rated current: $75 - 80$mA

shown in Equation 3.5.1 was used to simplify the process:

$$C_p = I^k \cdot t \qquad (3.5.1)$$

where C_p is the capacity at a one-ampere discharge rate, I is the actual discharge current, t is the actual time to discharge the battery and k is the Peukert constant.

The reason this criterion had been chosen as the main requirement for the batteries, is because eventually, the device needed to operate a specific time length for different measurements and experiments to be completed without interruption. Because the duration of each experiment was not yet known before construction, it was decided that the device needed to operate at least 10 hours before a recharge was needed. The values from Table 3.3 were used in order to choose a battery. Further aspects that were considered were the price, voltage, capacity, discharge rate, weight and size.

Eventually, it has been decided to obtain Li-Ion battery packs. The 3.7V Li-Ion Battery Pack delivers a capacity of 5000mAh, and there are two of these batteries that are used in the device. One battery is used for powering two of the vibration motors and the second battery is used in parallel with the first one to power the other motors and LEDs. The remaining components are powered through either the 3.3V or the 5V regulator on the controller. To charge these batteries, a Universal Series Bus (USB) Lipo Charger is used.

3.6   Prototype Manufacturing

After completion of the design process, the manufacturing stage began. All parts had to be available in the appropriate sequence for construction. With the aid of the facilities at Stellenbosch University mentioned in Chapter 3.1, all of the necessary parts were manufactured and put together. The manufacturing drawings for the final concept were then also set up. The components used to construct the control circuit are shown in Figure 3.4.
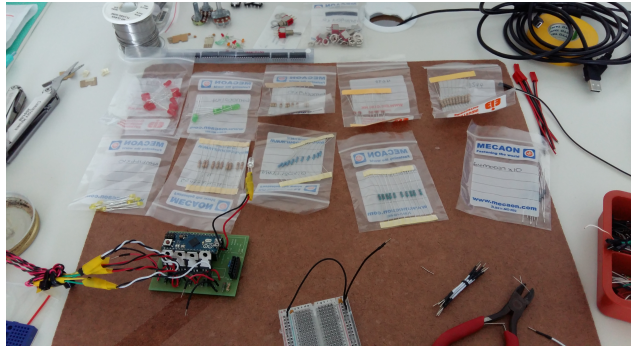
Figure 3.4: The necessary components for the circuitry

3.6.1   Control Circuit

During the manufacturing stage, it was important to have adequate knowledge of all the electronic and electric components. The best way to achieve this was to study their data sheets. It was noted that the vibration motors each has a voltage range of $2.5 - 3.8$V. Although the *Arduino Micro R3* has an input voltage of $7 - 12$V, it can deliver 5V with a maximum current of 20mA per input-output pin.

This voltage would have been satisfactory for the motors, but to reduce the cost of batteries, it has been decided to operate two motors in parallel, which means that the current needed ($\pm$85mA) would be more than the pins could provide. For this reason, a control circuit needed to be specially designed to control the vibration motors via the *Arduino*, while powering them with separate Li-Ion batteries. The circuit consists of NMOS transistors that act as switches. A voltage signal from the *Arduino*-pins is sent to the gate of the transistor, after which the drain and source respectively complete the current from the battery source to the ground. The circuit (Figure 3.5) was first designed and simulated in *Fritzing* - an open-source hardware initiative, after which the final PCB was designed in EAGLE® PCB Design Software, and sent to Trax® Interconnect (Pty) Ltd. for final manufacturing. Figure 3.6 shows the PCB design, with the final printed board.

3.6.2   Battery Level Indicators

It was necessary to know at which point the device needed to be charged. Because of the fact that an average rehabilitation session was planned to have a duration of 15 to 20 minutes without interruption, it was of utmost importance to monitor the battery levels during operation. For this reason, a battery level indicator circuit was built using a variation of LM339D-comparators and LEDs. The circuit schematic and final manufactured indicators are shown in Figure 3.7 and Figure 3.8.
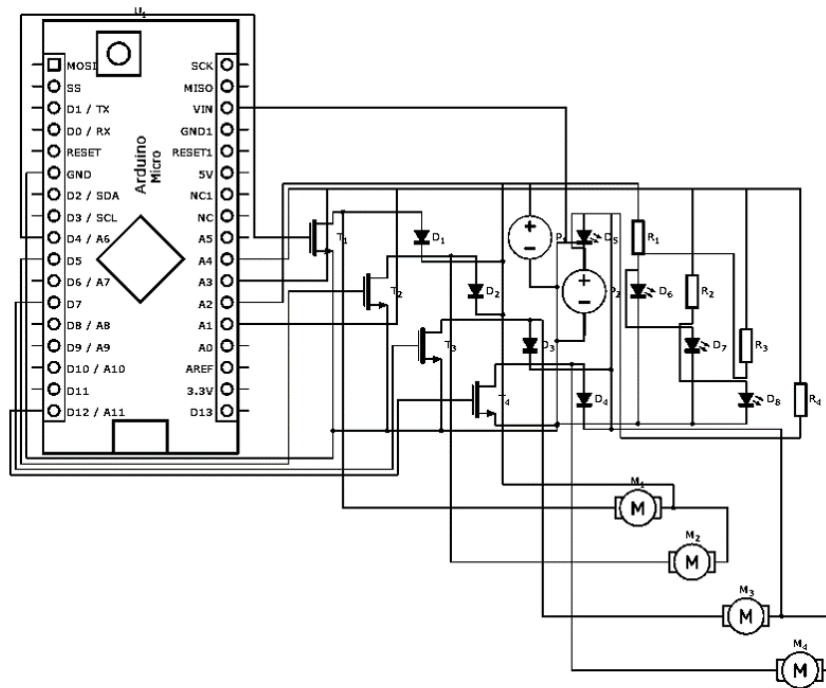
Figure 3.5: Circuit design created in Fritzing (Knörig *et al.*, 2009)
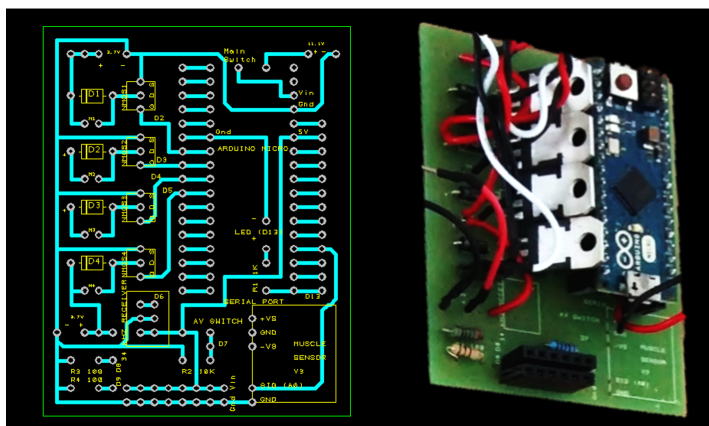

Figure 3.6: PCB design (left), and the final printed board with components (right)

3.6.3   Interface LEDs and Switches

For the operator to interact with the device and send different commands to the vibration motors and LEDs, a user controlled interface was necessary. To establish this, there were four red LED pushbuttons and eight toggle switches incorporated in the prototype. Each LED served as both a feedback mechanism and interface component for input. When the pushbutton is open (unpressed) there is no connection between the connecting wires of the pushbutton, so the pin is connected to ground (through the pull-down resistor) and a LOW is read through the *Arduino*. When the button is closed (pressed), it makes a
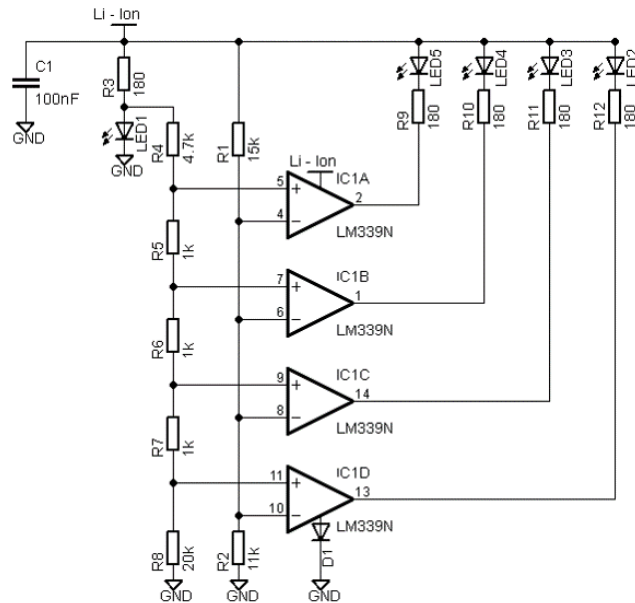
3. CONCEPT DESIGN

Figure 3.7: Battery Level Indicator circuit schematic

Voltage (V)	GREEN	GREEN	YELLOW	YELLOW	RED
4.2					
4.0					
3.8					
3.6					
3.4					

Figure 3.8: Battery Level Indicators. The indicators are designed to measure two 3.7 V rechargeable batteries on the following levels: 4.2 V - 100%; 4.0 V - 80%; 3.8 V - 60%; 3.6 V - 40%; 3.4 V - 20%

connection between its two legs, connecting the pin to 5 volts, so that a HIGH is read. These states made it easier to monitor manual feedback commands without any trouble.

3.6.4 Device Housing and Protection

The housing of the electronics of the device was chosen to be a thin wooden box, cut according to the correct size to contain the control circuit, battery level indicators, batteries, switches and LEDs. A final 3-D printed lid was made and and attached to the side in order to have easy access to the interior of the box. The vibration motors were lengthened using standard wires, to

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about 1 meter in length. The adhesive backing cover was removed and the motors were stuck to the inside of the wristband. The final prototype is shown in Figure 3.9.
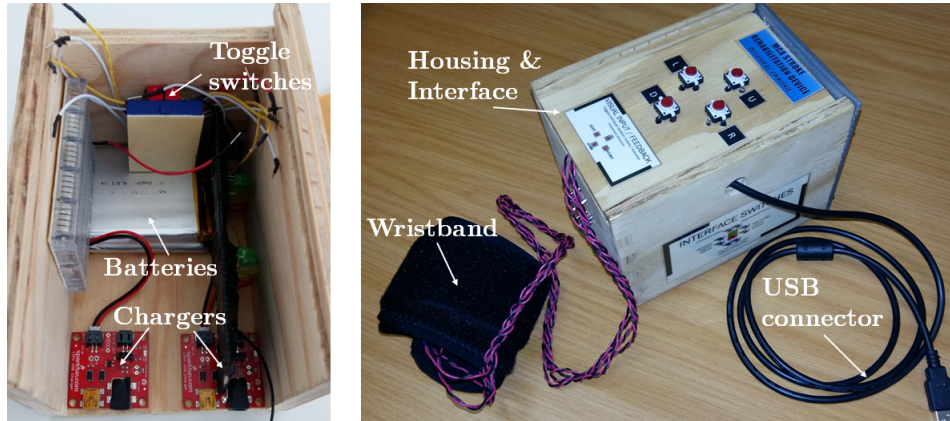

Figure 3.9: The chosen concept, with the wooden box containing some of the components (left) and the final prototype (right)

3.7 Control

With the finished prototype ready, the last task before it was fully functional, was to finalize the programming for control and communication. For the serial communication with the operator, a wired USB to Serial converter communication was implemented. These systems were incorporated in the device, and programmed via the *Arduino*, *MATLAB*, and *EEGLAB* software to carry out the necessary tasks when interacting with the operator, patient and/or environment (Banzi, 2008) (MATLAB, 2014), (Delorme and Makeig, 2004). The control scripts can be viewed in Appendix D. During the device operation and experiments, the Universal Synchronous/Asynchronous Receiver/Transmitter (USART) or Serial port of the controller was used to detect keystrokes sent by the operator on the keyboard of the computer, after which the keystrokes were shown on the *Arduino* environment's built-in serial monitor using the command "Serial.read()"-command. Figure 3.10 illustrates a rough process flow diagram of the software that was used during the experiments.

3.8 Operation

Finally, a user manual was created for operating the prototype during future neurorehabilitation sessions of MCA stroke patients. The goal is for an accompanying physiotherapist, who does not necessarily have the engineering knowledge, to understand the device and its operation. The manual will also speed up the understanding of engineering terms and concepts used throughout the sessions, and will allow the user to understand the developer. The

3. CONCEPT DESIGN
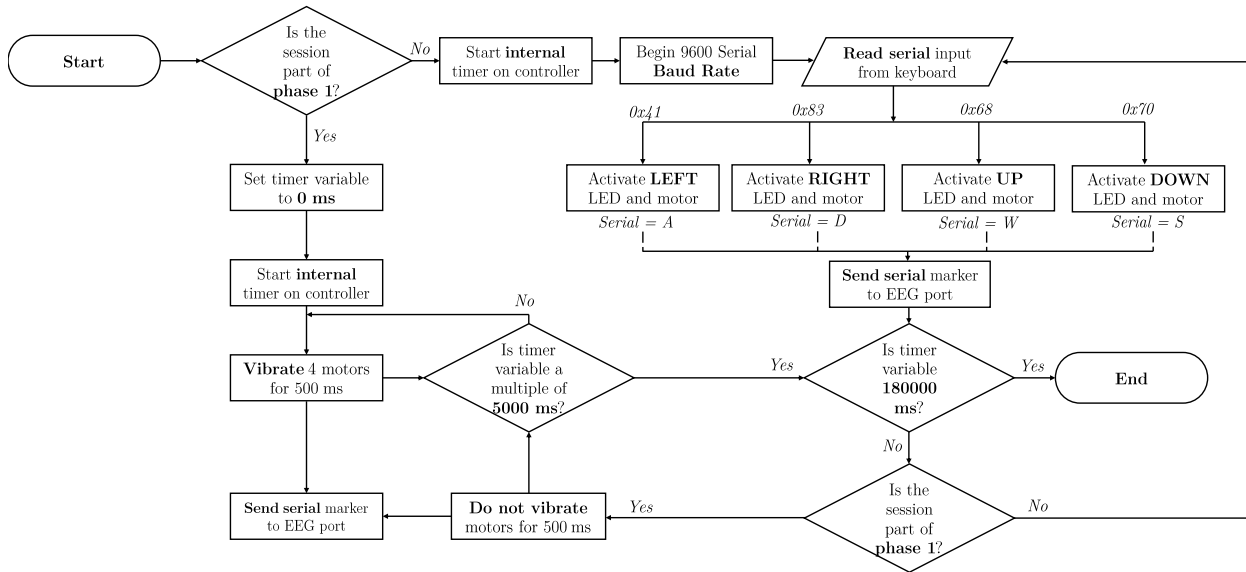
Figure 3.10: The flow diagram of the software used in the main experiment

manual summarizes the session preparations, device setup and how to conduct neurorehabilitation sessions. It can be viewed in Appendix A. The final prototype, with both its mechanical and electronic systems working, was then tested and demonstrated in a laboratory environment, followed by the experimental phase and its particular study - an observational study.

Chapter 4

Experimental procedure

4.1   Overview

This chapter discusses the experimental setup and procedures necessary for the observational study. The experimental sessions were conducted on healthy volunteers. The study is called an observational study, because the subjects that partook in the experiments were observed and variables of interest were measured without assigning treatments to the subjects. Before future tests could be run on patients with any symptoms of stroke, it was first necessary to test the device in terms of its ability to measure data and obtain significant results that prove it is in working order for its use in an EEG experiment. The study primarily focused on the feedback component, controller, and EEG headset. More specifically, in order to answer the research question, the goal was to investigate the prototype's ability to relay sensory information to the brain and evaluate this ability by means of Event-Related Potentials. The study will be considered successful if the feedback provided by the prototype can be sensed and analyzed by the EEG headset, making it suitable for future stroke rehabilitation.

EEG biofeedback data was captured by the *Emotiv Insight* EEG headset and monitored in real-time. The data was then analyzed offline to establish whether the EEG data can be analyzed to identify the occurrence of:

1) evoked action potentials in response to said sensation

2) evoked action potentials in anticipation of a somatic sensation (oddball event)

3) an abstract action potential given as a mental command in response to visual stimulus.

4.2   Theory

The theory behind Event-Related Potentials is discussed in Chapter 2.5.2. From the literature review, it was found that ERP occurence in the brain is

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independent of damage to the cortical activity of subjects, which makes it the perfect tool to use during a study that experiments on healthy subjects, but in the future, aims to rehabilitate post-stroke subjects. Furthermore the characteristic of ERPs as a real-time index of cortical neural activity makes them an apt tool for identifying whether any activity takes place in response to discrete events.

In order to obtain more than one set of data, it has been chosen to focus on the P_{200} and P_{300} ERP components. This will result in the acquirement of enough information from EEG data on which to base results obtained from previous similar ERP experiments. Considering the prototype, the visual- and haptic feedback both pertain to P_{200} characteristics, and the oddball event (i.e. no vibration) pertain to P_{300}. This thoroughly gives three different datasets that can be compared with other studies, which are adequate to result in substantiated data that can be extrapolated to provide further recommended results.

The following keywords and their definitions will aid in the comprehension of the methods that follow:

Events: This is a term that describes the measurements that will be taken during the experiment. An event consists of a latency and amplitude.

Latency: The latency is the duration of the EEG measurement in milliseconds (ms) and is described by the delay between a stimulus and response.

Amplitude: Also referred to as 'Deflection' or 'Potential'. This indicates the highest voltage displacement of the EEG wave above its baseline. It is measured in micro-volts (μV).

Stimuli: Events that evoke a specific functional reaction on the user. The events are classified as vibratory (i.e. a vibration on the arm) and visual (i.e. a visual indicator / LED).

Epoch: An instant in time that is of a certain duration in seconds, in other words, a time interval.

P_{200} **and** P_{300}**:** These are the events that will be studied. P_{200} is a positive (P) wave occurring more or less at 200 ms after a stimulus, and P_{300} occurs at more or less 300 ms after a stimulus.

4.3   Ethical Consent

The study complies with the SA National Health Act No. 61 2003, as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. Ethical approval was obtained from the Tygerberg Human Research (Humanities) Ethics Committee for research involving (anonymous) human participants and clearance was given 2 December 2015 with the protocol number M15/10/042. All the participants who contributed to this study signed a written consent form after having received a full explanation of the expected

results and possible side effects. The proof of Ethical Approval can be viewed in Appendix E

4.4   Subjects

The study was conducted on eleven healthy participants during two different experimental phases. According to Nel (2016), this number of subjects is statistically adequate when three different measurements are taken in relation to the same study. The participant information is shown in Table 4.1 (27% female, mean age = 23.72 years, range 21-26 years). There were no significant differences among participants relative to age, education, ethnicity, gender, and self-reported symptoms of depression. All participants were recruited via an online call for participation at the Biomedical Engineering Research Group of the Faculty of Engineering, University of Stellenbosch. The following exclusion criteria were enforced to minimize possible confounding effects of co-morbid factors known to adversely impact cognition:

1. Cognitive impairment, like medical problems or cognitive deficits resulting in a mini-mental status examination (MMSE) score of < 24 (Folstein *et al.*, 1975)

2. Intended or actual participation in any other study

3. Any sign of significant pain - this was determined by means of a visual analogue (VA) scale, for which a score of < 4 was needed (Sengupta *et al.*, 2004)

4. Upper and lower limb treatment with anti-spasticity drugs in the previous 6 months.

4.5   Apparatus

4.5.1   EEG headset

EEG data was collected with the *Emotiv* EEG headset in tandem with the *Emotiv* User Interface API. The electrodes cover five scalp sites according to the 10-20-system (see Figure 2.17 in Chapter 2.5), and are digitized at a rate of 128 samples per second per channel. Each EEG channel of the headset has a resolution of 14 bit per channel and a Least Significant Bit (LSB) resolution of 0.51 μV @ 14 bit. Since the *Insight* electrode locations cover AF_3, AF_4, T_7, T_8 and P_z, the channel of interest was P_z - this is the parietal lobe electrode placed on the scalp midline referenced to the left earlobe, and from the literature review, this channel in particular delivers the best results for the P_{200} and P_{300} ERPs. EEG data was recorded using the *Emotiv Testbench* software bundle. The software receives EEG data packets from the headset's USB

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Table 4.1: Participant Information and inclusion results displaying gender, age (years), visual analog scale (out of 5) results and mini-mental state examination score (out of 30).

Participant	Gender	Age	VA-Scale	MMSE-scale
1	M	21	1	29
2	M	22	2	24
3	F	24	3	28
4	M	24	3	30
5	F	23	2	30
6	M	25	2	27
7	M	26	3	27
8	M	23	2	26
9	M	24	2	30
10	F	25	2	26
11	M	24	1	30

dongle. Recorded data can then be converted to comma separated values file to be interpreted by *MATLAB* and *EEGLAB*.

4.5.2 Feedback Device

The rehabilitation system's control circuit integrated the five-channel *Emotiv Insight* EEG headset and the prototype rehabilitation device via a standard USB to serial converter. The feedback components of the device consist of the four vibration motors and four LEDs controlled via the *ATmega32U4* microcontroller. The rest of the circuit is powered through a serial connection established by the microcontroller to a computer.

During the experiments, the vibration motors were placed into contact with the right arm of each participant above the wrist by an *Orthofit* wristband. The four motors were positioned in four directions (up, down, left and right) in the standard anatomical position (see Figure 4.1).

4.6 Method

Figure 4.1 shows the physical experimental setup of the study. Two experimental phases were conducted at 15-minute intervals and repeated three times for each subject. Figure 4.2 illustrates the process flow and methodology of the observational case study. An explanation of each phase follows.

① **Prepare Environment:** A personal computer was used to aid in the experiment, and was controlled by the operator. Environmental noise in the recording room was excluded by removing any unnecessary sources of electromagnetic (EM) noise from the room and its immediate vicinity,
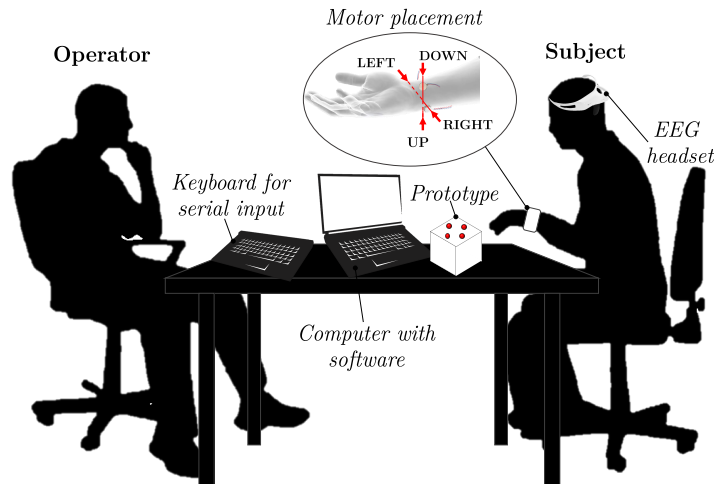
4. EXPERIMENTAL PROCEDURE

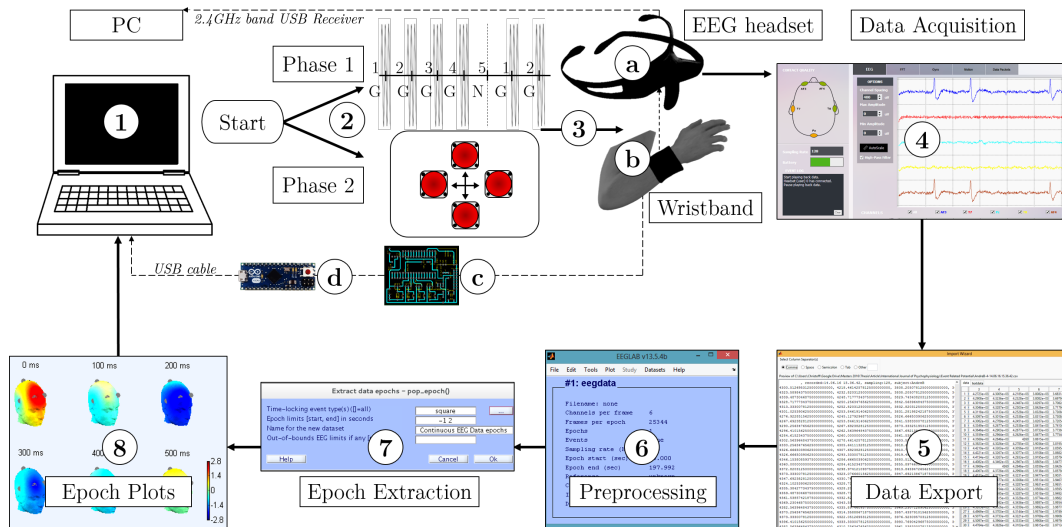**Figure 4.1:** Physical Experimental Setup

Figure 4.2: Case Study Methodology

and, where possible, replacing equipment using alternate current with equipment using direct current (such as direct current lighting). EMG noise caused by muscle movement was avoided or reduced by asking the participants to find a comfortable position and relax before the start of a recording session.

(2) **Start Experiment:** Phase 1 consisted of a three-minute session where a single-stimulus procedure was frequently presented to each participant, with no other stimuli occurring. The vibration stimulus was presented on the right arm of each participant in a sequence of four seconds, with no stimulus applied sequentially each fifth second, i.e. *GO, GO, GO, GO, NOGO*. The goal was to first capture the P_{200}-exogenous event, thereby identifying evoked action potentials in response to a somatic sensation

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and to capture the P_{300}-endogenous event to identify a potential in response to the anticipation or absence of an anticipated stimulus event.

Phase 2 consisted of a two-minute session where a single visual stimulus was frequently presented to each participant, with no other stimuli occurring. The visual stimuli were presented to the participants in the form of four red LEDs positioned in four directions (up, down, left and right). Here, the goal was to capture EEG data to identify the stimulus, followed by a response selection, and the execution of the correct movement of the participant - these reactions link to the P_{200}-ERPs. Another goal was to find a correlation between the deflection of the different P_{200}-events of the two phases and to determine whether any difference in amplitude might be due to exogenous factors (vibration vs. visual stimulus), and also due to the length and number of repetitions.

③ **Feedback:** ⓐ The *Emotiv Insight* EEG headset constantly recorded the EEG data from the participant (wearer) through both phases and transferred this data to the computer via a 2.4 GHz wireless USB dongle. The wristband ⓑ contained the vibration motors that were used as feedback during phase 1. During phase 2, the participants were instructed to move their right arm (with the wristband) in the direction of the given visual stimulus. The circuit ⓒ connected the vibration motors to an external power source, and also ensured a connection with the *ATmega32U4* microcontroller ⓓ. Automatic stimuli were sent using markers during phase 1 (see ④). Manual stimuli and visual instructions for phase 2 were executed via serial input (keystrokes) by the operator to the computer ① from a separate keyboard. During the experimental phases, the serial port of the microcontroller was used to detect keystrokes sent on the keyboard, after which the keystrokes were shown on the *ATmega32U4* microcontroller environment's built-in serial monitor.

④ **Data Acquisition:** Data acquisition of events took place during the EEG experiments through real-time EEG capturing. Event-recording refers to an automatic serial 'mark' sent to *Emotiv Testbench* during the presentation of stimuli. This records the time of stimulus occurrence and stores it as part of the data packets received in JSON format from the Wireless USB dongle. In phase 1, events were stored at each second. In phase 2, each event was recorded at the particular point in time before the movement was executed. Reaction time and action duration were not recorded for the second phase. All of the continuous EEG segments (Phase 1 and Phase 2) were recorded as an array of events using the EEG headset in ③. EEG data variables consisted of event times (ms), peak latencies (ms) and deflections (μV).

⑤ **Data Export:** After the experiment data was recorded, the headset was removed from the participant and turned off. The data acquisition soft-

ware files from ④ were stored in European Data Format (EDF) - a standard file format designed for exchange and storage of medical time series. This file then underwent a conversion to Comma Separated Values (CSV) format to be interpreted by *MATLAB*. Using *MATLAB*, the data columns containing the 128 samples per second, the deflections of the five channels of the EEG headset and the event-data were imported and stored as a matrix for each participant.

⑥ **Preprocessing:** Next, the matrix was imported in *EEGLAB* to be available for preprocessing. The preprocessing steps are described in detail in Chapter 4.7.1, and included: Data averaging and filtering, ICA Decomposition, Artifact Rejection, and Baseline Removal.

⑦ **Epoch Extraction:** After preprocessing, the data was ready to be extracted. This was done by running a modified script (Appendix D). Both the *GO-* and *NOGO*-events corresponding to four-second interval vibrations of phase 1 were extracted 900 ms before and after each stimulus. The visual events from phase 2 were extracted at 1 second before and 2 seconds after each stimulus. The extracted epochs were then saved as a new set of continuous EEG data for the three events. Detailed steps are provided in Chapter 4.7.2.

⑧ **Epoch Plots:** The data was then ready to be plotted. The *EEGLAB* Graphical User Interface (GUI) was used to assist in plotting figures for ERP analysis. Furthermore, the channel locations, channel spectra and maps, channel ERP with scalp maps, and component maps were available to plot. This final step allowed the data to be evaluated visually and provided several useful modes of visualization of the averaged and single-trial data.

4.7   Data Processing

This section explains in more detail, the data acquisition and preprocessing stages (stages 4-8 of the methodology), followed by the theory and application of topographical visualization analysis after data extraction. Figure 4.3 shows the steps involving acquiring, exporting and editing the raw EEG data.

4.7.1   Preprocessing

The interactive *MATLAB* toolbox for processing continuous and event-related EEG data (*EEGLAB*) was used to import raw EEG data, after which it incorporated several preprocessing techniques, like independent component analysis (ICA), time/frequency analysis, artifact rejection, and event-related statistics.

Data Averaging: To obtain ERPs, the dataset epochs needed to be averaged. This would then produce a clear ERP graph that can be analyzed
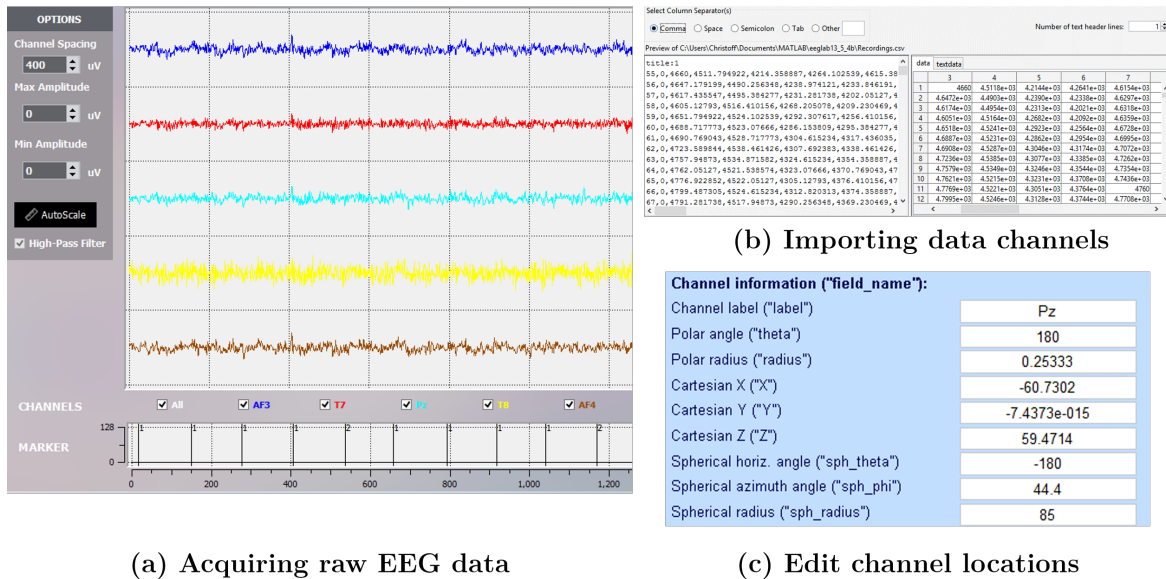
4. EXPERIMENTAL PROCEDURE

(a) Acquiring raw EEG data

(b) Importing data channels

(c) Edit channel locations

Figure 4.3: Data acquisition and exportation: (a) The five channel raw EEG data. An event marker is applied as either '1', '2' or '3', which corresponds to the P_{200}-, P_{300}- and visual-events respectively. The data is then imported in *MATLAB*, (b), with each channel transposed to an array (columns 3-7). Finally, once the data is loaded in *EEGLAB*, the channel locations (c) are applied to the correct array according to the polar coordinates, Cartesian coordinates and spherical angles of the 10-20 system.

according to its latency and deflection. Data was also averaged to form a single power spectrum for each EEG segment, as averaging has the effect of canceling out unwanted, random noise and revealing the ERPs. The stimuli described in the two experimental phases were repeated 108 times in order to average several segments of the EEG signals during each event. Each raw EEG epoch was one second long (updated every 0.25 sec) with a frequency response of 0.5-43 Hz.

Filtering Continuous Data: Before averaging, it was necessary to apply a bandpass filter, and low-pass filters to remove signal noise. Filtering the continuous data also minimizes the introduction of filtering artifacts at epoch boundaries. Highpass- and lowpass filtering at 1 Hz and 20 Hz respectively were selected for bandpass filtering. This allowed post-processing to focus on the required states of frequencies in the brain. Furthermore, the signal-to-noise ratio was improved by removing the contaminating 50 Hz interference from the power line.

Removing Artifacts: Recorded activity that is not of cerebral origin is termed "artifact". Artifacts resulting from physiologic sources, such as eye movements, were manually checked removed. The manual rejection was done by physically scanning through the continuous EEG dataset of each participant, and removing noise by deleting the particular interval containing that noise. An example of a small artifact before it was manually rejected is shown in Figure 4.4*a*. Only segments with a stable baseline

and without high-amplitude artifacts were analyzed. As a premeasure, an Independent Component Analysis (ICA) was also applied. ICA was automatically done by running a predefined algorithm that is part of the *EEGLAB* toolbox, called *runica*, which calls the function `pop_runica()`. This function performs ICA decomposition of the input data using the logistic ICA algorithm of Bell and Sejnowski (1995), with the natural gradient feature of Amari *et al.* (1996). ICA can separate out artifacts embedded in the data, which automatically rejects artifacts not clearly visible via visual inspection. It also separates independent sources linearly mixed in the five channels.

Removing DC Offset: EEG data was stored as floating point values directly converted from the unsigned 14-bit Analog-to-Digital Converters (ADC) output from the headset, which meant the floating Direct Current (DC) level of the signal occurred at approximately 4200 μV. The negative and positive voltage values of the EEG waves were respectively transmitted as positive values less and greater than the average level. The DC offset was therefore removed before any further analysis was performed. This was done by applying a 0.5 Hz first order high-pass filter, which matches the characteristics of the *Emotiv Insight* EEG headset, (Appendix C3) to remove the background signal.
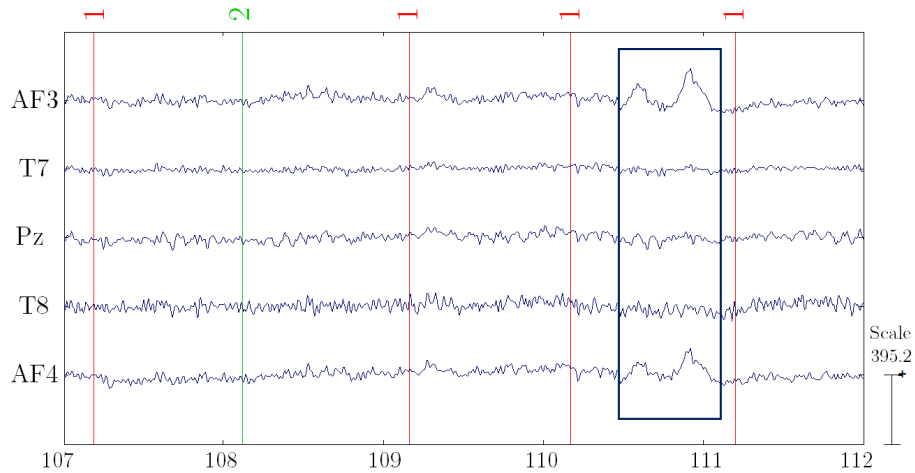
4.7.2   Epoch Extraction

In order to study the event-related EEG dynamics of the continuously recorded data, data epochs time locked to the onsets of the three classes of experimental stimuli were extracted by selecting the different events - either *GO* (1), *NOGO* (2) or *VISUAL* (3). Figure 4.4 illustrates the EEG data before and after extraction.

The ERPs of the epoched dataset were plotted as single-channel traces in their 2-D topographic arrangements. The P_z-channel location was then selected to plot its ERP data for a series of 2-D scalp maps representing potential distributions at a selected series of trial latencies. This was done in order to correlate the latency distribution of the ERP and compare that to ERP characteristics of previous studies.

Finally, an *EEGLAB* analysis was performed that contained readily optimally organized data in the 11 epoched datasets, for all phases and events. All the datasets originated from the single study and had comparable structure and significance for bivariate data analysis. Event-Related Spectral Perturbation (ERSP) and Inter-Trial Phase Coherence (ITC) images based on 148 trials of 230 frames sampled at 128 Hz were computed to determine the means of the combined epochs of all participants.

The datasets containing all the experimental results were analyzed with the use of *SATISTICA* (Dell Software, Round Rock, Texas). Repeated measures ANOVA with Least Significant Difference (LSD) and Bonferroni multiple

4. EXPERIMENTAL PROCEDURE

(a) Channel events
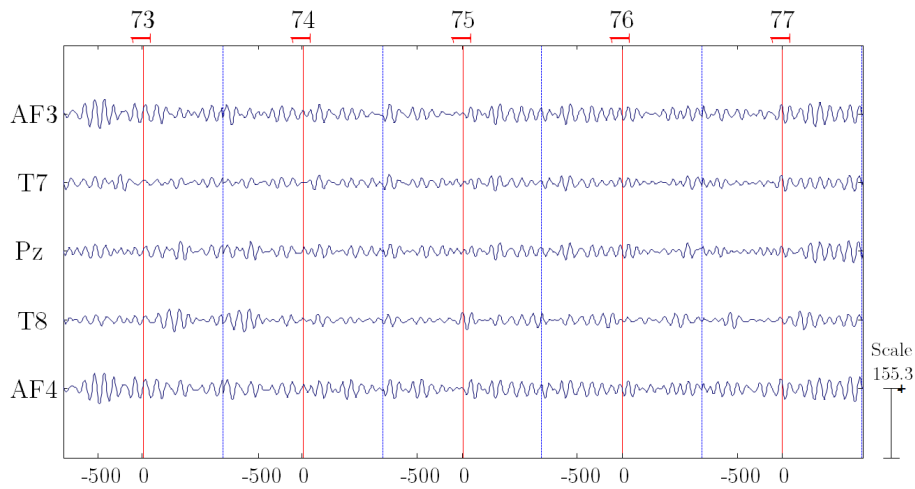
(b) Extracting epochs

Figure 4.4: Epoch extraction: (a) The time vs. channel plot in *EEGLAB*. The red and green markers indicate the time-locked epochs for the P_{200}- and P_{300}-events. An example of an eye-blink artifact is shown in the blue rectangle. Here, the artifact rejection step has not been applied yet. (b) EEG data packets after epoch extraction of the P_{200} (GO)-event, indicated by the red markers. The blue lines indicate the epoch barriers.

comparisons at each trial latency on the average ERPs were done. The goal was to show that the latencies between the P_{200}- and P_{300}-events were different and that there was no significant difference between the two P_{200}-categories of phase 1 and 2. The characteristics of the potentials that were captured were then compared to existing literature and theory to validate the feedback device's accuracy.

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Chapter 5

Results

The results of the observational study are summarized. The extraction data from all three events were analyzed using *EEGLAB* and figures were plotted using built-in *MATLAB* functions. All resulting figures contain the averaged data of all participants.

5.1   Phase 1 - P_{200}-Results

The *GO*-event corresponding to four-second interval vibrations was extracted 900 ms before and after the stimuli that occurred at each second. Figure 5.1a shows the resulting response after each *GO*-event, which illustrates the evoked action potentials in response to a somatic sensory stimulus. The power spectrum response for the event in Figure 5.1a was then plotted for the parietal lobe midline (P_z) electrode (Figure 5.1b). Latency distribution on the ERP image is typical for P_{200} varying between 150 and 275 ms after the onset of the *GO*-event. The P_{200} occurred as a positive deflection (2.469 μV) with a latency of 179.7 milliseconds from the onset of the vibration stimulus.

5.2   Phase 1 - P_{300}-Results

The *NOGO*-events that occurred were studied next. Epochs occurring at the time the vibration was omitted were extracted at 900 ms before and after the onset of the *NOGO*-event. Figure 5.2a shows the endogenous P_{300}-ERP traces in their 2-D topographic arrangements. From the data, a detailed representation was produced, (Figure 5.2b), with combined latencies and voltage deflections of all five channels. The P_z-channel is shown as the red voltage distribution. It can be seen that the P_z-channel peaks at 305.9 ms with an amplitude of 2.38 μV.
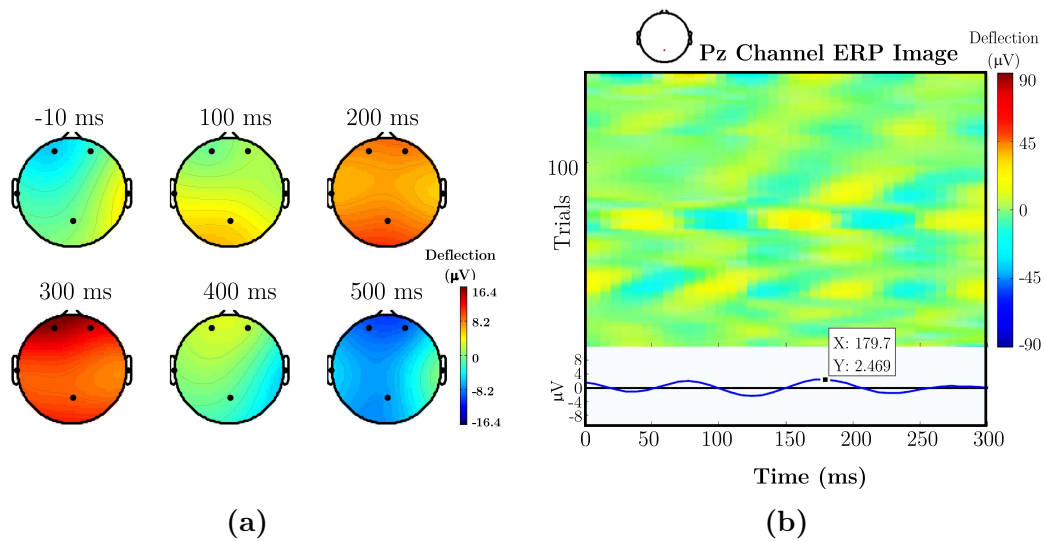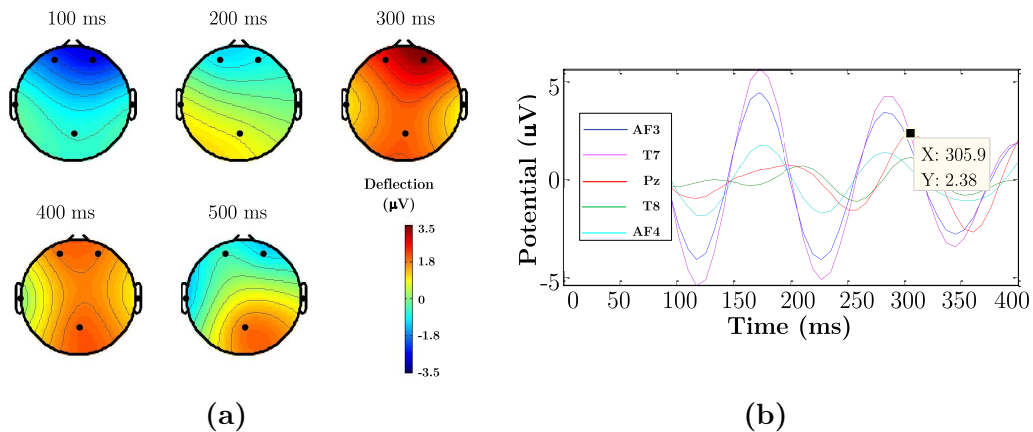
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(a)

(b)

Figure 5.1: *GO*-event results. (a) Exogenous P_{200}-ERP traces in their 2-D topographic arrangements. Increase in voltage amplitude is shown to occur between 200ms and 300ms. (b) Power spectrum graph with the latency of the P_{200}-sensory event in the P_z-channel. The peak voltage is indicated as 2.469 μV and occurs at 179.7 ms after the stimulus.

(a)

(b)

Figure 5.2: *NOGO*-event results. (a) Endogenous P_{300}-ERP traces in their 2-D topographic arrangements. Increase in voltage amplitude is shown to occur between 300 ms and 400 ms. (b) Latency (ms) and deflection (μV) of electrodes in response to no external stimulus. The red line shows the P_z-response, which increases in voltage after 250 ms and peaks at 305.9 ms
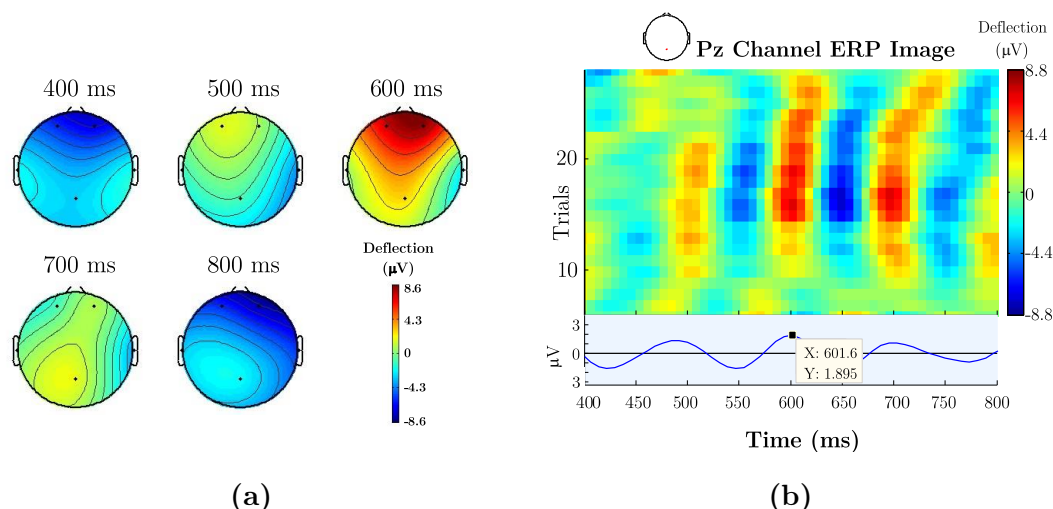
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Figure 5.3: *VISUAL*-event results. (a) Exogenous P_{200}-ERP traces in their 2-D topographic arrangements. Visual stimulus occurred at 400 ms. Increase in voltage amplitude is shown to occur at around 600 ms. (b) Power spectrum graph with the latency of the P_{200} visual event in P_z-channel. The peak voltage is indicated. Visual stimulus occurred at 400 ms. Increase in voltage amplitude is shown to occur at around 600 ms.

5.3   Phase 2 - P_{200}-Results

The final study focused on the third event - a visual instruction given to the participants during Phase 2. Figure 5.3a shows a representation of visual activity at about 200 ms after the visual stimulus (which in this instance occurred at 400 ms of the epoch). This also correlates to the characteristic latency of the P_{200}-potential. The latency and power spectrum of the P_{200} visual event in the P_z-channel were extracted (Figure 5.3b). Both figures illustrate that the P_{200} visual event potential occurred as a positive deflection (1.895 μV) with a latency of 201.6 milliseconds from the onset of the visual stimulus.

5.4   Statistical Analysis

The results of the study containing all 11 participants with their relevant data are shown in Table 5.1. Each trial contained samples from 898 ms before to 891 ms after the event.

Table 5.2 shows the analytical data necessary to analyze the two phases independently using confidence intervals.

Figure 6.5a and Figure 6.5b both illustrate the confidence intervals obtained from the Repeated Measures ANOVA test, which is an extension of the dependent t-test. The latencies of the Visual event and the P_{200}-event are

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Table 5.1: Combined maximum latencies (ms) and deflections (μV) of all participants during Phase 1 and Phase 2

Subject	P_{200}		P_{300}		Visual	
	Lat. (ms)	Def. (μV)	Lat. (ms)	Def. (μV)	Lat. (ms)	Def. (μV)
1	179.7	2.4690	359.4	1.4890	265.6	0.7716
2	203.1	0.3425	351.6	2.4730	164.1	1.6430
3	226.6	2.5013	305.9	2.3800	201.6	1.8950
4	195.3	1.3890	320.3	1.4270	257.8	1.4890
5	171.9	0.5204	390.6	1.4160	164.1	0.7453
6	179.7	2.4110	304.7	2.3800	250.0	0.5018
7	218.8	0.2291	343.8	2.8540	273.4	1.8680
8	250.0	0.0409	367.2	1.1010	265.6	0.7716
9	234.4	0.6157	335.9	1.0510	210.9	0.4024
10	257.8	2.3380	273.4	1.4880	234.4	0.5460
11	164.1	0.9133	273.4	2.2410	195.3	1.0670

Table 5.2: Analytical data for P_{200}- and P_{300}-latencies and deflections of both experimental phases. The ERP events are divided into the Phase 1, P_{200}- and P_{300}-potentials, and Phase 2 Visual potential. The average values and confidence intervals are shown for both the latencies and deflections

ERP Event Average	Latency (ms)	Deflection (μV)
Phase 1 P_{200}	207.40	1.2518
Phase 1 P_{300}	329.65	1.8454
Phase 2 Visual	225.71	1.0637
Confidence Interval		
Phase 1 P_{200}	21.68	0.6710
Phase 1 P_{300}	25.43	0.4216
Phase 2 Visual	27.26	0.3769

compared (F = 1.274, p = 0.28535), followed by the latencies of the P_{200} and the P_{300}-events (F = 64.253, p < 0.001). It can be seen that P_{200} and P_{300} from phase 1 differ significantly, whereas this was not the case for Visual vs. P_{200} (P > 0.05). These findings are confirmed in Figure 5.5 with the use of a Box-and-Whisker plot.
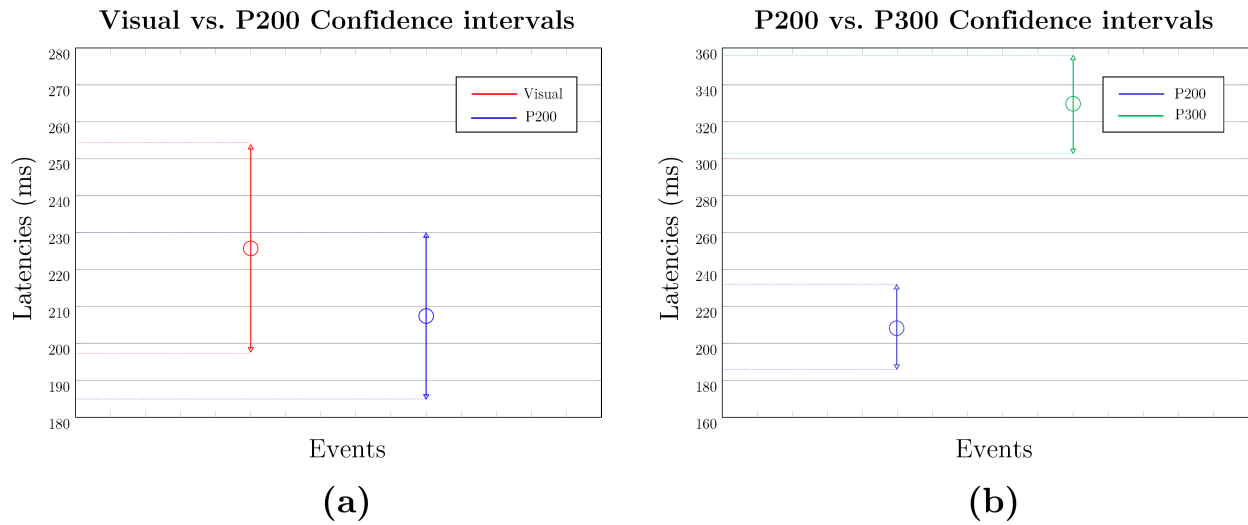
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Figure 5.4: Confidence intervals. 95% confidence intervals around the average for the latencies of the Visual vs. P_{200}-events (a) and the P_{200}- vs. P_{300}-events (b).
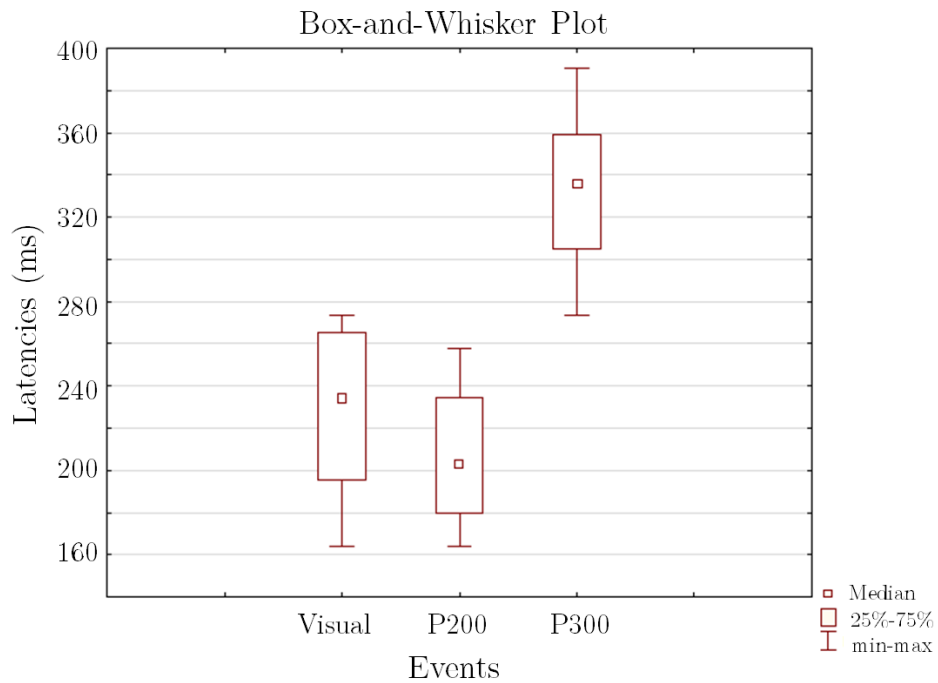

Figure 5.5: Box-and-Whisker Plot highlighting the middle half of the data points of the latencies of all three events.

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Chapter 6

Discussion

This chapter discusses the results that were obtained from the observational study and also introduces recommendations for future aims this project may manage to achieve, in terms of its clinical relevance. Statistically valid results of the observational study are compared with that of previous literature and their medical relevance is discussed. Furthermore, the research gaps that were identified in Chapter 2 are discussed, and what influence this project may have over these gaps.

6.1   Observational Study

6.1.1   Results Overview

The results have demonstrated the rehabilitation device's feasibility in detecting evoked action potentials in response to and in anticipation of somatic sensations, and visual stimuli in an EEG neurofeedback experiment. Three different event-related potentials were identified and their deflection and latencies were analyzed. Repeated Measures ANOVA tests revealed a significant difference between the two categories of exogenous and endogenous potentials. The P_{200}-component reflected the occurrence of general neural processes via the somatosensory and visual systems with similar latencies, but different amplitudes, which indicates that manipulations of sensory stimuli can be used to modulate the characteristics of the P_{200}.

It was observed that certain discrepancies may exist between the comparisons of the P_{200}-characteristics of phase 1 and 2. Visual processing in the multiple visual areas that exist in the brain will necessarily produce visual evoked potentials at a number of different latencies. The fact that the latency of the visual potential is similar to the latency of the P_{200}-event does not indicate that these events are likely not related to one another, although this observation does not influence the objectives of the study. The P_{300}-component was successfully recorded during the absence of the anticipated stimulus (i.e. "oddball") event. Results showing human processes of becoming aware of a

6. DISCUSSION

sensory stimuli and reaction time of simple tasks were successfully analyzed to reveal information about the values of the latencies and deflection amplitudes of event-related potentials.

6.1.2   Previous Literature

Latency and deflection variances obtained from control groups in ERP related literature are shown in Table 6.1. The results of the current study are included as "Heunis *et al.*".

Table 6.1: P_z-channel latencies (ms) and deflections (μV) of similar ERP-studies, compared to the current results

ERP events at P_z-channel	Latency (ms)	Deflection (μV)
Heunis *et al.* (2016)		
P_{200} (average)	164-266	0.23-2.20
P_{300}	305-391	1.05-2.85
Kropotov *et al.* (2016)		
P_{200}	140-240	16.0-17.1
P_{300}	390-530	6.25-6.65
Vaney *et al.* (2015)		
P_{200}	158-218	2.70-9.72
P_{300}	302-393	10.1-26.9
Krell-Rösch (2014)		
P_{200}	245-265	2.16-3.79
P_{300}	388-448	5.11-6.95
Andreadou *et al.* (2012)		
P_{200}	194-241	0.51-5.11
P_{300}	356-403	6.98-19.3
Anjana *et al.* (2010)		
P_{200}	156-232	1.23-8.85
P_{300}	317-419	8.12-27.3
Ozmenek *et al.* (2008)		
P_{200}	131-217	1.20-20.0
P_{300}	263-411	2.60-33.5

It is noted that the amplitudes of the deflections are inconsistent, which may be due to the differences in the amount of processing (i.e. level of attention) required by a given stimulus for each participant (Sur *et al.*, 2009). The average latency values are observed to be in correlation with the variances of other studies. The average P_{200} of the current study occurred at a latency of 207.4 ms during the *GO*-event and 225.71 ms during the visual event. It is also evident that the amplitude was affected by exogenous factors (vibration vs. visual stimulus), and also by the length and number of repetitions, which were associated with average amplitudes of 1.2518 μV and 1.0637 μV respectively.

From Figure 5.2, it is evident that when a stimulus was unexpectedly omitted in a sequence of stimuli presented regularly, a large amplitude positive deflection appeared at the P_z channel, in spite of the absence of an external stimulus. This endogenous component appeared at the moment when the stimulus was expected. The results of the *NOGO*-events agree with the studies of Fabiani *et al.* (2000), Makeig *et al.* (2004) and Sur *et al.* (2009), which show a positive deflection in the 2-5 μV range with a latency range of 250-400 milliseconds from the onset of a stimulus. According to the analytical plots, the Visual-, P_{200}-, and P_{300}-components are visible with a latency of 225.71 ms, 207.40 ms and 329.65 ms from the stimulus onset, and it is consistent (as in Figure 5.2b) in the region of the parietal lobe (i.e., P_z).

6.2 Future Work

As discussed in objective number 10, an objective that was planned to assist with the project development, was to conduct a clinical trial study in order to evaluate possible neuroplasticity through the use of rehabilitation of adequate post-stroke test subjects. Hence, a clinical trial study would have contributed to this objective. Though this phase had indeed been set into progress, and the literature reviews assisted with its planning, unfortunately, due to time constraints, not enough stroke patients could be recruited for statistically valid results. The following sections thus serve as guidelines for future use and continuation of the rehabilitation device, and may be used when similar rehabilitation projects are planned to be undertaken. Future recommendations will include the planned study description, patient criteria, methodology and stipulated results necessary for project continuation.

6.2.1 Clinical Trial Overview

During the planning of the clinical trial, the proposed rehabilitation treatment was compared to therapy treatment that is already available and in it, a control group and experimental group were established. The clinical trial focused on the analysis of EEG data captured from MCA stroke patients. It aimed to demonstrate the practical evaluation of possible neuroplasticity through the use of the alternative rehabilitation device and recorded EEG data, ERP analysis, and Functional Motor Assessments. Rehabilitation was planned to be conducted over a period of twelve weeks, in consideration of the hospitalization period. The evaluation included measurements of brain waves, cognitive function and BSI values.

6.2.2 Subjects

Determining the sample size required, to adhere to specific objectives, is one of the first steps in designing a study. The results, therefore, needed to be

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statistically valid to detect a clinically relevant treatment effect. Keeping this statement in mind, together with the future aim of trying to prove a faster decrease rate of BSI of the experimental group (see Chapter 2.5.3), the sample size was calculated using Equation 6.2.1, provided by Noordzij *et al.* (2010):

$$n_S = 2\frac{(a+b)^2 \sigma^2}{(\mu_A - \mu_B)^2} \tag{6.2.1}$$

n_S = the sample size in each of the groups
μ_A = population mean in treatment Group A
μ_B = population mean in treatment Group B
$\mu_A - \mu_B$ = the difference the investigator wishes to detect
σ^2 = population variance (SD)
a = conventional multiplier for alpha = 0.05
b = conventional multiplier for power = 0.80

When the significance level alpha is chosen at 0.05, one should enter the value 1.96 for a in the formula. Similarly, when beta is chosen at 0.20, the value 0.842 should be filled in for b in the formula - these are multipliers for conventional values of alpha and beta (Gogtay *et al.*, 2010). Suppose a BCI difference of 0.2 between the treated and the control group ($\mu_A - \mu_B$) was chosen as clinically relevant after three months and it was specified that the effect should be detected with 80% power (0.80) and a significance level alpha of 0.05. Past experience with similar experiments, with similar measuring methods and similar subjects, suggests that the data will be approximately normally distributed with an SD of 30% (Stojanović and Đurašić, 2013). Entering the values in the formula yields:

$$n = 2\frac{(1.96 + 0.842)^2 \cdot 0.3^2}{0.2^2} = 35.33 \tag{6.2.2}$$

This means that a sample size of at least 36 subjects per group should be adequate to conduct the clinical trial. Inclusion criteria for stroke patients were:

1. Patients should be hospitalized and receiving occupational therapy and physical therapy at a Western Cape Mediclinic between March 2016 and August 2016

2. Hemiparetic left or right MCA stroke patients with stroke onset within 1-3 months

3. Patients should be able to follow verbal instructions, and communicate to a certain level

4. Patients should be able to perform all tests of the rehabilitation sessions

5. Light cognitive function failures that scored between 18 and 23 on the mini-mental state examination (MMSE)

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6. Barthel Index between 50 and 60 (for consistency)

7. Motor Assessment Scale Index of between 25 and 45 (this interval pertains to adequate motor function of a patient that requires little no assistance)

6.2.3 Apparatus

The apparatus that are part of the clinical trial are the same apparatus used during the observational study. It includes the rehabilitation device, the *Emotiv Insight* EEG headset, and a personal computer (laptop). The EEG software used for data acquisition can be viewed in detail in Appendix A. It additionally includes the *Emotiv Xavier* Testbench, *Emotiv Insight Emokey*, *EmoComposer*, and *PuTTY*. Following the acquisition, the recorded data was converted to comma separated values files to be interpreted by *MATLAB*.

6.2.4 Method

Rehabilitation needed to occur as follow: Control group (A) receives occupational therapy and physical therapy, for half an hour, five times a week, for six weeks. The experimental group (B) receives the same rehabilitation as the control group with additional feedback training with the rehabilitation device, for 15-20 minutes, twice a week, for six weeks. Exercises should be prescribed and supervised by one or two experienced physical therapists.

The rehabilitation sessions were divided into three different training phases: Algorithm-, Vibratory Feedback-, and Vibratory and Visual Feedback Training. Data collection should take place in real time, while the stroke patient wears the *Emotiv Insight*. Figure 6.1 shows the steps involved in the preparation, execution, and analysis of the stroke experimental sessions. A more detailed explanation of the materials and methodology involved in the planned sessions is provided in the user manual (Appendix A). Data analysis involves spectral- and ERP-analysis. Data visualization for the spectral analysis can be done by means of a spectogram, which is a visual representation of the spectrum of frequencies.

Unfortunately, due to time limitations, not enough stroke patients were available for testing. From the three patients that gave written consent, two patients withdrew from the study before rehabilitation sessions could be completed, and one patient underwent only one rehabilitation session before he was discharged. The patient was recruited at the Cape Gate Therapy Centre and underwent the session in the Cape Gate Mediclinic.

6.2.5 Data Analysis

Spectral analysis, which decomposes a signal into its constituent frequency components, is an important method to investigate brain activity. In general,
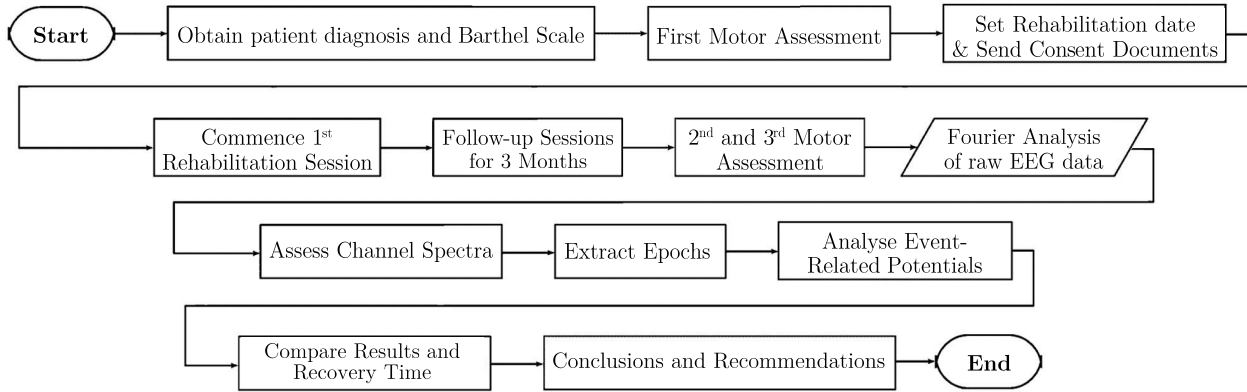
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Figure 6.1: Rehabilitation Methodology

autonomic nervous activity shows increased variations that are manifested as fluctuations in heart rate, blood pressure, and respiration. These variations can be used to determine which frequency band occurs more frequently, as well as whether it is more intense, i.e. whether it produces a stronger signal. Ultimately, the two hemispheres of the stroke patients can be compared to see whether the spectral density of the affected hemisphere, for example, the left hemisphere, correlates to the right one. It can also be deduced which hemisphere has increased in activity, and whether the experimental group provides better results than the control group during and after rehabilitation.

The raw data for data analysis was acquired and preprocessed by means of exactly the same methodology steps as those used in the observational study. An adjustment was made to the bandpass filter range during the filtering of the continuous data, in order to compensate for the additional analysis technique (Fourier decomposition). For bandpass filtering, Butterworth first order highpass- and lowpass filters were applied at 0.1 Hz and 30 Hz respectively to focus on the range of the five frequency bands.

6.2.5.1   Fourier Decomposition

To analyze and divide the EEG data into different frequency bands, the time-based data needs to be converted into frequency-based data using Fourier Decomposition. The Discrete Fourier Transform is a method that takes a complex waveform and decomposes it into a set of component sine waves. Before executing a Fast Fourier Transform (FFT), a window function (Hanning transform) was applied to ensure there were no wrapping artifacts where the FFT treats the data as an infinitely repeating sequence (Weisstein, 2009). This is defined by (with *hav* for the *haversine* function):

$$\omega(n) = 0.5\Big(1 - cos\frac{2\pi n}{N-1}\Big) = hav\frac{2\pi n}{N-1} \qquad (6.2.3)$$

hav = Haversine Function

n = Frequency over the sampling period

N = Width, in samples, of a discrete-time, symmetrical window function

ω = Discrete-time, symmetrical window function

The five channel signals of the headset are continuously sampled at a rate of 128 (N) samples per second and can then finally undergo spectral analysis via application of an FFT, which computes the discrete Fourier transform $\mathscr{F}[n]$ of each sequence $f[k]$:

$$\mathscr{F}[n] = \sum_{k=0}^{N-1} f[k] e^{-j\frac{2\pi}{N}nk} \qquad (6.2.4)$$

$\mathscr{F}$ = Fourier Transform function

k = Sample number in the time domain

N = Total number of samples

n = Individual sample

6.2.5.2 Frequency Extraction

After the Fourier transformation of the EEG data, the relevant frequencies can then be extracted. Parameters used by previous studies can be applied to these frequencies and then analyzed to create certain index ratios that can assess the values of quantified EEG in the follow-up of a stroke (Giaquinto *et al.*, 1994). For each of the five channels of the EEG headset the coefficients of five frequency bands can be extracted:

Beta: 14-30 Hz
Alpha: 8-13.9 Hz
Theta: 4-7.9 Hz
Delta: 0.1-3.9 Hz

The above frequency bands can be used to give an indication of the different fluctuations of the autonomic nervous activity of the patient. As proposed by Giaquinto *et al.* (1994), for each channel and each frequency band, the following parameters should then be calculated:

- **Absolute Power** (the total mean power)
- **Relative Power** (the ratio between the absolute power of the band and the absolute power of the total spectrum)
- **Mean Weighted Frequency**
- **Asymmetric Index** (the ratio between the absolute power on the uninjured- and injured hemispheres)
- **Reactivity Index** of the alpha-band (the ratio between the absolute power at "eyes open" and the absolute power at "eyes closed")

6.2.5.3 Marthel ADL Index

According to O'Sullivan *et al.* (2013), the Barthel scale or Barthel ADL index is an ordinal scale used to measure performance in activities of daily living (ADL). Each performance item is rated on this scale with a given number of points assigned to each level or ranking. The Motor Assessment Scale is designed to assess the ability of stroke patients to perform functional tasks rather than isolated patterns of movement or synergies (Malouin *et al.*, 1994). It is comprised of eight items corresponding to eight areas of motor function. Patients perform each task three times and the best performance is recorded.

A higher Barthel score is associated with a greater likelihood of being able to live at home with a degree of independence following discharge from a hospital. The patients should be divided into groups with more or less the same Barthel Index, for example, a score of less than 60 at admission. In contrast, a Barthel score of over 60 means much better prognosis. Motor functions and Motor Scales should be assessed three times. First, on admission to the study, then after the first and third months respectively. After completion of the clinical trial, these two scales should be compared between the two groups.

6.2.6 Planned Results

As mentioned, one patient (a 58-year old male) underwent a successful rehabilitation session. The patient had a right-sided stroke ten days before the first session, with a Motor Assessment score of 42 on admission. He also had a left 75% stenosis (abnormal narrowing) of the extracranial vessels, as observed from an ultrasound. The Motor Assessment Scale sheet, proof of prognosis, and the CT-Angiography results of the extracranial vessels and Carotid Doppler results can be studied in Appendix F. Unfortunately, this session did not receive a follow-up, as the patient was discharged before the next session could be scheduled, and hence rehabilitation was ceased.

As the results of the clinical trial could not be statistically verified, a few recommendations were made for future use of the rehabilitation device in a clinical setting. It is hypothesized that power spectrum density can be used to differentiate the brainwave characteristics of the different stroke groups. The following speculations supported by previous studies (Giaquinto *et al.* (1994), Leamy *et al.* (2014) and Wolf *et al.* (2016)) were also made with regards to the planned results:

EEG results: Before recovery, the quantified EEG results should be significantly abnormal in the affected hemisphere of the two study groups. The alpha mean weighted frequency of the injured hemisphere should also be slower than that of the contralateral side.

EEG power spectra: Longitudinal recordings should show a significant improvement of the EEG power spectra in the first 3 months. Depending

on the site and side of the lesion, power spectra comparisons as shown in Figure 6.3, should improve.

Frequency Bands: The relative and absolute EEG powers in the delta, theta, alpha, and beta bands should show changes over the three months of recording, with an increase in power of both the alpha and beta bands, and a decrease in delta and theta waves.

Motor Assessment / ADL: All patients are speculated to improve in motor performance and ADL, with the greatest gain in the first 3 months. The experimental group is hypothesized to show a faster rate of recovery.

Clinical Relevance: A correlation between quantified EEG and clinical testing should be found.

Spectra Symmetry: To verify patient recovery, the EEG spectra should become more symmetrical over the left and right hemispheres. This can also be correlated with follow-up MRI scans to confirm the hypothesis.

As an example, Figure 6.2 shows the average power plot, together with topographic maps of different frequency bands of the stroke patient that underwent a rehabilitation session. The average frequencies of the bands (2, 6, 10 and 20 Hz) were selected. The patient is shown to have very low beta and alpha frequencies, while higher powers of theta and delta (the lowest frequency) are prominent. They are linked with depressive and tiredness conditions, as well as very slow patterns. It can be argued that the right side (affected side) of the patient's brain controls the ability to pay attention, and influences the patient's sense of recognition and awareness, due to the right side having a lower density than the left side. From the five frequency bands, it can be seen that the topographical EEG spectra are asymmetrical over the left and right hemispheres, with a greater density in the left hemisphere (which can also be supported by the fact that the patient has had a right-sided stroke). Figure 6.3 shows how a comparison can be made between two channels of interest, for example AF_3 vs. AF_4. The power density of AF_3 (left) is more than that of AF_4 (right), which corresponds to the asymmetric power distribution.

6.3   Medical Relevance

The medical relevance of the results of the observational study can be contributed to the fact that the rehabilitation device is a reliable and feasible source of sensory feedback. The fact that three different types of Event-Related Potential stimuli were accurately identified, contributes to the fundamental purpose of sensory rehabilitation, i.e. utilizing neural plasticity mechanisms (sensory stimuli) to aid in the recovery of somatosensory function after stroke. This feasibility of the device shows that it is practicable to use it to rehabilitate cognitive and sensory-motor functions through repetitive motor activities and decision-making events.
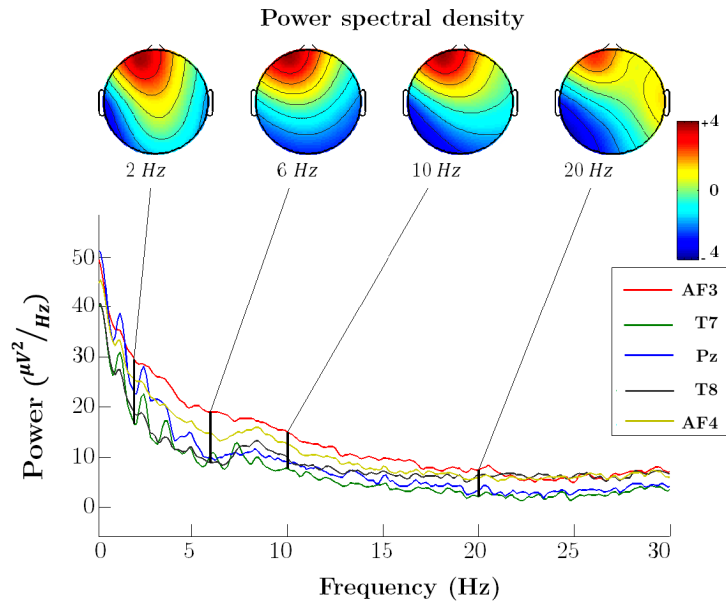
6. DISCUSSION

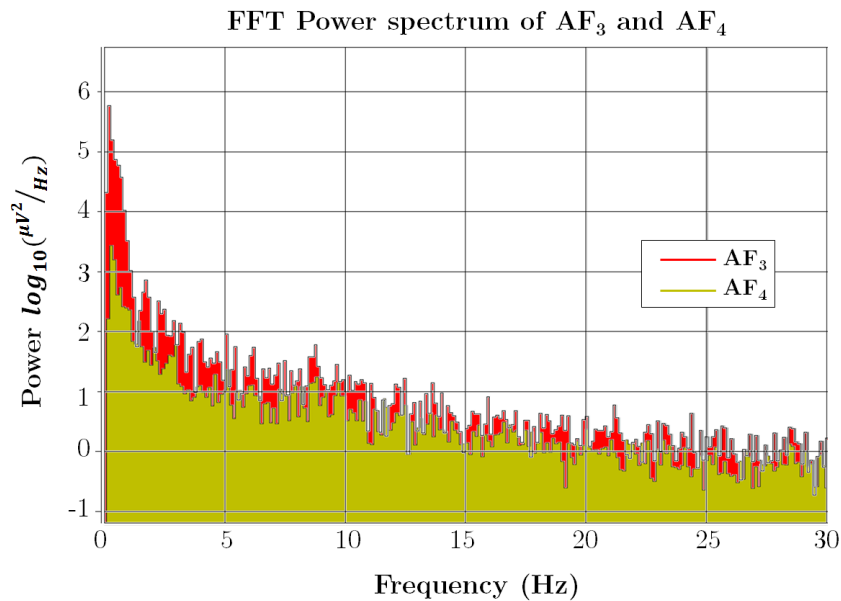**Figure 6.2:** EEG channel spectra and maps of the stroke patient

Figure 6.3: EEG channel spectra of AF_3 and AF_4 after FFT

The observational study revealed that the feedback component can be used to influence EEG measurements of Event-Related Potentials (ERPs) in order to detect, identify and initiate external stimuli, and to replicate the ERP characteristics of previous ERP studies. This observation of accuracy implies that ERP experiments can be conducted in relation to a neurorehabilitation program. During the research phase, some practical and economical concerns raised towards stroke recovery programs in developing countries were addressed. Even though the scope of the observational study did not extend to a consideration of the influence of the prototype on the recovery period of

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stroke patients, the design thereof still included the construction of a device aimed to be potentially cost-saving, that provides a solution to the lack of services of therapists, as well as addressing the patients' inability to access the stroke rehabilitation centers. The following areas of interest may assist with the solutions to these concerns:

Accessible The ease of access of the device allows it to be used at home without the constant guidance or presence of a therapist. It will be portable, easy to charge once the batteries are depleted, and the raw data acquired from the EEG device will be easy to convert on a computer to be interpreted by a professional. Since it will be easy accessible, it may benefit patients being cared for in stroke units in the acute stage (i.e. an earlier stage than usual).

Ease of use The device was developed to be used before and/or during rehabilitation programs. As mentioned, a user manual was set up specifically for rehabilitation sessions of stroke patients. As a result of its ease of use functionality, it was tested and operated by two different physiotherapists after the observational study, and an operator other than the principle investigator, and no problems or misunderstandings of the specific operating procedures were reported.

Therapy service From Chapter 4, two experimental phases were conducted at 15-minute intervals. This results in a 30 minute therapy session for each individual. When considering the time physiotherapists need to spend with patients, one such an additional therapy session may prove to relieve the, discomfort and possible morbidity that usually result from excessive medical and/or physical treatment. The proposed device may reduce these factors in the long run, as training and rehabilitation require minimal interaction with the therapist, and zero medical treatment. This could then benefit both the patient, and physiotherapist.

Cost-Saving In the future, repetitive sessions of this rehabilitation device may result in a decrease in the frequency of patient-therapist interaction, which could then decrease the costs involved in post-stroke rehabilitation programs.

Medical Contribution The device combines therapy methods used by physiotherapy and neurorehabilitation sessions. It is solitary in type to its value and contribution to research in the field of stroke therapy. Typically, stroke patients undergo core muscle skill therapy, with no sensory feedback mechanisms present. This device can address more specific muscle groups on certain limbs, and provide additional stimuli during therapy sessions in order to aid in sensorimotor recovery. Similar devices that can be used as such in the clinical setting, do not exist yet.

6.4   Limitations

The possible limitations to the investigation imposed by time and financial constraints entailed the interaction the principle investigator wished to achieve with stroke patients during the clinical trial. Financial constraints were also limitations in the course of this project. Therefore it was important to run a full assessment regarding the cost analysis of this project. This included the expenses regarding engineering labour, the cost of components and additional running costs.

A final limitation was to obtain enough data from enough samples. Recorded data cannot be analyzed sufficiently for statistical purposes if only a few post-stroke patients were tested. There were various factors that contributed to motivation regarding the small/limited sampling size of the patients:

- Access to a **limited sample population**: Due to the area the project formulation and execution took place, it was difficult to obtain enough patients in a certain radius that had the same diagnosis as required.

- **Testing time**: All ethical aspects of this project needed to be proactively addressed and ethical approval from the HREC had to be obtained. The testing phase only occurred after research approval was given - this was a parallel phase in the project formulation. It ran independently from the main objectives and needed to be approved by the Tygerberg HREC.

- **Limited funds**: This project was funded by Public Funds, and the National Research Foundation during the two consecutive years of the degree. The Public Funds needed to be discussed with the Director of the Technology Transfer Office (TTO) in Stellenbosch, as well as the National Intellectual Property Management Office (NIPMO). These companies were obliged to comply with the national legislation on Intellectual Property. The specific funds during 2015 were, therefore, limited and influenced the amount that could be spent on the components and capital costs of this project.

- **Proof of concept study**: The Tygerberg HREC decided the maximum sampling size according to the feasibility of the project proposal. This could therefore only be determined after approval had been given, which was 2 December 2015.

- **Limited time for study**: The time to complete the research was limited to the degree of study. The estimated completing time for a normal Master's degree in Research is 24 months. The testing phase could therefore only be a certain length.

Chapter 7

Conclusion

This document served as the thesis for a master's project in Biomedical Engineering. This project covered the design and construction of a sensory feedback prototype to serve as a possible future rehabilitation device for MCA stroke victims, with the aid of the concept of neuroplasticity. In summary, the design itself comprises a wearable device and all of the mechanisms necessary for its feedback control and reactive behavior. The device interacts with an EEG headset, which enables an operator to monitor and assess the wearer's EEG activity during feedback sessions on a specific limb.

After an introduction and literature study containing information about the human nervous system, the specified stroke and its methods of rehabilitation, and after the evaluation of current designs similar to the proposed design, the objectives, assumptions, and initial engineering specifications were provided to the reader, as well as a clearly stipulated method of experimentation and results. All of the planned activities that had to be done before the completion of the project, were discussed. All of the objectives necessary to adhere to the project aims were successfully completed. This included the mechanical design and construction of the prototype, the execution of an observational study and the practical demonstration of the feasibility of the device using adequate healthy test subjects.

Due to time constraints, one of the objectives (i.e. conducting a clinical trial study in order to evaluate possible neuroplasticity of stroke patients' cognitive functions) was not possible to achieve, though several recommendations and approaches to achieve this objective were discussed thoroughly.

7.1   Aims

The aims identified to successfully complete this project are discussed below:

Aim 1: A wearable prototype was successfully designed and constructed. This prototype uses two different methods of sensory feedback: haptic feedback (vibration) and visual feedback (through the use of LEDs). From the literature review, the methods used during the experimental sessions

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were similar to those used during neurorehabilitation and physical therapy sessions for patients with ischemic stroke. As with a neurofeedback training session, the operator has interacted with a subject using different feedback examples. And as with physiotherapy sessions, subjects were asked to move their lower limbs of their arms during sessions.

Aim 2: The feasibility of the prototype was thoroughly tested by obtaining electrobiological measurements (ERPs and EEG data) of healthy subjects through an observational study. The ERP results were compared with previous studies, and their accuracies were discussed.

Overall, the different types of feedback provided by the prototype were proven to be sensed and analyzed by the EEG headset as different electrobiological potentials. The feedback was accurately measured as three discrete Event-Related Potentials, and thus resulted in a successful solution to the research question.

7.2 Contribution to the field

This project may benefit both patients who have suffered MCA stroke, as well as their corresponding physiatrists, doctors, and/or physiotherapists. This means the patient may either improve in movement and level of independence or, in the long run, show that neuroplasticity through sensory stimulation therapy can be achieved by devices that are easily accessible, easy to use, decrease patient-time engagement and possibly result in cheaper alternatives for post-stroke rehabilitation devices. Consequently, the mentioned medical practitioners will benefit from this project by being able to sell or recommend the device to their patients. This would ensure the distribution and effectiveness of the device as a medical product.

By continuing the planned course of methodology for the proposed clinical trial, EEG results may reveal focal abnormalities that are undetected by coarse clinical evaluation, monitor mechanisms of local repair and also to detect changes in the affected and unaffected hemispheres of stroke patients.

7.3 Recommendations

7.3.1 Prototype Design

The current prototype uses wired USB connection in order to transfer feedback data to a computer. It could potentially benefit from a transmitter that relays wireless information. When it contains a microprocessor that constantly correlates feedback with measured brain activity, it can relay this information to the patient's physiatrist or doctor via wireless communications, which means that data can be transferred instantly and across great distances. This would

allow the physiatrist/doctor to interact with the patient in a mobile, flexible and convenient way.

It is recommended that an EEG device with more channels should be obtained to result in more conclusive EEG evidence, although this will cause an increase in project costs.

7.3.2   Clinical Trial

Obtaining more stroke patient sources would have also contributed to a better sample size for rehabilitation during the clinical trial. As part of future research, the rehabilitation device can be used as part of neurorehabilitation programs to provide support for neuroplasticity. Future results may indicate that low-cost alternative rehabilitation techniques are possible in their use for recording and analyzing EEG feedback in stroke victims, and can contribute to the results of previous ERP studies on MCA and other stroke patients.

In addition, the permission was given to implement the device in a 3-month rehabilitation program undertaken at the Cape Gate Mediclinic (Cape Town, South Africa), where stroke patients will complete weekly sessions of rehabilitation. Finally, as a research tool, the device can be used to monitor the time it takes on average, for a stroke patient to show signs recovery after a stroke, and to optimize stroke rehabilitation programs.

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Appendices

Appendix A

User Manual for Rehabilitation Sessions

A.1   Session Preparation

For each 15 minute session, certain preparation steps, procedures and methods are repeated. During sessions that can not be conducted by the principle investigator, accompanying therapists are urged to use this user manual that was specially compiled for the project. The following check-list is necessary to conduct a rehabilitation session:

1. ***Emotiv* EEG headset**

2. **Visual & Vibratory Feedback Device** This device (henceforth referred to as the "rehabilitation device") is the final chosen concept

3. **Windows 7 compatible Laptop / Computer**

4. ***Emotiv Xavier* Controlpanel 3.1.19 (build 200):** The *Emotiv* Control Panel is a software that allows the user to monitor the status and features of the *Emotiv Insight*. After cognition detections during training are mapped to keystrokes using *Emokey*, users calibrate their focus and training with each of four different driving commands. The users should each be instructed to train their "Left" and "Right" skills in order to activate the vibration motors in those directions. It is recommended to consider using "Lift" and "Drop" as replacements for "Push" and "Pull" respectively for the top and bottom vibration motors, as being able to move the cube up, down, left, and right makes for a more useful mental model for general 2D cursor GUI control.

5. ***Emotiv Xavier* Testbench 3.1.19:** Data collection will take place in real time, while the subject wears the *Emotiv Insight*. The *Emotiv* Testbench runs as a background process on your computer. Any EEG recorded data will then be exported to *Excel* compatible csv. format.

6. **Emotiv Insight Emokey:** The *Emotiv EmoKey* program is used to receive detections from the EEG Headset via the *Emotiv* Control Panel in real-time, or pre-scripted detections from the *EmoComposer* utility. *EmoKey* translates these detections into keystrokes which are issued to the interface through *PuTTY*, for activating the different vibration motors worn by the user.

7. **Putty:** *PuTTY* is an Secure Shell (SSH) and Telnet client, developed originally by Simon Tatham for the *Windows* platform. The use of *PuTTY* in this manual is for picking up the keystrokes that are pressed on the keyboard, or to detect Serial Data that is transferred by *Emotiv Insight Emokey*, and relay that information to the microcontroller of the rehabilitation device.

Figure A.1: Preparing for the Rehabilitation Session

A.2 Device Setup

A.2.1 Battery Check

Before starting the training sessions, the *Emotiv Insight* headset must be switched on and it should be verified that the built-in battery is charged and is providing power. If the headset battery needs charging, the power switch should be set to the **off** position and plugged into the laptop / computer, using the mini-USB cable provided with the headset.

Next, the battery level indicators on the rehabilitation device must be checked. This can be done by switching the two middle interface toggle

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switches (Figure A.2) to the **on** positions. The indicators (Figure A.3) then indicates the voltage levels of the batteries. If the rehabilitation device needs charging, the switches should be set to the **off** position, after which the mini-USB cable provided with the device should be plugged into the battery charger ports on the side, and into a laptop / computer.
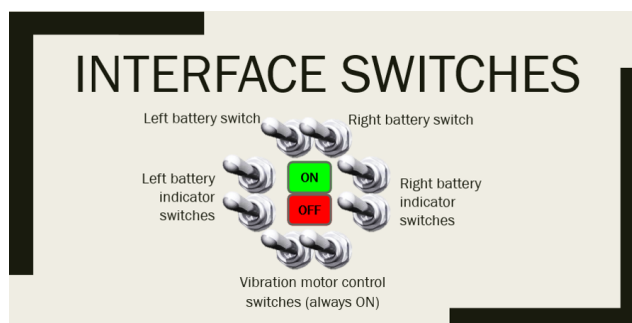
Figure A.2: The Interface Switches
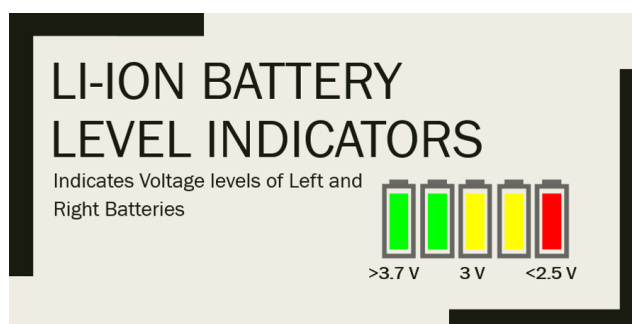
Figure A.3: Battery Level Indicators

A.2.2 Setting up the Device

The device can now be set up for each patient. The following steps must be followed before starting a training session:

Step 1: Hydrate the Sensors Assemble the headset (refer to Figures 2.3 and 2.4). Fully saturate the felt pads using saline solution. When the headset is placed on your scalp, the pads should feel wet.

Step 2: Put on Headset Place the headset on the patient's head (see Figure A.6) and make sure good contact is made by the EEG electrodes on the scalp of the operator.
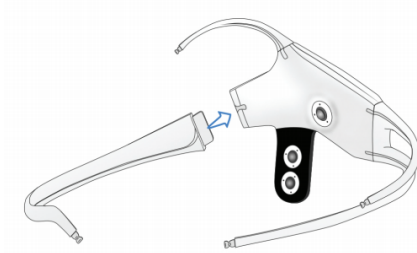
Figure A.4: Assembling the *Emotiv* (a)
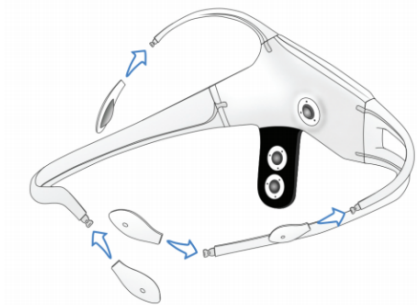
Figure A.5: Assembling the *Emotiv* (b)

Step 3: Position Electrodes Position the reference sensors to touch the skin behind the ear. It is critical that the reference sensors make contact with the skin behind the ear.
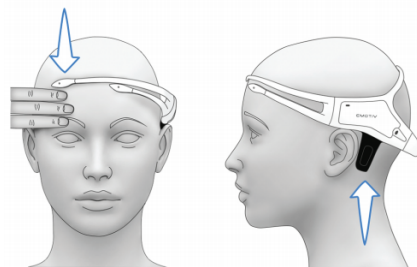
Figure A.6: Positioning Electrodes

Step 4: Insert Dongle Plug the dongle into your device's USB port. When a headset is paired, the indicator light should flicker rapidly (Figure A.7). If it is blinking slowly or is not illuminated, reinsert the dongle and try again.

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Paired
The second LED will
be lit,and the LED
above
the power symbol
becomes fainter
and
flickers rapidly.

Figure A.7: Reading Dongle Status

Step 5: Launch Software On your Laptop / Computer, launch *Emotiv Xavier* Testbench, *Emotiv Xavier* Controlpanel, *Emokey* and *PuTTY*.

Step 6: Turn on Headset The power switch is at the rear of the headset. A light indicates when the headset is on.

Step 7: Verify Signal Quality Verify that the Wireless Signal reception is reported as Good by looking at the Engine Status box in the *Emotiv Xavier* Controlpanel. If it is not, make sure that the *Emotiv Insight* SDK Dongle is inserted into a USB port on your computer and that the single LED on the top half of the dongle is on continuously or flickering very rapidly.

A.3   Training Sessions

The rehabilitation sessions are divided into three different phases:

1. Algorithm Training

2. Vibratory Feedback Training

3. Visual + Vibratory Feedback Training

A.3.1   Recording EEG data

Each training phase is executed in parallel with the *Emotiv Xavier* Testbench software. Before initiating a training phase, a new recording session in the *Emotiv Xavier* Testbench programme must be started:

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A. USER MANUAL FOR REHABILITATION SESSIONS

1. Open *Emotiv Xavier* **Testbench**

2. Click on **"Save Data"** (Figure A.8)

3. Enter the **configuration** for the output file (Figure A.9)

4. Click on "**Start**"

At the same time, the session can be recorded with a voice recording application on a mobile phone (in order to keep track of the session durations).
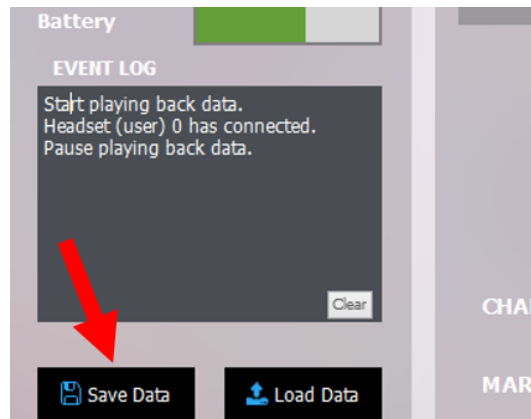
Figure A.8: Save Data
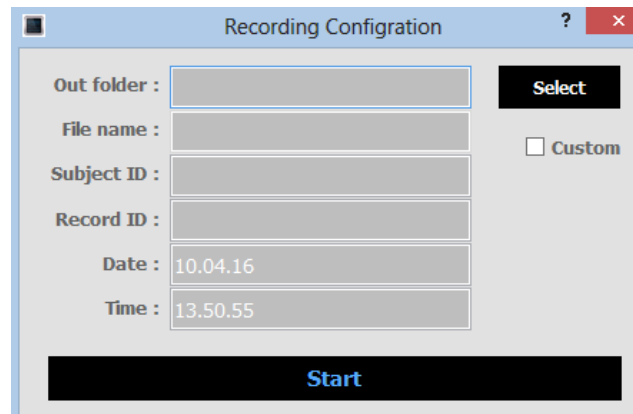
Figure A.9: Enter Configuration

A.3.2 Phase 1 - Algorithm Training

Since EEG data is being recorded, the first phase of training is ready to be executed. The following steps should be followed:

1. Open *Emotiv Xavier* **Controlpanel**

A. USER MANUAL FOR REHABILITATION SESSIONS

2. In the Controlpanel, in the top left, go to Options > Detections > **Mental Commands** (See Figure A.10)

3. Above the "Action" tab, go to Add User > Create **New Profile** and enter patient's details

4. Switch to the **Training** Tab

5. **Train Neutral** - The user will need to train the software to recognize their "Neutral" state - that is the user should sit still, and look away from the screen, clear their mind and try not to think about anything in particular

6. When Neutral training is complete, go to Options > **Calibration**

7. Train **Eyes open** and **Eyes Closed**. This is to distinguish between the Beta and Alpha brainwaves.

8. Under "Live Metrics", press **Start Recording**

9. Go back to Options > Detections > **Mental Commands**

10. Under "Action", add **Left** and **Right** directions

11. **Train** these directions. Once trained, the software will attempt to detect the difference which occurs in the user's brainwaves between the neutral state and the patterns which occur when the user thinks about moving the box.

12. If the patient struggles to concentrate, change **sensitivity** if necessary (Under the "Advanced" tab)

13. Under "Challenge", start 3 **Challenges** for the trained directions (1 minute each)

14. Do the same for **Lift** and **Drop**

A.3.3   Phase 2 - Vibratory Feedback Training

In the second phase of training, more or less the same procedures are followed as in the first phase, but instead, the patient receives feedback via the vibration motors. Hence, the wristband of the rehabilitation device should be strapped to the wrist of the patient. Placement of the motors must be according to Figure A.11 (U = Up, D = Down, L = Left, R = Right).

The following steps should then be followed:

1. First of all, connect the **USB cable** of the rehabilitation device to the laptop/computer

A. USER MANUAL FOR REHABILITATION SESSIONS
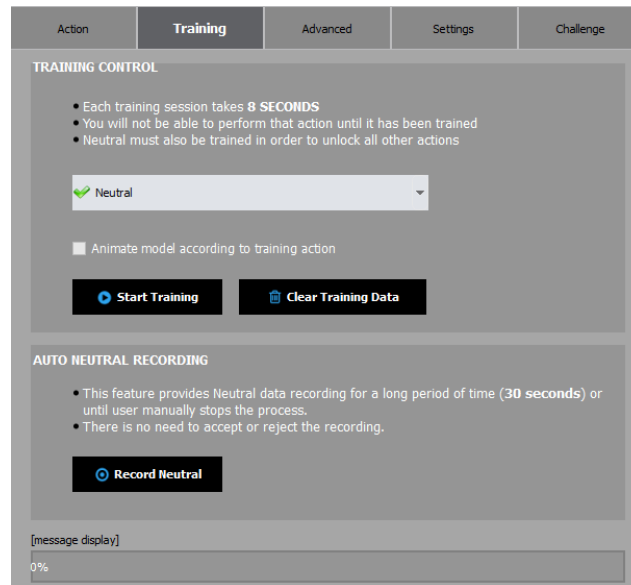
Figure A.10: The Mental Commands Window
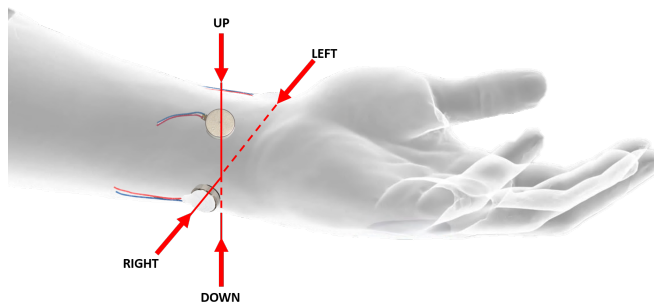
Figure A.11: Positioning the Motors

2. **Turn on** the rehabilitation device by turning all the toggle switches in the "up" positions (See Figure A.2)

3. Next, take note of the COM port port that is in use. To do this, use the following steps:

   - On the **keyboard**, press ⊞ + R to open the shortcut menu (command prompt)

   - In the **search** box, type in "mmc devmgmt.msc" (See Figure A.12)

   - Press **OK**. Go to Ports (COM & LPT), and view the Arduino Micro port to see the Component Object Model (COM) number

4. Keep the ***Emotiv Xavier* Controlpanel** and ***Emotiv Emokey*** open

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A. USER MANUAL FOR REHABILITATION SESSIONS
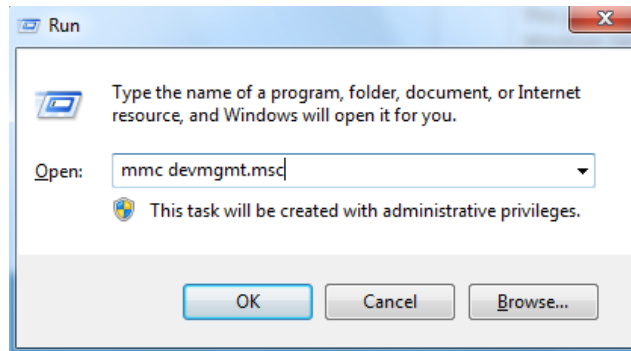
Figure A.12: Accessing Device Manager through Command Prompt
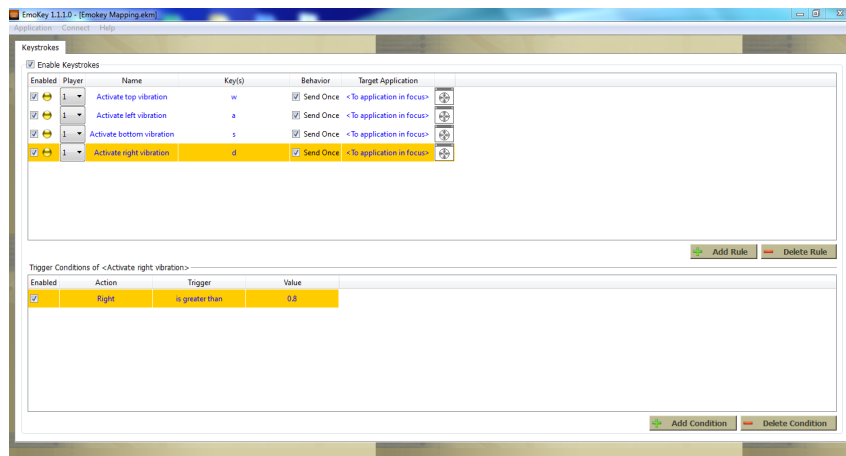
Figure A.13: *Emokey* Mapping

5. In the *Emokey* menu, load the **mapping file** (See Figure A.13), by going to Application > **Load Mapping.** The directory of the mapping file will be on the desktop of the computer. The file is called "*Emokey Mapping.emk*".

6. Open the **PuTTY** window

7. In the **PuTTY configuration**, select the correct serial line (COM port number from Step 3) and Speed (Baud rate Rate = 9600) for the *Arduino Micro* (See Figure A.14) > Click **Open**

8. Next, the **PuTTY Serial Monitor** will open. In the *Emokey* window, double-click on "Target Application" for each command and select the target as the Serial Monitor using the "Window Pick" function shown in Figure A.15 > Click on **Apply**. The training can now start.

9. Open the Control Panel and, again, commence Challenges for all directions. Now, the user will feel the feedback on his/her arm during each Challenge.
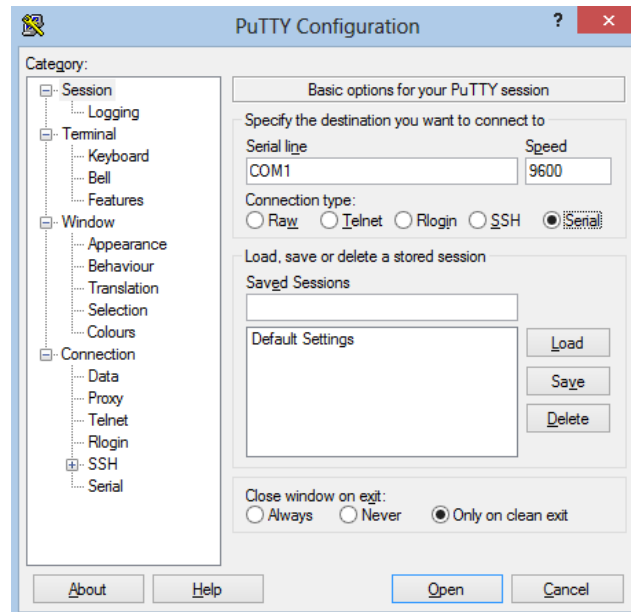
Figure A.14: *PuTTY* Configuration
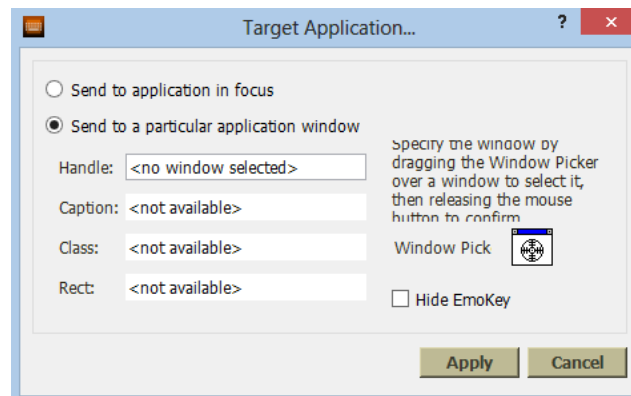
Figure A.15: Window Pick Function

A.3.4   Phase 3 - Vibratory and Visual Feedback Training

In the third and final phase of training, the instructor should indicate different sequences in which the vibration motors will vibrate. The goal is for the patient to constantly monitor the LED push-buttons on the device, to ensure visual feedback. For each sequence, the patient should be instructed to try and mimic the directions specified by the instructor, e.g. When the instructor says "Left", the input for the left vibration motor is pressed simultaneously (by the instructor), after which the patient should try to move his / her hand in said direction. The following keystrokes are assigned to each direction:

"Left" = A

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"Right" $=$ ⎡D⎤
"Up" $=$ ⎡W⎤
"Down" $=$ ⎡S⎤

The following steps should be followed for the third and final phase:

1. Keep the **_Emotiv Xavier_ Controlpanel**, **_Emotiv Emokey_** and **_PuTTY_** windows open

2. Instruct the patient to **monitor** the LED push-buttons on the rehabilitation device

3. Next, execute a number of **sequences** according to Table A.1

4. For each sequence, the patient should try and **mimic** the directions specified by the instructor, by moving his/her hand in the direction that illuminates on the device.

Table A.1: Sequences for Phase 3 Training

Sequence Type	Keystrokes
Horizontal	⎡A⎤ , ⎡D⎤ , ⎡A⎤ , ⎡D⎤
Vertical	⎡W⎤ , ⎡S⎤ , ⎡W⎤ , ⎡S⎤
Sequential	⎡A⎤ , ⎡W⎤ , ⎡D⎤ , ⎡S⎤
Random	⎡A⎤ , ⎡D⎤ , ⎡S⎤ , ⎡A⎤ , ⎡W⎤ , ⎡A⎤

A.4   Ending the Training

After the three phases have been completed, all that remains is to stop the recording of the EEG data in the sessions:

As with the training phases, the following steps are executed in order to finish the training:

- The first recording session is in the _Emotiv Xavier Testbench_ programme:

  1. Open **_Emotiv Xavier_ Testbench**

  2. Click on the Recording Configuration (Figure A.8) and **Stop** the recording.

  3. Under Options > **Tools** > Launcher EDF to CSV Converter, be sure to save the CSV file in the same directory as well.

- The next session is in the _Emotiv Xavier Controlpanel_ programme:

1. Open *Emotiv Xavier* **Controlpanel**

2. Go to Options > **Calibration** > Under "Live Metrics", press **Stop Recording** session > View Report > Screenshot

- Finally, stop the recording session on your phone.

You have now successfully completed the rehabilitation training!

Appendix B

Concept Development

This appendix contains all necessary data that was complimentary to the mechanical development of the rehabilitation device and the rest of the mechanical aspects presented in this thesis. It discusses the mechanical concept development process and it contains the assembly drawings for some of the proposed prototype designs of the concepts that led to the choosing of the final concept.

B.1   Concept Generation

This section explains the concept generation process. A brief overview of each of the concepts that were generated will be given. This includes a description, summary, and figures of each. The images shown to display the concepts are all designed and generated in *Solidworks Professional$^{®}$ 2014)*.

B.1.1   Concept A

Components:

- Tuff-Luv Universal Sports Armband
- Piezo Vibration sensor
- Muscle Sensor Kit (EMG sensor)
- Vibration motors

The first concept design is shown in Figure B.1. Concept A comprises a design that acts as the prototype for an EMG-based system. It shows the wearable device, containing all the proposed components that were necessary to sense and process the movements of the patient. The electronic design of the microprocessor was initialised afterward. Other components (chargers, sensors, storage shield, etc.) were ordered from catalogs early enough to be available for the testing stage.

TuffLuv **Universal Sports Armband**   This sports armband was perfect to use as a means to keep all the sensors together. *TuffLuv Uni-Sex Uni-*
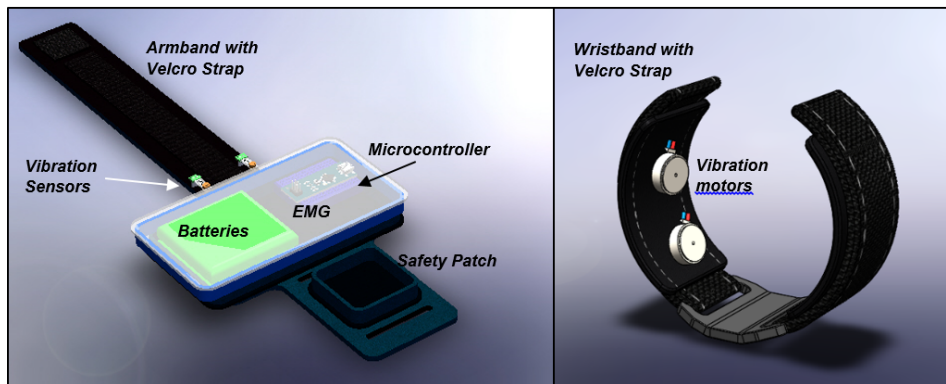
B. CONCEPT DEVELOPMENT

Figure B.1: Concept A components: Armband (left) with Wristband (right) (Source: *Solidworks Professional 2011*)

versal Sports Armband and Sportsband (TuffLuv, Weybridge, England) is an adjustable removable pouch for Smartphones. The idea was for the device to be accessible while using the armband. This particular armband was ideal, because this meant the controller and all the sensors could be inserted into the safety patch (which is secured with a Velcro function). The muscle sensor electrodes could also have been attached to the inside of the armband, which would then allow for direct contact with the skin of the patient.

The large clear plastic window supplies the user with complete visibility, which could have been used to make sure all the components were in working order, and also to keep track of the battery power indicators. The additional removable pouch on the side of the armband would have allowed for extension cables to be stored (like the charger and the USB access cable).

***Piezo* Vibration sensor**   During calibration of the patient's body part movements and exercises, it was necessary to determine certain thresholds to the extent to which the patient can move his or her body parts, like an arm that flexes its biceps. In order to compare these movements to that of an uninjured person, it was necessary to have some kind of sensor to measure each maximum level per patient.

The *Piezo* Vibration Sensor was ideal for this. This type is a low-cost cantilever-type vibration sensor that is loaded by a small mass to offer high sensitivity at low frequencies. The machine pins on the sensor allow for horizontal mounting, making it perfect to fit into the armband. It has a wide dynamic range, giving the candidate the perfect opportunity to specify a certain threshold to which the sensor needed to respond.

Muscle Sensor Kit   The Muscle Sensor Kit that was part of the first concept contains an EMG circuit and sensor that picks up any action potential generated by the patient's muscle activity. This sensor measures the filtered and rectified electrical activity of a muscle after which it outputs a voltage in

the range of 0-5 Volts, depending the amount of activity in the selected muscle. The kit also includes 60 cm cable leads and the necessary surface electrodes.

Shown in Figure B.2 is the proposed concept of both the armband (now enclosed on the upper right arm) and the placement of the wristband. Concept A was planned to be worn in such a way that the extension and flexion of the arm, as well as the external and internal rotations, were monitored. This design was then created in *Solidworks* (Figure B.3), with the placement of the EMG surface electrodes.
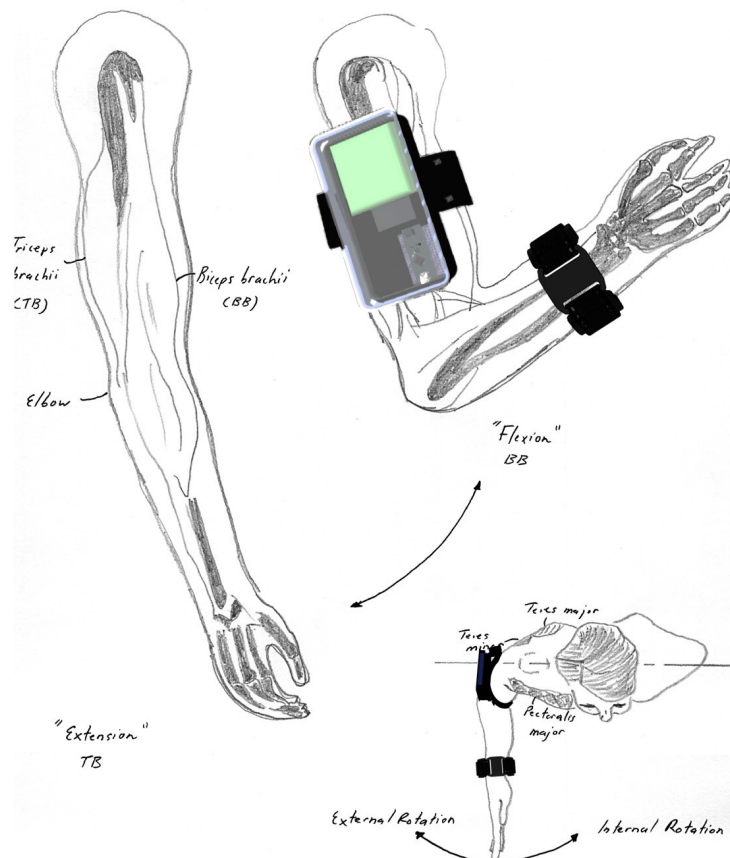
Figure B.2: Position of the proposed design of Concept A

B.1.2 Concept B

Shown in Figure B.4, Concept B is an amendment made to the first concept of both the armband (now enclosed on the upper right arm) and the placement of the wristband. Here, the factor of aesthetics was incorporated and combined with Concept A. The controller unit and batteries, as well as the wiring could then be disclosed and hidden from view, which would have given a neat appearance. Figures B.5 to B.8 show the design process of Concept B.

B. CONCEPT DEVELOPMENT
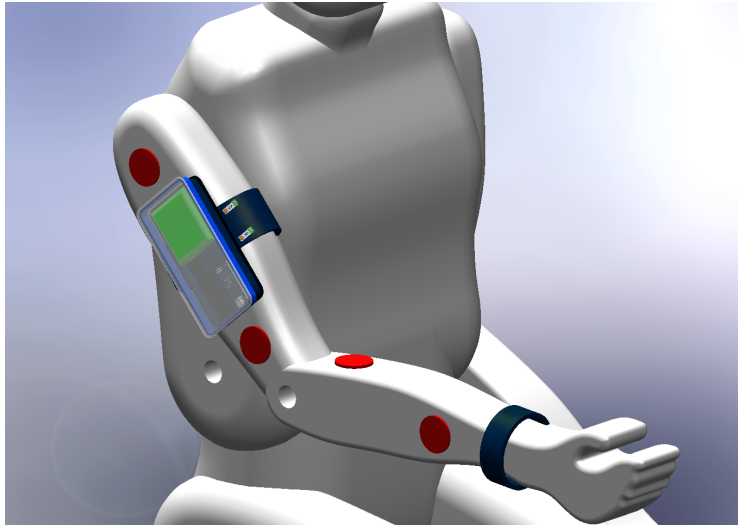
Figure B.3: *Solidworks* design of Concept A on patient

B.1.3 Concept C

Added components:

- Micro SD shield
- SD adapter and Card

Concept C was brought into consideration owing to the fact that the previous concepts lacked storage media.

The best way to record all the muscle activities of the patient was to store it, either by wired storage or via wireless communication. The most cost effective way to achieve this was to make use of a Micro SD shield. When soldered onto the correct pins of the *Arduino Micro*, the SD Shield equips the microcontroller with mass-storage capability, which meant that it could be used for data-logging.

The reason this storage was planned to be used was mainly to keep track of the muscle activity data, but also to allow the patient to store his / her activities independently of a physiatrist. Activities can be downloaded to a personal computer and then uploaded to an online drive (with adequate internet connection), to be accessed by the specific patient's physiatrist. To accompany the shield, an 8GB Micro SD card with an SD adapter was added for storage.

B.1.4 Concept D

Added components:

- Infrared Sensor
- Accelerometer
- *Emotiv* Headset

B. CONCEPT DEVELOPMENT

Figure B.4: Position of Concept B (wiring and electrodes not included)

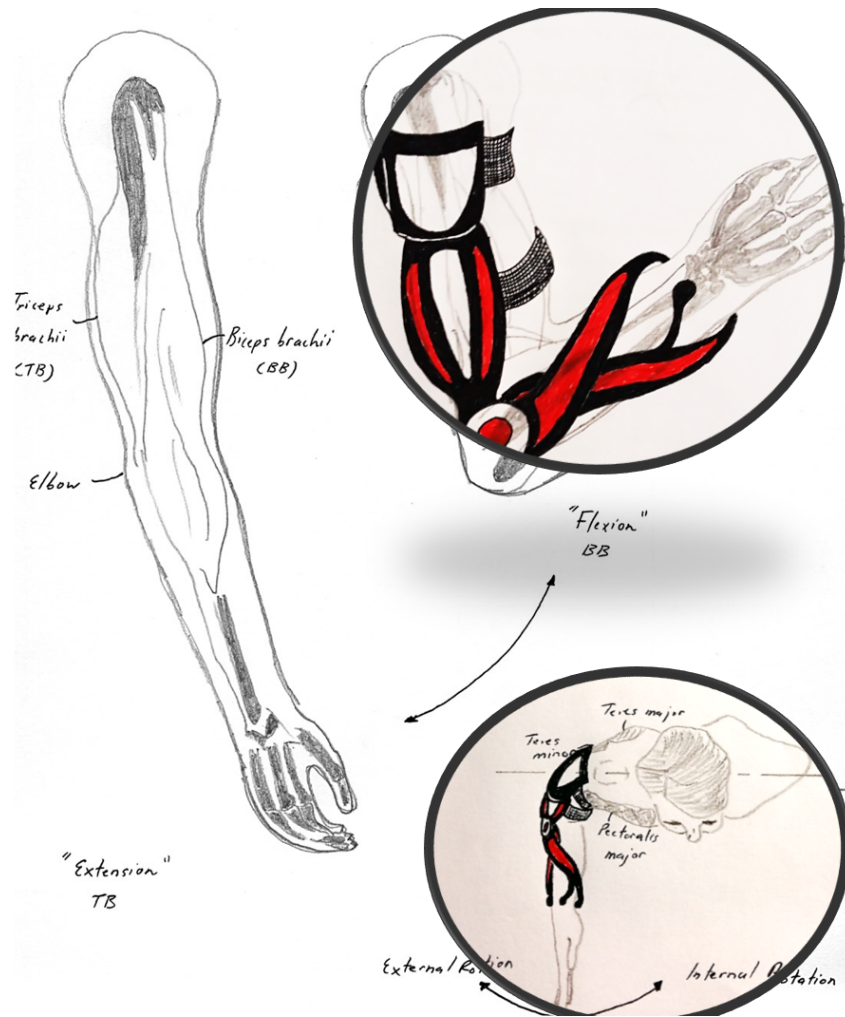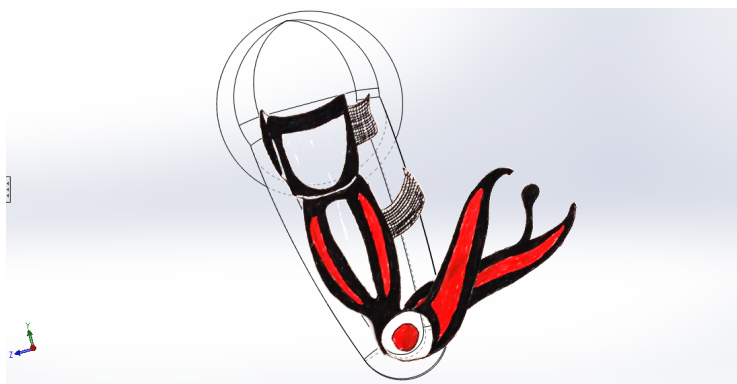**Figure B.5:** Reverse Engineering design of the sketch

Ease of access was required after the design for the third concept was finalized. As part of the project motivation, the goal was for the patient to use, understand and assemble or configure the device with ease, however, the goal

B. CONCEPT DEVELOPMENT
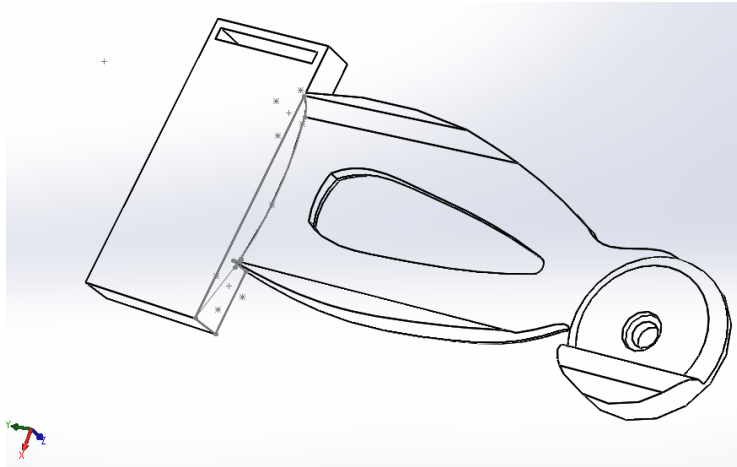
Figure B.6: Design of lower part of device
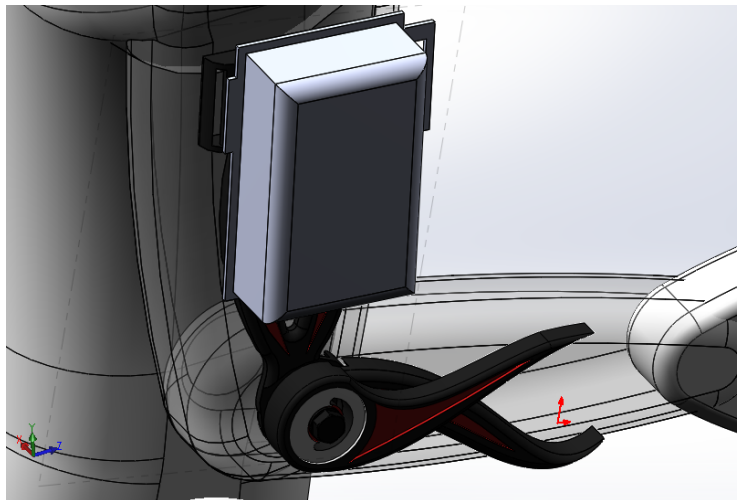
Figure B.7: *Solidworks* design of Concept B on patient

was also for the device to reduce the invasion of privacy involved in cognitive rehabilitation therapy or physical therapies. Physical contact and constant monitoring were planned to be reduced by incorporating a remote control feature using an infra-red sensor, which could be controlled by an infra-red remote. The *NEOMART Raspberry Pi HX1838* Infrared Remote Control IR Receiver Module Kit was bought and constructed. This was controlled by an *Arduino* IR Remote. Another component that was planned to be used as an input to the system was an *ADXL335* Accelerometer.

Overall activation of the vibration motors was planned to be obtained through two separate inputs: (1) Activation from the accelerometer, worn on the left wrist and (2) Activation from the *Emotiv Insight*, worn on the patient's head. Manual activation of the vibration motors will be acquired through the use of input received from an accelerometer worn on the left arm. The interface circuit connects between the *Arduino*'s digital pins and the wires of the vibra-

110
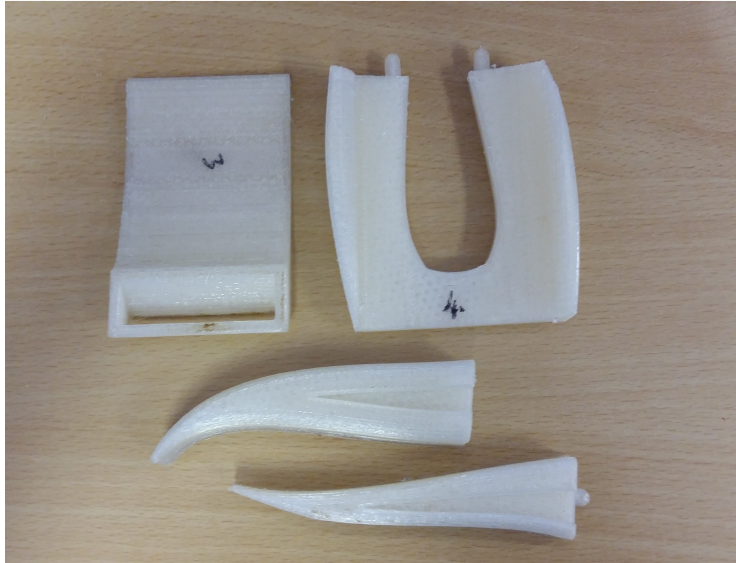
Figure B.8: Some of the 3-D printed parts for Concept B

tion motors. When the *Arduino* receives a command from the accelerometer (i.e. when the unaffected arm of the patient is moved), the vibration motors will activate. When the *Arduino* receives a command from the computer (i.e. through the *Emotiv Insight*), it causes the circuit to "fool" the vibration motors into thinking that the operator has moved the accelerometer, hence also activating the vibration motors.

B.1.5   Concept E

Final Concept:

- *Emotiv* Headset
- Vibration motors
- Serial Input
- Neurofeedback

Finally, the concept that was eventually used in the therapy sessions was constructed by combining some of the components of the previous concepts. This concept was chosen mainly because of its long operating time. The *Emotiv* has an internal Lithium Polymer battery that has 4 hours minimum run time, and the rehabilitation device can be operated for at least 2 hours before a recharge is needed. The following tests were run, followed by changes to the device's programming in order to have it perform optimally:

Battery life: The device was operated as part of full-length (15-20 min) sessions until the batteries were drained. Notes were taken on the battery life, and how often a recharge was needed. The duration of a recharge was also noted and corroborated in Appendix B.

B. CONCEPT DEVELOPMENT

Dimensions: The final dimensions of the device were measured, and packaging for transport and safety of the device was obtained. The device with all its components, EEG headset, battery chargers and USB cords all fit into a 48cm *BIG JIM* Toolbox, which is sturdy enough and easy to carry around.

Ease of use: At this stage, the final concept of the prototype was evaluated and adhered to the engineering specifications. The prototype was evaluated on the basis of the guidelines provided in Table 3.1 and the main objectives provided in Chapter 1.4. The device was assessed on its ease of use by the principle investigator, and also given to physiotherapists and stroke patients to assess by asking whether the device is comfortable.

Appendix C

Datasheets

C.1 *Arduino Micro*

Arduino Micro

A000053

Arduino Micro Front

Arduino Micro Rear

Overview

The Arduino Micro is a microcontroller board based on the ATmega32u4 ([datasheet](#)), developed in conjunction with [Adafruit](#). It has 20 digital input/output pins (of which 7 can be used as PWM outputs and 12 as analog inputs), a 16 MHz crystal oscillator, a micro USB connection, an ICSP header, and a reset button. It contains everything needed to support the microcontroller; simply connect it to a computer with a micro USB cable to get started. It has a form factor that enables it to be easily placed on a breadboard. The Micro is similar to the Arduino Leonardo in that the ATmega32u4 has built-in USB communication, eliminating the need for a secondary processor. This allows the Micro to appear to a connected computer as a mouse and keyboard, in addition to a virtual (CDC) serial / COM port. It also has other implications for the behavior of the board; these are detailed on the [getting started page](#).

Summary

Microcontroller	ATmega32u4
Operating Voltage	5V
Input Voltage (recommended)	7-12V
Input Voltage (limits)	6-20V
Digital I/O Pins	20
PWM Channels	7
Analog Input Channels	12
DC Current per I/O Pin	40 mA
DC Current for 3.3V Pin	50 mA
Flash Memory	32 KB (ATmega32u4) of which 4 KB used by bootloader
SRAM	2.5 KB (ATmega32u4)
EEPROM	1 KB (ATmega32u4)
Clock Speed	16 MHz

Schematic & Reference Design

EAGLE files: [arduino-micro-reference-design.zip](#)
Schematic: [arduino-micro-schematic-rev3b.pdf](#)

Power

The Arduino Micro can be powered via the micro USB connection or with an external power supply. The power source is selected automatically.
External (non-USB) power can come either from a DC power supply or battery. Leads from a battery or DC power supply can be connected to the Gnd and Vin pins.

The board can operate on an external supply of 6 to 20 volts. If supplied with less than 7V, however, the 5V pin may supply less than five volts and the board may be unstable. If using more than 12V, the voltage regulator may overheat and damage the board. The recommended range is 7 to 12 volts.
The power pins are as follows:

+ **VI.** The input voltage to the Arduino board when it's using an external power source (as opposed to 5 volts from the USB connection or other regulated power source). You can supply voltage through this pin.
+ **5V.** The regulated power supply used to power the microcontroller and other components on the board. This can come either from VIN via an on-board regulator, or be supplied by USB or another regulated 5V supply.
+ **3V.** A 3.3 volt supply generated by the on-board regulator. Maximum current draw is 50 mA.
+ ≜ Ground pins.

Memory

The ATmega32u4 has 32 KB (with 4 KB used for the bootloader). It also has 2.5 KB of SRAM and 1 KB of EEPROM (which can be read and written with the EEPROM library).

Input and Output

Each of the 20 digital i/o pins on the Micro can be used as an input or output, using pinMode(), digitalWrite(), and digitalRead() functions. They operate at 5 volts. Each pin can provide or receive a maximum of 40 mA and has an internal pull-up resistor (disconnected by default) of 20-50 kOhms. In addition, some pins have specialized functions:

+ **Serial: 0 (RX) and 1 (TX).** Used to receive (RX) and transmit (TX) TTL serial data using the ATmega32U4 hardware serial capability. Note that on the Micro, the **Serial** class refers to USB (CDC) communication; for TTL serial on pins 0 and 1, use the **Serial1** class.
+ **TWI: 2 (SDA) and 3 (SCL).** Support TWI communication using the Wire library.
+ **External Interrupts: 0(RX), 1(TX), 2 and 3.** These pins can be configured to trigger an interrupt on a low value, a rising or falling edge, or a change in value. See the attachInterrupt() function for details.
+ **PWM: 3, 5, 6, 9, 10, 11, and 13.** Provide 8-bit PWM output with the analogWrite() function.
+ **SPI: on the ICSP header.** These pins support SPI communication using the SPI library. Note that the SPI pins are not connected to any of the digital I/O pins as they are on the Arduino Uno, they are only available on the ICSP connector and on the nearby pins labelled MISO, MOSI and SCK.
+ **RX_LED/SS** This is an additional pin with respect to the Leonardo. It is connected to the RX_LED that indicates the activity of transmission during USB communication, but is can also used as slave select pin (SS) in SPI communication.
+ **LED: 13.** There is a built-in LED connected to digital pin 13. When the pin is HIGH value, the LED is on, when the pin is LOW, it's off.
+ **Analog Inputs: A0-A5, A6 - A11 (on digital pins 4, 6, 8, 9, 10, and 12).** The Micro has a total of 12 analog inputs, pins from A0 to A5 are labelled directly on the pins and the other ones that you can access in code using the constants from A6 trough A11 are shared respectively on digital pins 4, 6, 8, 9, 10, and 12. All of which can also be used as digital I/O. Each analog input provide 10 bits of resolution (i.e. 1024 different values). By default the analog inputs measure from ground to 5 volts, though is it possible to change the upper end of their range using the AREF pin and the analogReference() function.

There are a couple of other pins on the board:

AREF. Reference voltage for the analog inputs. Used with analogReference().
Reset. Bring this line LOW to reset the microcontroller. Typically used to add a reset button to shields which block the one on the board.

Pinout

C.2   Vibration Motors

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PRECISION MICRODRIVES™

310-101
10mm Shaftless Vibration Motor
3.4mm Button Type

Specification	Value
Voltage [V]	3
Frame Diameter [mm]	10
Body Length [mm]	3.4
Weight [g]	1.2
Voltage Range [V]	2.5~3.8
Rated Speed [rpm]	12000
Rated Current [mA]	75
Start Voltage [V]	2.3
Start Current [mA]	85
Terminal Resistance [Ohm]	75
Vibration Amplitude [G]	0.8
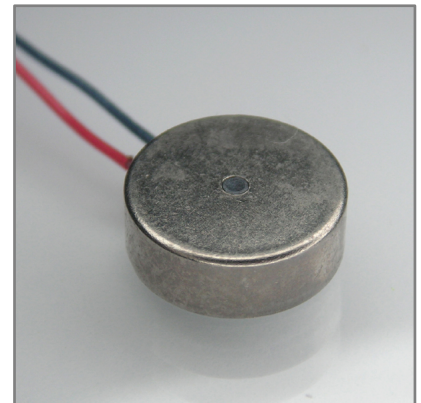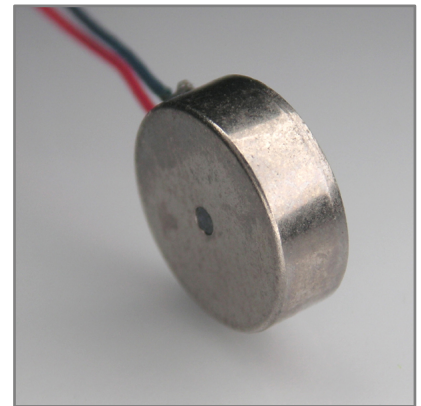
www.precisionmicrodrives.com

Tel: +44 (0) 1932 252482
Fax: +44 (0) 1932 325353
Email: sales@precisionmicrodrives.com

DESCRIPTION:

310-101.945

UNLESS OTHERWISE SPECIFIED:
DIMENSIONS ARE IN MILLIMETERS
SURFACE FINISH: N6
TOLERANCES:
  LINEAR:
    .XX± 0.01
    .X± 0.1
  ANGULAR: ±0.5°

3RD ANGLE PROJECTION

DO NOT SCALE DRAWING

DRAWING:
310-101.945

A4

REVISION:

SHEET 1 OF 1
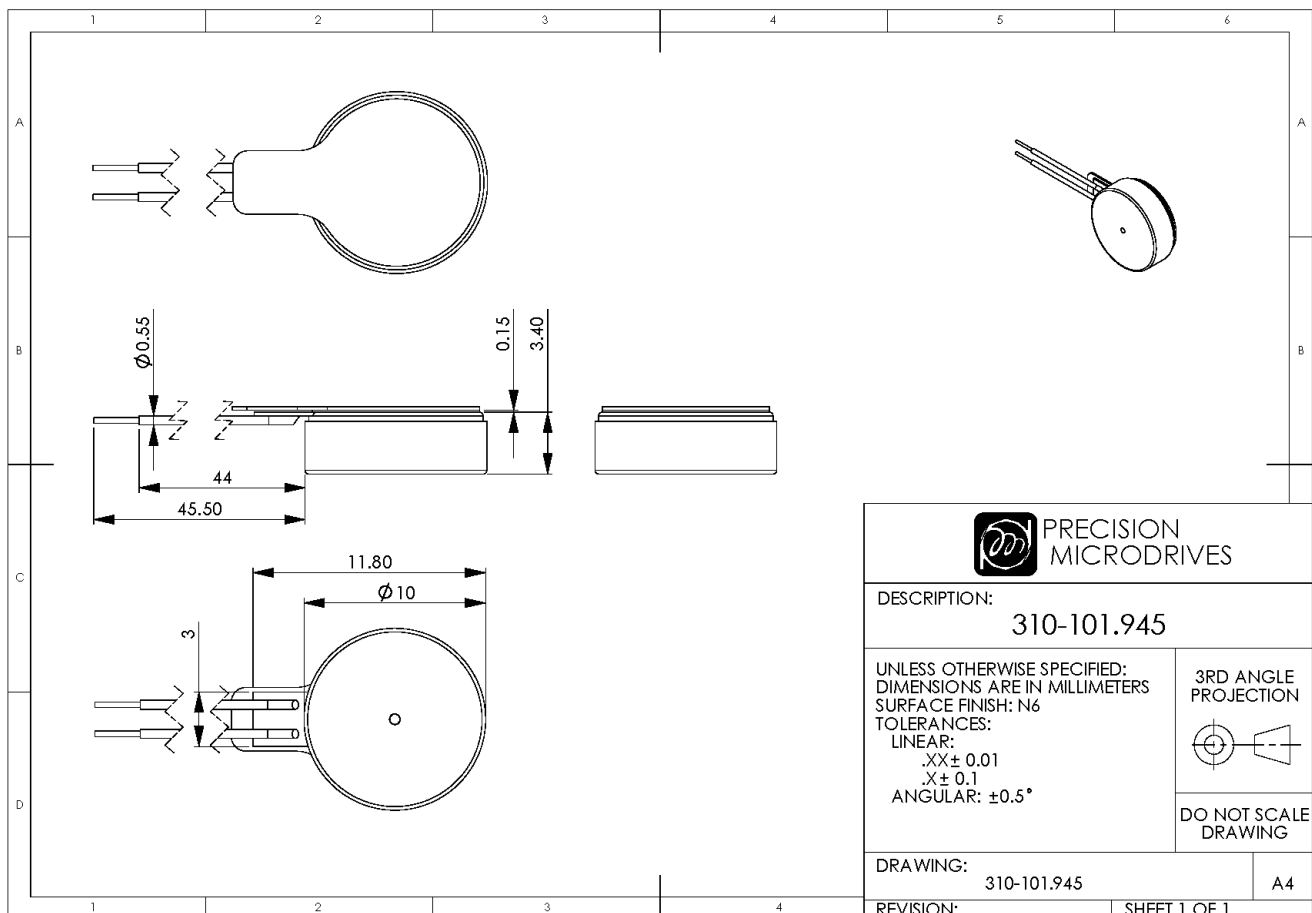
C.3   *Emotiv Insight*

Emotiv Insight
Brain Activity Tracker

A sleek, 5 channel, wireless headset that records and translates your brainwaves into meaningful data you can understand.

EDISON AWARDS

Emotiv Insight is the only device on the market that offers 5 EEG + 2 reference sensors for a higher spatial resolution that provides you with more in depth information on your brain activity.

Optimize, Measure & Create

- Optimize your brain fitness and performance.

- Measure you or your family's cognitive health and wellbeing.

- Create amazing applications with our APIs and analysis tools.

Detect Performance
Insight measures and tracks your Attention, Focus, Engagement, Interest, Excitement, Affinity, Relaxation and Stress levels.

Detect Mental Commands
Insight deciphers basic mental commands such as push, pull, levitate, rotate and hard to visualize commands such as disappear.

Detect Facial Expressions
Insight detects facial expressions such as blinks, winks, frown, surprise, clench and smile.

Sensor Technology
Insight uses a proprietary polymer sensor that offers great electrical conductivity without any preparation whatsoever.

Advanced Electronics
Insight uses advanced electronics that are optimized to produce clean, robust signals during everyday use.

Compatibility
Insight is fully compatible with Android, iOS, Mac, Linux and Windows Platforms.

Technical Specifications

Signals
5 channels: AF3, AF4, T7, T8, Pz
2 references: Left Mastoid Process

Battery
Internal Lithium Polymer battery 480mAh, 4 hours minimum run time

Wireless Data transmission
Bluetooth 4.0 LE
Proprietary wireless, 2.4GHz band

Signal Resolution
Data transmission rate:
128 samples per second per channel

Minimum voltage resolution:
0.51uV least significant bit

Ship & Release Dates

December 2014
Kickstarter Backer devices ship

Spring 2015
General release

EMOTIV

Mission
Empower individuals to understand their own brain and accelerate brain research globally.

Founded
August 2011

More Information
hello@emotiv.com
www.emotiv.com

Social Media
@emotiv
facebook.com/emotiv

C.4   Comparator

LM339, LM339E, LM239, LM2901, LM2901E, LM2901V, NCV2901, MC3302

ON Semiconductor®

Single Supply Quad Comparators

These comparators are designed for use in level detection, low–level sensing and memory applications in consumer, automotive, and industrial electronic applications.

Features

- Single or Split Supply Operation
- Low Input Bias Current: 25 nA (Typ)
- Low Input Offset Current: ±5.0 nA (Typ)
- Low Input Offset Voltage
- Input Common Mode Voltage Range to GND
- Low Output Saturation Voltage: 130 mV (Typ) @ 4.0 mA
- TTL and CMOS Compatible
- ESD Clamps on the Inputs Increase Reliability without Affecting Device Operation
- NCV Prefix for Automotive and Other Applications Requiring Unique Site and Control Change Requirements; AEC–Q100 Qualified and PPAP Capable
- These Devices are Pb–Free, Halogen Free/BFR Free and are RoHS Compliant
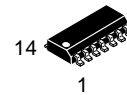
SOIC–14
D SUFFIX
CASE 751A

14
1
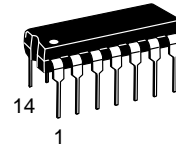
PDIP–14
N, P SUFFIX
CASE 646

14
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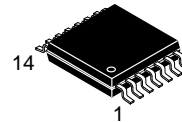
TSSOP–14
DTB SUFFIX
CASE 948G

14
1

PIN CONNECTIONS

Output 2	1	14 Output 3
Output 1	2	13 Output 4
V_{CC}	3	12 GND
– Input 1	4	11 + Input 4
+ Input 1	5	10 – Input 4
– Input 2	6	9 + Input 3
+ Input 2	7	8 – Input 3
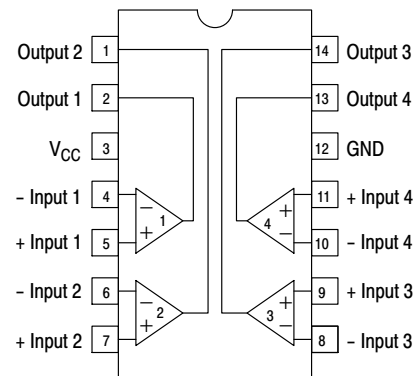
(Top View)

ORDERING INFORMATION

See detailed ordering and shipping information in the package dimensions section on page 7 of this data sheet.

DEVICE MARKING INFORMATION

See general marking information in the device marking section on page 8 of this data sheet.

LM339, LM339E, LM239, LM2901, LM2901E, LM2901V, NCV2901, MC3302

MAXIMUM RATINGS

Rating	Symbol	Value	Unit
Power Supply Voltage LM239/LM339, E/LM2901, E, V MC3302	V_{CC}	+36 or ±18 +30 or ±15	Vdc
Input Differential Voltage Range LM239/LM339, E/LM2901, E, V MC3302	V_{IDR}	36 30	Vdc
Input Common Mode Voltage Range	V_{ICMR}	−0.3 to V_{CC}	Vdc
Output Short Circuit to Ground (Note 1)	I_{SC}	Continuous	

Power Dissipation @ $T_A = 25°C$
    Plastic Package
    Derate above 25°C
	P_D
	
	$1/R_{\theta JA}$
		
		1.0
		8.0
			W
			mW/°C

Junction Temperature	T_J	150	°C

Operating Ambient Temperature Range
            LM239
            MC3302
            LM2901, LM2901E
            LM2901V, NCV2901
            LM339, LM339E
	T_A	−25 to +85
		−40 to +85
		−40 to +105
		−40 to +125
		0 to +70
			°C

Storage Temperature Range	T_{stg}	−65 to +150	°C

ESD Protection at any Pin (Note 2)
        Human Body Model
        Machine Model
	V_{ESD}	
		1500
		200
			V

Stresses exceeding those listed in the Maximum Ratings table may damage the device. If any of these limits are exceeded, device functionality should not be assumed, damage may occur and reliability may be affected.

1. The maximum output current may be as high as 20 mA, independent of the magnitude of V_{CC}. Output short circuits to V_{CC} can cause excessive heating and eventual destruction.
2. V_{ESD} rating for NCV/SC devices is: Human Body Model – 2000 V; Machine Model – 200 V.
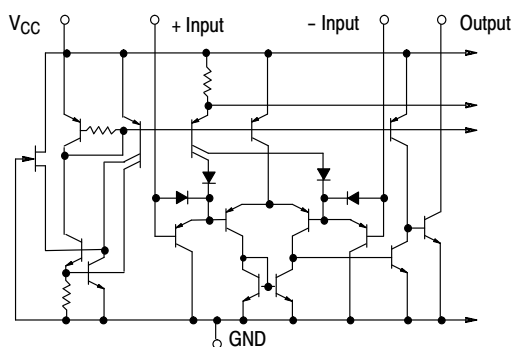
NOTE: Diagram shown is for 1 comparator.

Figure 1. Circuit Schematic

LM339, LM339E, LM239, LM2901, LM2901E, LM2901V, NCV2901, MC3302

ELECTRICAL CHARACTERISTICS (V_{CC} = +5.0 Vdc, T_A = +25°C, unless otherwise noted)

Characteristic	Symbol	LM239/339/339E			LM2901/2901E/2901V /NCV2901			MC3302			Unit
		Min	Typ	Max	Min	Typ	Max	Min	Typ	Max	
Input Offset Voltage (Note 4)	V_{IO}	–	±2.0	±5.0	–	±2.0	±7.0	–	±3.0	±20	mVdc
Input Bias Current (Notes 4, 5) (Output in Analog Range)	I_{IB}	–	25	250	–	25	250	–	25	500	nA
Input Offset Current (Note 4)	I_{IO}	–	±5.0	±50	–	±5.0	±50	–	±3.0	±100	nA
Input Common Mode Voltage Range	V_{ICMR}	0	–	V_{CC} −1.5	0	–	V_{CC} −1.5	0	–	V_{CC} −1.5	V
Supply Current $R_L = \infty$ (For All Comparators) $R_L = \infty$, V_{CC} = 30 Vdc	I_{CC}	– –	0.8 1.0	2.0 2.5	– –	0.8 1.0	2.0 2.5	– –	0.8 1.0	2.0 2.5	mA
Voltage Gain $R_L \geq 15$ kΩ, V_{CC} = 15 Vdc	A_{VOL}	50	200	–	25	100	–	25	100	–	V/mV
Large Signal Response Time V_I = TTL Logic Swing, V_{ref} = 1.4 Vdc, V_{RL} = 5.0 Vdc, $R_L = 5.1$ kΩ	–	–	–	300	–	–	300	–	–	300	–	ns
Response Time (Note 6) V_{RL} = 5.0 Vdc, $R_L = 5.1$ kΩ	–	–	–	1.3	–	–	1.3	–	–	1.3	–	μs
Output Sink Current $V_I (-) \geq +1.0$ Vdc, $V_I(+) = 0$, $V_O \leq 1.5$ Vdc	I_{Sink}	6.0	16	–	6.0	16	–	6.0	16	–	mA
Saturation Voltage $V_I(-) \geq +1.0$ Vdc, $V_I(+) = 0$, $I_{sink} \leq 4.0$ mA	V_{sat}	–	130	400	–	130	400	–	130	500	mV
Output Leakage Current $V_I(+) \geq +1.0$ Vdc, $V_I(-) = 0$, $V_O = +5.0$ Vdc	I_{OL}	–	0.1	–	–	0.1	–	–	0.1	–	nA

3. (LM239) T_{low} = −25°C, T_{high} = +85°
    (LM339, LM339E) T_{low} = 0°C, T_{high} = +70°C
    (MC3302) T_{low} = −40°C, T_{high} = +85°C
    (LM2901), LM2901E T_{low} = −40°C, T_{high} = +105°
    (LM2901V & NCV2901) T_{low} = −40°C, T_{high} = +125°C
    NCV2901 is qualified for automotive use.
4. At the output switch point, $V_O \simeq 1.4$ Vdc, $R_S \leq 100$ Ω 5.0 Vdc $\leq V_{CC} \leq$ 30 Vdc, with the inputs over the full common mode range (0 Vdc to V_{CC} −1.5 Vdc).
5. The bias current flows out of the inputs due to the PNP input stage. This current is virtually constant, independent of the output state.
6. The response time specified is for a 100 mV input step with 5.0 mV overdrive. For larger signals, 300 ns is typical.

LM339, LM339E, LM239, LM2901, LM2901E, LM2901V, NCV2901, MC3302

PERFORMANCE CHARACTERISTICS (V_{CC} = +5.0 Vdc, T_A = T_{low} to T_{high} [Note 7])

Characteristic	Symbol	LM239/339/339E			LM2901/2901E/2901V /NCV2901			MC3302			Unit
		Min	Typ	Max	Min	Typ	Max	Min	Typ	Max	
Input Offset Voltage (Note 8)	V_{IO}	–	–	±9.0	–	–	±15	–	–	±40	mVdc
Input Bias Current (Notes 8, 9) (Output in Analog Range)	I_{IB}	–	–	400	–	–	500	–	–	1000	nA
Input Offset Current (Note 8)	I_{IO}	–	–	±150	–	–	±200	–	–	±300	nA
Input Common Mode Voltage Range	V_{ICMR}	0	–	V_{CC} –2.0	0	–	V_{CC} –2.0	0	–	V_{CC} –2.0	V
Saturation Voltage $V_I(-) \geq$ +1.0 Vdc, $V_I(+)$ = 0, $I_{sink} \leq$ 4.0 mA	V_{sat}	–	–	700	–	–	700	–	–	700	mV
Output Leakage Current $V_I(+) \geq$ +1.0 Vdc, $V_I(-)$ = 0, V_O = 30 Vdc	I_{OL}	–	–	1.0	–	–	1.0	–	–	1.0	μA
Differential Input Voltage All $V_I \geq$ 0 Vdc	V_{ID}	–	–	V_{CC}	–	–	V_{CC}	–	–	V_{CC}	Vdc

7. (LM239) T_{low} = −25°C, T_{high} = +85°
   (LM339, LM339E) T_{low} = 0°C, T_{high} = +70°C
   (MC3302) T_{low} = −40°C, T_{high} = +85°C
   (LM2901, LM2901E) T_{low} = −40°C, T_{high} = +105°
   (LM2901V & NCV2901) T_{low} = −40°C, T_{high} = +125°C
   NCV2901 is qualified for automotive use.
8. At the output switch point, $V_O \simeq$ 1.4 Vdc, $R_S \leq$ 100 Ω 5.0 Vdc $\leq V_{CC} \leq$ 30 Vdc, with the inputs over the full common mode range (0 Vdc to V_{CC} −1.5 Vdc).
9. The bias current flows out of the inputs due to the PNP input stage. This current is virtually constant, independent of the output state.
10. The response time specified is for a 100 mV input step with 5.0 mV overdrive. For larger signals, 300 ns is typical.

$$V_{ref} \approx \frac{V_{CC} R1}{R_{ref} + R1}$$

$$R3 \simeq R1 // R_{ref} // R2$$

$$V_H = \frac{R1 // R_{ref}}{R1 // R_{ref} + R2} [V_{O(max)} - V_{O(min)}]$$

$$R2 \gg R_{ref} // R1$$

Figure 2. Inverting Comparator with Hysteresis

$$V_{ref} = \frac{V_{CC} R1}{R_{ref} + R1}$$

$$R2 \approx R1 // R_{ref}$$

Amount of Hysteresis V_H

$$V_H = \frac{R2}{R2 + R3} [(V_{O(max)} - V_{O(min)})]$$

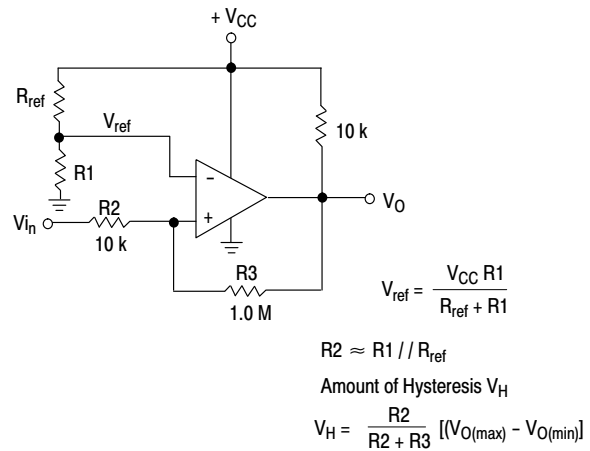**Figure 3. Noninverting Comparator with Hysteresis**

Appendix D

Control Scripts

D.1 *Arduino* Code

```
//Created by CM HEUNIS (cmheunis@sun.ac.za) Acknowledgements:
    \textit{Arduino}.
// GLOBALS:
////////////////////////////////////////////////////////////////LED's
// set pin numbers:
const int ledPin1 = A1;    // the number of the DOWN LED pin
const int ledPin2 = A2;    // the number of the LEFT LED pin
const int ledPin3 = A3;    // the number of the UP LED pin
const int ledPin4 = A4;    // the number of the RIGHT LED pin
int led = 13;
////////////////////////////////////////////////////////////////MOTORS
const int motor_l = 7;     // the number of the LEFT LED pin
const int motor_d = 12;    // the number of the DOWN LED pin
const int motor_r = 4;     // the number of the RIGHT LED pin
const int motor_u = 5;     // the number of the UP LED pin
///////////////////////////////////////////////////// MODES /
    STATES
// variables will change:
int buttonState1 = 0; // variable for reading the t pushbutton status
int buttonState2 = 0; // variable for reading the b pushbutton status
int buttonState3 = 0; // variable for reading the l pushbutton status
int buttonState4 = 0; // variable for reading the r pushbutton status
int stage = 0;
long previousMillis = 0;   // variable for GO event
long NOGOmillis = 0;       // variable for NOGO event
long intervalGO = 1000;    // interval at which to vibrate (ms)
long intervalNOGO = 5000;  //interval at which NOT to vibrate
long intervalEND = 180000; //interval to end events
int counter = 0;   //counter for loop
//------------------------------------------------------------------
// SETUP \ LOOP :
```

D. CONTROL SCRIPTS

```
void setup() {
  // initialize the LED pins as outputs:
  pinMode(ledPin1, OUTPUT);
  pinMode(ledPin2, OUTPUT);
  pinMode(ledPin3, OUTPUT);
  pinMode(ledPin4, OUTPUT);
  // initialize the motor pins as outputs
  pinMode(motor_u, OUTPUT); //Top motor (UP)
  pinMode(motor_l, OUTPUT); //Left motor (LEFT)
  pinMode(motor_d, OUTPUT); //Bottom motor (DOWN)
  pinMode(motor_r, OUTPUT); //Right motor (RIGHT)
  pinMode(led, OUTPUT);
  Keyboard.begin();
  Serial.begin(9600);     //Serial communication used for manual
                          //operation via keyboard
}
void loop() {
  unsigned long currentMillis = millis();
  //Constantly monitor the serial data from the keyboard:
  int inByte = Serial.read();
  if (inByte == '1') {  // turn MOTOR (DOWN) on:
    digitalWrite(motor_d, HIGH);
    Serial.print("Down activated");
    Serial.println();
    Serial.print(currentMillis);
    Serial.println();
    delay(500);
    digitalWrite(motor_d, LOW); }
  else if (inByte == '2') {
    // turn MOTOR (LEFT) on:
    digitalWrite(motor_l, HIGH);
    Serial.print("Left activated");
    Serial.println();
    Serial.print(currentMillis);
    Serial.println();
    delay(500);
    digitalWrite(motor_l, LOW); }
  else if (inByte == '3') {
    // turn MOTOR (UP) on:
    digitalWrite(motor_u, HIGH);
    Serial.print("Up activated");
    Serial.println();
    Serial.print(currentMillis);
    Serial.println();
    delay(500);
    digitalWrite(motor_u, LOW); }
  else if (inByte == '4') {
```

D. CONTROL SCRIPTS

```
  // turn MOTOR (RIGHT) on:
  digitalWrite(motor_r, HIGH);
  Serial.print("Right activated");
  Serial.println();
  Serial.print(currentMillis);
  Serial.println();
  delay(500);
  digitalWrite(motor_r, LOW); }
///////////////////////////////////////////////// REHAB SESSION
    3
// read the state of the pushbutton value:
// check if the pushbutton is pressed / keyboard letter is pressed:
else if (inByte == 's') {Keyboard.write(0x70)
  // turn DOWN LED on:
  digitalWrite(ledPin1, HIGH);
  digitalWrite(motor_d, HIGH);
  digitalWrite(led, LOW);
  Serial.print("Down + LED activated");
  Serial.println();
  Serial.print(currentMillis);
  Serial.println();
  delay(500);
  digitalWrite(ledPin1, LOW);
  digitalWrite(motor_d, LOW);
  digitalWrite(led, HIGH); }
else if (inByte == 'a') {Keyboard.write(0x41);
  // turn LEFT LED on:
  digitalWrite(ledPin2, HIGH);
  digitalWrite(motor_l, HIGH);
  digitalWrite(led, LOW);
  Serial.print("Left + LED activated");
  Serial.println();
  Serial.print(currentMillis);
  Serial.println();
  delay(500);
  digitalWrite(ledPin2, LOW);
  digitalWrite(motor_l, LOW);
  digitalWrite(led, HIGH); }
else if (inByte == 'w') {Keyboard.write(0x68)
  // turn LED on:
  digitalWrite(ledPin3, HIGH);
  digitalWrite(motor_u, HIGH);
  digitalWrite(led, LOW);
  Serial.print("Up + LED activated");
  Serial.println();
  Serial.print(currentMillis);
  Serial.println();
```

D. CONTROL SCRIPTS

```
    delay(500);
    digitalWrite(ledPin3, LOW);
    digitalWrite(motor_u, LOW);
    digitalWrite(led, HIGH); }
  else if (inByte == 'd') {Keyboard.write(0x83)
    // turn LED on:
    digitalWrite(ledPin4, HIGH);
    digitalWrite(motor_r, HIGH);
    digitalWrite(led, LOW);
    Serial.print("Right + LED activated");
    Serial.println();
    Serial.print(currentMillis);
    Serial.println();
    delay(500);
    digitalWrite(ledPin4, LOW);
    digitalWrite(motor_r, LOW);
    digitalWrite(led, HIGH); }
  else if (currentMillis == intervalGO && currentMillis !=
      intervalNOGO
   && currentMillis < intervalEND) {
    intervalGO = currentMillis + 1000;
    // turn MOTORS (LEFT AND RIGHT) on:
    Serial.println();
    digitalWrite(motor_r, HIGH);
    digitalWrite(motor_l, HIGH);
    Serial.print("Event activated");
Serial.write(1);
    Serial.println();
    Serial.print(currentMillis);
    Serial.println();
    delay(400);
    digitalWrite(motor_r, LOW);
    digitalWrite(motor_l, LOW); }
  else if (currentMillis == intervalNOGO && currentMillis <
      intervalEND) {
    intervalNOGO = currentMillis + 5000;
    intervalGO = currentMillis + 1000;
    Serial.println();
    Serial.print("Event not activated");
    Serial.write(2);
    Serial.println();
    Serial.print(currentMillis);
    Serial.println(); }
  else if (currentMillis == intervalEND) {
    Serial.println();
    Serial.print("Events ended");
    Serial.println();
```

```
    Serial.print(currentMillis); }}
```

D.2 *MATLAB* Code

```matlab
tbdata = importdata('Recordings.csv'); %import data from testbench
    csv file
eegdata = tbdata.data;
eegdata(:,12:19) = []; %remove unwanted fields
eegdata(:,8:10) = [];
eegdata(:,1:2) = [];
eegdata = eegdata';
eeglab %Prepare data in EEGLAB
EEG = pop_importdata('data',eegdata,'srate',128); %import data
from MATLAB array
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 0,'setname',
'eegdata','gui','off');
EEG = eeg_checkset( EEG );
EEG = pop_chanevent(EEG, 6,'edge','leading','edgelen',0);
% event channel
EEG = pop_chanedit(EEG, 'load',{'emotiv.ced' 'filetype'
    'autodetect'});
% channel locations
EEG = pop_eegfilt(EEG, 1, 0, [], [0]); % highpass filtering at 1Hz
EEG = pop_eegfilt(EEG, 0, 20, [], [0]); % lowpass filtering at 20Hz
eeglab redraw
EEG = pop_saveset(EEG,'data');
EEG = pop_epoch(EEG, {'1'}, [-0.9 0.9], 'newname', 'epochs_t'); %
    targets
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 1,'gui','off');
EEG = eeg_checkset( EEG );
EEG = pop_rmbase( EEG, [-898.4375 0]); % remove baseline
eeglab redraw
EEG = pop_saveset(EEG,'epochs_t');
EEG = pop_epoch(EEG, {'2'}, [-0.9 0.9], 'newname', 'epochs_nt'); %
    targets
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 1,'gui','off');
EEG = eeg_checkset( EEG );
EEG = pop_rmbase( EEG, [-898.4375 0]); % remove baseline
eeglab redraw
EEG = pop_saveset(EEG,'epochs_nt');
```

Appendix E

Proof of Ethical Approval

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Approval Notice
Response to Modifications- (New Application)

02-Dec-2015
Heunis, Christoff CM

Ethics Reference #: M15/10/042

Title: **Designing a rehabilitation device for paediatric Middle Cerebral Artery stroke victims to reinforce neural pathways and synapses during treatment**

Dear Mr. Christoff Heunis,

The **Response to Modifications -** *(New Application)* received on , was reviewed by members of **Health Research Ethics Committee 1** via Expedited review procedures on **02-Dec-2015** and was approved.
Please note the following information about your approved research protocol:

 Protocol Approval Period: **02-Dec-2015** -**01-Dec-2016**

Please remember to use your **protocol number** (**M15/10/042**) on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

After Ethical Review:
Please note a template of the progress report is obtainable on www.sun.ac.za/rds and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.
Translation of the consent document to the language applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 483 9907) and Dr Helene Visser at City Health (Helene.Visser@capetown.gov.za Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.
For standard HREC forms and documents please visit: www.sun.ac.za/rds

If you have any questions or need further assistance, please contact the HREC office at .

 Included Documents:
 ICF & Information leaflet
 Investigator CV - C Heunis
 Assent Form

271115 Mods requested - Application Form

271115 Mods requested - Assent Form

Supervisor CV - P Fourie

Supervisor CV - J van der Merwe

Description of study site

Motor Activity log

271115 Mods requested - Clinical Trial Data

Clinical Trials Checklist

Investigator CV - R van Toorn

271115 Mods requested - Protocol Synopsis

Protocol

Investigator Declaration - C Heunis

271115 Mods requested - Consent Forms

271115 Mods requested - Consent forms

ICF English

271115 Mods requested - Protocol

Supervisor Declaration - J vd Merwe

Application Form

Protocol Synopsis

Flow Chart

Supervisor Declaration - P Fourie

271115 Mods requested - Response letter

Cover Letter

Investigator Declaration - van Toorn

(HREC COORDINATOR NOT DEFINED - CONTACT MODULE ADMINISTRATOR)

Appendix F

Stroke Patient Data

Figure F.1: The Motor Assessment Scale sheet

F. STROKE PATIENT DATA

Met ondersoek:
Bloeddruk:145/80   Pols 67/minuut
Geen anemie, edeem of limfadenopatie nie
Kardiovaskulêr: Nie K4 hoorbaar nie.
Respiratories : Longe belug goed.
Buik: sag en obees
Neurologies: Hy het nie fokale neurologie nie.
Fundoskopie: Hipertensiewe veranderinge met fundoskopie, sonder enige bloedings.
Random HGT: mmol/l

Mens moet hier 'n vaskulêre tipe demensie oorweeg. 'n Binswangers variant wat soms met strawwe hipertensie geassosieer word, moet ingedagte gehou word, asook multi infarkte demensie in die lig van sy vorige AF. Dit is egter nog nie weer gedokumenteer nie. 'n Opvolg Minimental sal belangrik wees en 'n opvolg skandering mag ook van waarde wees om seker te maak die pasiënt kry nie multi infark demensie nie. Dit behoort ook die beeld van Binswangers te wys, indien dit wel teenwoordig is. Ek volg hom op.

Medikasie :
- Accu Check Active Strips
- Glucophage 850bd
- Diagluzide 80mg bd
- Ciplavasc 5mg per dag
- Bilocor 10mg per dag
- Co-Diovan 160mg per dag
- Aspavor 10mg per dag
- Puricos 300mg per dag
- Tegretol 400mg saans

Vriendelike groete

Figure F.2: Proof of prognosis, patient discharge and list of medication

F. STROKE PATIENT DATA

History: Right-sided stroke 10 days ago. Left 75% stenosis at ultrasound at outside institution.

CT ANGIOGRAPHY EXTRA CRANIAL VESSELS

Findings:

Vasculature:
Configuration of the aortic arch is normal.

Right: Calibre of the brachiocephalic artery, subclavian artery and common carotid artery within normal limits. Calcified and non-calcified atheroma at the right carotid bulb. The narrowest diameter of the right carotid bulb is 4.2 x 5.6 mm with an area of 18.2 mm², compared to the mid to distal ICA diameter of 4 x 4.3 mm and an area of 13.7 mm². No calculable stenosis according to NASCET. There is calcified atheroma of the right cavernous segment of the intracranial ICA. Taparing and short segment stenosis of the right M1 segment which is discontinuous over a short segment. Filling of the M2 segment again, but of smaller calibre compared to the contralateral side.

Left: Good opacification of the left CCA. Calcified and non-calcified atheroma at the left carotid bulb. The narrowest diameter of the left carotid bulb is 2.6 x 3.5 mm with an area of 6.9 mm², compared to the mid to distal ICA diameter of 5.1 x 5.4 mm and stenosis of 68%. Immediately distal to the stenosis is an intimal flap resulting in a similar degree of short segment stenosis. Remainder of the ICA demonstrate normal opacification. Good opacification of the intracranial internal carotid circulation on the left side.
2/.........

Figure F.3: CT-Angiography results of the extra cranial vessels

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F. STROKE PATIENT DATA

AROTID DOPPLER EXTRACRANIAL, BILATERAL

ndings:
here is a high-grade stenosis at the origin of the left internal carotid artery caused by calcified and soft plaque,
ith elevation in peak systolic velocity to 370 cm/sec, and internal carotid artery/common carotid artery ratio 4.3.
he intima on the left is thickened, with average of 1.09 mm. There is no stenosis of the common carotid artery
external carotid artery. The left vertebral artery has antegrade flow at decreased velocity of 13 cm/sec.

n the right, calcified plaque in the carotid bulb is extensive, no plaque ulceration and no haemodynamically
gnificant stenoses at the carotid bulb or at the origin of the internal or external carotid artery. The velocities
ithin the internal carotid artery are maintained and the colour Doppler flow spectrum normal. The right common
arotid artery intima media thickness on the near wall is increased, on the far wall of the vessel it measures 0.65
m which is within normal range. The right vertebral artery has antegrade flow at normal velocity of 30 cm/sec.

RT		LT
0.65	COMMON CAROTID intima media thickness (mm)	1.09
68.1	Peak systolic velocity (cm/s)	85.2
16.8	Peak diastolic velocity (cm/s)	21.6
58.7	INTERNAL CAROTID peak systolic velocity	369.6
23.0	Peak diastolic velocity	163.9
70.4	EXTERNAL CAROTID peak systolic velocity	80.5
28.8	VERTEBRAL ARTERY peak systolic velocity	13.2
0.9	Peak systolic ICA/CCA ratio	4.3
1.4	Peak diastolic ICA/CCA ratio	7.6
	INTERNAL CAROTID %age stenosis	75%
	EXTERNAL CAROTID %age stenosis	

Figure F.4: Carotid Doppler results showing artery conditions