Copyright Warning & Restrictions

The copyright law of the United States (Title 17, United States Code) governs the making of photocopies or other reproductions of copyrighted material.

Under certain conditions specified in the law, libraries and archives are authorized to furnish a photocopy or other reproduction. One of these specified conditions is that the photocopy or reproduction is not to be "used for any purpose other than private study, scholarship, or research." If a, user makes a request for, or later uses, a photocopy or reproduction for purposes in excess of "fair use" that user may be liable for copyright infringement,

This institution reserves the right to refuse to accept a copying order if, in its judgment, fulfillment of the order would involve violation of copyright law.

Please Note: The author retains the copyright while the New Jersey Institute of Technology reserves the right to distribute this thesis or dissertation

Printing note: If you do not wish to print this page, then select "Pages from: first page # to: last page #" on the print dialog screen



The Van Houten library has removed some of the personal information and all signatures from the approval page and biographical sketches of theses and dissertations in order to protect the identity of NJIT graduates and faculty.

ABSTRACT

THE CREATION AND TESTING OF A MOCK FUNCTIONAL MAGNETIC RESONANCE IMAGING FACILITY FOR PAIN PATIENTS

by Gladstone Vincent Reid

Unfamiliarity with functional Magnetic Resonance Imaging (fMRI) facilities leads to unwanted stress-related disturbances in the processing of fMRI data. A mock fMRI facility was developed to increase familiarization among subjects participating in fMRI studies and to alleviate the time and cost of familiarizing each subject in an actual fMRI facility. A decommissioned Magnetic Resonance Imaging (MRI) unit was remodeled to visually and aurally resemble the Siemens Magnetom Allegra 3 Telsa fMRI machine currently used at the University of Medicine and Dentistry of New Jersey (UMDNJ), Newark, New Jersey. Instrumentation was developed using LabVIEW software which presented subjects with recreated sounds of the UMDNJ fMRI unit, displayed interactive Pain Descriptor Differential Scales to the subject, collected and displayed electrocardiogram (ECG), blood pressure (BP), and questionnaire data to the operator. In addition to these tasks, the LabVIEW program triggered the Medoc Neuro-Sensory Analyzer to begin producing warm stimuli to patient's forearm, in synchrony with the order of the study. A pilot experiment was conducted to assess if subjects became more habituated to the fMRI environment after two mock fMRI experiences. ECG, BP, and questionnaire data for two subjects in the mock fMRI unit for two sessions were compared. The results support that the subjects were more comfortable, relaxed, and familiar with the experiment and the fMRI environment during the second session.

THE CREATION AND TESTING OF A MOCK FUNCTIONAL MAGNETIC RESONANCE IMAGING FACILITY FOR PAIN PATIENTS

by Gladstone Vincent Reid

A Thesis Submitted to the Faculty of New Jersey Institute of Technology In Partial Fulfillment of the Requirements for the Degree of Master of Science in Biomedical Engineering

Department of Biomedical Engineering

August 2005

 \langle

APROVAL PAGE

THE CREATION AND TESTING OF A MOCK FUNCTIONAL MAGNETIC RESONANCE IMAGING FACILITY FOR PAIN PATIENTS

Gladstone Vincent Reid

Stanley Reisman, PhD, Thesis Advisor Professor of Biomedical Engineering, NJIT

Date

Michael T. Bergen, Thesis AdvisorDateVA New Jersey Health Care System, East Orange, New JerseyAdjunct Professor of Biomedical Engineering, NJIT

Tara Alvarez, PhD Committee Member Assistant Professor of Biomedical Engineering, NJIT

Date

BIOGRAPHICAL SKETCH

Author: Gladstone Vincent Reid

Degree: Master of Science

Date: August 2005

Undergraduate and Graduate Education:

Master of Science in Biomedical Engineering New Jersey Institute of Technology, Newark, NJ, 2005

Bachelor of Science in Electrical Engineering New Jersey Institute of Technology, Newark, NJ 2003

Major: Biomedical Engineering

To Jesus Christ, the Author and Finisher of my faith. To my parents Gladstone Sr. and Annette. Also to my brothers and sisters: Alecia, Wade, Daviot, Thomas, and Venessa.

ACKNOWLEDGEMENT

Special thanks to Professor Michael T. Bergen for his continual help in the completion of this research. Thanks to the War Related Illnesses and Injuries Study Center in the Department of Veterans Affairs (DVA) for allowing me to contribute to the ongoing research to help United States veterans. I would like to thank Dr. Dane B. Cook for allowing me to work with him to prepare the apparatus necessary for the study of pain in Gulf War veterans. Special thanks to Dr. Stanley Reisman and Dr. Tara Alvarez who have both played an important role in the completion of my master's program at NJIT.

I would also like to take this opportunity to thank several individuals, departments, and organizations at NJIT that have helped me throughout my college career. The individuals are: Mr. Lawrence T. Howell, Mrs. Kim Akhtab, Mr. Carlo Ontenada, Mrs. Gloria Williams, Mrs. Rosalind Newton, Ms. Lynn Riker, Ms. Sanjeanetta Worley, and Mrs. Clarisa Gonzalez-Lenahan. The departments are: The Educational Opportunity Program, The Center for Pre-College Programs, Residence Life, The Career Development Services, The organizations are: The Caribbean Student Organization, The Intervarsity Christian Fellowship (IVCF), National Society of Black Engineers, and Inroads.

Thanks to the IVCF that provided encouragement and spiritual strength to help me complete my studies. I would also like to thank my family, my stepfather Thomas Newell, and my friend Tamara B. Davis who have helped me all the way through. Special thanks to the some of the staff at the DVA: Scott Soldan, Robert DeMarco, Michael Ocasio, Lynn Auger, and Florence Chua, Mary-Carol Rossignol, and Jose Chua.

Chapter Pa	ige
1 INTRODUCTION	1
1.1 Objective	1
1.2 The Brain: Pain and its Perception	2
1.2.1 Pain Processing	4
1.2.2 Stress Processing	5
1.3 Functional Magnetic Resonance Imaging	6
1.4 Functional Magnetic Resonance Imaging to Study Pain	9
1.5 Blood Pressure	.12
1.6 Electrocardiogram	14
1.7 The Effect of Stress on Cardiovascular Measures	.15
2 CREATION OF MOCK fMRI: HARDWARE	17
2.1 System Overview	.17
2.2 Mock fMRI Unit	.18
2.2.1 Mock FMRI Face Circuitry	.19
2.2.2 Mirror Attachment	.22
2.2.3 Audio Simulation	.24
2.3 Audio Mixer	.24
2.4 Patient Visual Display System	26
2.5 Patient Response Unit	.28
2.6 Neuro-Sensory Analyzer (Heat Stimuli Machine)	.31
2.7 Finapres	33

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

Chapter Page
2.8 Dinamap
2.9 Electrocardiogram Amplifier and Filter
2.10 Video Camera
2.11 Computer System
CREATION OF MOCK fMRI: SOFTWARE41
3.1 LabVIEW Program
3.2 Displaying Analog Signals43
3.3 Patient Response to Pain Scales45
3.4 Neuro-Sensory Analyzer Triggering and Visual Indicator
3.5 Organization of all Collected Data
3.6 MRI Sound Simulation
4 METHODOLOGY
4.1 System Setup
4.2 Physiological Connections54
4.3 Procedures
4.4 Habituation Validation
5 SIGNAL PROCESSING AND ANALYSIS
5.1 Signal Processing of Electrocardiogram 57
5.2 Signal Processing of Blood Pressure
5.3 Signal Processing of Mock MRI Questionnaire Responses

TABLE OF CONTENTS (Continued)

Chapter	Page
6 RESULTS	65
6.1 Results of System	65
6.2 Results of ECG Signal Processing	65
6.3 Results of Blood Pressure Signal Processing	71
6.4 Results of Mock MRI Questionnaire	78
7. CONCLUSION	80
APPENDIX A - FINAPRES SPECIFICATIONS	82
APPENDIX B - MOCK MRI QUESTIONNAIRE	83
APPENDIX C - PAIN INTENSITY SCALE	85
APPENDIX D - PAIN UNPLEASANTNESS SCALE	86
APPENDIX E - PROVIEW SCHEMATIC MONITOR PART 1-4	87
REFERENCES	91

|--|

Figu	re Page
1.1	The Anatomy Trail of Pain Processing by the Brain
1.2	Cerebral Cortex Four Divisions and Thalamus
1.3	Cingulated Gyrus and Insular Cortex
1.4	Affective and Sensory Numerical Descriptors Scales10
1.5	Traditional Sphygmomanometer and Stethoscope13
1.6	Blood Pressure Waveform14
1.7	Electrocardiogram Waveform15
2.1	Block Diagram of Mock fMRI System19
2.2	Remodeled Picker 2055 Vista HPQ 0.5 Telsa unit20
2.3	MRI Face Display21
2.4	Mirror Attachment for Siemens fMRI23
2.5	Schematic of the Mirror and its Attachment for the Mock MRI23
2.6	Mirror Attachment for Mock fMRI23
2.7	Speakers used for T1 and T2 Sound Simulation
2.8	Audio Mixer Setup Schematic
2.9	Investigator's Microphone, Speaker and Audio Mixer
2.10	Circuitry inside Proview Monitor
2.11	Screen Shot of Reversed Monitor
2.12	Proview 17" Monitor
2.13	Patient Response Unit

LIST OF FIGURES (Continued)

Figu	re P	age
2.14	Patient Response Unit Connection Diagram	30
2.15	Medoc TSA II Neuro-Sensory Analyzer	. 33
2.16	Medoc Square Thermode	33
2.17	Ohmeda Finapres Blood Pressure Monitor	34
2.18	Critikon Dinamap Blood Pressure Monitor	35
2.19	Electrocardiogram Amplifier and Filter	38
2.20	fMRI Video Camera and Monitor	39
3.1	Front Panel in LabVIEW	42
3.2	Block Diagram in LabVIEW	42
3.3a	Analog Input Configuration Block in LabVIEW Block Diagram	44
3.3b	Analog Input Start Block in LabVIEW Block Diagram	44
3.3c	Analog Input Read Block in LabVIEW Block Diagram	45
3.4	Block Diagram of DDS Pain Intensity and Unpleasantness Scales	47
3.5	Block Diagram of In Range and Coerce Block in LabVIEW	47
3.6	Sequence of DDS Pain Intensity and Unpleasantness Scales	48
3.7	Digital Line Output Block in LabVIEW	50
3.8	Patient Identification Sub Virtual Instrument in LabVIEW	51
3.9	File Storage and Organization in LabVIEW	52
3.10	Write to Spreadsheet Block in LabVIEW	52
3.11	Sound Play Wavefile block in LabVIEW	53
5.1	Threshold Peak Detector Block in LabVIEW	58

LIST OF FIGURES (Continued)

Figu	re Page
5.2	Front Panel of LabVIEW HR Calculation Program
5.3a	Block Diagram of LabVEW HR Calculation Program Stage 159
5.3b	Block Diagram of LabVEW HR Calculation Program Stage 2
5.3c	Block Diagram of LabVEW HR Calculation Program Stage 360
5.3d	Block Diagram of LabVEW HR Calculation Program Stage 460
5.4	Peak Detector block in LabVIEW61
5.5	Front Panel of LabVIEW BP Calculation Program
5.6a	Block Diagram of LabVIEW BP Calculation Program Stage 162
5.6b	Block Diagram of LabVIEW BP Calculation Program Stage 263
5.6c	Block Diagram of LabVIEW BP Calculation Program Stage 363
5.7	Microsoft Excel Spreadsheet of Responses from Mock MRI Questionnaire64
6.1	Subject 1 Herat Rate Comparison for Sessions 1 and 267
6.2	Subject 2 Herat Rate Comparison for Sessions 1 and 267
6.3	Subject 1 Heart Rate Trend in Session 1
6.4	Subject 1 Heart Rate Trend in Session 2
6.5	Subject 2 Heart Rate Trend in Session 170
6.6	Subject 2 Heart Rate Trend in Session 2
6.7	Subject 1 Finapres Blood Pressure comparison for Sessions 1 and 273
6.8	Subject 2 Finapres Blood Pressure comparison for Sessions 1 and 273
6.9	Subject 1 Blood Pressure Trend in Session 174
6.10	Subject 1 Blood Pressure Trend in Session 275

LIST OF FIGURES (Continued)

Figu	re Pag	ge
6.11	Subject 2 Blood Pressure Trend in Session 17	'6
6.12	Subject 2 Blood Pressure Trend in Session 27	'6
6.13	Subject 1 Dinamap BP comparison for Sessions 1 and 2	77
6.14	Subject 2 Dinamap BP comparison for Sessions 1 and 2	77
6.15	Overall Habituation Level for Subject 1 and 2 for Sessions 1 and 2	78

CHAPTER 1

INTRODUCTION

1.1 Objective

Musculoskeletal pain is the fourth prevalent complaint reported by Persian Gulf War veterans (GWV) that participated in the Gulf Health Registry. Dane B. Cook Ph.D., a researcher in the Department of War Related Illness and Injury Study Center (WRIISC) at the Department of Veterans Affairs (DVA) in East Orange, New Jersey, is currently studying pain perception by GWV. His research requires the use of a 3 Telsa functional Magnetic Resonance Imaging (fMRI) unit in the Advances Imaging Facility at the University of Medicine and Dentistry of New Jersey (UMDNJ). fMRI identify regions of the brain that are activated during painful stimuli. By locating the regions of the brain are responsible for pain processing and correlate the intensity of the stimuli to the perception in the brain. As a part of his research Dr. Cook has proposed to build a mock fMRI facility at the DVA that will habituate test subjects to being in an fMRI environment and participating in a pain perception study, before they go to the actual fMRI at UMDNJ.

The objective of this thesis was to create and test the mock fMRI facility in the WRIISC at the DVA that will be used in the pain perception studies of GWV. This option, of creating the mock fMRI, was chosen because of the expense to habituate subjects in the real fMRI facility. The virtual fMRI facility should give the perception to the subject that he/she is in a real fMRI facility, through mimicking the look and sound of

the MRI facility located at the Advanced Imaging Center at UMDNJ. This paper will discuss the entire project and will give background information about pain, fMRI, stress, electrocardiogram (ECG), and blood pressure (BP).

The proposed test was to try and habituate two volunteer subjects by connecting them to the system and recording cardiovascular measure namely, BP and ECG. In addition to BP and ECG, their response to a questionnaire was used to determine whether or not they became more comfortable after being in the mock fMRI two times.

1.2 The Brain: Pain and Its Perception

In order to test for pain perception, it is necessary to have a good understanding of what pain is and how the human body perceives it. The sequence pain goes through from point of contact to being processed in the brain will be discussed. There are different definitions for pain which all involve sensations that are usually described as pricking, burning, aching, stinging, or soreness. The simplest definition of pain is the sensation experienced in response to an undesirable or harmful input to sensory detectors on the body [4]. There are two types of pain, nociceptive and neuropathic. Nociceptive pain is caused by an injury or disease outside the nervous system, while neuropathic pain is cause by damage to the nerve tissue. This experiment only focuses on nociceptive pain. Examples of nociceptive pain include sprains, bone fractures, burns, bumps, bruises, inflammation, obstructions, and muscle pain [5].

The anatomy trail of nociceptive pain (see figure 1.1) begins with noxious insults, which are harmful stimuli to the skin or subcutaneous tissue. Noxious insults activate nociceptors, which are specialized sensory receptors in tissue. The information collected

by the nociceptors travels through nociceptive afferent fibers to the back of the spinal cord. This nociceptive information is transmitted from the spinal cord to the thalamus and cerebral cortex (see figure 1.2) along five ascending pathways namely spinothalamic, spinoreticular, spinomesencephalic, cervicothalamic, and spinohypothalamic tract [4].



Figure 1.1 The anatomy trail of pain processing by the human body.[4]



Figure 1.2 Cerebral Cortex in its four divisions (left). The Thalamus (right)[6]

1.2.1 Pain Processing

The processing of pain takes place in the cerebral cortex. Neurons in several regions of the cerebral cortex have shown a response to nociceptive inputs [7]. Pain is a complex perception and is influenced by prior experiences and the context within which noxious stimulus occurs; therefore, it would have to be linked to a part of the brain that also processes memory and perception. It has been determined that the cingulated gyrus (figure 1.3), the insular cortex, and the thalamus, three sections of the cerebral cortex, are involved in the response to nociception. The cingulated gyrus is believed to be involved in the processing of the emotional component of pain. The insular cortex is a structure of the human brain that lies deep in the brain's surface within the lateral fissure and separates the temporal and inferior parietal cortices [8]. It is believed to be involved in the processing of information regarding the internal state of the body such as disgust and feelings of unease, and contribute to the autonomic component of the overall pain response [4]. The thalamus modulates and transfers sensory signals to and from the cerebral cortex. It receives inputs from the nociceptive receptors through the spinal cord and coordinates the release of hormones that cause a person to move or tense up in response to perceived threats. [8]



Figure 1.3 Location of the Cingulated Gyrus and the Insular Cortex. [6]

1.2.2 Stress Processing

Stress is very similar to pain, but stress can be present without noxious stimuli. Stress is a summation of anxiety, fear, confusion, distress, frustration, and tiredness [9]. The processing of stress is similar to that of pain, since pain incorporates similar emotional reactions. There are three major brain regions that are responsible for the processing of stress in the form of anxiety and fear, namely the prefrontal cortex, the amygdala, and the hypothalamus. It is common in the clinical field that anxiety about pain can exacerbate the pain sensation [10]. An fMRI experiment that compared activation responses to noxious thermal stimulation while perceived pain intensity was manipulated by changes in either physical intensity or induced anxiety showed that the areas responsible for pain processing responded differently to identical noxious stimuli. The different responses were dependent on whether the perceived pain intensity was enhanced by pain-relevant anxiety or not [10]. This demonstrates that the presence of anxiety can cause incorrect and inconsistent subjective response to painful stimuli. This suggests that if a person is familiar with a procedure about to be done on him/her, he/she will respond more accurately.

1.3 Functional Magnetic Resonance Imaging

Magnetic Resonance Imaging is a method of creating images of the inside of opaque organs in living organisms as well as detecting the amount of bound water in geological structures [12]. MRI relies on the relaxation properties of excited hydrogen nuclei in water. When the object to be imaged is placed in a powerful uniform magnetic field, the spins of the atomic nuclei, within the tissue all align in one of two opposite directions: parallel to the magnetic field or anti-parallel. The magnetic dipole moment of the nuclei then precesses around the axial field. The frequency with which the dipole moments precess is called the Larmor frequency (ω). The tissue is then briefly exposed to pulses of electromagnetic energy (RF pulse) in a plane perpendicular to the magnetic field, causing some of the magnetically aligned hydrogen nuclei to assume a temporary non-aligned high-energy state. The frequency of the pulses is governed by the Larmor Equation ($\omega = \gamma$ B). In the Larmor Equation ω is the Larmor frequency; γ , gama, is the gyromagnetic ratio a constant that is unique to the nucleus of the hydrogen element; and the B, is the strength of the magnetic field meausred in Telsas. [12,13,14]

In order to selectively image the different voxels (3-D pixels) of the object being imaged, three orthogonal magnetic gradients are applied. The first is the slice selection gradient, which is applied during the RF pulse. Next, is the phase encoding gradient, and lastly, the frequency encoding gradient, during which the tissue is imaged. Various combinations of the gradients can be combined during the process so that slices can be taken in any orientation, not just X, Y, and Z. As the high-energy nuclei relax and realign, they emit energy which is recorded to provide information about their environment. The realignment with the magnetic field is termed longitudinal relaxation and the time in milliseconds required for a certain percentage of the tissue nuclei to realign is termed "Time 1" or T1. This is the basis of T1-weighted imaging. T2-weighted imaging relies upon local dephasing of spins following the application of the transverse energy pulse; the transverse relaxation time is termed "Time 2" or T2. Both T1- and T2-weighted images are acquired for most medical examinations. [12,13]

In order to create the image, spatial information must be recorded along with the received tissue relaxation information. For this reason, magnetic fields with an intensity gradient are applied in addition to the strong alignment field to allow encoding of the position of the nuclei. A field with the gradient increasing in each of the three dimensional planes is applied in sequence. When received, the signals are recorded in a temporary memory termed K-space; this is the spatial frequency weighting in two or three dimensions of a real space object as sampled by MRI. The information is then inverse Fourier transformed by a computer into real space to obtain the desired image. This image contains detailed anatomical information. Typical medical resolution is about 1 mm^3 , while research models can exceed $1 \mu \text{m}^3$. [12,13]

fMRI is an upgrade to Magnetic Resonance Imaging (MRI). MRI belongs in the family of imaging technology such as X-ray and Computer Aided Tomography (CAT scan). All of these take multiple images of a body region and reproduce a 3-dimensional anatomical image of the area of interest. Both X-Ray and CAT use X-rays emitters and detectors to produce an image. However, MRI employs the use of magnetic fields to

produce images as discussed above. fMRI uses MRI technology, but in addition, tracks the activity of regions in the brain by locating areas that employ more oxygen while a person is performing a task. Positron Emission Tomography (PET) is similar to fMRI, but uses CAT technology to produce images instead of magnetic fields. fMRI and PET scans show functionality in the brain. fMRI can determine which parts of the brain are activated by different types of physical sensation or activity, such as sight, sound or the movement of a subject's fingers. Synaptic activity generates increases in cerebral blood flow (CBF). This physiological fact is the basis for both PET and fMRI. fMRI uses MRI imaging to measure the quick, tiny metabolic changes that take place in an active part of the brain. The most common used method in fMRI is the Blood Oxygen Level Dependent The BOLD fMRI estimates neural activity by detecting local (BOLD) method. hemodynamic changes, which are related to synaptic activity [15]. This technology helps radiologists, doctors, and researchers to determine precisely which part of the brain is handling critical functions such as thought, speech, movement, and processing of sensations. [15]

1.4 Functional Magnetic Resonance Imaging Use in Studying Pain

People that suffer from musculoskeletal disorders such as Fibromyalgia, experience frequent episodes of pain. Fibromyalgia is musculoskeletal pain and fatigue disorder whose cause has not been determined. Its symptoms are muscle and joint aches, stiffness of joints, and extreme fatigue. FM is believed to be related to disorders in an individual's neural triggering and processing of pain. Since fMRI scanning can detect activity in the CNS caused by various activities, it is ideal in comparing healthy and FM subjects to

determine differences in pain processing. By delivering painful and non-painful stimuli to a subject during fMRI scanning, analysis can be done to examine which areas of the brain are active for each stimulus. In a study by Gracely, et al it is shown that fMRI brain responses to experimental pressure pain, set at either similar stimulus levels or similar subjective pain levels, were amplified in FM patients compared to healthy controls [19]. This shows that FM patients have a more exaggerated perception of pain.

Other methods can be used to provide painful stimulus to a subject during fMRI scanning. One method is to use a temperature sensory stimulator instead of pressure stimulator. The main advantages of using a temperature sensory stimulator versus a pressure stimulator are faster response time by subject to painful stimulus, less interaction between subject and administrator. The temperature sensory stimulator uses Peltier which allows it to reach its target temperature at a faster time than it would take the pressure stimulator to reach its target pressure, since it uses a mechanical system. Temperature sensory stimulators also have remote contact with subjects, allowing the subject to wear the object producing the stimuli versus an administrator.

Nociceptive pain is processed in the central nervous system (CNS), in several interrelated but different regions. The regions proven to be active during the processing of painful stimuli in healthy people are: the posterior insular cortex, anterior cingulated cortex (ACC), prefrontal cortex, periaqueductal gray region, thalamus, basal ganglia and cerebellum. These regions are inter-related in pain response, but some have shown distinct functions in response to pain. Pain intensity has been shown to correlate with

neural activity in the somatosensory cortex, while pain unpleasantness ("how much a given sensation bothers you" [18]) correlates to activation of the ACC. [15, 18, 19].

Pain intensity and unpleasantness (figure 1.4) can be very different based on the preference and environment. An experiment conducted by Price et al, showed that women in labor and cancer patients experienced similar pain intensity, but had very different responses to pain unpleasantness [20]. Women in labor experienced greater unpleasantness; this is due to attention and other cognitive processes such as anxiety and stress that modify pain perception. [21]

Affective

Sensory



Figure 1.4 Affective and sensory numerical descriptors scales used to measure evoked pain dimensions of affective unpleasantness and sensory intensity. [20]

Two pain perception studies conducted using fMRI have asked the subject to rate or evaluate the intensity and unpleasantness of a painful heat or pressure stimulus as it is applied to the subject's thumb nail for pressure, and thenar eminence for heat. The BOLD method was used to determine what areas of the brain are experiencing more than resting synaptic activity. Images of the brain are taken while the subject receives stimuli. The number of images correlates to the number of slices the total brain structure will be divided in. For each slice, an image is taken. An increase in the number of slices causes an increase in the resolution of the brain. During processing, fMRI software is used to reconstruct the images and identify the areas in the brain that experienced more than resting synaptic activity. This information is correlated with the range of stimuli given and the time each stimulus was given. Then analysis is done to compare times when there is more activity in some areas of the brain versus others. During the analysis stage, functional images of the brain are first realigned to make sure all the images taken are all aligned properly on top of each other. Then co-registration is done. This process entails checking all functional images to make sure he brain is in the same position for all images. Interpolation corrects slight movements of the patient's head. Then the images are normalized the size of a standard brain. Normalization entails reshaping the structural and functional images to fit the size of a template image which represents the gold standard for the size of a human brain. After the processing, the images are analyzed, by inputting the times when stimuli were given and the duration of the stimuli. This aids in identifying the images of interest to determine how they compare to images when no stimuli were given, or lesser intense stimuli were given. [15]

1.5 Blood Pressure

Blood pressure is the pressure exerted by blood on the walls of blood vessels. BP generally refers to arterial BP which is the pressure in the large arteries, such as brachial artery located in the arm. The pressure in other vessels, such as the finger, is lower than the arterial BP, because those blood vessels are much smaller. The highest pressure in the arteries during the cardiac cycle is the systolic pressure, and the lowest pressure during the relaxation phase of the cardiac cycle is the diastolic pressure. Healthy adults typically have an arterial blood pressure of approximately 120 mmHg systolic and 80 mmHg diastolic, written as 120/80 mmHg. Blood pressure is not static, but undergoes natural variations from one heartbeat to another. It also changes in response to stress, nutritional factors, drugs, or disease. [1]

Blood pressure can be measured in two ways, invasively and non-invasively, the most accurate being invasively, which is done by placing a catheter inside the blood vessel with a pressure sensor at the other end of the catheter. The less accurate method, non-invasively, can be done by using a sphygmomanometer, an inflatable cuff attached to a manometer, and a stethoscope (shown in figure 1.5). This is the standard method of taking BP measurements. The pump attached to the cuff is squeezed to inflate the cuff until the artery is completely occluded. Pressure is slowly released, while the stethoscope is placed at the site of measurement to listen for the flow of blood to begin. When the blood begins to flow, it makes a swooshing sound. The pressure at which the flow of blood begins is the systolic BP. As the pressure is continually released all noise will stop. The pressure at which the noise stops is the diastolic pressure.



Figure 1.5 Traditional sphygmomanometer (left) and Stethoscope (right).

With new technology, there are many ways to measure BP non-invasively. Most technology integrates similar principles as just described, but instead of manually pumping the cuff and listening for flow sounds, they employ an electronic pump and use a pressure transducer. Small oscillations are created in the cuff as the brachial artery expands during the decrease in pressure. It is these oscillations that are used in some new technology to calculate systolic and diastolic pressures. This automated cuff method is the basis of the technology behind the Dinamap that will be discussed in Chapter 2.

Other methods used to measure BP, monitor changes in BP over time yeilding a continuous waveform. One of these methods measure changes in arterial BP in the finger. The device used for this pilot experiment, the Finapres, uses a servo valve to produce a pulsating pressure in a small cuff attached to the finger. In the finger cuff is electronic pressure trancducer that measures the pressure throughout the cardiac cycle. Within the cuff there is also a photoplethysmograph that helps to maintain a fixed diameter around the finger. The waveform that is created using continuous BP monitoring devices resemble the waveform for BP (figure 1.6)



Figure 1.6 Blood Pressure Waveform

1.6 Electrocardiogram

An electrocardiogram (ECG or EKG, abbreviated from the German Elektrokardiogramm) is a graphic representation of the electrical voltage measured at the surface of the skin during the cardiac cycle [2]. The ECG (figure 1.7) is used to determine whether the heart is functioning normally or if it suffers from abnormalities.

An ECG is formed through the measurement of voltage difference between several points on the body. There are two types of configurations to collect the ECG signal from the body, namely bipolar and augmented. Bipolar configurations (Lead I, Lead II, and Lead III) record the difference in voltage between two extremities. Lead I is the difference in the voltage between left and right arm. Lead II is the difference in voltage between left leg and right arm. Lead III is the difference in voltage between the left leg and left arm. Augmented configurations (augmented voltage right arm (aVR), augmented voltage left arm (aVL), and augmented voltage left foot (aVF)) are known as unipolar because the voltage is measured from one extremity instead of two as in bipolar. For the experiment conducted, we used the Lead I configuration to record the ECG signal. [3]

The ECG signal was used to determine the heart rate of the subject during the experiment. The heart rate is calculated by subtracting the distance (in time) between R-waves. This interval is used to divide into sixty to acquire the HR in beats per minute. HR= $60[sec] / (R_{n+1} - R_n)[mins*sec/beats]$. A program was designed using LabVIEW software to process the collected ECG waveform to determine the HR. This program will be discussed further in Chapter 3. [2,3]



Figure 1.7 Electrocardiogram waveform

1.7 The Effect of Stress on Cardiovascular Measures

Stress in the form of fear and anxiety does affect a person's cardiovascular measures. A study examined blood pressure (BP) and heart rate (HR) of students undergoing a medical licensing examination sought to assess the effect of a real life mental stress situation on HR and BP [11]. The findings of this study showed that diastolic BP (DBP)

increased by approximately 6% during and 8.6% after undergoing a stressful situation. Systolic BP (SBP) did not increase significantly; it increased 3.8% during and 3% after undergoing a stressful situation. HR decreased significantly by 12.3% during and 16.7% after the exam in comparison to before the exam. One thing that was not included in the study was to have the students undergo the exam once again and compare their BP and HR between the two sessions. This would tell us if familiarity with the exam caused them to be more relaxed

CHAPTER 2

CREATION OF MOCK fMRI: HARDWARE

2.1 System Overview

The pilot experiment entailed the creation of an MRI facility to simulate MRI experiments. In addition to the subject's perception, there had to be collection of cardiovascular measures to evaluate the subjects' reaction to the MRI environment. The main purpose of creating this facility was to increase subject comfort and compliance in a real MRI unit while participating in a pain study. An experiment was constructed to have subjects lay in the MRI unit and go through the pain study twice while their electrocardiogram (ECG), and blood pressure (BP) were collected. The BP was collected with the Dinamap (Section 2.8) from the upper arm and from their index finger with the Finapres (Section 2.7). The Dinamap BP was taken every 2 minutes. The Finapres BP was collected every 3 seconds. The Dinamap BP was collected to validate the accuracy of the Finapres BP measurement.

To accomplish these goals a LabVIEW[™] program was created to collect data from the ECG and Finapres instruments, and store them on a computer for offline analysis. The program interacted with these instruments while triggering an instrument used to produce warm stimuli to the subject, called the Medoc TSA II Neuro-Sensory Analyzer (Section 2.6). The program also output MRI scanning sounds to the unit, and turned on and off an LED that indicated to the experiment administrator to place and remove the thermode extension of the Medoc TSA II Neuro-Sensory Analyzer on the subject's forearm. The thermode is discussed in more detail in Section 2.6 The pain study entailed applying warm stimuli to a subject's forearm, then allowing the subject to rate the intensity and unpleasantness of each stimulus received. The stimulus is applied by the administrator in the MRI room. The administrator is given a cue each time to place the thermode on the subject's forearm and to remove it, so the subject can rate the intensity and unpleasantness. This is repeated for 10 warm stimuli. This study will be conducted at UMDNJ, and it is important that the subject is comfortable during the experiment so their complete concentration can be on the stimulus they are receiving. This will help to better isolate the areas that are processing pain perception during the study. By increasing the subject's exposure to a MRI surrounding and training the subject to rate the intensity and unpleasantness of a stimulus, more accurate analysis can be done to precisely identify regions of the brain that are responsible for pain processing. Figures 2.1 shows how the medical instruments were arranged to form the system necessary for the habituation experiment.

2.2 Mock fMRI Unit

The mock MRI unit was constructed using a decommissioned Picker 2055 Vista HPQ 0.5 Telsa MRI unit as shown in figure 2.2. This unit did not have a magnet and was not able to perform scans. It consisted of a gantry, base, MRI face, bore, and head coil. To make this unit resemble and sound like the Siemens Magnetom Allegra 3 Telsa fMRI Scanner at UMDNJ, several changes were made to the Picker unit, such as powering the faceplate and programming its light emitting diodes (LEDs) to display information available in the Siemens MRI unit. A mirror was mounted in the head coil to allow the subject to see the monitor behind him/her. PC speakers were mounted in the bore of the unit to play the sounds that the Siemens unit made while scanning the sequence of scans the subject would get through at UMDNJ.



Figure 2.1 Block Diagram of fMRI System

2.2.1 Mock fMRI Face Circuitry

To try to convince the subject that the unit was real and to provide the experimenter with visual feedback, the MRI face alphanumeric light emitting diodes (LEDs) were programmed to display static values of cardiovascular measures and status of the unit.

The face displayed: Ready for Scanning, Heart Rate, Blood Pressure, and Time Elapsed (Figure 2.3). The Picker unit was equipped with LEDs and buttons; however, controller for these circuits was destroyed. Reverse engineering of the LED circuitry was necessary to allow the newly developed system to program of the LEDs. The LEDs and buttons were connected to a two 60-pin bus connectors. Twenty-five pins on each of the 60 pin buses were connected to the computer via a PCI 96 Digital Input/Output channel card that was controlled using LabVIEW software.



Figure 2.2 Remodeled decommissioned Picker 2055 Vista HPQ 0.5 Telsa unit.


Figure 2.3 MRI face display

The LabVIEW program developed allowed the user to type in the message he/she would like to display, then when the program commenced the user designated where he/she would like to display the words and or numbers; in the right or left side of the face display. The LabVIEW program was designed to display these messages was separate from the program developed for the pilot experiment. This program was developed by Robert DeMarco, an engineer at the DVA in East Orange. This program has a list of all the binary codes for each character in the ASCII system. The program compares the desired text that the user enters to the binary code for each letter, number or symbol and writes it to a LED in the assigned column and row.

On the MRI face an LED was also programmed to act as an indicator to the person administering the heat stimuli to the subject. The LED was already a part of the circuit board that came with the unit, but the connection was broken to the board and was connected to one of the digital outputs on the BNC 2090 (discussed in Section 2.11). As the LED illuminates, the administrator uses this as a cue to place the thermode on the subject's forearm, the LabVIEW program then triggers the Neuro-Sensory Analyzer to send a warm stimulus to the thermode. This eliminated verbal directions and caused the

system to be more automated. Once the stimulus was finished, the LED was turned off indicating to the administrator to remove the thermode from the subjects forearm. This sequence of events will be discussed in more detail in the Chapter 4.

2.2.2 Mirror Attachment

The Siemens Unit at UMDNJ has a mirror attached to the head coil that allows patients to see the display screen behind them. A similar attachment was developed to allow subjects to see the screen behind them in the mock MRI unit. Figure 2.4 shows the Siemens design and Figure 2.5 shows the schematic for the design used in the mock fMRI unit.

For our design, a custom made mirror similar to the shape of the mirror used on the mirror attachment at UMDNJ was developed at Orange Valley Glass Company in Orange, NJ. This mirror was attached to a painted piece of wood using a bracket that swings freely. Restraint washers were applied to cause the mirror to move only when a small amount of pressure is applied. The wood and mirror were then attached to the head coil, now allowing a view of the monitor attached to the back of the MRI unit (see figure 2.6). A computer monitor was placed behind the machine, which will be discussed in Section 2.4. The monitor displayed the Descriptor Differential Scales (DDS) for Pain Intensity and Unpleasantness (Appendices D and E) to the subject participating in the experiment.



Figure 2.4 Mirror Attachment for Siemens MRI unit at UMDNJ.



Figure 2.5 Schematic of the mirror and its attachment for the mock MRI facility.



Figure 2.6 Mirror Attachment in Head Coil

2.2.3 Audio Simulation

To give the subject the illusion of a working MRI machine, computer speakers were installed in the bore of the unit (see figure 2.7) that simulated the sounds from the gradient coils within the Siemens unit at UMDNJ. Within the LabVIEW program created for the pilot experiment, we included commands for LabVIEW to play a recorded sound that the MRI unit makes during a T1 scan and a T2 scan. These sounds are caused by the electrical switching of the magnetic fields, which is dependent on the parameters the investigator chooses to use. Both sounds differ from each other because there is different electrical switching done to accomplish either scan. The speakers were positioned toward the upper sides of the circular bore for better sound quality throughout the unit. The speakers were connected to the sound card of the computer that played the sounds stored on the computer for the T1 scan and the T2 scan.



Figure 2.7 Speakers used to play T1 and T2 sounds

2.3 Audio Mixer

In the real fMRI there is two-way communication between the subject and the investigator. We used an audio mixer (MXE-812, Nandy Audio) to provide this two-way communication in the mock MRI. The system was designed to match the schematic shown in figure 2.8. This was done by connecting a microphone (Shure 550L) that was

located in the control room to one input channel of the audio mixer. A mini microphone that is attached in the bore of the unit was connected to the 2nd input channel. Two self-powered speakers were connected to the output of the mixer along with an Audio Technical Studio Phones headphone. One speaker was positioned in the control room and only sounds from the microphone in the bore could be heard through that speaker. The other speaker was positioned in the fMRI room to output instructions given using the control room microphone to the person applying the stimuli in the room. Headphones were worn by the subject to hear feedback from the investigator in the control room. Figure 2.9 shows the mixer with its connections and settings.



Figure 2.8 Audio Mixer Setup Schematic



Figure 2.9 Investigator's Microphone and Speaker, Audio Mixer.

2.4 Patient Visual Display System

The real MRI unit at UMDNJ has a visual display system that uses a projector to display figures, or scales that investigators want patients to see. A similar system was needed to display DDS pain intensity and unpleasantness scales to the subjects that will participate in the study to allow them to rate the heat stimuli that will be applied to their forearm. Due to space limitations a projector could not be used, so a 17 inch Proview Monitor (figure 2.12) was used as a part of our visual display system. Because the subject is lying down and looking through a mirror, the image on the display needed to be reversed. Proview provided a schematic of the monitor wiring. This schematic was used to identify the wires responsible for the horizontal scan of the display. These wires (red and yellow) were switched (figure 2.10) causing the horizontal scan of the display to change from scanning left to right left, to scanning right to left as displayed in figure 2.11. Appendix F

shows the schematic given to us by the company and also the pins that were switched to cause the correct flipping of the monitor display.



Figure 2.10 Circuitry inside Proview monitor.



Figure 2.11 Screen Capture of DDS Pain Intensity Scale on Reversed Monitor.



Figure 2.12 Proview 17" Monitor (that was used to display DDS pain intensity and unpleasantness scales).

2.5 Patient Response Unit

A custom response unit was required by the investigator that would allow subjects to respond to the DDS pain intensity and unpleasantness scales with little movement of the hand while in the MRI unit. This response unit would also be used in the Siemens MRI unit, so it had to contain minimal ferrous components. A Digitus Magic-Click mouse was remodeled (see figure 2.13) to serve as our patient response unit. This ergonomic mouse was ideal to make it easier for the subject to respond without moving his/her hand. A potentiometer was mounted by the thumb placement on the mouse to be used as a knob to scroll up and down the DDS pain intensity and unpleasantness scales. When a suitable answer is determined by the subject, he/she then uses the push button located below the index finger to select the corresponding number as his/her rating. The patient response unit was connected to the BNC 2090 that allowed interaction between the subject and the pain intensity and unpleasantness DDS scales that were shown on the reversed Proview monitor. One of the three necessary connections was to an analog input channel. This connection read the potentiometer position through 0 to 5 volts in 21 increments. The other connection was the push button to another analog input channel, which generated a

5-volt pulse when the button was pressed. Another connection was to the 5-volt output of the BC 2090 which powered the response unit. The complete connection diagram for the response unit system is shown in figure 2.14. An older model that was used in previous studies consisted of the same potentiometer and a similar type of push button, but the shape was rectangular forcing the subject to move his/her hand while responding. Movement of the hand also produces brain activation during an fMRI scan, so creating an MRI compatible response unit that required less movement of the hand while responding to the stimuli, would help to minimize activation of brain regions that may or may not be responsible for pain processing.



Figure 2.13 Patient Response Unit.



Figure 2.14 Patient response unit connection diagram

2.6 Neuro-Sensory Analyzer

To administer warm stimuli to the subjects we used the Medoc TSA II Neuro-Sensory Analyzer (Figure 2.15). This Neuro-Sensory Analyzer unit can warm and cool water at a rate of 0.3°C / second between the range of 0 ° - 50 °C. The water flows through two rubber tubes to a thermode. The thermode is encased in a 30mm x30mm plastic box. The thermode is made up of a Peltier type of sensor. The principle behind Peltier sensors is the Peltier effect, which is caused when an electric current (I) flows across the junction of two different types of semiconductors (A and B). The Peltier effect causes heat to move from one material to the other in the direction of the current. The rate at which heat is produced (\acute{W}) is equal to the difference in the Peltier coefficients (Π_A and Π_B) of the semiconductors multiplied by the current (I). This is illustrated in the equation: $\dot{W} =$ $(\Pi_A - \Pi_B)^*I$. W can be negative or positive depending on the direction of the current. When positive it represents the rate at which heat is produced and when negative it represents the rate that heat is removed. In the thermode, an aluminum-coated plate that comes in contact with the skin is placed adjacent to one of the semiconductors (A). The plate is cooled or heated depending on the direction of the current. The other semiconductor (B) is buffered by water that at 20 °C, which acts as a heat sink or source depending on the direction of current. The temperature at the surface of the aluminum plate is measured through a thermocouple made of copper and constantan wires that produce a voltage difference in response to change in temperature. [16]

For the pain study discussed in Section 2.1, temperatures of 44-50 degrees Celsius were used. The square thermode that is shown in Figure 2.16 was placed on the subject's

dominant forearm in ten locations and the Neuro-Sensory Analyzer produced the desired temperature via the thermode.

The laptop that is attached to the system runs a program that controls the output of the Neuro-Sensory Analyzer. The program used was Covas 3.13, which allowed three different options for sending a trigger to begin the stimuli. One option was an automatic trigger, where the program waits for an assigned time between 1 and 60 seconds and then sends the signal on its own. Another option is a manual trigger, where the program waits for the person administering the stimuli to push the space bar or any key on the keyboard. when he/she is ready to begin the stimuli. The third option is an external trigger that allows the click of either the patient response unit (patient mouse) or a click of the administrator's mouse to begin the stimuli. Option three was used. A 9 pin serial connector was connected to the patient's response serial input of the Neuro-Sensory Analyzer. Pins 6, 7, and 9 were wired to a relay. Pins 7 and 9 were jumpered and wired to the ground terminal of the relay, and pin 6 was wired to the output of the relay. The LabVIEW program was programmed to send a 5-volt signal pulse through digital input channel 0 to power the relay that initialized the Neuro-Sensory Analyzer as a trigger to begin stimuli. This allowed for more control over the timing synchronization, which has not been reported in similar studies.



Figure 2.15 Medoc TSA II Neuro-sensory Analyzer



Figure 2.16 Square Thermode used for Medoc TSA II Neuro- Sensory Analyzer

2.7 Finapres

The Finapres, made by Ohmeda is a continuous BP monitor. Finapres, an acronym for FINger Arterial PRESsure, continuously tracks changes in BP at the finger. The Finapres is based on a volume clamp method developed by Penaz [17]. In the Finapres is a finger cuff inflates to a pressure that clamps the finger arteries with a fixed diameter. The finger cuff is made of an inflatable bladder that receives the external pulsating pressure via a reactive servo system. The servo system continuously counterbalances the finger arterial pressure, which physically clamps volume oscillations of the arterial walls, nullifying pulsations. The fixed diameter is determined by measurements from an infrared

plethysmograph, mounted in the cuff, so that pressure through the arterial wall is zero and intra-arterial and cuff pressure are always equal. Figure 2.17 shows the Finapres and its connectors. There are several controls and outputs at the back of the unit. There is one for volume control of the alarms, another for a BNC output of the signal as it is also shown on the screen of the Finapres, and there is one for pulse rate output. The 2nd output was used to display the waveform of the BP via a BNC cable that was attached to the DAQ card via the BNC 2090 connector. The waveform consisted of voltages proportional to the BP with a scaling factor of 1volt/100mmHg. This signal was one of the analog inputs into the LabVIEW program and displayed on the Front Panel (Section 3.1) and the data were stored in a text file. [17]



Figure 2.17 Ohmeda Finapres BP Monitor

2.8 Dinamap

There were two instruments used to collect BP, one was the Finapres as previously discussed and one was the Dinamap made by Critikon, which is shown in figure 2.18. The Dinamap uses a pneumatic module to control pressure provided by an air pump to fill the cuff. The air pump is a rotary-driven pump that is powered by a pulse width

modulated dc voltage supplied by the power converter circuit. When blood pressure is measured, the air pump fills the cuff to a pressure of 178 +/- 15 mmHg. This will stop blood flow in the arm. Pressure is slowly released and the oscillations in the cuff caused by the blood flow are used to calculate the SBP and DBP. The Dinamap allows manual arterial BP recordings in increments of 1 minute to 1 hour. There are two modes of operation, namely manual and automatic. In manual mode the Dinamap takes the subject's BP when the start button is pressed, while in automatic mode the operator chooses the time interval that the Dinamap will automatically take the subject's BP.

For the pilot experiment, the manual option was used and the BP was collected at specific intervals. The Dinamap was set to collect BP twice during the 5 minute baseline stage, twice during the T1 stage, once at the end the 1 minute baseline stage, twice during the T2 stage and once during the Recovery stage.



Figure 2.18 Critikon Dinamap Blood Pressure Monitor

2.9 Electrocardiogram Amplifier and Filter

To measure the subject's electrocardiogram (ECG), a Coulbourn amplifier and filter were used (figure 2.19). The amplifier has the capability to connect up to 6 leads to the subject with 7 different configurations. It has the capability to amplify the signal collected off the body by a gain of 10,000. The filter receives the output of the amplifier and filters out noise (any other signal that distorts the signal you is interested in collecting) within the frequency range of 0 to 100 KHz. The filter operates as a band pass filter with a low and high frequency cutoff. The frequencies between the low and high cutoff frequencies will be kept, and frequencies outside this range are removed form the signal. Noises that are common to the ECG signal are, 60 Hz noise caused from power lines that operate at that frequency, and movement of the electrode that occurs at a very low frequency within the range of 0.01 - 1.0 Hz. To remove these artifacts, the band pass filter was used that had a low frequency cutoff of 0.1 Hz, and a high frequency cutoff of 55 Hz.

After the signal is amplified and filtered, the signal is converted from an analog (continuous), to a digital (discrete) set of samples. A continuous signal has an infinite number of data points. No computer can process an infinite number of data points, so the signal has to be digitized. Digitizing a signal involves sampling the signal at the correct rate with sufficient amplitude intervals (levels). Choosing the sampling rate is assigning the number of data points to be read per second. The sampling rate has to follow the Nyquist sampling Theorem that states that a signal has to be sampled at rate greater than twice its bandwidth. The amplitude interval, the smallest quantized step in amplitude, correlates to the resolution of the signal. An increase in the number of sampling intervals

(A/D) conversion. A/D conversion was done through the use of the 6024E National Instrument Data Acquisition (DAQ) card. This card, which is installed in the main computer, has sixteen 12-bit analog input channels each channel has a full range of =/- 10 volts up to 100,000 scans/second. The configuration used for the pilot experiment used 2 channels at 1000 scans/second each; one for BP and one for ECG. The quantization level or these conversions were: delta Q = Range / # of levels = 20 volts / 4096 = 4.88 mV.

The ECG signal is a result of electrical activation sequences of the ventricles in the heart that produce an action current that flows in the thorax. The action potentials produced by the heart resonate throughout the body and on its surface. The potential differences are determined by placing electrodes on the surface on the body. Electrodes are placed on different equal potential lines of the electric field of the heart to produce a non-zero potential difference. Standard positions are used in the evaluation of the ECG because different pairs of electrodes placed at different locations cause different voltages. This occurs because the electric field of the heart is spatial dependent. In the experiment, ECG was detected through the use of three leads connected to three electrodes on the subject's thorax. One electrode was placed on the right pectoral region of the thorax, another on the right pectoral region of the thorax, and one on the bottom right region of the thorax. This configuration follows the Lead I connection (LA and RA). Three leads were connected to the electrodes and transmitted voltage differences between the electrodes detected at the surface of the skin during the activation sequence of the heart ventricles. The leads were connected to an amplifier that amplified the signal received from the body from milli-volts to volts. The amplification used was 2 V/mV (2000 times in magnification). The signal was sent through two filters to remove noise (unwanted

signals) such as 60-Hertz noise, which is caused from the electrical line and other devices that are in operation, and noise caused by small movement. To accomplish this, the signal was filtered through a low pass filter with a cutoff frequency of 0.1Hz to remove small movement noise, and then the signal was filtered through a high pass filter that removed frequencies higher that 55Hz to remove 60Hz device noise. These settings were within the estimated ranges for a healthy adult. If connected to a child or a patient with a diseased heart, significant signal loss would occur. A better method to remove the 60 Hz noise would have been to use a notch filter instead of a low pass filter. [3]



Figure 2.19 Electrocardiogram Amplifier (top) and Filter (bottom)

2.10 Video Camera

The real fMRI has a large open glass window that allows the investigator to look in at the subject while he/she is in the unit. To minimize construction in our facility, a video camera located in the mock fMRI room connected to a small television in the control room was used to view the subject during the experiment. A video camera (Defender

Security, model B2-835) and the television monitor (Panasonic, model (TR-124) were used. (Figure 2.20)



Figure 2.20 fMRI Room Video Camera and Monitor

2.11 Computer System

The computer is the main controller for the experiment. It provides outputs and records inputs from the systems discussed. The computer used was a Dell Pentium 4, 2.0 GHz computer with 512Mb Random Access Memory. An addition to the computer for this experiment was a Matrox Power Desk – HF dual video card. This allowed up to three separate monitor displays. Two displays were used, one to display the cardiovascular measures being collected and to maneuver controls such as stopping and running the program for the operator and the other display was used to display the pain intensity and unpleasantness scales to the subject.

The next two additions to the computer were for the Analog to Digital (A/D) Conversion and acquiring the signal. A National Instrument Data Acquisition (DAQ) card was installed in an available PCI slot in the computer. Two separate cards were used to meet the needs of the experiment. The first need was to communicate to the MRI Face (to display heart rate, blood pressure and time elapsed. For this a PCI DIO 96 DAQ card was used since task entailed only digital communication. This card offers 2 sets of 50 digital outputs. For each side of the MRI face 25 digital inputs were needed, so this card was the most suitable to fulfill the needs.

The second need was to communicate with the Finapres, Coulbourn electrocardiogram amplifier and filter, the response unit for the subject, the Neuro-Sensory Analyzer, and the administrator's visual indicator. A PCI 6024E DAQ card was used to accomplish these requirements. This card connects to a BNC 2090 connector that has 16 analog input channels, 8 digital input/output channels with 2 digital grounds and a 5-volt output. The first analog input channel was used to input the ECG signal, the second to input the BP signal from the Finapres, and the third and fourth to input the response the subject chose from the pain scales. The 5-volt output was used to power the patient response unit. One digital output connected to the digital output channel 1 was used to trigger the Neuro-Sensory Analyzer, and digital output 0 was used to trigger the administrator's visual indicator.

CHAPTER 3

CREATION OF MOCK fMRI SOFTWARE

3.1 LabVIEW Program

To control the components of the hardware system and to record the data from the instruments, a software program was required to perform this custom task. LabVIEW (Laboratory Virtual Instrumentation and Experimentation Workbench by National Instruments) was chosen as the programming language because of its ability to interface with the environment outside the computer and to display, process, analyze and store data.

LabVIEW is set up with two main windows or interfaces, one called the Front Panel and the other is called the Block Diagram. The Front Panel or user interface, displays information that is generally seen on the display of any electronic device such as graphs, indicators and strings of numbers (see figure 3.1). These displays are connected in the block diagram, which represents all the wiring within the casing of a device (see figure 3.2). The block diagram is an object oriented programming language

For this pilot experiment, the main interest was detecting, displaying, storing, and analyzing cardiovascular measures, namely blood pressure (BP) and electrocardiogram (ECG). The hardware setup for both of these was previously discussed in Sections 2.7 and 2.9. It is important to understand how the software and hardware work together to achieve the goals of detecting, displaying, storing, and analyzing physiological data.



Figure 3.1 Front Panel in LabVIEW for mock MRI cardiovascular measures collection



Figure 3.2 Block Diagram in LabVIEW for mock MRI cardiovascular measures collection

3.2 Displaying Analog Signals

LabVIEW was used to collect and display the analog ECG and BP from the body. In LabVIEW analog signals are processed in the following manner: The analog input is configured to handle the data being collected using the analog input configuration (AI Config) block shown in figure 3.3a. This block represents a subroutine that allows the programmer to choose which device or DAQ card to read the information through, what channels to read, and the buffer size. For the pilot device 1 as selected, reading channels 0 to 4. The buffer size was set to 100,000 scans to facilitate the large number of scans read per second (100). Then there is an initializing stage where the signal collection starts and the rate at which the signal is collected is specified. This occurs in the analog start (AI Start) block shown in figure 3.3b. At this point the A/D converter will begin sampling at the specified rate (1000 scans/sec). Using direct memory access, it stores the data into the buffer. Then LabVIEW needs to be told how many scans to read at a time out of this buffer. It is more efficient to read the data from the buffer in blocks than trying to process one sample at a time. This is done using the analog input read (AI Read) block shown in figure 3.3c. The output of the AI Read can be in the form of 2dimensional scaled data, binary data, or waveform data. The ECG signal can be displayed using either 2-dimensional scaled data or waveform data. The three analog input blocks are connected to each other by the task ID output of each block. The next step in displaying the ECG data is connecting the output of the AI Read block to a waveform chart. This gives a visual representation of the data being collected. The filter parameters used, were a low cutoff frequency of 0.1 Hz and a high cutoff frequency of 55 Hz (Section 2.9)



Figure 3.3a Analog Input Configuration block in LabVIEW



Figure 3.3b Analog input Start block in block diagram.



Figure 3.3c Analog Input Read block in block diagram.

3.3 Patient Response to Pain Scales

In addition to collecting cardiovascular measures, LabVIEW software was used to read movement up and down the DDS pain intensity and unpleasantness scales and to identify when an answer was selected using the patient response unit. One channel of A/D was used to read the array of scrolls and another to read when an answer was selected. This was done by using the same sequence of blocks as discussed above, but the array read the first channel was the input of the pain intensity and unpleasantness scales. The value read through the other corresponds to the values where the button on the response unit was pressed.

The voltage supply available through the BNC2090 was 5 volts. Both intensity and unpleasantness scales ranged from 0 to 20, limiting each rating to an increment of 0.2381 volts. The 0 to 20 DDS scales were preferable over the 0 to 10 scales, because they gave the subject more choices so he/she can accurately identify how intense and unpleasant the stimulus received felt. The 5 volt supply and ground are fed to the ends of the potentiometer. The potentiometer acts as a voltage divider and the voltage out is the proportional to the subject's response. The range of the output of the potentiometer had to be divided into 20 levels, which corresponded to the 20 response choices. The 'In Range and Coerce' block was used, as shown in figure 3.5 to set the ranges for each value on the DDS scales. The lower limit is the previous rating voltage value and the upper limit is the voltage value of the rating of interest. The 'x' value is the position of the potentiometer on the response unit.

The output value used was the 'In Range?' which was attached to a Boolean on the front panel (shown in Appendices E and F) with the corresponding rating value. This output was also fed into the 'Boolean to (0,1)' block and multiplied by the value of the selected rating. If the potentiometer was on a value of 4.76 volts for example, the Boolean on the front panel corresponding to the rating number 19 would turn white in contrast to the color it previous was (yellow-Intensity or green-Unpleasantness). The 'Boolean to (0,1)' block would output a 1 and this value would be multiplied by 19 and added with zeros in the 'Compound Arithmetic' block since none of the other ratings would produce a one, only zeros. The value selected is indexed for storage. Once the summation is complete, another loop begins in the FOR loop and the response of 19 is stored in the master program. The FOR Loop's repetition condition was the size of the potentiometer range divided by two allowing the program to move on when the array changed or a value was selected. Since this was embedded in the master program as a sub VI, the properties in terms of window appearance and method of execution had to be changed. The sub VIs (Pain Intensity and Unpleasantness) were set to show front panel when called and close after.



Figure 3.4 Block Diagram of DDS Pain Intensity and Unpleasantness Scales.



Figure 3.5 The In Range and Coerce block in LabVIEW.

In the overall program, both the DDS pain intensity and unpleasantness scales were sequenced using a flat sequence structure (see figure 3.6). First, the subject would be presented with a red cross (a sub VI developed previously by Lynn Auger, an engineer at the DVA in East Orange) for 10 seconds. Then the subject would receive a warm stimulus, then the pain intensity scale would come onscreen replacing the red cross at the end of the stimulus and the subject would then use the response unit to scroll up and down the scale to find the intensity he/she perceived the warm stimulus to be using the potentiometer. When the subject reaches a rating that corresponds to their perception, he/she would press the button on the response unit to select the rating as their response. After an answer is selected, the subject is then presented with the pain unpleasantness scale and the subject then has to use the response unit to rate how unpleasant the warm stimuli felt to him/her. After the subject has answered, the program moves on to save the subject's response and repeat the loop. The loop is repeated for the number of stimuli that the investigator wishes to give to the subject.



Figure 3.6 Sequence of presentation of Pain Intensity and Unpleasantness scales

3.4 Neuro-Sensory Analyzer Triggering and Visual Indicator

LabVIEW was used to trigger the Neuro-Sensory Analyzer and to indicate to the administrator of the machine when to apply stimuli. This was done by using the digital output channels 0 and 1, along with the digital ground terminals on the BNC 2090. In the block diagram the digital output channels of the BNC 2090 were wired to a Digital Line Output (Digi-Line) block shown in figure 3.7. This block writes a 5 volt pulse to the selected channel, depending on whether the state of the line was true or false. If the state was False, then 0 volts was sent and if true, a 5 volt pulse was sent. Case structures (similar to traditional If-Then statements) were used to organize when in a loop the trigger should be sent to the Neuro-Sensory Analyzer, and when the LED should turn on, on the MRI face to indicate to the administrator to place the thermode on the subject's arm.

For the triggering of the Neuro-Sensory Analyzer we used a relay that was normally closed. The relay was powered with 5 volts from the BNC 2090 digital channel output number 1. In the LabVIEW Program, the Dig-Line block was placed in the beginning of the program and set to true, causing 5 volts to power the relay constantly. Then to trigger the Neuro-Sensory Analyzer, the line was set to false for 0.5 seconds and then set back to true. This was done to simulate a mouse button click. The program, Covas 3.13, that operated the Neuro-Sensory Analyzer allowed for a manual trigger, an automatic trigger and an external trigger. The manual trigger would ask the administrator to press enter on the keyboard to begin a stimulus. The automatic trigger would begin the stimulus after a designated time. The external trigger would wait for a click on a mouse connected to the response unit serial port on the Neuro-Sensory Analyzer. A 9 pin serial male connector, wired with two wires to the relay was used instead of the mouse. This would allow the investigator to have the Neuro-Sensory Analyzer triggered in sequence with the subject's response to the pain intensity and unpleasantness scales. This was necessary since each person took a different amount of time to respond.

In efforts of making the system even more automated, LEDs were connected in the mock MRI face circuit. The purpose of these LEDs were to signal the person administering the thermode to the forearm of the subject, when to place and remove the thermode between stimuli. The same Digi-Line block in figure 3.7 was used. The LED was connected to digital output channel 0 of the BNC 2090. In the LabVIEW Program, we placed the Digi-Line block in the beginning of the program and set the line state to false, causing the LED to normally be off. When the thermode was to be placed on the person's forearm, the LED would illuminate, representative of the line state set to true. When the thermode was to be removed for the subject to rate the given stimulus, the LED would not illuminate representative of the line state being set to false. The sequence of the LED, trigger and pain scales can be seen in figure 3.6.



Figure 3.7 Digital Line Output block in LabVIEW

3.5 Organization of all Collected Data

The LabVIEW Program was also used to organize the subject's data being collected. This was done by using a Patient ID sub VI (see figure 3.8). This sub VI allowed the user to enter the patient's identification number, and to select a file path to save the data. The sub VI was sequenced in the beginning of the program and would cause the program to wait until this section was completed to begin the experiment. In the path that was selected to store the data, several files were created once the program started. A text file was created for each stage of the program, and within each stage a BP file and an ECG file were created, see figure 3.9. In addition to those two files, an answer file was created during the T2 stage when the patient was given the warm stimuli.



Figure 3.8 Patient ID sub VI in LabVIEW



Figure 3.9: File Storage and Organization



Figure 3.10 Write to Spreadsheet block in LabVIEW

3.6 MRI Sound Simulation

LabVIEW was also used to play the sounds that the real MRI would make during T1 (anatomical scan of the brain) and T2 (functional scan of the brain). For this we recorded the sounds from the real MRI unit at UMDNJ and used Cool Edit Audio software to amplify the sounds collected. Cool Edit software was used to make a 5 minute long T1 sound and a 20 minute long T2 sound. Within LabVIEW the Sound Play Wave File

block (see figure 3.11) was used to play the sound files. This block inputs the file path that the sound is saved in and plays it until it is finished. The T1 file path was connected to the Sound Play Wave File block during the T1 stage where the subject remained still and viewed a red cross on the screen. The T2 file path was connected to the Sound Play Wave File block during the T2 stage, where the subject remained still while receiving the designated number of stimuli and rating each one's intensity and unpleasantness.

Figure 3.11 Sound Play Wave File block in LabVIEW

CHAPTER 4

METHODOLOGY

4.1 System Setup

The mock fMRI is designed to mimic the fMRI system at UMDNJ. Therefore, we set up a control room was set up adjacent to the fMRI room. In the control room, there was the master computer that was connected to, the Finapres via the DAQ BNC 2090 connector, the ECG amplifier via the same DAQ connector, the speakers in the fMRI unit that play the simulated sounds recorded during a real fMRI scan, and the patient monitor via video card. To view the fMRI room a video monitor was connected to the video camera in the room. To listen to the subject while he/she was in the mock fMRI, an omni-directional microphone was connected to the audio mixer and the output was directed to the right speaker located in the control room. To speak to the subject a PA microphone was connected to the audio mixer that was outputted to the headphones the subject was wearing and the left speaker that was located in the fMRI room. There was wallpaper put up in the mock fMRI room that is similar to wallpaper at the real fMRI room at UMDNJ.

4.2 Physiological Connections

Each subject is connected to the ECG amplifier using a 10 foot long ECG cable. We used the Lead I connection, placing electrodes on the right arm, left arm, and right leg. Each subject wore the upper arm Dinamap BP cuff and received stimuli from the thermode attached to the Neuro-sensory Analyzer on the non dominant arm. The Finapres finger BP cuff and the response unit were attached on the dominant arm. Only the Dinamap cuff and the thermode were MRI compatible. The Finapres BP, and ECG signal would not be monitored during the study at UMDNJ, but were useful to determine change in stress response for the pilot experiment. The Finapres was also used in a previous study that did not entail the use of an MRI, and in order to compare these data, the Finapres was necessary during the piloting stage.

4.3 Procedures

In order to test that all the equipment worked in the correct manner, a similar experiment as the investigator's (Dr. D. Cook) was created. A program in Covas 3.13 was developed, that would give the two subjects, 10 warm stimuli, between 38 and 42 degrees Celsius. One subject was a male in between ages of 25-30, and the second subject was a female between the ages of 18-25. All sessions were conducted in the afternoon at least an hour after lunch. Both sessions were conducted over two weeks, with no less than on week between each session.

First, each subject received a presentation of each the procedures and received information about each scale and how to rate. The subject was connected to both BP units and the ECG unit. Then he/she lay down on the gantry and was pushed manually into the bore and head coil. The subject adjusted the mirror to make sure he/she could clearly see the monitor. A practice program was run in which the subject had a chance to practice using the patient response unit to rate on both scales. When the subject was familiar with using the response unit, the practice program was stopped and the LabVIEW program began to collect cardiovascular measures for 3 minutes while the subject viewed the cross on the patient monitor (Stage 1: 3 minute baseline). As the

subject remained still and continued to look at the cross, the T1 sound was played for 4 minutes (Stage 2: T1). Then the T1 sound was stopped and subject remained still for 1 minute, which represented the recovery period in the real fMRI (Stage 3: 1 minute recovery). Then the T2 sound was played. The administrator saw the green LED, indicating that s/he should place the thermode on the subject's arm and then after 15 seconds the thermode was removed and the subject rated the warm stimuli they felt on their arm. The subject while laying down first saw the pain intensity scale and the program waited for a response. Then the pleasantness scale was presented to the subject and the program waited for a response. Then the subject was presented with the cross, while the administrator's visual indicator came back on. These procedures were repeated 9 times until all the stimuli were given and all responses were received (Stage 4: T2). Then the subject remained still for another 1 minutes of recovery (Stage 5: 1 minute recovery) and then the program stopped and the subject was slowly pulled out of the bore and was detached from all the equipment.

4.4 Habituation Validation

In addition to validating that the system worked correctly, we performed a pilot experiment to see if the system decreases anxiety by the subject. This validated that the system really does habituate subjects to the fMRI. For this experiment we repeated the procedures in section 4.3 a second time to collect cardiovascular measures and to compare them to those collected during the first run. We also had each subject fill out a questionnaire (see Appendix G) that asked them to compare their first and second run in the fMRI.
CHAPTER 5

SIGNAL PROCESSING AND ANALYSIS

5.1 Signal Processing of Electrocardiogram

The ECG signal collected from each subject was collected at a scan rate of 1000 scans per second. This scan rate was chosen by Dr. Cook, to match the scan rate of his previous studies and is appropriately greater than the Nyquist frequency. The block in LabVIEW that was used to write the files was the 'Write to Spreadsheet' block (figure 3.10). There were five stages in total: stage one was a baseline period that lasted for 5 minutes during which the subject remained still while cardiovascular measures were being collected, stage 2 was the simulation of a T1-wieghted anatomical scan which lasted for 4 minutes, stage 3 was a rest period in between scans that lasted for one minute, stage four was the simulation for a T2-weighted functional scan that lasted for 5-10 minutes, and stage five was a recovery period which normally follows a functional scan to see how the brain recovers to its non stimulated state that lasted for 2 minutes. For efficiency, the LabVIEW program was constructed to write the data collected after each 100 scans were read into the buffer. This caused the file that was created to have 100 columns and many rows. The first processing step was to re-organize the data collected into one column. This was done by re-writing the collected file to a new file, reading row by row and placing all data in one column. This step can be seen in figure 5.6a.

Once the data were re-organized, a search was done for all R-waves in the ECG signal. This was done using the 'Threshold Peak Detector' block shown in figure 5.1. The ECG signal was fed into the 'X' input and the threshold was set by looking at the

57

ECG signal. The count output displayed the number of peaks found throughout the entire ECG signal. For each peak found that was above the threshold, its position in time was recorded via the indices output. Each R-wave was validated by comparing the difference between its index and that of the following index with the approximate distance between both R waves.





The indices of the occurrence of each R-wave in time were then subtracted to find the R-R interval between all R-waves detected (see figure 5.3b). The outcome of this calculation was then divided by the scan rate to get the actual distance in real time. This distance is then fed into the equation: $HR = 60[sec] / (R_{n+1} - R_n)$ [mins*sec/beats].

dit Operate Tools gravme Window deto 2 30 million Application Font v Renv deta deta deta v	
Converting saved waveform (10 columns) to single column Path of columns to single column	Ladculation of H. R interval and Heart Rate
Printer and Annual Printer	- 19 A Strawyor
Deter Just of Poeks in composing thate	Conference (second to are instant factors (space for the
Therease and the second	
el estrene branced	
	金云 联邦 的复数形式 正规 计分析法

Figure 5.2 Front Panel of Heart Rate calculation program in LabVIEW



Figure 5.3a Block diagram of LabVIEW heart rate calculation program. Stage 1, identifying R-waves in the ECG signal.



Figure 5.3b Block diagram of LabVIEW heart rate calculation program. Stage 2, Validation of R-waves in the ECG signal.



Figure 5.3c Block diagram of LabVIEW heart rate calculation program. Stage 3: Calculating the time interval between R-waves in the ECG signal.



Figure 5.3d Block diagram of LabVIEW heart rate calculation program. Stage 4: Calculating heart rate from the time interval between R-waves in the ECG signal.

5.2 Processing of Finapres Blood Pressure

Similarly to the ECG collection, the Finapres signal from each subject was collected at a scan rate of 1000 scans per second, reading 100 scan each time into the buffer. The same block in LabVIEW was used to write the data to a spreadsheet and the same problems

were present. The first processing step was to re-organize the data collected into one column. This was done by re-writing the collected file to a new file, reading row by row and placing all data in one column. This step can be seen in figure 5.6a.

Once the data was re-organized, a search was done for the peaks and valleys in the BP signal. The peaks represent the systolic BP and the valleys represent the diastolic BP. This was done using the Peak Detector block shown in figure 5.4. This block was used instead of the Threshold Peak Detector block because it outputs the value of the amplitudes in addition to their location, unlike the Threshold Peak Detector block that only outputs the location or index. The BP signal was fed into the 'X' input and the threshold was set for a value determined by looking at the BP signal. The '# found' output displayed the number of peaks found throughout the entire BP signal. For each peak found that was above the threshold, its position in time was recorded via the location output. Each Peak or valley was validated by comparing the difference between its location and that of the one that follows location with the normal anticipated distance between both peaks and valley. The amplitudes that were valid were multiplied by 100 to arrive at the systolic and diastolic BP. Both these files were stored and then graphed in Microsoft Excel to show comparison.



Figure 5.4 Peak Detector block in LabVIEW



Figure 5.5 Front Panel of Blood Pressure calculation program in LabVIEW



Figure 5.6a Block diagram of LabVIEW Blood Pressure calculation program. Stage 1, Re-writing Files of collected data.



Figure 5.6b Block diagram of LabVIEW Blood Pressure calculation program. Stage 2, Detection and Validation of Peaks and Valleys.



Figure 5.6c Block diagram of LabVIEW Blood Pressure calculation program. Stage 3, Calculating and writing BP to files.

63

5.3 Processing of Mock MRI Questionnaire Responses

To get subjective feedback as to how comfortable the procedure was, a mock MRI questionnaire (shown in Appendix C) was developed. Microsoft Office Excel was used to graph the responses from the mock MRI questionnaire. Each question on the questionnaire had answers that were weighted between -2 and 2. This made the least comfort experienced to be a -22 and the most comfort experienced to be a 22, based on the scaling in the mock MRI questionnaire. Each subject had to fill out the questionnaire after the completion of each session. The responses were added together and compared between both sessions. The total score of each session was graphed using a bar graph. Each overall score represented the comfort level of the subject during the experiment. From the graph one would be able to determine if the subject was more comfortable in one session versus the other and how much more comfortable.



Figure 5.7 Microsoft Excel Spreadsheet of responses from mock MRI Questionnaire.

CHAPTER 6

RESULTS

6.1 Results of System

According to the specifications given by the investigator, all the equipment worked together, in synchrony as anticipated. The sounds played at the right time and for the correct duration. The cross was presented to the subject at all times except for when the pain scales were being presented. The pain scales were shown on screen at the correct times and did wait for a response. The patient response unit did scroll up and down the pain scales smoothly. The program did recognize when an answer was selected and stored the selected answer. The analog to digital conversion of the ECG and Finapres BP signals showed the absence of 60 Hz noise. Some noise was noticed in the T2 stage during post processing that occurred because of movement when the subject was rating using the response unit. The ECG and BP data were stored for all stages along with the answers selected during the T2 stage. In addition to these, the triggering of the Neuro-sensory analyzer worked and was synchronized with the sound playing, and presentation of the scales.

6.2 Results of ECG Signal Processing

To test if the system habituated subjects, changes in cardiovascular measures were examined. These changes helped to facilitate whether or not the subject was more comfortable during their second session or their first. For this the heart rate and blood pressure collected in both sessions were compared for each subject.

65

The heart rate of subjects 1 and 2 for both sessions are shown in figure 6.1 and 6.2. From the graphs, it can be shown that in session 2 the subject's heart rate was lower than in session 1. The average heart rate during session 1 was 57.5 and 58 respectively, while the average heart rate in trail 2 was 56.3 and 55.8 respectively. The average heart rate was also calculated for both sessions and the percentage of decrease between session 1 and session 2 were determined for both subjects. For subject 1, the average heart rate decreased by 2.23% between session 1 and 2. For subject 2 the average heart rate decreased by 4.10% between sessions. This shows that there was no significant change in heart rate between the two sessions. This small change in HR can be attributed to a number of things. One way to see if the mock fMRI unit truly habituates is to compare the heart rate between multiple sessions.

The graph does show that session 1 lasted longer than session 2. All the stages in the program were restricted to a set time. The only stage that was dependent on the subject's response was the T2 stage, when the warm stimuli were given. In this stage, the program waited on the subject to respond on the pain intensity and unpleasantness scales. This means the subject took less time to complete the pain intensity and unpleasantness scales in session 2 than they did in session 1. This finding supports the hypothesis that multiple exposure to the environment will cause the subject to be less anxious and complete the task at a faster pace.



Figure 6.1 Subject 1 Heart Rate comparison for sessions 1 and 2.



Figure 6.2 Subject 2 Heart Rate comparison for sessions 1 and 2.

Stressful situations can cause changes in cardiovascular measures. It was expected that when the T1 and T2 sounds were played, and the warm stimuli were applied the HR of each subject would increase signifying a stressful situation, and decrease during recovery stages signifying removal of stress. Successful habituation would cause the percent change in HR to decrease during the second exposure to the stressful situations. Analysis of the heart rate changes between stages were done to examine if the percentage of change in HR during the stages decreased in the second session for both subjects. The last minute in the 3 minute baseline stage was compared to the average HR of the first minute in the T1 stage (comparison 1). The average HR of the last minute in T1 stage was compared to the average HR of 1 minute Recovery (comparison 2). The average HR of 1 minute Recovery was compared to the average HR of first minute in T2 stage (comparison 3). The average of the first minute, midpoint and last minute of the T2 stage were compared (comparison 4). The average of the last minute of the T2 stage was compared to the average of the final 1 minute recovery (comparison 5).

During session 1 for subject one, it is noticed from the graph in Figure 6.3 that when the T1 sound was played it caused an increase in the HR which continued to ascend until the sounds stopped. When the sounds stopped the HR decreased by 4.0% during the 1 minute recovery. This decrease in HR continued throughout the beginning and middle of the T2 stage when the warm stimuli were delivered to the subject and the T2 simulated sounds were being played. This decrease implies that the subject became more comfortable hearing the sounds. It would be expected that the HR would have increased even more than in the T1 stage, since both sound distraction and a warm stimuli were presented to the subject at once. Towards the end of the T2 stage HR increased by 9.1%, but still did not climb to the HR observed during T1 stage. The HR then decreased by 3.1% during the 1 minute recovery stage as expected since no warm stimuli nor sounds were presented to the subject.



Figure 6.3 Subject 1 Session 1 HR trend

In session 2, the same trend occurred between the end of the 3 minute baseline, the T1 stage and the 1 minute recovery period. However, the average HR that were compared, were less for each time in the stages, and the percent change between all comparisons were less. This supports the view that subject 1 was less anxious during session 2. One major difference observed between the two sessions, is that in session 2 instead of HR decreasing at the beginning of the T2 stage as it did in session 1, it increased by 3.7% for the 1st minute and then decreased as in session 1. This was the expected trend, but it did not occur in session 1.



Figure 6.4 Subject 1 Session 2 HR trend

Similarly to subject 1, subject 2 experienced an increase in average HR when the T1 sound began to play. The HR of subject 2 then decreased towards the end of the T1 stage and increased in HR during the recovery period. This implies that subject 2 became used to hearing the sound, but became anxious as he/she remained still in the unit awaiting the next stage. The percent change in HR during the T1 and 1 minute recovery stages were below 5%, so they could be attributed to normal heart rate variation. During the T2 stage it is observed that the HR decreased between the start of the stage to the middle of the stage but then increased at the end. This same trend was noticed in subject 1 for both sessions. This implies that the subjects became more comfortable midway through the T2 stage, but then became anxious towards the end as the sound and warm stimuli continued. The HR then decreased by 1.35% during the recovery period.





During session 2, subject 2 showed an increase in HR when the T1 sound was played, however, the average HR decreased by more than 8% during this time. Similar to subject 1, the HR continued to increase until the sound stopped and then decreased. It is not clear why subject 2 experienced an increase in HR during the 1 min recovery stage after the T1 sound was played in session 1 but experienced a decrease in HR of approximately 9.0% during session 2. When the T2 sound and the warm stimuli were presented the subject, he/she experienced an increase in HR of 3.3%, which continued to ascend until the end of the stage. The change in average HR during session 2, followed the expected trend, but cannot be explained from this analysis why it was so different from session 1.



Figure 6.6 Subject 2 Session 2 HR trend

6.3 Results of Blood Pressure Signal Processing

In addition to HR comparison, BP comparison was done for both sessions with data collected from the Finapres and the Dinamap. The Finapres gave continuous BP samples every 3 seconds, monitoring any change in BP. The Dinamap was set to collect BP twice during the 5 minute baseline stage, twice during the T1 stage, once at the end the 1 minute baseline stage, twice during the T2 stage and once during the Recovery stage.

The BP of subjects 1 and 2 for both sessions are shown in figure 6.7 and 6.8. From figure 6.7 it can be shown that there were no noticeable changes to either the systolic blood pressure (SBP) or diastolic blood pressure (DBP) across the two sessions for subject 1. The average BP during session 1 for subject 1 was 115.4/55.8 mmHg, while the average BP in session 2 was 117.3/55.2 mmHg. It is inconclusive whether or not the slight increase in SBP in session 2 means that the subject experienced more stress in this session than in the first. From figure 6.8, it can be shown that there was no noticeable change to the SBP, but there was greater change in DBP across the two sessions for subject 2. The average BP during session 2 for subject 2 was 107.4/62.8 mmHg, while the average BP in session 2 was 111.5/53.2 mmHg. The decrease in SBP and DBP in session 2 implies that the subject experienced less stress in this session than in the first.

The average BP was also calculated for both sessions and the percentage of decrease between session 1 and session 2 were determined for both subjects. For subject 1, the average SBP increased by 1.7% between session 1 and 2 and the average DBP decreased by 1.0%. For subject 2, the average SBP decreased by 3.8% between session 1 and 2 and the average DBP decreased by 15.3%. The decrease in the DBP indicates that the subject was more relaxed during session 2 since this average BP was closest to their baseline BP

Similarly to the HR graphs, the BP graphs show that session 1 lasted longer than session 2. This supports the hypothesis that multiple exposure to the environment will cause the subject to be less anxious and complete the task at a faster pace.



Figure 6.7 Subject 1 Finapres Blood Pressure comparison for sessions 1 and 2



Figure 6.8 Subject 1 Finapres Blood Pressure comparison for sessions 1 and 2

Similarly to HR, stage by stage analysis was done to further explore the changes in BP for both subjects. The average BP of the last minute in the 3 minute baseline stage was compared to the average BP of the first minute in the T1 stage. The average BP of the last minute in T1 stage was compared to the average BP of 1 minute recovery. The average BP of 1 minute recovery was compared to the average BP of first minute in T2 stage. The average BP of the first minute, midpoint and last minute of the T2 stage were compared. The average BP of the last minute of the T2 stage was compared to the average of the final 1 minute recovery.

It was observed form the graphs shown in figure 6.9 ad 6.10 that there was little if any change in both the average SBP and DBP for subject 1 during and between both sessions. All average percent changes in SBP and DBP were below 2.5% during the sessions. Changes of this magnitude do not reveal much about the impact of stress on the cardiovascular system, since these changes are within normal expected variations. According to Zeller, et al, changes of 5% or greater in DBP and SBP accurately depict changes in cardiovascular measures in response to stress in the form of anxiety. [11]



Figure 6.9 Subject 1 Session 1 BP



Figure 6.10 Subject 1 Session 2 BP

For the second subject there were greater average BP changes observed during and between both sessions. During session 1, SBP increased by 3.6% when the T2 stage began, but only increased by 1.9% in session 2. Such a small increase in SBP cannot accurately be correlated to stress response, however it does show that subject 2 SBP increased by a smaller percentage in session 2. For comparison 2, it is observed that both the percent decrease in SBP and DBP, increased between session 1 and session 2. The SBP decreased by 0.8% when the T1 sound was stopped in session 1, and decreased by 3.3% in session 2. This suggests that subject 2 became more relaxed in session 2 after the T1 sound stopped than in the first session. It is also noticed that during session 2 the SBP did not increase as much as the first session when the T2 stage began. These results imply that even though subject 2 had a greater increase in BP during the start of session 1, the subject became more relaxed for the remainder of the experiment, experiencing changes of less than 2% in SBP. Similarly to SBP in comparison 2 between both sessions, DBP decreased by a greater percentage during session 2 than in session 1. In session 1 DBP for comparison 2 decreased by 0.3%, but decreased by 5% in session 2. There was a greater increase in DBP during session 2 for comparison 3, but for the remainder of the session DBP increased and decreased at lower percentages than in session 1.



Figure 6.11 Subject 2 session 1 BP



Figure 6.12 Subject 2 session 2 BP

Similar trends were noticed in HR and BP. For subject 1, when HR increased or decreased, SBP and DBP similarly followed for all comparisons in session 1, and all but the 4th comparison in session 2. For subject 2, when HR increased or decreased, SBP followed for all but the 3rd comparison in session 1 and all but the 4th comparison in session 2. The DBP followed increase and decrease in HR for all but the 3rd comparison in session 2.

The Dinamap recordings were handwritten and then transferred to Microsoft Excel. The data acquired are shown in figure 6.13 and 6.14. Data were acquired from the Dinamap to see how closely, it correlated to the data collected from the Finapres. Finapres cannot be used in an fMRI because of its metallic components, so both devices were used in the mock fMRI facility. This was done to allow comparability with previous studies that used Finapres to measure BP response to stress in the form of pain outside of an fMRI environment. The trend of the Dinamap BPs is the same as those in the Finapres data findings.



Figure 6.13 Subject 1 Finapres and Dinamap BP comparison for sessions 1.



Figure 6.14 Subject 2 Finapres and Dinamap BP comparison for sessions 1

6.4 Results of mock MRI Questionnaire

In addition to cardiovascular changes, subjective changes were recorded to further analyze whether each subject was more or less habituated to the environment. The mock MRI questionnaire (Appendix B) was used for this evaluation. All thirteen questions, except for questions one and five, on the questionnaire had answers that were weighted between -2 and 2. An index score of comfort was created by summing the response of the eleven weighted questions. This made the least comfort experienced to be a -22 and the most comfort experienced to be a 22, based on the scaling in the mock MRI questionnaire. Each overall score represented the comfort level of the subject during the experiment. Both subjects were naïve to the goal of the experiment during the first session. The result of the mock MRI questionnaire showed that both subjects experienced more comfort and less anxiety during the second session (see figure 6.3). Subject 1 experienced 53.3% more comfort during the second session. Subject 2 experienced 17.6% more comfort during the second session. Even though these results are subjective, they do show that both subjects experienced some greater comfort in the second session.



Figure 6.15 Overall Habituation Level for subject 1 and 2 for session 1 and 2.

CHAPTER 7

CONCLUSION

The aim of the pilot experiment was to test all the devices that are a part of the mock fMRI facility and to test if the environment habituates subjects to an fMRI environment. Based on the results there is evidence that the system works correctly. From the questionnaire results it is also evident that the system does habituate subjects to the fMRI environment. The pilot experiment showed that the hypothesis of habituating subjects does cause a significant increase in the subject's familiarity of the surrounding and reduces anxiety.

The LabVIEW program worked correctly, in that it saved subject data to the correct files, it measured and recorded the ECG signal from the body, it recorded the BP signal from the Finapres, it sequentially turned on and off the LED for the administrator, it sequentially trigger the Neuro- Sensory Analyzer, it played the MRI sounds of the T1 anatomical and T2 functional scans, and it sequentially presented the red cross, pain intensity and unpleasantness scales to the subject.

For future experiments, it would be interesting to run subjects through the fMRI a third time to see if over time, subjects become more comfortable in the fMRI or if they get more anxious after a while. To truly test habituation the ideal experiment would compare cardiovascular measures and questionnaire data between the mock MRI and the real MRI facility at UMDNJ for two groups of subjects while observing differences in fMRI scans. Due to the noise distortion caused by the magnetic field on the ECG signal, and metallic components of the Finapres, some of the cardiovascular measures cannot be recorded in the real MRI unit at UMDNJ, but the Dinamap and questionnaire data in addition to fMRI scans could produce valuable results.

APPENDIX A

FINAPRES SPECIFICATIONS

Specifications

NOTE: All specifications in this manual are nominal and subject to change without notice.

MEASUREMENT RANGE :	Pulse Rate: Pressure:	12 to 175 bpm 20 to 260 mm Hg (3 to 35 kPa)
ACCURACY:	Pulse Rate:	+/-5 bpm or +/-5% of reading (whichever is greater)
	Pressure Transducer Span & Linearity:	+/-2 mm Hg (+/-0.25 kPa)

POWER:

AC input voltage selectable at power input module on the rear panel (see Figure 16 on page 62). Both AC input lines are fused. Ground wire resistance: 0.1 Ohms maximum Leakage Current: 100 microamps RMS maximum

Voltage +/-10% @ 47-63 Hz	Rated Current as noted on rear panel	Puse Rating	
100V	1.50 Amp	1.50 Amp	
120V	1.50 Amp	1.50 Amp	
220V	0.75 Amp	0.75 Amp	
240V	0.75 Amp	0.75 Amp	

х.		Reight	Width	Depth
DIMENSIONS:	Monitor Unit:	15.5 cm (6.1 in.)	30 cm (11.8 in.)	42.5 cm (16.7 in.)
	Patient			
	Interface Mod:	4.14 cm {1.63 in.}	6.98 cm (2.75 in.)	9.9 cm (3.9 in.)
	Patient Interface Cable	: 5m ()	16 ft.)	
WEIGHT:	Monitor Unit: Shipping (compl	11.9 : ete): 14.1 :	Kg (26.2 lb.) Kg (31 lb.)	
ENVIRONMENT RANGE:	Temperature: Op	erating, 10	to 40 °C (50	to 102 °F)

INVIRONMENT	RANGE :	Temperature:	Operating,	10 to	40 °C	(50 to	102	°F)
		-	Storage,	-18 to	> 52 °C	(0 to	125	°F)
		Humidity:	10 to 90% r	elative	, non-	conden	sing	
•		Altitude:	0-3,333 met	ers (0-	-10,932	feet)	-	

APPENDIX B

MOCK MRI QUESTIONNAIRE

2.	If you were in	an MRI in the	past, what was y	our experience lik	e? (Please circle one)
	-2 Varri	-l Slightler	U Oliveri/ NA	l Slightly	Voru
	Distrogation	Distractul	Okay/ NA	Comfortable	Comfortable
	Distressful	Distressiui		Comfortable	Connorable
3.	How did you	feel about being	in the mock MR	I before laying in	it? (Please circle on
	Very	-1 Slightly	Okay	Slightly	Verv
	Uneasy	Uneasy	Okay	Calm	Calm
4.	How did you	after you laid in	the mock MRI?	(Please circle on	e)
	-2	-1	0	1	2
	Very	Slightly	Okay	Slightly	Very
	Uneasy	Uneasy		Calm	Calm
5.	If you wear g	lasses, what is y	our uncorrected	vision?	_(eg. 20/20, L/R)
5.	How well cou	ld you see the sc	ales on the moni	tor behind you?(Please circle one)
	-2	-1	0	1	2
	Very	Slightly	Okay	Slightly	Very
	Blurry	Blurry		Clearly	Clearly
7.	What did you	think about the	colors of the res	ponse scales? (Pl	ease circle one)
	-2	-1	0	1	2
	Very	Moderately	Okay	Moderately	Very
	Dim	Dim	-	Clear	Clear
3.	How easy was	it to adjust the	mirror? (Please	circle one)	
	-2	-1	0	1	2
	Very	Slightly	Okay	Slightly	Very
	Difficult	Difficult	2	Effortless	Effortless
).	How much of	a challenge was	it to use the resp	oonse unit? (Pleas	e circle one)
	-2	-1	0	1	2
	Very	Slightly	Okay	Slightly	Very
	Difficult	Difficult		Effortless	Effortless
10.	How much di	d the sounds int	erfere with vour	concentration? (]	Please circle one)
	-2	-1	0	1	2
	Very Much	Much	Okay	A Little	Very Little
1.	How did you	feel while receiv	ing the warm sti	muli? (Please circ	te one)
	-2	-1	0	1	2
	Very	Slightly	Okay	Slightly	Very
	Worried	Worried	·	Relaxed	Relaxed
2.	What was you	ır overall opinio	n on the MRI fac	cility? (Please cire	cle one)
	-2	-1	0	1	2
		Slightly	Okay	Slightly	Verv
	Very	Singhuy	Okdy	Singlicity	VCIY

13. If you were to undergo these same procedures another time would you feel calmer? (Please

-2	-1	0	1	2
Definitely Not	Maybe Not	Not sure	Maybe yes	Definitely Yes

circle one)

APPENDIX C

DDS PAIN INTENSITY SCALE.VI



APPENDIX D

DDS PAIN UNPLEASANTNESS SCALE.VI







PROVIEW MONITOR SCHEMATIC: SECTION A AND B PART ì

87



.

PROVIEW MONITOR SCHEMATIC: SECTION A AND B PART 2

APPENDIX E





APPENDIX E

68

υ <u>Š</u> Re -(1211) CB46 E E B E ß Particle La Caracter maine a La Jan 1 7561/2004 200-1.03 - 700/1 7511/2014 200-1.03 - 700/1 7511/2014 200-05-0 \odot 8-3 6 여 a the first g Ē ٩ŀ Service Servic 9 **5** 8 8 Ē¥ Ê 30.21 PCE1 NUME AND THE REAL PROPERTY. ĥ D71C į 36. BU ÷ ŧ TANK THE LIVE e Ê 262 Ē 0.24,4H 1.6K,1.4H 745-200-900 D. 8311,4300 d. 89,511 ß Ĩ Ĩ f 뚢 214 ELCE 7-15-200-7001 2.71,1-41 Ē 1.5,3.1 Į 금 <u>⊢-ŧ</u> tì 0.01 **a**3 BC 8 F, Ē G SF. HERSING 10713 X021 Ē US-19 BLIG 22193 a a -帽品 Ē. 13 đ IRFROM 5323 8 ξį. ELU щ Ĵ. 5 旧作品 818 11: ģ 뿬 NAN ANA ₽ ₩ ₩ <u>0000</u>ma Į. E 18 174 HOUT H DCK NUTE זיפא 巖 萨 FE TUUN **POL** 0 26 ЯB ÌÌ õ ĂЙ **ACT** ኅ THE 琵 0 FE ō HOR ţ 115t 1230 1230 CR328

PROVIEW MONITOR SCHEMATIC: SECTION C, D AND E PART 2

APPENDIX E

REFERENCES

- [1] <u>Blood Pressure</u>. Wikipedia. <u>http://en.wikipedia.org/wiki/Blood_Pressure</u> June 2005.
- [2] <u>Electrocardiogram</u>. Wikipedia. <u>http://en.wikipedia.org/wiki/Electrocardiogram</u> June 2005.
- [3] John G. Webster, <u>Medical Instrumentation: Application and Design</u> 3rd Edition. John Wiley & Sons, Inc 1998.
- [4] Kandel, Eric; Schwartz, James; Jessell, Thomas. <u>Principles of Neural Science:</u> 4th Edition. McGraw Hill Companies, 2000.
- [5] Understanding Chronic Pain: Nociceptive Pain. Spine Universe. http://www.spineuniverse.com/displayarticle.php/article2258.html June 2005.
- [6] Casey, Kenneth. Forebrain mechanisms of nociception and pain: Analysis through imaging. Proc. Natl. Acad. Sci. USA Vol. 96, pp. 7668–7674, July 1999.
- [7] Jones, Anthony. Pain, Its Perception, and Pain Imaging. IASP Newsletter Technical Corner. www.iasp-pain.org/TC97MayJune.html
- [8] <u>Pain. Wikipedia. http://en.wikipedia.org/wiki/Pain</u> June 2005.
- [9] <u>Stress and Anxiety</u>. Wikipedia. <u>http://en.wikipedia.org/wiki/Stress and Anxiety</u> June 2005.
- [10] Ploghaus, Alexander et al. Exacerbation of Pain by Anxiety Is Associated with <u>Activity in the Hippocampal Network</u>. The Journal of Neuroscience, December 15, 2001, 21 (24): 9896-9903.
- [11] Zeller A, Handschin D, Gyr N, Martina B, Battegay E. <u>Blood pressure and heart</u> <u>rate of students undergoing a medical licensing examination</u>. Blood Pressure, 2004; 13 (1): 20-24.
- [12] Magnetic Resonance Imaging. Wikipedia. <u>http://en.wikipedia.org/wiki/</u> <u>Magnetic Resonance Imaging</u> June 2005.
- [13] Bushberg, Jerrold T., Seibert, J. Anthony, Leidholdt, Edwin M. JR., and Boone, John M. <u>Magnetic Resonance Imaging, Chaper 15</u>. The Essential Physics of Medical Imaging, Second Edition. Pennsylvania: Lippincott Williams and Wilkins, 2002.
- [14] Functional MR Imaging Brain. Radiological Society of North America. www.rsna.com/fMRI April 2004.

- [15] Porro, Carlo Adolfo, Fausta Lui, Patrizia Facchin, Marta Maieron, Patrizia Braldi. Precept-Related activity in the human somatosensory system: functional magnetic resonance imaging studies. Magnetic Resonance Imaging, October 2004, 22 (2004) 1539-1548.
- [16] Marius A. Kemler, Jos P. H. Reulen, Gerard A. M. Barendse, Maarten van Kleef, Henrica C. W. de Vet, Frans A. J. M. van den Wildenberg. <u>Impact of Spinal Cord</u> <u>Stimulation on Sensory Characteristics in Complex Regional Pain Syndrome</u> <u>Type I.</u> Anesthesiology, 2001 95: 72-80.
- [17] Peñáz, J. Photoelectric measurement of blood pressure, volume, and flow in the finger. Digest of the 10th International Conference on Medical and Biological Engineering (1973):104.
- [18] Richard H. Gracely, Frank Petzke, Julie M. Wolf, and Daniel J. Clauw. <u>Functional Magnetic Resonance Imaging Evidence of Augmented Pain</u> <u>Processing in Fibromyalgia</u>. Arthritis and Rheuamtism, May 2002, Volume 46: pages 1333-1343.
- [19] Dane B. Cook, Gudrun Lange, Donald S. Ciccone, Wn-Ching Liu, Jason Steffener. <u>Functional Imaging of Pain in Patients with Primary Fibromyalgia</u>. Journal of Rheumatology, 2004; Volume 31: 2.
- [20] Frank Petzke, Richard E. Harris, David A. Williams, Daniel J. Clauw, Richard H. Gracely. <u>Differences in unpleasantness induced by experimental pressure pain</u> <u>between patients with fibromyalgia and healthy controls</u>. European Journal of Pain, 2005; 9: 325-335
- [21] Price DD, Harkins SW, Baker C. <u>Sensory-affective relationships among different</u> types of clinical and experimental pain. Pain, 1987; Volume 28:297-307