Measuring Brain Activation through Functional Magnetic Resonance Imaging (FMRI) during Visual Task Learning

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Measuring brain activation through functional magnetic resonance imaging (fMRI) during visual task learning

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Engineering

by

Mohd Saif Usmani
B.S.F.A.B.E, Ohio State University, 2012

2015
Wright State University
I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY Mohd Saif Usmani ENTITLED Measuring brain activation through functional magnetic resonance imaging (fMRI) during visual task learning BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF Master of Science in Engineering.

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ABSTRACT

Usmani, Mohd. M.S.Egr., Department of Biomedical, Industrial, and Human Factors Engineering, Wright State University, 2015. Measuring brain activation through functional magnetic resonance imaging (fMRI) during visual task learning.

The purpose of this study is to understand the brain activity associated with learning a visual task by utilizing the applications of functional magnetic resonance imaging in cognitive neuroscience. The study was performed using two visual tasks referred to as aircraft and control, respectively. We compared the brain activation of these two visual tasks to understand the learning process of the participants. Fifteen young adults, ten males and five females, ranging in age from 19 to 35 years, participated in a ten-week study. Eight participants dropped out either voluntarily or were excluded for different reasons. The data analysis was completed with the remaining seven right handed participants. The study included seven behavioral sessions and three brain imaging sessions (weeks 2, 6 and 10). The collected data were analyzed using FMRIBs Software Library (FSL) and statistical analysis was performed using JMP 12. The brain activation associated with the aircraft task increased from week 2 to week 6 and then decreased by week 10, whereas the activation associated with the control task did not yield any significant increase or decrease but rather stayed the same across the three imaging sessions.
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Dedicated to

my mother, Mrs. Kahkashan Alavi
Introduction

The aim of this study is to understand brain activity that is associated with practice and learning in a visual recognition task. The brain activity in this study is measured through an imaging modality known as functional magnetic resonance imaging (fMRI). The images of the brain are acquired using an MR scanner which is discussed in detail in the upcoming chapters.

The motivation behind this study is to advance the science of learning and skill acquisition. This is done in this study by identifying brain activity associated with learning a visual task. Cognitive models along with fMRI can be used to build training systems which could predict when and where a learner might fail and improve upon those failing areas by providing some feedback related to the task. In this study, we will not be dealing with cognitive models but rather focus on the brain activity associated with learning over a period of time.

In the next chapter, we will discuss the fundamental principle of magnetic resonance imaging (MRI) along with the concept of acquiring an image. The two types of designs such as block design and event related design are discussed in this chapter as well. The studies related to cognitive neuroscience and fMRI along with the brain’s learning and control architecture are also discussed in great detail in the background chapter. In the methods chapter, the procedure of data collection along with the data analysis is discussed. Chapter 4 of the thesis summarizes all the results while Chapter 5 reflects light on the discussion and conclusion of the results and future work respectively.
Background

2.1 Magnetic Resonance Imaging

Magnetic resonance imaging, popularly known as MRI, is an imaging modality which uses non-ionizing radiation to produce anatomical images of the human body for diagnostic and research purposes. Dr. Herman Carr is said to be one of the first scientist to introduce the magnetic resonance imaging technology in the early part of 1950 [1]. An example of MR scanner is seen in the Figure 2.1, usually housed in hospitals or research institutions.

Figure 2.1: Classical MRI machine in hospitals or research institutions (Courtesy of Dr. Kashou).
2.1.1 Basic MR physics

A crucial factor behind acquiring an image in MRI is the presence of water molecules in the human body. These water molecules contain hydrogen nuclei which precess at a rate of 42.58 MHz/Tesla. Precession is a change in the positioning of the revolving axis of the rotating body. The orientation of the hydrogen nuclei in the human body is random and hence there is no net magnetization. In order to create net magnetization we need a magnet, three gradients and a radio frequency (RF) coil which are the main components of MRI for obtaining an image. The strength of the magnet could range from 1.5 to 7 Tesla, but the ones mostly used are either 1.5 Tesla or 3 Tesla [2]. The random orientation of the human body when not in an external magnetic field is shown in Figure 2.2. The participant

![Figure 2.2: Random orientation of the hydrogen atoms in the human body outside the MR scanner [2].](image)

is placed in the MRI scanner after completing the safety screening of any ferrous materials. At this time, a net magnetization (M) is created by the magnet in the direction of magnetic field which is $B_0$. This happens due to the protons aligning with the magnetic field of the scanner. An RF pulse is sent at the correct precession frequency of hydrogen nuclei based on the Larmor equation given by

$$\omega_0 = \gamma B_0$$

(2.1)

where $\omega_0$ is the angular frequency, $\gamma$ is the gyromagnetic ratio and $B_0$ is the strength of the magnetic field of the scanner [2].

This RF pulse is sent at an angle of 90° which tips the protons of interest over by 90°
and, then these protons start to absorb energy while they are realigning with the magnetic field. When the RF pulse is turned off, these protons come back to their original orientations and exude energy in the form of radio waves. This process is called relaxation when the protons return to their original state [2]. T1 and T2 are the two components of relaxation which are commonly known as spin-lattice and spin-spin interactions respectively. T1 relaxation time measures the time it takes for the protons to realign with $B_0$, which is the strength of the magnetic field of the scanner. In other words, it means the time taken by z-component of the protons magnetic field to return to the equilibrium. T2 relaxation measures the time taken by protons to interact with each other. In other words, time taken by xy-component of the protons magnetic field to return to its equilibrium. These two time constants are different for different tissues in the human body and are used to measure the repetition time (TR) and echo time (TE) [3].

![Illustration of protons aligning with the magnetic field and then returning to their original state, also known as T1 and T2 relaxation times [2].](image)

Generally, one of the gradients will phase encode, second one will do the frequency encode, and last one will preform slice encode. These 3 gradients correspond to the coordinates in the x, y, and z direction. Different locations of the tissues in the human body can be imaged by changing these gradients slightly [3]. The slice encode regulates the thickness and slice location dependent on the pulse bandwidth as determined by the user [2]. A coro-
nal, sagittal or an axial scan is produced based on the direction of the slice select gradient. An axial scan looks from the superior to inferior part of the brain, coronal scan looks from anterior part of the brain to the posterior part of the brain, and sagittal scan looks at lateral coordinates of the brain. These gradients are custom made to the protocol to get the best possible image [3]. T1-weighted and T2-weighted image contrasts are acquired based on the values of echo time (TE) and repetition time (TR). The echo time is the time between the RF pulse and the highest amount of the output signal whereas time between two RF pulses is called the repetition time [3].

When the RF pulse is sent at the precessing frequency of the hydrogen nuclei, the net magnetization vector can be divided into two components. They are longitudinal ($M_z$) and transverse ($M_{xy}$). The equations for the two components are given below.

\begin{align}
M_z &= M_0(1 - e^{\frac{-t}{T_1}}) \\
M_{xy} &= M_0(e^{\frac{t}{T_2}})
\end{align}

where $M_0$ is the equilibrium magnetization when there is no excitation and T1 and T2 are time constants. These time constants have already been explained above.

When the subject is placed under the scanner, a net magnetization (M) is created by the magnet in the longitudinal z-direction ($M_z$) when some of the hydrogen atoms align with the magnetic field $B_0$. This is when an RF pulse is sent at the precessing frequency of the nuclei which tips the nuclei by 90° into the transverse plane. This causes a net magnetization in the XY plane ($M_{xy}$). The magnetic field $B_0$ will cause the longitudinal magnetization to align with the z-axis again and dephase the transverse magnetization in the XY plane respectively. This process of longitudinal and transverse relaxation is illustrated in Figure 2.3. The frequencies are acquired using the magnet, a radio frequency (RF) coil and three gradients which are then converted to an image space, forming an image of the
desired location. The inverse fast fourier transform (IFFT) converts the frequencies into an image [2].

2.2 Study designs in fMRI

The most common method used to study the brain function is known as the BOLD (blood oxygenation level dependent) contrast imaging. The underlying principle of this method is based on changes in the state of oxygenation of the hemoglobin [4]. The magnetic properties of the hemoglobin are based on the concentration of oxygen molecule present in it. When the concentration of oxygen is very high in hemoglobin (oxy-hemoglobin), it acts as diamagnetic substance. However, when the concentration of oxygen is low in hemoglobin, it becomes para-magnetic. The ratio of oxy-hemoglobin to deoxy-hemoglobin within a voxel (volume element) of the brain governs how the signal will show up in a BOLD image. The areas of the brain with higher concentration of oxy-hemoglobin will give brighter images compared to those with lower concentration of oxygen in hemoglobin [5].

![Hemodynamic Response Function - HRF](image)

Figure 2.4: An example of HRF showing BOLD signal change with initial dip and an undershoot [5].

When an individual sees an stimulus under the scanner, it leads to a brief increase in
the deoxy-hemoglobin concentration which is also known as the initial dip \[6\]. This is the first thing that happens during the initial stimulus presentation stage. An increase in the oxy/deoxy-hemoglobin ratio leads to a higher MR signal which in turn leads to an increase in the BOLD effect. The BOLD effect is directly proportional to the neuronal activity of the brain \[7\]. The BOLD effect reaches a plateau when the stimulus is maintained for a good amount of time \[8\]. Once the stimulus has been stopped, the signal returns to the baseline and underpasses it which is called the undershoot effect \[9\]. Please refer to Figure 2.4 to see an illustration of this concept. Once a subject performs a cognitive task, an increase in the neuronal activity can be seen by using BOLD images. The underlying principle of fMRI is to collect BOLD images of the brain while the subject is performing cognitive tasks inside the scanner.

\subsection{2.2.1 Block design}

The Block experimental paradigm is the most commonly used technique in fMRI studies today. It is based on maintaining a state of cognitive engagement of a task by presenting a stimulus to the individual followed by a period of rest. These states could be referred to as ‘AB’ block or ‘on-off’ blocks. ‘On’ referring to the state when an individual is engaged in a task whereas ‘off’ refers to the state of rest when the individual is not engaged \[5\]. This technique drew much criticism due to many assumptions involved with this design. However, this technique is still valuable today due to increased statistical power \[10\] and greater BOLD signal change with respect to baseline \[9\].

\subsection{2.2.2 Event related design}

In an event related design, different stimuli are presented in a random fashion. This type of design is more suited to behavioral studies as compared to the block design. In behavioral studies stimuli such as pictures or words are presented in a random order separated by an
ISI (inter-stimulus interval) of a specified length [5].

Event related design helps with analysis related to individual responses to trials which in turn helps in analyzing neural coordinates of the behavioral responses [5]. This technique is not that sensitive to the head motion artifacts [11] and lets the experimenter randomize the order of conditions [12]. The experimenter can also adjust the time between stimulus presentation, also known as inter-stimulus interval (ISI). The subject will then not be able to predict what will happen next, hence keeping a consistent level of attention across the experiment [13, 14]. Another advantage of event related design is the use of post hoc methods to detect the subjective perception of a state not influenced or controlled by the experimenter [15]. The paradigms used in event related design helps in having greater flexibility and randomization as compared to block design, thus making the experiments tricky and less predictable. The third type of design is the mixed design which combines both block and event related design. These three designs are depicted in Figure 2.5.
2.3 Cognitive Neuroscience

In 1993, there were only 20 or fewer articles published on the studies related to functional magnetic resonance imaging (fMRI). The number rose from 20 to 1800 about the number of articles published on fMRI by 2003. This shows that a lot of research has been done in the field of fMRI. The classical approaches used for applying the fMRI data to understand the neural mechanisms of brain are studied in the upcoming sections [16].

The most common approach of the researchers has been driven by an interest in localization of psychological functions to different regions of the brain. The goal of the neuro-cognitive scientists has been to determine the brain behavior correlations. In other words, it means to know the localization of psychological processes in the brain tissue. Knowledge of localization helps in understanding the normal organization of modules of processing and to infer the nature of deficits that appear to show up when brain tissue is damaged [16].

One of the examples of studying localization of the brain approach could be found in a study [17] where they were driven to find out if object recognition utilizes the same neural mechanism irrespective of the object being recognized or there are modules of processing in the brain custom-made to specific classes of objects. These authors were particularly concerned with finding brain regions responsible for identifying parts of the human body. The findings showed that there was an exceptional consistency among the subjects in the activation of an area in right occipitotemporal cortex of the brain. This region of the brain responded more strongly to images of the human bodies than to any other classes of objects [16]. One of the issues with this approach is that the organization of the human brain is modular. It cannot be explicitly stated that there is a one to one mapping of psychological functions onto brain regions. Studies such as recognition of parts of the human body [17] and face recognition [18] propose that there may be a one to one mapping of functions to brain regions but Haxby explains that coding of neural pathways is more complex than one to one brain mapping discussed above [19]. Haxby suggested a model of object recognition
where the processing of faces and other objects is distributed over a broad range of brain regions [19]. They proposed that it is the pattern of activation over the regions critical to identification of objects that is important to object recognition rather than individual brain areas that are activated specifically for different stimuli. The investigators discovered a novel sequence of neural activity in ventral temporal cortex (VTC) of the brain for the classification of human faces, houses and several man made objects [16]. The patterns of activation in ventral temporal cortex showed that the objects were being recognized at an accuracy of 96% which agrees with regional specificity as inferred from the research of Downing [17]. One of the important things to note is that when the region that responded to faces more than any other objects was taken out from the analysis, regions of ventral temporal cortex still recognized the objects with 94% accuracy. This shows us that ventral temporal cortex could be the area important for visual object recognition. It can be inferred from the results that studies of localization should not be limited to one to one brain to behavior mapping [16].

In this study, our goal is to understand the brain activity associated with learning and practice in two visual tasks. The use of an unfamiliar aircraft as a visual task is what differentiates this study from the similar brain imaging studies. It has already been established that continuous practice is associated with diminutions in brain activity in task specific brain regions but this only applies when there is uniform mapping between the stimuli and responses. Also, no change in strategy is expected to take place during practice and learning [20]. However, increases in brain activity has been reported for practice and learning for experimental designs that are created for skill acquisition and strategy shifts are observed as an after effect of training [21].

### 2.3.1 Studying Placebo effect through fMRI

In this section, one of the study is examined in which regional activation of brain from one task is equivalent to activation from another task. An example of this concept can be seen
in the work of Wager [22] on understanding the neural mechanisms behind the placebo effect. He found that reduced activation in regions receptive to physical pain was related to placebo anesthesia. These regions are insula, thalamus, and anterior cingulate cortex [22]. In other words, it was found out that these regions were common for reduced activation by placebo to those with increased activation to physical pain. It was inferred from this study that placebos work by reducing the activation in brain regions that are receptive to physical pain [22].

Some fMRI studies focus on the commonalities of brain activation whereas some focus on studying the differences across the individuals. Canli [23] studied activation in amygdala by making participants see fearful facial expressions and happy facial expressions. They found out that there was a consistent activation in amygdala when participants looked at fearful faces. However, there was an inconsistent activation when the same participants looked at happy faces. This inconsistent activation in amygdala when watching happy faces was measured by a score on an extraversion scale. The higher score on this scale would mean higher activation in amygdala of brain. The difference between the consistent and inconsistent responses of the fearful and happy faces was attributed to the adaptive value by the authors of this study [16].

2.3.2 Application of fMRI in tracking mental states while using an intelligent tutoring system

In this study, neural imaging was used for the purpose of enabling student modeling in an intelligent tutoring system [24]. These models would then help in improving mathematical solving capabilities of the student. Functional MRI data were collected while the participants worked with a system that taught solving an algebra problem. A cognitive model was used to predict the time taken by students to complete a problem based on the difficulty level of the problem. An algorithm was used to combine the two models (fMRI and
cognitive model) to foretell the mental states of students during problem solving. The two objectives of this approach are to recognize intervals of time when the student is engaged or disengaged in problem solving and the next one is to identify the problem they were solving and their progress towards the solution of that particular problem. The students solve the problem using several clicks on a system based on tutoring software. The number of clicks would give us the degree of difficulty of a particular problem [24].

The model’s performance was determined based on fMRI only algorithms, cognitive model algorithm and a combination of both. The performance of the model is measured by looking at the difference between the ground truth state and predicted state. The difference of 0 implied that the algorithm correctly predicted the state of the scan. If the difference was a positive value then the predicted state was too late whereas if the difference was a negative value then the predicted state was too early. The model ‘both’ correctly recognizes 86.6% of the total scans and on day 5, it correctly recognizes 83.4% of the total scans [24]. However, the fMRI-only algorithm correctly identifies 43.9% of the totals scans on day 1 and 30.6% of the total scans on day 5. For, model-only algorithm, the results look like 21.9% on day 1 and 56.9% on day 5 [24]. This clearly shows that using fMRI-only and model-only approach are not that good because of the results shown above. The ‘both’ model approach is considerably better and that is why it is important to integrate the knowledge from both the approaches together to make any concrete conclusions. On the brighter side, the study showed that it is possible to merge the brain imaging with cognitive models to learn about the participants’ approach to learning [24].

2.3.3 Learning and control architecture of the human brain

In this paper, an organized learning structure which consists of three systems related to brain learning will be studied. This is revealed when there are changes in the brain activity as a new activity is learned. Each of these systems has a unique role in learning and each have a unique pattern of learning-dependent plasticity. The underlying principle of
human cognition is that it specifically utilizes those brain circuits that are tailor made for the specific task at hand. In other words, only those areas of the brain will be active that are specialized to deal with the current task. This feature of selectively activating distinct brain areas in an organized manner is a function of the brain’s learning and control-cognitive architecture [25].

According to Chein and Schneider, people tend to use less of the brain’s resources once they have mastered at completing a specific task [20]. Some research regarding brain studies have shown that there are patterns for experience dependent plasticity. However, an important point to be noted is that all the regions of brain are not uniformly affected by the experience. There are different patterns of plasticity for different regions of the brain [25].

In this paper, three stages of learning are studied starting from the initial development of a new trait, through a disciplined implementation of that behavior, and finally to a phase where the learned task is carried out with relative ease [25]. This system of learning is explained in Figure 2.6. The three systems of organization also known as the ‘triarchic

![Figure 2.6: Three systems of organization within the human brain [25].](image)

theory of learning’ consists of a representation system, cognitive control network system and a metacognitive system. Each of these systems plays an important role in the processing of information and learning in the brain. The main function of the representation system is to pick up the regularities and the predictions based on people’s experience of working
on a simple task. In other words, it makes predictions on a task based on people’s learning experience. The representation system is a place of storage of learned knowledge based on experience [25]. This system is based on the concept that brain cells that fire together get wired together. This is also known as Hebbian theory or connectionism. This system is a slow learner as the neural changes in the brain occur gradually and incrementally over a period of several days of practicing a particular task. It can be seen from a study that this slow learning is crucial as it makes sure that important information in the system does not get lost by unusual experiences [26]. Schneider and Chein found that this representation system can process information without the support of certain important mechanisms of cognitive control network, and hence decreases the response time to familiar or emotional stimuli which leads to automaticity of the task [27].

The main role of the cognitive control network is to sequence and monitor the flow of information in the representation system. This network directs attention to information wherever it is needed the most for processing. This network allows subjects to remain focused on their goal of completing a complex goal oriented task and keeps all the unnecessary information out of the mind [25]. Even though it is a very organized and integrated network, this network is comprised of different brain areas each having a distinguished role [28]. One of the important difference between the representation system and cognitive control network is that the cognitive control network processes complex learned information that could be applied in novel surroundings to accommodate novel information [29]. Various neuroimaging studies have shown that when people work on broadly varied tasks, a strong activation can be seen in the lateral prefrontal cortex of the brain during early performance whereas weaker activation after the task has been mastered by the people [20]. Thus, after learning the task, representation system can work on its own whereas the work of cognitive control network is reduced at that point of time [25].

Another system important to human learning is the metacognitive system. The main goal of this system is to administer the behavior of the cognitive control network. This
system could make changes to the cognitive control network such as starting or aborting certain routines or modifying them in order to enhance the performance and learning. The regions associated with this system are anterior prefrontal cortex, posterior cingulate cortex, claustrum, and the anterior half of the temporal lobes. It has been hypothesized that individuals who are really good at performing novel and complex tasks have a very well developed metacognitive system. This allows these individuals to quickly learn new behavioral routines and consider the effect of the alternating different learning strategies [30].

Figure 2.7: Engagement of three systems of organization of the human brain during learning [25].

The human learning is based on three important learning systems mentioned above and their relative engagement can be seen in Figure 2.7. They work together in an organized fashion to carry out the process of learning very effectively. During the early stages of learning, metacognitive system works on initiating and regulating the brain so it can carry out a new routine. Then, the cognitive control network carries out controlled execution of
the task by removing any irrelevant information and allowing the brain to work on the task at hand. After repeating the task several times, automaticity is attained and the activity then moves to the representation system which then helps in performing the task with relative ease. Without these systems, it would have been really difficult to perform simpler tasks. With these systems, individuals can perform and learn easily [25].
Methodology

3.1 Subjects

Fifteen young adults, ten males and five females, ranging in age from 19 to 35 years, participated in a ten-week study. Eight participants dropped out either voluntarily or were excluded for different reasons during the study. One of the subjects was removed from the study due to a technical failure in image acquisition. That data could not be used for analysis. Another subject did not show any learning during the visual tasks and hence their data was removed as well. Another subject had issues with seeing the visual stimuli in the scanner due to their vision and hence was removed from the imaging sessions but finished all of the behavioral sessions. Other subjects quit voluntarily from the study. The results presented in the thesis are based on the data analysis of the remaining seven right handed participants with normal or corrected to normal vision. For this study, subjects were asked to look at a visual stimulus which was an object they have not seen before. There were 75 of them which were referred to as aircraft task and there were 52 of the familiar stimuli which were called the control task. These stimulus were shown to the subjects using Presentation (Neurobehavioral Systems, Inc.) software.
3.2 Pilot study

A pilot study was conducted to evaluate the feasibility of the proposed study. This would help in modifying the proposed study if such a situation arise.

There were two interfaces designed namely training and testing. As the name suggests training sessions provided the subjects with training by providing feedback. This session consisted of 3 rounds and each round displays 127 images described above. Once this session is finished, a testing session would start to test the knowledge of the subjects showing the same images as shown in the training session. This session did not provide any type of feedback but accuracy scores were shown in both the interfaces once the task was completed. These two interfaces were updated after several trials and testing by individuals from the lab before starting the pilot study so as to make sure that no error exists in the training and testing UI.

The pilot study was advertised in classes at Wright State University and a pool of subjects were made. Five subjects were chosen randomly using a random number generator and were contacted. Institutional Review Board (IRB) at Wright State University approved the pilot study. The subjects were given a consent form, a summary of the pilot study and a pre-study questionnaire.

A PowerPoint presentation was used to give instructions to the subjects before beginning the pilot study. This was a six session study and the subjects were trained 2 times per week. Most of the participants finished the study in 3 weeks and some completed in 4 weeks. This difference in finishing the study is due to conflict in schedule of each participant. The two interfaces were designed such that it would take 42 minutes to finish the whole session, but subjects were given the discretion to take a short break if they were tired. This made the task about 45-50 minutes in duration.
3.3 Main study

3.3.1 Subject recruitment

Once the main study was approved by Institutional Review Board (IRB) at Wright State University, it was advertised on the campus. The students were recruited from Engineering and Psychology department. An email was sent to the students through the Engineering department and Psychology department.

A pool of students interested in the study was created. Each student in the pool was assigned a number and these numbers were put in lisp (programming language) to generate 15 random numbers in order to select 15 students for the study. The selected students were then called to complete a telephone screening form as part of the selection protocol. The screening form consisted of the exclusion and inclusion criteria in order to determine whether the student was eligible to participate in the study. If the student was not found to be eligible then another student was selected from the pool through a random number generator.

The selected students were then informed of their selection and they were requested to provide their schedule for the study which spanned across 10 weeks. On the first day of the study, students were given a consent form to sign, a short summary of the study, pre-study questionnaire to complete and a short power-point presentation of the behavioral tasks. The selected students were assigned subject numbers in order to protect the privacy of the students. An activity log for each student was maintained by the research assistant conducting the behavioral experiment. All of the aforementioned documents were safely handed over to the principal investigator at the Wright State University.
3.3.2 Study design

There were a total of 10 sessions conducted over the course of 10 weeks for each subject. 7 out of 10 sessions were the behavioral sessions conducted in the department of Psychology. All of the seven sessions were comprised of 3 training rounds and 1 testing round. There were 75 aircraft images and 52 control images shown in each round. Overview of the 10 week study depicting type of rounds can be seen in Table 3.1. The subjects recorded their responses by choosing one of the four options they thought could be correct. Figures 3.2 and 3.3 are shown here for reference. In training rounds, subjects were given the feedback and score whereas the testing round did not provide any feedback and score.

<table>
<thead>
<tr>
<th>Week</th>
<th>Type of Rounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 Training and 1 Testing</td>
</tr>
<tr>
<td>2</td>
<td>1 Testing</td>
</tr>
<tr>
<td>3</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>4</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>5</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>6</td>
<td>1 Testing</td>
</tr>
<tr>
<td>7</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>8</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>9</td>
<td>3 Training and 1 Testing</td>
</tr>
<tr>
<td>10</td>
<td>1 Testing</td>
</tr>
</tbody>
</table>

Table 3.1: Each week corresponds to type of rounds which were carried out in a single session. Weeks 2, 6 & 10 correspond to the brain imaging sessions and rest of them were behavioral sessions.

The duration of the shown image was set to 4 seconds, also known as a trial. Presentation software was installed on the Mac computers which was used to show the stimuli to the participants. A randomized presentation run was used for each session and the same run was shown to all the participants. Jittering was used between trials to account for sampling of different time points at each stimulus presentation. In other words, jittering allows for different delays between the start of the stimulus presentation of the participant and the start of the sampling of brain images [5]. An overview of the presentation sequence can
Figure 3.1: A sample of the stimulus presentation sequence. ‘A’ refers to the aircraft image, ‘C’ refers to the control image, and ‘J’ refers to the jitter. The total time of the presentation sequence is approximately 10 minutes and 30 seconds.

be seen in Figure 3.1. The behavioral sessions were held in sound proof booths. An eye tracker named EyeLink 1000 was also installed to track the eye movement of the participants. For this study, a desktop mount version of EyeLink 1000 was used. It tracked the pupil along with the corneal reflection (CR). EyeLink 1000 desktop mount comprised of an infra red (IR) Illuminator along with a high speed binocular camera. The high speed camera could be adjusted using a camera angle adjustment and it could also be moved back and forth using a pan or tilt adjustment. The eye tracking files were saved to the desktop after the completion of the session. Figure 3.2 is one of the 75 images of the aircraft task

Figure 3.2: Example image of the aircraft task.
as mentioned earlier. Similarly, Figure 3.3 is one of the 52 images of the control task. The images of the control task were divided into 4 categories and those categories are the four options shown in Figure 3.3.

Figure 3.3: Example image of the control task.

3.3.3 Acquiring fMRI scans

The set up of the fMRI data collection was done at Wright State Physicians office. Brain imaging scans were acquired on weeks 2, 6, and 10 of the study. A 1.5 Tesla GE (General Electric) MR scanner with eight channel head coil was used to acquire the brain imaging data. Visual task images, also known as stimuli, were shown to the participants using an LCD projected screen located at the bottom end of the scanner inside the room. The projector showing the stimuli was connected to a HP laptop running Presentation software. A Lumina response pad equipped with two buttons on each side of participants’ hand was used to record their responses.

There were several scans done during the session. The first couple of scans were the prep scan and the localizer scan which spanned around 30 seconds. We also collected high
resolution T1-weighted scans using the Fast Spoiled Gradient Recovery Echo (FSPGR) sequence. These are also called the structural scans of the brain. This scan runs for about 7 minutes. There were 162 slices acquired parallel to the anterior commissure (AC)-posterior commissure (PC) line for this scan. The participants were requested not to move their head during the scan and stay relaxed. The music of their interest was played on radio during this scan. The functional scans ($T2^*$-weighted images) were acquired using echo-planar sequence sensitive to BOLD contrast. In this scan participants performed the visual task using the provided Lumina response pad to respond with their middle finger and index finger on both sides to record their responses to the visual task. This scan lasted for 10 minutes and 32 seconds. The details of the scanning parameters can be found in Table 3.2. The music was stopped during this scan in order to avoid any false positives that may come up on the images due to brain responding to music. This was followed by resting state scan where the participant did not have do any tasks. They were requested to stay calm and relaxed during this scan. The last two scans were a Diffusion Tensor Imaging (DTI) and Magnetic Resonance Spectroscopy (MRS) scans which were done as a part of data collection process. The imaging data from the computer was immediately saved on a compact disk after each session. All the CD’s containing the imaging data were handed to the principal investigator (PI).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Anatomical scan</th>
<th>Functional scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echo time (TE)</td>
<td>3.2 ms</td>
<td>35 ms</td>
</tr>
<tr>
<td>Field of view</td>
<td>24 x 24 cm²</td>
<td>24 x 24 cm²</td>
</tr>
<tr>
<td>Flip angle</td>
<td>12°</td>
<td>90°</td>
</tr>
<tr>
<td>Matrix</td>
<td>240 x 240</td>
<td>64 x 64</td>
</tr>
<tr>
<td>Repetition time (TR)</td>
<td>8.3 ms</td>
<td>2000 ms</td>
</tr>
<tr>
<td>Slices</td>
<td>162</td>
<td>30</td>
</tr>
<tr>
<td>Voxel size</td>
<td>1 x 1 x 1 mm³</td>
<td>3.75 x 3.75 x 4.50 mm³</td>
</tr>
</tbody>
</table>

Table 3.2: Overview of the scanning parameters.
3.4 Data Analysis

The analysis for the fMRI data was done in two levels namely individual level and group level using fMRI Expert Analysis Tool (FEAT) in FMRIB’s Software Library (FSL) package [31].

3.4.1 Individual level

The data from the subjects was collected in the form of NIfTI images (.nii.gz). The fMRI data from the subjects included images of the functional scan, structural scan, resting state scan, Diffusion Tensor Imaging (DTI) and Magnetic Resonance Spectroscopy (MRS). The functional scans are of the main interest here as they are the actual tasks that the participants performed in the scanner. These scans were followed up with the resting state scan where the participants did not have to perform any task.

Before delving into FSL, a MATLAB (The MathWorks, Inc.) code was written to create text files which had stimulus onset time for aircraft and control groups. The first trial from each of the two text files was removed from the data set to correct for a MRI machine artifact. The brain was extracted using a Brain Extraction Tool (BET) from FSL when the structural image was fed into FSL. Now, the functional scans (4D fMRI data) of each subject were entered into FSL and the parameters were set. These parameters were set to a TR of 2 s and a high pass temporal filter cutoff of 90 s was applied. Spatial smoothing was applied using a full width half maximum (FWHM) of 5 mm. A cluster threshold (Z) of 1.96 was set with a ‘p’ value of 0.05. No slice timing correction was used for the individual analysis.

Once the pre-processing was performed, a general linear model (GLM) was created by defining two exploratory variables (EV’s) for each aircraft (EV1) and control (EV2). The on periods of the aircraft and control were determined using the stimulus onset text files. These exploratory variables were made by convolving the model with a hemodynamic
response function (HRF) modeled by the custom optimal basis functions with a 0 s phase offset. Four contrasts were created in the model. The first one applied a value of 1 to the aircraft (EV1) and 0 to the control (EV2), second one applies a value of 0 to the aircraft (EV1) and 1 to the control (EV2), third contrast applies a value of 1 to the aircraft (EV1) and -1 to the control (EV2), and the final one applies a value of -1 to the aircraft (EV1) and 1 to the control (EV2). The first two contrasts represents activation for the aircraft and control tasks respectively whereas contrasts 3 and 4 represents ‘aircraft - control’ activation and ‘control - aircraft’ activation respectively. Z statistic images were thresholded using clusters determined by $Z > 1.96$ and significance threshold of $p = 0.05$. FSL completed the analysis for one subject in about 15-20 minutes. A FEAT folder was created in the output directory which contains all the activation images and important fMRI results.

The analysis done in this study is called the univariate analysis. In other words, it is also called the voxel by voxel analysis. General linear model is the univariate analysis we did in this study. It is generally represented by the following equation

$$y(t) = \beta * x(t) + c + e(t)$$

(3.1)

Here, $y(t)$ is our data and a 1D vector of intensity values. Then, $x(t)$ represents the model and $\beta$ gives us the parameter estimate for $x(t)$. The constant is given by $c$ and $e(t)$ represents the residual error between our data and the model. The fundamental assumption here is that the BOLD signal is linear time invariant (LTI). In other words, it can be inferred that the response of the BOLD signal can be predicted by convolution of the hemodynamic response function with the neuronal activity of the brain [32]. This convolution can be done in number of ways but for this study we chose double gamma HRF and custom/optimal basis functions.

Double Gamma HRF is a combination of two gamma functions. One of the gamma function is a standard positive function at normal lag and the other one is a small, delayed,
inverted gamma which models the late undershoot [33]. The double gamma is mathematically represented as follows

\[
h(t) = A \left( t^{\alpha_1 - 1} \frac{\beta_1^\alpha_1 e^{-\beta_1 t}}{\Gamma(\alpha_1)} - c \frac{t^{\alpha_2 - 1} \beta_2^\alpha_2 e^{-\beta_2 t}}{\Gamma(\alpha_2)} \right)
\]  

(3.2)

In the equation above, \( A \) refers to the amplitude, \( \alpha \) and \( \beta \) are the parameters that control the shape and scale, respectively, and the ratio of the response to undershoot is given by \( c \). \( \Gamma \) is the gamma function which is a normalizing parameter in this equation [33].

The custom/optimal basis function allows the user to use a customized set of basis functions. This function uses FMRIB’s Linear Optimal Basis Set (FLOBS) which has a capability of producing a set of functions that optimally covers the range of likely hemodynamic response shapes (HRF’s) found in the data [34]. The masks for the region of interests (ROI) in the brain were created using Talairach labels [35, 36]. Activation is calculated by taking the mean of nonzero voxels of regions of interest in the brain. On the other hand, percent extent is calculated by dividing the size (mm\(^3\)) of the regions of interest for nonzero voxels by the size of regions of interest (mm\(^3\)).

### 3.4.2 Group level

The group level analysis is also called as the higher level analysis. This is where the first level/individual level analysis was combined. Generally, a second level is used to analyze across subjects and a third level is used to analyze across several sessions. For our analysis, only a second level was done to get the group results. The inputs for the group level analysis could be the lower level FEAT directories or 3D cope images from the given FEAT directories. If the lower level FEAT directories are chosen as inputs, then higher level design is applied across them. Every one of the lower level FEAT directories expresses a single session in a multiple-session higher level analysis or a single subject in a multiple subject analysis. For this analysis, we chose to input the 3D cope images from the FEAT
directory. This is the option to use if we would like to perform higher level analysis across the multiple contrasts (copes) in the FEAT directory.

### 3.4.3 Exploratory analysis

This analysis was conducted for the individual FSL analysis. In this analysis, clusters from the FEAT post stats were selected for each subject for each week. The number of clusters within each week varied depending upon the activation. Each cluster had number of voxels that were active above the threshold. Each cluster had several indices along with their coordinates. These coordinates were used to locate the regions of brain that were potentially active while participants were performing complex visual tasks. Talairach daemon software was used to generate labels of brain using the coordinates from the clusters indices [35, 36]. These labels were put in excel cell with respect to their clusters for each subject for each week. Many labels generated from the software were redundant so they were cleaned up manually and were then put into the word document. They were then divided into the gyri of the right cerebrum frontal lobe or left cerebellum parietal lobe etc. An example of this can be seen in Table 3.3.

<table>
<thead>
<tr>
<th>Right Cerebrum Occipital Lobe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lingual Gyrus Brodmann area 18</td>
</tr>
<tr>
<td>Lingual Gyrus Brodmann area 17</td>
</tr>
<tr>
<td>Cuneus Brodmann area 17</td>
</tr>
<tr>
<td>Cuneus Brodmann area 18</td>
</tr>
<tr>
<td>Inferior Occipital Gyrus Brodmann area 17</td>
</tr>
<tr>
<td>Inferior Occipital Gyrus Brodmann area 18</td>
</tr>
<tr>
<td>Fusiform Gyrus Brodmann area 18</td>
</tr>
<tr>
<td>Fusiform Gyrus Brodmann area 19</td>
</tr>
<tr>
<td>Middle Temporal Gyrus Brodmann area 19</td>
</tr>
</tbody>
</table>

Table 3.3: An example of the gyri of right cerebrum occipital lobe.

Once the labels were put in the above format, the word document was converted to text file format so that it could be read by MATLAB. The text files were converted into
an array. A MATLAB code was written in order to find the common elements of two files such as week 2 & week 6, week 6 & week 10, and week 2 & week 10. A MATLAB code was also used to perform operations such as 'week 2 - week 6' and 'week 6 - week 2'. This was done to find out the labels found in week 2 but not in week 6 and vice-versa. This would help in knowing which brain regions emerge or decline after several weeks of learning aircraft and control task. Each cell of the matrix represented in Table 3.4 was put in an excel worksheet. All the clusters of activity were identified as function of session and task. A cluster of activity was defined as the adjacent voxels activated above threshold. There were three sessions (week 2, 6, & 10) and two tasks (aircraft & control) as mentioned earlier in this chapter. The number of local maxima was observed for each cluster and the brain regions were listed for these maxima. Local maxima could be defined as a set of coordinates in the brain with the maximum activation. We assumed the number of local maxima to signify the extent of task related activity in that region of the brain. For example, a brain region that was active at week 6 and not week 10 was considered a declining region (Week 6 - Week 10) and a brain region that was active at week 10 but not at week 6 was considered an emerging region (Week 10 - Week 6). In Table 3.4, the upper right half of the matrix contain declining regions and lower left half of the matrix contains emerging regions. The diagonal matrix in Table 3.4 represents brain regions active at week 2, week 6 and week 10.

<table>
<thead>
<tr>
<th>Week 2</th>
<th>Week 2 - Week 6</th>
<th>Week 2 - Week 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6 - Week 2</td>
<td>Week 6</td>
<td>Week 6 - Week 10</td>
</tr>
<tr>
<td>Week 10 - Week 2</td>
<td>Week 10 - Week 6</td>
<td>Week 10</td>
</tr>
</tbody>
</table>

Table 3.4: Emergence and Decline matrix.
Results

In this section, we will discuss the results of individual level analysis and the statistical analysis done using JMP 12 by SAS Institute, Inc.

4.1 Individual level

Figure 4.1 compares the mean accuracy scores of the participants over 3 weeks of imaging sessions for aircraft and control group.

It can be seen from Figure 4.2 that there is no discernible pattern of activation for the control task. It rather stays low and same over the course of the 3 fMRI sessions. However, there is an interesting pattern to be noted for the aircraft task. The activation increases from the week 2 to week 6 which can be referred to as the learning phase and then decreases from week 6 to week 10.

Next, we will take a look at the graph of mean activation extent by week and task. Activation extent refers to the numbers of voxels activated above threshold whereas activation intensity is the magnitude of the BOLD signal relative to the baseline. In Figure 4.3, mean activation extent plotted against the imaging sessions for both control and aircraft group.

It can be seen from Figure 4.3 that the activation extent for aircraft task increases from week 2 to week 6 and then decreases from week 6 to week 10. This observation is similar
Figure 4.1: Comparison of mean accuracy of the participants over 3 weeks (imaging sessions) for aircraft and control. Each error bar is constructed using 1 standard error from the mean.

to what was seen in Figure 4.2. For the control task, it increases slightly from week 2 to week 6 and then decreases a little from week 6 to week 10.

Next, we analyze the differences observed in activation between the aircraft and control task. From Figures 4.4 and 4.5, it can be seen that the maximum activation for both aircraft and control can be noted in fusiform gyrus, middle occipital gyrus, and superior parietal lobule. These brain regions are involved in the visual processing and recognition of objects [37]. Also, other notable activation could be seen in inferior frontal gyrus, inferior parietal lobule, medial frontal gyrus and middle frontal gyrus. These regions are believed to exhibit the retrieval and cognitive control mechanisms of the brain [37].
Figure 4.2: Mean activation intensity \((p < 0.05, \text{magnitude of signal relative to baseline})\) as a function of week and task. Task 1 refers to aircraft and task 2 refers to control group. Each error bar is constructed using 1 standard error from the mean.

### 4.2 Statistical analysis

In this analysis, JMP was used to perform analysis of variance (ANOVA) which is the primary theme of discussion in this section. Subjects, regions of interest (ROI), weeks, and tasks are chosen as factors and activation intensity is chosen as the independent variable. Table 4.1 shows a list of all the regions of interest of this study.

In Figure 4.6, the p-value of the model (Prob > F) is much smaller than 0.0001 which suggests that the model is pretty significant. Similarly if we study the effect tests, all of the effects and their interaction are significant except for the interaction between ROI and week. The p-value for the interaction between ROI and week is 0.8474 which much higher than 0.05 and hence the interaction is not significant. Now, using student’s t test we will
Figure 4.3: Mean activation extent ($p < 0.05$) as a function of week and task. Task 1 refers to aircraft and task 2 refers to control group. Each error bar is constructed using 1 standard error from the mean.

Figure 4.4: Mean activation ($p < 0.05$) as a function of regions of interest for the aircraft task. Each error bar is constructed using 1 standard error from the mean.
Figure 4.5: Mean activation ($p < 0.05$) as a function of regions of interest for the control task. Each error bar is constructed using 1 standard error from the mean.

<table>
<thead>
<tr>
<th>Number</th>
<th>Regions of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Caudate</td>
</tr>
<tr>
<td>2</td>
<td>Hippocampus</td>
</tr>
<tr>
<td>3</td>
<td>Insula</td>
</tr>
<tr>
<td>4</td>
<td>Post-central gyrus</td>
</tr>
<tr>
<td>5</td>
<td>Pre-central gyrus</td>
</tr>
<tr>
<td>6</td>
<td>Fusiform gyrus</td>
</tr>
<tr>
<td>7</td>
<td>Middle Occipital gyrus</td>
</tr>
<tr>
<td>8</td>
<td>Superior temporal gyrus</td>
</tr>
<tr>
<td>9</td>
<td>Medial frontal gyrus</td>
</tr>
<tr>
<td>10</td>
<td>Anterior cingulate</td>
</tr>
<tr>
<td>11</td>
<td>Superior parietal lobule</td>
</tr>
<tr>
<td>12</td>
<td>Inferior parietal lobule</td>
</tr>
<tr>
<td>13</td>
<td>Middle frontal gyrus</td>
</tr>
<tr>
<td>14</td>
<td>Inferior frontal gyrus</td>
</tr>
</tbody>
</table>

Table 4.1: List of chosen regions of interest.

study the statistical significance of some of the interesting factors and their interactions. We will study the differences in week and task using the Student’s t test. In Figure 4.7, we study the least squares means table with $\alpha = 0.05$ and $t = 1.96$. The levels 2, 6, and 10 denote three weeks of imaging study and the corresponding letters denote whether the difference in activation between the three tasks is significant. Then, we also have the least square mean values next to them. We can see from the figure that levels not connected by
Figure 4.6: Model showing summary of fit, analysis of variance, and effect tests.

same letter are significantly different.

In Figure 4.7, it can be noted that activation between week 2 and 6 does not seem to be significantly different than each other. However, activation in week 10 is significantly different than both week 2 and week 6. The two levels of the task factor are 1 and 2 which represent aircraft and control group respectively. The activation between two of them is significantly different as levels are connected by different letters A and B. Now, this leads us to discussing the results of the two way interactions between the week and task. The two
Figure 4.7: Connecting letters report for week and task.

Figure 4.8: Connecting letters report for interaction between week and task.
interaction shown in Figure 4.8 has six levels. The first level is represented by 6,1 which means week 6 and task 1. In other words, this level represents interaction between week 6 and airtrack task. If we carefully observe all the six levels, we can see that the activation between all the weeks (2, 6, and 10) for task 1 (aircraft task) are significantly different. The levels (6,1), (2,1) and (10,1) are connected by different letters A, B and C respectively which implies that they are significantly different. However, if we look at all the weeks (2, 6 and 10) of control task we can say that none of them is significantly different. The corresponding letters to the levels (10,2), (2,2) and (6,2) are the same (D) and hence they are not significant.

Figure 4.9: Connecting letters report for interaction between ROI and task.

Now, we study the interaction between the factors ROI and task using Figure 4.9. The activation observed for middle occipital gyrus, fusiform gyrus, and superior parietal lobule for airtrack task is significantly different than the activation for the same regions for the control task. It can be seen in Figure 4.9 that these regions mentioned above are denoted
by different letters. For example, middle occipital gyrus for aircraft task (represented by 1) is denoted by A and middle occipital gyrus for control task (represented by 2) is denoted by H and I which implies that the activation between them is significantly different. This difference between the aircraft and control task for the aforementioned ROI’s is reflected in Figures 4.4 and 4.5. The residual analysis of the data has been done for completeness and can be referred to in the Appendix B.

4.3 Exploratory analysis

Figure 4.10: Number of local maxima as a function of hemisphere, task and week.

In Figure 4.10, it can be noted that the activation in the left hemisphere is comparatively higher than the right hemisphere for the aircraft task. However, this is not true for the control task. The only inference that can be made here about the control task is the decrease in brain activity of the left hemisphere. Similarly, Figure 4.11 shows number of local maxima in frontal lobe as a function of week and task. It can be deduced from Figure 4.11 that there is much more activity in the aircraft task especially in the left hemisphere of
the frontal lobe. The activity in the brain decreases quite a bit with practice in the control task. However, the activity in the aircraft task stays at a comparatively high level.

Figure 4.11: Number of local maxima in frontal lobe as a function of week and task.

Number of local maxima was also plotted for other lobes such as temporal lobe, parietal lobe, occipital lobe and cerebellum as a function of week and task but there were no distinct patterns of practice related changes found for the two tasks and hence not included here.
Discussion, Conclusion & Future Work

5.1 Discussion & Conclusion

The results found in this study suggest that progression of learning is different in two tasks. The higher level of accuracy ($\approx 96\%$) in the control task was observed throughout the 3 imaging sessions. However, the accuracy of the aircraft task was $33.9\%$ in week 2, $72.19\%$ in week 6 and $80.57\%$ in week 10. This shows that the participants’ accuracy improved drastically for the aircraft task over the course of the 3 imaging sessions. It can be inferred from the results that the activation for the aircraft task was significantly higher than the activation for the control task. The activation during the aircraft task significantly increased from week 2 to week 6 and then decreased by week 10. This may suggest that the aircraft task uses more brain resources compared to the control task as the participants exhibit significantly higher brain activation. However, activation in the control task did not yield any significant increase or decrease but rather stayed the same throughout the three imaging sessions. This may also suggest that the participants mastered the control task easily and hence did not use much of their brain resources. This was reflected by participants achieving very high accuracy scores ($\approx 96\%$) and no significant change in brain activity. Improvement in the accuracy scores in the aircraft task could mean that participants are becoming better in performing the visual task and are using brain regions associated with learning, memory and representation. Higher accuracy in the control task for all three imaging sessions means that this task reaches high levels of automation which is associated
with no significant change in brain activity and hence the activation stays low compared to
the aircraft task. It was observed that the highest brain activation for aircraft and control
task could be seen in middle occipital gyrus, fusiform gyrus and superior parietal lobule as
discussed in the results chapter. The results of this study support the view that practice is
associated with different brain activity patterns in the aircraft and control task.

5.2 Future work

One way to improve this study would be to use different software for conducting data
analysis. There are several other software that could be used for data analysis of brain
imaging data apart from FMRIB’s software library. These are Statistical Parametric Map-
ing (SPM), Analysis of Functional NeuroImages (AFNI) and FreeSurfer. We could also
try to use eye tracking software during the brain imaging sessions to observe the eye move-
ment of the participants. Along with the functional scans, we also collected the resting
state scan, Magnetic Resonance Spectography (MRS) scans and Diffusion Tensor Imaging
(DTI) scans. Due to the scope of the study only functional scans were analyzed but it would
be interesting to analyze the resting state, MRS and DTI scans.
Bibliography


Appendix A

Activation Images

In this appendix, all the activation images for the frontal lobe and occipital lobe for all three weeks (week 2, week 6 & week 10) for all the subjects are shown here.

The cross hairs (intersection of two green lines) in all the figures points to the coordinates in brain region that was active. This coordinate was same for 3 weeks as it was chosen as a reference and it was unique for each subject. This enabled us to show the same slices of the brain (for 3 weeks) for each subject. Figures A.1 and A.2 depict the aircraft

![Activation Images](image)

Figure A.1: Activation images for subject 1 showing activation in frontal lobe for three weeks.
Figure A.2: Activation images for subject 1 showing activation in occipital lobe for three weeks.

Figure A.3: Activation images for subject 2 showing activation in frontal lobe for three weeks.

and control activation for subject 1. Figures A.3 and A.4 depict the aircraft and control activation for subject 2. Figures A.5 and A.6 depict the aircraft and control activation for
Figure A.4: Activation images for subject 2 showing activation in occipital lobe for three weeks.

Figure A.5: Activation images for subject 3 showing activation in frontal lobe for three weeks.

subject 3. Figures A.7 and A.8 depict the aircraft and control activation for subject 4. Figure A.9 depict the aircraft and control activation for subject 5. Figures A.10 and A.11 depict the aircraft and control activation for subject 6. Figures A.12 and A.13 depict the
Figure A.6: Activation images for subject 3 showing activation in occipital lobe for three weeks.

Figure A.7: Activation images for subject 4 showing activation in frontal lobe for three weeks.

aircraft and control activation for subject 7.
Figure A.8: Activation images for subject 4 showing activation in occipital lobe for three weeks.

Figure A.9: Activation images for subject 5 showing activation in occipital lobe for all three weeks.
Figure A.10: Activation images for subject 6 showing activation in frontal lobe for all three weeks.

Figure A.11: Activation images for subject 6 showing activation in occipital lobe for all three weeks.
Figure A.12: Activation images for subject 7 showing activation in frontal lobe for all three weeks.

Figure A.13: Activation images for subject 7 showing activation in occipital lobe for all three weeks.
Appendix B

Residual Analysis

It can be seen from Figure B.1 that the normality assumption has been satisfied. The variance in residual activation in Figure B.2 exhibited similar distribution for all the subjects.

![Figure B.1: Normal Quantile Plot of the residual activation created using JMP 12.](image)

The variance in residual activation in Figure B.3 exhibited similar distribution for all the weeks. Therefore, the condition for equal variance for weeks has been satisfied. The variance in residual activation in Figure B.4 exhibited similar distribution for both the tasks.
Figure B.2: Residual activation plotted as a function of subjects to check for equal variance.

Therefore, the condition for equal variance for tasks has been satisfied.
Figure B.3: Residual activation plotted as a function of weeks to check for equal variance.
Figure B.4: Residual activation plotted as a function of tasks to check for equal variance. Task 1 refers to the aircraft task and task 2 refers to the control task.