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ARTICLE

Functional Magnetic Resonance Imaging (fMRI): A Brief Exercise for an Undergraduate Laboratory Course

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Functional neuroimaging represents an important technique for the study of the brain. However, the skills necessary for collecting, processing, and analyzing functional magnetic resonance imaging (fMRI) data sets are complex and relatively few undergraduate programs offer students an opportunity to acquire these skills or to observe functional neuroimaging.

We report here on our experiences working with functional neuroimaging in an undergraduate laboratory course and suggest resources for the implementation of a similar exercise in a comparable setting. This exercise is structured so that four class meetings are devoted to functional neuroimaging. During these sessions, we discuss the basics of fMRI, study design, the advantages and disadvantages of this technique for the study of brain function as well as a general overview of data processing and analysis. Due to the college's proximity to a medical school, we are able to offer students an opportunity to observe functional neuroimaging sessions (however, this component is not critical for the completion of this exercise). Two final class sessions are devoted to data processing and presentation as well as writing up the experimental results. The exercise culminates in a paper based on the American Psychological Association format for a small number of subjects. At the conclusion of the exercise, students were surveyed to assess their impressions of the lab sessions. The results from these surveys indicate that students found this portion of the laboratory course to be a very positive experience.

While this lab exercise does require some initial set up, we believe it stimulates the development of critical thinking skills with a technique that is used increasingly in neuroscience research. Both print and online resources are suggested to assist faculty in setting up a similar exercise.

Key words: functional magnetic resonance imaging (fMRI); laboratory course; behavioral neuroscience; neuroinformatics

Laboratory experiences are an essential component of any undergraduate neuroscience curriculum. These exercises stimulate critical thinking skills and introduce students to important techniques that are used in the field. Some of these techniques may involve animals and could include experiences in sterile surgical procedures, cannulation, brain lesions, pharmacological manipulations, electrophysiology and histology (see e.g., Barnes, et al, 2003; Hall and Harrington, 2003; Land et al., 2001; Mickley et al., 2003). Laboratory exercises that involve humans are equally as important and could provide students with important experiences involving motor control, electroencephalogram recordings (EEG), event-related potentials (ERP) and electromyography (EMG) (Lennartz, 1999; Buford, 2005). However, these types of experiences in human research are perhaps more difficult to obtain at a primarily undergraduate institution; funding and space may be limited for the purchase of equipment necessary to conduct, for example, EEG or ERP research in the context of a course.

Another important set of techniques that students should be exposed to in an undergraduate laboratory is functional neuroimaging (e.g., functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), or positron emission tomography (PET)). Indeed, the use of functional neuroimaging techniques in neuroscience has grown rapidly in recent years (Hennig et al., 2003; Van Horn et al, 2004). Yet experiences involving functional neuroimaging may be even rarer at undergraduate institutions given the expense of the equipment involved and the specific training required to collect and analyze neuroimaging data. These types of experiences are likely to be limited to either Research I universities or medical centers.

However, an advanced undergraduate cognitive neuroscience course has been described by Dr. Kevin Wilson (http://www.sinauer.com/pdf/fMRI_Course.pdf); he discusses his experience in developing an entire course around functional neuroimaging at an undergraduate institution. We have developed a similar, briefer exercise that also exposes undergraduate students to functional neuroimaging. Here we describe our experiences with students enrolled in PSYC 364, Laboratory in Physiological Psychology, an undergraduate course at the College of Charleston, in which we have implemented fMRI in one segment of the course.

BACKGROUND

This one credit course covers selected research topics in Physiological Psychology and methods typically used in this field of study. The associated lecture course (PSYC 214, Physiological Psychology) is generally taken during the second or third year. The laboratory course normally begins with a short review of research methodology and statistics. We also discuss ethics in the context of physiological research and focus on specific examples of ethical and unethical behavior in animal and human research. The final segment of this section involves a review of neuroanatomy using sheep brain dissection; a practical and functional exam follows this review in which students identify neuroanatomical structures and describe their function.

The remainder of the course involves conducting and writing up three physiological experiments. Traditionally, this course has focused on animal related experiments. For example, rats, mice, and zebrafish have been used extensively in this course. Zebrafish have been used for pharmacology experiments in which the animals are exposed to agents such as melatonin, ethanol, and caffeine and various behaviors are measured (e.g., locomotor behavior, conditioned place preference). Learning and memory experiments involving mice (e.g., Morris water maze, plus maze, Y-maze experiments) and zebrafish (t-maze experiments) have also been conducted.

However, students often express a keen interest in physiological experiments that involve human subjects. Consequently, we developed a brief, small subject design involving a functional neuroimaging experiment for this course so that students could observe and develop some of the skills required to process and analyze fMRI data. While not an essential component of this exercise, we have utilized the fMRI suite at the Medical University of South Carolina (MUSC) so that students can observe a functional neuroimaging session. Additionally, we developed several learning objectives for this exercise and describe our implementation and outcomes below. To assess how students reacted to this exercise, we asked them to complete a brief survey in which they rated their experiences in fMRI. We conclude our discussion with suggestions for other instructors that might be interested in implementing a similar exercise in an undergraduate laboratory course.

LEARNING OBJECTIVES

After completing this segment of the Physiological Psychology course (PSYC 364) students should be able to:

1. discuss the use of fMRI in Physiological Psychology as well as the design of studies and hypothesis testing in fMRI.
2. describe the process of data collection in fMRI, discuss safety issues related to MRI, and develop some of the technical skills required to process and analyze these data.
3. explain the cautions of data interpretation in fMRI.
4. present and discuss functional neuroimaging data in a written format.

IMPLEMENTATION

We use a four step process to achieve these learning objectives. First, we provide students with a general overview of fMRI using a lecture format within the lab (Learning Objectives 1 and 2). Discussion and questions are encouraged throughout this class meeting so that students have an opportunity to ask questions about fMRI. There are numerous published resources that can be used for the development of this presentation (e.g., see Arthurs and Boniface, 2002; Cacioppo, et al., 2003; Huettel et al., 2004; Sharma and Sharma, 2004; Amaro and Barker, 2006; Nielsen et al., 2006). In addition, there are prepared PowerPoint slide decks available online as well (see http://www.cofc.edu/neuroscience/fmri/ for links). During this discussion, a general overview of fMRI is provided, the advantages and disadvantages of block and event-related designs, and the data collection process and analysis are discussion topics (Arthurs and Boniface, 2002; Cacioppo, et al., 2003; Amaro and Barker, 2006).

Second, since MUSC is close to campus, students are able to view a functional neuroimaging session in the late afternoon or early evening and observe two fMRI studies (Learning Objective 2). During this time, students are able to ask questions, interact with investigators using fMRI to study the brain and they also view a short safety video on MRI produced by Philips (Andover, MA, USA). Next, they observe the informed consent process for human subjects (we also have a brief discussion of the Health Information Portability and Accountability Act (HIPAA; Annas, 2003) at this time). Students then watch the collection of functional neuroimaging data on a Philips 3 Tesla (T) MRI scanner. In general, this process involves a structural brain anatomy scan followed by a series of functional scans of subjects while they engage in motor behavior. We selected motor behavior because it is simple and the areas of activation in the brain have some familiarity for students because they typically discuss the motor system in PSYC 214. For this exercise, subjects are asked to perform the following simple motor tasks while in the MR scanner: finger tapping (each finger is touched to the thumb in random order) and foot flexion and extension. Again, this component is not essential since it is possible to analyze previously collected data sets (see below).

The third component of this exercise involves data processing and analysis (Learning Objectives 2 and 3). Because this segment is perhaps the most time consuming, we describe here some general considerations for the implementation of this portion of the exercise.

HARDWARE. Students will need access to fairly current personal or Macintosh computers in order to analyze the data for this exercise. At this writing, an Intel Pentium IV based PC or dual-core Intel processor Macintosh with one gigabyte of RAM (random access memory) should be sufficient for data analysis.

SOFTWARE. There are a number of different software packages that may be used for data analysis including SPM, AFNI, FSL, BrainVoyager, VoxBo as well as others (see Cox, 1996; Cox and Hyde, 1997; Nielsen et al., 2006). Some programs may only be executed in the Microsoft Windows operating system (OS) while others require UNIX, a Linux OS or Macintosh OS X for execution of the programs. Note that it is also possible to run these operating systems simultaneously using virtual environment software within a primary OS in order to compare different analysis software on the same dataset (e.g., SPM (Windows) and AFNI or FSL (Linux); see below as well as the following address for details: http://www.cofc.edu/neuroscience/fmri/). This virtual environment software allows the instructor the option of teaching and comparing two different types of software packages on the same dataset within a familiar OS (i.e. Microsoft Windows).

For instructors working in a Windows environment, one of the most popular programs is SPM (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, London, UK). There are a number of advantages to working with SPM: it is a free program, it is widely used by many researchers, and there are a number of resources available for it on the Internet. However, it is not a freestanding program in that it must be executed within MATLAB® (Mathworks, Natick, MA, USA; http://www.mathworks.com) for the actual data analysis. Currently, student licenses for classroom use may be obtained through Mathworks for $44 each for 10 or more seats. However, a larger number of licenses (>25 seats) may be purchased at a discounted price.

For instructors in a Macintosh environment, FSL (FMRIB Software Library; http://www.fmrib.ox.ac.uk/fsl/) and AFNI (Analysis of Functional NeuroImages; http://afni.nimh.nih.gov/afni/) may be used for data analysis. Both software packages are freestanding and are available free of charge. In addition, several excellent resources are available for learning more about data processing and analysis in these packages at the following addresses: http://www.fmrib.ox.ac.uk/fslcourse/ and http://afni.nimh.nih.gov/afni/doc/. There are other software packages that may be used for analysis of functional neuroimaging data as well (e.g., BrainVoyager, VoxBo, etc.), some of these are commercial products (BrainVoyager) and some require MATLAB® in order to be executed (VoxBo; see e.g., Gold et al., 1998, Nielsen et al., 2006). We continue to use SPM and AFNI because of their popularity (Nielsen et al., 2006) and because we have colleagues that also use these software packages extensively.

For the data processing phase of the exercise, it is necessary to discuss the pre and post-processing phases of data analysis in class (see e.g., Sharma and Sharma, 2004; Vincent and Hurd, 2005; Nielsen et al., 2006). For the pre-processing phase of data analysis, it is important to discuss data conversion from proprietary formats that are common for scanner data acquisition. In our case, this requires data conversion from a Philips format to header and image files that can be analyzed in SPM. Philips creates a single file during data acquisition that must be broken down into individual header and image pair files that SPM can read for analysis. For this data conversion, we use a software package called MRICro by Chris Rorden (http://www.sph.sc.edu/comd/rorden/). This excellent, freely available software package allows the conversion of data into files that can be analyzed by SPM (as well as a number of other software packages). This data conversion is relatively quick and is conducted as an in class exercise as part of the data processing discussion. Once the data have been converted and broken down into these separate files, the data must be post-processed. However, since data post-processing is often lengthy and this exercise is intended to be a brief exposure to fMRI, post-processing can be carried out by the instructor outside of class, or if a very detailed protocol is provided, as a homework assignment (see http://www.cofc.edu/neuroscience/fmri/ for links). Additionally, both SPM and AFNI offer datasets that can be downloaded from the following locations: http://www.fil.ion.ucl.ac.uk/spm/data/ and http://afni.nimh.nih.gov/afni/download. Recall that AFNI datasets may only be processed in Linux or on a Macintosh.

The final component of this exercise focuses on exposing students to some of the issues associated with data interpretation and presentation (Learning Objectives 3 and 4). For example, we discuss some of the issues associated with mapping areas of activation to brain atlases (Talairach and Tournoux, 1988; Van Essen, 2002). This discussion focuses on a general overview of methods that are available for indicating where the areas of activation observed (see Figure 1) are actually located in the brain and the limitations of these different methods (Van Essen, 2002).

In their paper, students are required to write a full manuscript on the experiment including a title page, abstract, introduction, method, results, and discussion sections with references and figures. For this dialogue, we again revisit concerns about interpretation of these data (Cacioppo et al., 2003). Students must generate and interpret several figures from the data sets (e.g., see http://www.cofc.edu/neuroscience/fmri/ and Figure 1 below). Additionally, they must discuss the anatomical localization of motor activity for these tasks according to Brodmann's areas (Talairach and Tournoux, 1988).

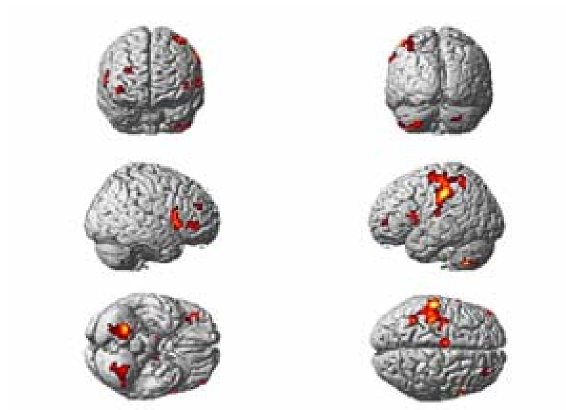

Figure 1. An example of a functional MRI image generated during data post-processing. This graphic image is a representative example of post-processed images that are generated within Statistical Parametric Mapping (SPM) software (http://www.fil.ion.ucl.ac.uk/spm/). The activation is mapped onto a standard generic brain image. For students engaged in the laboratory course, these images are included and interpreted in their manuscripts. Note the activation in the primary motor cortex (e.g., middle row, right column) and cerebellum (e.g., bottom row, left column) during this finger tapping task with the right hand. Also note the color of activation on the images; yellow indicates the most intense activation, red indicates less intense activation.

Understandably, this portion of the exercise can become very complicated due to issues associated with mapping areas of activation on the brain (Van Essen, 2002). Our primary goal for this segment of the exercise is for students to gain a general understanding how these areas of activation are produced during post-processing of data. The final images are included, interpreted, and discussed in their manuscript as a product of this exercise.

OUTCOMES

Thus far, we have exposed 30 students to this fMRI exercise in the undergraduate laboratory course. After the initial group of students (N=10) took part in the exercise, the response was so enthusiastic that we have continued to offer an experience in fMRI to subsequent classes of students. We were interested in quantifying the comments that we received from the first group of students. To that end, we developed a survey to assess the student's perception of the exercise and administered the survey at the conclusion of the neuroimaging session to the next two groups of students (N=20). The survey consisted of two sections: the first set of questions was designed to assess the demographics of the population. These questions indicated that 75% of the students were female, the mean age was 22, and 90% were seniors.

The second portion of the survey consisted of a set of questions and a Likert scale that ranged from 1 to 7 in which students were asked to indicate whether they strongly agree (7) or strongly disagree (1) with the statements outlined in the table below.

Additional Questions: Likert scale	**Mean**	**SEM**
1. I learned a great deal about fMRI as a result of this exercise.	6.2	0.2
2. This exercise clearly demonstrated the importance of fMRI in Neuroscience.	6.2	0.3
3. I learned more about the importance of fMRI than if I had not participated in this exercise.	6.6	0.2
4. Today's exercise was <u>not</u> an efficient use of my time.	2.6	0.4
5. I would recommend this course to my colleagues because of this exercise.	5.7	0.3
6. The instructor should use this exercise again in future classes.	6.5	0.2
7. This exercise is an enjoyable experience.	6.2	0.2

Table 1. Likert scale survey questions for students enrolled in the laboratory course. The number in the column labeled Mean indicates the mean student rating based on the Likert scale (N=20). The SEM (standard error of the mean) for each question is given in the final column of the table.

The survey results indicate that students generally agreed that the exercise was meaningful (questions 1, 2, 7) and that they learned more about fMRI from the experience. Questions 3 and 6 indicated stronger agreement that the exercise should continue to be offered in the course.

EVALUATION AND DISCUSSION

Our results indicate that students exposed to functional neuroimaging found the exercise to be very instructive. Several verbal comments from the students were even more effusive (e.g., “Thank you for offering us this opportunity – I learned so much during this experiment” to “This was way cool” and “This was an awesome experience”).

While not every institution has access to an MRI facility, faculty interested in attempting to offer a functional neuroimaging exercise within a laboratory might consider contacting a nearby hospital or medical center. There is no guarantee that they will be engaged in collecting functional neuroimaging data as they may only gather structural images for diagnostic purposes. However, if the institution is involved in collecting functional data, it may be possible to set up an interaction to facilitate this brief exercise. Interested individuals might try contacting the public relations department to determine if collaborations may be developed. This department will likely be able to direct anyone interested in learning more about fMRI to the person in charge of the MRI facility. From that point, it should be possible to gauge the potential to observe a data collection session or possibly if a data set might be available for processing in the classroom. The interaction between the College of Charleston and MUSC developed out of an introduction to the functional neuroimaging group by a colleague; collaborations seemed to develop fairly naturally from that point on. Additionally, for institutions that lack proximity to a medical center, there are several resources for data sets online. Some of the motor data sets discussed in this paper may be downloaded from the following address: http://www.cofc.edu/neuroscience/fmri. Additional links as well as data analysis protocols and links to other data sets are provided for instructors interested in conducting this project in class.

We believe that this laboratory exercise is an important experience for students to be involved in because it exposes them to some of the issues associated with collecting and processing fairly large data sets with this technique. We also believe that this exercise emphasizes the importance of developing information technology skills for data collection and analysis – an important skill for students to develop regardless of their career choice. Indeed, other authors have highlighted the importance of technical skills training in managing large data sets, for future employment as well as competency in professional programs (Scott, et al., 2000; Chao et al., 2003; Insel et al., 2004; Van Horn et al., 2004). We also believe it is important to encourage the development of these skills during the undergraduate years; such experiences and skills may provide students with a competitive edge for graduate or professional school admission.

Neither of the authors was exposed to such experiences as an undergraduate because this technology did not exist at that time. Although we found our way to functional neuroimaging through neuroscience/informatics

(MWH) and physics/mathematics (DJV), we hope that this experience might influence student's future decisions about pursuing a career in science or perhaps a specialization if they pursue a medical degree (e.g., Radiology or Neurology). Ramirez (2005) has suggested the importance of encouraging students to pursue careers in science. If students are to make good career choices and select vocations related to science, we believe that they need to be exposed to a variety of different opportunities as undergraduates. This brief exercise may stimulate students to pursue an interest in this area based on their written and verbal reactions.

There is some preparation time involved in getting this exercise set up, but we believe it has value because it teaches an important skill set and critical thinking about a technique that is becoming more frequently used in neuroscience. This exercise represents our attempt to provide undergraduates with a novel experience in a physiological psychology laboratory. While the exercise described in this paper is not as extensive as an entire course dedicated to fMRI (e.g., Dr. Kevin Wilson's advanced undergraduate cognitive neuroscience course, http://www.sinauer.com/pdf/fMRI_Course.pdf), we believe that it emphasizes the importance of exposure to fMRI during an undergraduate's career. Such experiences need not necessarily be limited to fMRI, but this is an area where knowledge and experience with information technology greatly facilitate data collection and analysis. Faculty that currently utilize technology in their research program or that have an interest in applying technology in the classroom (e.g., Griffin, 2003; McGrath et al., 2003; Evert et al., 2005) might consider developing comparable exercises and, if the possibility exists, setting up similar collaborations between institutions. Finally, exercises such as those described above may not only motivate the students to develop skills in these techniques, this exercise may also invigorate teaching and research programs because of discussions that develop between faculty and/or institutions.

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