VERY BASIC SAMPLE EXPERIMENTAL DESIGN FOR A FUNCTIONAL MRI (fMRI) RESEARCH PROJECT

The following material is provided to help investigators finalize the experimental design of the pilot project. The RIC Technical Director, MR physicist, and or MR Research Technologist can help to fine-tune this design. Information on the hardware and software used in fMRI experiments will also be needed to write a Human Subjects Protocol.

SUBJECT PREPARATION

The subject fills out a standard MRI questionnaire to be sure that they are not precluded from the MRI study due to existing medical conditions. Safety precautions (as indicated on the questionnaire, e.g. use of earplugs) are implemented. After giving informed consent, the subject lays supine on the MRI table, and the RF coil is placed around the subject's head. Head motion restraints are placed. For visual stimuli, the subject puts on special MR compatible LCD display goggles. For auditory stimuli, the subject puts on MR compatible earphones. The table is then moved, placing the subject's head at the center of the magnet.

STRUCTURAL MRI

A high resolution fast spin echo sequence is run first to provide proton density and T2 weighted images in the same planes that the activation studies will be done (typically coronal with 6 mm thickness and 2 mm gap). The scan parameters for this scan are: Fast spin echo, Coronal plane, TR=3100, Effective TE: 36 and 136, Echo train: 8, Matrix: 256 x 256, FOV: 22 cm, Slice thickness: 6 mm, Gap: 2 mm, Slice range: Posterior 96 mm to Anterior 88 mm typically, 24 slices. These scan parameters can be changed to vary spatial resolution and scan time, but the changes should be strongly justified by the experiment because image quality is affected by any changes.

FMRI SCAN PROCEDURES

For detection of brain activation during stimulus presentation, echo planar imaging is performed with the following scan parameters: Echo Planar scans: Gradient recalled echo, Coronal plane, TR=2000, Effective TE: 40 ms, FA: 90 degrees, Matrix: 64 x 64, FOV=22 cm, Slice thickness: 6 mm, Slice gap: 2 mm, Slice range: Posterior 64 mm to Anterior 56 mm. Some of these scan parameters can be changed to vary temporal and spatial resolution, but the changes should be strongly justified by the experiment because image quality is affected by any changes. The timing of the visual and auditory stimuli is controlled by a PC and tied to the MR imaging sequence. During each scan the subject is experiencing one of two conditions, labeled A and B. Following 32 seconds of baseline image acquisition during which the subject is in a resting condition, condition A is initiated. Condition A is continued for 16 or 32 seconds (set prior to scan as part of protocol), and then condition B is initiated. Condition B is continued for the same 16 or 32 seconds. The total number of A-B cycles is 8 if 16 second ½ cycles are used, and 4 if 32 second ½ cycles are used. Therefore, each EPI scan is 4 minutes 48 seconds. Typically, in each scan 16 slice locations with 2 second temporal resolution are acquired, so 2304 images are obtained in a typical 4 minute 48 second scan (16 slices and 144 repetitions). Alternatively, fewer slices can be obtained with higher temporal resolution, with some loss of signal to noise due to the shorter TR. The total study time is approximately one hour 30 minutes. Total setup and teardown time by physicist and technologist may be 2 or more hours.

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Auditory and visual stimuli are controlled by a PC (the stimulus computer) and delivered to the subject through MRI compatible headphones and goggles. A video projection system is also used. For auditory studies, audio file composed of words or sounds prepared by the investigator, and inserted in time order into a presentation file that can be read by a stimulus presentation program such as Presentation on the PC. The PC thus controls the stimulus presentation, and can be controlled by triggers from the MRI system, or vis-versa. In most experiments, the switch between stimulus condition A and B is automatic in the change of auditory stimulus in the presentation file. In studies of the motor cortex, the conditions are often different types of finger tapping or fist clenching by the subject. In these studies, the subject requires an auditory or visual signal to switch between conditions, at 16 or 32 second intervals typically. In studies of the sensory cortex, stimulation is provided on the subjects hand with a brush or other coarse surface. The investigator or assistant applies the stimulation with cues from the auditory file to switch the conditions. Painful stimuli has been implemented in fMRI studies, using milliampere level electrical shock, commonly used in anesthesiology to test subject wakefulness. A skin heating/cooling (peltier) device has also been used in other sensory cortex studies. Switches between conditions A and B are controlled by the investigator or assistant via knobs on the device.

IMAGE PROCESSING

During image reconstruction of the k-space data using the 2D Fourier Transform, an additional algorithm is applied to the data to remove ghost artifacts. Ghost artifacts arise from unequally spaced echos in the MR signal train generated by rapid gradient switching used in EPI. This algorithm examines pixel values outside the physical extent of the object to estimate the temporal offsets of each of the echo trains. The algorithm then corrects the raw data by phase shifting the k-space data in accordance with the Fourier transform shift theorem, and image reconstruction is redone. This correction removes about 85% of the ghost artifact, and restores signal intensity within the image of the object. Currently, image reconstruction and ghost correction is carried on a Linux Workstation at the RIC.

STATISTICAL ANALYSIS

A program called BrainMRI is available for investigators using the Research Imaging Center. A technique based on linear vector space mathematics described in the article by Bandettini (see References) is used to correlate activation response with a reference vector. We have limited our reference vector to boxcar to represent switching between two conditions, and computed values of the correlation function at 0, 2, 4, 6, 8, and 10 second time offsets at each pixel to find the offset of maximum correlation. The correlation threshold was set to exclude lower correlation from display in the image overlay.

HARDWARE AND SOFTWARE FOR FUNCTIONAL MRI

The following information is provided to help the investigator understand the special hardware requirements of functional MRI and provide information for human subject review committee protocols.

Scanner Hardware

The GE Signa NV/I MRI system provides high duty-cycle and speed of echo-planar pulse sequences to achieve whole-brain imaging as required for understanding complex cognitive processes. The system provides single image acquisition in 28 ms, and using a TE of 40 ms, up to 12 images per second sustained. The MR system includes gradient coils that produces high gradient strength and rapid switching needed for rapid spatial encoding in any direction, and a high sensitivity birdcage RF coil for signal reception and transmission. The RF coil is slid over the subject's head and extends below chin level to image the cortex and cerebellum.

Software User Interface

Programs such as AFNI, MedX, SPM, and Analyze are also available. BrainMRI is a locally-developed image display and processing program for fMRI analysis, that runs on SGI systems running IRIX. Functional MRI offers unique requirements for software development in particular because of the large number of images that can be generated. While statistical analysis software for single slice data analysis has been developed for PET, the analysis of spatial and temporal correlations of activations in different cortical areas is poorly developed. In the BrainMRI program, the user can draw closed regions of interest (ROI), label them and generate numerical files for statistical analysis using SAS or other program. Regions of interest can be defined over the 3D spatial extent of images. Plots of signal data versus time can be displayed so that the user can assess whether or not there is activation. The BrainMRI interface allows clicking on a pixel or group of pixels and displaying a plot of the average signal versus time in those pixels. Activation patterns can be observed in graphical form (increase in signal about 3-8% at 1.5T), where signal changes are readily assessed. Anatomical distortion in the EPI images requires correction. High resolution scans using conventional fast GRE or spin echo sequences are performed before and after the functional studies, with the intent to overlay EPI activation maps onto the high resolution images. Algorithms developed at UC Davis and elsewhere dewarp the EPI image based on image landmarks are based on a map of the main field of the magnet.

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