

FBIRN Phase II Multi-site fMRI programs

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Overview

The FBIRN has as its aim to develop initial multi-site, imaging calibration methods and the shared data storage infrastructure. Despite its great potential value, there are significant problems in employing fMRI in multi-institutional studies. Multi-site functional imaging data include the same variability sources as single-site data (e.g., subject and population variability), as well as new sources of variability, such as differences in scanner equipment and methods. fMRI instrumentation and acquisition protocols vary greatly across imaging centers, and methods for data analysis and quantification vary similarly. Even more problematic are the myriad of psychological challenge tasks during which activations are elicited. Finally, the network, storage, and database infrastructure necessary to share and analyze collaboratively the multi-terabyte data sets resulting from multi-institutional fMRI studies do not exist.

Following the first phase of sending the same subjects to all the sites using a common initial protocol (Phase I Traveling Subjects dataset, data and programs available on www.nbirn.net/Resources/Downloads), a revised protocol was used in a multi-site study of both schizophrenic and control subjects. The stimuli and responses were presented and collected using E-prime software, using an SRBox response device (see Psychology Software Tools, Inc., <http://www.pstnet.com/products/e-prime/>). These E-Prime programs are now available.

Study Design:

These programs as released require E-Prime to be installed, and an SRBox be connected to the computer. If an SRBox is not connected, then many of these programs will not run. Double-clicking the .es files for each task should start E-prime, which can then be run as usual.

At each site, subjects were scanned according to the same protocol. The paradigms consisted of:

The sensorimotor task (SM); the breathhold task (BH); a Serial Item Recognition Paradigm (SIRP); and an Auditory Oddball task (AO). Information on these tasks, the instructions given for training, and the details of the paradigm can be www.nbirn.net/Resources/Downloads. The file [fBIRN_phaseII_scanchecklist_Version2_0_1-27-2005.doc](#) includes the step by step scanning protocol. It assumes that the various programs and instructions have been downloaded and installed.

The stimuli and programs are www.nbirn.net/Resources/Downloads. All stimuli presentation and subject response recordings were performed using E-Prime software (Psychology Software Systems, Pittsburgh). The stimulus generation computer and scanner were linked by a trigger signal so that timing of the paradigm and scanner are precisely matched. Visual stimuli were delivered using various methods. Several sites in the consortium use an LCD projector, with the presentation focused onto a back-projection screen mounted in the magnet bore. Several sites were using projectors onto head coil-mounted mirrors; others used MRI-compatible goggles.

Auditory stimuli were standardized as much as possible by using the AuditorySetup program. The stimuli were delivered using pneumatic, sound-insulated headphones adjusted to a comfort level per subject, which was recorded (using the Audio Setup E-prime file). The background noise levels at

each site are different, given their different scanners and pulse sequences; thus, calibrating to a constant dB level was found to be impractical and ineffective. Responses were monitored using keypads, and reaction times were recorded for subsequent psychophysical analysis of timing and accuracy of task performance. Prior to scanning, subjects practiced the tasks in front of a monitor with headphones and a button response box using the same stimulus delivery software as for the fMRI scanning. A basic reaction time task was used once subjects were inside the scanner, for comparison of response devices across sites (using the Reaction Time E-prime file).

Scanner triggering: Different scanners allowed for different triggering mechanisms. The file Fbirn_triggersetup4.ppt includes an explanation of the different scanning options that were included in each E-prime program. Certain scanners could send trigger signals to start the E-prime programs, and others could not. Scanner triggers could come in on Line 4 or Line 5 of the SRBox. This information is needed in running several of the programs.

The user is responsible for making the correct choice in the opening screens on each program, to determine whether the E-prime program is triggering the scanner, or vice versa, and which line on the SRBox is sending or receiving the trigger impulse. All button box data is saved in .edat file and can be viewed in E-Data Aid.

All of these paradigms were designed to run with a 2 s TR on the scanner. For more specifics on the imaging details used in data collection, see the Scanning Checklist.

Summary of the paradigms:

1. The Audio Setup task is used to adjust headphone placement and/or headphone volume that result from improper headphone placement and/or headphone malfunction. Auditory stimuli are presented with E-Prime programming software and Avotec headphones. No earplugs are used. Phases 1 and 2 are done before any scans are performed, but with the subject positioned on the scan table supine, with headphones on and bite bar in place inside the headcoil. Phase 3 is done during a functional scan to obtain the volume thresholds with this background noise, although no scan data are recorded.

The task consists of 3 phases:

Phase 1, Test tones. Produces tone in left, right and both ears, sequentially. Subjects press any button on the button box to confirm that they can hear tones as they are presented. If the subject is unable to hear the tones, adjust the headphones or increase the master volume.

Phase 2, Balance setup. Allows subject to adjust left/right balance of sound, by pressing buttons 1 or 2 to alter volume balance. The tone is first presented at -500 (left, 5 dB higher). Button 1 is pressed to move tone to the left ear, and button 2 is pressed to move tone to the right ear. The minimum step size is 100 (1 dB). Button 3 is pressed when the tone sounds equal in both ears. The balance is recorded in E-Data Aid, and can be obtained by loading and running the analysis file: Balance.anl.

Phase 3, Volume setup. A tone is played at -5000 (-50dB). Subjects press button 1 to increase volume and 2 to decrease volume. The minimum step size is 200 (2 dB). Button 3 is pressed when subject feels that the tone is set to a comfortable volume level (not too loud and not too soft). The balance is recorded in E-Data Aid, and can be obtained by loading and running the analysis file: VolumeLevel_ver#.anl.

The obtained balance levels and volume thresholds obtained should be calculated immediately following the completion of the entire audio setup task, as this data is required to run the Sensory-Motor and Auditory Oddball tasks. Do not exit the task until phases 2 and 3 are complete.

All scanning paradigms began with a 6-second (3 TR) count-down of black screens with the words "Please wait...", to allow for dummy acquisitions.

2. The SIRP timing and design are as follows (see Figure, below). Instructions to run the E-prime program are similar to those listed in the Auditory Oddball Task.

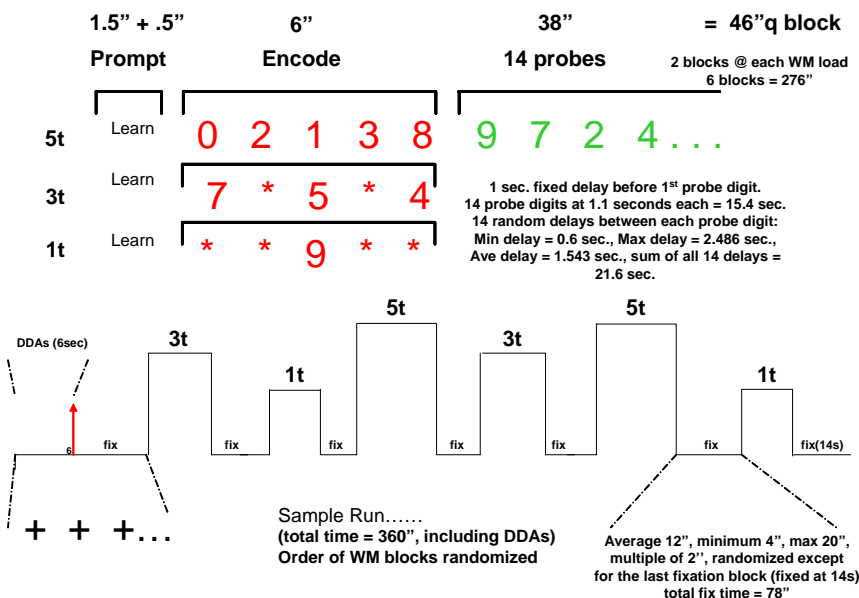
Prior to the start of this task, subjects need to position the button box so that the right index finger is placed on button 1, and the right middle finger is on button 2. The Sternberg Item Recognition (SIRP) task is a continuous performance, choice reaction time task that requires working memory (WM). Subjects memorize a set of targets (e.g., digits). They are then presented with probes (single digits) and respond by indicating whether the probe is a target (a member of the memorized set) or a foil (not a member of the memorized set). Correct responses are predicated on an accurate representation of the targets in WM for the duration of the block. The number of targets can be varied to produce conditions with a range of working memory loads. This version of the SIRP task consists of three working memory loads, where subjects are shown a set of 1, 3 or 5 target digits in red, followed by a series of probe digits in green. For each run or scan, two sets of target digits for each of the three loads, or conditions, is presented. Each set has three portions: learn, encode, and probe epochs. Subjects are asked to learn the sets of red digits and are instructed to press “1” if the green probe digit matches one of the targets and “2” if it does not.

The behavior can be analyzed using E-Prime Data Aid.

The order of the three conditions is pseudorandom. In between conditions, subjects fixate on a flashing cross. Psychophysical data include button box responses, which are analyzed in E-Data Aid using the analysis files mean_reac.anl, and num_correct.anl, which provide the mean accuracy and reaction time for each condition in the data file. The screen is set for 1024x768.

Working Memory (WM) WM conditions: Each WM condition begins with the prompt “Learn”. This alerts the subject to memorize the digit(s) that follow.

This prompt is followed by a 6 second “encode” epoch consisting of the presentation of a set of target digits. The targets are presented in red. To match for visual stimulation, for the 1 and 3 target condition, asterisks (*) are used in place of digits.



Following the encode epoch, there is 2.7 s “delay” and a longer “probe” epoch. During the probe epoch, subjects are shown 14 individual WM probes in green. The subjects are trained to respond with an index finger press if the probe digit is a target (a member of the memorized set), and a middle finger press if the probe digit is a foil (not a member of the memorized set). Within each WM condition,

half of the probes are targets, half are foils, and each member of the target set is presented at least once. Probe digits are random integers between 0 and 9, and are not repeated within a single memory set; no more than 3 consecutive digits are targets within a memory set. The timing of the probe digits is 2.7 s, made up of random jitter around a 1.1 s display. The overall probe epoch lasts 37.8 s.

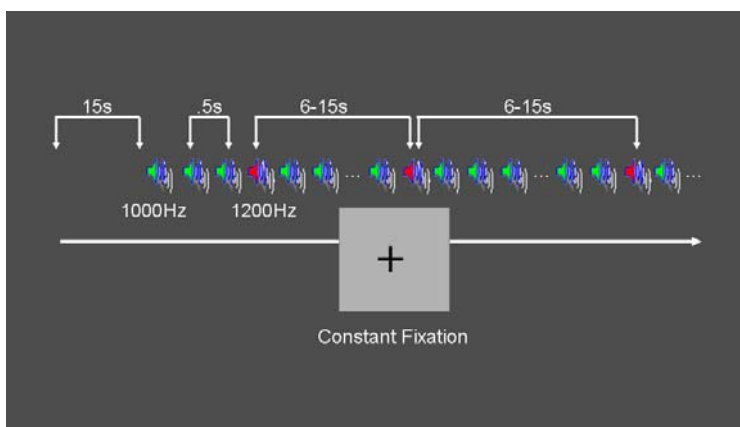
Fixation condition and timing: During fixation epochs, a single, flickering cross-hair (“+”) appears during which time the subject relaxes. The flickering interval is 2s: 1.85s on, and 0.15s off, (with exception to the first interval, which lasts 2.8s). A fixation epoch occurs at the beginning of each WM block.

3. The **Auditory Oddball timing and design** are as follows:

In the auditory oddball task the subject is presented with a continuous sequence of discrete stimuli comprising Standards and Targets. Standards are either physically identical or members of the same stimulus category. Standards typically appear on 80-90% of trials. Targets are distinct from Standards, occur infrequently (5-10% of trials), and require a differential response. This task has been used to investigate auditory “automatic” involuntary sensory processing regions.

The auditory oddball task consists of two practice runs and 4 experimental runs each having a duration of 280s (4.67 minutes). Each run consist of a standard tone (1000 Hz) and an oddball tone (1200 Hz). A gray screen with a black fixation cross in the middle of the screen is presented for the duration of each run. The subject is instructed to focus on the fixation point while listening to the tones and to respond with a button press when they hear a deviant tone. See Figure below.

After 6s (3 TRs) of discarded and deleted acquisitions, the task begins with a fixation block of silence (15s). This is followed by the presentation of a series of standard tones (1000Hz; ISI=500ms; duration=100ms). Every 6-15s the oddball tone is presented (1200Hz; ISI=500ms; duration=100ms). The task consists of 95% standard tones and 5% oddball tones. The task finishes with a second fixation block of silence (15s). Subjects are instructed to press button 1 to the oddball tone.



Instructions for running the Auditory Oddball task

1. Start E-prime and load the Auditory Oddball script
2. Using the menu at the top of the screen, select 'E-run', then 'Run'. This should prompt E-prime to run the script.
3. Next the script will ask you to specify several experimental parameters.
 - a. Subject Number: Enter the subject number.
 - b. Session Number: Enter the subject's session number (run number).

- c. Enter Balance: Select the option that the subject indicated was the most balanced during the calibration. See the Audio Task Setup section for more details.
- d. Enter Volume: Select the volume level that the subject indicated was the most comfortable during the calibration. See the Audio Task Setup section for more details.
- e. Select a run number: Select the appropriate run. Depending on where you are in the experiment you should select one of the two practice runs or one of the four experimental runs.
- f. Select a trigger setup: Select the way in which you wish to have the task be triggered.
 - i. 'Scan Start' specifies a non-Siemens scanner as the trigger to start the task.
 - ii. "E-prime Start" specifies that you will trigger the task by clicking on the space bar.
 - iii. 'Siemens Start' specifies a Siemens scanner as the trigger to start the task.
- g. Select scan trigger line: This option lets you determine how the script should communicate with the button box. You can choose line 4 or line 5. The choice should be determined based on the hardware configuration for your task computer.

4. Summary of Startup information: Once all the selections have been made E-prime reviews the options and asks if you want to proceed. If you are satisfied with your selections, click 'OK'.

- a. If you selected 'Scan Start' or 'Siemens Start' as the trigger setup, the scanner will automatically trigger the task to begin.
- b. If you selected 'E-prime Start' as the trigger setup then click on the spacebar when the screen turns gray and says 'preparing to start'.

5. When the scan ends E-prime will save a text file and .edat file to the directory in which you ran the E-prime script. You can identify the file name by finding the file that has the subject number incorporated into the name.

4. The **SM timing and design** are as follows:

Total task time: 4:06 (includes 3 discarded acquisitions (DDAs) w/TR = 2s)

Time frames: 123 (includes 3 DDAs)

The task consists of a block design with block durations of 16s on/off. During the on-block, a checkerboard stimulus appears at irregular intervals. When checkerboard appears, subjects press button "1" on the SRBox using their dominant hand only. This is a block design with intentionally short block durations of 16s on/off. The off-block is fixation/no tapping. The sequence begins with an off block.

On block parameters: ISI ranges from 500-1000ms, average ISI = 762ms, std dev = 156ms. 21 checkerboard flashes per on block, each checkerboard flash duration = 200ms. 15 total 16s blocks. Total task time: 240s + 6s countdown (246s total). The screen is set for 1024x768. Psychophysiological data recorded with E-Prime and saved in respective *.edat file.

5. The **BH timing and design** are as follows:

Total task time: 4:06 (includes 3 DDAs w/TR = 2s)

Time frames: 123 (includes 3 DDAs)

Total task time: 240s + 6s countdown (246s total).

This task is used to measure subjects' global vascular reactivity. The task consists of a block design with alternating on/off blocks of 16-second periods of breath holding and normal breathing. During the off-block, the subject sees a green screen during which they are to breathe normally. During the last 2s of the off-block, the screen becomes yellow, signifying to the subject to take a deep breath in and hold. During the on-block (16s), the subject is shown a red screen, during which time they should hold their breath. The subject resumes breathing when they see a green colored screen. There are 15 total blocks of 16 s each.

Task instruction and stimuli are presented visually with E-Prime programming software. No psychophysical data are recorded. The screen is set for 1024x768.

Relevant publications and conference presentations analyzing data collected with these paradigms include (available at www.nbirn.net):

1. S.G. Potkin; G.G. Brown; G.H. Glover; G. McCarthy; K. O. Lim; R. Gollub; B. Rosen; A. Toga; R. Kikinis; A. Dale; J. Lauriello; D. O'Leary; J. Lieberman; A. Belger; D. Greve; L. Friedman; T. Cannon; D.B. Keator; J.S. Grethe; J.A. Turner; Function BIRN. (2004). Functional Biomedical Informatics Research Network: Multi-Center fMRI Methods. *American College of Neuropsychopharmacology Meeting*, San Juan, Puerto Rico.
2. Turner, J., Potkin, S. G., Brown, G. G., Glover, G. H., Fallon, J. H., McCarthy, G., Lim, K. O., Gollub, R. L., Rosen, B. R., Toga, A. W., Kikinis, R., Pieper, S., Dale, A. M., Lauriello, J., O'Leary, D. S., Lieberman, J. A., Belger, A., Greve, D. N., Friedman, L., Cannon, T. D., Keator, D. B., Grethe, J. S., Function BIRN. (2005) . Multi-Center fMRI Methods And Design: Function BIRN. *International Congress of Schizophrenia Research*, Savannah GA.
3. Friedman, L., Krenz, D., Magnotta, V., Functional BIRN (2005): Isolated Spike-Like Transients (ISLTs) in Functional MR Timeseries: Evidence for Vendor and Field Strength Effects on Rates. *13th Annual Meeting of the International Society for Magnetic Resonance Imaging (ISMRM)*, Miami Beach, FL.
4. Keator, D.B, Grethe, J., Ozyurt, B., Gadde, S., Wei, D., Turner, J.A., Potkin, S.G., Brown, G.G., McCarthy, G., Glover, G.H., Stern, H., Lauriello, J., Friedman, L., Belger, A., Lim, K.O., Pieper, S., Greve, D., FBIRN. (2006). Function Biomedical Informatics Research Network (FBIRN) Open Source fMRI Informatics, Calibration, and Data Tools Repository. *Annual Meeting of the Organization for Human Brain Mapping*, Florence, Italy, June 11-15, 2006.
5. Yendiki, A., Wallace, S, Vangel, M., Clark, V., Lim, K.O., Andreasen, N., Greve, D., Manoach, D.S., Gollub, R.L. (2006). Multi-site characterization of an fMRI working memory paradigm: Reliability of activation indices. *Annual Meeting of the Organization for Human Brain Mapping*, Florence, Italy, June 11-15, 2006.
6. Turner, J.; Potkin, S. G.; Brown, G. G.; Stern, H. S; Glover, G. H.; McCarthy, G.; Greve, D. N.; Friedman, L.; Keator, D. B.; Grethe, J. S. Fallon, J. H.; Lim, K. O.; Gollub, R. L.; Rosen, B. R.; Toga, A. W.; Kikinis, R.; Pieper, S.; Lauriello, J.; O'Leary, D. S.; Belger, A.; Function BIRN. (2006). Multi-center fMRI methods and design: Function BIRN. *Annual Meeting of the Society for Neuroscience*, Atlanta, GA.