Functional Imaging Paradigms

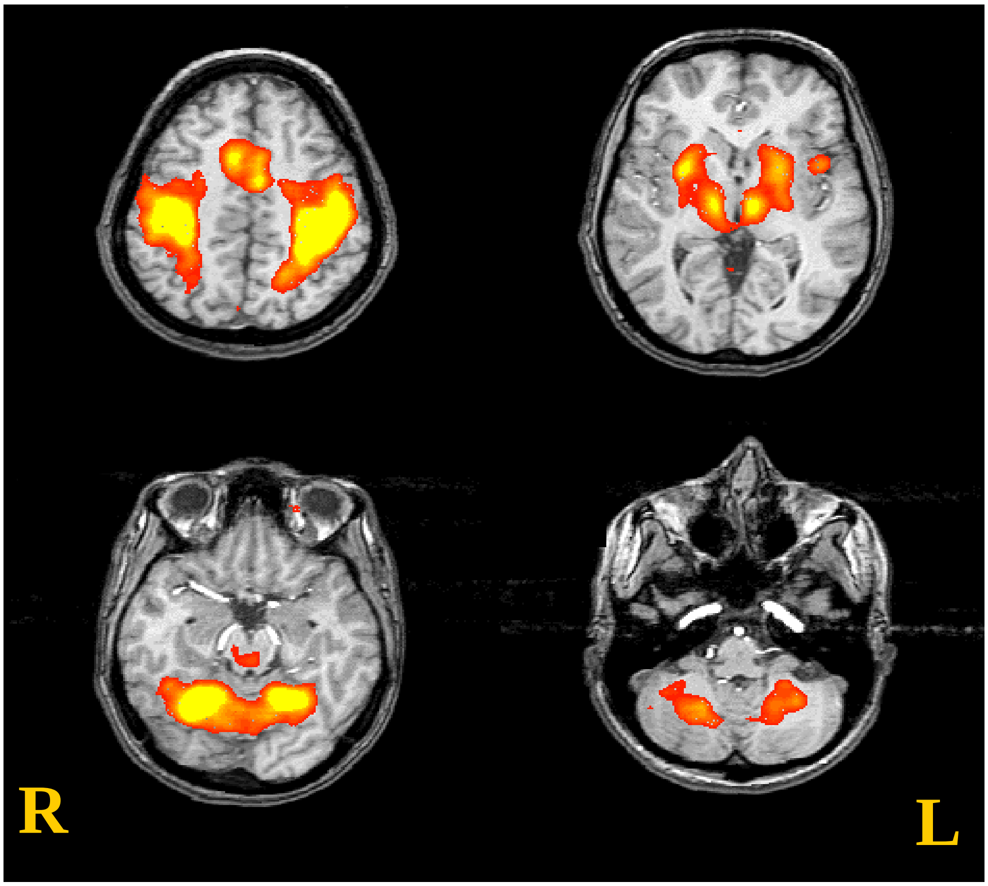
This “Functional Imaging Paradigm” section contains brief fMRI paradigm descriptions that were requested from presenters in the fMRI portion of this meeting. The authors have all had experience and success using these specific paradigms for presurgical mapping and other clinical scenarios. Not all ASFNR speakers submitted a paradigm or all of the paradigms used at their respective institutions. There are undoubtedly successful paradigms at other institutions not represented here. Also, specific paradigm timing parameters are influenced by field strength, coil design, delivery systems, other environmental factors, and post-processing strategies. Consequently, differences in paradigm parameters described here are less pertinent to the educational effort than the overall paradigm designs. The section contains a variety of paradigms for mapping motor, premotor, speech and language, vision, and memory functions that are intended to promote the translation of clinical presurgical mapping services among the institutions of meeting attendees. However, the standardization of presurgical mapping paradigms is an evolving process, and the contents herein do not represent an official recommendation or endorsement by the ASFNR.

Motor and Premotor

Paradigm Title: Bilateral Complex Finger Tapping

Paradigm description: bilateral simultaneous complex finger tapping. Subjects tap fingers bilaterally in the sequential order of 1, 3, 5, 2, and 4. The subjects are instructed to tap the fingers of both hands on there thighs in a comfortable location. The important aspect of he task is the sequencing of the finger movements, rather than location. The task is repeated as rapidly as possible without making mistakes. The dexterity requirements of the task generate robust M1 and premotor activity.

Paradigm parameters: EPI gradient echo two-dimensional pulse sequence. TR = 2 seconds, TE = 30 ms, matrix = 64 x 64, Field of view 240 x 240, slice thickness 3.8 mm, 32 slices. Simple rest/tapping block paradigm with four cycles. Audible cues to stop and start tapping are given via a MRI compatible sound system. Task performance is assessed using fiber-optic MR compatible gloves.



Activation patterns: Paradigm provides robust activation in the bilateral sensorimotor cortex, bilateral SMA, bilateral basal ganglia, bilateral thalami, and bilateral superior cerebellum. Additional areas of activation are oftentimes noted in the bilateral premotor regions.

Comments: This is a robust motor task that produces activation throughout the motor and premotor pathways. Extensive activation requires a relatively high activation threshold at 3T, to visualize functional anatomy. Task is difficult for some patients to perform, particularly those with neurodegenerative processes such as Parkinson's disease or multiple sclerosis, or those with compromised motor function due to an underlying tumor and edema. Musicians and others with dexterity training may produce lesser activity.

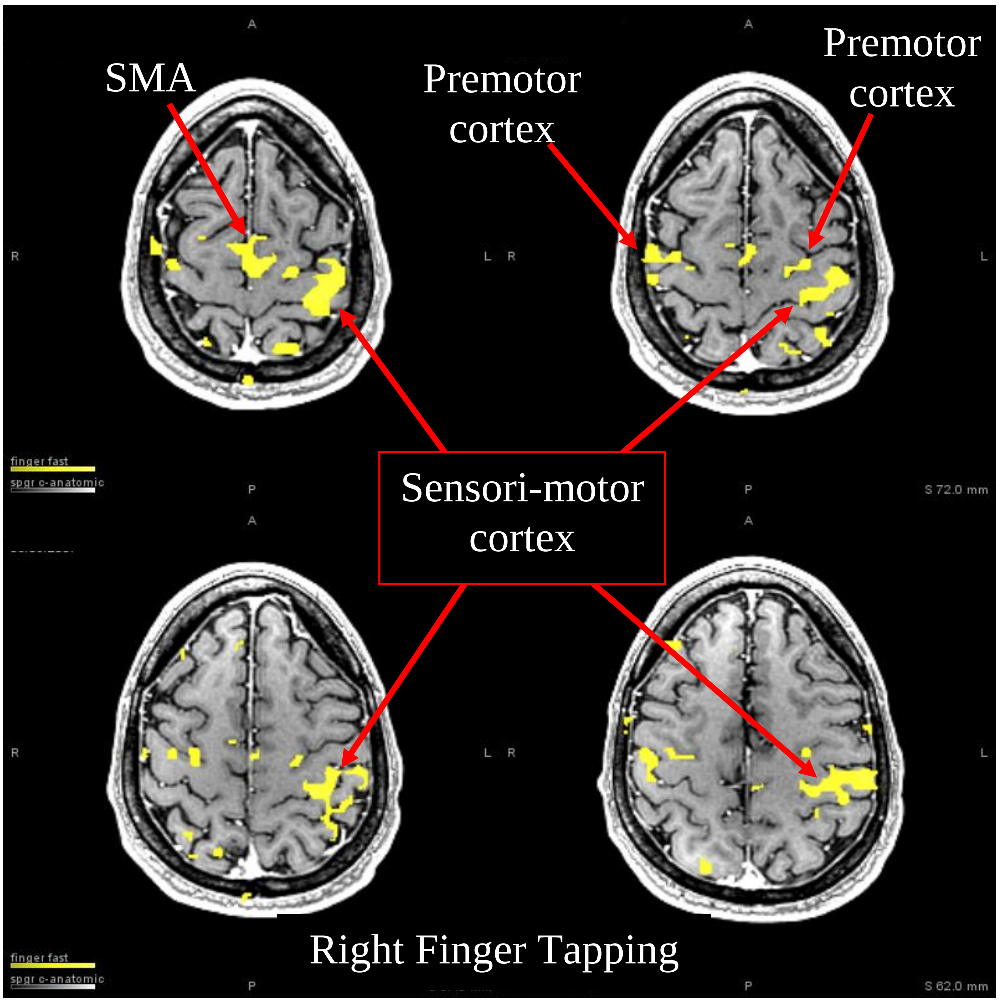
References:

Lowe MJ, Lurito JT, Mathews VP, Phillips MD, Hutchins GD. Quantitative comparison of functional contrast from BOLD-weighted spin-echo and gradient-echo echoplanar imaging at 1.5T and H2150 PET in the whole brain. *J Cereb Blood Flow Metab* 20(9):1331-1340,

Paradigm Title: Unilateral Sequential Finger Tapping

Paradigm Description: Sequential finger tapping results in robust premotor and primary sensori-motor activation and is easily performed by most subjects. Some patients with neurological cortical spinal deficits may not be able to carry out finger tapping tasks. In this case, a hand grasping or index finger-to-thumb task is preferred. For the sequential finger tapping task, the patient is asked to tap their thumb to each finger of their hand in a sequential manner at a self-paced rate on a "go" command and to continue tapping until a "stop" command is presented. During the scan, the scanner operator visually confirms that the finger tapping is performed during the "go" period. Alternatively, a response keypad or MR compatible glove can be used to monitor the task more precisely.

Paradigm Parameters: Block design with a visual stimulus presentation and stop/go commands. Three cycles, 60 seconds/cycle or epic (30 second half cycles). TR = 3 sec.. 20 volumes scanned per complete cycle. Total scan duration 3 minutes, 12 seconds. Four discarded acquisitions preceding stimulus presentation (12 seconds).



Activation Patterns: Unilateral sequential finger tapping results in robust activity within cortex about the superior lateral central sulcus, in the expected somatotopic location for this body part. In addition to primary sensori-motor activation, robust SMA activation is seen, with contralateral dominance. However, the contralateral dominance is more striking when sequential finger tapping is carried out on the dominant compared to the nondominant side. Secondary somatosensory activation may also be observed. Premotor cortex and cerebellar activation is common.

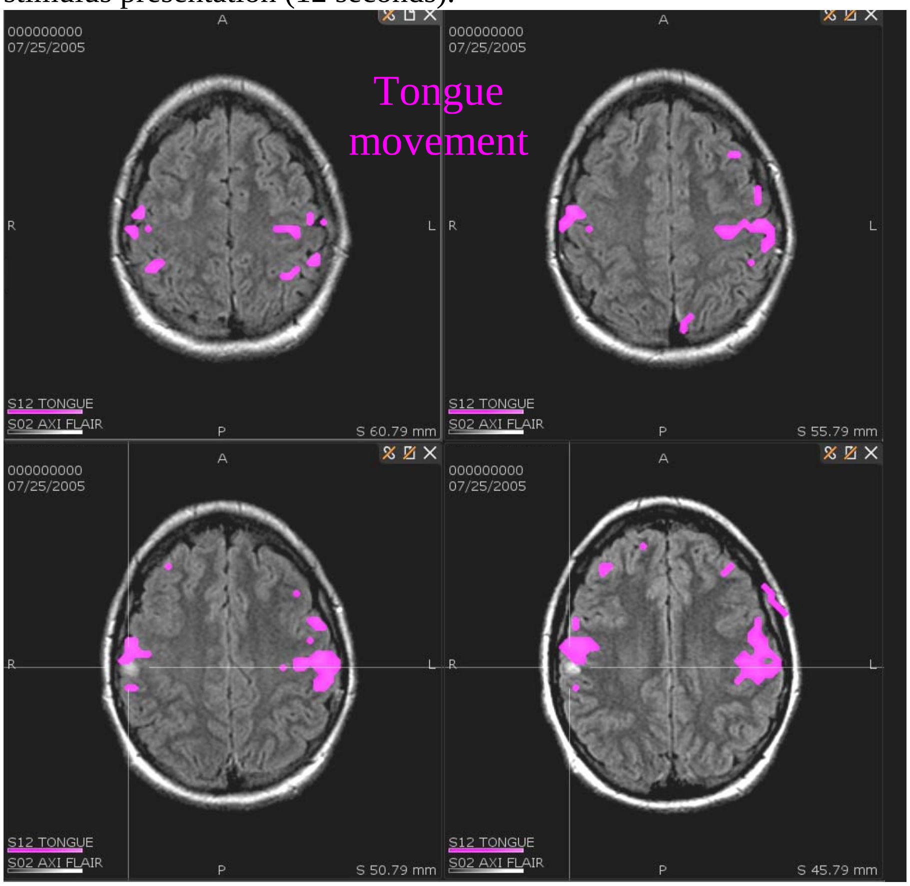
Comments: The sequential finger-tapping task can be performed by most subjects, although the rate of finger tapping varies considerably. Given that rate can influence the activated area of the sensori-motor cortex and if rate is not controlled by a visual cue, this must be considered in the interpretation. In those subjects that cannot perform a sequential finger-tapping task, an alternative hand opening and closing paradigm can be employed. In subjects who cannot perform a hand grasping task, passive movement paradigms are employed. Sequential finger tapping often results in ipsilateral activation within the anterolateral precentral gyrus located anteriorly and laterally to the primary motor cortex of the contralateral body part.

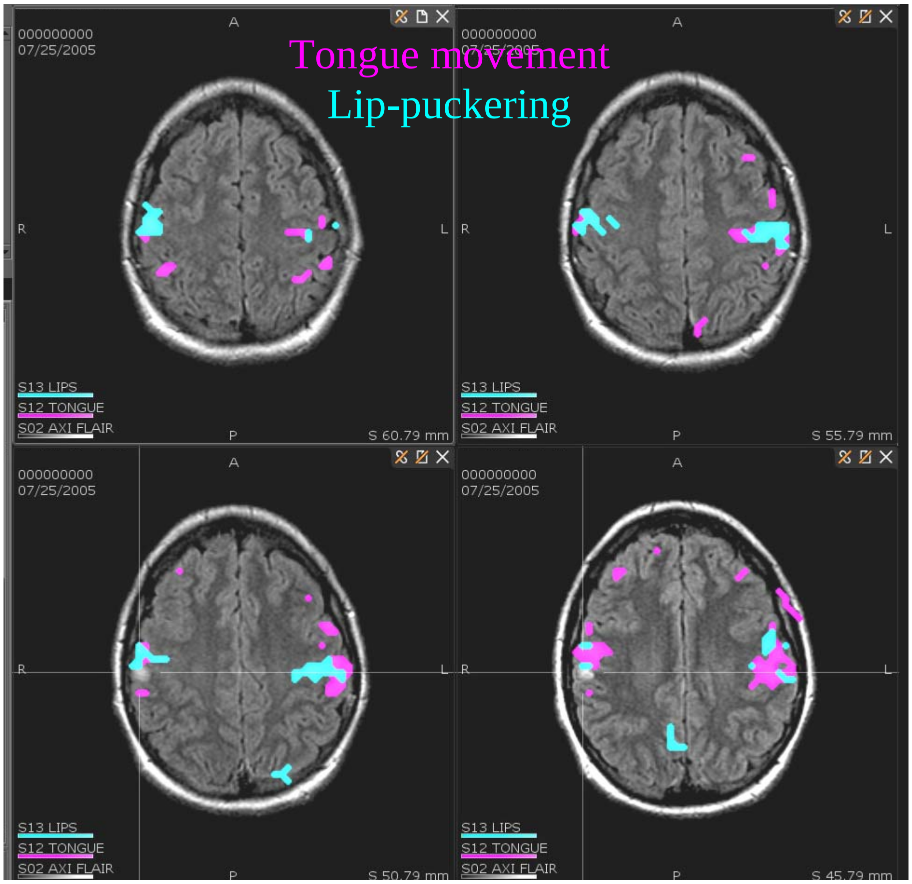
References: Too numerous to list.

Paradigm Titles: Lip Puckering and Tongue Movement

Paradigm Description: Identification of the corticobulbar motor cortex is important, because this cortex efficiently reorganizes, particularly in a nondominant hemisphere. Consequently, the border between cortico-spinal motor cortex (poor reorganization potential) and cortico-bulbar motor cortex is of interest to Neurosurgeons. For lip-puckering, patients are asked to pucker their lips repeatedly on a visually presented, or auditory, “go” command and to continue doing so until the “stop” command is presented. This is carried on for at least three cycles. Moving the tongue back and forth within a closed mouth can activate the lower extent of cortico-bulbar motor cortex, overlapping with and just below the activation response to lip-puckering. For the tongue movement task, patients are asked to wiggle their tongue back and forth in a closed mouth on a “go” command and continue so until the “stop” command is presented. To monitor lip-puckering, an MRI suite video system is required. Monitoring of tongue movement requires a modification of the task; moving the tongue from side-to-side outside of the mouth. However, this may increase jaw motion. The lip-puckering and tongue movement paradigms are simple to perform and, therefore, the vast majority of patients can perform them effectively.

Paradigm Parameters: Block design with a visual stimulus presentation and stop/go commands. Three cycles, 60 seconds/cycle or epic (30 second half cycles). TR = 3 sec.. 20 volumes scanned per complete cycle. Total scan duration 3 minutes, 12 seconds. Four discarded acquisitions preceding stimulus presentation (12 seconds).





Activation Patterns: The lip puckering task will result in activation about the lateral central sulcus in the expected somatotopic location for lower face sensori-motor cortex. Secondary somatosensory, premotor cortex, and SMA activation are also observed. Tongue movement will activate similar areas, but with primary sensori-motor cortex located along the homunculus lower than, and overlapping with, that produced by lip-puckering. Cerebellar activation is commonly observed.

Comment: Virtually all patients can perform these tasks, even those with facial and lingual deficits. Activation of corticobulbar motor cortex can cause head movement. Lip-puckering can be performed by most individuals (approximately 80%) without excessive head motion. In 10-15% of subjects head motion will be present, but will not impact the ability to localize primary sensori-motor cortico-bulbar cortex. In up to 5% of patients, head motion renders this task nondiagnostic or nearly nondiagnostic. The tongue movement task results in excessive head motion in approximately 50% of patients. In up to 25% of patients, head motion may render this paradigm nondiagnostic.

References:

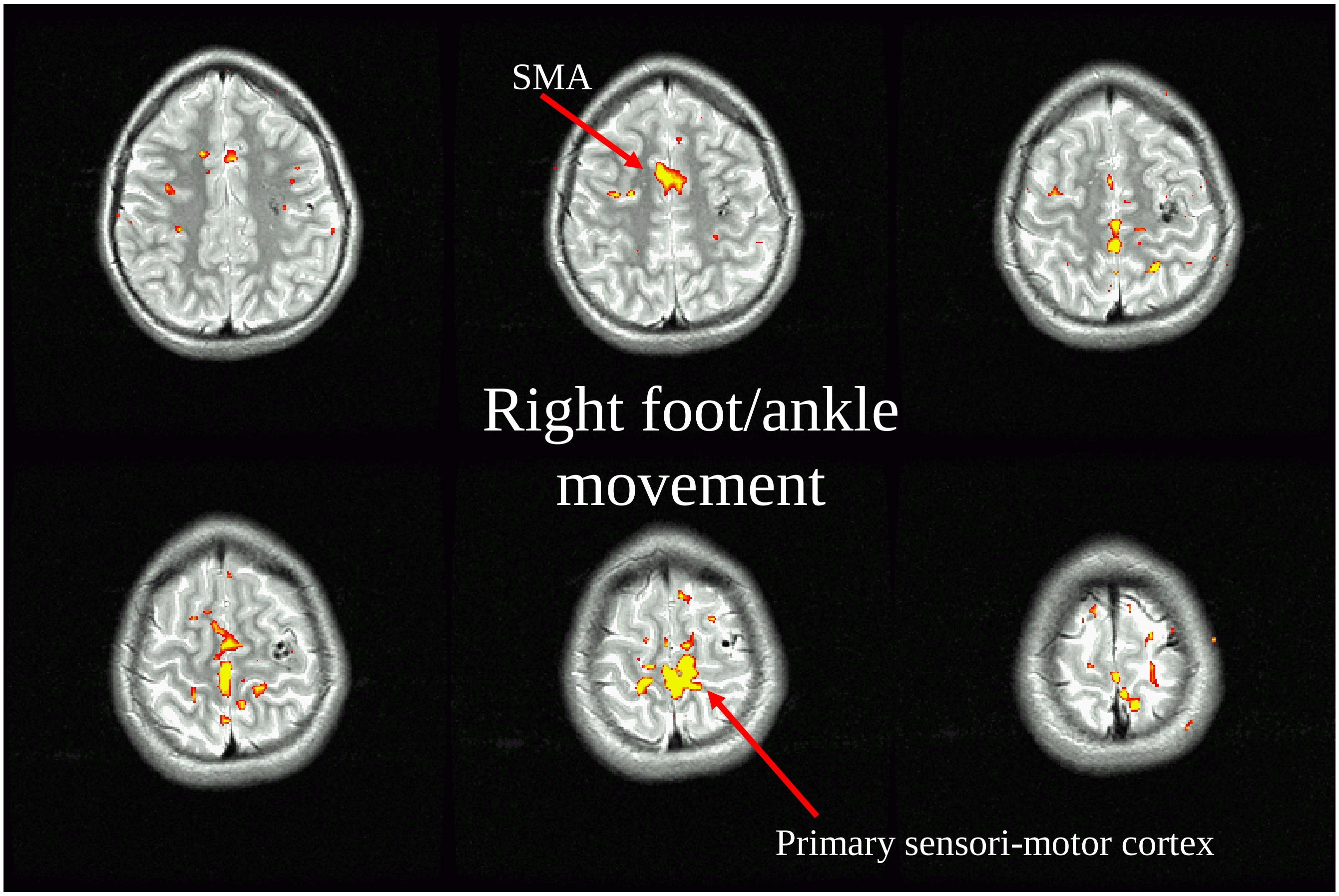
Kocak M. Functional MR imaging of the motor homunculus: Toward optimizing paradigms for clinical scenarios. *Proceedings of the American Society of Neuroradiology*, Vancouver, Canada. May 13-17, 2002.

Ulmer JL, Hacein-Bey L, Mathews VP, Mueller W, DeYoe, EA, Prost R, Meyer G, Wascher TM, Krouwer HG, Schmainda KD, Lowe M. Lesion-induced pseudo-dominance at fMRI: Implications for Pre-operative Assessments. *Neurosurgery* 55:569-581(2004).

Paradigm Title: Unilateral Foot/Ankle Movement

Paradigm Description: Foot/ankle movement results in premotor and primary sensori-motor activation and can be performed by most patients. Some patients with neurological cortico-spinal deficits may not be able to carry out finger tapping tasks. For the foot/ankle movement task, the patient is asked to dorsiflex and plantar flex the foot and ankle in a smooth, steady manner at a self-paced rate on a "go" command and to continue tapping until a "stop" command is presented. During the scan, the scanner operator visually confirms that the foot/ankle movement is performed during the "go" periods. The patient in belted to the scanner table around his /her pelvis to minimize cranial-spinal axis motion. The lower leg is elevated off the scan table using a foam cushion, placed at the knee or just above the ankle. When the cushion is placed at the knee, the patient must extend the knee to perform the task. This may add sparse motor activation in response to isotonic knee extension. Foot/ankle movements are monitored by the scan operator. Visual cues can be used to control movement rate.

Paradigm Parameters: Block design with a visual stimulus presentation and stop/go commands. Three cycles, 60 seconds/cycle or epic (30 second half cycles). TR = 3 sec.. 20 volumes scanned per complete cycle. Total scan duration 3 minutes, 12 seconds. Four discarded acquisitions preceding stimulus presentation (12 seconds).



Activation Patterns: Unilateral foot/ankle results in robust activity within cortex about the superior termination of the central sulcus and in the paracentral lobule, in the expected somatotopic location for this body part. In addition to primary sensori-motor activation, SMA activation is seen. Secondary somatosensory activation may also be observed. Premotor cortex and cerebellar activation is variable.

Comments: The foot/ankle movement task can be carried out by most subjects, although the rate may vary. Given that rate can influence the activated area of the sensory motor cortex and if rate is not controlled, this must be considered in the interpretation. A rapid rate will induce excessive head motion and a too-slow rate with elicit little activity. A rapid-as-possible rate while keeping the movement smooth and steady is preferable (usually about 1 Hz). A visual cue can be used to control movement rate. Up to 25 % of patients will exhibit excessive head motion, rendering the task nondiagnostic. An alternative movement is to rotate the foot and ankle from side-to-side, which may reduce head motion. Because SMA and primary motor cortex for the lower extremity may lay adjacent to one another, distinguishing the border between the two areas can be problematic.

References:

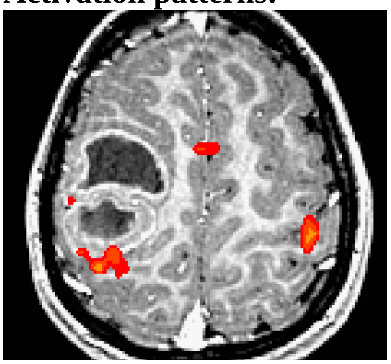
1) Kocak M. Functional MR imaging of the motor homunculus: Toward optimizing paradigms for clinical scenarios. *Proceedings of the American Society of Neuroradiology*, Vancouver, Canada. May 13-17, 2002.
2) Ulmer JL, Hacein-Bey L, Mathews VP, Mueller W, DeYoe, EA, Prost R, Meyer G, Wascher TM, Krouwer HG, Schmainda KD, Lowe M. Lesion-induced pseudo-dominance at fMRI: Implications for Pre-operative Assessments. *Neurosurgery* 55:569-581(2004).

Paradigm Title: Passive hand stimulation

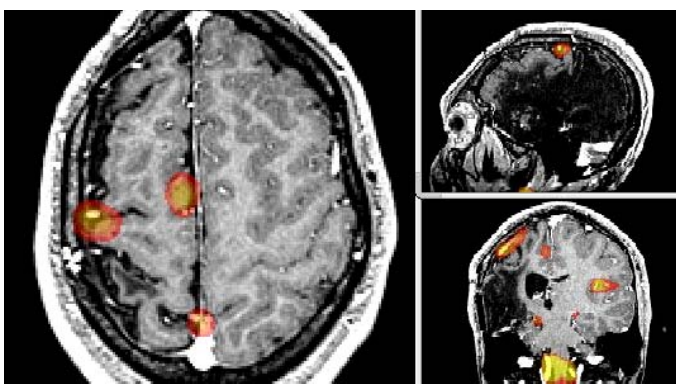
Paradigm description: Somatosensory .stimulation of the patient's palms / fingers. Primarily targeted at upper limb primary sensorimotor localization in central sulcus. Application is to sedated / unresponsive patients (e.g., pediatric or comatose[2]), or patients lacking motive control of upper limb (e.g., neurological deficit or cerebral palsy). Putative supplementary motor area responses can often be identified.

Paradigm parameters: Stimulation of the hands, either uni- or bilaterally, performed with the investigator's fingertips or a mildly abrasive device such as a toothbrush. Continuous stimulation of the entire hand, including palm and fingertips, can be expected to yield a robust response in upper limb region of contralateral central sulcus. Stimulus is performed as a block paradigm alternating with condition of non-stimulation. Example: Four 20sec iterations of stimulus blocks interleaved and book ended with 20sec blocks of non-stimulus. TR = 2sec; 10 data points per block; scan duration = 3min.

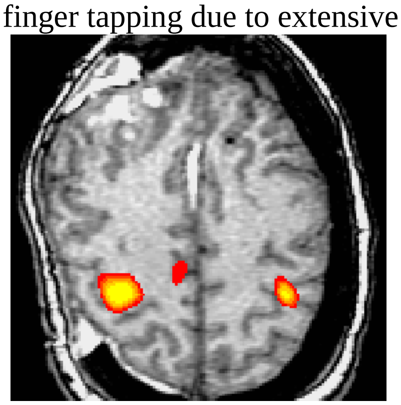
Activation patterns:



Bilateral hand tactile stimulus in sedated 3yr. old presurgical patient .



Left hand unilateral tactile stimulus in 19yr old epilepsy patient. Patient was unable to perform left hand finger tapping due to extensive right frontal-temporal infarct.



Bilateral hand tactile stimulus in comatose traumatic brain injury patient[2].

Comments: Patient's hands should be extended at their side to minimize proximity to head coil and possible artifact due to disruption of magnetic field. Passive stimulus fMRI of sedated patients can yield variable results, depending on the patient's level of sedation.

References:

1. Yetkin FZ, Mueller WM, Hammeke TA, Morris GL 3rd, Haughton VM. Functional magnetic resonance imaging mapping of the sensorimotor cortex with tactile stimulation. Neurosurgery. 1995 May;36(5):921-5

2. Moritz C, Rowley H, Haughton V, Swartz K, Jones J, and Badie B. Functional MR imaging assessment of a non-Responsive brain injured patient. Magnetic Resonance Imaging 19: 1129-1132, 2001.

Paradigm Title: Motor Task

Paradigm description: Intended to show sensory-motor regions involved in hand and foot movements

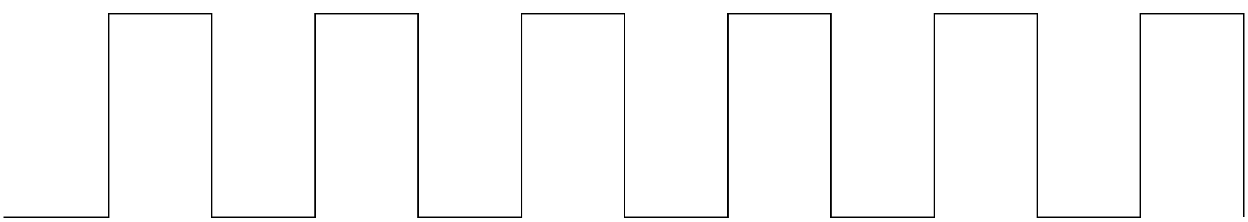
Paradigm parameters: The protocol consists of movement of hand/foot during the activation states (30sec duration, 6 conditions) and rest during the rest states (30sec duration, 6 conditions). Depending upon the task the subject is given the following instructions.

Hand Movement: In this study when you hear a start command please start performing left hand finger to thumb movement at your own pace until you hear the stop command. This start and stop cycle will be repeated several times and please pay attention to the instructions. During the rest time please do not move your hands and try to keep your head still throughout the study. Also please keep your eyes closed throughout the study.

Foot Movement: In this study when you hear a start command please start flexing and relaxing your foot your own pace until you hear the stop command. This start and stop cycle will be repeated several times and please pay attention to the instructions. During the rest time please do not move your foot and try to keep your head still throughout the study. Also please keep your eyes closed throughout the study.

The block diagram of the paradigm used is shown below. The total imaging time is 6 minutes.

Stop **(5:00)** Stop **(4:00)** Stop **(3:00)** Stop **(2:00)** Stop **(1:00)** Stop**(0:00)**



↑ ↑ ↑ ↑ ↑ ↑

Start **(5:30)** Start **(4:30)** Start **(3:30)** Start **(2:30)** Start **(1:30)** Start **(:30)**

Activation patterns: Hand: Contra-lateral superior Fronto/Parietal (Peri-rolandic fissure)
Foot: Contra-lateral medial mid Fronto/Parietal region

Speech and Language

Paradigm Title: Auditory Responsive Naming Task (Aural/Visual)
by Nicole Petrovich Brennan (Dr. Andrei Holodny's Lab MSKCC)

Paradigm Description: An auditory responsive naming paradigm is useful for language lateralization and particular localization of posterior (Wernicke's) language areas. The task also localizes frontal speech areas as it requires that the patient generate a word to a given verbal descriptor. (e.g. What do you sit in?) Presented visually, the task targets parietal structures involved in reading. Further, if presented visually, the task can be designed to be forced choice and the patient's performance can be monitored using a button box. The task is performed as a block design with 12 epochs total. (6 'on' and 6'off'). The patient is asked to read the sentence and push the button corresponding to the correct choice. (It is useful to have a practice run using the button box and a computer outside the scanner) Each 20 second stimulation epoch includes 4 stimuli. When presented aurally, the patient is instructed to silently generate a word that fits the description. The baseline is a resting baseline for the aural presentation and a nonsense baseline (perceptual control) for the visual presentation (eg &#&%& #^%)*&%). Control stimuli are jittered in length allowing for a non-periodic design that may be more sensitive to small temporo-parietal signals (*see Veltman D et al. Neuroimage 2002*)

Paradigm Parameters:

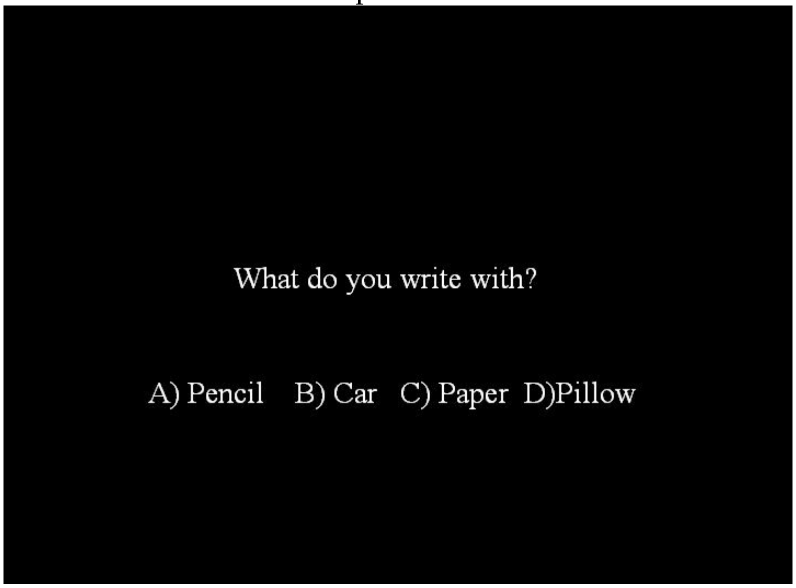
The following parameters are employed at 1.5T Tesla:

Gradient Echo-EPI pulse sequence
TR: 4000 msec
TE: 40 msec
FOV 24 x24
Matrix 128 x 128

Block design with visual or aural stimulus presentation.
12 epochs total (6 stimulation 6 control)
20 seconds per stimulation cycle and control length is variable
60 volumes scanned per complete cycle
Total scan duration: 4 min 12 seconds (3 dummy scans or 12 sec)

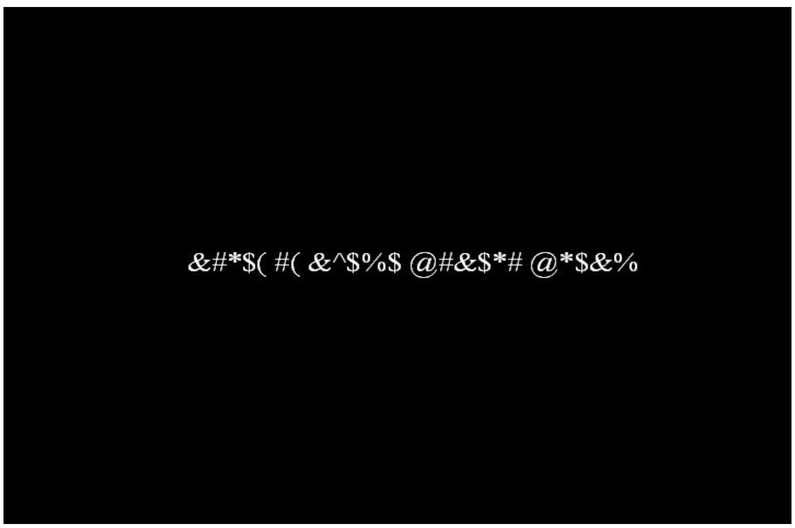
Stimuli are presented every 5 seconds for a duration of 5 seconds with a total of 4 stimuli per 20 seconds per stimulation epoch.

Sample Stimuli



Stimulation

Baseline



Monitoring: Four button finger switch (2 per hand)

Paradigm Activation Patterns:

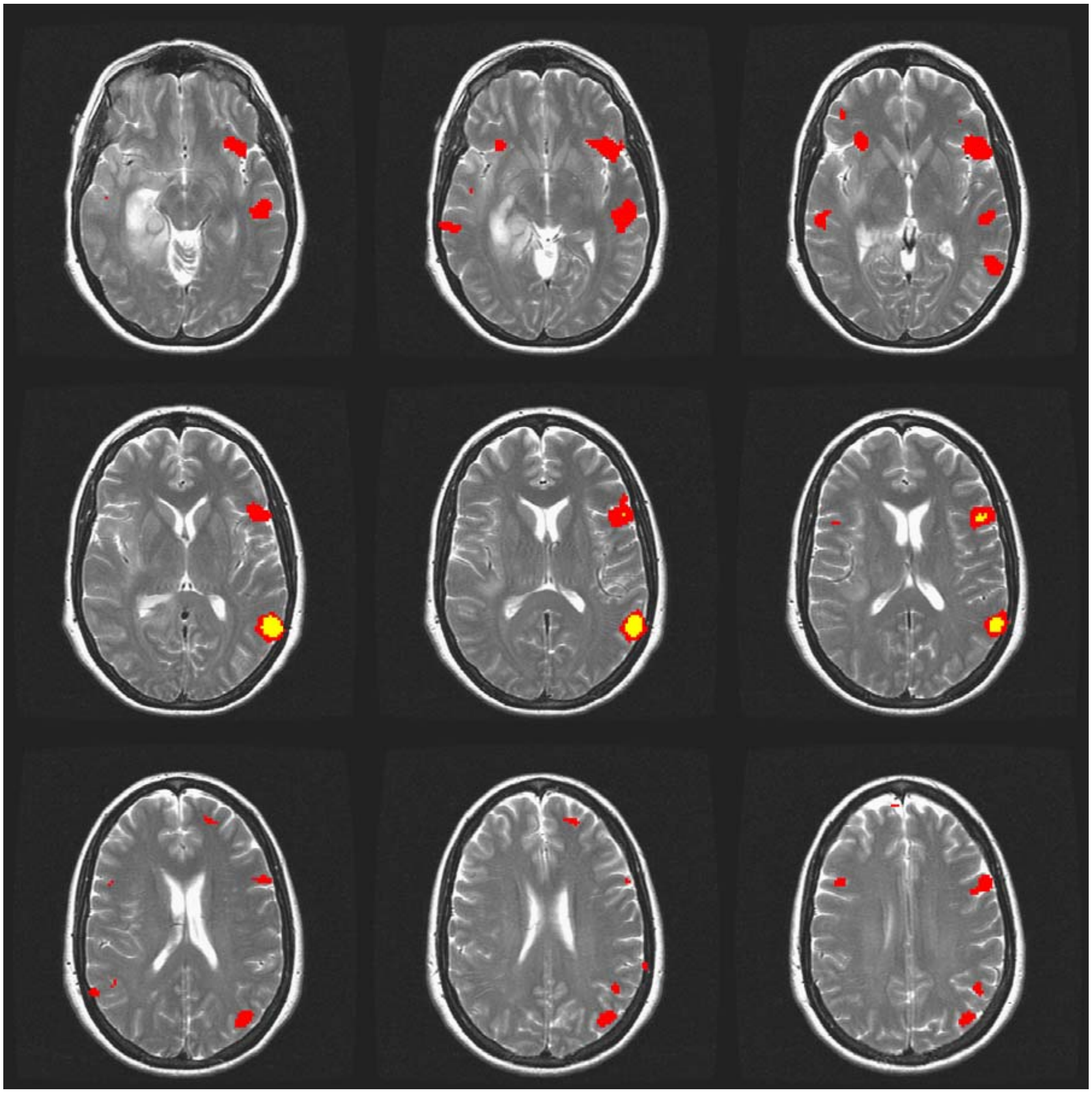


Figure 1. : Typical single patient fMRIat 1.5T. Auditory responsive naming map. Predominate areas of activation are inferior frontal, superior temporal, bilateral heschl's (primary auditory), and middle frontal gyri. Parietal structures activate variably.

Comments: The advantage of this task is that it tends to activate posterior language areas reliably. This can be difficult in patient populations. Another advantage of this paradigm is its ease of use in the operating room during electrocorticography. The task has been used to localize Wernicke's Area and may be a more sensitive measure than the typical object naming during electrocorticography. (*see Hamberger MJ et al. Brain, 2005*) The visual forced choice version of this task is not generally appropriate for profoundly aphasic patients. These patients perform better on a modified version of the aural task, where the patients are asked autobiographical information about themselves over headphones. (e.g. What is your address?)

Paradigm Title: Semantic Decision Task (Visual)

Paradigm Design: Mary Machulda, PhD, L.P. Mayo Clinic, Rochester
Clinical Implementation: Kirk Welker, M.D. Mayo Clinic, Rochester

Paradigm Description: A semantic decision paradigm is useful for language lateralization and localization of inferior frontal, posterior temporal, and inferior parietal speech areas in the dominant cerebral hemisphere[1-4]. This particular task is performed as a block paradigm with six to eight cycles. The "active" task consists of word pairs where one word represents a superordinate category (e.g. fruit) and the other word represents a subordinate category exemplar (e.g., apple.) For a six-cycle task, twenty of the word pairs consist of correct pairings (fruit - apple) and ten word pairs consist of incorrect pairings (fruit – shoe). The word pairs are visually presented every 6 seconds. Subjects are asked to respond "yes" using the fMRI response hand switch when the pairings are correct. They are asked to respond "no" when the pairings are incorrect. The "control" portion is a visual perceptual decision task and consists of two sets of 4 lines grouped together. The lines are either vertical (||||) or slanted (////). Subjects are asked to respond "yes" when the two sets of lines are identical (e.g., both are either vertical or slanted) and "no" when they are different (i.e., one set vertical, one set horizontal). These control stimuli are also presented every 6 seconds.

Paradigm Parameters:

The following parameters are employed at 3 Tesla:

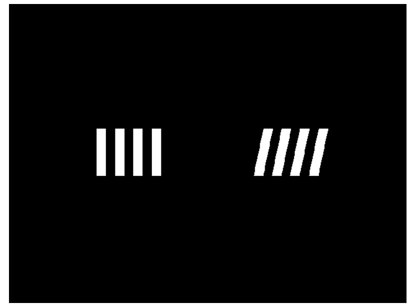
Gradient Echo-EPI pulse sequence
TR: 3000 msec
TE: 25 msec
FOV 20 cm by 20 cm
Matrix 64 x 64

Block design with visual stimulus presentation.
6 1/2 cycles
60 seconds /cycle or epoch (30 second half cycle)
20 volumes scanned per complete cycle
Total scan duration: 6 min 42 sec.
4 discarded acquisitions preceding stimulus presentation (12 sec)

First 30 second half cycle (control task) is not typically processed to allow for cognitive equilibrium.

Stimuli are presented every 6 seconds for a duration of 6 seconds with a total of 5 stimuli per 30 second half cycle.

Sample Stimuli



For the 30 semantic decisions presented, 20 are “yes” pairings and 10 are “no” pairings and these are randomly ordered. For the 30 visual perceptual decisions used as the control task 20 are “yes” pairings and 10 are “no” pairings. (Excludes, the first half cycle of visual perceptual decisions which is typically discarded.)

Monitoring: Two button finger switch (yes/no) buttons, HR, respiration, eye camera

Paradigm Activation Patterns:

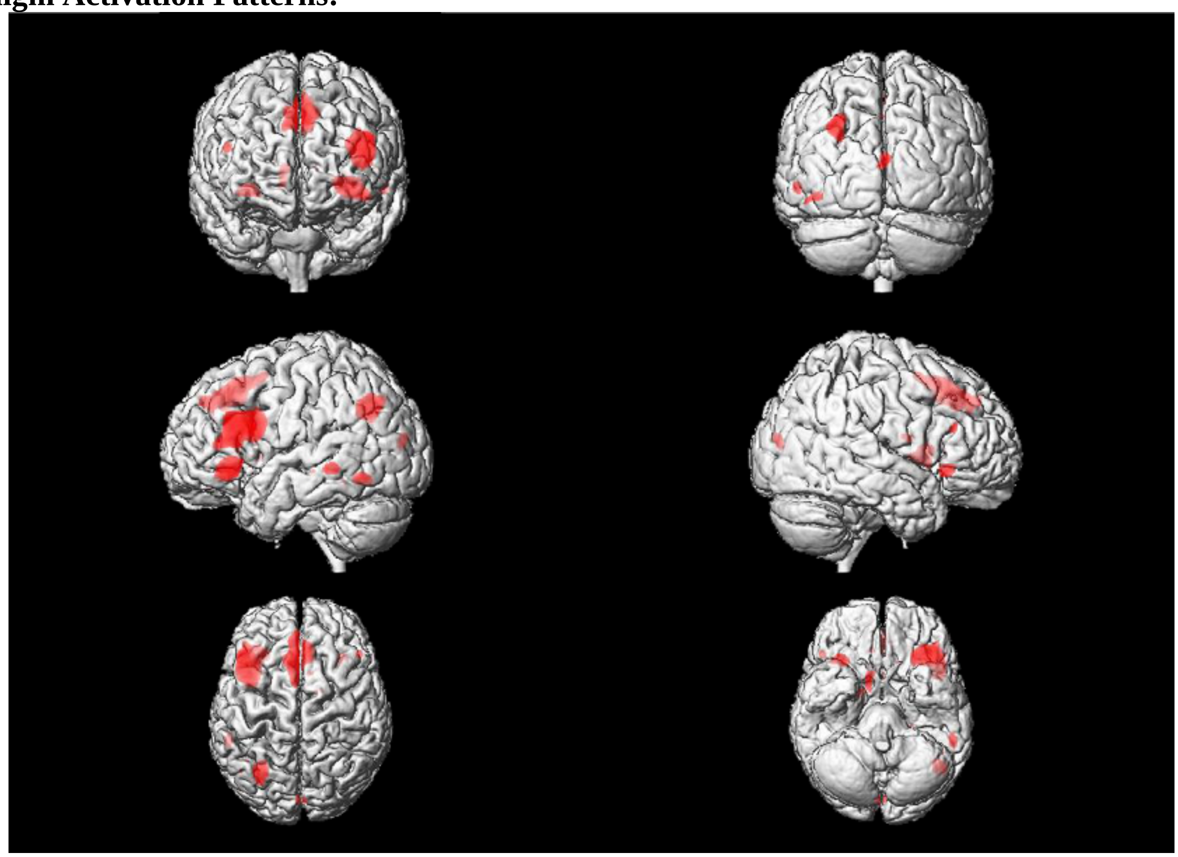


Figure 2. : Composite 3 Tesla fMRI activation map from 15 subjects derived from the semantic decision task. There is activation in the left Broca’s area, left inferior dorsolateral prefrontal cortex, junction of posterior superior temporal gyrus and supramarginal gyrus of the parietal lobe, left middle and left inferior temporal gyri. Less robust homologues noted in the opposite hemisphere. Activation also noted in supplemental eye fields, frontal eye fields and to a small degree the primary visual cortex bilaterally. Courtesy of Mary Machulda, PhD

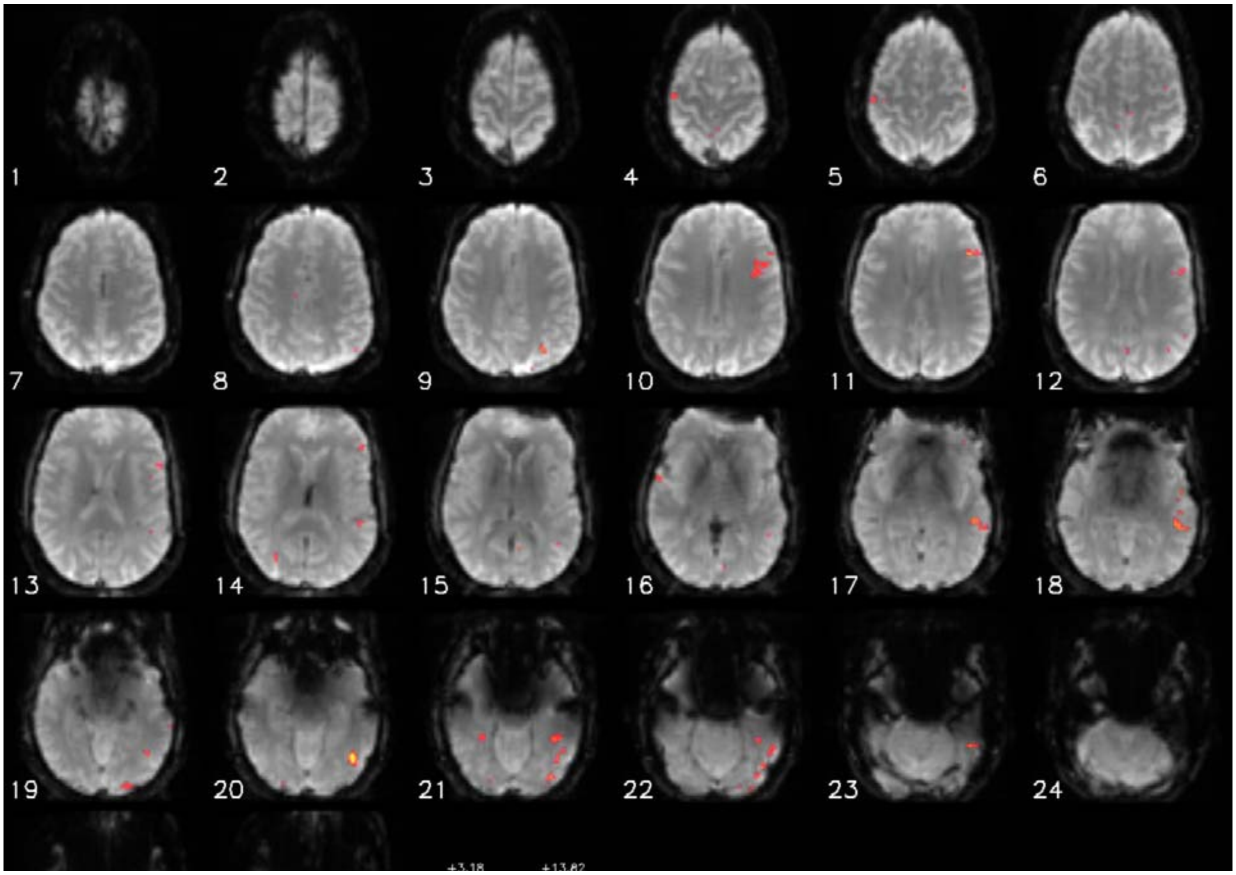


Figure 3. Semantic decision task performed in a single subject at 3T and fused onto the first GRE-EPI volume of the scan. Note prominent activation of left inferior dorsolateral prefrontal cortex (images 10-11), Broca's area (images 12-13), the posterior superior temporal gyrus(image 14) and middle and inferior left temporal gyri (images 17-18, 21-22) Note relative suppression of primary visual and frontal lobe visual attention activations in the single subject.

Comments: Advantages of this task include robust language lateralization of both frontal and temporal language regions and the ability to measure behavioral data related to task performance. The middle and inferior temporal activations are believed to correspond with semantic processing regions that are known to exist in these locations. Large amount of activation in the inferior dorsolateral prefrontal cortex also corresponds with known semantic processing at that site. Using the visual perceptual decision as a control task partially suppresses activation in primary visual cortex and visual attention regions of the frontal lobe as well as motor activity related to finger switch operation. This task is simple to perform for most patients and works well even in patients that are slow readers.

References: Paradigm developed by Mary Machulda, PhD, L.P. Mayo Clinic, Rochester

Paradigm Title: Text reading vs. non-linguistic symbols

Paradigm description: Visual presentation of descriptive text alternating with non-linguistic symbols (e.g., Marlett font). Primarily targeted at localization of language comprehension areas in dominant hemisphere region of posterior superior temporal gyrus / parietal angular gyrus (Wernicke's area). Usually yields an additional language response in region of dominant hemisphere lateral inferior / middle frontal gyri (Broca's area). Conditional contrast with visual presentation of non-linguistic symbols emphasizes language-specific mapping by subtraction of most primary and association visual responses. Application is to presurgical mapping of language, particularly in patients with temporal lesions.

Paradigm parameters: Visual presentation of short (2-4 sentences) narrative paragraphs for 10sec each; two consecutive narrative text presentations per 20sec block. Text blocks alternate with visually presented condition of non-linguistic symbols. Text for adult patients is equivalent to 6^{th} grade reading level; simpler text may be used for pediatric patients. Visual content of symbols is approximately same as text sentences to control for visual presentation. Patient is instructed to concentrate on reading and comprehending the text blocks and merely attend to the symbols. Example: Five 20sec iterations of text blocks interleaved and book ended with 20sec blocks of symbols. TR = 2sec; 10 data points per block; scan duration = 3min 40sec.

Sample task epoch, illustrating two task conditions of text vs. non-linguistic symbols. Each visual presentation follows consecutively at 10sec intervals:

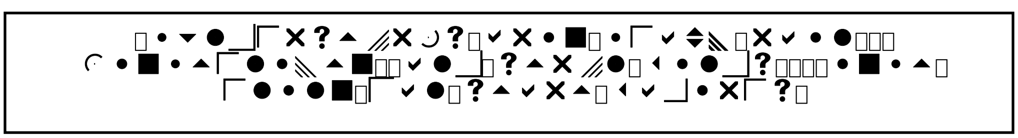
10sec presentation, first half of a 20sec text block:

Thunderstorms bring heavy rain, lightening, and strong winds.
Lightening can start fires, snap off branches, and cause power failures.
Strong winds can break glass and even uproot trees.

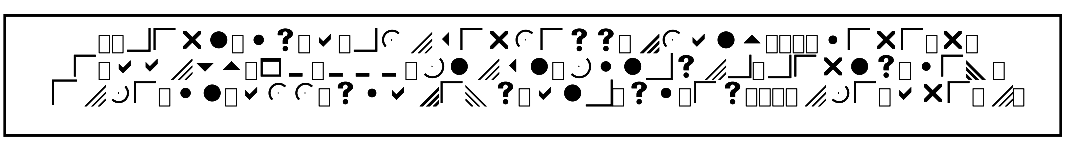
10sec presentation, second half of a 20sec text block:

A fern is a flowerless plant. There are about 10,000 known kinds of ferns.
They come in all shapes and sizes. Some are so small they look like moss.
Other kinds grow to be as tall as trees. Ferns grow in places all over the world.

10sec presentation, first half of a 20sec symbols block:

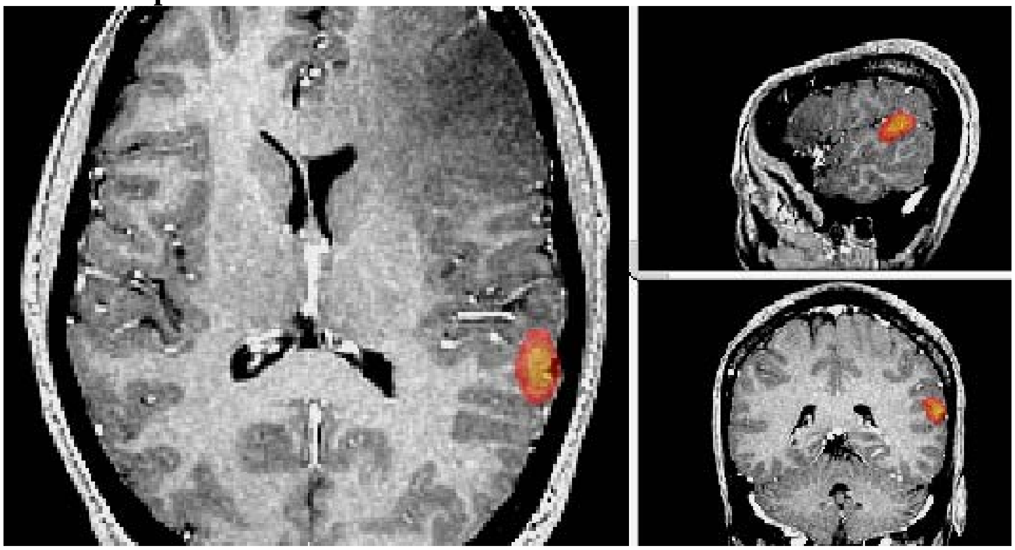


10sec presentation, second half of a 20sec symbols block:

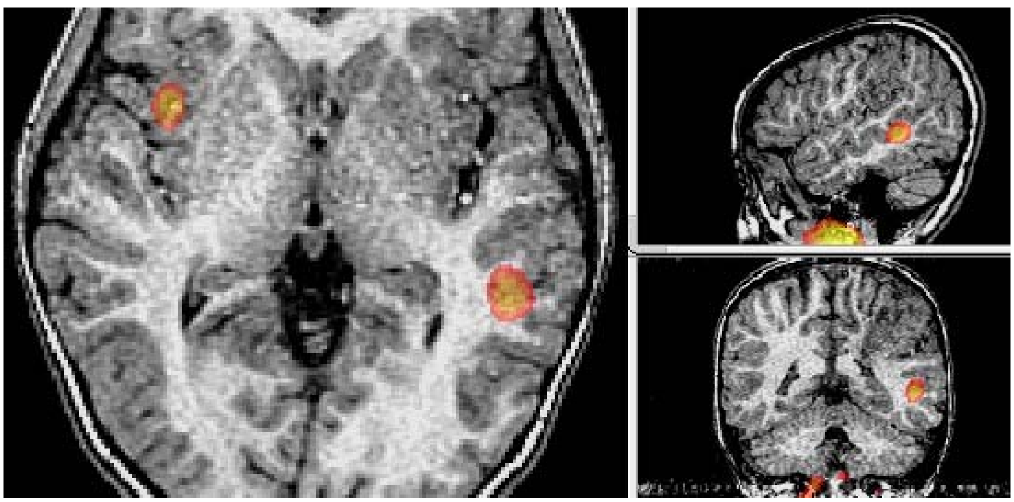


Alternating conditions are repeated five times in total, each presentation with different text and symbols.

Activation patterns:



Left posterior superior temporal gyrus response in 30yr old presurgical patient with left frontal tumor.



Left posterior superior temporal response in 9yr old presurgical patient with left temporal parietal AVM.

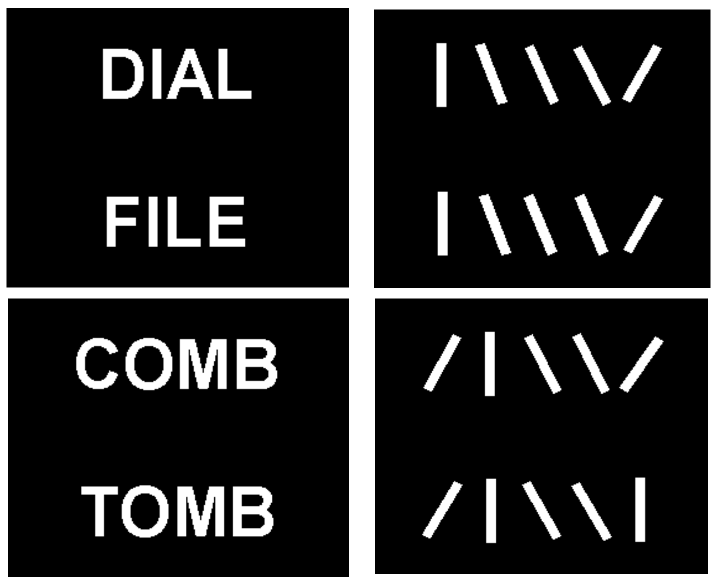
Comments: Paradigm results can be compared to a similar presentation of text reading blocks alternating with blank screen fixation. Language-specific responses should be similar across the two paradigms, with the exception that visual association responses should be minimized with the text vs. non-linguistic symbols contrast.

Reference:

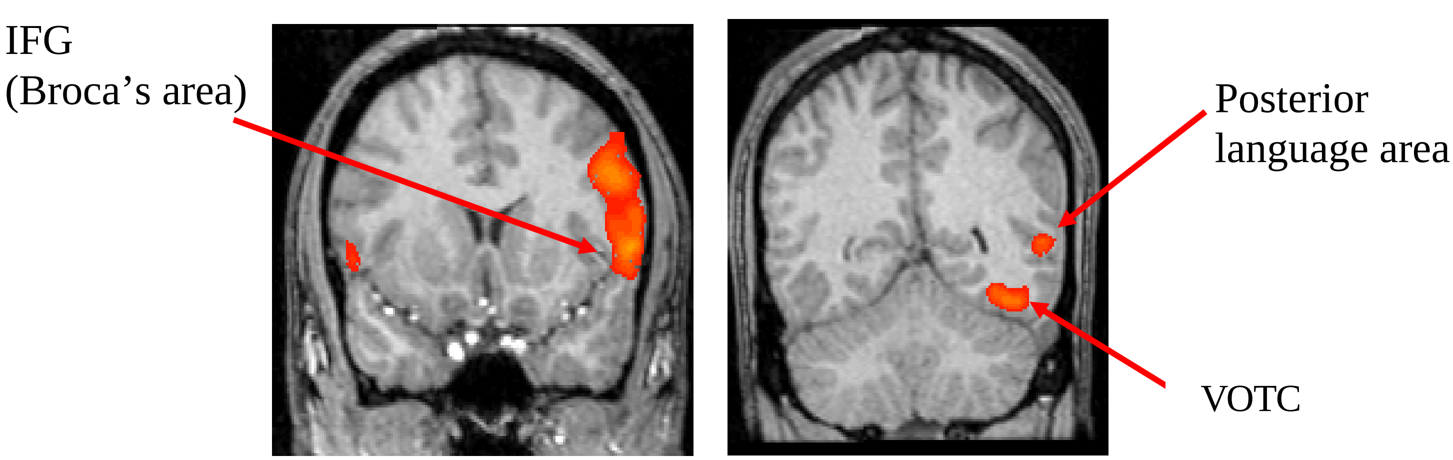
W.D. Gaillard, MD, L.M. Balsamo, MA, Z. Ibrahim, BA, B.C. Sachs, BS and B. Xu, PhD. fMRI identifies regional specialization of neural networks for reading in young children. *Neurology* 2003;60:94-100.

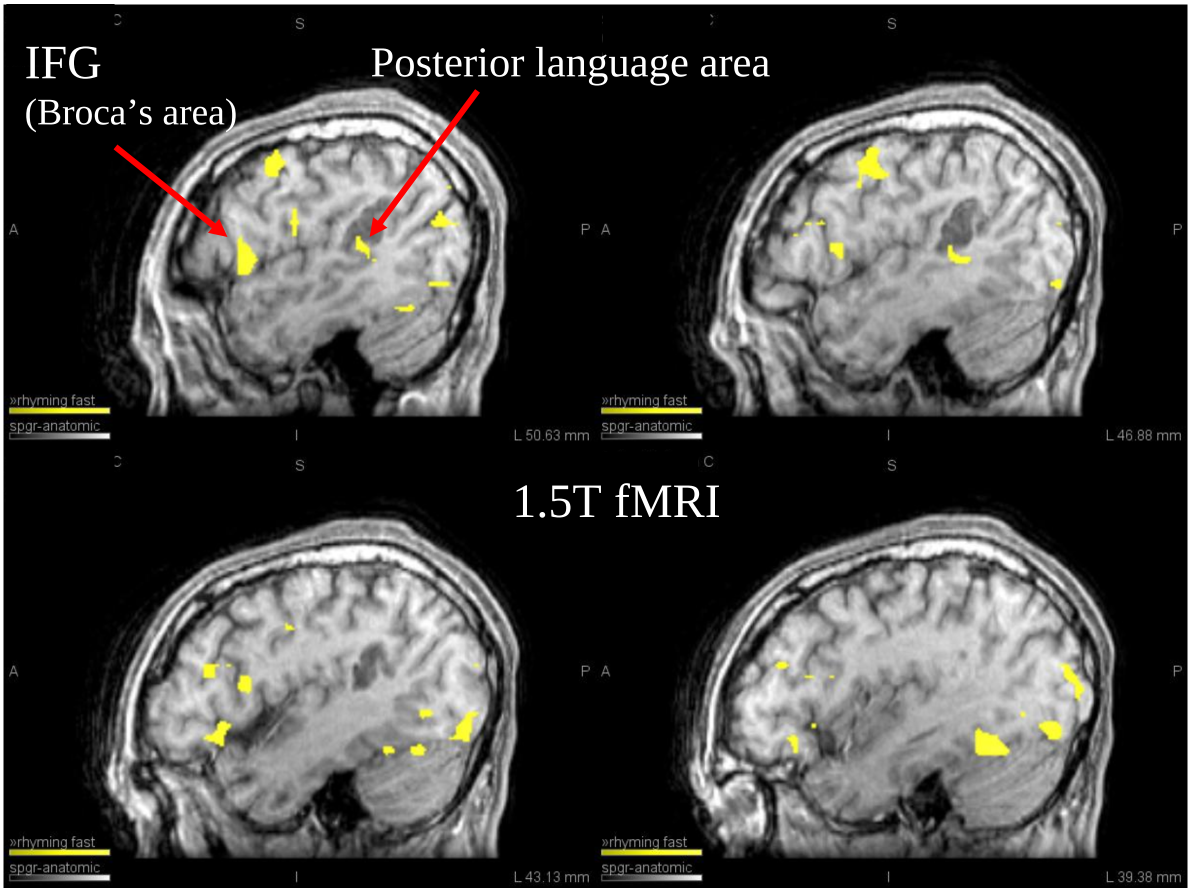
Paradigm Title: Rhyming

Paradigm description: This task presents visually rhyming and non-rhyming word pairs. The control condition presents paired bar patterns that match or do not match. Subjects are asked to determine whether words rhyme or do not rhyme in the activation state and asked to determine whether the bar patterns match or do not match during the control condition. Patients can indicate a rhyming word pair or matching bar pattern pair by a button response or simply lifting one of two index finger to designate an answer to the challenge. Word pairs contain a mix of words that are spelled similar and rhyme, spelled similar and do not rhyme, spelled differently and rhyme, and spelled differently and do not rhyme. This ensures that the subject must recite each word silently to perform well on the task. This point will become clear to the patient during training. Normal patients can perform the task at a rate of one word pair or bar pattern pair every 3 sec.. Compromised patients may require a task frequency of one every 5 sec..



Paradigm parameters: EPI gradient echo two-dimensional pulse sequence. TR = 2 seconds, TE = 30 ms, matrix = 64 x 64, Field of view 240 x 240, slice thickness 3.8 mm, 32 slices. Simple block paradigm with four cycles. Stimuli are presented using either fiber-optic goggles or back projection. Task performance is easily assessed on a simple two-button response unit or designated finger movements.





Activation patterns: Typical activation seen includes the dorso-lateral prefrontal cortex, interior frontal gyrus, and superior temporal gyrus and cortex lining the superior temporal sulcus. Additionally, the fusiform gyrus/ventral occipito-temporal cortex (VOTC) also demonstrates activation, typically left hemispheric dominant corresponding to the visual word area. Dorso-lateral prefrontal and premotor/SMA activity is minimized by the control condition.

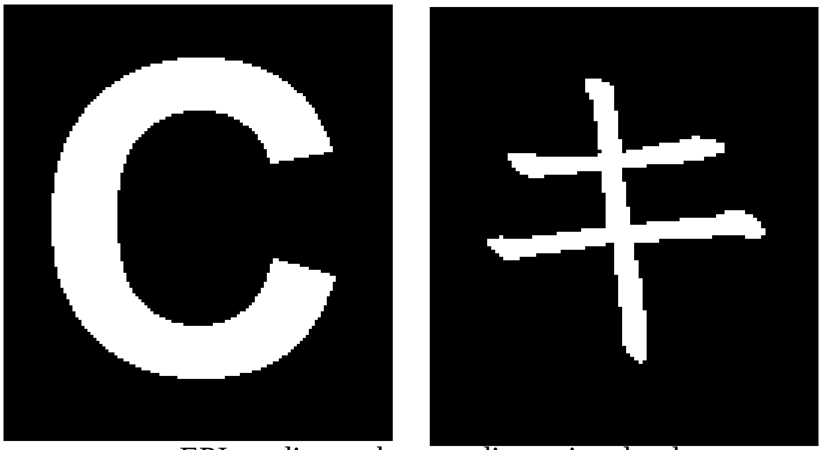
Comments: The pattern of activation seen during rhyming appears to be more specific for Wernicke's and Broca's area in comparison to typical fluency or word generation tasks. The test provides feedback with regard to test performance. The overall extent of activation appears less than that seen in typical word generation tasks. The task yields best results on a higher field strength magnet (3T).

References:

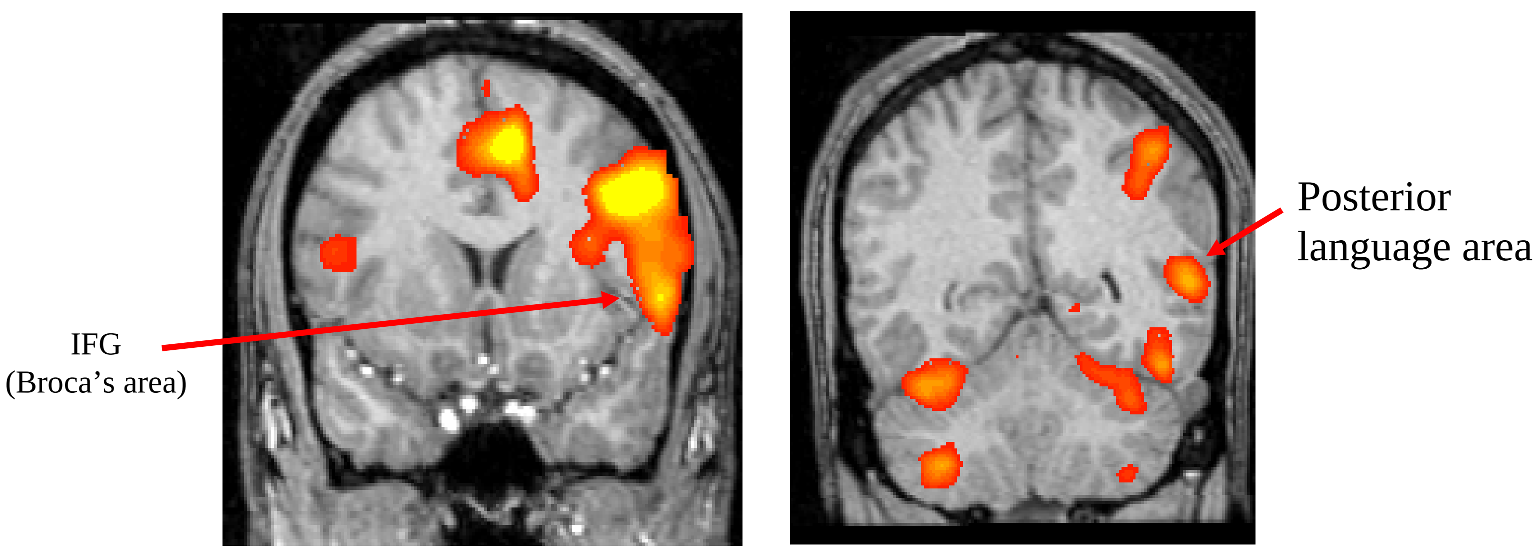
1) Paradigm developed by JT Lurito, MD, PhD
2) Laurito JT, Bryan RN, Mathews UP, Ulmer JU, Lowe MJ. Functional Brain Mapping, Categorical Course in Diagnostic Radiology: Neuroradiology, Oak Brook, IL RSNA 2000; 79-104.
3) Salvan CV, Ulmer JL, DeYoe EA, Wascher T, Mathews VP, Lewis JW, Prost R. Visual Object Agnosia and Pure Word Alexia: Correlation of fMRI and Lesion Localization. *JCAT*: Vol. 28(1) 63-67, 2004.

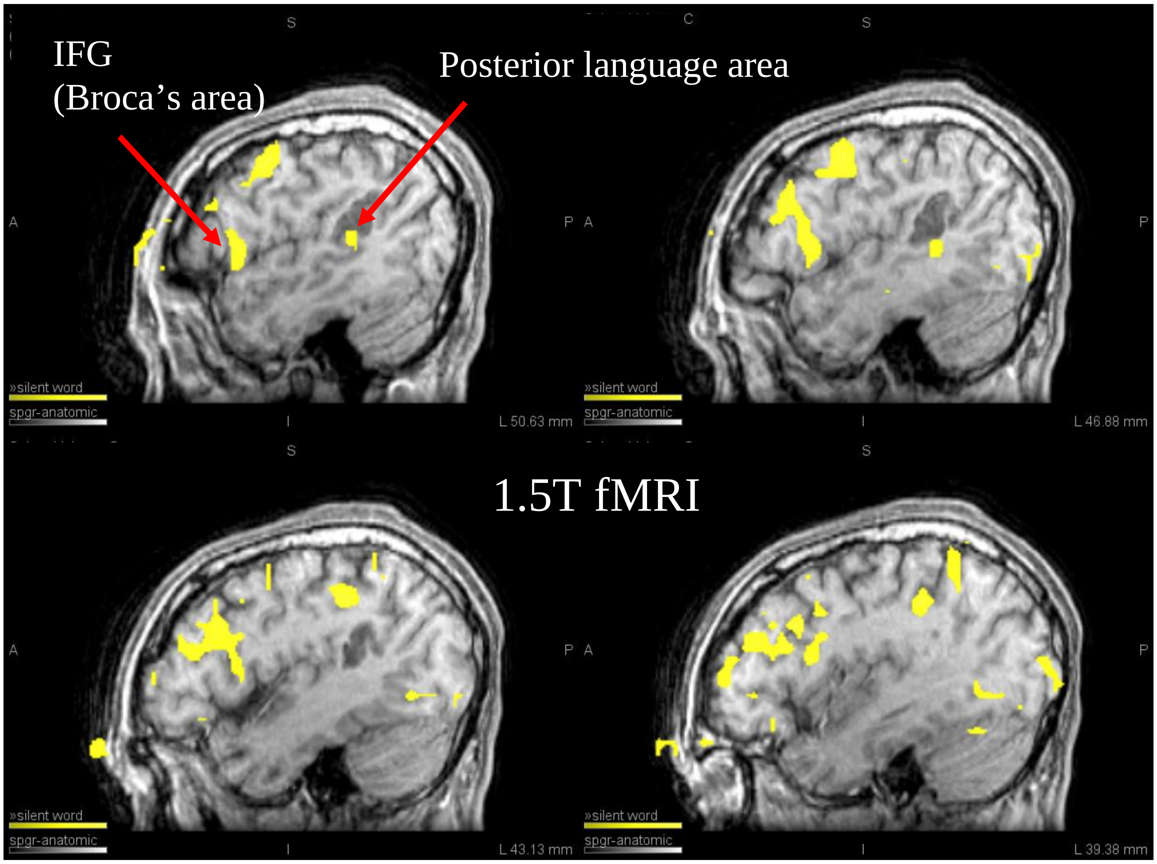
Paradigm Title: Silent Word Generation

Paradigm description: This task visually presents letter during the activation state and a nonsense symbol during the control condition. During letter presentation, patients are instructed to think of as many words as possible that begin with the letter presented on the screen. There are instructed not to use variations of the same word such as runs, running, ran. During the control tasks are instructed to simply look at the symbol. The letters and foreign script symbols (Mandarin, Arabic, Hebrew) are displayed at equal size. The foreign characters are "letter-like", but are meaningless to the patient. For patients with vision deficits, the letters can be delivered through head-phones. Between auditory letter epics, computer generated noise at the same frequency of letter presentation may be used as a control state. A typical rate of letter presentation during the active state is one letter every five sec..



Paradigm parameters: EPI gradient echo two-dimensional pulse sequence. TR = 2 seconds, TE = 30 ms, matrix = 64 x 64, Field of view 240 x 240, slice thickness 3.8 mm, 32 slices. Simple block paradigm with four cycles There is no measurement task performance for this paradigm.





Activation patterns: Activation is typically identified within the dorso-lateral prefrontal cortex, inferior frontal gyrus, variably within cingulate language regions, SMA, premotor and motor regions. Posterior language cortex may also activate to this task. Small amounts of activity can be seen in the ventral occipito-temporal cortex.

Comments: This task produces robust activation and effectively lateralizes speech functions, and posterior language functions when activated. There is no monitoring of task performance. Distinguishing exact borders between Broca's area and dorsolateral prefrontal or premotor cortex can be problematic, requiring anatomic correlation.

References:

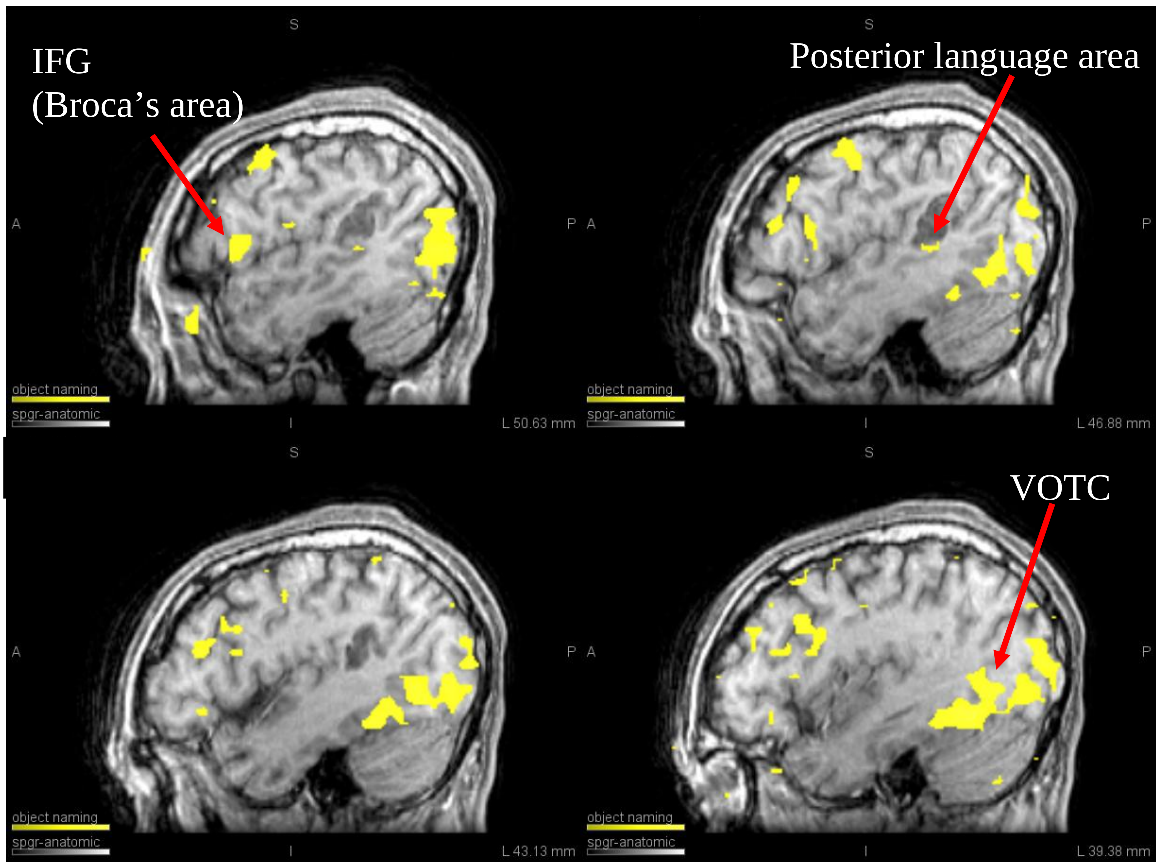
1) Yetkin FZ, Swanson S, Fischer M, Akansel G, Morris G, Mueller W, Haughton V. Functional MR of frontal lobe activations: comparison with Wada language results. *AJNR: Am J Neuroradio* 19(6): 1095-1098, 1998.

2) Many other references in the literature too numerous to list.

Paradigm Title: Simple object naming

Paradigm Description: Simple object naming is intended to activate speech and language cortical functions for language lateralization and localization of inferior frontal and posterior parietal temporal speech and language areas of the dominant hemisphere. This task is performed as a block paradigm with three cycles or epics. The active tasks consist of presenting simple objects that the subject names silently, at a rate of approximately one object every 3 seconds. The control task utilizes a nonsense symbol for visual fixation and to minimize elementary visual cortical activation. Subjects are asked to simply name the object silently to them-selves when an object is presented during the active portion of the paradigm. The objects can be presented in color or in black and white, though ventral occipito-temporal cortex activation patterns may vary.

Paradigm Parameters: Block design with visual stimulus presentation. Three cycles, 60 seconds/cycle or epic (:30 second half cycle). 20 volumes scanned for a complete cycle. Total scan duration 3:12. 4 discarded acquisitions preceding stimulus presentation (12 seconds).



Activation Patterns: Simple object naming results in activity within the inferior frontal gyrus (frontal operculum), dorsal lateral prefrontal cortex, or premotor cortex, SMA, ventral occipito-temporal cortex (VOTC), and to a variable extent within the posterior temporo-parietal language cortex. Inferior temporal gyrus activation is also seen commonly. The task will also variably cause activation of posterior temporal or temporo-parietal opercular cortex, corresponding to language relevant cortex. Activation in the posterior inferior temporal gyrus and in bilateral VOTC is seen in response to object recognition. Activation in the VOTC necessary for object recognition is adjacent to and may overlap with the visual word-form area, which may be induced by other visually delivered speech and language tasks. Activation is also commonly seen in the visual parietal areas, including the intraparietal sulcus, necessary for visual attention and visuo-spatial processing.

Comments: There is no monitoring of task performance. This task is not up to nearly as lateralizing as a word generation task and some other speech and language paradigms. Instead, it is one of the simplest tasks for subjects to carry out and is complimentary to other speech and language paradigms, to confirm and support identification of the location of Brocca's area and often Wernicke's area. It is occasionally useful for assessing higher visual functions in the VOTC area and the visual parietal areas. VOTC activation patterns may vary based on content in the images. The task also results in robust SMA activity, representing premotor speech functions, which can be useful in tumors when there are tumors in this vicinity.

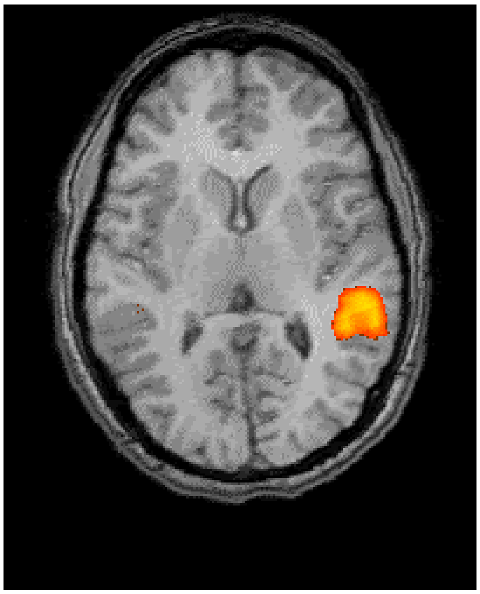
References:

1) Paradigm developed by JT Lurito , MD, PhD
2) Laurito JT, Bryan RN, Mathews UP, Ulmer JU, Lowe MJ. Functional Brain Mapping, Categorical Course in Diagnostic Radiology: Neuroradiology, Oak Brook, IL RSNA 2000; 79-104.
3) Salvan CV, Ulmer JL, DeYoe EA, Wascher T, Mathews VP, Lewis JW, Prost R. Visual Object Agnosia and Pure Word Alexia: Correlation of fMRI and Lesion Localization. *JCAT*: Vol. 28(1) 63-67, 2004.

Paradigm Title: Passive Listening

Paradigm description: This paradigm delivers passive listening of speech (a narrative) during the active state and backward speech during the control condition. An example would be a passage from Harry Potter and the sorcerer's Stone, which allows for use both adults and children to comprehend the passage.

Paradigm parameters: EPI gradient echo two-dimensional pulse sequence. TR = 2 seconds, TE = 30 ms, matrix = 64 x 64, Field of view 240 x 240, slice thickness 3.8 mm, 32 slices. Simple block paradigm with four cycles.



Activation patterns: Activation is most typically seen within the superior temporal gyrus and cortex lining the superior temporal sulcus, in the expected region of Wernicke's area. Additionally there's typically activation identified within the superior temporal sulcus and middle temporal gyrus more anteriorly. A smaller but significant portion of patients will demonstrate activation within the inferior frontal gyrus.

Comments: Passive task may have no real assessment of task performance. A post examination quiz or verbal account of the story can be employed to assure attentiveness. Very robust and easy for patients to perform, even many of those with compromised language functions. Typically, very robust and reproducible across subjects. Lateralizes temporal language functions, but more lateralized response seen in males compared to females.

References:

Phillips MD, Lowe MJ, Lurito JT, Dzemidzic M, Mathews VP. Temporal Lobe Activation Demonstrates Sex-Based Differences During Passive Listening. *Radiology* 220(1): 202-207, 2001.

Paradigm Title: The Visual Language Comprehension Task

Paradigm Description: A visual language comprehension task is useful for clinical questions regarding language localization in Broca's area (inferior frontal lobes) and Wernicke's area (posterior superior temporal sulci) and hippocampal structures. Eye movement areas (precentral sulci, medial frontal lobes, intraparietal sulci), unilateral thumb movement (finger switch in dominant hand), working memory (middle frontal gyri) and primary and associative visual areas (occipital areas) are also mapped. This task is performed as a two-condition, block paradigm with six and half cycles beginning and ending on the control condition of central fixation. The "active" task consists of sentence-question pairs requiring a YES/NO answer by pushing a 2-button finger switch held in the dominant hand. Task difficulty is controlled by choosing the number of sentence-question pairs. The simplest task uses 3 pairs per block. An intermediate task has 4 pairs. The most difficult task uses 5 pairs. Stimuli are presented at a fixed pace, equally spaced across the active blocks. The sentence-questions pairs of each entire paradigm are in English, Spanish or any other language required for the patient population. The paradigm should be used in the native language. The two conditions are not matched in luminance to ensure that there is visual activation. Hand movement is not matched across blocks to ensure that hand activation is present. These features become control areas of activation for internal quality assurance. For patients with visual acuity difficulties, who are too young to read or who are illiterate, the same paradigm can be presented as an auditory paradigm. The audio version uses only three sentence-question pairs per block as listening is slower than reading. The audio task should also be in the native language.

This paradigm was run on MRIx Technologies hardware platform as avi file format.

Paradigm Parameters:

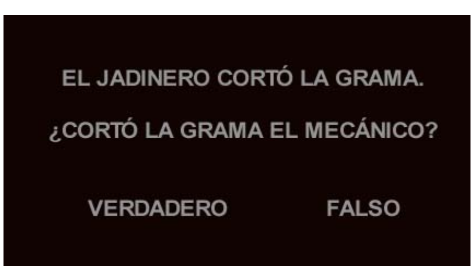
The following parameters are employed at 3 Tesla:

Gradient Echo-EPI pulse sequence
TR: 3000 msec
TE: 30 msec
FOV 20 cm by 20 cm
Matrix 64 x 64

Block design with visual stimulus presentation.
6 1/2 cycles
60 seconds /cycle or epoch (30 second half cycle)
20 volumes scanned per complete cycle
Total scan duration: 6 min 42 sec.
4 discarded acquisitions preceding stimulus presentation (12 sec)

First 30 second half cycle (control task) is not typically processed to allow for cognitive equilibrium.

Sample Stimuli



Monitoring: Two button finger switch (yes/no) buttons, HR, respiration, eye camera

Paradigm Activation Patterns:

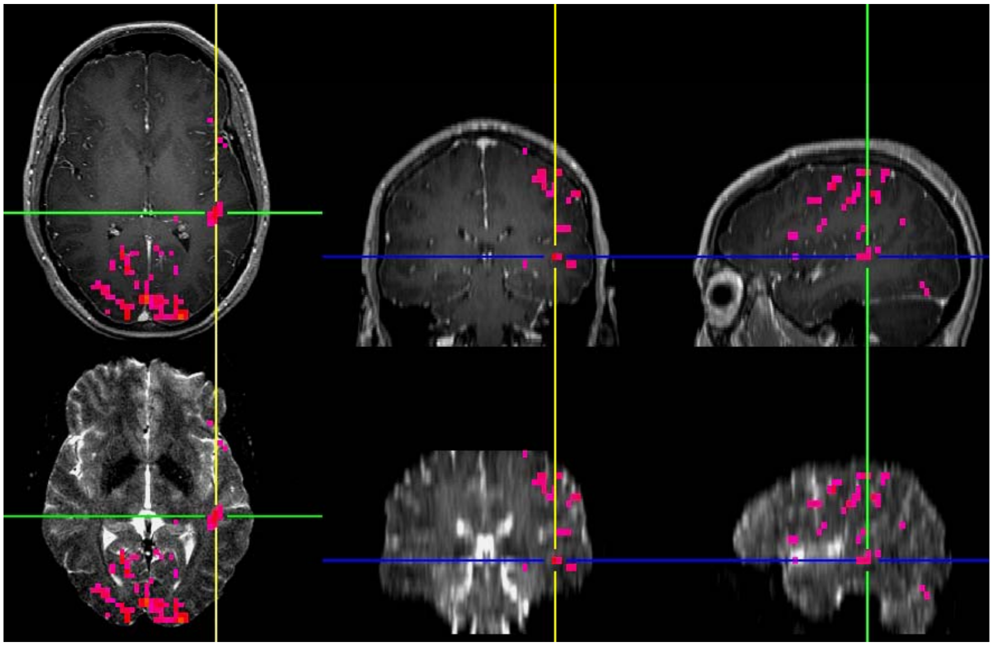


Figure 4. Three-plane view of 3 Tesla fMRI activation map from a single patient for the reading language comprehension task. There is activation in the left Broca's area in left inferior frontal cortex, posterior superior temporal gyrus and occipital lobes. Activation on other images is noted in supplemental eye fields, frontal eye fields, hippocampal areas and prefrontal cortex. Top row is activation over IR fSPGR images (dark cerebrospinal fluid). Bottom row is activation over SE EPI images (bright cerebrospinal fluid).

Comments: Advantages of this task include robust language lateralization of both frontal and temporal language regions and the ability to measure behavioral data related to task performance. This task is simple to perform for most patients and works well even in patients that are slow readers.

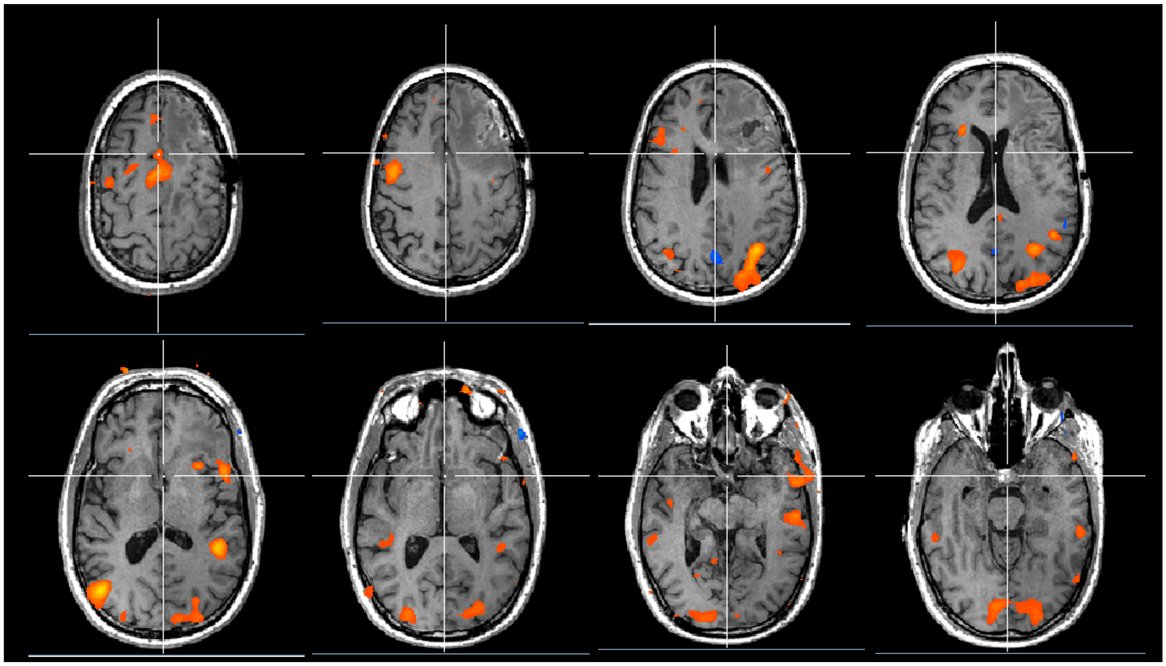
References:

Paradigm developed by Keith Thulborn, MD, PhD, L.P. University of Illinois, Chicago (kthulbor@uic.edu).

Paradigm Title: Silent Verb Generation Task (JHH)

Paradigm description: Patient generates verbs related to visually presented written nouns. Delivered via LCD projector and mirror setup as visual stimuli.

Paradigm parameters: Block design using 30 sec blocks, alternating with 30 sec of flashing fixation point (pound signs)--
Starting with fixation for 30 sec, followed by verb gen 30 sec, and thus alternating for total of 5 minutes.



Activation patterns: Mostly receptive speech areas in frontal regions, but Wernicke's activation is inconsistent.

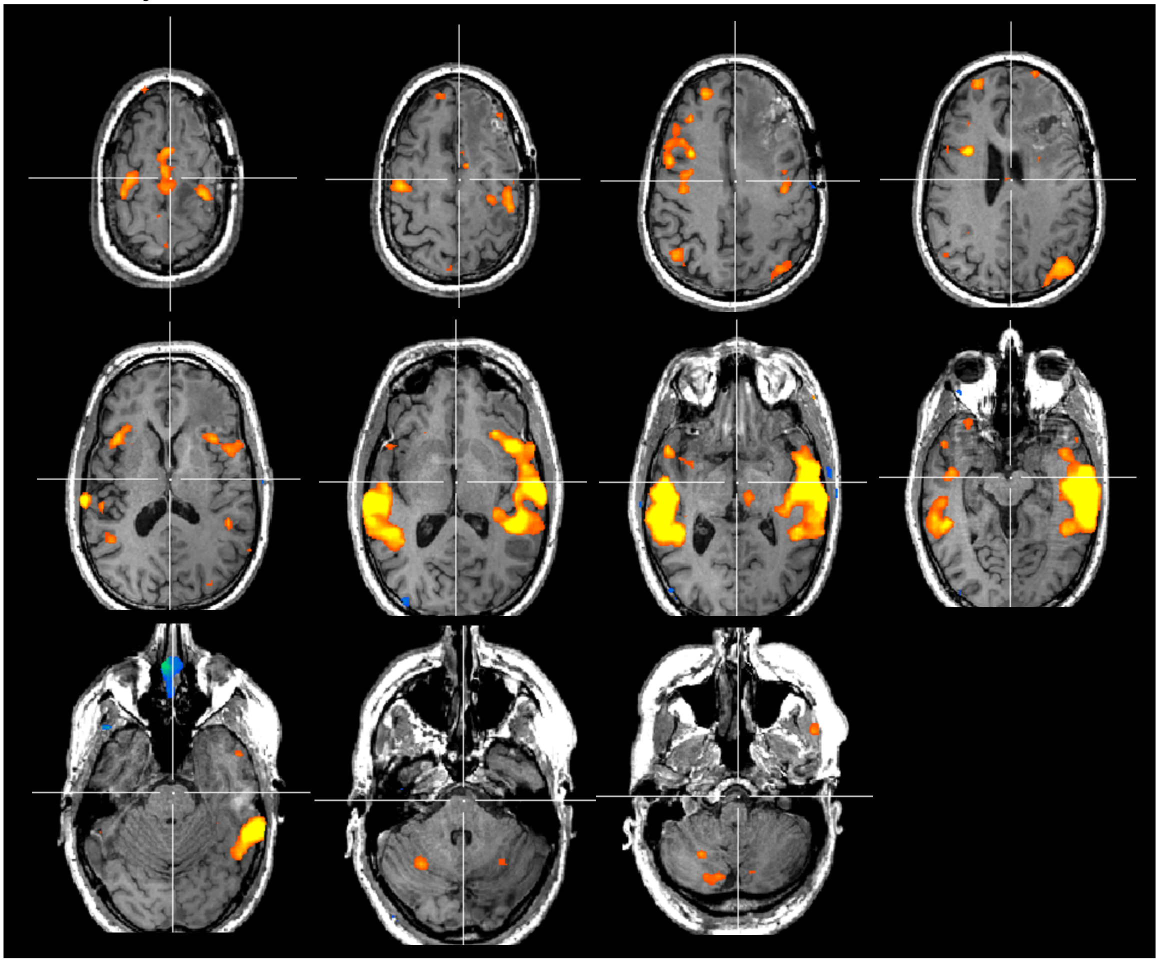
Comments: Works well at 3T.

References: Too numerous to list.

Paradigm Title: Word Listening Task (JHH)

Paradigm description: Receptive speech task in which subject listens to a presented word (auditory stimulus) via headphones.

Paradigm parameters: Single block design with first 45 seconds of visual fixation on pound signs alone, followed by 45 seconds of auditory stimuli [patient hears words (nouns) each repeated three times, during which he/she is supposed to repeat the words silently] accompanied by visual fixation, followed by 45 seconds of fixation alone.



Activation patterns: Temporal receptive speech areas including Wernicke's area, bilateral temporal primary auditory cortex, primarily.

Comments: Works well (including variations of this task) for selective receptive language localization at 3T

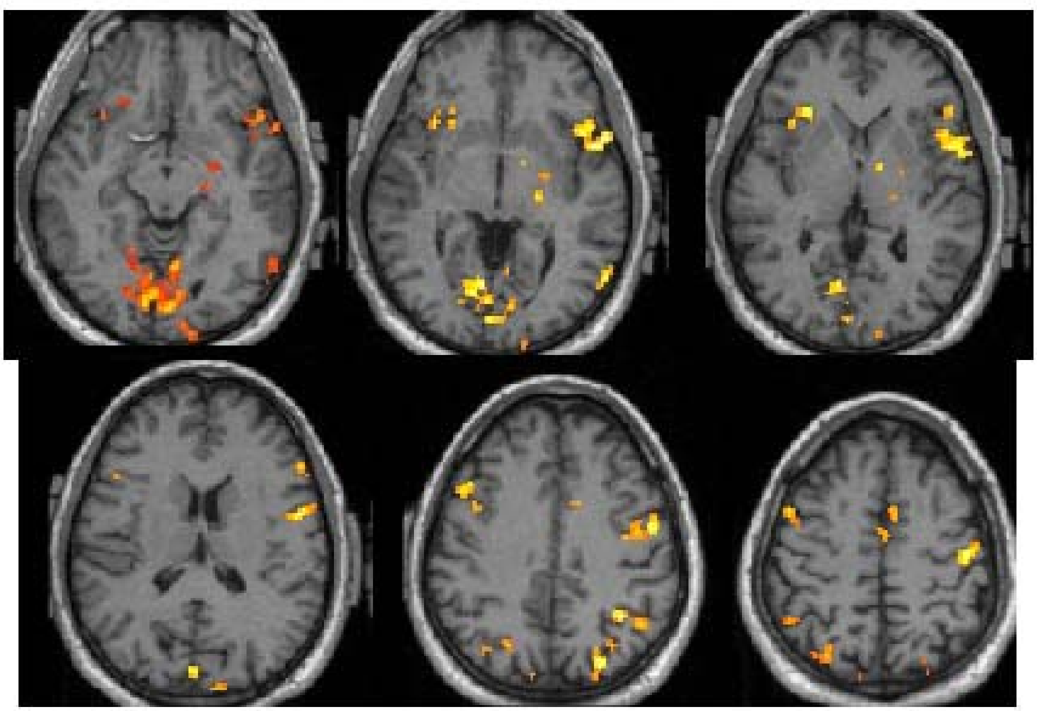
References:

Hirsch, J., M. I. Ruge, et al. (2000). "An integrated functional magnetic resonance imaging procedure for preoperative mapping of cortical areas associated with tactile, motor, language, and visual functions." Neurosurgery **47**(3): 711-21; discussion 721-2.

Paradigm Title: Phonological (Rhyming) Task (MCG)

Paradigm description: Good lateralizing primarily expressive speech task using visual stimuli presented via video goggles in which a pair of words is presented via Psyscope. For the experimental task, the subject is shown a pair of words that either rhyme or don't rhyme; for pairs that rhyme, the right button is pressed, and for those that don't, the left button is pressed. For the control task, subjects are shown nonsense line drawings with a + sign in one of the lower corners of the slide. The subjects are instructed to press a button on the left side of keypad if the + sign is in the left corner or a button on the right if the sign is in the right corner. Performance on the control task is monitored. Left and right button presses are balanced for the experimental and control tasks.

Paradigm parameters: Block-design paradigm, lengths of visual stimulus presentation--5 seconds each, identical lengths of activation and control blocks. 20-second blocks of the experimental task alternate with 20-second blocks of the control task for total task duration of 6 minutes. For the experimental task, the subject is shown a pair of words that either rhyme or don't rhyme; for pairs that rhyme, the right button is pressed, and for those that don't, the left button is pressed. For the control task, subjects are shown nonsense line drawings with a + sign in one of the lower corners of the slide. The subjects are instructed to press a button on the left side of keypad if the + sign is in the left corner or a button on the right if the sign is in the right corner. Performance on the control task is monitored. Left and right button presses are balanced for the experimental and control tasks.



Activation patterns: Classic activation patterns in frontal expressive speech areas including Broca's area, with variable Wernicke's area activation

Comments: Works well at 1.5T for reliable lateralization.

References:

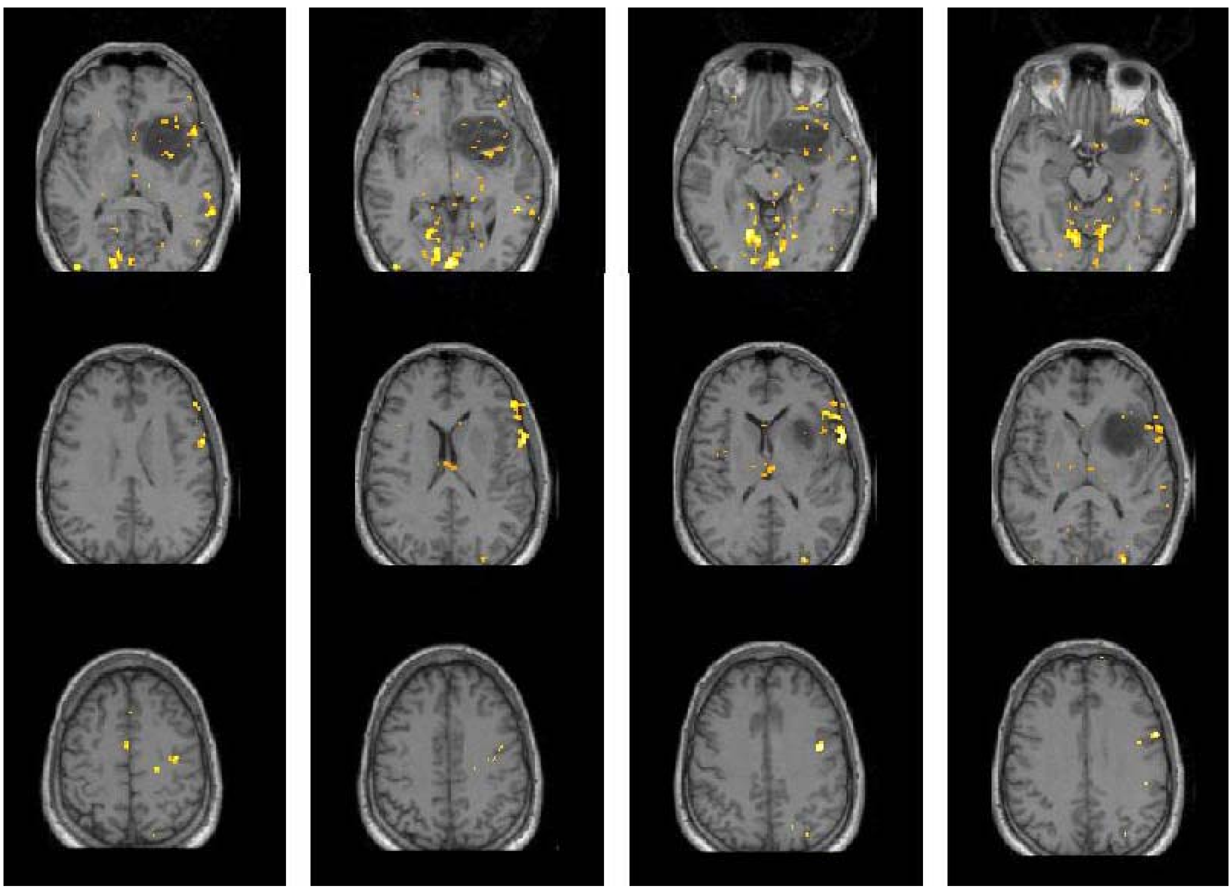
1) Pillai JJ, Allison JD, Sethuraman S, Araque JM, Thiruvaiyaru D, Ison CB, Loring DW, Lavin T. Functional MR imaging study of language-related differences in bilingual cerebellar activation. *AJNR Am J Neuroradiol*. 2004;25(4):523-32.

2) Pillai JJ, Araque JM, Allison JD, Sethuraman S, Loring DW, Thiruvaiyaru D, Ison CB, Balan A, Lavin T. Functional MRI study of semantic and phonological language processing in bilingual subjects: preliminary findings.*Neuroimage.* 2003;19(3):565-76

Paradigm Title: Noun-verb semantic association task (MCG)

Paradigm description: Good lateralizing task for expressive and receptive speech utilizing visual stimuli presented via video goggles (with Psyscope as stimulus presentation software) in which a semantic decision needs to be made regarding which of two presented verbs is more stongly semantically associated with a particular presented noun. For the experimental task, the subject is shown a pair of verbs on a line below a presented noun. If the verb on the right is more strongly semantically associated with the presented noun, the right button is pressed, and if the verb on the left is more strongly associated with the presented noun above, the left button is pressed. For the control task, subjects are shown nonsense line drawings with a + sign in one of the lower corners of the slide. The subjects are instructed to press a button on the left side of keypad if the + sign is in the left corner or a button on the right if the sign is in the right corner. Performance on the control task is monitored. Left and right button presses are balanced for the experimental and control tasks.

Paradigm parameters: Block-design paradigm, lengths of visual stimulus presentation--5 seconds each, identical lengths of activation and control blocks. 20-second blocks of the experimental task alternate with 20-second blocks of the control task for a total of 6 minutes task duration.



Activation patterns: Both receptive and expressive speech areas consistently activated;
Comments: Works well at 1.5T for reliable lateralization

References:

1) Pillai JJ, Allison JD, Sethuraman S, Araque JM, Thiruvaiyaru D, Ison CB, Loring DW, Lavin T. Functional MR imaging study of language-related differences in bilingual cerebellar activation. *AJNR Am J Neuroradiol*. 2004;25(4):523-32.
2) Pillai JJ, Araque JM, Allison JD, Sethuraman S, Loring DW, Thiruvaiyaru D, Ison CB, Balan A, Lavin T. Functional MRI study of semantic and phonological language processing in bilingual subjects: preliminary findings.*Neuroimage.* 2003;19(3):565-76.

Vision

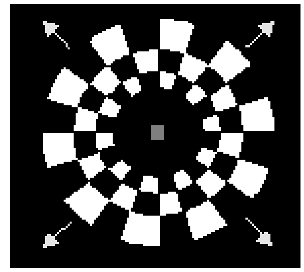
Paradigm Title: Vision - Temporal Phase Mapped Visual Field

Author: Edgar DeYoe, Medical College of Wisconsin, Milwaukee

Paradigm description: This paradigm can be used to efficiently map visually responsive brain areas that are retinotopically organized. It is particularly advantageous for pre-surgical mapping because the resulting brain map can be colored to identify each quadrant of the visual field and to distinguish central (foveal) from peripheral vision, the latter being critical for reading

Paradigm parameters:

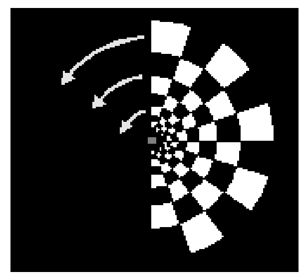
Visual Field Eccentricity (Expanding Rings):



To map visual field eccentricity (distance from the center of gaze), subjects view a counterphase-flickering (8 Hz) black and white checkered annulus (mean luminance approx. 35 cd/m^2) expanding from 1.6° to 24° in 32 seconds, repeated 5 times in a single run. Step size, check size, and width are scaled in proportion to eccentricity. Check contrast is 98%. Two or three runs are typically averaged.

The task of the subject is to maintain gaze on the central fixation point (dot in center of display), without moving the eyes. To enhance activation and help maintain attention and arousal, subjects are required to press a button when they detect brief (200 msec), random disappearances of the fixation point.

Polar Angle (Rotating Wedges):



To map angular positions within the visual field, subjects view a counterphase-flickering (8 Hz), black and white checkered hemifield (mean luminance approx. 35 cd/m^2) that rotates completely about a central fixation point in 32 seconds, repeated 5 times in a single run. Two or three runs are typically averaged.

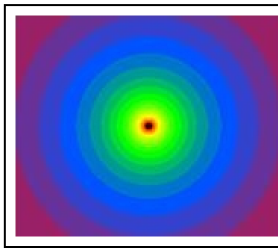
The task of the subject is the same as for the eccentricity mapping task.

Neurons responding preferentially to visual stimulation at different locations in the visual field are activated at different times during each of the stimulus sequences. Corresponding differences in the temporal phase of the fMRI responses thus indicate the eccentricity and polar angle (i.e. location in the visual field) represented by each brain voxel.

Activation patterns:

Figure 1 illustrates activation patterns obtained with the expanding rings, eccentricity mapping stimulus. Here, the color code represents the eccentricity to which the voxel responds best during the rings series, not amplitude of the BOLD response. (Case BWT)

Legend at right shows approximate color code for relative eccentricity. Note that representation of foveal eccentricities (red, yellow) is disproportionately expanded in the cortex due to “cortical magnification”.



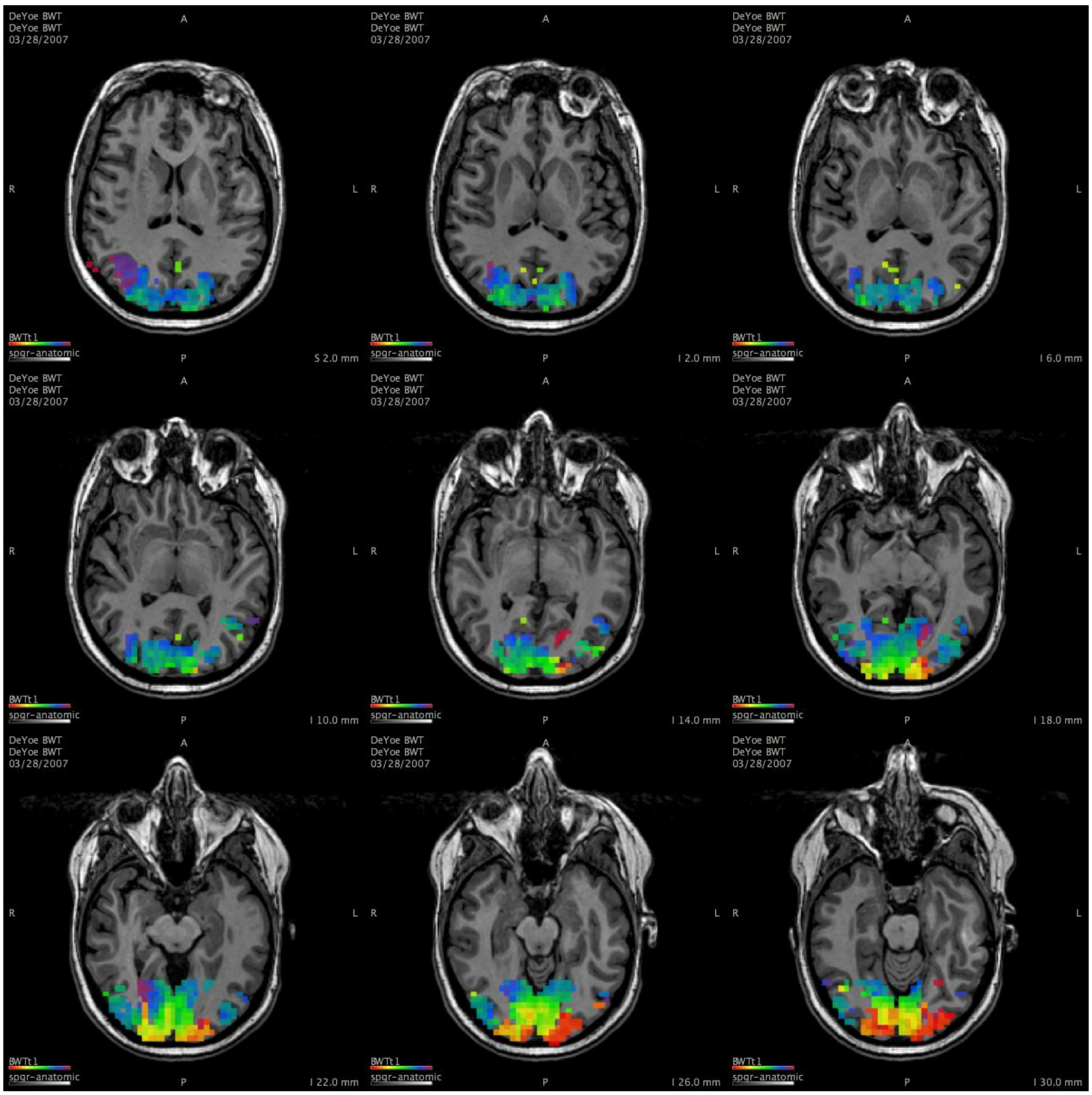


Figure 1

Figure 2 illustrates the pattern of activation for the rotating, checkered hemifield used to map polar angle representations.

Legend at right shows color code for polar angle.

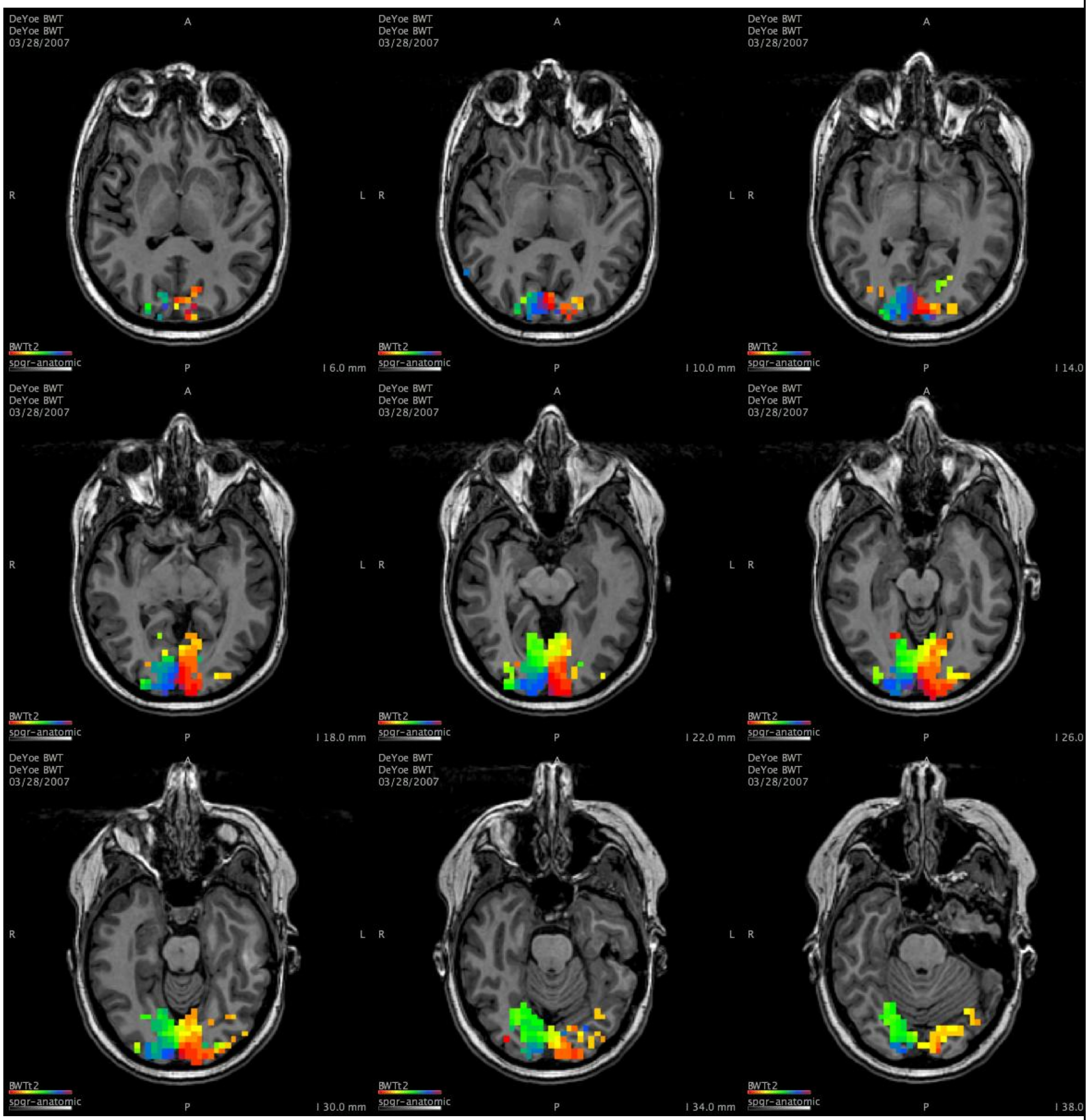


Figure 2

Comments: This is a very robust paradigm, especially for eccentricity mapping. It requires the subject to fixate, but momentary lapses are well tolerated. Poor fixation will typically destroy the activation, not produce a distorted mapping. A minimum run of one repetition of the eccentricity and polar angle paradigms can be completed in 15 minutes or less. For greatest accuracy, 3 repetitions of each stimulus is optimal and can be completed in 30-40 minutes.

Analysis: The Hilbert-Delay plugin for AFNI provides a convenient algorithm for analyzing the phase mapped data. This routine provides the delay, correlation coefficient, and covariance of a best-fit, reference waveform (typically a sinusoid of appropriate temporal period). The correlation coefficient can be used as an acceptance criterion and thresholding parameter. Color coding the delay values as illustrated above provides highly informative brain maps. An alternate approach is to fourier-transform the timecourse data and use the resulting temporal phase information as the encoding parameter. In either case, the color code for eccentricity or polar angle should be corrected to compensate for the BOLD hemodynamic lag if absolute eccentricity and angle measurements are desired.

References:

1. DeYoe, E. A., Bandettini, P., Neitz, J., Miller, D. & Winans, P. Functional magnetic resonance imaging (FMRI) of the human brain. Journal of Neuroscience Methods 54, 171-187 (1994).
2. DeYoe, E. A., Carman, G., Bandettini, P., Glickman, S., Wieser, J., Cox, R., Miller, D. & Neitz, J. Mapping striate and extrastriate visual areas in human cerebral cortex. Proceedings of the National Academy of Sciences - USA 93, 2382-2386 (1996).
2. Saad, Z. S., Ropella, K. M., Cox, R. W. & DeYoe, E. A. Analysis and use of FMRI response delays. Human Brain Mapping 13, 74-93. (2001).
3. Saad, Z. S., DeYoe, E. A. & Ropella, K. M. Estimation of FMRI response delays. Neuroimage 18, 494-504 (2003).

Memory

Paradigm Title: Novel vs Familiar Face-Name Memory Encoding/Retrieval Task [1] (Duke)

Paradigm description: This paradigm employs a variation of a face-name associative memory encoding task developed by Sperling et al in young adults [2], and later applied to elderly subjects and patients with Alzheimer's disease [3]. Subjects are required to encode and later retrieve face-name associations of two conditions, novel face-name pairs and familiar face-name pairs, which are delivered via MR compatible audiovisual goggles.

Paradigm parameters: Sixty novel and two familiar face-name pairs, drawn from *The AR Face Database* [4], are presented within a block design. Faces are balanced for age, race and gender. Behavioral responses are monitored via a fiber optic button box within the scanner. For control purposes, subjects are also told to provide a button response during the encoding period indicating whether or not the name matched the face. The experimental paradigm was divided into three runs, each run, lasting 6 minutes 50 seconds, including two sets of four blocks separated by a brief fixation cross. Both sets of four blocks included encoding of ten novel face-names, encoding of two familiar face-names x 5, retrieval of ten novel face-names, and retrieval of two familiar face-names x 5. The activation during the familiar condition for encoding or retrieval provided the control for the novel condition of that same task (Figure 1).

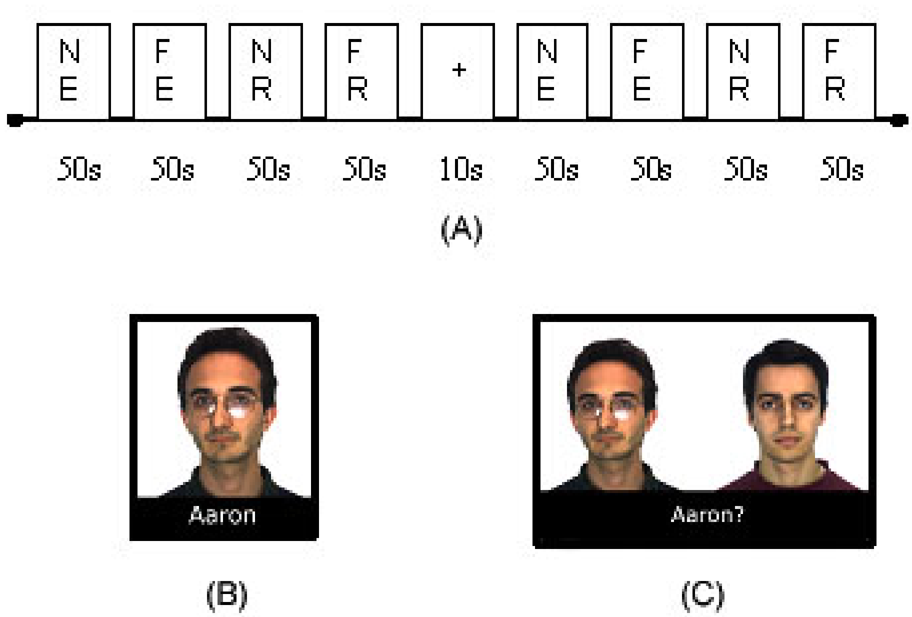


Figure 1: (a) Schematic of one run of the behavioral paradigm. Each block represents 10 trials. NE = novel encode; FE = familiar encode; NR = novel retrieval; FR = familiar retrieval. There is no inter-trial interval. (b) Example of an encode trial. (c) Example of a retrieval trial. (Reproduced from Petrella et al.[1]).

Activation patterns: Prefrontal cortex, parietal and medial temporal lobes (Figure 2).

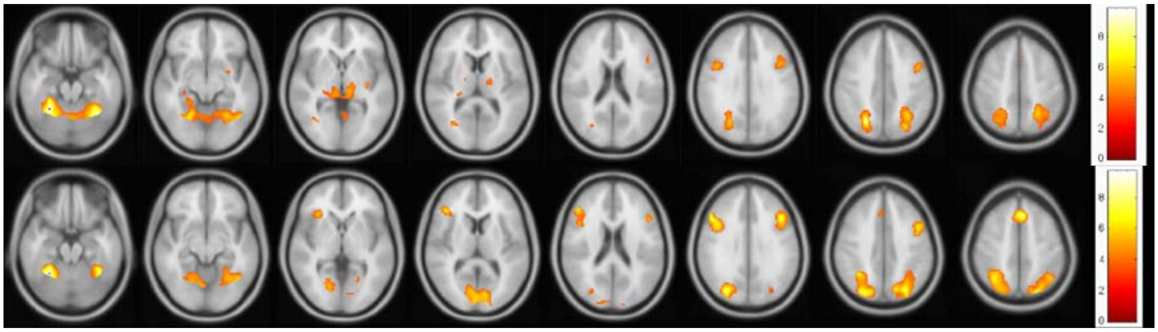


Figure 2: Task related Areas of Activation**:** Axial images of fMRI activation maps during encoding (top row) and retrieval (bottom row) created using SPM ANOVA (*p*=0.001 uncorrected threshold for statistical significance and minimal cluster size=10 voxels). Anatomical images are from the SPM T1-weighted single subject canonical brain. Thresholded activation is displayed as a color overlay of t-values. (Reproduced from Petrella et al.[1]).

Comments: Variations include novel verses familiar complex color scene encoding [5, 6].

References:

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Paradigm Title: Visual Memory Paradigm

Paradigm description: This is a two-condition block design task using 6.5 cycles, beginning and ending with a central fixation condition. The first active condition (encoding) is a list of colored object pictures that the patient is instructed to remember. The subsequent active blocks (retrieval) are lists of colored object pictures that contain one or two pictures from the first list that was to be remembered. The objects are identified as in (YES) or not (NO) in the first list by a manual finger switch response using the dominant hand. The pictures are in the center of the field of view of the visor screen suspending a small visual angle that does not require much eye movement.
The difficulty of the task is determined by the number of objects to be remembered (5 or 10). The objects are presented uniformly spaced in time.

This paradigm was run on MRIx Technologies hardware platform as avi file format.

Paradigm Parameters:

The following parameters are employed at 3 Tesla:

Gradient Echo-EPI pulse sequence
TR: 3000 msec
TE: 30 msec
FOV 20 cm by 20 cm
Matrix 64 x 64

Block design with visual stimulus presentation.
6 1/2 cycles
60 seconds /cycle or epoch (30 second half cycle)
20 volumes scanned per complete cycle
Total scan duration: 6 min 42 sec.
4 discarded acquisitions preceding stimulus presentation (12 sec)

First 30 second half cycle (control task) is not typically processed to allow for cognitive equilibrium.
The encode cycle can also be removed from the other cycles to allow activation maps based only on the retrieval cycles that are using memory recall.

Sample Stimuli

Monitoring: Two button finger switch (yes/no) buttons, cardiac and respiration rates, eye camera

Paradigm Activation Pattern:

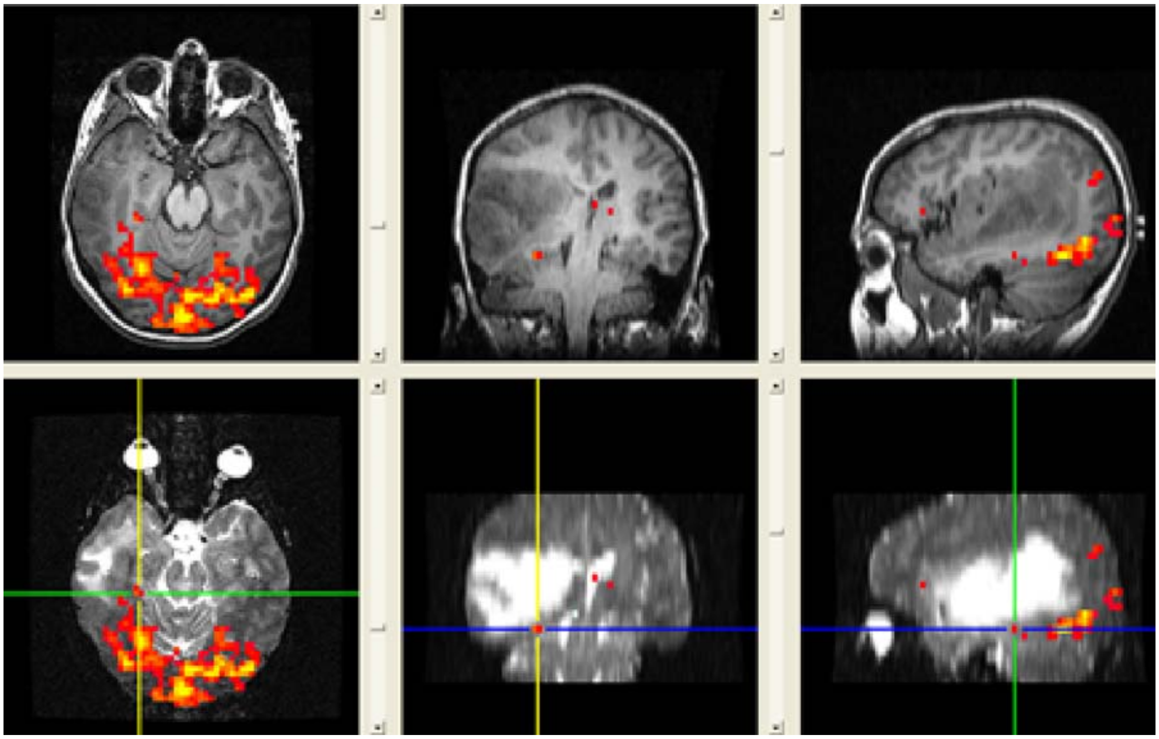

Figure 5. Three-plane view of 3 Tesla fMRI activation map from a single patient with right temporofrontal tumor for the visual memory task. There is activation in the right hippocampus (cross-referenced on bottom row) and visual activation in the occipital lobes. Top row is activation over IR fSPGR images (dark cerebrospinal fluid). Bottom row is activation over SE EPI images (bright cerebrospinal fluid).

Comments: Advantages of this task include robust memory localization in both mesiotemporal and dorsolateral prefrontal cortex regions and the ability to measure behavioral data of task performance. This task is simple to perform for most patients. The motor area for the hand and visual cortex are activated and serve as control areas. Eye movement is present but not great as in the reading language comprehension task as the pictures are confined to the central filed of view (<5° visual angle).

References:

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