


3 T MR Angiography in Spinal Dural Fistula
A Pictorial Presentation

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Key words: 3 T MRI, angiography, spinal dural AV fistula, DAVF

A 63-year-old man with a probable dural arteriovenous fistula of the spine underwent angiography which failed to demonstrate many of the metameric arteries. The patient’s age and the severe arteriosclerotic alterations of the aorta precluded catheterisation of the fine arteries involved.

The patient was then studied by 3 T fast MR angiography with gadolinium injection to identify the fistula and thereby avoid myelography. MR angiography was performed using a 3 D FAST SPGR coronal acquisition with k-space segmentation by TRICKS (Time Resolved Imaging in Contrast Kinetics) technique having the following parameters: TR 3.8 ms, TE 1.5 ms, Flip Angle 20°, Matrix 384×192, THK 2 mm, FOV 35, GAP –1 mm, NEX 0.50, Temporal Resolution 5.1 s, AT 1.5 min. The nine acquisition phases resulted in eight coronal MIP formatted images.

A large fistula appeared clearly and a cine view demonstrated the caudal direction of the flow and the origin from the sixth metameric artery on the right side. This new 3 T diagnostic approach is not only safer than other conventional techniques, but allows a diagnosis which would otherwise be impossible.
Pre-Surgical Use of Functional Paradigms in Brain fMRI Mapping: Our Initial 3 T Experience

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Key words: 3 T MRI, brain fMRI, neurosurgery

INTRODUCTION – Mapping eloquent brain areas by fMRI only belongs to recent history, but has already proved an essential tool in the pre-surgical evaluation of patients with brain lesions. The reasons for this include the fact that fMRI is a non-invasive technique, enabling us to examine patients safely and to repeat the scans several times for follow-up purposes. Other non-invasive techniques like positron emission tomography (PET) and magnetoencephalography (MEG) are also available for this purpose, but the higher fMRI temporal (as to PET) and spatial (as to MEG) resolution and the wide availability of fMRI functional paradigms make this technique the most suitable way to provide an accurate evaluation of eloquent brain areas. Brain functional mapping has dramatically improved post-surgical neurological sequelae, providing patients with a better quality of life and a longer life expectancy. The accurate definition of functionally eloquent areas allows surgeons to spare as much eloquent tissue as possible and, at the same time, gives them an important cue to adjust the surgical approach pathway. Merely anatomical landmarks are seldom reliable for this purpose, owing to the frequent healthy tissue displacement by the lesion and to the high interpersonal variability. All these advantages, together with the development of 3 T instruments, offering higher spatial definition analysis in a shorter time, have resulted in an increasing diffusion of fMRI and a wide variety of functional MRI paradigms. The aim of this paper is to describe our initial fMRI experience in the pre-surgical evaluation of patients with brain lesions and to explain the functional paradigms we used and why.

“Suitability”

The paradigms described in literature are many and choosing the most suitable ones for pre-surgical purposes may be difficult.

To be defined as “suitable” a paradigm should be:

1. Reliable: activated areas have to be unambiguous and specific.
2. Reproducible: activated areas have to remain the same across different trials made in the same and/or different sessions thus allowing patient follow-up.
3. Plain: the clearer and less ambiguous the task to be performed is, the less the influence of unknown interfering variables to be interpreted, because results are not mixed with extraneous elements.
4. Easy: the task has to be easily learned by patients of different cultures and backgrounds. Otherwise poor patient compliance may result in suboptimal activation.
5. Short-lasting: an appropriate task duration enables the patient to maintain an adequate concentration throughout the task. Unfortunately, an optimal duration is only a compromise between the time spent by the patient in the magnet and the need to acquire enough data for statistically significant mapping. Usually, a fMRI session including 4-5 paradigms has a duration of 40-50 minutes.

One may infer from literature that para-
digms having all these characteristics are rare. The first inconsistency is the high individual variability: the higher the task complexity, the higher the physiological function involved, the higher the individual variability. This may be why literature reports often suggest performing multiple tasks to infer an actual eloquent area.

We focused our attention on the above suitability characteristics and tried to extract from literature the most suitable paradigms for our aims and apply them to healthy individuals and patients.

After a brief description of our experimental design and acquisition parameters, each paradigm is addressed.

Each task is preceded by a short description and discussion of the main task-specific paradigms used in literature, followed by an example of each paradigm we obtained in our Department on a 3 T MR GE Signa System.

**Block Design and Rest Condition**

Usually, pre-surgical fMRI paradigms are performed as a "block design" instead of an "event related" or a "single trial" design. This choice is due to the higher power of the block paradigm design. In a block design, two different tasks alternate with each other, namely the "activation condition" (A) and the "rest condition" (B). In our experiments, both conditions

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**Figure 1** The paradigm and image reconstruction. A) The paradigm, applied to all tasks, consisted of 30 s activation followed by 30 s rest, both repeated 5 times, for a total time of 5 minutes. B) The logic of image reconstruction is shown: the functional coloured map obtained by Functool (I) is superimposed on the anatomical map (II), giving the anatomical location of eloquent brain areas (III).
last the same length of time, the rest condition acting as the baseline of activation. During data processing, the activity detected in the rest condition is subtracted from the activity detected in activation condition: the remaining activity is the specific effect we are looking for. This is why the rest condition is so important, often crucial to disclose activation areas, especially if they are small. Obviously, the rest condition may vary depending on each particular kind of task.

The paradigms we used in all tasks were organized in a block design, in which 30 s of activation alternated with 30 s of rest (five periods of activation and five of rest, for a total acquisition time of five minutes) (figure 1A).

Acquisition Parameters

We performed all paradigms on our 3 T GE Signa Excite MR system, installed in our Department in February 2004. All sequences were acquired using an 8-channel phased array coil. Blood oxygen level-dependent (BOLD) fMRI imaging data were acquired using a Single-shot Gradient-echo echoplanar sequence, with the following parameters: TR 3000, TE 40, FA 90, NEX 1, Matrix 128×128, FOV 24, THK 4 mm, Gap 0 mm. Conventional anatomical Flair T1-w and FR-FSE T2-w images were also acquired.

fMRI data were processed off-line on an independent ADW 4.1 Workstation using the GE proprietary software Functool (version 2). Parametric activation maps of the correlation coefficient were calculated using a significance level of P<0.001. The activation maps calculated were superimposed on anatomical Flair T1-w and FR-FSE T2-w images (figure 1B).

fMRI data were also processed on-line on the same workstation by BrainWave software and 3D images were reconstructed by GE BrainWave Software using an isovolumetric sequence with the following parameters: TR 7.3, TE 3.2, FA 1.0, NEX 1.0, Matrix 288×288, FOV 29, THK 1.0, Gap 0. Also in this case, parametric activation maps of the correlation coefficient were calculated by using a significance level of P<0.001.

Paradigms

Motor paradigms

Motor paradigms, together with tactile stimulation, were the first paradigms performed by fMRI imaging. A wide spectrum of tasks is available to explore eloquent motor areas (flexion, extension, supination, pronation of the limbs; tapping of the fingers and/or toes/feet; keyboard, mouse or joystick manipulation; lip smacking, tongue movements, etc.)20,21,26,27,28. By combining all these paradigms, one may activate the whole contralateral primary motor area of the pre-central gyrus (BA 4), the supplementary motor area (SMA) lying in the paracentral lobule and posterior portion of the superior (medial) frontal gyrus (BA 6α) and the pre-supplementary motor area (pre-SMA) lying medially just anteriorly to the SMA (BA 6β); and also: thalamus, basal ganglia and ipsilateral superior cerebellum. In general, the more complex of motor task, the wider the activated motor area is9,23. However, owing to the presence of the sensimotor homunculus, the wider areas of fingers, hands, tongue and lips are the most suitable to produce the highest BOLD signal. Furthermore, hands/fingers and lips/tongue are very important anatomical effectors, involved, respectively, in day-to-day manual activities and speaking. As a consequence, finger tapping and lip smacking are the most used tasks to explore the activity of the primary motor cortex. However, when the lesion is located near the convexity of the brain, flexi-extension of the foot is also used.

Rest condition may be performed as a complete lack of movement or as a movement of the contralateral limb. Figure 2 shows an example of eloquent cortex activated by finger tapping (2A), lip smacking (2B) and foot flexi-extension (2C).

Tactile Stimulation Paradigms

Also in this case there are many ways to perform tactile stimulation. The most frequently used tools are: simple plastic toothbrushes, blunt nails, and even the examiner’s fingertips. In more sophisticated paradigms, an air puff was also used. The activated areas include the whole sensory strip of the post-central gyrus in the parietal lobe (BA 3-1-2)20,21. Here, again, the sensimotor homunculus is present and it should be noted that palm tactile stimulation activates
Figure 2  Eloquent areas activated by our motor paradigms: finger tapping of the right hand (A), flexo-extension of the right foot (B), and lip smacking (C). For each row (A, B or C), the 1st column (I) shows the parametric activation map of the eloquent area and the related Region Of Interest (ROI, the green or pink circle); the second column (II) shows the exact anatomical location of the ROI; the third column (III) shows the ROI temporal correlation to the paradigm (movement-rest alternation).
eloquent areas whose localization is very similar to that produced by finger tapping.

The tactile stimulation paradigm has the advantage of being a passive task allowing it to be performed also on uncooperative patients (anaesthetized, unconscious, neurologically impaired, disabled, aged, babies, etc.).

Figure 3 shows an example of eloquent cortex activated by tactile stimulation of the left hand palm by means of a soft brush.

Auditory Paradigms

Auditory paradigms suffer from an obvious but important problem: the noise produced by the scanner, which may reach 100 dB, even though this can be drastically reduced by the use of earplugs or earphones. The scanner noise not only may activate the auditory cortex by itself, but also interferes with the experimental auditory paradigm giving unpredictable results. This is especially true if one wants to examine pure tone thresholds or foreground-background discrimination, owing to the masking effect of the noise. Functionally speaking, scanner noise may be considered a source of distraction acting as a factor increasing the difficulty of the task, especially when the task difficulty is high, e.g. phonetic discrimination, or when higher cognitive processes are studied in event-related paradigms. Under these conditions, scanner noise should be carefully addressed. However, in the case of a block design paradigm, the scanner noise is present in both the rest and the active conditions and the noise of the two conditions will be subtracted from each other. Moreover, for pre-surgical purposes, there is only the need for a paradigm generating a clear-cut acoustic activation. A good way to obtain this is to listen to orchestral music, which consists of many frequencies resulting in a wide activation of the tonotopic auditory cortex (Heschl's gyri, BA 41, 42). Simple music listening is again a passive task, having the same advantages mentioned for tactile stimulation paradigms. Figure 4 shows an example of acoustic areas activated by simple music listening.

Visual Paradigms

Visual stimulation paradigms are commonly used to explore not only visual system activation, but also language and memory function (together with many auditory paradigms). The most frequent ways to present visual tasks to the patient are by means of MRI-compatible goggles or by video screen. Goggles have the advantage of permitting monocular activation and to assure the patient of better concentration, because s/he is allowed to see only the stimulus and is not distracted by the surroundings. Hence, goggles permit a better control of the paradigm. Once again, a wide variety of tasks have been used in literature to produce activations ranging from the primary visual cortex to the more specific visual association...
areas. For pre-surgical purposes, we need a task activating as much of the occipital visual cortex as possible as a whole. Alternating checkerboard activates mainly, if not only, the primary visual area (V1) in the striate cortex and calcarine fissure (BA 17), whereas alternating vertical bars also activates complex neurons in the surrounding higher visual areas, giving a wider activation area. We chose this last task and used a block paradigm composed of alternating vertical black and red bars (active state) and a black screen having at the centre a dark purple fixation cross (rest state). This paradigm application produced a strong activation of a wide area in the occipital visual cortex.

Language and Lateralization

Classically, the main cerebral areas involved in language processes are two: Broca’s area in the posterior-inferior part of the third frontal convolution (triangular portion and anterior part of the operculum of the inferior frontal cir-cumvolution, BA 44 and posterior part of BA 45), and Wernicke’s areas in the posterior part of the superior temporal region (BA, 22), both located in the left hemisphere. Broca’s area is mainly involved in language production, whereas Wernicke’s area is mainly involved in language comprehension.

The location of Broca’s and Wernicke’s areas in the left hemisphere is not casual. Language areas are not bilateral, but mainly unilateral and are located in the so-called dominant hemisphere. Language location in the dominant hemisphere is called lateralization. The dominant hemisphere is usually, but not always, the left hemisphere and the problem to define such hemispheric specialization for language is a long-standing issue. Among other things, a variable dominance has been shown among right-handers, left-handers and ambidextrous subjects. Moreover, brain lesions or other pathologies may cause displacements.
of these areas, leading to an even higher variability and consequently a higher pre-surgical risk, also considering the importance of this function. As a result, brain location of language areas is quite unpredictable and the use of mere anatomy is not sufficient. Instead, we need to know the exact locations of language production and comprehension eloquent areas.

Up to now, a variety of new language-exploring paradigms have replaced the more invasive Wada test and are used for pre-operative fMRI imaging. Generally speaking, language-exploring paradigms are divided into two main types: expressive language paradigms and receptive language paradigms.

**Expressive language paradigms**

Expressive language paradigms are used to determine location and lateralization of expressive language areas: Broca’s areas in the inferior frontal gyrus (BA 44, and posterior part of BA 45) and surroundings (BA 47), together with premotor, supplementary and pre-supplementary motor areas (pre-MA, SMA, pre-SMA, BA 6, 8)\(^2\). Hence they are employed in patients with frontal lesions. Owing to the frequent motor artefacts of lips, tongue and head in actively generating words, the patient is taught to generate covertly the corresponding associated verb (ex. food → to eat; dog → to bark; car → to drive, etc.). This test is the most suitable to disclose lateralization. As expected, the activated areas are: Broca’s area in the inferior frontal gyrus (BA 44, and posterior part of BA 45) and the surroundings (BA 47), the middle frontal gyrus (BA 46, 9) implicated in working memory, and other superior frontal areas (BA 6, 8) as well as prefrontal and posterior temporal cortices in the dominant hemisphere, the anterior cingulate, and the contra-lateral cerebellum.\(^2,16,26,30\).

Figure 6 shows an example of the eloquent areas activated by the word-verb paradigm in a left-dominant hemisphere subject.

**Semantic decision test**. There are different versions of this test. In one paradigm, a sequence of words or pairs of words is presented, visually or aurally, to the patient, who has to decide whether they belong to a given category stated before, e.g. abstract vs. concrete\(^13,15,30\), synonyms vs. antonyms\(^26\), living vs. non living\(^15\), positive vs. negative connotation\(^1\), etc. The activation condition, requiring semantic analysis, is also called deep encoding\(^10,19\). When this task is presented aurally, in the rest period the patient has to decide if pairs of tones are the same or not. When this task is presented visually, in the rest period the patient has to decide, for instance, if a sequence of letters are shown in uppercase or lowercase. The resting condition, not requiring semantic analysis but perceptual encoding decision (auditory or visual-orthographic analysis), is also called shallow encoding\(^10,19\). In another version of the paradigm, the target category is presented at the beginning of the activating period (e.g. if an animal lives in the United States and if it is used by man); then the patient has to decide whether the sequence of animals presented belongs to that category (e.g. turtle, rabbit, etc.)\(^5,6\).

The result of the semantic decision paradigm application is the activation of the inferior prefrontal cortex (IPFC, BA 45,46,47) of the dominant hemisphere\(^15\). This activation is specifically related to semantic encoding and not to task difficulty\(^15\). The middle temporal gyrus is also activated and temporal activation spreads ventrally to the inferior temporal gyrus, fusiform and parahippocampal gyri in the ventral temporal lobes\(^5,46\). Also activated, though to a lesser extent, are the cingulate cortex (BA 32) and the superior frontal region (BA 8), both in the dominant hemisphere\(^2,22,42\).

Figure 7 shows an example of the eloquent areas activated by a semantic decision task in a left-dominant hemisphere subject.

**Verbal fluency.** In this task, the subject has to generate covertly as many words as possible according to a key given, visually or aurally, at the start of each activation period. If the key is a phonological key\(^16\), the patient has to generate words beginning with a certain letter (ex. C: coat, church, ceiling, etc.), if the key is a semantic key\(^7\), the patient has to generate words belonging to a certain semantic category (e.g. Animals: cat, dog, rabbit, etc.). In the rest condition, the patient may think of nothing, may repeat a single word, count, or recite the alphabet.

Both paradigms activate the inferior frontal gyrus (BA 44, 45) and sulcus, the middle frontal gyrus (BA 46, 9), the anterior insular cortex and the supplementary motor/cingulate areas in the dominant hemisphere\(^2\). Comparative studies
Figure 5 Visual paradigm and the resulting activated area. A) The paradigm: 30 s activation, consisting of alternating red and black vertical bands (500 ms interval), followed by 30 s resting, consisting of a dark purple cross on a black field. Visual stimuli were delivered bilaterally by MRI-compatible goggles connected to a PC video. B) (I) parametric activation map and (III) the related green ROI; (IV) anatomical location of the ROI; (II) ROI temporal correlation to the paradigm.
Figure 6  Eloquent brain areas activated by noun→verb paradigm. A) The paradigm. A sequence of nouns was presented for 30 s at the rate of 1 noun every 2 s (activation). Then a silence period of 30 s followed (rest). B) Left-hemisphere dominant subject. In the upper part: 3D representation of the left hemisphere with activation areas in orange-yellow. In the lower part (from left to right): axial, coronal and sagittal views (respectively) of the activated areas. Note the activated cortex in Broca’s area and the temporal lobe.
Figure 7  Eloquent brain areas activated by semantic decision – tone decision subtraction paradigm. A) The paradigm. A sequence of couples of synonyms mixed with some (25%) couples of antonyms was presented aurally for 30 s at the rate of 1 couple every 2 s (activation); then a period of 30 s followed, in which a sequence of couples of tones, 25% of which were identical, was presented (rest). The subject had to recognize the couple of antonyms in the active state and the couple of identical tones in the resting state. B) Left-hemisphere dominant subject. In the upper part: 3D representation of the left hemisphere with activation areas in orange-yellow. In the lower part (from left to right): axial, coronal and sagittal views (respectively) of the activated areas. Note the activation areas in the left inferior frontal lobe and the temporal lobe.
Figure 8  Eloquent brain areas activated by passive listening. A) The paradigm. The subject listened to a newspaper reading for 30 s (activation), then a silence period of 30 s followed (rest). B) Left-hemisphere dominant subject. In the upper part: 3D representation of the cut hemisphere with activation areas in orange-yellow. In the lower part (from left to right): axial, coronal and sagittal views (respectively) of the activated areas. Note that the bilateral temporal activated areas are not symmetrical, but on the left side, the activated area is wider (Wernicke’s area + acoustic areas).
have shown that phonological fluency produces wider and more reproducible frontal activation areas than semantic fluency 13.

However, the wider and stronger activation produced by the aforesaid word-verb paradigm makes this one more suitable in evaluating frontal lobe activation for pre-surgical purposes.

Receptive language paradigms

Receptive language paradigms are employed in temporal and inferior parietal lesions and used to determine lateralization and location of receptive language areas, that is to say Wernicke’s area and surrounding perisylvian areas. Wernicke’s area is a poorly defined area anatomically. It consists of the very posterior part of the superior temporal gyrus (posterior part of BA 22), the planum temporale (including also part of the surroundings perisylvian areas) and the multimodal belt in the superior temporal sulcus (BA 37, 39, 40) 27. Here, again, many paradigms are employed: story listening, text reading, covert sentence repetition, semantic fluency task. Among them, story listening (auditory input) and text reading (visual input) have proved to be more reliable 31,39.

Story listening. This is a passive task and has the advantage that it can also be performed on uncooperative patients (cf. tactile stimulation). During the active condition, the patient listens to a short story, during the rest condition, the patient may listen either to the same story played backwards, to subtract the auditory component, or may listen to nothing and lie relaxed with eyes closed (in this case the bilateral activation of primary and secondary auditory cortex have to be considered). This paradigm results in activation in the following areas of the dominant hemisphere: the classical Wernicke’s area (posterior BA 22), midsuperior temporal sulcus (midportion of BA 21 and BA 22) and the anterior-superior and middle temporal gyri (anterior BA 22). “These latter two areas are believed to represent language association cortex that overlaps with the auditory cortical network” 24. Two more areas may be also activated: the angular (BA 39) and supramarginal (BA 40) gyri; these inferior parietal areas, together with superior-temporal areas, form a continuous area along the superior temporal sulcus of the dominant hemisphere. Last but not least, eloquent areas are: the superior middle and inferior frontal gyri and the supplementary motor/cingulate areas 1,22. Figure 8 shows an example of the eloquent areas activated by the passive listening task in a left-dominant hemisphere subject.

Conclusions

The use of appropriate fMRI paradigms makes the localization of functional eloquent brain areas not only possible but also reliable. By performing an fMRI standardized battery of tasks, we can obtain a standardized and non invasive pre-surgical mapping of critical functions to be spared by neurosurgery. This enables a better assessment of surgical risk and facilitates the planning of surgical routes, thereby allowing the best outcome for the patient.

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