Can fMRI replace Wada in pre-surgical evaluation of language dominance?

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Introduction: The intracarotid amytal procedure (IAP), also referred to as the Wada test, has for many years been regarded as the gold standard to assess functional lateralization. However, a recent study[1] has shown that the community standard of care is shifting away from a routine use of this invasive technique. Functional MRI (fMRI) is becoming an increasingly viable alternative and has shown better prediction of cognitive decline than Wada[2]. FMRI is a non-invasive MRI technique that uses blood oxygen level-dependent signal changes to map functional areas of the cortex, which are activated in response to specific tasks such as language. The technique has been extensively and reliably used to determine functional abnormalities in patient populations when comparing to neurologically normal participants. Studies of patients undergoing anterior temporal lobectomies (ATL) have found a good correlation between fMRI results, using a number of language tasks, and the Wada test [3, 4]. However, there are great challenges when performing these exams in individual patients for clinical evaluation, since presently there is no standardized procedure and patterns of activation differ widely between patients. Nevertheless, when a battery of a few different tests is performed in an individual patient, a consistency of activation can help to identify functional localization. We performed a retrospective study which aimed to determine if functional MRI, using a battery of language tests, is able to provide enough information to replace the invasive Wada procedure for language lateralization for pre-surgical planning.

Methods: Functional MRI tests were performed on a 3 Tesla GE MRI scanner (General Electric, Milwaukee WI USA) using a battery of five language tests: Verb generation (generating verbs associated with the presented noun), Verbal fluency (generating words beginning with a letter or belonging to a category), Boston Naming Test (naming the object in a drawing) and Descriptive naming (naming the object described in a phrase). All tasks were designed for patient use and were all presented visually, in a block design, with each tests lasting between 3 and 4 minutes. The whole procedure was designed to last between 30 and 45 minutes, to insure maximum cooperation from impaired patients. All patients had to practice the tests to be performed, just before entering the scanner. Data was processed using commercial software (GE BrainWave PA) and visually inspected to determine language localization. A total of 16 patients with various diagnoses such as mesial temporal sclerosis (n=6), low grade glioma (n=2), cavernous angioma (n=1), gliosis (n=1), DNET (n=2), low grade ganglioglioma (n=1), arachnoid cyst (n=1) and seizures with no obvious lesions on diagnostic imaging (n=2), underwent both fMRI, using the battery described above, and Wada test for the localization of language and memory functions. The Edinburgh handedness inventory was used to determine handedness in these patients: 13 were right handed and 3 were ambidextrous.

Results: Functional MRI results were interpretable in 15 patients. In one patient motion artifacts rendered the study difficult to assess while Wada found bilateral language suggesting a possible dissociation between expressive (bilateral) and receptive (primarily left sided) language. In 14 cases there was agreement between fMRI and WADA regarding language lateralization (Table1). Thirteen patients (11 right handed and 2 ambidextrous) showed left hemisphere dominance (Fig1 shows an example). One right handed patient with focal seizures and a low grade glioma in the left temporal lobe, showed atypical language localization in the right hemisphere (Fig2). In one case, a patient with multiple surgeries, the WADA test performed before her first surgery found left hemisphere language. However, fMRI performed before her 3rd and 4th surgical procedures, consistently found bilateral language activation, possibly indicating language reorganization (Fig 3).

Table1: Language hemisphere dominance as determined by fMRI and Wada (n_R-number of right handed patients; n_A-number of ambidextrous patients).

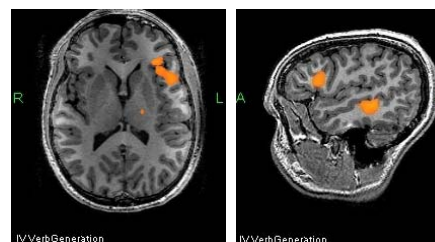|	Wada Left	Wada Bilateral	Wada Right
fMRI Left	13 (n_R=11; n_A=2)	1 (n_A=1) fMRI inconclusive	0
fMRI Bilateral	1 (n_R=1) multiple surgeries	0	0
fMRI Right	0	0	1 (n_R=1)

Fig. 1 Right handed patient with left hemisphere language
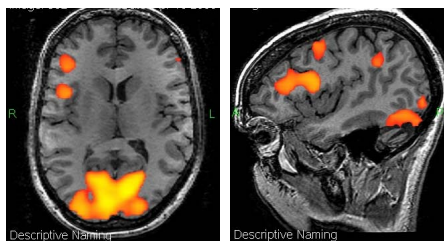

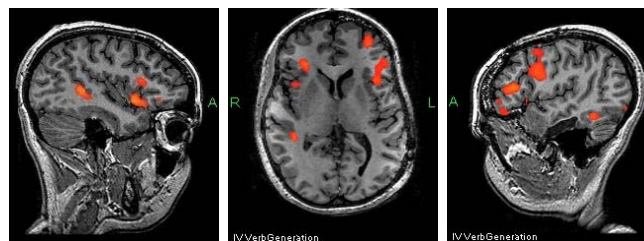**Fig. 2 Right handed patient with right hemisphere language**

Fig. 3 Right handed patient with bilateral language

Discussion: FMRI using a battery of language tests is more reliable than a single test in assessing language hemispheric dominance in patients with brain lesions and/or epilepsy, even when there is atypical dominance (right handed patient with right hemisphere language language).The use of a number of tasks improves the ability to interpret the results and will reduce the number of non-findings. Although our experience with performing fMRI clinically showed promising results, the technique is not yet able to entirely replace the Wada procedure. However, fMRI can be used as a screening tool and limit the need of invasive Wada procedures. When fMRI results are difficult to interpret, either due to atypical language localization or due to difficulties in obtaining good quality data, Wada can be performed to identify hemispheric dominance. Standing issues, such as the existence of a standardized procedure across centers, will need to be resolved before a complete transition from the invasive WADA test to the non-invasive and less expensive fMRI can take place.

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