

CAN *f*MRI SUBSTITUTE FOR THE WADA TEST?**Intrasubject Reproducibility of Presurgical Language Lateralization and Mapping Using *f*MRI**

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PURPOSE: Functional magnetic resonance imaging (*f*MRI) is becoming a standard tool for the presurgical lateralization and mapping of brain areas involved in language processing. However, its within-subject reproducibility has yet to be fully explored. We evaluated within-test and test–retest reliability of language *f*MRI in consecutive patients undergoing evaluation for epilepsy surgery.

METHODS: Thirty-four unselected patients were investigated once (within-test reliability) and 12 patients twice (test–retest reliability). The imaging series consisted of an alternating 25-second synonym judgment condition with a 25-second letter-matching condition repeated 15 times. Reproducibility of activation maps of the first and second half of session 1 or activation maps of sessions 1 and 2 was evaluated by comparing one global and three regional lateralization indexes (Broca's area, remaining prefrontal cortex, temporoparietal area) and on a voxel-by-voxel basis (intraclass correlation coefficient, percentage overlap, correlation of *t* values).

RESULTS: Global and regional language lateralization was achieved with high reliability within and across sessions. Reproducibility was evenly distributed across both hemispheres but not within each hemisphere. Frontal activations were more reliable than temporoparietal ones. Depending on the statistical threshold chosen, the voxel-by-voxel analysis revealed a mean overlap of activations derived from the first and second investigation of up to 48.9%.

CONCLUSIONS: Language *f*MRI proved sufficiently reliable for the determination of global and regional lateralization of language representation in individual unselected patients with epilepsy.

COMMENTARY

The intracarotid sodium amobarbital (Wada) test remains the standard method for lateralizing language and memory before epilepsy surgery. However, the test requires catheterization for amobarbital administration. With the advent of more and more sophisticated imaging techniques, there has been hope that a noninvasive method might someday replace this test. In principle, functional magnetic resonance imaging (*f*MRI) should be the most straightforward way to do this, and so a number of groups have worked to define the utility of *f*MRI for language lateralization.

In a previous article, Fernández et al. asked patients to indicate whether two words did or did not match semantically (1). The control condition consisted of pairs of unpronounceable words. They used *f*MRI to image the brain regions activated by the target task. Their *f*MRI algorithm allowed lateralization and mapping to occur within 15 minutes, making the method useful for clinical applications. However, as Fernández and colleagues pointed out, *f*MRI is an activation procedure. Practically, this means that the test demonstrates areas that participate in a task but does not necessarily demonstrate all areas necessary for accomplishing that task. Further, it is possible that an area might not sufficiently activate on *f*MRI, but removal of the area still could result in language difficulties. For this reason, the investigators pointed out that the test might not be able to localize all critical language areas.

Another critical issue for any test is its reproducibility. The goal of a second article by Fernández et al. was to compare studies performed on two different occasions in the same individual (2). The researchers found that language lateralized in the same way on consecutive studies. However, localization was more consistent for the frontal sites and more variable for temporal sites. Moreover, considerable voxel-by-voxel variability was found between the two studies. As the authors pointed out, this finding means that cortical stimulation will remain necessary before resecting potentially critical cortex. Nonetheless, this work, along with that of others, indicates that *f*MRI may eventually replace the Wada test for language lateralization (2–5).

A third problem is that the Wada tests two functions: language and memory. Reports, such as this one, indicate that we may be close to developing an *f*MRI test that can lateralize language. Parallel work is being performed to develop *f*MRI-based

tests that reliably lateralize memory (6–9). Here again, the issue will be not only to determine what areas are activated by a test but also to assure that removal of an area would not adversely alter memory function.

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