A new method to quantify language lateralization in fMRI using whole brain analysis

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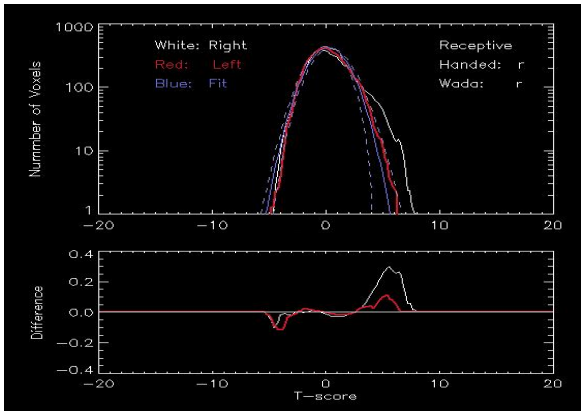
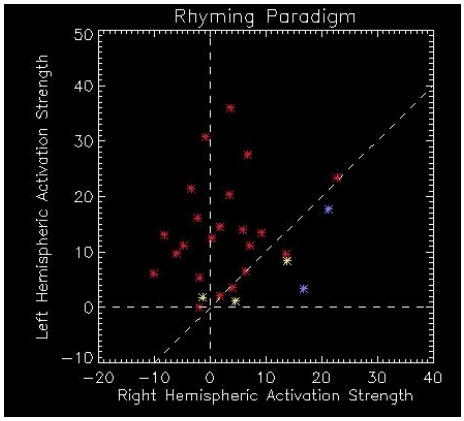
INTRODUCTION: For many patients with intractable epilepsy the only effective treatment is surgical resection of hypersensitive brain parenchyma. Naturally this radical treatment must be balanced by the expected loss of normal functions, of which language is particularly important. Language is further problematic by lateralizing to one hemisphere, typically the left, for which pre-surgical determination can be essential. The intracarotid amobarbital (Wada) test [1] is the most trusted technique to determine language lateralization, however its invasiveness can carry significant comorbidities. The advent of fMRI provides an enticing non-invasive alternative to determine language hemispheric dominance. However, agreement is not complete between fMRI lateralization and the Wada test. The quantify language lateralization, various laterality indexes (LI) have been proposed, many of which suffer from hypersensitivity to predetermined statistical thresholds for activation [2-3]. It is not known to what extent these differences are due to systematic differences, or variability in the underlying cognitive activity. The purpose of this study is to develop a new language lateralization index that does not depend on the use of any predetermined threshold.

METHODS: 26 epileptic and brain tumor patients were retrospectively selected who underwent both fMRI and WADA tests. The fMRI studies were performed with a 3 Tesla Siemens Trio MRI Scanner with paradigms for motor and language activation, the latter including rhyming, verb generation, and receptive speech paradigms. Student t-score maps were separated for left and right cerebral hemispheres, and whole-hemispheric histogram distributions of the t-score were generated. As a control comparison to an expected histogram distribution occurring with no activation, a Gaussian distribution was fit to the most dominant portions of the data. The control Gaussian distribution was calculated separately for each axial level, whose variance provided and estimate for errors of fit. The difference between the data histogram distribution and the Gaussian fit distribution was typically largest in the tail, and was visually best evident using a log scale, in effect weighting differences in the tail. These departures from a Gaussian fit typically reflect activation from the paradigm. These departures were collected from all patients and a scatter plot produced.

RESULTS: Histogram departures from the Gaussian fit distribution provide an alternative visualization for hemispheric activity that is sensitive to small activation; however this occurs at the expense of localization. The top of Fig. 1 shows an example for a receptive speech paradigm for a patient with right-sided Wada lateralization. The white line (right side) at high t-score departs significantly from the red line (left side) and blue line (Gaussian fit). The bottom graph shows the logarithmic difference, which weights small departures in the tail. An activation strength score is calculated from the area under this curve, integrated over positive t-scores. Figure 2 shows a scatter plot of these strength scores for a rhyming paradigm: the x-axis shows the right hemispheric score and the y-axis shows the left hemispheric score. Points above the diagonal line represent left-sided dominant tasks, while points below the diagonal line represent right-sided dominant tasks. Red, blue and yellow points are patients with left, right, and bilateral Wada lateralization, respectively. Note the strong grouping of these Wada lateralization cohorts above, below, and along the diagonal line (respectively), reflecting a high correlation with our new activation strength parameter.





DISCUSSION & CONCLUSIONS: We present a new method to quantify global fMRI activation in the cerebral hemispheres in an objective and automated way, which highly correlates with Wada results during language paradigms. Unlike previous measures of laterality index, this method does not require input of an *a priori* threshold. Also, this method is visually sensitive to small activations, and can occasionally reveal language lateralization when a reader viewing standard planar images reports no significant activation.

REFERENCES:

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