# Test-retest reproducibility of language paradigms for fMRI used in pre-surgical planning

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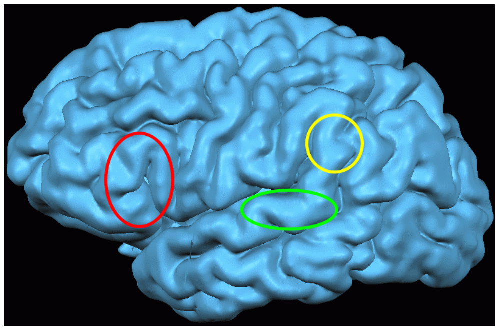
**Purpose:** As part of evaluation of reliability of paradigms for pre-surgical planning, the purpose was to determine the test-retest precision of functional MR maps of important language function regions of the brain activated by three different language paradigms.

**Introduction:** Mapping of eloquent cerebrocortical areas before neurosurgery is gaining popularity worldwide. The selection of cortices mapped is expanding beyond primary motor cortex, and many centers perform fMRI-experiments to delineate language areas with probable aphasia if damaged, in order to minimize postsurgical neurological deficits. In published studies a variety of paradigms are used to stimulate these language areas, and this study aims at investigating the quality of three such paradigms in terms of their test-retest reproducibility.

**Methods:** Gradient echo EPI's were acquired at 3.0 T (Phillips Intera) with voxel size 2 x 2.x 2 $mm^3$ in nine healthy volunteers (eight right-handed, one left-handed) aged 20-42 during three different "classical" language paradigms: Word generation, object naming and a visual responsive naming paradigm. All three paradigms stimulate language production, while the naming task also stimulate language comprehension. All paradigms were identically designed as on-off block paradigms, stimulating language in four 27 s blocks, interleaved with five equally long periods of crosshair gaze fixation. The testing was repeated, in the same subjects, 4-7 weeks after the first session. Data preprocessing included head movement correction and temporal smoothing with high, and low-pass filtering. No spatial smoothing was done. Signal-changes in the time-series on a voxel-by-voxel level were fitted to a Boynton-type hemodynamic response function, and the condition effects were estimated according to the general linear model. VOI analysis was performed on areas with probable aphasia if damaged in dominant hemispheres: Brocas area, Wernickes area and the angular gyrus (figure 1).

**Figure 1:** Regions of interest used in analysis:
Red area: Brocas area.
Green area: Wernickes area.
Yellow area: Angular gyrus.



Activated voxels in each area was counted at a strict statistical threshold (the same for all runs and paradigms for each subject, and for the two sessions). Results were compared with a ratio of the number of voxels activated in both iterations of the tasks in proportion to the voxels maximally activated by either iteration of the task (called "reproducibility index"). Ideally, a full reproduction would yield a ratio of 0.5, while activation of an area in only one run and not the other gives a ratio of 1.

**Results and discussion:** The three different paradigms showed varying levels of activation of the language areas with probable aphasia if damaged (see table 1). Using a strict statistical threshold (z-scores 5.5-7), only the word generation paradigm always "activated" Brocas area, with a "reproducability index" ranging from 0.56 to 0.65. Only the word generation paradigm may thus be named a "robust activator" of Brocas area. Both Wernicke's area and angular gyrus showed varying patterns of activations, and it was concluded that none of the paradigms can robustly activate these areas at a strict threshold. Lowering the threshold makes activation boundaries blurry and confluent with activations in other parts of the brain, making them less suitable for delineation of functionality to be used in pre-surgical planning. A high level of inter-individual variability in areas activated is also seen, making strict thresholding in identifying language areas difficult.

| Subject | Word Generation | | | Naming Task | | | Object Naming | | |
|---|---|---|---|---|---|---|---|---|---|
| # | Broca | Angular gyrus | Wernicke | Broca | Angular gyrus | Wernicke | Broca | Angular gyrus | Wernicke |
| 1 | 0.60 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0.56 | 0.51 | 0.56 | 1 | 1 | 1 | 1 | 1 | 1 |
| 3 | 0.63 | 1 | 0 | 0.64 | 1 | 0.53 | 0.63 | 1 | 0 |
| 4 | 0.60 | 0 | 0.53 | 1 | 1 | 1 | 1 | 0 | 0 |
| 5 | 0.62 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| 6 | 0.65 | 1 | 0 | 0.60 | 0.54 | 0.56 | 0.58 | 0 | 0 |
| 7 | 0.65 | 0.75 | 0.77 | 0.60 | 0.64 | 0.80 | 0.78 | 0 | 0.58 |
| 8 | 0.56 | 0 | 0 | 0.53 | 0.78 | 0 | 0.52 | 0 | 0.63 |
| 9 | 0.58 | 0 | 1 | 0.66 | 1 | 0 | 0.61 | 0 | 0 |

**Table 1:** "Reproducability index" of activations in VOI's. 0 denotes no activation in either run, 1 denotes activation in one of the two runs, values 0.5-1 denotes index ratio of voxels activated in both runs in proportion to the number of voxels activated in the most "effective" run.