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Effects of task complexity on activation of language areas in a semantic decision fMRI protocol

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ABSTRACT

Language tasks used for clinical fMRI studies may be too complex for some patients with cognitive impairments, and "easier" versions are sometimes substituted, though the effects on brain activity of such changes in task complexity are largely unknown. To investigate these differences, we compared two versions of an fMRI language comprehension protocol, with different levels of difficulty, in 24 healthy right-handed adults.

The protocol contrasted an auditory word comprehension task (semantic decision) with a nonspeech control task using tone sequences (tone decision). In the "complex" version (CV), the semantic decision task required two complex semantic decisions for each word, and the tone decision task required the participant to count the number of target tones in each sequence. In the "easy" version (EV), the semantic task required only a single easier decision, and the tone task required only detection of the presence or absence of a target tone in each sequence. The protocols were adapted for a Brazilian population.

Typical left hemisphere language lateralization was observed in 92% of participants for both CV and EV using the whole-brain lateralization index, and typical language lateralization was also observed for others regions of interest. Task performance was superior on the EV compared to the CV ($p=0.014$). There were many common areas of activation across the two version; however, the CV produced greater activation in the left superior and middle frontal giri, angular gyrus, and left posterior cingulate gyrus compared to the EV, the majority of which are areas previously identified with language and semantic processing. The EV produced stronger activation only in a small area in the posterior middle temporal gyrus.

These results reveal differences between two versions of the protocol and provide evidence that both are useful for language lateralization and worked well for Brazilian population. The complex version produces stronger activation in several nodes of the semantic network and therefore is elected for participants who can perform well these tasks.

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1. Introduction

Language lateralization is an important issue in the context of presurgical evaluation of patients with focal epilepsies, because language representation may determine the prognosis related to verbal memory and naming losses (Binder et al., 2008a; Sabsevitz et al., 2003; Sveller et al., 2006).

Several functional magnetic resonance imaging (fMRI) protocols are available for measuring language lateralization in the clinical setting, such as paradigms emphasizing verbal fluency (Bonelli et al., 2011; Friedman et al., 1998; Phelps et al., 1997) or language comprehension. However, there is no universally accepted standard language protocol for presurgical evaluation. One of these protocols is the semantic decision vs. tone decision, which works well because the tone decision task prevents semantically mediated "mind wandering" while also providing a control for low-level auditory, general executive, and motor requirements of the semantic task. In addition, it produces a strong left lateralization in regions such as the prefrontal, temporal, angular, retrosplenial, and thalamocapsular regions (Binder et al., 1997; Frost et al., 1999).

However, the semantic and tone decision tasks used by Binder et al. are demanding and may not be suitable for children or for adults with cognitive deficits, such as memory loss, dysexecutive function, or inattention. Although easier versions of these tasks

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have been developed and are sometimes used in the clinical setting, there are no previous studies comparing their patterns of activation and language lateralization with the more complex version (Binder et al., 1995).

Some neuroimaging studies have addressed the question of how the brain deals with task complexity and have concluded that cognitive functions are not restrained to a particular area, because they depend on diffuse networks which support the main function (Papathanassiou et al., 2000; Stowe et al., 1998). Nonetheless, other studies have demonstrated that the brain has to activate other regions related to additional cognitive functions that are not associated with the evaluated domain (Drager et al., 2004; Just et al., 1996).

Therefore, the objective of this study was to compare areas of fMRI activations directly related to language lateralization produced by two different versions, in complexity, of the language protocol, i.e., the more complex version developed by Binder et al. (1995) (with high cognitive demand) and an easier version with lower cognitive demands. Our experiment was not designed to investigate other cognitive aspects but to compare two protocols.

In addition, we aimed to develop and test a semantic decision/tone decision fMRI protocol using a different language (Portuguese) in a distinct cultural context (Brazil). Understanding the activation patterns and other involved aspects of each version will help us to better choose a task for our neurologically impaired patients.

Our first hypothesis predicted that activation patterns in our population would be similar to those observed previously, despite differences in language and culture. We also predicted that there would be many common language areas between both versions; however, the complex version would present more widespread activations, involving some areas not shared by the easy version.

Moreover, we hypothesized that subjects would perform better in the easy version; however, due to a higher demanding cognitive task elicited by the complex version, we predicted that it would provide stronger activations, especially in the dominant hemisphere for language.

2. Materials and methods

2.1. Subjects

We studied 24 healthy Brazilian volunteers (9 men; mean age 26 ± 3.3, range 20–31 years), all native Portuguese speakers, from the University of Campinas (UNICAMP) with a mean educational level of 17.2 ± 2.4 years of study, ranging from 13 to 22 years, who indicated strong right-handed preferences-laterality quotient (89.5 ± 2.1, range 67–100) on the Edinburgh Handedness Inventory (Oldfield, 1971). Three volunteers reported a positive family history for left-handedness (parents, siblings, or grandparents). All volunteers included in this study signed informed consent that was approved by the Ethics Committee of the Faculty of Medical Sciences of UNICAMP.

2.1.1 fMRI images

All MRI images were acquired on a 3T Philips Achieva (Best, the Netherlands) with an eight-channel head coil at the Neuroimaging Laboratory, UNICAMP, Campinas, São Paulo, Brazil. The acquisition protocol included a T_1-weighted image (isotropic voxels of 1 mm, acquired in the sagittal plane, with 180 slices, 1 mm thick, no gap, flip angle = 8°, TR = 7.0 ms, TE = 3.2 ms, matrix = 240×240, FOV = 240×240 mm^2) for anatomical registration and two echo-planar imaging (EPI) sequences of 6 min 48 s for each version (voxel size = $3 \times 3 \times 3$ mm^3, 40 axial slices, no gap, FOV = $240 \times 240 \times 120$ mm^3, TE = 30 ms, TR = 2000 ms, flip angle = 90°) for functional inference.

2.1.1.2 fMRI language protocol. We developed two fMRI language protocols based on the semantic decision/tone decision study of Binder et al. (1995), which uses names of animals as language stimuli. As the original animal words were selected for an American study population, we created a new list of animal concepts appropriate for a Brazilian population. We first conducted Google searches to generate a list of common animals in Brazil and a list of animals that are not found in Brazil. By consensus, we chose 128 animals that are well known by Brazilians. Each animal name was then recorded by a male Brazilian native speaker in a sound-insulated audio studio. Subsequently, these audio files were edited to remove transients and other artifacts and normalized for intensity. The tones were original audio files used by Binder et al. (1995). Both fMRI protocols were presented using an MRI-compatible audio system (MR Confon GmbH, Leibniz-Institute for Neurobiology at Magdeburg, Germany) and a PC running a MRI-triggered paradigm, enabling time synchronization with the fMRI acquisitions.

We instructed all volunteers to keep their eyes closed during scanning. Two different versions of the protocol were applied. In the complex version (CV), the semantic decision task required volunteers to press a button (using their left hand) if they heard the name of an animal that is both found in Brazil (excluding zoos) and used by people (for food, farm work, clothing, or as a pet). This complex version of the semantic decision task thus requires evaluation of two distinct criteria, both of which are somewhat complex and ambiguous.

During the CV tone decision task, volunteers heard brief sequences of 3–7 high (750 Hz) and lower (500 Hz) frequency tones and were instructed to press the button (with the left hand) for sequences containing exactly two high tones.

In the easy version (EV) of the protocol, the semantic task required volunteers to press the button if they heard the name of an animal that walks on four legs. In contrast to the CV, this version requires only a single criterion to be evaluated, which is relatively concrete and unambiguous. In the EV tone decision task, volunteers were instructed to press the button whenever they heard a sequence with at least one high tone. Compared to the CV version, the EV tone task did not require counting or monitoring of the entire tone sequence and thus made lower demands on working memory and attention.

Four EPI runs were acquired (we combined two runs for CV and two for EV), each alternating eight activation blocks of semantic decision with nine blocks of tone decision. Each block contained eight task trials and lasted 24 s, so the subjects had 3 s to listen to each stimulus and push the button. All participants performed both versions, but half of them performed the CV in the first two runs, and the other half started with the EV.

Participants were instructed that their most important goal was to engage as completely as possible in the tasks, and that they should not be concerned about occasional errors, given that familiarity and knowledge about animals varies from person to person.

2.1.1.3 Quantitative ROIs analysis. In order to calculate the lateralization index (LI) related to each version (EV and CV), we defined regions of interest (ROIs) using the WFU-PickAtlas toolbox (http://www.nitrc.org/projects/wfu_pickatlas/; Maldjian et al., 2003). Results from a previous study using the semantic decision/tone decision protocol in a large sample of healthy subjects (Frost et al., 1999) were used to guide selection of the gyri to be included in the ROIs. We defined the following ROIs in both right and left hemispheres: Hemisphere (the whole left and right hemispheres), Wernicke's area (Brodmann's areas 22, 39, 40), Broca's area (pars opercularis and pars triangularis or Brodmann's area 44 and 45), and a lateral temporal area (superior, middle, and inferior

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