3

Objective and Methods

3.1

General Objective

To study the brain circuitry that is involved in working memory tasks from different theoretical perspectives using functional magnetic resonance imaging (fMRI) meta-analysis.

3.2

Specific Objectives

- To test the theoretical models of Baddeley (2000), Cowan (2010), and Diamond (2013) using fMRI meta-analysis.
- To study phonological working memory in the brain using different stimuli that lead to encoding using fMRI meta-analysis.

3.3

Methods

The first step in the present study was to build a database of fMRI studies to perform the meta-analysis. We systematically searched theneurosynth.org (PubMed Automated Coordinate Extraction) database using the feature “working” to identify phonological working memory studies. We searched articles from the last 25 years that were published prior to August 2014. The search was limited to four languages: English, Portuguese, Spanish, and French (languages with which the author is familiar).

The second step was to identify missing articles from theneurosynth.org database by searching other databases. We used the keywords “working” + “fMRI” to identify working memory studies in the following databases: *PLoS One*, ScienceDirect (e.g., *NeuroImage*, *Neuropsychologia*, *Brain Research*, *Cortex*, etc.),Wiley & Sons (e.g., *Brain and Behavior*, *Human Brain Mapping*, etc.), Elsevier, *Journal of Neuroscience*, and Oxford University Press (e.g., *Brain*, *Cerebral Cortex*, etc.).

The third step involved applying inclusion and exclusion criteria to the search results and presenting the final findings for the systematic study. Article titles and abstracts were scanned to exclude articles based on the exclusion criteria. In case of doubts, the methods section of the articles was reviewed to determine whether it would be excluded. We then retrieved the full-text article to build a complete database, including authorship, year of publication, sample size, electromagnetic field of the fMRI machine (measured in Tesla), the task that was executed inside the machine, types of stimuli, a brief description of the task, and the contrast that was observed in the functional images. Coordinates were extracted from the results, and the meta-analysis was performed using the Activation Likelihood Estimation (ALE) method, which is explained below.

3.3.1
Inclusion and exclusion criteria

The inclusion criteria included the following: normal adult participants only, whole brain scans using fMRI only (positron emission tomography, magnetoencephalography, electroencephalography, and other imaging techniques were excluded), experiments in which English, Italian, French, German, Polish, Spanish, Russian, Dutch, Danish, and Portuguese languages were spoken by monolingual or first-language-only participants (Eastern languages that use other than the Latin or Cyrillic alphabet and its variations were excluded, such as Japanese, Chinese, Malayan, and Korean), and studies that provided brain coordinates in their results. Studies that compared groups (sex, normal control, and pathologies, etc.) were excluded. Duplicate articles that were indexed in multiple databases were excluded.

3.3.2
Meta-analysis: Activation Likelihood Estimation

Activation Likelihood Estimation meta-analysis is a method of conducting statistical analyses of human brain imaging studies using published coordinates in Talairach or Montreal Neurological Institute (MNI) space. Activation Likelihood Estimation was originally developed by Peter Turkeltaub (Turkeltaub, Eden, Jones, & Zeffiro, 2002). It has come to also mean “anatomic likelihood estimate” when used in conjunction with anatomic data, such as the voxel-based morphometry database. Activation Likelihood Estimation uses a null-hypothesis test for each voxel to be activated during a task. Much criticism has been given to the uncertainty in spatial coordinate determination in neuroimaging studies. Turkeltaub et al. (2002) suggested that each focus is best viewed not as a single point but rather as a probability distribution that is centered around a peak at the reported coordinates. By evaluating the union of these distributions for all brain locations, a map for the entire brain that represents the differential likelihood of activation at all locations can be generated.

To organize our database, we adapted the MNI coordinates to Talairach space using icbm2tal transformation (Lancaster et al., 2007). We then separated the database by type of stimuli and lastly conducted the ALE analysis to test significant differences between networks by considering the types of stimuli, with code types as the independent variable. We used three different software programs to conduct the analyses: GingerALE (Eickhoff et al., 2009; to test the null-hypothesis),icbm2tal transformation (Lancaster et al., 2007; to transform MNI data into Talairach space), and Mango 2.1 (to generate the images).