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Mapping lexical-semantic networks and determining hemispheric language dominance: Do task design, sex, age, and language performance make a difference?

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ABSTRACT

Blocked and event-related fMRI designs are both commonly used to localize language networks and determine hemispheric dominance in research and clinical settings. We compared activation profiles on a semantic monitoring task using one of the two designs in a total of 43 healthy individual to determine whether task design or subject-specific factors (i.e., age, sex, or language performance) influence activation patterns. We found high concordance between the two designs within core language regions, including the inferior frontal, posterior temporal, and basal temporal region. However, differences emerged within inferior parietal cortex. Subject-specific factors did not influence activation patterns, nor did they interact with task design. These results suggest that despite high concordance within perisylvian regions that are robust to subject-specific factors, methodological differences between blocked and event-related designs may contribute to parietal activations. These findings provide important information for researchers incorporating fMRI results into meta-analytic studies, as well as for clinicians using fMRI to guide pre-surgical planning.

1. Introduction

Two major types of experimental designs that have been employed to localize language networks and to identify the language-dominant hemisphere with functional magnetic resonance imaging (fMRI) are blocked and event-related designs. Both designs are frequently implemented in research and clinical settings and are thought to have different advantages. Blocked designs generally have large blood-oxygen-level-dependent (BOLD) signal changes relative to the baseline, resulting in high statistical power in a short time frame (e.g., Birn, Cox, & Bandettini, 2002; Friston, Zarahn, Josephs, Henson, & Dale, 1999). Thus, blocked designs may be more appropriate if the research goal is to localize a specific cognitive function or to detect subtle differences in BOLD response between different task conditions, especially in clinical settings that require efficiency (Chee, Venkatraman, Westphal, & Siong, 2003). Conversely, event-related designs are believed to have the advantage of reducing participant's expectation of subsequent stimuli, providing greater specificity, and reducing motion artifacts when estimating the hemodynamic response (e.g., Birn et al., 2002; D'Esposito, Zarahn, & Aguirre, 1999; Friston et al., 1999; Liu, Frank, Wong, & Buxton, 2001). Thus, the choice of experimental design often depends upon the nature of the research or clinical question and the relative importance of each of these factors to answering the proposed question.

Despite the number of papers that have alluded to the relative merits of each design, only two papers have directly compared blocked versus event-related designs for identifying language networks in healthy controls or preoperative patients. In a small sample of young adults (n = 8–12 per group), Chee et al. (2003) used a semantic judgement task and found strong concordance in language activation patterns between blocked and event-related designs. In contrast, Tie et al. (2009) examined language processing in six healthy controls and eight patients with brain tumors using an antonym generation task and reported a relatively high degree of discordance between task designs. In fact, their event-related design produced more robust activations in putative language areas, including the inferior frontal gyrus and posterior superior temporal gyrus, relative to the blocked design. In addition, the blocked design was more likely to show activations outside of the core language network, including right frontal lobe and precuneus

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in a subset of healthy controls. These findings led them to conclude that their event-related design produced maps with both greater sensitivity and specificity to language networks relative to their blocked design.

Understanding the similarities and differences between blocked and event-related designs is critical for at least two reasons. First, this information can facilitate the comparison of fMRI findings across different studies aimed at identifying common brain regions involved in a specific cognitive function. Despite the growing number of systematic reviews and meta-analyses on fMRI activations associated with language and other cognitive functions, the variability in experimental designs is rarely considered (Costafreda, 2009). Second, fMRI is increasingly used in the clinical setting as a non-invasive tool for pre-operative mapping of language networks and determination of language-dominance in pre-surgical planning for patients with epilepsy and brain tumors. Most published pre-surgical language fMRI studies utilize a blocked design (e.g., epilepsy: Desmond et al., 1995; Woermann et al., 2003; brain tumor: Stippich et al., 2007) because it is believed to be simpler to implement, time efficient, and has a higher detection power (e.g., Chee et al., 2003; Donaldson & Buckner, 2001). However, as noted above, there is some evidence that event-related designs may provide comparable or even higher detection power for determining language lateralization compared to blocked designs (Tie et al., 2009). Thus, understanding core differences between the two designs is critical for clinicians who must select the most robust task for clinical decision-making in the context of pre-surgical planning. This is particularly relevant for patients with temporal lobe epilepsy or frontotemporal brain tumors where the goal is to identify the language-dominant hemisphere so as to not surgically encroach upon eloquent brain regions.

In present study, we build upon a surprisingly small literature that has compared blocked and event-related designs for identifying language networks and determining hemispheric language dominance in healthy controls. However, we augment the existing literature in two important ways. First, we include a large group of healthy controls (N = 43) who span a broad age range (19–72 years) and broad language performance (see Table 1) to parallel the variability seen in pre-surgical populations. Second, we stratify participants according to demographic variables (i.e., age, sex) and language performance (i.e., high versus low performer) to explore whether there are main effects of these variables on language activation patterns or interactions between these subject-specific characteristics and fMRI experimental designs. We use a semantic monitoring task to measure language lateralization in this study due to the importance of temporal lobe neocortex in pre-surgical planning for two of the most common patient populations for which fMRI is used: patients with temporal lobe epilepsy (e.g., Benke et al., 2006; Carpentier et al., 2001) and patients with temporal lobe brain tumors (e.g., Tomczak et al., 2000).

2. Methods

2.1. Participants

This study was approved by the Institutional Review Board at the University of California, San Diego (UC San Diego) and informed consent was collected from all participants. A total of 50 healthy adults were recruited in this study. The final sample included 43 healthy adults; seven participants were excluded from the final analyses due to excessive head motion during fMRI scanning. Twenty-one participants completed the blocked design version of the task, whereas 22 completed the event-related design. All of the participants were screened for neurological or psychiatric conditions.

2.2. Materials and procedures

2.2.1. Neuropsychological tasks

Participants were administered the Boston Naming Test, a visual confrontation naming measure (BNT; Kaplan, Goodglass, & Weintraub, 1983); Auditory Naming Test, an auditory naming test in which participants are provided with verbal cues (ANT; Hamberger & Seidel, 2003), and Category Fluency (CF) and Letter Fluency (LF) subtests from the Delis-Kaplan Executive Function System (Delis, Kaplan, & Kramer, 2001), as part of a larger neuropsychological test battery.[1] Age and education-corrected z-scores were calculated for the BNT based on normative data provided in the test manuals, and education-corrected z-scores were calculated for the ANT based on normative data published in Hamberger and Seidel (2003). Age-corrected z-scores were calculated for the CF and LF.

Table 1
Descriptive statistics for the demographic/performance characteristics for the participants in the blocked and event-related designs.

Variables	Blocked	Event-Related
Sample Size	21	22
Demographic		
Sex (Male/Female)	9/12	11/11
Handedness (Right/Left/Ambidextrous)[+]	19/1/1	21/1/0
Language (Monolingual/Bilingual)	14/7	17/5
Age[*]	37.14 (20–65)	36.64 (19–72)
Education[*]	16.05 (12–20)	15.64 (13–20)
Language Performance		
Language Composite[*]	0.68 (−0.69 to 1.56)	0.62 (−0.74 to 1.50)
Boston Naming Test (BNT)[*]	0.29 (−1.00 to 2.00)	0.20 (−1.00 to 2.00)
Auditory Naming Test (ANT)[*]	0.51 (−0.77 to 0.94)	0.07 (−0.77 to 0.94)
Category Fluency (CF)[*]	0.98 (−1.33 to 3.00)	1.11 (−1.33 to 2.67)
Letter Fluency (LF)[*]	0.93 (−1.00 to 3.00)	1.02 (−1.33 to 3.00)

[+] The handedness was measured by Edinburgh Handedness Inventory.
[*] Mean (Minimum − Maximum).

2.2.2. FMRI language task

The blocked and event-related fMRI tasks were designed to be as comparable as possible, using the same stimuli, general timing, task instructions, and approximate length of each task run. During each task, four types of stimuli were presented visually on the screen as light gray letters on a black background in Arial font. These four types of stimuli included novel words (NW) that were presented only once, repeating words (old) that were presented more than once, false font (FF) stimuli, and target words (i.e., animals). The NW stimuli were nouns with 4–8 letters, with a written lexical frequency of 3–80 per 10 million (Francis & Kucera, 1982). The old words were repetitions of the novel words. The FF stimuli were comprised of alphabet-like characters that were matched in size and number of characters to each NW stimulus in order to control for visual features of the stimuli, but not lexical, syntactic, or semantic content (McDonald et al., 2009). The target words consisted of moderate to low frequency animal names. In the task, participants were asked to respond to the presence of target words by pressing a button. The task response occurred only to target words to avoid motor contamination in the main contrast of interest (NW and FF). Presentation software (Neurobehavioral Systems, Inc, Albany, CA, U.S.A.) was used to present stimuli and collect participants' responses. For the purpose of this study, the contrast between NW and FF stimuli was used as the primary contrast to model lexical-semantic processing in the blocked and event-related designs.

[1] Language performance were measured by the four neuropsychological tasks of language, which was performed on 39 participants. Three participants did not perform all the neuropsychological tasks; two participants did not perform Boston Naming Test, and one participant did not perform Auditory Naming Test.