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Role of the left hemisphere in visuospatial working memory

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ABSTRACT

Visuospatial processing deficits are typically associated with damage to the right hemisphere. However, deficits on spatial working memory have been reported among some individuals with focal left hemisphere damage (LHD). It has been suggested that the left hemisphere may play a role in such non-verbal working memory tasks due to the use of subvocal, verbally-mediated strategies. The current study investigated the role of the left hemisphere in spatial working memory by testing spatial span performance, both forward and backward, in a large group of individuals with a history of left hemisphere stroke. Our first aim was to establish whether individuals with LHD are indeed impaired on spatial span tasks using standardized span tasks with published normative data. Our second aim was to identify the role that language plays in supporting spatial working memory by comparing LHD individuals with and without aphasia, and by relating spatial span performance to performance on a series of language measures. Our third aim was to identify left hemisphere brain regions that contribute to spatial working memory using voxel-based lesion symptom mapping (VLSM), a whole-brain statistical approach that identifies regions critical to a particular behavior on a voxel-by-voxel basis. We found that 28% of individuals with LHD performed in the clinically-impaired range on forward spatial span and 16% performed in the clinically-impaired range on backward spatial span. There were no significant differences in performance between individuals with and without aphasia, and there were no correlations between spatial span performance and language functions such as repetition and comprehension. The VLSM analysis showed that backward spatial span was associated with a left fronto-parietal network consisting of somatosensory cortex, the supramarginal gyrus, lateral prefrontal cortex, and the frontal eye fields. Regions identified in the VLSM analysis of forward spatial span did not reach the conservative statistical threshold for significance. Overall, these results suggest that spatial working memory, as measured by spatial span, can be significantly disrupted in a subset of individuals with LHD whose lesions infringe on a network of regions in the left hemisphere that have been implicated in domain-general working memory and attentional control mechanisms.

1. Introduction and background

Working memory is typically described as a higher-order process that provides cognitive space for the temporary storage and manipulation of both verbal and spatial information (Baddeley, 1992; 2003). In research and clinical neuropsychology, working

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memory is often tested with span tasks that require examinees to reproduce a series of either verbal or visuospatial sequences (Baldo, Katseff, & Dronkers, 2012; De Renzi, Faglioni, & Previdi, 1977; Kessels, Kappelle, de Haan, & Postma, 2002; Kessels, van Zandvoort, Postma, Kappelle, & De Haan, 2000; Luciana, Burgund, Berman, & Hanson, 2001; Nys, van Zandvoort, van der Worp, Kappelle, & de Haan, 2006; Wilde, Strauss, & Tulsky, 2004). In visuospatial span tasks, the examiner points to a series of spatial locations on a board and the examinee is instructed to point to the locations in the same order (forward spatial span) or reverse order (backward spatial span; Corsi, 1972; Milner, 1971). Performance on spatial span is typically measured as accuracy in reproducing/reversing the sequences.

Early models of spatial working memory posited a visuospatial sketchpad that is activated in forward spatial span tasks to temporarily hold the locations and order in mind (Baddeley & Hitch, 1974), with additional engagement of the central executive for the manipulation of information required for backward spatial span (Baddeley, 1986; Hester, Kinsella, & Ong, 2004). More recent findings, however, have suggested that both forward and backward spatial span rely on common working memory mechanisms that engage central executive systems, with backward span requiring additional attentional control (Vandierendonck, Kemps, Fastame, & Szmalec, 2004; Wilde et al., 2004). In addition, domain-general theories suggest that attentional control processes are critical for working memory regardless of modality (Barrouillet, Bernardin, & Camos, 2004; Cowan, 1995).

Visuospatial functioning in general has been associated primarily with the right hemisphere and this holds true for visuospatial working memory as well (De Renzi et al., 1977; Jonides et al., 1993; Kessels et al., 2002, 2000a,b; Smith, Jonides, & Koeppe, 1996). Consistent with this notion, a few studies have shown that individuals with left hemisphere damage (LHD) perform well on spatial span tasks relative to individuals with right-hemisphere lesions or neurologically-intact individuals (Beeson, Bayles, Rubens, & Kaszniak, 1993; Corsi, 1972). However, other studies have reported that individuals with LHD do exhibit deficits on spatial span tasks (Burgio & Basso, 1997; De Renzi & Nichelli, 1975; Kasselimis et al., 2013).

There are a number of factors that might account for the discrepancy in spatial span findings in the literature. One of these factors is the presence/degree of aphasia in the samples, as verbal mediation has been suggested to play a role in spatial span performance (Postma & de Haan, 1996; Rausch & Ary, 1990). A few studies have looked at the potential role of aphasia/language abilities on spatial span and found that the presence or severity of aphasia or other phonological abilities have an impact on spatial span performance (Kasselimis et al., 2013; Lang & Quitz, 2012; Martin & Ayala, 2004; Potagas, Kasselimis, & Evdokimidis, 2011). Conversely, negative findings with respect to the impact of aphasia on spatial span performance have also been reported for both the presence and type of aphasia (Burgio & Basso, 1997; De Renzi & Nichelli, 1975; Kasselimis et al., in press). It is possible that this mix of positive and negative findings with respect to the role of language in spatial span is due to some studies relying solely on a general aphasia or subtype classification rather than assessing distinct language processes.

Another possible confounding factor in previous studies of spatial span in individuals with LHD is the specific location of lesions. Lesion site is typically not included as a factor in analyses and when included, has often been arbitrarily-defined or has included large regions of interest (e.g., anterior vs. posterior; Beeson et al., 1993; Burgio & Basso, 1997; De Renzi & Nichelli, 1975; Lang & Quitz, 2012). There is some evidence that posterior left hemisphere regions play a role in forward spatial span performance (De Renzi & Nichelli, 1975). However, other studies have not replicated this effect for forward spatial span (Beeson et al., 1993; Burgio & Basso, 1997) or backward spatial span (Kasselimis et al., 2013). In the neuroimaging literature, there is evidence for a domain-general dorsal attention network comprised of superior frontal cortex and the intraparietal sulcus that supports working memory, so that lesions in both anterior and posterior regions could affect spatial span (Majerus et al., 2016, 2012; Todd & Marois, 2004).

Yet another possible explanation for the mixed findings on spatial span in individuals with LHD is that the majority of studies have focused on forward spatial span alone (Beeson et al., 1993; Burgio & Basso, 1997; De Renzi & Nichelli, 1975; Martin & Ayala, 2004). As mentioned above, backward spatial span has been posited to engage additional rehearsal and/or manipulative mechanisms in some models. It may be that forward and backward spatial span are thus differentially affected in LHD individuals (Baddeley, 1986; Harnish & Lundine, 2015; Hester et al., 2004).

Last, spatial span performance is sometimes discussed as *relatively* preserved in individuals with LHD, without establishing whether spatial span performance is in fact in the "normal" range. Most studies have relied on previously published cut-off scores from a sample of patients hospitalized for non-neurological illnesses (De Renzi & Nichelli, 1975; Martin & Ayala, 2004; Potagas et al., 2011).

In summary, the literature on spatial working memory in LHD individuals has been mixed due to a number of factors: 1) presence/degree of aphasia and related language functions, 2) lesion site, 3) test conditions (forward vs. backward span), and 4) lack of normative data (i.e., establishing what is "impaired" performance). The first aim of this study was to identify whether the left hemisphere contributes to spatial working memory by evaluating spatial span performance in individuals with LHD using standardized span tasks with published normative data. The second aim was to determine whether language plays a role in supporting spatial working memory by comparing LHD individuals with and without aphasia and by assessing the relationship between performance on spatial span and specific language measures. The third aim was to identify which left hemisphere brain regions are critically related to spatial span performance using a whole-brain voxel-based lesion symptom mapping approach (VLSM), which allowed for the identification of brain regions that play a critical role in supporting spatial span performance.