



## Which perseverative behaviors are symptoms of spatial neglect?



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### ABSTRACT

Spatial neglect is characterized by a failure to attend or make movements towards left-sided stimuli. Common paper-and-pencil tasks to diagnose spatial neglect are sensitive to perseverative errors, including additional marks over already cancelled targets and “scribbling” out a target. Here, we examine whether functionally distinct perseverative behaviors are related to spatial neglect. Line cancellation tasks of 45 healthy controls and 220 right-hemisphere stroke survivors were examined for recurrent marks (RM) and continuous marks (CM) perseverations. We found that RM perseveration correlated with neglect severity, while CM perseveration did not. Examination of lesion profiles for the two groups indicated distinct anatomical correlates, with RM lesions overlapping regions implicated in spatial neglect including the rolandic operculum, superior temporal gyrus, and inferior parietal lobule.

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### 1. Introduction

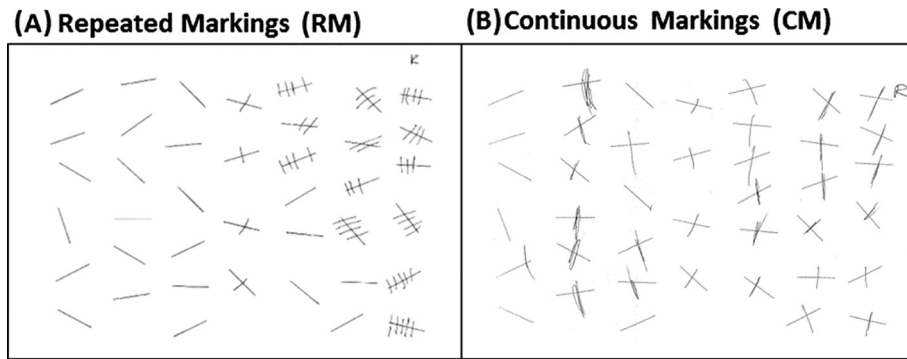
Spatial neglect is a failure to report, respond, or orient to stimuli in the side of space opposite a brain injury, causing functional disability (Barrett & Burkholder, 2006; Heilman, Watson, & Valenstein, 2011; Mesulam, 1999). To diagnose spatial neglect, it is common to use paper-and-pencil tasks that require manual responses, such as asking the participant to cancel all of the targets presented in an array (Albert, 1973). Individuals with spatial neglect often mark only those targets located on the ipsilesional side of the page, while failing to cancel those located on the contralesional side.

In contrast to healthy adults, who typically cancel targets with a single line, participants with neglect may not cancel contralesional targets, and often mark an ipsilesional target more than once

(Fig. 1A) or continuously mark it with a “scribble” (Fig. 1B). This unnecessary repetition or continuation of a response counter to instructions can be defined as *motor perseveration* (henceforth, perseveration). Co-occurrence of perseveration and spatial neglect is quite common, with rates of spatial neglect and perseveration reported from 30% to 90% (Pia, Ricci, Gindri, & Vallar, 2013; Toraldo et al., 2005). Perseverative ipsilesional behaviors may be functionally important, i.e. when they affect the type and direction of hand movements during wheelchair navigation. However, it remains unclear why perseveration and spatial neglect frequently co-occur. Attempts to explain why this relationship is so common fall largely under two theories: that perseveration is a symptom of spatial neglect (Manly, Woldt, Watson, & Warburton, 2002; Toraldo et al., 2005; Wansard et al., 2014) or that spatial neglect and perseveration are separate symptoms (Gandola et al., 2013; Ronchi, Algeri, Chiapella, Spada, & Vallar, 2012; Rusconi, Maravita, Bottini, & Vallar, 2002; Vallar, Zilli, Gandola, & Bottini, 2006). In past studies, conflicting evidence has been presented on the relationship between severity of neglect and severity of

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**Fig. 1.** The Albert Cancellation Task of the BIT assesses for the presence of spatial neglect (left sided omissions) as well as repetitive behaviors on cancelled targets. The participants below both demonstrate severe spatial neglect. Panel A demonstrates recurrent marking (RM) perseveration and Panel B demonstrated continuous marking (CM) perseveration.

perseveration (Manly et al., 2002; Na et al., 1999; Nys, van Zandvoort, Van der Worp, Kappelle, & de Haan, 2006). Manipulating stimuli so that there are no left-sided targets reduced perseveration in some cases (Manly et al., 2002), but not others (Pia et al., 2013). Co-occurrence of perseveration and neglect severity was also not replicated in some studies (Ronchi et al., 2012; Rusconi et al., 2002; Vallar et al., 2006). These conflicting results come from studies that examine a single type of perseveration, or do not separate participants according to their distinct perseverative behaviors. Some forms of perseveration may be neglect-related while others may occur independently.

Perseveration can be categorized into two types. In one type of perseveration, the participant is unable to change to a new motor response, inappropriately repeating a prior motor response. This type of perseveration has been called *inertia of program action* (Luria, 1965), or *recurrent perseveration* (Sandson & Albert, 1984). In the context of the current study, we refer to this type of perseveration as *recurrent markings* (RM) perseveration. Other examinations of motor perseveration have termed this *Type I* (Na et al., 1999), *Simple* (Rusconi et al., 2002), *re-markings* (Nys et al., 2006), and *Additional marks* (Gandola et al., 2013). RM perseveration is highlighted by the recurrence of a previous response after a delay and is manifest on a cancellation task as multiple distinct lines through a single target (Fig. 1A).

In the second type of perseveration, the participant continues to perform a movement even though the task is completed. Luria (1965) called this *effluent perseveration*, and Sandson and Albert (1984) referred to this as *continuous perseveration*. In the context of cancellation tasks, we refer to this as *continuous marking* (CM) perseveration (Fig. 1B). CM perseveration refers to the continuation of a response beyond the point of completion and is manifest as a “scribble” on a target. Other studies examining perseveration have described this form of perseveration as *Inkblot* (Torraldo et al., 2005) and *Scribble* (Gandola et al., 2013) perseveration. Recent research separating RM and CM perseverations by behavioral pattern found that these distinct types of perseveration differentially relate to spatial neglect (Gandola et al., 2013). In their study, RM errors, but not CM errors, were associated with spatial neglect severity. RM perseveration is assumed to be related to spatial displacement of a motor response to uncanceled targets, which could be directly related to spatial neglect. CM perseveration, or scribble perseveration, is assumed, in contrast, to stem from failure to appropriately end or complete a motor task, which may not be spatially specific and thus may not be related to spatial neglect.

RM and CM perseveration are also associated with different functional neuroanatomy. Lesion profiles in RM include the inferior frontal gyrus (IFG), superior temporal gyrus (STG), and rolandic operculum – areas also typically associated with the presence of

spatial neglect (Chen, Goedert, Shah, Foundas, & Barrett, 2014; Gandola et al., 2013). CM perseveration, however, is reflective of lesions or dysfunctions of frontal and subcortical structures (Gandola et al., 2013; Luria, 1965; Sandson & Albert, 1984).

In the present study, we had three goals. The first goal was to confirm that RM relates to spatially biased behavior, while CM is not specific to spatial bias. Thus, we expected that RM, but not CM, would be correlated with measures of spatial neglect severity. The second goal was to examine lesion profiles in the two identified specific types of perseveration, and their relationship with spatial neglect. Based on recent research utilizing similar categories of perseveration (Gandola et al., 2013), we expected that RM would be associated with lesions of the IFG, STG, and rolandic operculum, and CM associated with frontal and subcortical lesions of the basal ganglia. Our third goal was to examine how co-occurring perseveration and spatial neglect related to reduced functional independence. Based on previous research indicating that spatial neglect is associated with many adverse stroke outcomes, including reduced functional independence, increased falls, and difficulties in mobility, we expected that spatial neglect and perseveration may be associated with increased functional disability. (Chen, Hreha, Kong, & Barrett, 2015; Jehkonen, Laihosalo, & Kettunen, 2006; Nijboer, Kollen, & Kwakkel, 2014; Nijboer, van de Port, Schepers, Post, & Visser-Meily, 2013).

## 2. Materials & methods

### 2.1. Participants

After giving written informed consent, 45 healthy controls (52.2% female) ages 49–88 years ( $M = 64.56$ ,  $SD = 9.42$ ) and 220 right brain stroke survivors (48.5% female) ages 19–93 years ( $M = 65.36$ ,  $SD = 14.34$ ) in an inpatient rehabilitation facility were assessed for this study (see Table 1). Participants who had a first right brain stroke, no history of neurological or psychiatric disorders, no uncorrected ocular disorders (e.g. near-sightedness or cataract), and used their right hand to write were enrolled in the study. Patients were tested as part of their participation in ongoing spatial neglect research (clinical trials.gov: NCT00350012, NCT00989430) during the period 2008–2015.

### 2.2. Neuropsychological and functional assessments

Healthy adults and stroke participants were assessed with the Behavioral Inattention Test (BIT; Wilson, Cockburn, & Halligan, 1987). The BIT is a widely used paper-and-pencil assessment of spatial neglect with scores from 0 to 146. Here, we used published

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