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Author(s): Kettunen, Jani E; Nurmi, Mari; Dastibar, Prasun; Jehkonen, Mervi
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Recovery From Visual Neglect After Right Hemisphere Stroke: Does Starting Point in Cancellation Tasks Change After 6 Months?

J. E. Kettunen^{1,2}, M. Nurmi^{1,2}, P. Dastidar³, and M. Jehkonen^{1,2}

¹Department of Neurology and Rehabilitation, Tampere University Hospital, Tampere, Finland

²School of Social Sciences and Humanities, Psychology, University of Tampere, Tampere, Finland

³Regional Medical Imaging Center and Tampere Medical School, Tampere University Hospital, Tampere, Finland

In the acute phase of stroke, patients with left visual neglect (VN) automatically orient to the right hemisphere. This study examined the presence of rightward bias after right hemisphere stroke within 10 days of stroke onset and after 6 months. Our sample comprised 43 patients and 49 healthy controls. Presence of VN was evaluated with the six conventional subtests of the Behavioral Inattention Test (BITC). Starting points were determined in three BITC cancellation tasks by measuring the distance between the starting point and the median line of the stimulus sheet in centimeters. Activities of daily living (ADL) were assessed with the Barthel Index. At baseline VN patients showed more robust rightward bias than patients without VN. The magnitude of rightward bias decreased clearly in the VN patients at follow-up. A favorable ADL outcome was observed in 90% of the patients with VN and in all of the patients without VN. The magnitude of rightward bias differed clearly between the patient groups and controls. Our result implies that VN was likely to have improved as measured by BITC sum scores, but symptoms of rightward attention bias were still detected. We therefore suggest that, for clinical purposes, it is important that attention bias is measured accurately after right hemisphere stroke.

Keywords: Rightward bias; Recovery; Stroke; Visual neglect.

INTRODUCTION

Visual neglect (VN) is a disabling disorder that frequently occurs after right hemisphere stroke (Bowen, McKenna, & Tallis, 1999; Ringman, Saver, Woolson, Clarke, & Adams, 2004), suggesting a special role for the right hemisphere in spatial attention (Halligan, Fink, Marshall, & Vallar, 2003; Heilman, Watson, & Valenstein, 2003; Shulman et al., 2010). Neglect refers to failure to report, respond, or orient to stimuli on the contralesional side of space that cannot be accounted for by primary sensory or motor deficits (Halligan, Cockburn, & Wilson, 1991; Heilman et al., 2003; Robertson & Halligan, 1999). One prominent theory of this asymmetry in VN is that the left hemisphere controls shifts of attention in the rightward direction, while the right hemisphere controls shifts of attention in either direction (Mesulam, 1981).

Address correspondence to: Jani Kettunen, University of Tampere, School of Social Sciences and Humanities, FIN-33014 University of Tampere, Finland. E-mail: jani.e.kettunen@uta.fi

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Neglect is detected in several modalities (Barbieri & De Renzi, 1989), and it is associated with poor functional recovery (Cherney, Halper, Kwasnica, Harvey, & Zhang, 2001; Jehkonen, Laihosalo, & Kettunen, 2006). It occurs more often and is increasingly severe in older patients (Gottesman et al., 2008; Linden, Samuelsson, Skoog, & Blomstrand, 2005; Ringman et al., 2004). Clinical manifestations vary widely, which is consistent with the idea that neglect is a multicomponent syndrome (Vuilleumier et al., 2008).

Previous clinical studies (Azouvi et al., 2002, 2006; Jalas, Lindell, Brunila, Tenovuo, & Hämäläinen, 2002; Mattingley, Bradshaw, Bradshaw, & Nettleton, 1994; Nurmi et al., 2010; Samuelsson, Hjelmqvist, Naver, & Blomstrand, 1996) have found that stroke patients with or without VN show pathological attention processes, including a right-to-left visual scanning strategy. In the study of Jalas et al. (2002) the starting point in different cancellation tasks was designated right or left with respect to the center of the stimulus sheet. VN patients showed a strong tendency to start on the right, but half of the right hemisphere patients without VN demonstrated right bias at the acute stage of stroke, suggesting the presence of subclinical hemi-inattention (Jalas et al., 2002). In the study of Samuelsson et al. (1996) the stimulus sheets in the line and star cancellation tasks were divided into three columns on both sides of the midline, and the cancellation start column was recorded. Rightward bias was initially found in right hemisphere patients with or without VN, and patients with severe VN showed a strong tendency to start on the right hemispase, regardless of the type of task (Samuelsson et al., 1996). After a 7-month follow-up significant differences were found between healthy controls and patients with VN or patients who had recovered from VN (Samuelsson et al., 1996). In conventional VN tests automatic rightward bias is significantly associated with the presence of left VN (Samuelsson et al., 1996). Azouvi et al. (2006) later suggested that approximately 80% of healthy controls used a left-to-right visual scanning strategy, while the majority of VN patients used a reverse pattern. In their studies (Azouvi et al., 2002, 2006) the stimulus sheet was divided into seven columns (three on both sides and one in the middle) and the cancellation start column was operationally defined.

Rightward bias is evidently an essential element of neglect syndrome (Gainotti, D'Erme, & Bartolomeo, 1991; Lådavas, Carletti, & Gori, 1994; Mattingley et al., 1994). It is strongest in VN patients, but also evident in patients with milder attention deficits (Gainotti et al., 1991), regardless of the degree of neglect recovery (Mattingley et al., 1994). It seems that patients who tend to start cancellation tasks from the right hemispase also manage to search for targets on the left side using compensatory right-to-left visual strategies and thus do not meet typical neglect criteria. Latent residual VN that is not detectable in repeated tasks of VN may continue to cause difficulties in everyday life. It seems that patients with mild VN are able to anticipate their skewed spatial orientation and to compensate for VN in structured and predictable circumstances (Jehkonen et al., 2000), but novel situations are enough to result in failures and accidents (Webster et al., 1995). Several clinical studies based on paper-and-pencil tasks (e.g., Appelros, Nydevik, Karlsson, Thorwalls, & Seiger, 2004; Cassidy, Lewis, & Gray, 1998; Cherney & Halper, 2001; Jehkonen et al., 2000) have shown that VN typically resolves over time as measured by the number of omissions. Nonetheless there is evidence that

VN is detectable in the acute phase and may be observed up to several months post onset. This may indicate that the measures available for the assessment of VN are not sensitive enough to detect residual but clinically significant VN. Azouvi et al. (2002) found that the spatial location of starting point was the most sensitive measure of VN. Therefore, from a clinical point of view, it is important that starting points are determined in detail so that even patients with residual attentional impairments can be detected.

In this study our aims were to (1) examine the presence of rightward bias in patients with or without VN at baseline and after a 6-month follow-up; and to (2) compare the results with those from a healthy control group. In contrast to previous studies (e.g., Azouvi et al., 2002, 2006; Jalas et al., 2002; Samuelsson et al., 1996), we measured the magnitude of attention gradient in centimeters (cm) using three cancellation tasks. Earlier studies (Azouvi et al., 2002; Jalas et al., 2002; Mattingley et al., 1994; Samuelsson et al., 1996) have measured rightward bias using mainly dichotomous variables (left vs right) or an ordinal scale (columns), and functional and neurological outcomes have not been systemically reported (e.g., Jalas et al., 2002; Mattingley et al., 1994). Furthermore, results have only been reported for the acute phase of stroke (e.g., Jalas et al., 2004; Nurmi et al., 2010).

Our hypothesis in this study was that we would see a similar rightward bias after right hemisphere stroke as has been reported previously (e.g., Jalas et al., 2004; Samuelsson et al., 1996). Furthermore, we hypothesized that the magnitude of rightward bias will decrease during the follow-up in patients with VN, but differences between healthy controls and right hemisphere stroke patients will still remain.

METHOD

Patients

The patients for this study who were admitted to a university hospital as emergency cases between June 2005 and June 2008 were selected on the basis of an acute focal neurological deficit (left hemiparesis or left-sided weakness). Brain infarct was verified with computerized tomography (CT). Patients with a previous neurological or psychiatric history and aged 80 years or over were excluded. Only right-handed right hemisphere patients with first-ever stroke were included. In our study there were 10 patients with and 27 without VN, and 49 healthy controls. Figure 1 describes the process of patient selection.

The study was approved by the ethics committee of the university hospital. During their hospital stay all patients received physiotherapy or occupational therapy according to the hospital department's standard protocol for stroke patients. The patients did not receive any cognitive rehabilitation. Informed consent was obtained from all the participating patients.

PROCEDURE

The patients were examined at two time points. The first neuropsychological examination was conducted on average 3.6 days (± 1.8 ; range 1–9 days), and the first

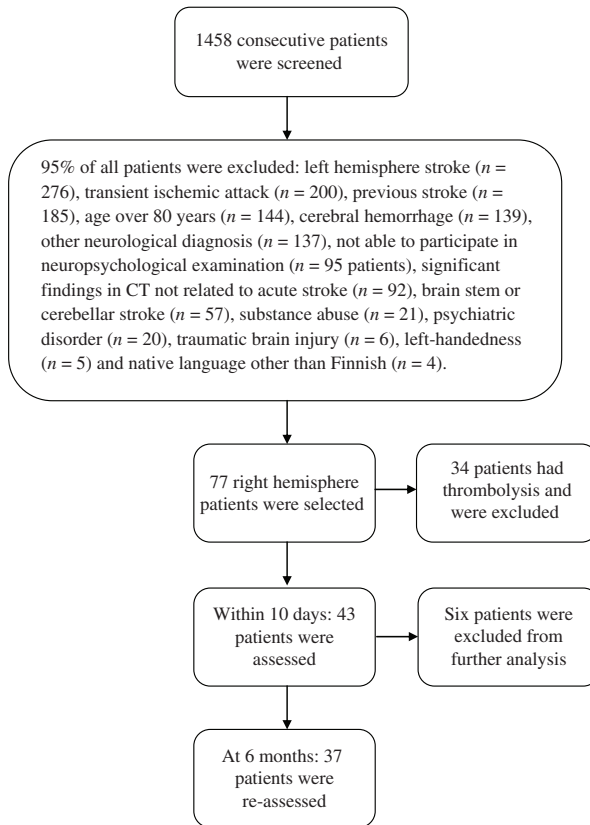


Figure 1. Selection criteria for acute ischemic right hemisphere stroke patients

neurological examination on average 3.6 days (± 2.2 ; range 1–10 days) post-stroke. Follow-up neuropsychological and neurological examinations were carried out on average 189.5 days (± 10.6 ; range: 160–222 days) after completion of the first series of tests at the acute phase. None of the 37 patients had a recurrent stroke during the follow-up. All neuropsychological examinations were performed by the same neuropsychologist and neurological examinations by the same neurologist.

Presence of VN was evaluated with the six conventional paper-and-pencil subtests of the Behavioral Inattention Test (BITC) (Wilson, Cockburn, & Halligan, 1987). This standardized test battery for VN includes three distinct target cancellation tasks, figure and shape copying, line bisection, and representational drawing. The maximum total score is 146. Patients, who scored at or below the cut-off point (≤ 129) for the total BITC score, or below the cut-off score on at least two of the six BITC subtests, were considered to have VN. The cut-off points for each subtest were the same as used in Halligan, Marshall, and Wade (1989). VN was dichotomized as present or absent.

Starting points were determined using the line, letter, and star cancellation tasks. Each standard task sheet (A4) was placed directly in front of the patient and

aligned with his or her midsagittal plane. The patient was not allowed to move the sheet during the task, and no time limit was imposed. The patient's starting point was marked in each task and its distance was measured from the center of the page in centimeters. Values on the left of the true midpoint were given a negative sign, values on the right a positive sign. All patients were assessed in a sitting position.

A complete neurological examination including confrontational assessment of hemianopia was performed based on the National Institute of Health Stroke Scale (Goldstein, Bertels, & Davis, 1989) (NIHSS: 0–1 = none or minimal symptoms, 2–8 = mild symptoms, 9–15 = moderate symptoms, ≥ 16 = severe symptoms), the most commonly used test for evaluating outcome in acute stroke trials. Hemianopia was scored as absent or present. Basic activities of daily living (ADL) were measured using the Barthel Index (Mahoney & Barthel, 1965) (BI; range 0–100: 0–50 = full dependency, 55–90 = moderate dependency, 95–100 = functional independence), which comprises 10 items measuring feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, chair/bed transfer, ambulation, and stair climbing. The maximum score implies full functional independence, not necessarily a normal status. A good or favorable outcome at 6 months was defined as a BI score of 95 or 100.

CT of the brain was performed 3–4 hours from onset to verify the side and size of the infarction. Stroke location was evaluated by an experienced neuroradiologist who was blind to the neuropsychological and neurological data. Native axial 5-mm/7.5-mm slices were taken from the level of foramen magnum to the vertex of the skull on a modern 16 multi-detector CT machine (GELIGHTSPEED RT16, Wisconsin, USA). The sizes of the infarction were determined on the basis of the CT images by a method described by Broderick, Brott, Duldner, Tomsick, and Huster (1993).

Controls

A reference sample of 49 right-handed healthy controls was drawn for the neuropsychological examination from local pensioners' clubs and from among the researchers' acquaintances (e.g., family members, friends or volunteers who came to our attention by word of mouth). Before the examinations the control group was screened using a semi-structured interview for possible history of alcohol abuse and psychiatric or neurological disorders. The possible presence of general cognitive decline was evaluated with the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975); the cutoff score for exclusion from the study was 24. All the participants were Finnish, studied in their primary language, and were blind to the hypotheses of the study.

Statistical analyses

Since some of the parameters were not normally distributed and the sample sizes were small, we chose to use non-parametric tests for continuous variables. Group differences in continuous variables between patients with and without VN were analyzed using the Mann-Whitney U test. Differences in categorical variables were analyzed with the χ^2 test. Correlations between ADL outcome and starting

point in three cancellation tasks were analyzed according to Spearman rho. Recovery was measured in terms of change from baseline to follow-up. Changes between two time points were analyzed with the Wilcoxon test (continuous variables) or the McNemar test (categorical variables). Comparisons between all three groups (the two patient groups and the healthy control group) were carried out using the Kruskal-Wallis analysis of variance. Multiple pairwise comparisons between patient groups and healthy controls were conducted using the Mann-Whitney *U* test with Bonferroni corrections (*p*-values were multiplied by three). The level of statistical significance was set at 0.05 for all analyses. All reported *p*-values are based on two-tailed tests. Cohen's *d* (Cohen, 1988, 1992) was used for both within- and between-group comparisons: small effects ≤ 0.20 , medium 0.20 to 0.50, and large > 0.80 .

RESULTS

Baseline data

First, 34 right hemisphere patients who received thrombolytic treatment at the acute phase of stroke were excluded (five of them had VN and hemianopia). Second, six patients were excluded from further analysis because they did not participate in the follow-up study. These six patients did not differ significantly from the other right hemisphere patients with respect to age, education, gender, stroke severity, basic ADL, infarct size, BITC sum score, presence of hemianopia, or presence of VN. Two of the excluded patients had VN and one had hemianopia.

After application of the exclusion criteria, the final study group consisted of 37 right hemisphere brain infarct patients, 10 (27%) of whom had VN. The two groups (VN+ vs VN-) did not differ significantly with respect to age, gender, or presence of hemianopia. The VN+ group had a significantly higher NIHSS score ($p = .001$), larger infarct size ($p = .013$), lower BITC sum score ($p < .001$), were less educated ($p = .044$), and were more dependent in basic ADL ($p < .001$) than the VN- group. The patients' clinical characteristics are described in Table 1.

The right hemisphere lesions were mainly located in the following brain regions: 3 (11.5%) in the frontal area, 11 (42.3%) in the temporal area, 3 (11.5%) in the occipital area, 1 (3.8%) in the fronto-parietal area, 1 (3.8%) in the fronto-temporal area, 2 (7.7%) in the occipito-temporal area, 3 (11.5%) in the fronto-parietal-temporal area, and 2 (7.7%) in the parietal-temporal-occipital area. Most of the infarcts (69%) were located in the middle cerebral artery.

Table 2 shows the results of each conventional subtest and the total BITC score for each VN patient at the acute phase of stroke and after the 6-month follow-up. The scores of only two VN patients were not at or below the cut-off point (≤ 129) for the total BITC sum score. In the star cancellation task the results of all the VN patients were at or below the cut-off score. In the line cancellation task 90% of the VN+ group and 33% of the VN- group started from the right; in the letter cancellation task the figures were 50% and 4%; and in the star cancellation task 80% and 44%, respectively.

Table 1. Clinical and demographic characteristics of patients with or without visual neglect and healthy controls

Descriptive variables	VN+ (<i>n</i> = 10)	VN- (<i>n</i> = 27)	HC (<i>n</i> = 49)
Male/female	7/3	21/6	21/28
Age: Md (range)	65 (56–79)	62 (36–78)	59 (30–80)
Education (years): Md (range)	8.5 (6–10)	10 (6–20)	11 (5–17)
Infarct size: mean cm ³ (<i>SD</i>)	27.1 (23.5) ^a	7.1 (9.7) ^c	
Hemianopia: present (%)	1 (11)	3 (11)	
Neurological examination: mean (<i>SD</i>)	4.5 (2.8)	3.3 (1.9)	
Neuropsychological examination: mean (<i>SD</i>)	4.4 (2.6)	3.3 (1.5)	
Follow-up examination: mean (<i>SD</i>)	186.3 (10.7)	190.7 (10.4)	

Md = median; *SD* = standard deviation; VN+ = patients with visual neglect; VN- = patients without visual neglect; HC = healthy controls; ^amissing value for one patient; ^bthree patients had missing values; ^c12 patients had missing values; Neurological examination = days from onset to first neurological examination; Neuropsychological examination = days from onset to first neuropsychological examination; Follow-up examination = days from onset to second neuropsychological and neurological examinations.

Analyses of the starting points

Starting points revealed a clear rightward bias: the VN+ group started more often on the right side than the VN- group. Statistically significant differences were found in the line cancellation ($p = .004$, $d = -1.53$), letter cancellation ($p = .001$, $d = -1.48$), and star cancellation ($p = .003$, $d = -1.03$) task.

In the VN+ group four patients (40%) started all cancellation tasks (3/3) from the right; four patients (40%) started two tasks from the right (2/3), and two patients (20%) started one task from the right (1/3). In the VN- group one patient (4%) started three tasks from the right, five patients (19%) started two tasks from the right, and nine patients (33%) started one task from the right.

BI and starting point in the star cancellation task showed a statistically significant correlation ($r = -.443$, $p = .011$), indicating a possible impact of residual VN on daily functioning. None of the other differences was statistically significant.

Follow-up data

The results for the two time points are summarized in Table 3. At 6 months only two patients had VN and one patient had hemianopia. The VN+ group had more severe strokes ($p = .02$, $d = -0.98$) and lower BITC sum scores ($p = .013$, $d = 1.12$) than the VN- group.

In both groups the follow-up results for stroke severity and basic ADL showed a significant improvement compared to baseline. The VN+ group had significantly higher BITC sum scores at follow-up than at baseline. A favorable ADL outcome was found in 90% of the patients in the VN+ group and in 100% of the VN- group.

Table 2. Results of six conventional Behavioral Inattention Tests for patients with visual neglect at two time points

Patient number	Line cancellation	Letter cancellation	Star cancellation	Figure and shape copying	Line bisection	Representational drawing	Total BITC
	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd	1st/2nd
1	*14/36 (R/L)	*5/40 (R/L)	*8/54 (R/L)	*1/4	*0/8	3/3	*31/145
2	*17/36 (L/L)	*14/32* (R/L)	*17/46* (R/L)	*0/4	*0/9	3/3	*48/130
3	36/36 (R/L)	*22/34 (R/L)	*10/54 (R/R)	*2/4	*6/9	3/3	*74/140
4	36/36 (R/R)	*28/34 (R ^a)	*40/51* (R/L)	4/4	*6/9	3/3	*117/137
5	*32/36 (R/R)	33/37 (L/L)	*38/42* (R/R)	*3/4	8/9	3/3	*117/131
6	36/36 (R/R)	35/39 (L/R)	*46/52 (R/R)	*2/4	*2/9	3/3	*124/143
7	36/36 (R/L)	*27/36 (R/L)	*47/54 (R/L)	4/4	8/9	3/3	*125/142
8	36/36 (R/L)	34/40 (L/L)	*43/53 (R/R)	4/4	9/9	3/3	*129/145
9	36/36 (R/L)	34/32* (L/L)	*51/51* (L/L)	4/4	*7/9	3/3	135/135
10	36/36 (R/R)	38/36 (L/L)	*49/52 (L/L)	4/4	8/9	*2/ ^a	137/137

Starting points (L = left, R = right) in the three cancellation tasks are given in parentheses.

BITC = sum score of six conventional subtests of the Behavioral Inattention Test (range 0–146; ≤ 129 = visual neglect, ≥ 130 = no visual neglect); * = results at or below cut-off for each subtest and total BITC sum score within 10 days (1st) and at six months (2nd); ^amissing data.

Table 3. Sum scores of Behavioral Inattention Test, National Institute of Health Stroke Scale, Barthel Index, and starting points in three target cancellation tasks at each assessment in patients with or without visual neglect and comparisons between the two time points

Recovery group	Assessment time		<i>p</i> -value	<i>d</i> -cohen
	Within 10 days	6 months		
<i>VN+</i> group (<i>n</i> = 10)				
BITC: Md (range), mean (<i>SD</i>)	120.5 (31–137), 103.7 (38.3)	138.5 (130–145), 138.5 (5.4)	0.012	-1.27
BI: Md (range), mean (<i>SD</i>)	75 (30–95) ^a , 69.4 (21.9)	100 (85–100), 97.0 (4.8)	0.011	-1.74
NIHSS: Md (range), mean (<i>SD</i>)	6.5 (1–10), 6.1 (2.8)	1 (0–6), 1.9 (2.3)	0.007	1.63
Line cancellation: mean cm (<i>SD</i>)	9.4 (5.2)	-2.5 (11.2)	0.008	1.37
Letter cancellation: mean cm (<i>SD</i>)	0.7 (9.8)	-7.5 (8.1)	0.161	0.92
Star cancellation: mean cm (<i>SD</i>)	6.6 (9.8)	-1.6 (10.5)	0.110	0.80
<i>VN-</i> group (<i>n</i> = 27)				
BITC: Md (range), mean (<i>SD</i>)	143 (132–146), 142.6 (3.2)	144 (138–146), 143.2 (2.3)	0.604	-0.21
BI: Md (range), mean (<i>SD</i>)	100 (35–100) ^b , 92.9 (17.3)	100 (95–100), 99.3 (1.8)	0.041	-0.52
NIHSS: Md (range), mean (<i>SD</i>)	2 (0–8) ^b , 2.3 (2.0)	0 (0–2), 0.3 (0.6)	<.001	0.55
Line cancellation: mean cm (<i>SD</i>)	-3.9 (10.1)	-3.7 (10.2)	0.585	0.02
Letter cancellation: mean cm (<i>SD</i>)	-10.7 (4.7)	-11.7 (0.3)	0.777	0.32
Star cancellation: mean cm (<i>SD</i>)	-3.1 (9.0)	-4.8 (10.6)	0.233	0.17

Md = median; *SD* = standard deviation; VN+ = patients with visual neglect; VN- = patients without visual neglect; BITC = sum score of six conventional subtests of the Behavioral Inattention Test (range 0–146; ≤ 129 = visual neglect, ≥ 130 = no visual neglect); NIHSS = sum score of the National Institute of Health Stroke Scale (range: 0–34; 0 = no defect; 34 = severe stroke); BI = sum score of the Barthel Index (range 0–100; 0–50 = full dependency, 55–90 = moderate dependency, 95–100 = functional independence); ^amissing value for patient; ^bthree patients had missing values.

Table 4. Starting point locations in the three cancellation tasks and comparisons between the healthy controls and patients with or without visual neglect

Task	Group	Mean cm (<i>SD</i>)	Kruskal-Wallis	Compared pairs	Mann-Whitney U	<i>p</i> -value
Line cancellation	HC	8.7 (6.4)	2.906; <i>df</i> =2; <i>p</i> =0.234	HC vs VN–	496.5	<i>ns</i>
	VN–	–3.7 (10.2)		HC vs VN+	231.0	<i>ns</i>
	VN+	–2.5 (11.2)		VN– vs VN+	124.0	<i>ns</i>
Letter cancellation	HC	11.4 (1.0)	7.269; <i>df</i> =2; <i>p</i> =0.026	HC vs VN–	557.0	<i>ns</i>
	VN–	–11.7 (0.3)		HC vs VN+	130.5	0.036
	VN+	–7.5 (8.1)		VN– vs VN+	60.0	0.069
Star cancellation	HC	10.3 (4.7)	10.906; <i>df</i> =2; <i>p</i> =0.004	HC vs VN–	441.0	0.033
	VN–	–4.8 (10.6)		HC vs VN+	117.0	0.009
	VN+	–1.6 (10.5)		VN– vs VN+	109.0	<i>ns</i>

SD = standard deviation; VN+ = patients with visual neglect; VN– = patients without visual neglect, HC = healthy controls; *ns* = non significant.

Healthy controls and comparisons between the patient groups

The group of healthy controls comprised 49 participants, 28 (57%) of whom were men. The median age was 59 years (range: 30–80), median duration of education 11 years (range: 5–17), and median BITC sum score 142 (range: 133–146). None of the controls suffered from any neurological or psychiatric illness. The VN+, VN–, and healthy control groups did not differ significantly according to sex, $\chi^2(2) = 3.382$; *p* = .184, or age, $\chi^2(2) = 1.601$; *p* = .449, but significant difference was found years of education, $\chi^2(2) = 6.980$; *p* = .031. Duration of education was significantly longer in the control group than in the VN+ group (*p* = .010). The participants' clinical characteristics are described in Table 1.

Analyses of the starting points

The mean and standard deviation (*SD*) of starting points in the three cancellation tasks for all three groups are presented in Table 4. The Kruskal-Wallis test showed significant differences between all three groups in their starting point in the letter cancellation and the star cancellation tasks. More detailed analyses using multiple pairwise comparisons revealed that the healthy control group differed significantly from the VN+ group in the letter cancellation and the star cancellation tasks and from the VN– group in the star cancellation task. The VN+ group did not differ significantly from the VN– group in any tasks, but a tendency toward significance was found in the letter cancellation task. None of the other differences was statistically significant. Between two patient groups the effects size was small in line cancellation task (*d* = –0.11), medium in star cancellation task (*d* = –0.29), and large in letter cancellation task (*d* = –0.74).

In each task the healthy control group tended to start the cancellations mainly from the left side of the task sheet. In the line cancellation task 71% of the controls

started from the left; in the letter cancellation task the figure was 100%; and in the star cancellation task 80%. None of the healthy controls started all the cancellation tasks from the right; two (4%) controls started from the right in two tasks and four (8%) controls started from the right in one task.

In the line cancellation task 40% of the VN+ group and 41% of the VN– group started from the right; in the letter cancellation task the figures were 50% and 0%; and in the star cancellation task 40% and 26%, respectively. The results for individual tasks in the VN+ group indicated that one patient (1/10) started all three cancellation tasks from the right, one patient (1/10) started two tasks from the right, and four patients (4/10) started one task from the right. In the VN– group eight patients (29.5%) started from the right in two tasks, and three patients (11.1%) started from the right in one task (see Table 2).

DISCUSSION

In this study our aims were to examine the presence of rightward bias in right hemisphere patients with or without VN at baseline and at 6 months post-stroke, and to compare their results with those of a healthy control group. In contrast to the previous literature we measured rightward bias in centimeters at the acute phase and 6 months after stroke. We expected to find the same degree of rightward bias after right hemisphere stroke as has been reported earlier (e.g., Jalas et al., 2004; Samuelsson et al., 1996). We also hypothesized that the magnitude of rightward bias would decrease during the follow-up in patients with VN, but that differences between the healthy controls and right hemisphere patients will still remain. To the best of our knowledge this is first study where rightward bias in cancellation tasks has been measured in centimeters 10 days and 6 months after stroke.

At baseline the VN+ group showed clearly stronger rightward bias and they were more dependent in basic ADL than the VN– group. At follow-up the magnitude of rightward bias decreased in the VN+ group, but was still present. The VN+ group still showed stronger rightward bias than the VN– group, but a statistically significant difference was not found. Only a tendency toward significance was found in the letter cancellation task. A favorable basic ADL outcome was observed in 90% of the VN+ group and in the whole VN– group. Healthy controls differed significantly from the VN+ group in the letter cancellation and the star cancellation tasks and from the VN– group in the star cancellation task.

An important finding replicated in several studies (e.g., Gainotti et al., 1991; Jalas et al., 2004; Mattingley et al., 1994; Samuelsson et al., 1996) using different measures and different sample sizes of right hemisphere patients was that at baseline, rightward bias was more evident in VN patients than in patients without VN. Our results also suggest that not all VN patients showed a clear rightward bias and it might depend on the tasks used. An examination of individual starting points revealed that five VN patients started from the left in the letter cancellation task, one patient in the line cancellation task, and two patients in the star cancellation task. It has been suggested that a pseudo-random arrays stimulus sheet induces more rightward orienting than structured arrays (Jalas et al., 2002; Samuelsson et al., 1996; Weintraub & Mesulam, 1988). Samuelsson et al. (1996) proposed that the star cancellation task does not present distinct clues that force the patient to

start on the left or the right side of space. Our result might lend at least partial support to these arguments, but caution is needed when interpreting rightward bias as a sign of pathological performance (Jalas et al., 2002) in one type of cancellation task only. We also found that the star cancellation task was the only task in which all the VN patients showed a result at or below the cut-off score, confirming earlier suggestions that star cancellation might be particularly sensitive to identifying VN (Halligan et al., 1989; Jehkonen et al., 1998; Lindell et al., 2007).

The VN+ group showed stronger rightward bias than the VN- group in all three cancellation tasks at baseline. This is in line with results from previous clinical studies (Jalas et al., 2002; Samuelsson et al., 1996). Our result lends support to the assumption that an automatic orientation toward the right is an essential component behind VN (Gainotti et al., 1991; Mattingley et al., 1994). In additional analyses of individual test scores we found that only one patient in the VN- group started from the right in the letter cancellation task. Samuelsson et al. (1996) suggested that the letter cancellation task might include cues that forced patients to start the task from the left side, since reading and writing are from left to right in many languages. In our study a right-to-left strategy was uncommon in the letter cancellation task. In the star cancellation task almost half of the patients without VN started from the right, suggesting that some patients who according to BITC scores do not have clear-cut VN may still suffer from a residual inattention problem. The detection of these problems depends on the tasks used.

At follow-up the magnitude of rightward bias decreased clearly in the VN+ group compared to baseline, but the difference was statistically significant only in the line cancellation task. In the VN- group no such change was seen. Nevertheless the results in the VN- group showed stronger left-sided lateralization than the results in the VN+ group. This supports the assumption that residual attention problems were still present in the VN+ group even though most of the VN patients improved during the follow-up (as measured by BITC sum scores).

Some right hemisphere stroke patients who do not develop clear-cut VN may still suffer from rightward bias (Jalas et al., 2002). At follow-up, none of the patients in the VN+ group had VN according to their total BITC sum score. Nonetheless one patient started from the right in all three cancellation tasks, and four patients (40%) started from the right in two cancellation tasks. Rightward bias was also found in the VN- group. Eight patients (29%) in the VN- group started from the right in two cancellation tasks. These results might indicate that both right hemisphere stroke groups include patients who do not develop clear-cut VN as assessed with BITC, but they might have signs of residual VN (rightward bias). It is possible that when a patient is fully concentrating on a task, they may be able to compensate for their VN symptoms. It should be emphasized that the number of left-sided omissions should not be considered the sole marker of VN, but the pattern of visual scanning should also be taken into consideration (Azouvi et al., 2006).

Webster et al. (1995) reported that rightward bias in clinical tasks in right hemisphere patients was associated with an increased risk of wheelchair accidents. In our study we found a significant correlation between starting point in the star cancellation task and BI in VN patients, suggesting that residual VN has a possible impact on daily functioning. An association between BI and rightward starting point was seen only in the star cancellation task, which has been previously

described as the most sensitive cancellation task (Agrell, Dehlin, & Dahlgren, 1997; Halligan et al., 1989; Jehkonen et al., 1998; Lindell et al., 2007).

At follow-up a favorable ADL outcome (BI > 95) was found in 90% of the VN+ group and in the whole VN- group, but BI mean score for the two groups did not differ at follow-up. This result might be due to the small sample size and/or the evaluation method used. The BI scale measures only motor abilities and does not cover cognitive domains. Therefore it is recommended that future research examine whether rightward bias affects more complex functions such as employment or driving.

At follow-up both patient groups, and the VN+ group in particular, seemed to be more right-biased than the healthy controls. This result might indicate that recovery of attention was not complete 6 months post-stroke, and residual symptoms of VN were still evident at follow-up. Samuelsson et al. (1996) found similar results. Based on these findings it is suggested that clinicians schedule follow-up evaluations for VN no earlier than 6 months after initial evaluation at onset.

Although our patient sample size was small, one of the strengths of our study is that it was carried out in a homogeneous group of consecutive right hemisphere patients with or without VN who had suffered their first brain infarct. Second, the presence of VN was assessed in each patient using a systematic battery of standard paper-and-pencil tasks which is in widespread clinical use and focused on assessing extrapersonal neglect in near space. Third, the location of the starting point was measured in centimeters, which is a more accurate procedure than that used in previous studies.

The main limitation of our study is the small number of patients, which limits the generalizability of the results. Our findings should therefore be considered with caution. Due to the small group sizes we used a categorized variable when defining the presence of VN, and therefore all VN patients were grouped together. Because of this we were unable to examine the association between the subtype or severity (e.g., mild, moderate, severe) of VN and the starting points. We also excluded 34 right hemisphere patients who received thrombolytic treatment. Recent studies suggest that thrombolytic treatment is a significant predictor of earlier discharge to home (Ruskanen et al., 2010) and it is related to a favorable effect on visuoperceptual functions in acute phase of stroke (Laihosalo et al., 2010). We assume that the patients with thrombolysis have a favorable effect on cognitive function in acute phase of stroke and therefore they were excluded in this study. This needs to be more carefully examined in future studies.

Our healthy controls and patients in the VN- group appeared to have a longer education than the VN+ group, and at the second assessment, the BITC sum score was also higher in the VN- group than among the controls. In this study the right hemisphere patients were evaluated at two points of measurement (at baseline and at follow-up) using the same protocol, but the controls were evaluated only once. The results from the second assessment of the right hemisphere patients probably reflect at least some learning effect, which might at least in part explain the differences between the controls and the results for the VN- group. Azouvi et al. (2006) found that education had a significant effect on the performance of healthy controls in cancellation tasks: less-educated healthy participants had a greater

number of omissions than those with longer education. Our results suggest that caution is needed when interpreting the results for healthy participants, and these factors (e.g., education) should be given closer consideration in future studies.

The main conclusions of our study are as follows. At baseline, VN patients showed a strong rightward bias. At 6 months, VN was likely to have improved as measured by BITC sum scores, but symptoms of mild or residual attention (bias) problems were still detected. Our findings lend support to the multicomponent picture of VN. For clinical purposes it seems to make sense to determine patients' starting points in cancellation tasks after right hemisphere stroke in centimeters both at baseline and at 6 months. This might provide important additional information about the presence of mild or residual VN, which may have an impact on daily functioning.

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REFERENCES

- Agrell, B. M., Dehlin, O. I., & Dahlgren, C. J. (1997). Neglect in elderly patient: A comparison of five tests. *Psychiatry and Clinical Neurosciences*, *51*, 295–300.
- Appellos, P., Nydevik, I., Karlsson, G. M., Throwalls, A., & Seiger, Å. (2004). Recovery from unilateral neglect after right hemisphere stroke. *Disability and Rehabilitation*, *26*, 471–477.
- Azouvi, P., Bartolomeo, P., Beis, J.-M., Perennou, D., Pradat-Diehl, P., & Rousseaux, M. (2006). A battery of tests for quantitative assessment of unilateral neglect. *Restorative Neurology and Neuroscience*, *24*, 273–285.
- Azouvi, P., Samuel, C., Louis-Dreyfus, A.-L., Bernati, T., Bartolomeo, P., Beis, J.-M., et al. (2002). Sensitivity of clinical and behavioural tests of spatial neglect after right hemisphere stroke. *Journal of Neurology, Neurosurgery and Psychiatry*, *73*, 160–166.
- Barbieri, C., & De Renzi, E. (1989). Patterns of neglect dissociation. *Behavioural Neurology*, *2*, 13–24.
- Bowen, A., McKenna, K., & Tallis, R. C. (1999). Reasons for the variability in the reported rate of occurrence of unilateral neglect after stroke. *Stroke*, *30*, 1196–1202.
- Broderick, J. P., Brott, T. G., Duldner, J. E., Tomsick, T., & Huster, G. (1993). Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. *Stroke*, *24*, 987–993.
- Cassidy, T., Lewis, S., & Gray, C. S. (1998). Recovery from visuospatial neglect in stroke patients. *Journal of Neurology, Neurosurgery and Psychiatry*, *64*, 555–557.
- Cherney, L. R., & Halper, A. (2001). Unilateral visual neglect in right hemisphere stroke: A longitudinal study. *Brain Injury*, *15*, 585–592.

- Cherney, L. R., Halper, A. S., Kwasnica, C. M., Harvey, R. L., & Zhang, M. (2001). Recovery of functional status after right hemisphere stroke: Relationship with unilateral neglect. *Archives of Physical Medicine and Rehabilitation*, *82*, 322–328.
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates Inc.
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*, 155–159.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatry Research*, *12*, 189–198.
- Gainotti, G., D'Erme, P., & Bartolomeo, P. (1991). Early orientation of attention toward the half space ipsilateral to the lesion in patients with unilateral brain damage. *Journal of Neurology, Neurosurgery and Psychiatry*, *53*, 422–426.
- Goldstein, L. B., Bertels, C., & Davis, J. N. (1989). Interrater reliability of the NIH Stroke Scale. *Archives of Neurology*, *46*, 660–662.
- Gottesman, R. F., Kleinman, J. T., Davis, C., Heidler-Gary, J., Newhart, J., Kannan, M., et al. (2008). Unilateral neglect is more severe and common in older patients with right hemispheric stroke. *Neurology*, *71*, 1439–1444.
- Halligan, P. W., Fink, G. R., Marshall, J. C., & Vallar, G. (2003). Spatial cognition: Evidence from visual neglect. *Trends in Cognitive Sciences*, *7*, 125–133.
- Halligan, P., Marshall, J. C., & Wade, D. T. (1989). Visuospatial neglect: Underlying factors and test sensitivity. *Lancet*, *ii*, 908–911.
- Halligan, P., Cockburn, J., & Wilson, B. (1991). The behavioural assessment of visual neglect. *Neuropsychological Rehabilitation*, *1*, 5–32.
- Heilman, K. M., Watson, R. T., & Valenstein, E. (1993). Neglect and related disorders. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 279–336). New York: Oxford University Press.
- Jalas, M. J., Lindell, A. B., Brunila, T., Tenovuo, O., & Hämäläinen, H. (2002). Initial orienting bias in clinical tasks: Normal subjects and right hemisphere stroke patients with and without neglect. *Journal of Clinical and Experimental Neuropsychology*, *4*, 479–490.
- Jehkonen, M., Ahonen, J.-P., Dastidar, P., Koivisto, A.-M., Laippala P., & Vilkki, J. (1998). How to detect visual neglect in acute stroke. *The Lancet*, *351*, 727–728.
- Jehkonen, M., Ahonen, J.-P., Dastidar, P., Koivisto, A.-M., Laippala, P., Vilkki, J., et al. (2000). Visual neglect as a predictor of functional outcome one year after stroke. *Acta Neurologica Scandinavica*, *101*, 195–201.
- Jehkonen, M., Laihosalo, M., & Kettunen, J. E. (2006). Impact of neglect on functional outcome after stroke: A review of methodological issues and recent research findings. *Restorative Neurology and Neuroscience*, *24*, 209–215.
- Lädavas, E., Carletti, M., & Gori, G. (1994). Automatic and voluntary orienting of attention in patients with visual neglect: Horizontal and vertical dimensions. *Neuropsychologia*, *32*, 1195–1208.
- Laihosalo, M., Kettunen, J. E., Koivisto, A.-M., Dastidar, P., Ollikainen, J., & Jehkonen, M. (2010). Thrombolytic therapy and visuoperceptual functions in right hemisphere infarct patients. *Journal of Neurology*, *6*, 1021–1025.
- Lindell, A. B., Jalas, M. J., Tenovuo, O., Brunila, T., Voeten, M. J. M., & Hämäläinen, H. (2007). Clinical assessment of hemispatial neglect: Evaluation of different measures and dimensions. *The Clinical Neuropsychologist*, *21*, 479–497.
- Linden, T., Samuelsson, H., Skoog, I., & Blomstrand, C. (2005). Visual neglect and cognitive impairment in elderly patients late after stroke. *Acta Neurologica Scandinavica*, *111*, 163–168.
- Mahoney, F., & Barthel, D. (1965). Functional evaluation: The Barthel Index. *Maryland State Medical Journal*, *2*, 61–65.

- Mattingley, J. B., Bradshaw, J. L., Bradshaw, J. A., & Nettleton, N. C. (1994). Residual rightward attentional bias after apparent recovery from right hemisphere damage: Implications for a multicomponent model of neglect. *Journal of Neurology, Neurosurgery and Psychiatry*, *57*, 597–604.
- Mesulam, M. M. (1981). A cortical network for directed attention and unilateral neglect. *Annals of Neurology*, *10*, 309–325.
- Nurmi, L., Kettunen, J., Laihosalo, M., Ruuskanen, E.-I., Koivisto, A.-M., & Jehkonen, M. (2010). Right hemisphere infarct patients and healthy controls: Evaluation of starting points in cancellation tasks. *Journal of the International Neuropsychological Society*, *16*, 902–909.
- Ringman, J. M., Saver, J. L., Woolson, R. F., Clarke, W. R., & Adams, H. P. (2004). Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*, *63*, 468–474.
- Robertson, I. H., & Halligan, P. W. (1999). *Spatial neglect: A clinical handbook for diagnosis and treatment*. Hove, UK: Psychology Press.
- Ruuskanen, E.-I., Laihosalo, M., Kettunen, J. E., Losoi, H., Nurmi, L., Koivisto, A.-M., et al. (2010). Predictors of discharge to home after thrombolytic treatment in right hemisphere infarct patients. *Journal of Central Nervous System Disease*, *2*, 73–79.
- Samuelsson, H., Hjelmqvist, E., Naver, H., & Blomstrand, C. (1996). Visuospatial neglect and an ipsilesional bias during the start of performance in conventional tests of neglect. *The Clinical Neuropsychologist*, *10*, 15–24.
- Shulman, G. L., Pope, D. L. W., Astafiev, S. V., McAvoy, M. P., Snyder, A. Z., & Corbetta, M. (2010). Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal fronto-parietal network. *Journal of Cognitive Neuroscience*, *30*, 3640–3651.
- Vuilleumier, P., Schwartz, S., Verdon, V., Maravita, A., Hutton, C., Husain, M., et al. (2008). Abnormal attention modulation of retinotopic cortex in parietal patients with spatial neglect. *Current Biology*, *18*, 1525–1529.
- Webster, J. S., Roades, L. A., Morrill, B., Rapport, L. J., Abadee, P. S., Sowa, M. V., et al. (1995). Rightward orienting bias, wheelchair maneuvering and fall risk. *Archives of Physical Medicine and Rehabilitation*, *76*, 924–928.
- Weintraub, S., & Mesulam, M. M. (1988). Visual hemispatial inattention: Stimulus parameters and exploratory strategies. *Journal of Neurology, Neurosurgery and Psychiatry*, *51*, 1481–1488.
- Wilson, B., Cockburn, J., & Halligan, P. W. (1987). *Behavioural Inattention Test, manual*. Titchfield, UK: Thames Valley Test Company.