Universiteit Utrecht

Visual search in stroke patients using a digitized object cancellation test without markers

Abstract

Stroke patients can have problems regarding visual search, which could affect rehabilitation and activities of daily living (ADL). Lesions in the right hemisphere are associated with disorganized visual search. Visual search can be evaluated with a cancellation test, in which targets that are embedded in a set of distractors, are cancelled. The targets are marked in order to keep track of the search performance. In ADL however, no visual markers appear during visual search. In this study, visual search in stroke patients with lesions in the left hemisphere (LH) or the right hemisphere (RH) was explored with a digitized cancellation test with and without visual markers. The amount of omitted targets, perseverations, intersections, consistency in search direction and the duration of the test performance were extracted to evaluate visual search performance. It was found that more omissions and perseverations were made when no markers were provided. In contrast, search direction was more consistent. Furthermore, patients with lesions in the RH made more omissions, more intersections and showed a less consistent search direction on both versions. In addition, patients with lesions to the RH made more perseverations when no markers appeared in the test.

Name: Eileen Bousché
Email: e.bousche@students.uu.nl
Student number: 3377202

Supervisors
Name: Tanja Nijboer
Contact details: t.c.w.nijboer@uu.nl

Name: Teuni ten Brink
Contact details: t.t.brink@dehoogstraat.nl

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Introduction

In our day to day lives, we continuously scan our environment in order to find objects we can use to achieve our goals (Milne et al., 2013). Visual search can be defined as the cognitive process of finding a target among a set of distractors (Dowdall et al., 2012). Cancellation tests can be used in research regarding visual search. During a cancellation test, a participant is asked to cross out specific targets among distractors. The amount of omitted targets can be used as a measure for spatial inattention (Mark et al., 2004).

Currently, digitized versions of cancellation tests are available with additional software to analyse performance in depth (Dalmaijer et al., 2015). When the cancellation test is digitized, it can provide information about organization of visual search. Ten Brink et al. (2015) evaluated three organizational measures to study visual search strategies in stroke patients, 1) the amount of intersections of lines between consecutive cancelled targets, 2) the average distance between the sequential cancelled targets and 3) the consistency in search direction. They found that intersections were most strongly associated with disorganized search in stroke patients.

Although the cancellation test is a convenient tool to assess visual attention and visual search, still one problem arises with the visual feedback that comes with the marking of targets. Visual feedback in the cancellation test does not coincide with visual search in daily living, in the sense that no marker appears after searching a specific location. One way to overcome this problem is to leave out the markers, in that the cancelled target will not be marked on the computer screen.

In the current study, the first aim was to evaluate search organization of ischemic stroke patients and healthy controls on a cancellation test in a more ecologically valid fashion. In order to test this, organization of visual search on two versions of a cancellation test (with and without visual markers) were compared.

The second aim was to test whether the organization of visual search differed in ischemic stroke patients with either damage to the left hemisphere (LH) or the right hemisphere (RH) and healthy controls. The hypothesis was that stroke patients would search less organized than healthy controls, as Ten Brink et al. (2015) showed that disorganized search on the cancellation test *with* visual marking is correlated to stroke. In contrast, healthy controls tend to use organized search strategies and make few errors on cancellation tests (Warren et al., 2008).

In addition, in a lesion symptom mapping study by Ten Brink et al. (2016), it was found that disorganized search was associated with damage to the right hemisphere. Therefore, it was expected that the RH group would search less organized on both tests compared to the LH group.

Methods

Participants

The data that was used are of ischemic stroke patients who were admitted to De Hoogstraat rehabilitation center for inpatient rehabilitation.

For this study, inclusion criteria for the patients were: 1) ischemic stroke, first or recurrent; 2) lesion side, left or right hemisphere; 3) ability to use a computer mouse; 4) ability to understand and follow the instructions for the tests. Patients with 1) lesions in both hemispheres and 2) a diagnosis other than ischemic stroke were excluded from this study. In addition, healthy controls with the age between 40 and 70 years were included in this study. This range is to match with the age of the patients at group level. Healthy controls were rewarded 10 Euros for participation. Additionally, the consent and test procedures were conform to the standards of the Declaration of Helsinki.

Procedure and tests

Patients were tested between September 2014 to January 2016, within the first two weeks of their admission to the rehabilitation center. Tests that were used for the current study are from the neuropsychological neglect screening that is part of standard care. The whole neglect screening took 45 minutes and consisted of an extinction test and 8 digitized tests: 2 line bisection tests, 4 experimental tests and 2 conditions of an object cancellation test. The digitized object cancellation test was used for the current study and the conditions were: 1) with visual markers and 2) without visual markers.

This test was presented on a 23“ computer screen at a 35,5” distance from the participant. Participants were presented with a field (18,5° x 11°, w x h) of 54 targets (0.6° x 0.6°), and 75 distractors (0,95-2,1° x 0,45-95°) (Ten Brink et al., 2015).

For both conditions, instructions were to click once on every target in the field. The researcher canceled two targets at the bottom of the field as an example. In the condition with markers, after each click, a small circle appeared at the clicked location (i.e. the mark). In the condition without markers, the researcher mentioned that no circles would appear at the clicked location. The test was finished when the participant reported he/she has clicked on all the targets. There was no time limit.

Outcome measures

Demographic and stroke characteristics

The measures that are gathered from the patient's medical records are: age, gender, type of stroke (ischemic), lesion side, time post-stroke (in days), motor abilities that are measured on a Motricity Index (MI) (Fayazi, Dehkordi, Dadgoo & Salehi, 2012), overall cognitive abilities measured with the Mini Mental State Examination (MMSE) (Folstein, Folstein & McHugh, 1957), daily activities scored on the Barthel index (Liu, Unick, Galik & Resnick, 2015) and presence of language and communication deficits scored on the "Stichting Afasie Nederland" (SAN). For each test, the values of the ranges are displayed in Table 1.

The following measures are extracted from the cancellation tests:

- The amount of omissions. Omissions are unmarked targets that measure spatial inattention (Mark et al., 2004).
- The amount of perseverations. Here, additional marks to previously cancelled targets were considered perseverations (Mark et al., 2004; Nys, Van Zandvoort, Van Der Worp, Kappelle & De Haan, 2006). Only non-consecutive perseverations were analyzed: the clicks to targets that are marked again after at least one other target is cancelled in between (Ten Brink et al. 2015).

The organizational measures were based on the study by Ten Brink et al. (2015) and Dalmaijer et al. (2015):

- Intersections: The number of path crossings between consecutive marked targets, corrected for the total amount of cancellations.
- Consistency of search direction: This shows whether the participant is searching in one direction during the whole test. In order to calculate this, the Pearson correlation coefficient (r) is taken from the linear regression of the coordinates of the marked targets relative to the order of the marking process. The highest absolute

correlation of these two will be selected to represent the degree to which calculations were pursued orthogonally (Best *r*).

- Duration: total amount of time that the participant spends on one test.

Analyses

In order to evaluate whether the three groups (LH, RH and healthy controls) differed regarding age, a Kruskal-Wallis test was applied. The distribution of gender among the three groups was evaluated with a Chi square test. Additionally, the stroke characteristics of the two patient groups (LH and RH) were compared by using a Mann-Whitney test.

Furthermore, the data from the cancellation tests was processed using the software Cancellation-Tools by Dalmaijer et al. (2015). The omissions, perseverations, intersections, consistency of search direction and duration were extracted.

To answer the research questions, a mixed measures design analysis of variance (ANOVA) was performed for each measure derived from the object cancellation task (i.e. omissions, perseverations, intersections, consistency of search direction and duration). The within factor was Condition (markers versus no markers). The between factor was Group (LH, RH and controls). Bonferroni corrections and post hoc t-tests were applied to test which Group or Condition contributed to the significant difference.

In addition, to evaluate the interaction effects between Group and Condition, an post hoc ANOVA was conducted to test which group performance was modulated by the test condition.

For the first aim of this study, performance on both conditions of the cancellation test were compared for each measure. With the outcomes derived from the ANOVA, it was determined whether there was a main effect for the factor Condition and an interaction effect between the factors Group and Condition.

For the second aim, performance on the condition without markers was compared between the three groups. The results from the ANOVA were used to determine whether there was a main effect for the factor Group and an interaction effect for the factors Group and Condition.

Results

<u>Demographic and stroke characteristics</u>

The sample consisted of 158 participants, and the means and standard deviations of the demographic and stroke characteristics of this sample are displayed in Table 1. The three groups (LH, RH and controls) were equal in age [$H(2)= 5.26$, $p=.072$], and differed in distribution of gender [$\chi^2(2)= 8{,}688$ $p=.013$].

Furthermore, the two patient groups (LH and RH) were equal in time post stroke onset [$U= 2199.5$, Z= -.254, $p=.799$]; Mini Mental State Exam [$U= 114.0$, Z= -1.350, $p=.177$]; Barthel Index [$U= 1892.00$, Z= -.366, $p=.714$]; Motricity Index Arm [$U= 1854.5$, Z= -1.350, $p=.177$]; Motricity Index Leg [$U= 1997.5$, Z= -.691, $p=.490$]. Patients with left hemisphere lesions had a lower score on the SAN scale [$U= 1013.0$, Z= -5.341, $p< .001$], indicating more symptoms of aphasia in the patients with left hemisphere lesions.

Table 1
Means and standard deviations of demographic and stroke characteristics for each group.

	Controls (N = 20)	**LH** (N = 75)	**RH** (N = 63)
Gender (% male)	40	74.70	63.50
Age (years)	54.60 (8.48)	59.10 (11.85)	59.29 (10.96)
Time post stroke (days)	-	30.05 (36.83)	36.21 (70.78)
MMSE (0-30)	-	25.13 (5.48)	26.71 (3.38)
BI (0-20)	-	12.72 (5.62)	12.42 (5.32)
MI Arm (0-100)	-	67.55 (35.43)	57.10 (39.51)
MI Leg (0-100)	-	73.00 (33.05)	70.45 (32.64)
SAN (1-7)	-	4.33 (2.28)	6.29 (1.14)

Note: LH= Left Hemisphere; RH= Right Hemisphere; MMSE= Mini Mental State Exam; BI=Barthel Index; MI=Motricity Index; SAN=Stichting Afasie Nederland. The values of the range are between brackets behind each scale.

Outcome measures
The results of each outcome measure for each group and condition are depicted in Figure 1.

Omissions

There was a main effect for Condition (marking versus no marking) on the amount of omissions made [$F(1, 133)= 13.25$, $p<.001$, $\eta^2= 0.09$]. Pairwise comparisons revealed more omissions for the condition without marking than the condition with marking ($p<.001$). The post hoc test confirmed the significant difference between the two conditions [$t(139)= -4.88$, $p<.001$]. There was no interaction effect between Group (LH, RH versus controls) and Condition (marking versus no marking) [$F(2, 133)= 2.49$, $p=.08$, $\eta^2= 0.03$].

There was a significant main effect for Group (LH, RH versus controls) on the amount of omissions made [$F(2, 133)= 9.99$, $p<.001$, $\eta^2= 0.15$]. Multiple comparisons indicate that patients with RH made more omissions compared to patients with LH ($p=.001$) and the controls ($p=.002$). There was no difference between patients with LH and controls ($p>.05$). Post hoc tests revealed that patients with RH made more omissions compared to patients with LH on the *no marking condition* [$t(89)= -6.91$, $p=.002$], in contrast to *the marking condition* [$t(91)= -1.87$, $p=.064$]. In addition, patients with RH made more omissions compared to controls on both conditions (marking [$t(76)= 3.63$, $p=.001$]); no marking ([$t(58)= 5.35$, $p<.001$]). The results of the omissions are displayed in Figure 1A.

Perseverations

There was a significant main effect for Condition (marking versus no marking) on the amount of perseverations [$F(1, 133)= 22.71$, $p.=003$, $\eta^2= 0.17$]. Pairwise comparisons showed more perseverations were made on the cancellation test without marking ($p<.001$). The post hoc test confirms the significant difference between the two conditions [$t(139)= -5.97$, $p<.001$].

The effect of Condition (marking versus no marking) was modulated by Group (LH, RH versus controls) [Group x Condition, $F(2, 133)= 6.06$, $p<.001$, $\eta^2= 0.09$]. The post-hoc test [$F(2,136)= 7.06$, $p=.001$, $\eta^2= 0.07$] indicates that patients with RH made more perseverations on the *condition without marking* than patients with LH ($p=.001$) and the control group ($p=.008$). There is no difference between patients with LH and the control group (p=.770).

There was a main effect for Group (LH, RH versus controls) on the amount of perseverations made[F(2, 133)= 6.18, p<.001, η^2= 0.09]. Pairwise comparisons revealed that more perseverations were made by patients with RH compared to patients with LH (p=.005) and the control group (p=.039). There was no difference between the control group and patients with LH (p>.05). Post hoc tests indicate that patients with RH made more perseverations compared to patients with LH on the *no marking condition* [t(70)= 3.27, p=.002], in contrast to the *marking condition* [t(120)= -.79, p=.426]. In addition, there was no significant difference between patients with RH compared to controls on the marking condition [t(76)= -.54, p=.590], in contrast to the no marking condition [t(70)= 3.72, p=.042]where patients with RH made more perseverations compared to controls. The results of the perseverations are displayed in Figure 1B.

Intersections

There was no main effect for Condition (marking versus no marking) [F(1, 133)= 0.00, p=.98, η^2= 0.00] and no interaction effect for Group (LH, RH versus controls) x Condition (marking versus no marking)[F(2, 133)= 0.29, p=.74, η^2= 0.00].

There was a main effect for Group (LH, RH versus controls) on the amount of intersections made [F(2, 133)= 4.16, p=.018, η^2= 0.06], multiple comparisons indicate that patients with RH made more intersections compared to patients with LH (p=.031). Contrastingly, no difference exists between patients with RH and to the control group (p=.108). In addition, there is no difference between patients with LH and the control group (p>.05). Post hoc tests revealed no significant difference in the amount of intersections between patients with RH and patients with LH on the *marking condition* [t(59)= -1.64, p=.105], in contrast to the *no marking* condition, where patients with RH made more intersections[t(89)= -2.44, p=.017]. Additionally, patients with RH made more intersections compared to controls on the *marking condition* [t(58)= 5.35, p<.001] in contrast to the no marking condition [t(71)= 2.24, p=.028].

The results of the intersections are displayed in Figure 1C.

Consistency

There was a main effect for Condition (marking versus no marking) on the consistency in search direction [F (1, 133)= 13.67, p<.001, η^2= 0.10]. Pairwise comparisons indicate that the search direction was more consistent in the test condition without marking (p<.001). The post hoc test confirms the significant difference between the two conditions [t(139)= -3.24, p= .001]

There was no interaction effect between Group (LH, RH versus controls) and Condition (marking versus no marking) [F (2, 133)= 1.55, p=.21, η^2= 0.02].

There was a main effect for Group (LH, RH versus controls) [F (2, 133)= 12,83, p<.001, η^2= 0.19]. Pairwise comparisons revealed that patients with RH showed less consistency in search direction compared to patients with LH (p<.001) and the control group (p=.028). There was no difference between the control group and patients with LH (p>.05). Post hoc tests revealed that patients with RH was less consistent in search direction compared to patients with LH on both conditions (marking [t(77)= 3.83, p<.001]); (no marking [t(75)= 4.53, p<.001]). Additionally, there was no difference in search direction in the performance of patients with RH compared to controls on the *marking condition* [t(32)= -8.68, p=.392] in contrast to the *no marking condition* [t(55)= -3.51, p=.001]. The results of the consistency in search direction are displayed in Figure 1D.

Duration

There was no main effect for Condition (marking versus no marking) [F (1, 133)= 0.24, p=.62, η^2= 0.00], and no interaction effect between Group (LH, RH versus controls) and Condition (marking versus no marking) [F (2, 133)= 0.07, p=.93, η^2= 0.00].

There was a main effect for Group (LH, RH versus controls) on how long it took to take the individual tests [F (2, 133)= 5.99, p=.003, η^2= 0.09]. Multiple comparisons revealed that there was no difference between patients with LH and patients with RH (p>.05). However, the duration in the control group was shorter compared to patients with LH (p=.003) and patients with RH (p=.008). Post hoc tests confirmed the difference between controls and patients with LH (marking [t(81)= -5.41, p<.001]); (no marking [t(67)= -5.32, p<.001]) and patients with RH (marking [t(75)= 4.18, p<.001]); (no marking [t(73)= 4.38, p<.001]). The results of the duration are displayed in Figure 1E.

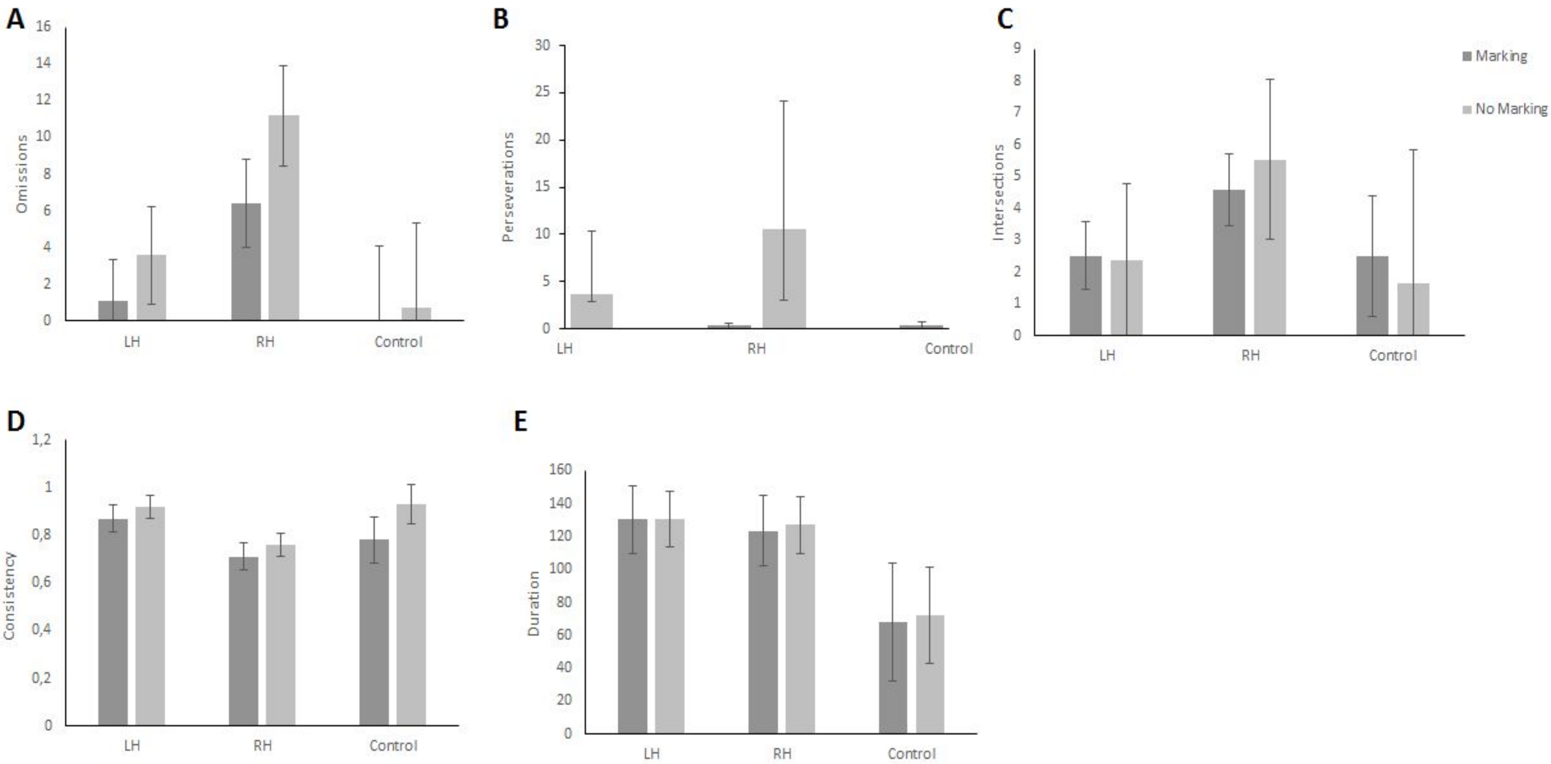

Figure 1. Means and 95% CI (error bars) for each outcome measure, group and condition.
Each graph displays the means of an outcome measure: A) omissions; B) perseverations; C) Intersections; D) Consistency; E) Duration.

Discussion

The first aim was to investigate search organization of ischemic stroke patients and healthy controls on a cancellation test in a more ecologically valid fashion. This was tested by comparing visual search performance on a cancellation task with visual markers and without visual markers. The second aim was to investigate whether the organization of visual search differed in ischemic stroke patients with either damage to the left hemisphere (LH) or the right hemisphere (RH) and healthy controls. This was tested by comparing the performance of the three groups on two versions of a cancellation test. The amount of omissions, perseverations, intersections, consistency in search direction and the duration of performance were evaluated for both aims.

Results indicated that more *omissions* were made when no visual markers were provided during the visual search test compared to the version with visual markers. The same effect was found for patients with RH, patients with LH and the healthy controls. More omissions indicate inattention in general (Mark, et al., 2004), and inattention can be revealed more clearly with the use of the cancellation test without marking, as is consistent with the study by Wojciulik et al. (2006). They pointed out that, compared to a cancellation test with visible markers, performance on a cancellation test without visible markers resulted in more omissions in the contralesional field of patients with hemi-inattention. Hemi-inattention is most often associated with lesions in the right hemisphere (Behrman & Shomstein, 2015; Ptak & Schnider, 2011). Although more omissions were made by the patients with RH in the present study, this effect was not found solely for the version without visual markers and this particular patient group. In that performance on the version without visual markers was not modulated by group type.

In contrast, an interaction effect was in fact found between group and the version regarding the amount of *perseverations*. Patients with RH made more perseverations when no visual markers appeared in the cancellation test compared to the other groups, and compared to the performance on the cancellation test with markers. This is in line with the study by Wojciulik et al. (2006) where more perseverations were found in stroke patients with hemi-inattention on the cancellation test without visual markers in comparison to the version with markers. In the study of Wojciulik et al. (2006), the perseverations were located in the ipsilesional field. The present study did not differentiate between the two sides of the template, which might be interesting to investigate in future research. Additionally, Nys et al. (2016) showed the same results regarding the amount of perseverations made by patients with either right or left hemi-inattention, and they pointed out that the location of the perseverations is more important than the amount of perseverations to differentiate between the two groups. However, the current study provides evidence that lesion side in fact does affect the amount of perseverations made on two versions of a cancellation test.

Furthermore, Nys et al. (2016) also report a significant relation between the amount of perseverations and executive dysfunctioning in subacute stroke patients without hemi-inattention or inattention in general. More specifically, perseverations can reveal inhibitory problems (Dalmaijer et al., 2015). Together with the results of the current study, it can be concluded that when no visual markers are provided, executive functioning is even more challenged than than during the original visual search assessment.

In addition, the amount of perseverations is associated with a spatial working memory deficit, which is often seen in hemi-inattention (Husain et al., 2005). When spatial working memory is impaired, the participant cannot keep track of the targets that are already cancelled. Spatial working memory may be the most important underlying cognitive mechanism in search organization when no visual marking is provided.

Despite the differences between the two versions regarding the amount of omissions and perseverations, the amount of *intersections* remained constant over the two versions of the cancellation test. According to Ten Brink et al. (2015) the amount of intersections is the most important measure to reveal disorganized search, therefore it was expected that the test without marking would elicit more intersections. This constancy in amount of intersections across test versions could be due to the fact that participants used a more consistent search path. On the cancellation test without marking, participants showed more *consistency* in search direction (Best R) in comparison to the condition *with* visual markers. This means that participants were using a more organized search strategy when no markers were given, possibly in order to keep track of the targets they already encountered. This might keep the amount of intersections low in the condition without marking. The number of intersections and the consistency in search direction may be related, except when the search path follows a circular pattern as can be seen in figure 2. Further support for this claim relates to the finding that the opposite pattern was observed in patients with RH: this group made *more* intersections and was *less* consistent in search direction compared to the patients with LH and the healthy controls. These findings overlap with the study by Ten Brink et al. (2016) that provided evidence for the relationship between disorganized search and right hemispheric damage.

Different outcomes were found for the *duration* of the test performance. For both patient groups, it took an equal amount of time to complete each version of the cancellation test. In contrast, it took longer for both patient groups to complete each version, compared to the control group. This may be due to the use of medication in patients, or executive dysfunctioning that is related to stroke (Dalmaijer et al., 2015.).

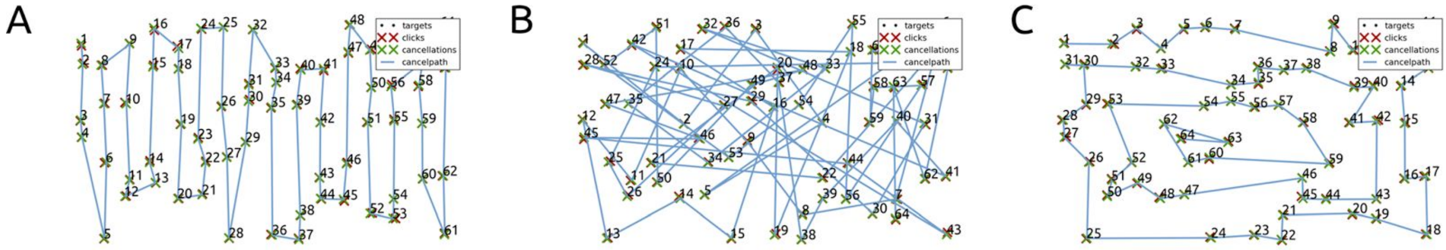

Figure 2. Examples of search paths by Dalmaijer et al. (2015). A= high consistency in search direction and low in intersections, B= low consistency in search direction and high in intersections, C= low consistency and low in intersections: path is circular.

Limitations of this study were the group compositions. As can be seen in figure 1, a large variance exists in the amount omissions, perseverations and intersections, especially in the version without markers. Further research can provide more insight in the effect of the composition of the groups on the visual search task without visual marking. For example, the effect of hemi-inattention can be included in further studies. This might explain the variance in the data, and could provide information for clinical purposes of a cancellation test without markers. Additionally, the two patient groups were based solely on the lesion side. It would be interesting to investigate what brain lesions contribute to disorganized visual search without markers. Therefore a lesion symptom mapping study is recommended to make a more solid statement about disorganized visual search without marking and the corresponding lesions.

Clinical implications are that the cancellation test without visual markers detect problems in visual search that may possibly generalize to daily living. According to Zihl (2000), problems in visual search are common in stroke patients and are associated with inattention and visual disorders. Moreover, problems in visual search lead to reading deficits and immobility which in turn have consequences for rehabilitation and activities of daily living. It may be relevant to investigate search strategies in stroke patients to overcome these problems. The visual search test without markers gets into the root of the problem by investigating several components that are associated with search organization and attention in a more ecologically valid fashion. Each affected component can be addressed in the rehabilitation process which could eventually lead to better outcomes.

In conclusion, through the evaluation of different organizational measures we found that the amount of perseverations differed most between versions. This may be due to the executive functioning and spatial working memory components that become more important during visual search without markers. In addition, the version without markers compared to the original cancellation test reveals more omissions and more consistency in search direction. The higher consistency in search direction is noteworthy, because it may indicate that the lack of visual markers makes people more vigilant to apply a more organized search pattern.

Finally, it is confirmed once more that performance of patients with damage to the left hemisphere are comparable to the performance of the healthy control group, with the exception for the duration it took to complete the tests. Furthermore, the group differences are attributable to right hemispheric lesions, which proves that the right hemisphere is indeed important in visual search tasks. Additionally, the lesions in the right hemisphere are most often associated with hemi-inattention. This raises the question of what the results would be if group selection was based on right or left sided inattention and lesion side.

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