Introduction

Many patients with unilateral neglect exhibit impaired space exploration when searching a visual scene, sensitively indexed by their tendency to mark fewer contralesional targets than ipsilesional ones on cancellation search tasks [1,2]. Recent reports have also noted that neglect patients often return to previously found ipsilesional targets [3–6]. While only a few studies have specifically investigated the cognitive mechanisms underlying space re-exploration, a number of alternate theoretical explanations have been proposed, which potentially offer important insights into this behaviour.

Some authors suggest that revisits might be a type of perseveration [3,4], such as an inability to suppress responses [7] to a just-visited target. By contrast, Manly and colleagues [6] proposed that revisits might be due to the influence of contralesional targets, which they argue result in either covert awareness of un-cancelled targets, spatial transposition of contralesional target locations into ipsilesional space (allochiria) or the displacement of movements towards contralesional targets to ipsilesional ones. Other investigators have used search tasks in which visible marks are not left on explored locations [8–10]. They demonstrated that many neglect patients return to target locations, often unaware they have searched there before, and proposed that these patients have a coexisting spatial working memory (SWM) deficit [8–10]. A failure to keep track of previously searched locations, when combined with a directional bias towards ipsilesional space, might account for re-exploratory behaviour.

In this study, we developed novel touchscreen search tasks to examine more closely space re-exploration in the neglect syndrome. First, our new tests enabled us to track the pattern of target-finding over time. We tested patients on analogues of traditional cancellation tests (in which located targets are marked), as well as on invisible cancellation tests (in which no visible marks are left). If revisits to ipsilesional targets are due to immediate perseveration they would occur directly after a visit to target. By contrast, a SWM deficit should lead to delayed revisits that occur after visiting other targets in the interim. By examining the interval between an initial visit and a return to a location — immediate or delayed — we distinguished between these possibilities.

Second, the mechanisms underlying revisits proposed by Manly et al. [6] all necessitate distinguishing in some way between un-cancelled targets and distractors in contralesional space. Patients with severe neglect, however, make few eye movements to contralesional space [8]. So Manly and colleagues used stimuli that were easily distinguishable in peripheral vision (Manly, personal communication). Conversely, minimizing the peripheral detection of targets should lead to little, or no, revisiting behaviour. Therefore, we used similar targets and distractors that could only be distinguished near fixation.

Third, we investigated the role of ipsilesional salience. Mark et al. [11] proposed that marking ipsilesional targets increased their salience relative to unmarked items, thereby drawing attention to that side of space and exacerbating neglect. The increased salience of cancelled targets might also draw patients to revisit them [4]. If marking targets causes target revisits, there should be fewer revisits on invisible cancellation (where the relative salience of ipsilesional targets is unchanged) than in the visible counterpart. In contrast, a coexisting deficit in SWM [9,12–14] predicts more returns to previously found ipsilesional
targets in invisible cancellation because there is no visual reminder of previously searched locations.

Finally, even if changes in ipsilesional stimulus salience do not cause revisits they might still modulate neglect. So we used two tasks to investigate this issue further. One was an erase task, similar to that of Mark et al. [11], in which targets were removed when touched. In this case, there should be less neglect than in visible cancellation because found targets are not longer marked by visibly salient cancellation marks. Moreover, there is reduced ipsilesional stimulus density because targets are erased. Our second condition was a bold task in which target outlines became thicker when touched, thereby increasing their salience without substantially changing overall stimulus density (as occurs in visible cancellation). Using these four types of search task – visible, invisible, erase and bold – we examined the nature of space exploration in right brain-damaged patients.

**Methods**

Twenty-two right-hemisphere stroke patients (Table 1) consented to participate, in accordance with the Helsinki agreement, and were divided evenly into two groups (n=11), neglect and non-neglect patients (mean age 63.2 years, SD 15.6 vs. 60.9, SD 14.6). The neglect group comprised patients who cancelled two or more targets on the right half of the screen than on the left in the visible cancellation task. Patients sat ~50 cm from the 20.1’’ LCD touchscreen (~45’’ × 35’’) with its vertical midline aligned with the body midline (Fig. 1a). The cancellation experiment was implemented using E-PRIME software (Psychology Software Tools Inc., Pittsburgh, Pennsylvania, USA).

Patients touched a central crossed circle (2.8’’ diameter) to trigger a search array, consisting of 192 black circular elements (64 targets and 128 distractors) on a grey background (Fig. 1a). Each array contained three types of element: whole circles (1.4’’ diameter), circles with a gap (~0.3’) at the top and circles with a gap at the bottom. Search screens comprised 16 columns each containing four of the three element types positioned pseudo-randomly with a jitter (±0.0-0.7’) applied independently to their x and y coordinates. Pilot experiments showed that reliable discrimination (>80% hit-rate) between these three types of stimuli was not possible at eccentricities >7.5’’ from fixation in uncluttered displays. Across all four tasks each participant searched for the same target (circle with a gap at the bottom or at the top), but target type was counterbalanced across individuals. Patients touched as many targets as they could find with no time limit. The four tasks – visible, invisible, erase and bold – were presented in pseudo-random order. In the visible task, an ‘X’-shaped cross was inserted into a touched target; in the bold task the targets’ outline became thicker; and in the erase task the target was deleted. Finally, in the invisible task no changes were made to the display if a target was touched. Data were analysed with Mann–Whitney and Wilcoxon non-parametric tests; high levels of performance of the non-neglect group meant that the data were not normally distributed.

**Table 1** Patient details

<table>
<thead>
<tr>
<th>Patient</th>
<th>Brain lesions†</th>
<th>Days from admission ‡</th>
<th>Neglect on ‡</th>
<th>Patient</th>
<th>Brain lesions†</th>
<th>Days from admission ‡</th>
<th>Neglect on ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.L.</td>
<td>O, T</td>
<td>12</td>
<td>+</td>
<td>B.N.</td>
<td>Ic</td>
<td>45</td>
<td>+</td>
</tr>
<tr>
<td>B.E.</td>
<td>No CT</td>
<td>10</td>
<td>+</td>
<td>C.E.</td>
<td>BG, Ic, I</td>
<td>24</td>
<td>–</td>
</tr>
<tr>
<td>B.Q.</td>
<td>P haem.</td>
<td>44</td>
<td>–</td>
<td>D.O. *</td>
<td>T, Th, BG</td>
<td>325</td>
<td>+</td>
</tr>
<tr>
<td>C.X.</td>
<td>F, P, T</td>
<td>103</td>
<td>+</td>
<td>F.T.</td>
<td>F, P</td>
<td>123</td>
<td>–</td>
</tr>
<tr>
<td>H.N. *</td>
<td>F, P</td>
<td>256</td>
<td>–</td>
<td>H.T. *</td>
<td>P</td>
<td>19</td>
<td>+</td>
</tr>
<tr>
<td>I.I.</td>
<td>F</td>
<td>19</td>
<td>+</td>
<td>K.X.</td>
<td>P, T, BG, Ic</td>
<td>28</td>
<td>+</td>
</tr>
<tr>
<td>K.C.</td>
<td>Sc</td>
<td>18</td>
<td>–</td>
<td>M.P.</td>
<td>F, P</td>
<td>10</td>
<td>–</td>
</tr>
<tr>
<td>K.S.</td>
<td>P, O, T, Th</td>
<td>14</td>
<td>+</td>
<td>N.B.</td>
<td>P, T</td>
<td>180</td>
<td>+</td>
</tr>
<tr>
<td>Q.S.</td>
<td>P haem.</td>
<td>9</td>
<td>+</td>
<td>O.P.</td>
<td>F, P, T</td>
<td>19</td>
<td>+</td>
</tr>
<tr>
<td>X.B.</td>
<td>F, T, BG</td>
<td>20</td>
<td>+</td>
<td>P.F.</td>
<td>Th haem.</td>
<td>21</td>
<td>+</td>
</tr>
</tbody>
</table>

†Denote involvement of frontal (F), parietal (P), temporal (T), occipital (O), basal ganglia (BG), thalamus (Th), internal capsule (Ic), striatocapsular (Sc) and insula (I) haem., haemorrhage.

‡Number of days following admission when patients participated.

Performance on BIT Star or Mesulam shape cancellation within 7 days of admission (Adm) and on the test day (T-day); a plus (+) denotes patients who cancelled two or more targets on the right than the left, a minus (−) the others.

No admission tests were available for two patients (N.B. and Q.Q) referred chronically. On the day of testing, three patients in the neglect group did not demonstrate a lateralized bias on traditional tests but did so on the visible touchscreen task (left−right differences of 7–14), the parameters of which (size, target distractor similarity, etc.) were chosen to maximize sensitivity. All three patients had shown considerable neglect on admission. One non-neglect group patient showed minor lateralized bias on a cancellation test but none on the more demanding touchscreen system. Asterisks indicate patients who performed the non-lateralized spatial working memory task.

**Results**

Across all tasks, neglect patients (1) cancelled fewer targets than the non-neglect group (mean 48 vs. 90%; U=3, P<0.001) and (2) demonstrated a lateralized difference in targets cancelled (z=2.93, P<0.01) (Fig. 2), which confirmed the validity of the patient groupings.

Neglect patients targeted location more often in the invisible task than in the visible task (mean 60.3 vs. 31.7; z=2.49, P<0.05) owing to a clear tendency to re-cancel previously touched targets (cf. Fig. 2a and c). Hence, extensive target revisits occur even when targets and distractors cannot be distinguished in peripheral vision. Strikingly, neglect patients cancelled fewer individual targets on the right in the invisible task than in the visible task, despite making more touches on target locations.
We distinguished between two types of re-cancellation: immediate revisits (directly after touching a target) and delayed revisits (cancelling other targets before returning). Re-cancellations in the invisible task consisted overwhelmingly of delayed revisits (Fig. 1b). For neglect patients, just over half (52%) of target touches in the invisible task were delayed revisits, and only 8% were immediate (the remainder were initial cancellations). The median number of intervening targets touched by neglect patients before a revisit was 8 (IQ range: 4.3–17.5) in the invisible task, which would not be expected from simple repetitive perseveration [for non-neglect patients the values were 21 (14.3–27.5)].

Neglect patients made significantly more delayed revisits than the non-neglect group ($U=23.5$, $P<0.05$). Friedman tests revealed a difference across tasks in the delayed revisit rate (neglect: $w^2=11.85$, $P<0.005$; non-neglect: $w^2=8.97$, $P<0.05$), which was attributable to increased revisits in the invisible task.

The large revisit rate in invisible cancellation, where stimuli remained unchanged, indicate that changes in the relative visible salience of ipsilesional targets cannot account for revisits. Nonetheless, changes in stimulus salience might still effect space exploration. Both patient groups touched more targets when they were erased (reducing the ipsilesional stimulus salience) than in the invisible task (neglect: $z=1.83$, $P<0.05$, one-tailed; non-neglect: $z=2.81$, $P<0.005$, one-tailed) (Fig. 1b), and neglect patients showed a similar trend between the erase and visible tasks ($z=1.6$, $P<0.1$, one-tailed). In the bold task, in which targets were marked without substantial changes to overall stimulus density, both groups performed identically to the visible task.

**Discussion**

In this study, we examined the performance of two groups of right-hemisphere stroke patients, with and without spatial neglect, across a range of search tasks. We compared performance on visible cancellation (analogous to pen-and-paper cancellation) and invisible cancellation tasks (in which no marks were left) to probe the mechanisms underlying target revisits. Both groups of patients showed substantial revisiting behaviour in invisible cancellation tasks consistent with the view that revisits result from separate mechanisms to those causing neglect. Neglect patients, however, made far more revisits than non-neglect
patients despite touching fewer unique targets (due to contralesional omissions), indicating that a SWM deficit may interact with the syndrome. High revisit rates occurred despite the use of stimuli that could not be distinguished peripherally.

Taken together, these findings suggest that the influence of contralesional targets, as proposed by Manly et al. [6], was not a primary cause of target revisits in our tasks. Furthermore, the very small number of revisits in visible tasks (in which cancelled targets were highly salient) and the relatively high number in invisible tasks (Fig. 2) indicate that revisits are not attributable to increased ipsilesional target salience. The vast majority of target revisits consisted of returns after cancelling targets at other locations, rather than immediate re-presses on a target. In the invisible task, revisits comprised over half of screen presses (Fig. 1b) and were biased to the right in neglect patients (Fig. 2c). Re-presses without intervening visits to other locations were rare, and only one neglect patient made more immediate revisits than delayed ones. This suggests that target re-presses by most neglect patients are not a consequence of immediate perseveration but might instead be due to a failure to keep track of searched locations. Such a deficit in SWM has been proposed to coexist and exacerbate the spatial bias defining neglect [15].

Of course, perseverative responses could possibly occur after intervening touches on other targets but we propose that a non-lateralized deficit in SWM, for which there is accumulating evidence [12–16], might explain another aspect of patients' performance. Neglect patients cancelled fewer ipsilesional targets in the invisible task than in the visible one (compare solid lines in Fig. 2a and c). Such a failure to cancel some targets on the right cannot be explained by an account based solely on perseveration. It would, however, be consistent with a SWM deficit, with patients erroneously considering an untouched target to be one they had already found. Thus, a deficit in keeping track of locations can explain both target omissions on the right and increased retouches on other targets on that side. Although not our primary aim, at the suggestion of a reviewer, we compared revisit rates on invisible cancellation and a non-lateralized measure of SWM we have developed [16]. For seven patients (four marked by an asterisk in Table 1 and three previously reported in a drug intervention study [17]) who had performed both tasks, we found a high correlation (r = 0.72, P < 0.05) between target revisits and spatial memory span.

Finally, in a task in which targets were erased we found a small reduction in neglect patients’ lateralized bias similar to, but of smaller magnitude than, that previously reported [11]. These results are consistent with explanations based on SWM, stimulus salience or both. Erasing stimuli means they reported may have been reduced in our paradigm by the presence of ipsilesional distractors, or by the additional SWM load imposed by these items. We also found that performance in the bold task (in which stimulus salience increased without altering display density) was indistinguishable from visible cancellation for the neglect group. This suggests that increases in element density are not critical for explaining the differences between the erase and visible tasks. It leaves open the possibility, however that the difference between the erase and visible tasks may be due to the increased salience of elements in the visible tasks.

Conclusion
Re-exploration of ipsilesional space is an important feature of spatial neglect patients’ search behaviour, especially when there are no visible reminders of explored locations. Revisits occur after intervening visits to other locations and are most prominent on the ipsilesional, supposedly ‘good’, side of space. Neglect patients’ exploratory behaviour appears to be modulated by both a deficit in keeping track of spatial locations and the visible salience of ipsilesional stimuli. Both SWM and the encoding of stimulus salience may be important features underlying normal space exploration.

Acknowledgements
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References