Is the intact side really intact? Perseverative responses in patients with unilateral neglect: a productive manifestation

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1. Introduction

Clinical descriptions of extra-personal spatial unilateral neglect typically emphasize a constellation of ‘negative’ symptoms. Patients fail to report and identify stimuli presented in the contralesional side of space and to explore this portion of space. The disruption of brain systems responsible for the orientation of spatial attention, the organization of motor responses, or the internal representation of the contralesional side of space provide current general explanations to this complex clinical picture, which is usually associated with damage in the right cerebral hemisphere [8,64]. Many observations suggest, however, that control of behaviour is altered also within the ipsilesional, putatively intact, side of space. Firstly, during the execution of cancellation tasks, when the contralesional and the ipsilesional sides are defined with reference to the mid-sagittal plane of the body, right-brain-damaged patients may omit targets in both sides of the sheet, though errors are fewer in the ipsilesional (right) side (e.g. [67,69]. Secondly, right-brain-damaged patients with left neglect...
may show disproportionately slow latencies to visual targets with a left-to-right gradient, rather than with a sharp dichotomy between a ‘preserved’ ipsilesional and a ‘disrupted’ contralesional side of space [15,35,59]. Thirdly, dichotic sound images may be perceived by right-brain-damaged patients with left spatial neglect as displaced towards the right ipsilesional side, throughout the whole auditory space [1,4]. Fourthly, in the phenomenon of ‘alloaesthesia’, which is frequently associated with right brain damage and left neglect, patients report visual or tactile stimuli delivered to the contralesional side of space or body, as if they had been delivered to the ipsilesional side [8,11,31]. A similar incorrect localization of items may be observed in tasks requiring the mental description of visual scenes [3], in copying a figure [25], or in drawing from memory, for example a clock face with all the hours on the right side [3,28,50].

All these manifestations of neglect, which may affect both sides of space, often with a left-to-right gradient of decreasing severity, may be regarded as defective or negative, disrupting visuo-motor exploration, as in cancellation tasks, or perceptual awareness, as in detection or identification tasks. Fewer reports are available on the so-called productive or positive manifestations of unilateral spatial neglect, which may concern the ipsilesional side (reviewed in [64]). Perseveration in drawing and visuo-motor exploratory tasks is a pathological behaviour repeatedly described in right-brain-damaged patients, which may be listed under the rubric of productive disorders [66]. In general terms, perseveration may be defined as the inappropriate iteration of a behaviour or experience, which continues steadfastly after the termination or change of task demands, or in the absence of the appropriate exciting stimulus (e.g. [23,51,56,57]). A manifestation of perseveration associated with right brain damage is the greater tendency of these patients to overscore lines already drawn and to add irrelevant graphic material on the right-hand side of the paper [21]. In a series of 10 right-brain-damaged patients with left spatial neglect, Mark et al. [40] reported that, in a cancellation task, erasing right-sided items improved left neglect, compared to simply marking them with a pencil. A corollary observation was that items cancelled in the ipsilesional space were often marked more than a single time (see other instances of perseveration in cancellation tasks in [7,12,49,63]). These observations were replicated and extended by Na et al. [48], who found perseveration in approximately 30% of 60 right-brain-damaged patients with left spatial neglect.

The present study aimed at investigating in a systematic fashion the relationships between perseverative behaviour in a visuo-motor exploratory task and unilateral spatial neglect, extending the assessment to other types of patients with focal or diffuse brain damage. To explore the specificity of the putative association between spatial neglect on the one hand and perseverative behaviour in cancellation tasks on the other, we did not confine our study to right- and left-brain-damaged patients with contralesional neglect, but included also patients with left- and right-sided hemispheric lesions without neglect, and patients suffering from senile dementia of the Alzheimer-type. Both left-brain-damaged patients (e.g. [21,51,57]) and patients with senile dementia (e.g. [23]) may exhibit perseverative responses in paper-and-pencil drawing tasks.

2. Materials and methods

2.1. Patients

A continuous series of 181 patients entered this retrospective study. Patients were divided into four groups: (i) 35 patients with contralesional spatial unilateral neglect (31 with right-sided hemispheric lesions and left neglect, four with left-sided lesions and right neglect); (ii) 60 patients with right-sided hemispheric lesion without neglect; (iii) 64 patients with left-sided hemispheric lesion without neglect; (iv) 22 patients with a probable senile dementia of the Alzheimer-type, according to the criteria set by McKhann et al. [44]. On the Mini Mental State Examination [20] patients with senile dementia scored 7.8 (d.s. 4.2, range 0–16), below the cut off of 24/30 [45]. In the 159 patients with unilateral focal damage, the site of the lesion was assessed by CT or MRI scan. The aetiology of the focal lesion was vascular in 140 patients and neoplastic in 19 patients. Duration of disease was computed as the number of days elapsed between stroke onset and time of testing. In patients with a neoplastic lesion duration of disease was arbitrarily set to 1. All patients were right-handed and had no history or neurological evidence of bilateral hemispheric damage, psychiatric disorders, or dementia. Contralesional motor, somatosensory and visual half-field deficits, including extinction to tactile and visual stimuli, were assessed by a standard neurological exam [9]. Specifically, visual half fields were assessed using the confrontation technique, with patients being required to detect the movement of the examiner’s index finger. The patients’ demographic features are summarized in Table 1.

2.2. Procedure

2.2.1. Circle cancellation task

Patients were given a visuo-motor exploratory task, widely used as a clinical test for the assessment of unilateral spatial neglect [6]. The patients’ task was to mark or cross out with a pencil all of the 13 circles 1 cm in diameter, printed on an A4 paper sheet (6 in the left
half, 6 in the right, and 1 in the centre). The centre of the sheet was aligned with the mid-sagittal plane of the patient’s trunk. Patients received instructions to commence the cancellation from the central target, which was pointed out by the examiner. This task, which can be easily performed and does not require complex verbal instructions, is suitable for patients suffering from dementia or dysphasia. Patients used the ipsilesional hand: right-brain-damaged patients their right hand, and left-brain-damaged patients their left hand. Throughout the execution of the cancellation task the examiner took care of ruling out the possibility that perseveration represented a defective reaching of the target itself. This possibility would be suggested by the behaviour of a patient who eventually crossed out the target, after a number of crossings in the vicinity of it. No patient showed such a behaviour. Patients who omitted to cross out one or more circles on either the left- or the right-hand side were classified as showing left or right extra-personal visuo-spatial neglect. Normal control subjects exhibit an errorless performance on this task [61].

The current operational definition of ‘perseveration’ included all drawing activities which continued steadfastly after the termination or change of the task demands, namely: circle cancellation. On the basis of previous work on perseveration in cancellation and drawing tasks [21,48], we considered two types of error: (i) ‘simple’ perseveration (i.e. any cancellation exceeding one single line, mark, or cross drawn on each circle or nearby it); (ii) ‘complex’ perseveration, including irrelevant graphic material added by the patient (e.g. a drawing, the patient’s signature, an extra target subsequently crossed out). The 1-cm-wide sector corresponding to the central circle was not considered for analysis. The lateral distribution of total perseveration errors was analyzed subdividing the response sheet into four columns: Each of the two central columns included four targets, each of the two lateral columns two targets, for a total of 12 targets. A preliminary inspection of the data revealed that most perseveration errors were confined to the neglect group. This made unrealistic the assumption that the observations were drawn from populations all of which have the same variance. Accordingly, non-parametric statistics were used [58].

### 2.2.2. Lesion analysis

The lesions of the 35 patients with contralesional neglect were classified, with reference to standard atlases [13,42], by a neurologist unaware of the neuropsychological data as (i) ‘posterior’ (i.e. involving the parietal, occipital, or temporal lobes, and sparing the frontal lobe); (ii) ‘anterior’ (i.e. involving the frontal lobe, with a possible extension to the posterior regions); and (iii) ‘subcortical’ (i.e. involving the grey nuclei, the subcortical white matter, or both, and sparing the cortex).

### 3. Results

Fig. 1 shows the average number of perseveration errors committed by the four groups. It is apparent that all patients’ groups made a negligible number of errors (on average, less than 1), with the exception of the patients with contralesional neglect. A Kruskal–Wallis one-way analysis of variance by ranks revealed a significant difference among groups (KW corrected for ties = 87.663; d.f. = 3; \( P < 0.0001 \)). Multiple comparisons revealed that the neglect group differed from the other three groups (\( P < 0.05 \), with no other comparisons being significant. Table 2 shows the number of patients who made at least one perseveration error. The close

<table>
<thead>
<tr>
<th>Group</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>Length of illness (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N+ (n = 35)</td>
<td>20/15</td>
<td>65.4 (11.5)</td>
<td>6.8 (1.7)</td>
<td>11.8 (12.2, 1–45)</td>
</tr>
<tr>
<td>RN− (n = 60)</td>
<td>32/28</td>
<td>63.5 (13)</td>
<td>7.3 (8.7)</td>
<td>11.5 (13.3, 1–50)</td>
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<tr>
<td>LN− (n = 64)</td>
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<td>60 (13.2)</td>
<td>7.4 (3.8)</td>
<td>13.8 (29.6, 1–60)</td>
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<tr>
<td>SDAT (n = 22)</td>
<td>9/13</td>
<td>70 (8.6)</td>
<td>6.1 (3.4)</td>
<td>–</td>
</tr>
</tbody>
</table>
association between perseveration and neglect was highly significant ($\chi^2 = 71.47$, $P < 0.0001$, d.f. = 1). Forty-seven patients (29.6%) out of the 159 with focal damage showed perseveration. Thirty-one such patients (66%), 28 with damage to the right hemisphere, three to the left hemisphere, showed contralesional neglect. The association between perseveration in the cancellation task and right brain-damage was further confirmed by the 16 patients without neglect on the circle cancellation task, who made perseveration errors. Seven right-brain-damaged patients made an average of 5.71 (range 3–9) errors, nine left-brain-damaged patients an average of 1.56 (range 1–3) errors (unpaired $t$-test $= 5.17$, d.f. = 14, $P = 0.00014$).

Fig. 2A shows the distribution of the perseveration errors made by the 31 patients with neglect in the four columns of the sheet. Most errors were confined to the two ipsilesional columns. The number of target circles was different in the four columns of the sheet: Two circles in each of the two lateral (left-sided and right-sided) columns, four in each of the two central (left-sided and right-sided) columns (see Fig. 4). Accordingly, the number of perseveration errors in pairs of contralesional and ipsilesional columns with the same number of targets was analyzed by the Wilcoxon signed rank test. Patients produced more perseveration errors in the ipsilesional than in the contralesional columns (central columns, 2 and 3 in the figure: $z = 3.98$, $P < 0.0001$; lateral columns 1 and 4 in the figure: $z = 4.28$, $P < 0.0001$). In the seven right-brain-damaged patients without neglect perseveration errors occurred mainly in the two central columns (68%).

Fig. 2B shows the distribution of omission errors made by the 35 patients with contralesional neglect. The vast majority of omissions occurred in the contralesional side of the sheet, with a lateral gradient opposite to that of perseveration. A Friedman two-way analysis of variance by ranks revealed a significant difference among columns ($\chi^2$ corrected for ties = 88.56, d.f. = 3; $P < 0.0001$). Multiple comparisons showed that ipsilesional positions 3 and 4 differed from contralesional positions 1 and 2 ($P < 0.05$).

Table 3 shows the lesion localization of the 31 right-brain-damaged patients (nos. 1–31) and of the four left-brain-damaged patients (nos. 32–35) with contralesional neglect, together with their perseveration and omission error scores. Twenty right-brain-damaged patients (nos. 1–20) had cortico-subcortical lesions, which in seven cases were confined to the posterior regions, sparing the frontal cortex (nos. 14–20). Eleven right-brain-damaged patients (nos. 21–31) had lesions confined to subcortical structures. The four left-brain-damaged patients showed minimal evidence of both omission and perseveration errors, with a maximum score of one in each conditions. These patients were not considered for further analysis.

The vast majority of patients showing perseveration had contralateral visual half-field deficits. These may reflect a primary sensory impairment (haemianopia), a manifestation of neglect (visual hemi-inattention), or the association of the two disorders [26,33,70]. The two patients with visual extinction (# 17 and # 34) did not make perseveration errors. The presence of visual field deficits does not appear to be necessarily associated
with both perseveration and, as it has long been known (see, e.g. [24,68]), with unilateral spatial neglect. Right brain-damaged patient # 25, who had preserved visual fields made three omissions, and five perseveration errors. Also left-brain-damaged patients # 32 and # 33, each of whom made one omission and one perseveration error, had normal visual fields.

As Table 3 also shows, 31 patients had suffered a cerebrovascular attack, four patients (# 3, # 17, # 19, # 25) had a space-occupying neoplastic lesion. The average number of perseveration errors was 5.61 (range 0–25) in the 31 vascular patients, 3.0 (range 0–25) in the 31 neoplastic patients. The average number of perseveration errors was 4.74 (range 1–9) in the vascular group, 4.5 (range 3–6) in the neoplastic group. The limited number of patients with neoplastic damage prevents, however, definite conclusions concerning differences in perseveration related to the aetiology of the lesion.

Fig. 3 shows the average number of perseveration and omission errors in right-brain-damaged patients with lesions including (nos. 1–13) and sparing (nos. 14–20) the frontal lobe, and in patients with subcortical damage (nos. 21–31). A Kruskal–Wallis one-way analysis of variance by ranks revealed a significant difference in the number of perseveration errors committed by the three groups (KW corrected for ties = 6.95; d.f. = 2; P = 0.031). Multiple comparisons revealed that the group with lesions sparing the frontal lobe differed from the other two groups (P < 0.05), which did not differ from each other. Omission errors, by contrast,

<table>
<thead>
<tr>
<th>Patient</th>
<th>Lesion side</th>
<th>Aetiology</th>
<th>Neurological deficits</th>
<th>Total number of perseverative errors</th>
<th>‘Complex’ perseverative errors</th>
<th>Number of omissions</th>
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</thead>
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<td>1</td>
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<td>F/V</td>
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<td></td>
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<td>5</td>
</tr>
<tr>
<td>2</td>
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<td></td>
<td>6</td>
</tr>
<tr>
<td>3</td>
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<td>F T P/N</td>
<td>+ + + 4</td>
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</tr>
<tr>
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<td>+ + + 3</td>
<td>1/3</td>
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<td>9</td>
</tr>
<tr>
<td>5</td>
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<td>F T P/V</td>
<td>+ + + 8</td>
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<td></td>
<td>4</td>
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<tr>
<td>6</td>
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<td>+ ext + 11</td>
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<td>3</td>
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<td>F T P O/V</td>
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<tr>
<td>8</td>
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<td>F T/V</td>
<td>+ + + 9</td>
<td>1/9</td>
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<td>6</td>
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<td>F T P/V</td>
<td>+ + + 1</td>
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<tr>
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<td>F P/V</td>
<td>+ + + 17</td>
<td>8/17</td>
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<td>3</td>
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<tr>
<td>11</td>
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<td>+ + + 9</td>
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</tr>
<tr>
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<td>2/9</td>
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</tr>
<tr>
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<td>F T P/V</td>
<td>+ ext + 4</td>
<td></td>
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<tr>
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</tr>
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<td>4/4</td>
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<td>1</td>
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<td>+ + + 25</td>
<td></td>
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<td>pwm/V</td>
<td>+ + + 13</td>
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<td>(+) − − 5</td>
<td>1/5</td>
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<td>27</td>
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<td>Th/V</td>
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<td>35</td>
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<td>+ + + 1</td>
<td></td>
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<td>1</td>
</tr>
</tbody>
</table>

Left/right (L/R), frontal (F), parietal (P), temporal (T), occipital (O), basal ganglia (BG), thalamus (Th), periventricular white matter (pwm), external capsule (ec), internal capsule (ic), insula (i), V (vascular), N (neoplastic), Motor (M), somatosensory (S), and visual (V) neurological deficits contralateral to the side of the lesion; +/− (presence/absence of deficit, minor motor deficit in brackets), ext (extinction to double simultaneous stimulation).
Fig. 3. Average number of perseveration (P) and omission (O) errors (S.E.) in 31 right-brain-damaged patients with left unilateral spatial neglect, by localization of the hemispheric lesion: A (‘anterior’: including the frontal lobe), P (‘posterior’: sparing the frontal lobe), SUBCO (confined to subcortical structures).

Fig. 4. Examples of perseveration errors committed by right-brain-damaged patients with left spatial neglect in the circle cancellation task. (A) Patient #8: spontaneous addition of crosses nearby (‘simple’ perseveration), after each circle had been crossed out, and of a target-circle subsequently crossed out (‘complex’ perseveration, indicated by a vertical arrow). (B) Patient #4: repeated cancelling out in the two right-sided circles of the right hand-side of the sheet (‘simple perseveration’) and spontaneous drawing of an incomplete hen (‘complex’ perseveration).
unilateral neglect were distinctive features of the performance of both left-brain-damaged patients and patients with senile dementia of the Alzheimer-type. Right neglect after damage to the left hemisphere is less frequent and severe than left neglect associated with right brain damage [8]. As to dementia, unilateral spatial neglect is not mentioned in comprehensive reviews as a main visuo-spatial component deficit (see, e.g. [60,75]). Left unilateral neglect in patients with dementia of the Alzheimer-type has, however, been observed using both line bisection [27,71], and cancellation [46,71] tasks, with no mention, however, of perseveration during cancellation. The absence of perseveration in patients with dementia in the present cancellation task may reflect the pattern of the cerebral metabolic dysfunction, which is prevalently biparietotemporal, with a relative sparing of the frontal regions, at least in the early course of the disorder, though there is a great variability across patients (reviewed in [43]).

Taken together, the present results suggest an association between unilateral spatial neglect and perseveration in visuo-motor exploratory cancellation tasks. In line with the hemispheric asymmetry which characterizes neglect, the association concerns mainly left neglect and perseveration errors prevalently produced in the ipsilesional, right, less neglected portion of the display. The association between perseveration and left neglect in cancellation tasks is further supported by the finding that, in the 16 patients without neglect, as assessed by the circle crossing out task, perseveration errors were definitely more frequent after right brain damage than after lesion in the left hemisphere. This difference, which parallels the well known hemispheric asymmetry of the defective manifestations of neglect (in the present study omissions in a cancellation tasks see review in [8]) may be accounted for by a distortion or instability of space representation or attention in right-brain-damaged patients. Such a spatial bias may be not detected by the circle cancellation task in terms of defective performance (omissions), allowing leeway, however, to perseveration. The view that in right-brain-damaged patients the ipsilesional perseveration in cancellation and drawing tasks depends mainly upon the ipsilesional bias which characterises neglect may account for a clinical observation by Maeshima et al. [39]. A right-brain-damaged patient, S.Y., with a right frontal lesion exhibited left neglect and ipsilateral perseveration in line cancellation and figure copying. A follow-up assessment showed improvement of neglect (reduction of omissions, more complete figure copying) and the disappearance of perseveration (Maeshima et al.’s Figs. 1 and 4 and 5).

General unitary interpretations of unilateral spatial neglect in terms of a merely defective, negative, phenomenon are unlikely to be able to account for the occurrence of positive manifestations, such as perseveration in cancellation tasks [64,66]. This difficulty applies to comprehensive theories suggesting that the basic dysfunction underlying neglect involves the defective orientation of attention towards the contralesional side of space [26,32], an impaired disengagement of attention from ipsilesional stimuli [54], the mere loss of the medium for contralesional space representation (see [2], for discussion), the ipsilesional rotation [30,72] or translation [67] of the egocentric frame of reference, or directional hypokinesia [74]. All these interpretations (reviewed in [8]), which share the view that conscious processing of contralesional stimuli is at some extent defective, may readily account for the impaired visuo-motor exploration of the contralesional side of space, with respect to a given reference frame. However, the occurrence of the positive pathological phenomenon of perseveration does not appear to be a direct consequence of these putative disorders.

We have focussed so far on the close association between perseverative behaviour and unilateral spatial neglect in a cancellation task. The present study also provides evidence that drawing perseveration and defective cancellation are, in some respects, distinct pathological phenomena, at both the functional and the anatomical level. As Table 3 shows, patients # 15 and # 17 showed a severe left neglect, omitting to cross out all left-sided circles, but did not produce any perseveration error. Furthermore, as Fig. 3 shows, the occurrence of perseveration was closely associated with damage involving the frontal cortex or confined to subcortical regions (white matter, grey nuclei). Fig. 3 also shows that perseveration can not be conceived as a positive manifestation of neglect which occurs when the latter deficit is most severe: The occurrence of omissions was comparable in the three anatomical groups. In line with these findings, the correlation between perseveration and omission errors was low. Similarly, Na et al. [48], found that perseveration was more frequent in patients with ‘anterior’ lesions than in patients with ‘posterior’ damage. Na et al.’s ‘anterior’ group pooled together patients with subcortical lesions (basal ganglia and white matter), patients with dorso-lateral frontal lesions, and patients with both lesion sites. In the present study the contrast was between extensive antero-posterior lesions (including the frontal lobe and subcortical lesions) on the one hand and posterior damage on the other.

As Table 3 shows, three patients (# 18, # 19, # 20) with posterior damage not extending to the frontal lobe made more than a single perseveration error, suggesting the existence of exceptions to the anatomo-clinical association between perseveration and frontal damage, revealed by the group analysis. Exceptions to a prevailing anatomo-clinical pattern are always difficult to interpret (discussion in [65]). Studies mapping local cerebral metabolism and perfusion have, however,
shown that the regions of functional depression may exceed the areas of structural damage, as assessed by TC or MRI. These well known remote effects of a focal vascular or neoplastic lesion (diaschisis: see [18]) have been found also in association with the neglect syndrome [19,52,53,73]. The possibility may be then entertained that in these patients a functional depression affecting the frontal and subcortical regions was present. It should be also noted, however, that the more severe manifestations of perseveration (e.g. patients # 6, # 10, # 23, # 24, # 29) were associated with structural lesions extending to the frontal lobe or involving the subcortical regions, in line with the view that damage to these areas plays a most relevant role. This conclusion is further supported by the finding that only damage involving the frontal lobe or confined to the subcortical structures was associated with ‘complex’ perseveration phenomena. These are likely to be a heterogeneous set of productive manifestations, which, we suggest, go under the rubric of ‘perseveration’, being, according to the present operational definition, more or less complex drawing activities, which continue steadfastly after the termination or change of the task demands (circle cancellation).

In the present study, the correlation between omission and perseveration errors was low. This result appears to differ from Na et al.’s [48] observation that neglect severity, as scored by the ratio of the number of cancelled lines on the left side of the page, compared to those cancelled on the right side of it, was greater in right-brain-damaged patients with perseveration. The parametric (t-test) analysis made by Na et al. [48] differs from the present correlative approach, however. A perusal of the individual scores of Na et al.’s [48] patients, reported in their Table 1, reveals dissociations similar to those observed in the present study. For instance, Na et al.’s [48] patient # 2 made three right-sided perseveration errors and omitted 19 out of 36 lines (18 on the left-hand side, 1 on the right-hand side) in the cancellation task. By contrast, patient # 18 made five right-sided perseveration errors, but no omissions in the line cancellation task. Finally, patient # 34 had an extremely severe neglect, crossing out only two out of 36 lines on the right-hand side of the display, but made only two right-sided perseveration errors. The correlation, computed on the data reported in Table 1 of Na et al. [48], between omissions and perseveration errors committed by 18 patients with ‘type I’ perseveration (comparable to the present ‘simple’ perseveration), was low (Kendall rank-order coefficient $T = 0.28$, $z = 1.63$, $p = 0.10$). To summarize, both Na et al.’s [48] and the present study show an association of prevalently ipsilesional, right-sided perseveration errors with left neglect in cancellation tasks. In both studies, however, the defective (omissions) and the productive (perseveration) impairments do not appear to be correlated in terms of severity.

The present results suggest that perseveration in visuo-motor exploratory cancellation tasks is a positive, productive, pathological phenomenon which may add to the defective, negative, component of spatial neglect (namely: omissions of contralesional targets in cancellation tasks), independent of the severity of the latter. The occurrence of perseveration in the writing and drawing behaviour of patients with damage to the frontal lobe, the basal ganglia and the anterior subcortical white matter is a well known phenomenon: the lesions are often bilateral with no definite hemispheric asymmetry [17,37,38,62]. Damage to the right cerebral hemisphere has been associated, however, with a variety of productive phenomena, ranging from ‘hypergraphia’ [76] and perseveratory verbal or gesturing response on stimulation of other patients in the same room (‘response-to-next-patient-stimulation’, see [10]), which may involve both sides of space, to ‘ipsilateral instinctive grasp reaction’ [47]. The latter phenomenon, which has been reported to be closely associated with right-sided lesions involving subcortical structures or the perisylvian regions including the frontal lobe, appears to be relevant to the interpretation of the present results, suggesting that right brain damage may bring about uncontrolled motor activity in the ipsilesional right side of space. An experimentally controlled counterpart to this clinical observation is the finding that in right-brain-damaged patients with left spatial neglect, contrary to the case of normal subjects, response speed and accuracy to ipsilesional stimuli improve with stimulus eccentricity; the more rightward the position of the stimulus, the faster and more accurate the patients’ responses [15,35,59]. This behaviour, termed magnetic attraction [15] or hyperattention [34], indicates that activity in the ipsilesional, putatively preserved, side of space may be set at an abnormally high level.

The drawing perseveration found in the ipsilesional side of the sheet may result from the combined effect of two pathological mechanisms, with discrete anatomical counterparts. Denny-Brown ([16], p. 22) draw a distinction between two impairments of exploratory behaviour, ‘frontal or magnetic apraxia’ and ‘parietal or repellent apraxia’, even though the use of the term ‘apraxia’ with reference to these disorders is questionable [14]. According to Denny-Brown the magnetic exploratory aspect of behaviour, involving ‘perseveration of all contactual reactions’, is managed by the parietal cortex, and released by frontal and temporal lesions. The repellent, negative, bias is determined by the premotor, cingulate and hippocampal regions, and released by parietal lesions. In the present series, the majority of patients showing perseverative behaviour had extensive antero-posterior lesions, or subcortical damage, which may disrupt connections with frontal lobe regions. Within Denny-Brown’s ‘magnetic versus repellent apraxia’ framework, these patients showed
repetitive drawing responses during cancellation in the ipsilesional sector of the sheet (where neglect abnormally restricted exploration) due to the pathological release of complex motor behaviour, brought about by the frontal damage. The presence of left neglect may therefore account for the occurrence of perseveration confined to the ipsilesional, right-sided, sector of the sheet. By contrast, when the lesion is confined to the posterior, mainly parietal, regions, the exploratory deficit has no positive, productive components, being limited to a negative bias towards the ipsilesional side. It is the combined effect of the pathological restriction to the contralesional side of the representation of extrapersonal space, on the one hand, and of the release of repetitive visuo-motor activity (drawing, in the context of a cancellation task) on the other, which brings about perseveration in patients with neglect. This two-component-deficit interpretation may account for both the association between contralesional neglect and ipsilesional perseveration, and the low degree of correlation between the severities of the defective (omissions in cancellation) and productive (perseveration errors) impairments. Perseveration in cancellation tasks is triggered by a rightward representational bias, which brings about left neglect. The actual manifestation and severity of perseveration depend, however, on an additional dysfunction, related to frontal lobe or subcortical damage.

The present results might be alternatively interpreted in terms of optic alloaesthesia, a pathological phenomenon whereby stimuli are displaced across the midline in the intact visual half-field ([11], p. 300). Similarly, perseveration in crossing out tasks may be conceived as an ipsilesional displacement of visuo-motor actions (i.e. cancellations) originally intended towards contralesional targets. This view predicts the existence of a relationship between contralesional omissions and ipsilesional perseverations. Fig. 4A illustrates a behaviour compatible with such an account. Patient # 8 made seven omissions (including the central circle) and eight ‘simple’ perseveration errors. However, in the group of neglect patients the correlation between perseveration and omission errors was low and not significant. This suggests that an optic alloaesthetic phenomenon may be a pathological factor contributing to perseveration, but does not provide a complete explanation of the disorder.

Finally, the ‘complex’ perseveration phenomena (see examples in Fig. 4) may be seen as a counterpart for the ipsilesional extra-personal space of the somatoparaaphrenic delusions concerning the patient’s contralesional side of the body [5,22]. A related observation was made by Marshall and Halligan [41], in a patient (# 5, in their series) who had suffered a right fronto-parietal infarct and showed left neglect on a standard battery. The patient, required to copy a potted plant (two flowers on two branches with a common stem), substituted the left-sided flower with a rabbit. Marshall and Halligan [41] referred to the rabbit as ‘hallucinatory’ and drew analogies to the ‘metamorphopsia’ described by Critchley [11], and to contralesional confabulations, such as somatoparaphrenia. A possible relationship between these phenomena and delusions concerning the contralesional side of the body is suggested by the behaviour of patient # 4 (see Fig. 4B), who made one ‘complex’ ipsilesional perseveration, and showed left somatoparaphrenia. These pathological drawing behaviours, which may occur in copying and cancellation tasks, either in the contralesional left (as in Marshall and Halligan’s [41] patient # 5, or in the ipsilesional right (as in patient # 4 in the present series) side of the display are likely to be an heterogeneous set of productive manifestations, with partly different underlying mechanisms. Taken together, these findings corroborate, however, interpretations of unilateral spatial neglect in terms of a higher-level representational disorder, which may be not confined to a mere deficit of exploration of the contralesional side of space (discussion in [8]).

Taking the view that spatial unilateral neglect is a multi-componential syndrome [64], the productive manifestations found in the present study (ipsilesional drawing perseveration in cancellation performance) may be considered as a discrete component deficit, which, when the responsible cerebral damage includes the frontal or subcortical regions, adds to the basic negative disorder of defective contralesional exploration and awareness. This may be produced by damage confined to the inferior-posterior parietal regions, at the tempo-parietal junction, which represents the more frequent anatomical correlate of visuo-spatial neglect [36,55,68].

Acknowledgements

We are grateful to Leonardo Chelazzi, who read an early draft of this paper for his suggestions, and to Anna Berti, Claudio Galletti, and Giovanni Zamboni for a helpful discussion. This work has been supported in part by grants from the MURST and the Ministero della Sanità to Giuseppe Vallar.

References


[61] Spinnler H, Tognoni G. Standardizzazione e taratura Italiana di Test Neuropsicologici. The Italian Journal of Neurological Sciences, Suppl. 8. 1987;1–120.