Relationship Between Closing-In and Spatial Neglect: A Case Study

Massimiliano Conson, PhD,* Claudia Nuzzaci, PsyD,† Laura Sagliano, PhD,* and Luigi Trojano, MD*

Abstract: We describe a right-brain-damaged patient with extrapersonal neglect, dysexecutive deficits, and closing-in. Because no study has investigated the relationship between spatial neglect and closing-in in patients with focal brain damage, we assessed how spatial factors (drawing direction: left-to-right, right-to-left, radial) and attentional load (single versus dual task copying; the concurrent task was counting aloud) interacted in determining our patient's closing-in. We found that her closingin was worst when she copied the stimulus (Luria's line) from left to right; greater attentional load significantly worsened her closing-in in the right-to-left direction. Closing-in seems to be caused by a pathologic release of motor behavior, analogous to other productive manifestations of extrapersonal neglect.

Key Words: closing-in, spatial neglect, productive disorders, pathologic approach behavior

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When performing a copying task, brain-damaged patients may tend to draw close to the model or even to overlap it. Such behaviors are manifestations of the phenomenon known as "closing-in" and are usually reported in patients with degenerative conditions, particularly Alzheimer disease (De Lucia et al, 2014; Mayer-Gross, 1935).

While early studies considered closing-in to be a form of constructional apraxia (Mayer-Gross, 1935), we now recognize that patients can develop closing-in independent of visuospatial constructional disturbances (Conson et al, 2009). Today, closing-in is usually considered a symptom distinct from constructional apraxia. Rather, closing-in has been related to frontal and executive impairments leading to the release of pathologic attraction of action and attention toward relevant visual stimuli (Ambron et al, 2009; Conson et al, 2009; De Lucia et al, 2014; Grossi et al, 2015; McIntosh et al, 2008).

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From the *Neuropsychology Laboratory, Department of Psychology, Second University of Naples, Caserta, Italy; and †Santa Chiara Institute, Lecce, Italy.

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Reprints: Massimiliano Conson, PhD, Neuropsychology Laboratory, Department of Psychology, Second University of Naples, Viale Ellittico 31, 81100 Caserta, Italy. E-mail: massimiliano.conson@ unina2.it.

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Sagliano et al (2013) demonstrated that healthy adults tend to draw close to the model when they are engaged in an attention-demanding concurrent activity, thus suggesting that a reduction in available attentional resources can release an attraction toward the model without being part of a brain disorder.

Only rarely has closing-in been reported in patients with focal brain lesions (Grossi et al, 1996). To the best of our knowledge, only one study reported a behavior resembling closing-in in a patient with neglect after a right frontal stroke (Lepore et al, 2005). The patient could draw clocks accurately from memory, but in clock copying tasks he transposed all numbers toward the model, ie, from the lower to the upper half of the dial. According to the authors, this response pattern resembled closing-in and could be ascribed to a pathologic approach behavior (Denny-Brown and Chambers, 1958).

Other frontal lobe-related pathologic approach behaviors in drawing tasks have been reported in patients with spatial neglect. In particular, during target cancellation tasks, patients with neglect may repeatedly cross out the same target (simple perseverations) or may draw extra targets and subsequently cross them out (complex perseverations) (Rusconi et al, 2002).

Ronchi et al (2009) suggested that perseveration in patients with neglect can be interpreted in the framework of a two-factor theory. The first factor is the release of complex motor activity as a result of lesions mainly involving the frontal lobes (Rusconi et al, 2002). The second factor, simultaneous with the first, is extrapersonal neglect triggering perseverations with an ipsilesional-tocontralesional gradient. According to the authors, this interpretative model can account for not only the association between concurrent perseveration and contralesional neglect, but also dissociations between perseveration and neglect in patients who have only one of the factors.

In the same vein, Ronchi et al (2009) found that higher attentional demands affected perseverations but not neglect severity, since perseverations were more frequent on a star cancellation task (high attentional load) than on a letter cancellation task (low attentional load), while frequency of omissions was not modulated by attentional load.

Here we describe a right-brain-damaged patient with left extrapersonal neglect, dysexecutive deficits, and closing-in in several formalized copying tasks. Starting from Ronchi et al's (2009) two-factor interpretative

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Test	Raw Score
Mini-Mental State Examination (Measso et al, 1993)	22/30
Digit span forward (Orsini et al, 1987)	6
Rey 15 auditory word learning test (Carlesimo et al, 1996)	
Immediate recall	35
Delayed recall	5 5
Street's Completion Test (Spinnler and Tognoni, 1987)	5
Copying of geometrical drawings (Spinnler and Tognoni, 1987)	6/14*
Rey Complex Figure (Bertolani et al, 1993)	,
Immediate reproduction	10.5*
Delayed recall	8
Categorical verbal fluency (Spinnler and Tognoni, 1987)	18
Phonological verbal fluency (Carlesimo et al, 1996)	31
Frontal Assessment Battery (Appollonio et al, 2005)	9*
Abstract verbal judgment test (Spinnler and Tognoni, 1987)	23*
Inverse motor learning test (right hand) (Spinnler and Tognoni, 1987)	15*
Line cancellation (Pizzamiglio et al, 1989)	6/21*
Star cancellation (Halligan et al, 1989)	27/54*
180 mm line bisection (mean rightward error in mm) (Bisiach et al, 1998)	12.2*

framework of perseverations in neglect, we assessed whether and how extrapersonal neglect can interact with manifestations of closing-in. We studied the patient's performance on an experimental copying task while manipulating the task's drawing direction and cognitive load. By these means we could collect new evidence on interactions between pathologic approach behavior and neglect-related impairments, eg, omissions (Vallar et al, 2006).

CASE REPORT

The patient was a 74-year-old right-handed housewife with 5 years of formal education. She had one son. She had no past history of relevant medical or psychiatric diseases.

She suddenly developed left hemiplegia and was admitted to the "Città di Lecce" (Italy) Hospital. A computed tomography scan showed a cortico-subcortical hyperdense lesion in the right frontotemporal region, consistent with a hemorrhagic stroke. On the day of admission, she underwent microsurgical clipping of a middle cerebral artery aneurysm, allowing her a good functional recovery. She returned home 2 weeks after the operation.

The patient and her relatives reported improvement in her clinical condition and motor function within a few days after she left the hospital, the only exception being weakness in her left arm. At home, she could stand and walk unaided, but could not resume her usual housekeeping activities, notwithstanding two 1-month periods of motor neurorehabilitation.

Ten months after the stroke, her left arm was still weak and she continued having general difficulties with common activities of daily life. She sought additional motor rehabilitation and was admitted to the Santa Chiara Institute, Presidio di Riabilitazione Funzionale, also in Lecce, Italy.

On evaluation, she was alert and cooperative. She showed left extrapersonal neglect, dysexecutive deficits, and constructional apraxia, without disturbances in verbal short-term or long-term memory, visual perception, or verbal fluency. Formal neuropsychological tests showed intact general cognitive function (Table 1). She did not evidence neglect in personal space; she could report left-sided tactile stimuli correctly.

In copying geometric figures (Figure 1), the patient always began drawing from one element of the model rather than the overall outline, and she tended to approach the model. Her drawings were severely distorted. In her immediate-recall reproduction of the Rey Complex Figure (Figure 2), she clearly showed concurrent spatial neglect and closing-in; in her delayed-recall reproduction, she rotated the figure 90° counter-clockwise, a phenomenon previously described only in patients with frontal damage (Molteni et al, 2014; Solms et al, 1998).

Because our patient systematically closed in on the model in repeated sessions several days apart, she enabled us to explore the relationship between closing-in and spatial neglect.

We performed the following assessment during the first month that she stayed at the rehabilitation center. When she was discharged and returned home, about a month later, she could move her left arm a little better and her left neglect was markedly reduced, but she still showed visuoconstructional apraxia and mild dysexecutive deficits, without closing-in.

The patient provided her written informed consent to participate in the experimental study, which was approved by the local Ethics Committee.

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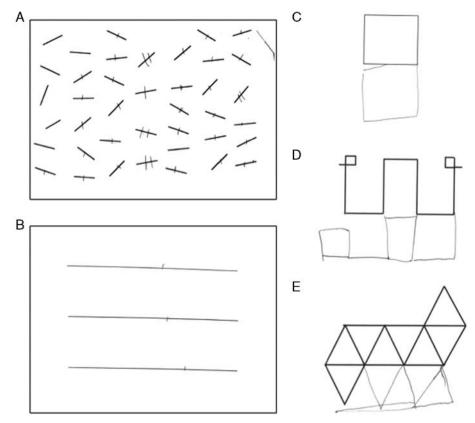


FIGURE 1. On cancellation (Panel A) and line bisection (Panel B) tasks, our patient clearly shows left spatial neglect. Her copying of geometric figures of different complexities (Panels C, D, and E) displays closing-in and constructional apraxia.

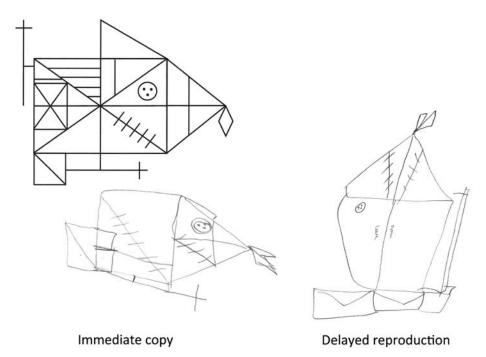


FIGURE 2. On her immediate-recall reproduction of the Rey Complex Figure (Bertolani et al, 1993), our patient shows both left spatial neglect and closing-in. On the delayed-recall reproduction, she rotates the figure 90° counterclockwise.

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TABLE 2. Experimental Task: Distances (mm) Between Our
Patient's Copies and the Model (Smaller Distance Indicates
Stronger Tendency for Closing-In)

Drawing Direction	Experimental Condition				
	Single Task		Dual Task		
	Mean	SEM	Mean	SEM	
Minimum distance					
Left-to-right	7.00	0.89	9.63	1.01	
Right-to-left	56.15	2.33	45.93	1.29	
Radial	21.48	1.86	26.00	1.44	
Final distance					
Left-to-right	7.59	1.24	7.48	1.29	
Right-to-left	62.78	4.11	46.82	1.67	
Radial	27.41	3.68	24.15	1.52	

SEM = standard error of the mean.

EXPERIMENTAL TASK

We derived the stimuli for the experimental copying task from Luria's figure (Luria, 1966). We started with a black baseline and superimposed 15 variations on it, as illustrated in Figure 3. By altering the number and types of variations, we developed 10 different black linear models (Sagliano et al, 2013). We printed each model in black ink on a separate size A3 sheet of white paper. Each model was 23 cm long and 0.1 cm thick.

The patient sat at a table with a rollerball pen. Author C.N. placed one sheet at a time on the table and aligned the midpoint of the model with the patient's midsagittal plane. Her task was to copy each of the 10 models in three different drawing directions:

- Left-to-right: Each linear model was printed in landscape (horizontal) orientation in the center of a horizontally oriented sheet of paper. A small black dot appeared 70 mm below the left edge of the model. C.N. instructed the patient to copy the model from the left to the right, starting her drawing at the printed dot.
- Right-to-left: The stimuli and the procedure were the same, but this time each horizontally oriented stimulus was in the lower part of the horizontal A3 sheet, and the black starting dot was 70 mm above the model's right edge. C.N. instructed the patient to copy the model from the right to the left, starting at the dot.
- Radial: The stimuli and the procedure were again the same, but now each model was centered in portrait (vertical) orientation on a vertically oriented sheet, with the black starting dot at the bottom. C.N. instructed the patient to copy each model starting at the black dot and drawing away from her body, ie, in a radial direction.

To manipulate cognitive load, we asked the patient to perform the task in two conditions: a single task condition, in which she just copied the models, and a dual task condition, in which she copied the models while counting aloud, starting at "one" and continuing until the end of each trial.

C.N. gave the patient a total of 60 experimental trials, one for each of the 10 models in each drawing

direction (left-to-right, right-to-left, or radial) and each experimental condition (single task or dual task). We randomized the order of drawing direction, but alternated the experimental conditions in an ABAB schema.

C.N. administered 30 of the trials during each of two 50-minute sessions held a week apart. No time constraint was imposed on the patient, and she was allowed to rest for about 10 minutes halfway through each session.

In analyzing the results for each stimulus, we estimated the patient's tendency to deviate toward the model, related to closing-in, by calculating the minimum distance (in millimeters) between her reproduction and the model, ie, the distance between the copy and the model at the point where they came closest together; the smaller the distance, the stronger the tendency to close in to the model.

Previous studies have shown that healthy participants (Sagliano et al, 2013) and patients with vascular dementia (De Lucia et al, 2013) tend to compensate for their deviation toward the model; therefore, those authors computed both the minimum distance and the "final distance," ie, the distance between the end point of the participant's drawing and the end point of the model. If participants reduced their approach toward the model, ie, final distance larger than minimum distance (De Lucia et al, 2013; Sagliano et al, 2013), it would mean that they had tried to compensate for closing-in.

On this basis, we decided to calculate both measures of closing-in for our patient. We assessed her closing-in separately from measures of her copying accuracy.

We analyzed minimum distance and final distance separately with repeated measures 2×3 analyses of variance, with drawing direction (left-to-right, right-to-left, or radial) and experimental condition (single task or dual task) as the within-subject factors. We used the Bonferroni test for post-hoc contrasts. We set the significance level at P < 0.05.

RESULTS

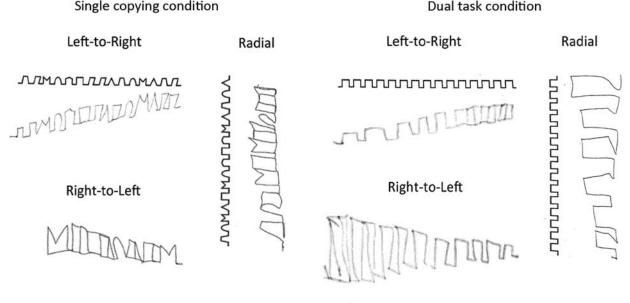
Table 2 shows the patient's performance (minimum and final distances) on the experimental task, for the three drawing directions and the two experimental conditions.

Analysis of variance on minimum distance showed a significant main effect of drawing direction: $F_{2,16} = 412.410$, P = 0.0001, $\eta_p^2 = 0.981$; but not of experimental condition, F < 1. The interaction between drawing direction and experimental condition was significant: $F_{2,16} = 9.065$, P = 0.011, $\eta_p^2 = 0.531$. Post-hoc contrasts on the main effect of drawing direction showed significantly shorter distances, ie, greater closing-in, in the left-to-right than the two other directions, and significantly shorter distances in the radial than the right-to-left direction (all Ps < 0.001). Post-hoc contrasts on the interaction showed significantly shorter distances in the interaction showed significantly shorter distances in the radial than the right-to-left direction (all Ps < 0.001). Post-hoc contrasts on the interaction showed significantly shorter distances in the dual task than the single task copying condition in the right-to-left direction (P = 0.012), but not in the other two directions (P > 0.05). Figure 3 shows some examples of the patient's closing-in.

Analysis of variance on final distance showed significant main effects of both drawing direction: $F_{2,16} = 149.667$, P = 0.0001, $\eta_p^2 = 0.949$, and experimental

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FIGURE 3. In these examples from the experimental task, our patient closes in when copying in all three drawing directions in both the simple and dual task conditions.

condition: $F_{2,16} = 13.149$, P = 0.007, $\eta_p^2 = 0.622$, with shorter distances in the dual task than the single task condition. The interaction between drawing direction and experimental condition was significant: $F_{2,16} = 5.237$, P = 0.045, $\eta_p^2 = 0.396$. Post-hoc contrasts on the main effect of drawing direction confirmed significantly shorter distances in the left-to-right than the two other directions, and in the radial than the right-to-left direction (all Ps < 0.001). Post-hoc contrasts on the interaction confirmed significantly shorter distances in the dual task than the single task copying condition in the right-to-left direction (P = 0.002), but not the other two directions (P > 0.05).

DISCUSSION

We report a patient with spatial neglect showing closing-in in copying tasks. In an experimental copying task, we concurrently varied drawing direction and cognitive load. We had two main findings:

- (1) Drawing direction strongly influenced closing-in, with a continuum of decreasing severity from the left-toright, to the radial, and to the right-to-left direction.
- (2) Although higher cognitive load significantly shortened the final distance of the patient's copies from the model, her closing-in increased in the dual task condition only when she drew from her right to her left (neglected) side.

Our results showed the same pattern when we took into account both the minimum and the final distance, although there tended to be less discrepancy between distances in the dual than the single task condition. Thus, our patient with neglect appeared partially able to detect her drift toward the model while copying, but she was less able to compensate for her drift when the task imposed a higher cognitive load. Her performance was similar to that observed in healthy participants (Sagliano et al, 2013) and in patients with vascular dementia (De Lucia et al, 2013).

Our first main finding suggests that stimulus saliency was an important determinant of closing-in, since the patient's closing-in was more severe in the ipsilesional than in the neglected space, where spatial exploration was more effective. In this sense, closing-in would resemble other "productive" manifestations of the neglect syndrome (such as perseverations in cancellation tasks), which are usually observed in the ipsilesional non-neglected space (Vallar, 1998; Vallar et al, 2006).

Our second main finding seems at odds with current interpretation of closing-in. Recent reports on both patients with dementia (De Lucia et al, 2014; McIntosh et al, 2008) and healthy participants (Sagliano et al, 2013) show that cognitive load can increase closing-in independent of drawing direction. Instead, our patient's closing-in during the minimal cognitive load increased significantly only when she drew toward the neglected space.

Our findings thus suggest the counterintuitive interpretation that cognitive load increased stimulus saliency in the neglected space. This interpretation would not fit evidence that neglect is exacerbated by higher concurrent cognitive load (Bonato, 2012). The only way to reconcile our findings with previous literature would be to hypothesize that higher attentional demand, such as our dual task, could interfere with a patient's on-line visuomotor control system (Milner and McIntosh, 2004), reducing monitoring of motor response (Pia et al, 2013) and increasing closing-in on the contralesional side.

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It has been suggested that "productive" and "defective" manifestations of spatial neglect, though associated, are independent disorders (Vallar et al, 2006). Consistent with this hypothesis, double dissociations between omissions and perseveration errors have been reported in patients with neglect (eg, Pia et al, 2009; Ronchi et al, 2009; Rusconi et al, 2002). However, the issue remains controversial. Toraldo et al (2005) suggested that perseverations correlate with neglect severity and can be ascribed to allochiria (perception of the targets in cancellation tasks as being transposed from the contralesional to the ipsilesional side of space). More recently, Gandola et al (2013) suggested that both perseverations and neglect share a common mechanism, namely an attentional disengagement deficit.

Closing-in, like other "productive" disorders, might be ascribed to a frontal-related pathologic release of motor behavior distinct from the ipsilesional spatial bias characteristic of neglect syndrome. Consistent with the approach-avoidance hypothesis of Denny-Brown and Chambers (1958), the idea that frontal damage can generate a release of motor approach behaviors has been considered in interpreting "multidirectional spatial transpositions" in a patient with neglect from a frontal lesion (Lepore et al, 2005).

Grossi et al (2004) used this interpretative model to account for the tendency of their patient with a right frontal lesion and neglect to transpose drawings from left to right and vice versa ("alternating constructional allochiria"), depending on whether the patient was starting the copies on the left or right.

More recent studies have suggested that a frontalrelated pathologic approach behavior accounts for closing-in in patients with neurodegenerative disorders (Conson et al, 2009; De Lucia et al, 2013). This is in line with the idea that closing-in can be related to defective inhibition of actions attracted by relevant visual stimuli in patients with dementia as well as in typically developing children (Gainotti, 1972).

Taken together, findings on closing-in and neuropsychological findings on perseveration in patients with neglect seem to converge toward Ronchi et al's (2009) two-factor interpretative framework of productive behaviors in neglect. In this framework, frontal-related pathologic behaviors and concomitant contralesional neglect lead to perseverations in the ipsilesional space. Although we did not obtain direct evidence that our patient's closing-in was a frontal-lobe-related phenomenon, our findings allow us to speculate that she would fit this model and to suggest that the two-factor account of perseveration can be extended to other forms of productive drawing phenomena in spatial neglect.

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