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Monocular patching affects inattention but not perseveration in spatial neglect

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Abstract

Monocular patching might improve perceptual-attentional, not motor-intentional deficits in a patient with chronic post-stroke left spatial neglect. Performing a line-cancellation task, his omission errors were associated with a perceptual-attentional “where” deficit, while perseverative errors were associated with “aiming” motor-intentional bias. Contralesional patching had no effect on the omissions ($p=0.871$), whereas ipsilesional patching reduced left-sided omissions compared with the unpatched condition ($p=0.016$). Neither patching condition altered perseverative errors. Further research is needed to examine whether targeting treatments to spatial neglect symptoms (omissions, perseveration) results in improved outcomes.

Introduction

Spatial neglect is a failure to report, respond, or orient to a novel or meaningful stimulus in the side of space contralesional to a brain lesion, associated with functional disability.^{1,2} As spatial neglect is associated with considerable morbidity and predicts poststroke loss of independence,^{2,3} better treatment approaches for these patients are needed.⁴ Optimal treatment for spatial neglect might involve deficit-specific, targeted therapies designed for an individual patient.⁵

Motor perseveration may be defined as the continuation or repetition of a behavior or experience that inappropriately persists after a change in task demands.^{6,7} Patients with spatial neglect have been observed to exhibit asymmetric perseverative behavior⁷ (e.g. patients may attempt to cancel the same target multiple times when completing a line-cancellation task⁸). Lesion studies have shown that frontal/sub-cortical brain injury is associated with perseverative responses.^{7,9} Thus, neglect-based perseveration may be a manifestation of compulsive approach behavior within the context of spatial neglect bias.^{7,9} However, the mechanisms of motor perseveration in spatial neglect are not yet completely understood.

Monocular patching of the right eye has been proposed as a treatment for spatial neglect.² By reducing input to the right eye - and secondarily the left superior colliculus - the right colliculus may be released from inhibition, in turn facilitating contralesional orienting.¹⁰ However, response to right monocular patching has not predictably followed this pattern.^{2,11}

Patients with spatial neglect may primarily manifest either “where” perceptual-attentional or primarily “aiming” motor-intentional deficits.^{2,13} Previous studies reported that monocular patching may primarily alter “where” perceptual bias,^{2,5} which may also underlie failures of stimulus detection (omission errors). Motor perseveration, in contrast, may be strongly associated with an “aiming” motor-intentional deficit.¹⁴ In this experiment, we wished to learn whether omission errors and perseveration errors are indeed associated with “where” and “aiming” bias, respectively, and whether monocular patching improves stimulus detection.

Subjects and Methods

Subject

Patient CB (62) had a right posterior cerebral artery stroke affecting right temporal-occipital cortex and frontal-subcortical system processing (See Figure 1). On neuropsychological evaluation one year post-stroke, he had amnesia, left spatial neglect and difficulty programming alternating hand movements, although he had no other signs of frontal lobe dysfunction. General neurological examination revealed only a left homonymous hemianopia. He had some perceptual difficulty with confrontation naming (47/60 Boston Naming Test¹² items named correctly), though he could name missed items to verbal description. He was unable to copy simple figures, and his writing was difficult to read because of poor spacing on the page. Canceling lines in an array⁹ he demonstrated left-sided omission errors and right-sided perseveration (See Figure 2). Line bisections revealed a rightward bias, but his performance was variable between trials.

Procedure

CB performed a video line-cancellation task to examine visual feedback versus motor feed-forward bias in line cancellation errors.¹³ In the **natural** condition, left/ right on the video screen corresponded with workspace left/ right. In the **reversed** condition, a 180° change in camera perspective reversed the image. Thus, in reversed trials, whenever the patient moved his hand rightward in the actual workspace, his hand would appear to move leftward on the screen, and vice versa.¹¹

“Where” perceptual-attentional bias may be altered by right-left reversal, whereas “aiming” motor-intentional bias may not.¹² Based on this knowledge, we predicted that right-left reversing the viewed workspace would alter omission, but not perseveration errors.

To investigate the effects of eye patching on perseveration versus omission errors, we had CB perform the line cancellation task while wearing a (1) contralesional (left) (2) ipsilesional, and (3) no monocular patch. CB canceled a total of 36 line arrays (6 per testing condition, including both natural and reversed conditions). We compared omission and perseveration asymmetry separately among the three patching conditions, analyzing omissions as described by Na et al (see Results, below).⁷ Perseverative errors were marks on already-cancelled lines, counted on each side; marks on the four central targets were not counted.

Results

Where/Aiming Bias Analysis

We performed an analysis of variance (ANOVA) with side of errors (right, left), viewing condition (natural/reversed) and patching condition (right, unpatched, left) as within-subject factors. This data analysis examined the effect of the natural and reversed viewing conditions on the subject's omission errors on the left and right side of space, while wearing a left or right eye patch, or while unpatched. Omission errors were the dependent variable, and viewing condition (natural vs reversed), side of space (left vs right), and patch side (left, unpatched, right) were within-subject factors. Greenhouse-Geisser correction was necessary as Maunchley's test of sphericity approached significance ($p = 0.052$) for the different patch conditions, indicating potential inhomogeneity of variance for this variable.

Omissions—(See Table 1). Omission errors were more frequent in the reversed condition (main effect of natural versus reversed viewing condition; $p = 0.005$). Omissions were more frequent on the left than on the right (main effect of side of omission errors; $p = 0.043$).

There was also a significant three-way interaction of natural versus reversed viewing condition, left versus right side of omission errors, and left, unpatched and right patched performance conditions (viewing condition $\times$ side $\times$ patch interaction $p = 0.003$). We performed followup pairwise comparisons to test the a priori hypothesis that left-right pattern of omission errors should be altered in the indirect condition (see last line, Introduction). We completed followup t-tests, using family-wise error correction. For each condition, four comparisons were performed relevant to the effect of the natural versus reversed condition, and thus the revised level of significance for these comparisons was $p = 0.0125$.

Pairwise comparison of the natural and reversed conditions for the left side of space and the right side of space yielded different results. On the left side of space, there was no difference between the natural and reversed conditions (natural mean 13.3, SD 0.56; reversed mean 13.7, SD 0.68, $p = 0.721$; 2-tailed). On the right side of space, more omission errors occurred in the reversed condition (natural mean 8.8, SD 0.75; reversed mean 14.4 SD 1.33; $p = 0.005$). A left-right difference in the change with visual feedback is consistent with spatially asymmetric omission errors associated with “where” perceptual-attentional bias.

Perseverations—An omnibus analysis of variance (ANOVA) was also performed to examine perseverative errors, with perseverative errors as the dependent variable, and viewing condition (natural vs reversed), side (left vs right), and patch (left, unpatched, right) as within-subject factors. Inhomogeneity of variance was detected for this data using Maunchley’s test of sphericity for a view $\times$ patch $\times$ side interaction ($p = 0.023$), but this was not relevant to the results obtained, below.

Perseveration occurred more frequently on the right than on the left (main effect of side; $p = 0.000$). There was also a main effect of natural versus reversed viewing conditions ($p = 0.003$), with fewer perseverative errors made in the reversed viewing condition than in the unreversed, natural condition. This may have been a result of increased omission errors in the reversed condition, rather than evidence of “where” spatial bias, however, since perseverative errors could not occur if a stimulus was omitted. Further, no viewing condition $\times$ side interaction was obtained ($p = 0.49$, n.s.).

The lack of an interaction including viewing condition and side of space for perseverative errors in the natural and reversed conditions suggests these perseverative errors may have been associated with an “aiming” bias.

Effect of Patching

Omissions—(See Figure 3) As above (*Where/Aiming Bias Analysis: Omissions*), a three-way interaction was observed, suggesting that eye patching influenced omission error performance, but that this might be spatially specific or specific to natural versus reversed visual feedback conditions. We performed further post-hoc pairwise analyses using family-wise error correction to address an effect of eye patching on “where” omission errors. For each condition, four comparisons were performed relevant to the current experiment and patching effects, and thus the revised level of significance for these comparisons was $p = 0.0125$.

Omission errors with left patching exceeded omission errors with right patching in the reversed condition, right space: 11.33 errors versus 9.33 ($p = 0.012$). Three other pairwise comparisons neared a revised significance level (omission errors with left patching exceeded omission errors with right patching in the natural condition, left space: $p = 0.022$; omission errors while unpatched exceeded omission errors with right patching in the natural condition, left space: $p = 0.029$).

Taken together, the above pairwise comparisons support a beneficial effect of right eye patching, as compared with the unpatched condition or left eye patching, on omission errors of the “where” perceptual-attentional type. The effect may have been more pronounced in the reversed condition, but pairwise comparisons do not support this specifically.

Perseverations—In the left patching condition, CB made a mean 2.5 (sd 3.21) left and a mean 8.67 (sd 5.50) right perseveration errors. In the right patching condition, he made a mean 6 (sd 4) left and a mean 6.67 (sd 3.39) right perseveration errors. The omnibus analysis above (*Where/Aiming Bias Analysis: Perseveration*) did not result in a significant interaction patch side $\times$ left/right space perseverative errors ($p = 0.109$). We did not perform further post-hoc analyses given the lack of a significant interaction to explore. However, this is a preliminary investigation in a single subject, and further investigation is warranted to examine whether an effect of eye patching on perseverative errors may be hemispatially segregated, or whether a subtle, spatially specific influence of visual feedback on these errors may be present.

Discussion

Based on our results, a stroke survivor with chronic left spatial neglect may have made perseverative errors on a line cancellation task associated with an “aiming” motor-intentional disorder. Unlike omission errors on the same task, which became more symmetric and more frequent with mirror-reversal of the stimulus array, our patient’s perseveration errors did not alter in spatial asymmetry with stimulus reversal.

Studies reported that frontal-subcortical brain lesions – particularly those affecting the basal ganglia - were associated with perseverative behaviors.^{7,9} The basal ganglia may play an important role in the inhibition of active motor patterns, with the basal ganglia on one side acting to inhibit ipsilateral movements.¹⁵ Thus, right frontal-subcortical injury could release inhibition of movement in ipsilesional space, allowing for abnormal compulsive approach behavior.^{7,9} Disinhibited movement, within the context of an ipsilesional “aiming” motor-intentional bias, may occur preferentially in ipsilesional space, resulting in perseverative responses on that side.. If monocular patching primarily affects “where” spatial bias^{2,5}, we expected it might alter omission errors but might not modify perseverative errors. Indeed, a right eye patch reduced the baseline preponderance of left-sided omission errors due to spatial neglect. As predicted, neither left nor right eye patching had a significant effect on perseverative errors, which may have been a manifestation of an independent “aiming” bias, as above. It is interesting to note, however, that although patching had no effect on perseveration asymmetry, mean errors were greater in the left hemifield with right versus left eye patching. It is possible that this deterioration in performance could have been caused by the facilitation of contralesional orienting caused by patching¹⁰, resulting in more opportunities for perseverative errors in the neglected hemifield with right patching. Thus, right patching may have increased left-sided perseveration through a secondary effect independent of the proposed primary “aiming” mechanism. The current study is a preliminary investigation in a single subject, and further investigation is warranted to examine whether an effect of eye patching on perseverative errors may be hemispatially segregated, or whether a subtle, spatially specific influence of visual feedback on these errors may be present. Further investigation of patching effects, including subjects with milder symptoms who may be able to tolerate prolonged testing and whose data may thus be more reliable to detect small effects, may shed light on these questions.

Our findings may be consistent with those of Vallar et al,¹⁶ in that “where” perceptual-attentional symptoms in this patient with chronic spatial neglect were observed to be independent of motor perseveration. Consistent with their findings, “aiming” perseverative

errors were associated with frontal-subcortical dysfunction. These authors also suggested, however, that perceptual-attentional or representational dysfunction (e.g. allochiria) may interact with asymmetric motor disinhibition in spatial neglect. We did not specifically explore representational function in the present study, but we did not find evidence that “where” perceptual-attentional processing influenced perseverative behavior.

The results of this case study may remind us that spatial neglect has more than one manifestation between and within subjects. Fractionating abnormal visuo-motor behaviors in one patient exposed potentially separate “where” and “aiming” spatial neglect bias, which appear to give rise to two different classes of error (omission and perseveration, respectively). The finding that an intervention (monocular patching) may alter one type of error (pathologic omission errors) more than it alters another error type (pathologic perseveration) makes this distinction even more significant. Error types in this laboratory study may correspond to dysfunctional natural behaviors causing disability in dressing, adaptive movement, or other self-care. If closer inspection of each neglect patient’s functional problems can identify deficits corresponding to “where” and “aiming” dysfunction, more specific treatments for some of these problems may be developed. This might increase the functional transfer of treatment effects.¹⁷ To apply more focused interventions, however, further study of specific neglect-related deficits and the degree of functional gain that can reasonably be expected by targeted rehabilitation is required.

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Figure 1.
A CT image of the patient's brain. Encephalomalacia is present in the right temporal-occipital region, which can be seen in the left side of the upper-left and upper-middle scan slices. A lacunar stroke in the right putamen can also be appreciated on the upper-right image, (left side of scan) with small foci of white matter hyperintensity visible in the right basal ganglia, suggestive of damage to frontal-subcortical system processing.

Figure 2.
Sample cancellation pattern performed by the patient in the current study in the free field. Left-sided omission errors (failure to cross out lines on the left) and right-sided perseveration (multiple cancellation of right-sided lines) are evident.

Figure 3.

CB?'s line-cancellation errors in the natural visual feedback condition under left eye patch, no patch, and right eye patch conditions. Right eye patching tended to reduce the mean number of left-sided omissions when compared to the left patch or unpatched condition (See text). Neither patching condition affected perseverative error asymmetry compared to the unpatched condition.

Table 1

Omission Versus Perseveration in Natural and Reversed Unpatched Conditions

	Left side of workspace Mean errors	Right side of workspace Mean errors
Omissions		
Natural Condition	13.3 (sd 0.56)	8.8 (sd 0.75)
Reversed Condition	13.7 (sd 0.68)	14.4 (sd 1.33)
Perseverations		
Natural Condition	4.30 (sd 1.97)	7.67 (sd 2.16)
Reversed Condition	2.17 (sd 1.17)	3.67 (sd 2.25)