Allocentric neglect strongly associated with egocentric neglect

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ABSTRACT

Following brain injury, many patients experience egocentric spatial neglect, where they fail to respond to stimuli on the contralesional side of their body. On the other hand, allocentric, object-based neglect refers to the symptom of ignoring the contralesional side of objects, regardless of the objects' egocentric position. There is an established tradition for considering these two phenomena as both behaviorally and anatomically dissociable. However, several studies and some theoretical work have suggested that these rather reflect two aspects of a unitary underlying disorder. Furthermore, in a recent large study Yue et al. [Archives of Physical Medicine and Rehabilitation 93 (2012) 156] reported that acute allocentric neglect is only observed in cases where substantial egocentric neglect is also present. In a new sample of right hemisphere stroke patients, we attempted to control for potential confounds by using a novel continuous measure for allocentric neglect (in addition to a recently developed continuous measure for egocentric neglect). Our findings suggest a strong association between egocentric and allocentric neglect. Consistent with the work of Yue et al. (2012), we found allocentric behavioral deficits only in conjunction with egocentric deficits as well as a large corresponding overlap for the anatomical regions associated with egocentric and with allocentric neglect. We discuss how different anatomical and behavioral findings can be explained in a unified physiologically plausible framework, whereby allocentric and egocentric effects interact.

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1. Introduction

Spatial neglect is a common consequence of right hemisphere brain injury, with patients classically failing to respond to stimuli on their contralesional side. For example, when asking patients to copy a complex scene composed of multiple objects, patients with neglect often miss the left half of the scene as well as missing the left side of objects throughout the whole scene (Gainotti, Messerli, & Tissot, 1972; Johannsen & Karnath, 2004). These patterns of behavior have traditionally been interpreted as evidence for two dissociable forms of spatial neglect: egocentric neglect (where stimuli are missed on the contralesional side with respect to the viewer) and allocentric, object-based neglect (where the contralesional side of stimuli are ignored, irrespective of the location of these stimuli to the patients' viewpoint). Several behavioral and theoretical studies have emphasized this distinction (e.g. Bickerton, Samson, Williamson, & Humphreys, 2011; Hillis et al., 2005; Kleinman et al., 2007; Marsh & Hillis, 2008; Medina et al., 2009; Ota,

Fujii, Suzuki, Fukatsu, & Yamadori, 2001), and some studies have suggested that these deficits may have separate anatomical correlates (for review Karnath & Rorden, 2012). However, theoretical and empirical work has also argued that these behaviors may not be distinct, but reflect different situations and strategies (Driver & Pouget, 2000; Karnath, Mandler, & Clavagnier, 2011; Karnath & Niemeier, 2002; Mozer, 2002; Niemeier & Karnath, 2002a, 2002b). Indeed, a recent study of 110 stroke patients by Yue, Song, Huo, and Wang (2012) has suggested that allocentric deficits are only observed in the presence of egocentric neglect. Much of this discrepancy may reflect different (and potentially insensitive) measures that have been used to identify these forms of neglect. Therefore, our aim was to develop and validate a robust measure for allocentric deficits (similar to recent developments with egocentric neglect [Rorden & Karnath, 2010]) to determine whether allocentric neglect typically represents a unique disorder, or rather is usually seen concomitant with egocentric neglect.

A popular measure for discriminating between egocentric and allocentric, object-based deficits is the defect detection task (see Fig. 1) developed by Ota et al. (2001), where individuals are asked to differentiate between whole objects (e.g. circle for one task, triangles for another) and objects where one side has a defect (e.g. a

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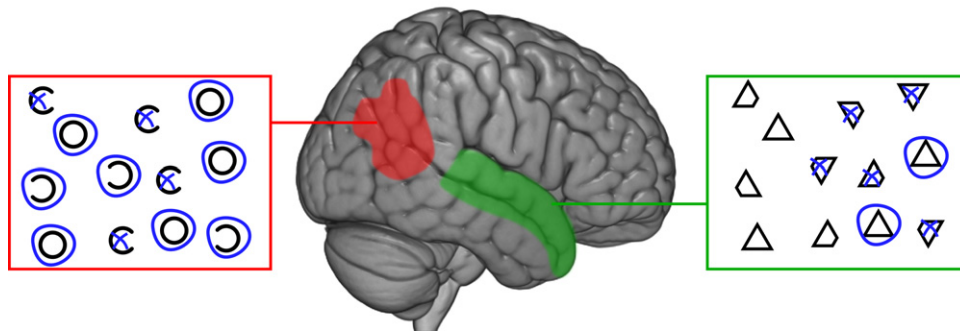
Fig. 1. The popular concept that egocentric and allocentric neglect dissociate behaviorally and anatomically, a view that the data of the present study challenges. Previous studies have suggested that performance on the defect detection tasks (Ota et al., 2001) differs between participants with egocentric and with allocentric neglect. The left and right panels show cartoons for the circle and triangle variants of this task (the actual tasks contain far more stimuli). In these examples the participants were simply asked to circle all the intact objects and cross out all those with a defect (though note that the present study applied these tasks differently; see Section 2). The patient with a lesion in the red territory (illustrated in the left panel) shows an allocentric bias: consistently missing features on the left side of objects, regardless of their position on the page. The patient with a lesion in the green territory (illustrated in the right panel) instead shows egocentric neglect: correctly discriminating items on the right side of the page, yet missing all information on the left half. This brain rendering was inspired by previous anatomical studies (for review, see Karnath & Rorden, 2012; Riddoch et al., 2010).

circle with a gap on the left or the right side, or a triangle with a wedge removed from the left or the right side). Ota et al. (2001) presented data from two patients with right hemisphere injury who showed very different performance – one individual consistently found features on the right side of the page (regardless of what side of the object) yet completely neglected stimuli on the left side of the page, whereas the other patient marked all the stimuli but incorrectly identified many of the circles with a gap on the left as being intact circles. While these patterns appear to provide a strong behavioral double dissociation, the small number of patients does raise the concern that these may not be representative of the population (Juola, 2000). More convincing evidence arguing for a dissociation between egocentric and allocentric neglect comes from work by Hillis et al. (2005). They investigated 50 individuals with acute right hemisphere stroke and observed eleven individuals who exhibited 'pure' egocentric neglect, four patients with 'pure' allocentric neglect and only a single patient with combined ego- and allocentric deficits (here we focus on right hemisphere injury; for studies of left brain injury see Bickerton et al., 2011; Gainotti et al., 1972; Kleinman et al., 2007). Marsh and Hillis (2008) tested acute stroke patients for egocentric and allocentric neglect. They used a visual and a tactile variant of the test suggested by Ota et al. (2001). Nineteen stroke patients showed spatial neglect in the visual modality (Marsh & Hillis, 2008). Seventeen of these patients demonstrated egocentric visual neglect, while 4 patients met the criteria for allocentric visual neglect. Only two patients showed both ego- and allocentric neglect. Medina et al. (2009) examined 171 patients with acute right hemisphere stroke. They observed 32 patients who showed 'pure' egocentric neglect, thirteen patients with 'pure' allocentric neglect and 12 patients with combined ego- and allocentric deficits. Bickerton et al. (2011) reported on 25 individuals with chronic brain injury (at least 9 months since injury, seven with left hemisphere injury and 18 with right hemisphere injury) using an 'Apples Test' (which is similar to the circle defect detection task described by Ota et al. (2001)). Two patients had pure allocentric deficits, five had pure egocentric deficits, and five patients presented both. Verdon, Schwartz, Lovblad, Hauert, and Vuilleumier (2010) studied 80 subacute patients (mean 14.8 days since injury) and found that allocentric errors in reading and the circle defect detection task correlated with each other, with this factor predictive of posterior temporal injury. Chechlacz et al. (2010) examined 41 individuals from the same database as Bickerton et al. (2011) with chronic brain injury (>9 months) and reported that egocentric and allocentric behavior were independent with egocentric

deficits associated with perisylvian regions while allocentric biases correlated with injury to the more posterior temporo-parietal junction. Likewise, Khurshid et al. (2012) examined 25 patients (tested at day 1 and again at day 3–5 after injury) and report that dorsal frontal–parietal reperfusion predicts recovery from egocentric neglect while more ventral posterior-temporal reperfusion correlated with improvements in allocentric neglect. Therefore, a number of studies have suggested that egocentric and allocentric deficits are dissociable, and they appear to suggest that posterior-temporal injury correlates specifically with allocentric deficits (see Fig. 1; as reviewed by Karnath & Rorden, 2012; Riddoch et al., 2010).

In sharp contrast to these findings, a large study by Yue et al. (2012) suggested that allocentric deficits are always observed in conjunction with egocentric deficits. Relying on a large sample, they tested 110 patients with acute right hemisphere stroke and found that from the 47 egocentric neglect patients who could be tested with the circle gap detection task (Ota et al., 2001), 63.8% exhibited also allocentric neglect. However, there were no cases of pure allocentric neglect. Rather, the presence of allocentric neglect predicted poor performance on a range of neglect tasks (including traditional measures of egocentric neglect such as line cancellation, star cancellation, egocentric biases in the defect detection task), suggesting that allocentric neglect is associated with cases of severe egocentric neglect. Also unlike the previously reviewed studies, this study did not reveal a dissociation in anatomical terms. Egocentric and allocentric deficits were not related to separate regions but were associated with lesions affecting the superior and middle temporal cortex and underlying white matter and insula (Yue et al., 2012).

How can we explain the discrepancy between the behavioral and anatomical findings of Yue et al. (2012) and the previous smaller studies that suggested ego- and allocentric symptoms are largely independent of each other? We suggest this might reflect the criteria used to dichotomize patients as having either egocentric or allocentric neglect. There is clear evidence that egocentric neglect presents with a range of severity (Rorden & Karnath, 2010). In contrast, most previous studies have coded allocentric neglect as categorical, i.e. as 'having' or 'not having' allocentric neglect. However, if severity varies across patients, it is reasonable to suggest that thresholds that dichotomize allocentric neglect may create apparent dissociations. More recently there have been attempts to code allocentric neglect as a continuous severity index (e.g. Bickerton et al., 2011; Chechlacz et al., 2010; Verdon et al., 2010). However, most of these measures for an allocentric deficit become
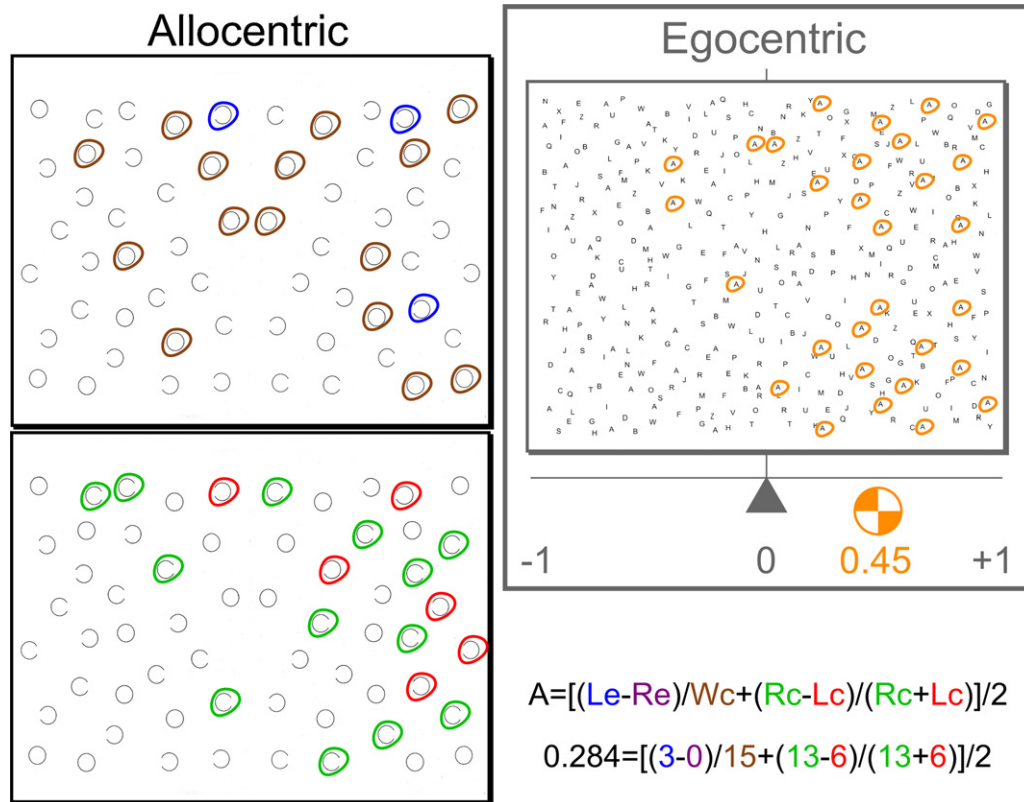
Fig. 2. Illustration of the measures for allocentric and egocentric neglect in the present study. These images show performance for a representative participant with a right-sided lesion, though note that all actual responses were made with a black pen (shown in color here for salience and to illustrate our formula). Main panel: allocentric neglect is based on two repetitions of the defect detection task (Ota et al., 2001). The participant was asked to find all the whole items (circles in this example) in one presentation (top) and asked to find all the defective items in a second presentation (bottom). Our measure of allocentric neglect was based on the number of correct whole items found (Wc, brown), the number of errors where the defect is on the contralesional left (Le, blue), and the number of errors where the defect is on the ipsilesional right (Re, purple – none in this example), the number of correctly identified items with a defect on the contralesional left (Lc, red) as well as the number of correctly identified items with a defect on the ipsilesional right (Rc, green). The formula (lower right) shows how our measure of allocentric neglect is computed with these values (here 0.284). *Upper right inset:* the center of cancellation (CoC) measure for egocentric neglect (cf. Rorden & Karnath, 2010) applied to the letter cancellation task. The participant is asked to find instances of a target in a cluttered field (the letter A in this example). Each potential target is given a weight of −1 (leftmost item) to +1 (rightmost item), with the CoC reflecting the mean weighted value for all targets detected (here 0.45). Note that the CoC values for the letter cancellation task (illustrated here) and the feature cancellation task (not illustrated) by Weintraub and Mesulam (1985) were averaged and served as our measure of egocentric neglect.

more conservative with neglect severity (a patient with an egocentric bias explores fewer items on defect detection tasks, and therefore the total number of possible allocentric errors is reduced). Likewise, the egocentric classifiers used in these studies (number of errors on either side of the page) have relatively low sensitivity for egocentric neglect severity (Rorden & Karnath, 2010). In sum, in order to properly investigate an association between egocentric and allocentric neglect, these deficits need to be assessed with continuous measures that can capture the severity of the deficits. We directly explore this hypothesis in the present work, by examining performance using appropriate continuous measures for both ego- and allocentric neglect.

One additional concern with regards to the study of Yue et al. (2012) is that it appears to classify patients as having both egocentric and allocentric neglect based on performance on a single circle defect detection task. Further, their task includes only 30 items (10 whole, 10 with left gaps, 10 with right gaps), rather that the 60-item task originally described by Ota et al. (2001). Specifically, participants were diagnosed with allocentric neglect if they omitted significantly more left than right gaps, or if they omitted more than 10% of left gaps while correctly identifying all right gaps (e.g. missing two left gaps but detecting all ten right gaps would have a chi-squared $p < 0.136$). Likewise, egocentric neglect was diagnosed when individuals neglected "some circles on the left of the test

paper, with other circles marked correctly". One concern with the method used in the study of Yue et al. (2012) is that acute performance may be noisy; therefore, relying on a single small test for the primary classification may be troublesome. Furthermore, the description of the egocentric classification is vague – does a single error on the left half of the page classify someone as having egocentric neglect? In our experience, many patients with severe neglect may miss a few items on the right side of the page, as well as all/most of the items on the left half (e.g., the individual we present in Fig. 2): it is ambiguous how these patients would be classified (as some items on the right of the test paper are marked incorrectly). In any case, one might argue that Yue et al. (2012) used a liberal measure to detect egocentric neglect, and therefore it is not surprising that all individuals with allocentric neglect also exhibited an egocentric bias (though note in the subsequent analyses the authors found that patients with both allocentric and egocentric neglect showed larger deficits on other classical neglect tests than individuals with only egocentric biases).

To resolve these concerns, we acquired data on a new group of stroke patients and have conducted an analysis where we attempt to measure the severity of egocentric and allocentric aspects of neglect by using a novel continuous measure for allocentric neglect, in addition to a recently developed continuous measure for egocentric neglect (Rorden & Karnath, 2010). Evidence from Yue

et al. (2012) predicts that we will find that allocentric neglect is only observed in combination with severe egocentric neglect, whereas other studies have suggested these deficits are independent.

2. Methods

We acquired data at the University Hospital Reykjavik from 36 right hemisphere stroke patients (mean 64.1 years, sd 14.75) with behavioral testing 10.3 days (sd 8.9) and magnetic resonance imaging 10.0 days (sd 9.0) post stroke. Lesion volume varied across participants (mean = 51cc, sd = 65cc; min = 0.52cc, max = 186cc). Each individual completed a battery of behavioral tasks that included both the circle and triangle versions of the defect detection task described by Ota et al. (2001) as well as the Letter and Feature cancellation tasks by Weintraub and Mesulam (1985). For the defect detection tasks, we had each participant perform four versions – for both the circle and triangle task the participant was asked to mark all whole circles/triangles in one presentation and then they were asked to mark all the circles/triangles with a defect on a separate sheet of the same stimulus array. To measure allocentric biases we counted the number of responses for each of five conditions: for the whole item detection task we determined the whole items correctly marked (Wc) as well as the errors for marks of items with a defect on the contralesional left (Le) and ipsilesional right (Re); for the detection task of items with a defect we measured the number of correctly detected items with a defect on the contralesional left (Lc) and on the ipsilesional right (Rc). From these values we computed (separately for the detection task with the triangles and with the circles) an allocentric score (A) for the right-sided lesioned patients based on the following formula:

$$A = \frac{[(Le - Re)/Wc + (Rc - Lc)/(Rc + Lc)]}{2}$$

By including the number of detected whole items in the denominator we take into account the extent of egocentric neglect, yet by placing the number of items detected (Rc + Lc) in the denominator, we do not understate allocentric neglect in individuals with substantial egocentric bias (unlike Bickerton et al., 2011). Note that this formula cannot be applied for patients who do not correctly detect any whole items in the whole item detection task (Wc = 0); such behavior could result if subjects, e.g., do not understand the instructions or simply have such severe egocentric neglect that the defect detection task is unable to measure an allocentric bias. The cancellation tasks were scored using the center of cancellation (CoC) measure and software (Rorden & Karnath, 2010). The CoC values for the letter cancellation task and the feature cancellation task were averaged and served as our measure of egocentric neglect. We conducted Pearson Product Moment Correlations by using OpenStat (http://www.statprograms4u.com/) to assess the strength of association between the allocentric and egocentric neglect measures. Our new allocentric measure and the CoC measure are illustrated in Fig. 2.

Brain imaging was acquired on a Siemens Avanto 1.5T scanner in all subjects. For 24 patients these data were available in digital format for further analysis. Lesions were delineated on fluid-attenuated inversion recovery (FLAIR) T2-weighted sequence with images reconstructed to $0.72 \times 0.72 \times 6.5$ mm resolution with 25 axial slices, TR = 9.0 s, TE = 11 ms. A high-resolution T1-weighted image was also acquired using an MP-RAGE sequence allowing isotropic 1 mm resolution. Raw DICOM data was converted to NIfTI format using dcm2nii (www.mricro.com). Images were spatially processed using the 'clinical toolbox' (Rorden, Bonilha, Fridriksson, Bender, & Karnath, in press) for SPM8 where the FLAIR images were initially coregistered to the T1 image, with parameters applied to the lesion masks. Subsequently, the T1 images were normalized with SPM8's unified segmentation normalization with lesion cost function masking (Brett, Leff, Rorden, & Ashburner, 2001), with the transforms applied to the coregistered lesion maps for use in voxelwise lesion-symptom mapping (Bates et al., 2003). Lesion symptom mapping was conducted using the t-test feature of our NPM software (Rorden, Fridriksson, Karnath, 2009).

3. Results

No defect detection task data was available for one patient, and three patients had such severe egocentric neglect (with a mean CoC score greater than 0.97) that we were unable to assess possible allocentric defects using the defect detection tasks (cf., Section 2 above). These participants were excluded from further analysis. A further patient completed the defect detection task with the triangles but not with the circles; this patient was excluded only from the analysis that contrasted these two tasks.

In order to validate our new measure of allocentric neglect, we tested whether performance in one test of allocentric neglect (e.g. the triangle defect task) predicted an individual's performance on a different test of allocentric neglect (e.g. the circle defect task). The 32 participants who completed both versions of the defect detection task (with the triangles and with the circles) exhibited
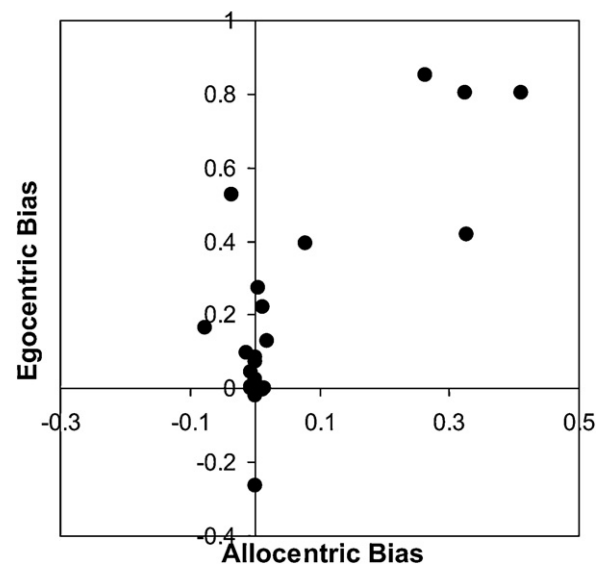
Fig. 3. Correlation of egocentric neglect (vertical axis) and allocentric neglect (horizontal axis). The egocentric neglect score is calculated using the averaged Center of Cancellation (CoC) measure (see Fig. 2) applied to the letter and the feature cancellation tasks by Weintraub and Mesulam (1985), such that values near 1 indicate that only the right-most items were detected while scores near zero reflect that targets were missed with equal distribution on both sides of the page or that all targets were correctly cancelled. The allocentric neglect score averages the allocentric scores (A; see Section 2) for both the circle and triangle defect detection tasks. Each dot represents values from a single participant. Note that allocentric neglect was highly correlated with egocentric neglect.

a Pearson product-moment correlation coefficient (PCC) of 0.349 ($t(30) = 2.03$, for a one-tailed $p < 0.025$). Therefore, as predicted, we found that higher values in one task would predict higher values in the other. Thus, for the next step of the analysis we averaged the allocentric scores for the defect detection task with the triangles and with the circles. Fig. 3 illustrates that for the 33 participants their allocentric neglect score was strongly correlated with their egocentric neglect score, with a PCC of 0.799 ($t(31) = 7.40$, $p < 0.00001$). Examining Fig. 3 revealed that substantial allocentric neglect was only observed in the presence of substantial egocentric neglect.

Voxelwise lesion-behavior statistics were calculated for the 24 patients with complete anatomical and behavioral data (cf., Section 2 above). This patient subset also showed a strong correlation between allocentric and egocentric neglect (PCC = 0.899). We conducted t-tests on voxels damaged in at least 25% ($n = 5$) of the population, and thresholded with a 5% false discovery rate to control for multiple comparisons. As shown in Fig. 4, regions associated with egocentric neglect (green) and allocentric neglect (red) largely overlapped (yellow).

4. Discussion

Many previous studies have argued that egocentric and allocentric deficits dissociate. Yue et al.'s (2012) recent large study of 110 patients as well as the present data suggests that this may be a false dichotomy. In both cases, a strong association was found between allocentric and egocentric neglect. We suggest that categorical measures for egocentric and allocentric deficits may explain some of the previously reported dissociations, whereas we here employed continuous measures for both aspects. Furthermore, we note that some previous studies have looked at chronic patients, used different tasks and provided different instructions. However, we assert that many of these studies were designed to explicitly
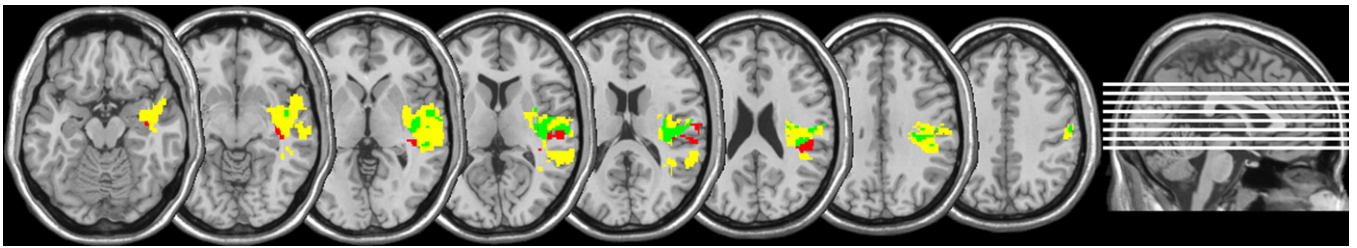
Fig. 4. Lesion-symptom mapping data showing regions that predict egocentric (green), allocentric (red) biases, and egocentric plus allocentric (yellow) neglect. This analysis is based on the structural scans from 24 of our stroke patients. Data are thresholded with a 5% false discovery rate. Illustrated slices correspond to −16, −8, 0, 8, 16, 24, 32 and 40 mm in standard stereotaxic space. Note that the anatomical dissociation predicted in Fig. 1 was not supported by our data, with large regions associated with both deficits.

dichotomize data, and therefore were destined to find dissociations in at least a portion of the participants.

The defect detection tasks by Ota et al. (2001) have been adopted by most of the previous studies of allocentric neglect. These tests are easy to administer in an acute clinical environment. Our analysis revealed that it also appears to be a relatively reliable measure of allocentric neglect (based on the fact that the index on the triangles task correlated with the same individual's bias on the circle task). However, note that we administered the defect detection task slightly differently from the conventional method where participants were asked to mark on the same sheet the broken items with one symbol (e.g. crossing out the circles that have a gap) and to identify the intact items with a different symbol (e.g. circling the complete circles). As noted by Bickerton et al. (2011), this procedure may not be an optimal method for assessing allocentric neglect. One issue is that the two simultaneously required tasks can cause problems for patients with perseverative deficits. Furthermore, since every item requires a response it may not be as sensitive as a more sparse displays, where distractor stimuli terminate searches. Similar to Bickerton et al. (2011), we required participants to complete two independent tasks with copies of the same display, directly addressing this criticism. One limitation of the defect detection task (Ota et al., 2001) and the Apples task (Bickerton et al., 2011) is that they do not provide accurate reliable measures of possible allocentric neglect when severe egocentric neglect is present. Perhaps in these instances, computerized tasks that only present a single item at a time, or eye tracking tasks can provide a robust measure of allocentric, object-based neglect (cf. Karnath et al., 2011), though these studies are more arduous.

As noted, our data as well as the data by Yue et al. (2012) suggest a strong association between egocentric and allocentric neglect that appears to be at odds with previously published studies. For example, Fig. 1 in the study of Chechlacz et al. (2010) suggests that robust allocentric biases are only observed when there is no egocentric bias, while our data shows that allocentric neglect is strongly correlated with egocentric neglect (Fig. 2). We assert that our choice of measures can explain some of these effects. However, with respect to this particular study it is also worth noting that these authors used a different test for allocentric neglect (the Apples task) and that they worked with chronic patients. Explicit rehabilitation or spontaneous recovery thus may also account for differences (though see Bickerton et al., 2011). We further wish to emphasize that our study had a relatively small number of patients and therefore must be interpreted with caution, though our findings were consistent with the study by Yue et al. (2012), which was based on a large sample size of 110 subjects.

The present data as well as those reported by Yue et al. (2012) fit with a clear record of empirical evidence and theoretical models which suggest that allocentric and egocentric effects interact.

Driver and Pouget (2000) noted that virtually all the evidence for allocentric neglect could be explained by a relative egocentric gradient. For example, consider that the left hemisphere has a very strong weighting for information on the extreme right hemifield with decreasing weight for information progressively on the left (which Driver and Pouget noted is similar to the effects found in single-cell recordings from primates). With such a model, if the right hemisphere is injured the right side of any object will be more salient than the left side of the object – regardless of the location of this object with respect to the body. This model would apply to all the tests of allocentric neglect described here. Mozer (2002) used similar principles for a simple neural network model that has no explicit object-based coding yet predicts 'allocentric' deficits on many tasks. Indeed, clear empirical evidence has been reported that egocentric position interacts with allocentric biases. Karnath and Niemeier (2002) compared the exploratory eye movement behavior of neglect patients during their spontaneous visual search of the entire surroundings versus when they had to concentrate their visual search on a discrete segment of the whole scene. They observed evidence that egocentric and allocentric neglect may not be distinct, but rather reflect different situations and strategies. One and the same physical stimulus at one and the same location in a scene was attended or, in another situation, neglected, just depending on the behavioral goal of the subject. More recently, Karnath et al. (2011) recorded neglect patients' eye and head movements while they explored objects at five different egocentric positions along the horizontal dimension of space. Data analysis revealed that allocentric, object-based neglect varied with egocentric position: while the neglect of the objects' left side was strong at contralesional egocentric positions, it ameliorated at more ipsilesional egocentric positions of the objects. These findings may indicate that visual input is coded in egocentric and object-based coordinates simultaneously (Niemeier & Karnath, 2002a, 2002b). Alternatively, the models of Driver and Pouget (2000) and of Mozer (2002) explain these effects without needing to invoke an allocentric frame of reference at all. In sum, these empirical data and theoretical models are in accord in suggesting that egocentric and object-based neglect may constitute different manifestations of the same disturbed system (Karnath & Niemeier, 2002; Niemeier & Karnath, 2002a). A simple analogy is to consider a zoom lens (e.g. Eriksen & St James, 1986) that adjusts its field of view based on the region of interest, such that the amount of allocentric bias reflects a pathological zooming onto one portion of the environment, e.g. zooming onto one particular object (cf. Niemeier & Karnath, 2002a). Therefore, the form of the task used and the strategy employed by the participant can influence the magnitude of the allocentric neglect; manipulations of the density of targets and task instructions may also influence the allocentric bias. Patients with egocentric deficits thus may exhibit allocentric biases but these effects appear to be influenced by the task, strategy and location of brain injury (Karnath et al., 2011; Karnath & Niemeier, 2002).

If allocentric and egocentric neglect are associated, why have some of the previously described studies found that individuals with allocentric neglect exhibit more posterior injuries than those without (Chechlacz et al., 2010; Hillis et al., 2005; Khurshid et al., 2012; Marsh & Hillis, 2008; Verdon et al., 2010)? One possibility could be that this simply reflects the vasculature of the middle cerebral artery territory – according to this model, mild neglect is associated with anatomical injury to the central portion of the middle cerebral artery territory, while more severe deficits accompany disruption of a larger portion of eloquent cortex and are therefore associated with damage to a larger region of middle cerebral artery territory (including more posterior regions). By this account, allocentric and egocentric neglect rely on one and the same underlying mechanism, yet allocentric deficits are subclinical for milder forms of neglect. Alternatively, it is possible that allocentric deficits are seen when there is a combination of disruption to the perisylvian regions responsible for egocentric neglect (Karnath & Rorden, 2012 for review) as well as injury to more posterior regions involved in visual processing. According to this view damage to the perisylvian regions is sufficient for egocentric deficits but allocentric deficits also require more posterior injury. This combination could explain why allocentric neglect is contingent on egocentric neglect, but egocentric neglect can be observed in isolation.

By either account, we note that data from a wide range of modalities (including single cell recording) might provide a physiologically plausible method for a 'zoom lens' mechanism for neglect (Halligan & Marshall, 1993, 1994) – with posterior regions found to effectively tune their receptive fields based on both bottom up and top down attentional demands. A recent review by Beck and Kastner (2009) summarizes elegantly this hypothesis: "… *directed attention can be described as causing a constriction of receptive fields (RFs) in V4 and TEO from 4° to 8° to about 2°, thereby presumably enhancing spatial resolution. This interpretation is compatible with behavioral studies showing that spatial attention improves acuity and is also supported by recent physiology findings of dynamic RF properties during the allocation of visual attention in macaque area MT. We should like to emphasize, however, that the concept of a shrinking RF is simply a convenient description of the data. Presumably, this apparent shrinking is the result of attention changing the weighting of the input to the cells, such that those cells that correspond to the attended stimulus are weighted more strongly than those that correspond to the unattended stimulus. In other words, the underlying mechanism of such 'shrinking' is the biasing of competition in favor of the attended stimulus.*"

In summary, we provide new evidence that allocentric deficits are strongly associated with egocentric neglect, based on a new continuous measure to assess allocentric neglect (in addition to our recently developed continuous measure for egocentric neglect). In a group study of (sub)acute right hemisphere stroke patients, we found that allocentric deficits were strongly correlated with egocentric neglect. In fact, allocentric neglect was only observed in conjunction with egocentric neglect. Further, neither the large study by Yue et al. (2012), nor the work we present here supported an anatomical dissociation between egocentric and allocentric neglect. However, we would like to emphasize that each of these studies has potential limitations. Yue et al. (2012) did not conduct objective statistics on their anatomical data, and as mentioned previously their classification of egocentric neglect may have been sensitive to allocentric biases. Further, our sample size was small, and thus in our anatomical analysis we were not able to control for lesion volume or directly model the interaction between behavioral measures (e.g. use VLSM to conduct an ANCOVA). In addition, both Yue et al. (2012) and our work rely on structural scans that may not identify the full extent of the functional disruption induced by a stroke. In any case, null results are always difficult to interpret. Future research thus is required to further investigate the anatomical relationship between allocentric and egocentric effects.

Acknowledgements

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