DISABILITY AND REHABILITATION, 2004; VOL. 26, NO. 12, 746–755

Taylor & Francis healthsciences

Role of disengagement failure and attentional gradient in unilateral spatial neglect – a longitudinal study

YARON SACHER†*, CORINNE SERFATY†, LEON DEOUELL‡, AYELET SAPIR§, AVISHAI HENIK§ and NACHUM SOROKER†

† Loewenstein Rehabilitation Hospital, Raanana, and Sackler Faculty of Medicine, Tel-Aviv University, Ramat Aviv, Israel

‡ Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel

§ Department of Behavioral Sciences and Zlotowski Center for Neuroscience, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Abstract

Purpose: To assess the importance of 'disengagement failure' and 'attentional gradient' in unilateral spatial neglect (USN) and in recovery from neglect.

Method: Eight right-hemisphere-damaged stroke patients performed the standardized Behavioural-Inattention-Test battery for visual neglect, line-bisection tests, and two computerized reaction-time (RT) tasks: a variant of Posner's 'Spatial-Cueing' paradigm (with special emphasis on the magnitude of leftward disengagement time) and a signal-detection task (marking the spatial gradient of attention by the distribution of RTs to target stimuli in different spatial locations). The correlation between the different measures was assessed at two points in time, before and after a period of rehabilitation treatment.

Results: A recovery pattern could be identified in both RT paradigms. However, the correlation between standard measures of neglect and performance on both, spatial-cueing and signal-detection tasks, was weak.

Conclusion: Neither difficulty disengaging attention from an ipsilesional stimulus nor changes in the attentional gradient can fully explain the processes underlying USN and its recovery. A large interpersonal variance exists among USN patients in the expression of disengagement and other spatial-attention deficits. Hence, individual patients should be tested by measuring different factors known to play a role in USN. This information is crucial for assigning the appropriate treatment for each patient in accord with the specific deficit revealed.

* Author for correspondence; Department of Neurological Rehabilitation, Loewenstein Hospital Rehabilitation Center, 278 Ahuza, Ra'anana, Israel 43100. e-mail: sacher@012.net.il

Introduction

Unilateral spatial neglect (USN; unawareness of objects located in the side of space contralateral to the side of a brain lesion) is one of the most devastating consequences of stroke, with prevalence as high as 35% in some studies.[1–4] The syndrome is much more frequent, persistent and severe among right-hemisphere damaged (RHD) patients. In RHD stroke patients with USN, processing of information in the left space is partial at best. They might fail to eat from one side of the tray, have trouble grooming the left side of their body, respond poorly to people standing on their left, have difficulty reading a paragraph or a word to its left margin (neglect dyslexia), and have difficulties initiating exploratory leftward movements. USN was found to be a very important negative prognostic factor in stroke rehabilitation.[5, 6]

Recovery from USN has been demonstrated by several studies.[3, 6, 7–11] However, recovery was often partial and significant differences were seen in the magnitude of the improvement, depending on the test used for measuring neglect.[7, 8] In a study carried out recently in the Loewenstein Rehabilitation Hospital, Israel,[12] the recovery of 29 RHD patients with left USN was evaluated using two major paradigms for the assessment of neglect – *Line Bisection* and *Target Cancellation* (the latter was assessed using the Star Cancellation subtest of the standardized Behavioral Inattention Test;[13] BIT). While improvement was evident in both testing methods, significant discrepancy was seen. Whereas in the Cancellation task an improve-

Disability and Rehabilitation ISSN 0963–8288 print/ISSN 1464–5165 online © 2004 Taylor & Francis Ltd
http://www.tandf.co.uk/journals
DOI: 10.1080/09638280410001704340

ment of 60% of the possible range of improvement was detected, in the Line-Bisection task the recovery was of only 29% of the possible range of improvement. The different expression of recovery in these two tasks probably suggests that they do not measure the same thing.[14] Cancellation tasks might assess a spatial dysfunction within an egocentric coordinate system while Line Bisection is probably more sensitive to dysfunction revealed within an object-based coordinate frame. This discrepancy formed the drive to evaluate further the recovery process in USN in its relation to the putative mechanisms underlying this syndrome. Better understanding of the mechanism of neglect, and of the factors operating in recovery from neglect, is crucial for development of efficient treatments for this disabling condition.

Several theories have been set forward to explain the syndrome of spatial neglect. Among them, failure in the representation of contralesional space,[15–19] in exploring the contralesional space (intention),[20–22] and in moving attention in space and the allocation of attention to spatially-tagged targets. The latter model, proposed by Posner and colleagues, has gained much influence.[23]

According to Posner's model, the covert movement of attention from one visual object to another can be described by a sequence of four steps, each having a distinct neurological organization. Attention is first *disengaged* from the location of the currently-attended stimulus; next it is *moved* to a new location, where *engagement* on a new stimulus takes place. After the location/stimulus has been screened, it is actively *inhibited* by the attentional system, relatively to other spatial locations, as a means to facilitate novelty-seeking behaviour. These functions were assigned to the parietal lobe (*disengagement*), the thalamus (*engagement*) and the tectal area of the midbrain (*move; inhibition of return*).[24–30] Posner and his colleagues have introduced a computerized paradigm (spatial-cueing paradigm) to test the four components of covert orienting of attention. According to their findings, parietal neglect (the most frequent form) is the result of *disengagement failure*.[25, 26]

Another attentional theory of USN, originally proposed by Kinsbourne, claims for the existence of an *attentional gradient* across the horizontal dimension. The damaged right hemisphere is said to exert less inhibition on the intact left hemisphere. As both hemispheres normally maintain a more or less balanced state by way of reciprocal inhibition, the result of left hemisphere disinhibition is an exaggerated bias of attention to the right side of space.[31] Mathematical models describing the impairment in the spatial distribution of stimulus salience in USN have been devised.[32]

Here we examined longitudinally the performance of RHD patients in standard paper-and-pencil tests of neglect and correlated them with parallel measurements of (a) magnitude of leftward *disengagement failure* (using the Spatial Cueing paradigm) and (b) magnitude of *attentional gradient* (using a signal detection task). Strong correlation between these two factors and performance in the standard tests would point to their importance in the pathogenesis of the syndrome. In addition, relatedness between amelioration of neglect and shortening of disengagement time or attenuation of the attentional gradient, would point to the role of these two factors in the mechanism underlying recovery from neglect. In order to verify the specificity of these factors to USN we tested also RHD patients without neglect, or with manifestation of neglect only in part of the classical measures.

Method

SUBJECTS

The study population included eight patients admitted to the Loewenstein Hospital for rehabilitation, who were able to perform the tests listed below and answered the following inclusion criteria: right handedness, first-episode stroke with solitary brain lesion (either ischemic or haemorrhagic) in the right hemisphere, intact visual fields on confrontation, negative neurological and psychiatric past history, willingness to participate and provision of informed consent. All patients were in a stable clinical and metabolic state and did not suffer from any active psychiatric disturbance. Detailed characteristics of the population referred to rehabilitation in this centre were presented elsewhere.[33] Lesion analysis was performed on the basis of follow-up imaging studies (CT/MRI). Patients' demographic and lesion characteristics are presented in table 1.

Six of the eight patients (LZ, BA, SY, ZL, KY, AS) manifested extinction of tactile stimuli on the left, and two patients (SY, ZL) manifested in addition extinction of visual stimuli appearing in the left visual field, in conditions of bilateral simultaneous stimulation. On admission to the study three patients (SY, ZL, AS) showed neglect according to the total score in the Behavioural Inattention Test (BIT) battery for visual neglect or according to their score in one or more of the subtests of the BIT* These and two more patients (LZ, KY)

*AS, with BIT score below the cut-off point for normality did not show significant asymmetry in the cancellation subtests.

Table 1 Patients' demographic and lesion data

Patient	*Age*	*Sex*	*Edu.*	*Lesion Type*	*Involvement*	*TAO I*	*TAO II*	*FIM adm*	*FIM dis*
LZ	72	F	10	I	I, EC, LN, ALIC, CN, IHWM	35	67	66	82
BA	66	M	15	H	Thalamus, PLIC, IHWM	33	68	76	104
SY	65	M	5	I	Pi, Odl, LN, PLIC, IHWM	29	66	75	96
ZL	49	M	12	I	Fi, Ts, Pi, I, EC, LN, ALIC, IHWM	31	91	78	108
KY	59	M	0	H	Thalamus, PLIC, LN, EC, I, IHWM	47	91	47	92
AS	29	M	10	H	Ts, Pi	34	70	104	116
LT	44	F	12	I	Fi, Ts, I, EC, LN, PLIC, ALIC, IHWM	24	65	93	116
SI	47	M	12	I	Fi, m, IHWM	33	68	103	123
Mean	54	–	9	–	–	33	74	80.25	104.6

Abbreviations: Edu. = Education (years); Lesion Type: I = Ischemic, H = Hemorrhage; Involvement: F, P, T, O = Frontal, Parietal, Temporal, Occipital; s, m, i, dl = superior, middle, inferior, dorso-lateral gyri; I = Insula, EC = External Capsule, LN = Lentiform Nucleus, ALIC = Anterior Limb of Internal Capsule, PLIC = Posterior Limb of Internal Capsule, CN = Caudate Nucleus, IHWM = Intra Hemispheric White Matter; TAO = Time (days) after stroke onset of first (I) or second (II) examination; FIM = Functional Independence Measure (total score at admission and discharge from the Loewenstein Hospital).

manifested pathological rightward deviation in bisection of 180 mm horizontal lines. The remaining three patients (BA, LT, SI) did not show neglect either in BIT or in Line-Bisection performance, although one of them (BA) manifested tactile extinction.

PROCEDURE AND TESTS

The patients were examined at two points in time. The first examination took place 4 ± 2 weeks after stroke onset, and the second examination was carried out 6 ± 2 weeks after completion of the first series of tests. Demographic and clinical anamnestic data were collected, and lateral dominance for hand, leg, ear and eye was assessed using a questionnaire. On each of the two test series several measures were taken.

Neurological examination and testing for neglect

Special consideration was given to signs of USN in performance of ADL tasks, and to the phenomenon of extinction upon bilateral simultaneous stimulation, both in visual and tactile modalities. Neglect was assessed using the *Behavioural Inattention Test*.[13] This widely used standardized test battery for neglect in the visual modality includes three distinct target-cancellation tasks (lines, letters, stars); figure and shape copying; line bisection; and representational drawing. Maximal total score is 146 and cut-off for normality is 130 points. In addition we employed a *Line Bisection task* where the patient was asked to mark the middle of a black horizontal line presented in the middle of an A4 sheet of white paper. Three line lengths (36, 90, and 180 mm) were used, each appearing 10 times in pseudo random order. The deviation (in mm accuracy) of the point marked (subjective midpoint) from the true midpoint was measured. Positive sign was given to rightward deviations while deviations to the left were assigned as negative.

Measurement of signal detection – 'Starry Night' Test[34]

The test is carried out with the patient sitting in front of the computer screen (16° and 12° visual angles, in horizontal and vertical dimensions, respectively). The screen is virtually divided into a 7×7 matrix with a distractor placed in each division. Every trial begins with the distractor in each cell being randomly visible or invisible. Every 50–250 ms (exact interval selected randomly) one cell of the matrix is chosen randomly and the status of its distractor is toggled so that if it was invisible it would become visible and vice versa. The exact location of the distractor within the cell is also varied at random. This pattern gives the appearance of a starry night, hence the nickname 'Starry Night' test. Seven hundred to 2100 ms from the beginning of the trial a target stimulus, distinct from the distractor stimuli, appears in the middle of one of the virtual cells while the distractors continue to flicker as described above. The patient is instructed to hit a specified key as soon as the target stimulus is detected. If the examinee has hit the key before the actual appearance of the target, the response is defined as false alarm. If she or he did not respond within 3000 ms of the appearance of the target, a miss trial is recorded. Missed trials are not replaced. The test starts with a training block of 49 trials, in which the target appears once in every location in random order. The test itself is divided into 10 blocks of 49 trials. Alltogether, the target appears 10 times in each cell of the virtual matrix. The target stimuli were 4 mm (0.22°) filled red circles whereas the distractor stimuli were 2 mm (0.11°) filled green circles. The independent variable was the horizontal location of the target stimulus on the screen and the dependent variables were the reaction time to the target stimulus and the hit rate.

Measurement of disengagement time – Spatial Cueing paradigm

This paradigm was developed by Posner and his colleagues to investigate the mechanism responsible for covert orienting of attention in space.[23, 24] In the present study we used a version of the test where the patient is presented with 3 dim white boxes in middle, right, and left positions on the computer screen. A trial begins with the appearance of a fixation cross in the centre of the middle square, where the patient is instructed to focus. The cross disappears after 1500 ms and 500 ms later luminance increases in one of the lateral boxes for 200 ms. After another interval the target stimulus is presented, either in the cued box (a valid trial) or in the opposite one (an invalid trial). The stimulus-onset-asynchrony (SOA - time interval between cue brightening and the appearance of the target) is 50, 150, 500 and 1000 ms. The target stimulus is presented until it is detected, but not longer than 3000 ms. Each trial is separated from the next one by a 2000 ms interval. The ratio between the number of valid trials and invalid trials was 1 : 1, i.e., the cue was not predictive of the ensuing target location. Each session consisted of 704 trials, divided as follows: each one of the 16 possible conditions (target side [2] by SOA [4] by trial validity [2]) was repeated 40 times, with the addition of 10% catch trials, in which no target appeared. The purpose of the catch trials was to prevent the patient from pressing the button each time a trial begins. The different trial conditions were presented in random order.

Results

RECOVERY PATTERN IN PATIENTS WITH NEGLECT ACCORDING TO TARGET CANCELLATION SUBTESTS OF THE BIT

Trying to recruit appropriate subjects for this study we found that patients with low BIT scores experience great difficulty answering the demands imposed by the Spatial-Cueing task as used in this study. Of the eight RHD patients who were able to complete the Spatial-Cueing test and formed eventually the study group, only two patients (SY, ZL) manifested clear neglect with asymmetric performance in Target-Cancellation subtests of the BIT. As a consequence, it is not surprising that neither the group total score on the BIT, nor the scores obtained at the group level in the different subtests, reveal significant change in paired *t*-test with time (second vs. first session). Nevertheless, revealing patterns emerge when the performance of individual patients is examined.

As can be seen in table 2, the two patients who showed neglect in the BIT with contralesional disadvantage in Target Cancellation (SY, ZL), manifested neglect

Table 2 Temporal dynamics in the different measures of spatial asymmetry

Patient	*Behavioral inattention test (BIT)* Total score		*Behavioral inattention test (BIT)* Star cancellation		*Line bisection 180 mm*		*Signal detection laterality index*		*Disengagement laterality index*	
TAO	1	2	1	2	1	2	1	2	1	2
LZ	140	142	54	52	**7.1**	2.5	0.02	0.05	**0.16**	0.01
BA	144	144	53	53	− 0.6	− 2.3	**0.06**	− 0.01	− 0.04	0.08
SY	**131**	129	**47**	50	**5.4**	13.6	**0.20**	0.19	**0.36**	− 0.11
ZL	**125**	137	**43**	54	**9.1**	5.9	**0.33**	0.19	**0.39**	0.12
KY	138	122	53	51	**5.6**	5.1	− 0.01	0.01	0.03	0.30
AS	118	135	54	52	**7.3**	8.6	**0.05**	0.06	**0.33**	0.03
LT	146	146	54	54	1.4	1.1	− 0.02	0.02	− 0.06	− 0.21
SI	142	143	54	53	− 0.4	1.8	**0.05**	− 0.01	− 0.05	0.04
Mean	135.50	137.25	51.50	52.38	4.36	4.54	0.09	0.06	0.14	0.03

Abbreviations: TAO = Time after stroke onset of first (1) or second (2) examination. Bolded scores = cases of marked contralesional disadvantage, as revealed in the different measures at TAO 1. Line Bisection: Mean signed displacement (mm) of the subjective midpoint from the objective midpoint in bisecting lines of 180mm, + / − = rightward/leftward error, respectively.

Signal Detection Laterality Index derived from the Starry Night test = Mean RT in 3 contralesional columns minus mean RT in 3 ipsilesional columns divided by mean RT in all 6 lateral columns.

Disengagement Laterality Index derived from the Spatial-Cueing test = Contralesional validity effect minus ipsilesional validity effect divided by mean RT in all 4 conditions (contralesional valid and invalid trials and ipsilesional valid and invalid trials) in Stimulus Onset Asynchrony (SOA) of 500 ms.

also in Line Bisection. These two patients showed the most prominent attentional gradient, as revealed in the laterality index of signal-detection time in the 'Starry Night' test. They also showed the most prominent leftward disengagement failure, as revealed in the disengagement laterality index derived from the Spatial Cueing test (see table 2). These associations seem to support theories of neglect suggesting a causative role for *attentional gradient* and *disengagement failure* in USN (but see further analysis of the data in the Discussion section).

The two patients dissociate however in their recovery patterns. While patient SY did not improve significantly in either total BIT score, the Star-Cancellation subtest, or the Line-Bisection task (actually he worsened from the first to the second session in the latter task), patient ZL showed significant improvement in all three measures. The dynamics in signal detection (the 'Starry Night' test) follow a similar pattern – no improvement in patient SY and improvement in patient ZL. The dynamics in disengagement time was different: in both patients the laterality index derived from the Spatial-Cueing paradigm (reflecting the difference in the magnitude of the cue-validity effect on both sides) became smaller with time, indexing a shift towards normalization. In patient SY the index actually became negative, meaning that in the second session the difference in RTs between valid and invalid trials was smaller for left (contralesional) targets than for right (ipsilesional) targets. Therefore, in this case lack of recovery in Target-Cancellation, Line-Bisection and signal-detection speed is coupled with marked improvement in leftward disengagement time, at least in SOA of 500 ms (see table 2).

RECOVERY PATTERN IN PATIENTS WITH NEGLECT ACCORDING TO LINE-BISECTION PERFORMANCE

Table 2 presents the mean error in bisection of 180 mm horizontal lines in the two sessions (data obtained from bisection of shorter lines is not presented). Five patients (LZ, SY, ZL, KY, AS) manifested contralesional (left) neglect, as evidenced by marked ipsilesional (right) deviation of the subjective midpoint in relation to the objective midpoint. Of these five patients only two (SY, ZL) showed neglect in the Target-Cancellation subtests of the BIT, and as discussed earlier, these two patients showed the most prominent attentional gradient, as reflected in signal-detection time to right and left target stimuli. Of the three patients with neglect on Line Bisection but not on Target Cancellation (LZ, KY, AS), only one patient (AS) showed a significant attentional gradient (see table 2). Four of the five patients with neglect on Line Bisection (LZ, SY, ZL, AS) showed asymmetry of disengagement time in the Spatial Cueing task. In these patients leftward disengagement time was longer than rightward disengagement time, a pattern compatible with contralesional disengagement failure. These findings probably suggest that disengagement failure is more relevant to manifestation of neglect on Line Bisection, whereas attentional gradient is related more to manifestation of neglect on Target Cancellation (see further analysis in the Discussion section).

The change in bisection error over time did not follow a uniform pattern. Of the five patients with neglect on Line Bisection, three improved with time (LZ, ZL, KY) and two performed worse on the second session (SY, AS). As can be seen in table 2, in some patients the dynamics either in magnitude of attentional gradient or in severity of leftward disengagement failure did not correlate with the Line Bisection dynamics. For example, patient SY with marked worsening in Line-Bisection performance over time did not exhibit a concomitant increment in attentional gradient nor prolongation of leftward disengagement time. In contrast, patient KY with some improvement in Line Bisection on the second session showed a significant increment in leftward relative to rightward disengagement time.

ATTENTIONAL GRADIENT AS REVEALED IN SIGNAL-DETECTION TIME

On admission to the study, five RHD patients (BA, SY, ZL, AS, SI) showed contralesional disadvantage in signal detection, as evidenced by significant difference in RT to right and left target stimuli (comparison of mean RT in the left three columns of the 'Starry Night' with mean RT in the right three columns, paired t-test, $p < 0.01$). It is of interest that two (BA, SI) of the five patients did not show neglect either on the BIT (or any of its Target-Cancellation subtests) or on Line-Bisection performance. This finding could represent merely a greater sensitivity of the computerized 'Starry Night' test compared with the classical paper-and-pencil paradigms (Target Cancellation and Line Bisection). However, the occurrence of pathological rightward deviation on Line Bisection coupled with symmetric signal detection (patients LZ and KY) forms a 'double dissociation' pointing to a fundamental distinction between attentional gradient and neglect by Line Bisection.

ANOVA was applied to RT data with *Horizontal Location of Stimulus* (one to seven) and *TAO* (time after stroke onset – I, II) as within-subject variables and *Neglect in the BIT* (+ , –) as a between-subjects variable. Main effects were found for *TAO* ($f = 49$, $p < 0.001$), with shortening of RTs in the second session, *Horizontal Location of Stimulus* ($f = 67$, $p < 0.001$), with reaction to targets on the three left columns being significantly slower compared with the three right columns, and *Neglect in the BIT* ($f = 682$, $p < 0.001$) with slower responses recorded among patients with neglect by BIT. The following interactions between variables reached significance: *TAO* by *Neglect in the BIT* ($f = 11.4$, $p = 0.001$) resulting from greater improvement between the sessions in patients with abnormal BIT (or BIT subtests), *and Horizontal Location of Stimulus* by *Neglect in the BIT* ($f = 48$, $p < 0.001$) as a consequence of the greater asymmetry in signal detection in patients with USN according to BIT.

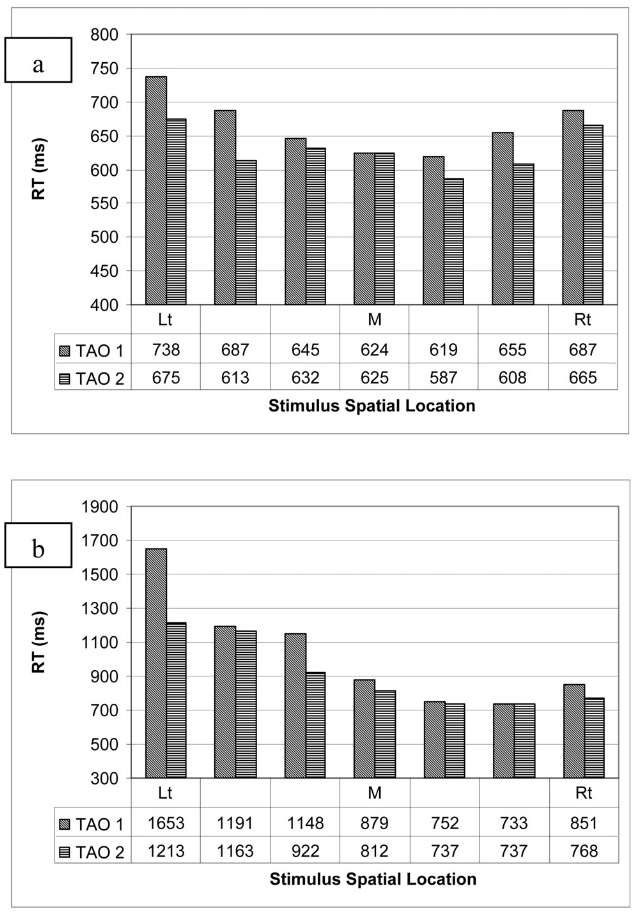

Figure 1 Attentional-gradient recovery pattern in RHD patients without (a) and with (b) USN according to BIT. Signal-detection data derived from the 'Starry-Night' test.

Mean RT according to the horizontal location of the stimulus in RHD patients who did not show USN by the BIT, is depicted in figure 1a comparatively for TAO I and TAO II. As can be seen, these patients show a mild disadvantage on the left. In TAO II, a slight overall improvement is noted (more speedy RTs) and the initial rightward bias is less pronounced. RHD patients who had USN by the BIT, showed a much more pronounced right-left asymmetry with left side disadvantage (figure 1b). Here examination in TAO II reveals improvement which is more evident on the contralesional left side.

DISENGAGEMENT FAILURE

On admission to the study, four RHD patients (LZ, SY, ZL, AS) showed significant prolongation of leftward (contralesional) disengagement time, relative to rightward (ipsilesional) disengagement time, at SOA of 500 ms. Disengagement failure is revealed in these patients in the laterality index derived from comparison of leftward and rightward cue-validity effects on the Spatial Cueing task (see table 2). With time, the relative contralesional disadvantage in disengagement time was reduced in all the four patients (see table 2).

The four patients who showed leftward disengagement failure manifested also neglect on Line Bisection, pointing to the possible connectedness of the two phenomena. However, the temporal dynamics in Line Bisection performance showed amelioration only in two of these patients (LZ, ZL). Patients SY and AS did not show recovery of neglect on Line Bisection, and actually performed worse at TAO II, while at the same time showing improvement in leftward disengagement time.

The variance in performance of the Spatial-Cueing task was analysed by a model that included the following parameters: *TAO* (I, II) as a within-subject variable and *Target Side* (right, left), *Trial Validity* (valid, invalid), *SOA* (50, 150, 500 and 1000 ms), and *Attentional Gradient in Signal Detection* (+ / –) as between-subjects variables. Significant main effects were found for *TAO* ($f = 11$, $p = 0.01$) as RTs shortened on the second session, and *Target Side* ($f = 18$, $p < 0.001$) resulting from slower responses to left-sided targets. *Trial Validity, SOA* and *Attentional Gradient in Signal Detection* did not have a significant main effect. Significant interaction was found between *TAO* and *Target Side* ($f = 6.3$, $p = 0.014$) resulting from greater shortening of RTs between subsequent sessions for left-sided targets. Figure 2 presents the RTs for right and left targets in valid and invalid trials across SOA's, in TAO I (figure 2a) and TAO II (figure 2b).

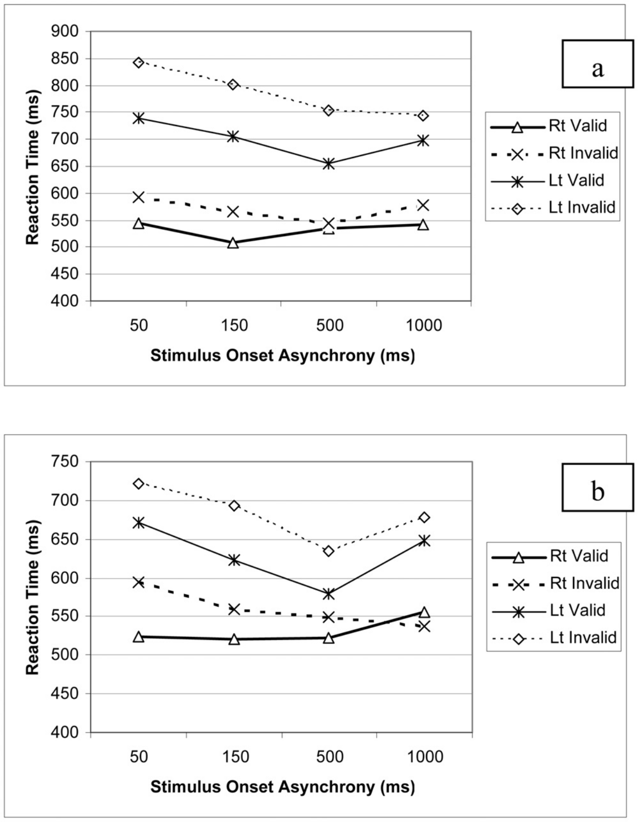

Figure 2 Dynamics in performance of the Spatial-Cueing test between first (a) and second (b) session.

TEMPORAL DYNAMICS IN DIFFERENT MEASURES

In order to evaluate the relationship between the different tests used to assess spatial attention, several parameters were calculated: (a) *BIT* (total score): (b) *Line Bisection* (mean signed displacement of the subjective midpoint from the objective midpoint, in mm, for each line length): (c) *Signal Detection Laterality Index* - the difference between mean RT in the left three columns of the 'Starry Night' and mean RT in the right three columns, divided by the mean RT in the six columns (using this laterality index we aimed to cancel the overall interpersonal variance in RT in this task): (d) *Spatial-Cueing* data (trial validity effect for left targets; trial validity effect for right targets; disengagement laterality index based on the difference between left and right validity effects at SOA of 500 ms divided by the mean RT at the same SOA across conditions [left valid and invalid trials and right valid and invalid trials]).

Examination of the temporal dynamics (difference in performance between first and second sessions) in these parameters, separately for each patient, reveals concordant trends in some patients (e.g., patient ZL in whom reduction of left-side disadvantage with time was observed in all parameters), and discordant trends in others (e.g., patient SY in whom deterioration in Line-Bisection performance was accompanied by improvement in leftward disengagement). Table 2 presents the dynamics in each parameter, separately for each patient.

In order to investigate the congruity of dynamics in different measures across patients, the recovery patterns (difference in performance between TAO I and TAO II) revealed in all the above parameters, was entered into a correlation matrix. The following correlations reached significance at the 0.05 level: bisection error in 36 mm lines and BIT total score ($r = -0.87$); ipsilesional (right target) validity effect and bisection error in 180 mm lines ($r = 0.77$).

Discussion

USN is a frequent sequel of vascular brain damage bearing grave implications on the rehabilitation process and its outcome.[5, 6] Impaired mechanisms of spatial attention were claimed to play a major causative role in this syndrome. The theoretical framework proposed by Posner and colleagues describes how attention is moved and allocated in space, provides a powerful tool (the Spatial-Cueing paradigm) to measure the different components of the process, and enables detection of specific attentional disturbances consequent of lesions to different brain structures. In the case of parietal neglect, use of the Spatial-Cueing task suggested that failure disengaging from a currently attended object, in order to relocate attention on a different object positioned on its left, is of specific importance.[25, 26] A different attentional theory of USN, originally proposed by Kinsbourne, claims for the existence of an exaggerated attentional gradient across the horizontal dimension, causing bias of attentional resources to targets on the right side of space.[31]

In the present study we aimed to evaluate further the importance of disengagement failure and attentional gradient as etiological factors in USN, with special emphasis on their role in recovery from neglect. For this aim we correlated recovery, as revealed in standard widely used paper-and-pencil tests of neglect, with parallel changes in (a) leftward disengagement time (derived from the Spatial-Cueing task), and (b) magnitude of the attentional gradient (evidenced by the difference in signal detection time for right and left visual stimuli in the 'Starry Night' test).

The research paradigm employed in the present study has limitations similar to those of earlier efforts to correlate impairment in clinical tests of neglect with malfunctioning of putative mechanisms.[35] The basic difficulty stems from the fact that there is no golden standard for the diagnosis of USN, and classical measures, like Line-Bisection, Target Cancellation, Copying or Drawing tasks often dissociate in the same patient. In earlier group studies, the frequency of double dissociations among classical symptoms and signs of neglect raised questions regarding the logic of applying a common name to this myriad of phenomena.[35] However, there seems to be a common denominator to all neglect phenomena and that is – impaired processing of information in the contralesional space. It is not clear why in one patient this impairment is manifested in Line Bisection and not in Target Cancellation while in another patient the opposite pattern is revealed. It is possible that one theoretical mechanism has greater impact on one measure of neglect (e.g., ipsilesional deviation on Line Bisection) and another mechanism has a greater impact on another measure (e.g., tendency to omit contralesional target stimuli in Cancellation tasks). Moreover, the two theoretical mechanisms studied in the present study are not mutually exclusive and may coexist in different degrees of malfunctioning in different patients.

The RHD patients who participated in the present study revealed marked variance in the expression of neglect on admission, and marked variance in the recovery patterns shown in different measures of neglect (see table 2). As a consequence, group analyses performed on the different parameters are probably less revealing than examination of relationships between measures, done separately for each patient. The only measures in which group temporal dynamics (change in performance between first and second examination sessions) revealed significant correlations were: error in bisection of short lines vs. BIT score, and error in bisection of long lines vs. ipsilesional cue-validity effect). Given the small number of participants in the study and the heterogeneity of neglect manifestations (two patients with neglect manifested both in Target Cancellation and Line Bisection, and another three patients with neglect manifested only in Line-Bisection performance), the meaning of the above concordant patterns of recovery is hard to interpret. For the same reason, lack of correlation between different measures in the group analyses is even less informative.

In contrast, the associative and especially the dissociative patterns shown by individual patients are revealing. Detailed description of concordant and discordant patterns in individual patients is to be found in the Results section. The major findings and conclusions are as follows:

(1) RHD patients who perform normally on Target Cancellation, Copying and Drawing tasks (comprising the BIT battery) may nevertheless show neglect on Line Bisection. Such decomposition of USN symptomatology was observed repeatedly in earlier studies, e.g.,[35] It points to the multifactorial and multifaceted nature of USN and underlines the importance of applying different diagnostic tests to assess different aspects of spatial inattention.

(2) RHD patients who perform normally on all standard paper-and-pencil tests of neglect (including Target Cancellation and Line Bisection) may nevertheless show a clear *attentional gradient* with attenuated signal detection on the left. Measurement of reaction time to left and right target stimuli seems to be more sensitive than regular Cancellation tests for detection of lateral asymmetries in information processing. Patients with delayed response to contralesional stimuli suffer probably from a milder form of impairment compared with patients manifesting full-blown neglect. Although these patients detect the stimuli on the left, it takes them much more time. In conditions where rapid stimulus detection and production of a quick response are crucial, for example, in driving, prolongation of response time can be very dangerous.

(3) Neglect on Line Bisection and *attentional gradient* show 'double dissociation' (i.e., neglect on Line Bisection can be seen in RHD patients who do not show an attentional gradient, and attentional gradient can be seen in RHD patients who do not show neglect on Line Bisection). According to the classical notion of 'double dissociation' introduced by Teuber,[36] this finding points to independence of the two phenomena.[37] Thus, it is unlikely that attentional gradient plays an important causative role in neglect on Line Bisection. This conjecture is supported by 'double dissociation' shown also in the patterns of recovery of Line Bisection errors and attentional gradient.

(4) All the patients in the present study who showed significant leftward *disengagement failure* on the Spatial-Cueing task had neglect on Line Bisection. This association may suggest a causative role for disengagement failure in neglect on Line Bisection. However, anatomical proximity of

processors responsible for distinct unrelated operations can also result in association of impairments following localized brain damage. The latter possibility is supported here by the demonstration of significant improvement in leftward disengagement time, with normalization of the disengagement laterality index, yet with parallel aggravation of neglect on Line Bisection (such longitudinal course was demonstrated by patients SY and AS, see table 2). Additional support for this possibility comes from demonstration of negative temporal dynamics in leftward disengagement time coupled with positive dynamics in Line Bisection performance (patient KY, see table 2).

(5) Improvement in leftward disengagement time does not necessarily imply amelioration of neglect on Target Cancellation. It is of interest that such dissociation in recovery patterns was found in a patient with parietal neglect (SY). According to Posner and colleagues[25, 26] the parietal lobe is responsible for disengagement, and parietal neglect is said to be caused specifically by disengagement failure.

(6) Finally, *attentional gradient* and *disengagement failure* – two putative mechanisms of USN belonging in neglect theorizing to the group of 'attentional' accounts - double dissociate, both on admission and in the recovery pattern. According to the classical notion of 'double dissociation', the implication of this finding is that none of these impairments fully explains the other.

The present research provides interesting information on the fate of the attentional gradient following right brain damage (see figure 1). The group analysis shows two significant aspects of the temporal dynamics: (a) overall shortening of signal-detection time in all spatial sectors, and (b) reduced left-right asymmetry. The first aspect points to the importance of a general, non-spatial, factor. In recent years the role of non-spatial factors in USN gets more attention,[38] and in one study recovery from neglect was shown to correlate with amelioration of non-spatial deficits.[39] The second aspect of the recovery process – flattening of the spatial gradient – is also of interest. If the attentional gradient reflects a state of imbalance between opposing hemispheric spatial biases, where the normal balance prior to the occurrence of brain damage was maintained by way of reciprocal inhibition,[31] flattening of the gradient in the recovery process should signal restitution of inhibitory forces of the damaged right hemisphere. In two patients (ZL, SI) shortening of RTs on the left was actually accompanied by prolongation of RTs on the right (so that RT on the right in TAO II was longer than in TAO I). Possibly this pattern represents spatial relocation of limited attentional resources, as improvement in one spatial location results in worsening in another.

The present research sheds light also on the fate of impairments in mobilization of attention consequent upon right hemisphere damage (see figure 2). Group analysis of the temporal dynamics in Spatial-Cueing performance demonstrates significant shortening of RT across conditions, which is more pronounced on the left (main effect for *TAO* and interaction of *TAO* and *Target Side*). As can be seen in figure 2, on first examination, the cue-validity effect (difference in RT between valid and invalid trials) was bigger on the left (indicating leftward disengagement failure). The improvement with time was asymmetric. For SOA of 500 ms (generally showing the best overall performance with shortest RTs on both sides) there is reduction of the validity effect on the left coupled with some enlargement of the validity effect on the right. This trend, which did not reach statistical significance, is quite similar to the pattern of dynamics observed for the attentional gradient.

Despite the introduction of various treatment modalities in the last two decades, USN still poses a significant challenge in rehabilitation medicine, as the functional sequels of the problem are extremely grave.[5, 6] There is no single therapeutic approach that seems to help all patients. This fact is in accord with the multifactorial nature of neglect and the multiple ways of its manifestation. The findings of the present research add to this complex picture new data on the nature of recovery processes in USN. Here also, dissociative patterns were found to occur commonly. Of special importance is the demonstration, in one and the same patient, of discordant dynamics in different measures of neglect, and in putative underlying mechanisms. The occurrence of discordant dynamics for different aspects of neglect suggests the possibility that a specific treatment exerts a beneficial effect on one aspect leaving important others unaffected.

This state of affairs calls for an effort to develop a novel, theory-motivated, taxonomy of spatial neglect. A comprehensive taxonomy would facilitate the appreciation of the relative effectiveness of different treatment modalities. It is unclear whether a classification based on phenomenological clustering (as in the case of aphasic syndromes) is operational and justified. On the other hand, the current level of neglect theorizing is probably at a stage where classification based on impairments to different cognitive mechanisms would fail to cover and explain all the relevant behavioural aspects. Our study, through the evaluation of patterns of recovery from USN, shows that neither *disengagement failure* nor *attentional gradient* provide the pathogenetic basis for all cases of USN. Moreover, none of these putative mechanisms seems to explain entirely the variance revealed in performance of classic neglect tests. More research, in large groups of patients, is needed in order to understand better the relationship between impaired cognitive processes and neglect phenomena. Progress along these lines is necessary for development of better treatment strategies targeting USN phenomena at their roots.

References

1 Diller L, Weinberg J. Hemi-inattention in rehabilitation: The evolution of rational remediation program. In: EA Weinstein, RP Friedland (eds) *Advances in Neurology*. Vol. 18. New York: Raven Press, 1977; 63–82.
2 Hier DB, Mondlock J, Caplan LR. Behavioural abnormalities after right hemisphere stroke. *Neurology* 1983; **33**: 337–344.
3 Kinsella G, Ford B. Hemi-inattention and the recovery patterns of stroke patients. *Int Rehabil Med* 1985; **7**: 102–106.
4 Kotila M, Niemi ML, Laaksonen R. Four-year prognosis of stroke patients with visuospatial inattention. *Scandinavian Journal of Rehabilitation Medicine* 1986; **18**: 177–179.
5 Katz N, Hartman-Maeir A, Ring H, Soroker N. Functional disability and rehabilitation outcome in right hemisphere damaged patients with and without unilateral spatial neglect. *Archives of Physical Medicine and Rehabilitation* 1999; **80**: 379–384.
6 Jehkonen M, Ahonen JP, Dstidar P, Koivisto AM, Laippala P, Vilkki J, Molnar G. Visual neglect as a predictor of functional outcome one year after stroke. *Acta Neurologica Scandinavica* 2000; **101**: 195–201.
7 Campbell DC, Oxbury JM. Recovery from unilateral visuo-spatial neglect? *Cortex* 1976; **12**: 303–312.
8 Hier DB, Mondblock J, Caplan LR. Recovery of behavioral abnormalities after right hemisphere stroke. *Neurology* 1983; **33**: 345–350.
9 Wade DT, Wood VA, Hewer RL. Recovery of cognitive function soon after stroke: a study of visual neglect, attention span and verbal recall. *Journal of Neurology, Neurosurgery and Psychiatry* 1988; **51**: 10–13.
10 Cassidy TP, Lewis S, Gray CS. Recovery from visuospatial neglect in stroke patients. *Journal of Neurology and Neurosurgery* 1998; **64**: 555–557.
11 Stone SP, Patel P, Greenwood RJ, Halligan PW. Measuring visual neglect in acute stroke and predicting its recovery: the visual neglect recovery index. *Journal of Neurology, Neurosurgery and Psychiatry* 1992; **55**: 431–436.
12 Serfaty C. *et al*., Personal communication. Unpublished data, 2001.
13 Wilson B, Cockburn J, Halligan PW. *Behavioral inattention test*. Titchfield, Hants: Thames Valley Test Company, 1987.
14 Binder J, Marshall R, Lazar R, Benjamin J, Mohr JP. Distinct syndromes of hemineglect. *Archives of Neurology* 1992; **49**: 1187–1194.
15 Bisiach E, Luzzati C, Perani D. Unilateral neglect: Representational schema and consciousness. *Brain* 1979; **102**: 609–618.
16 Bisiach E, Capitani E, Luzzati C, Perani D. Brain and conscious representation of outside reality. *Neuropsychology* 1981; **19**: 543–551.
17 Bisiach E, Capitani E, Porta E. Two basic properties of space representation in the brain: evidence from unilateral neglect. *Journal of Neurology, Neurosurgery and Psychiatry* 1985; **48**: 141–144.
18 Halligan PW, Marshall JC. Spatial compression in visual neglect: a case study. *Cortex* 1991; **27**: 623–629.
19 Bisiach E, Pizzamiglio L, Nico D, Antonucci G. Beyond unilateral neglect. *Brain* 1996; **119**: 851–857.
20 Weintraub S, Mesulam M-M. Right cerebral dominance in spatial attention. Further evidence based on ipsilateral neglect. *Archives of Neurology* 1987; **44**: 621–625.
21 Tegner R, Levander M. Through a looking glass. A new technique to demonstrate directional hypokinesia in unilateral neglect. *Brain* 1991; **114**: 1943–1951.
22 Kim M, Anderson JM, Heilman KM. Search patterns using the line bisection task for neglect. *Neurology* 1997; **49**: 936–940.
23 Posner MI. Orienting of attention. *Quarterly Journal of Experimental Psychology* 1980; **32**: 3025.
24 Posner MI, Cohen Y, Rafal RD. Neural systems control of spatial orienting. *Philosophical Transactions of the Royal Society of London Biology* 1982; **298**: 187–198.
25 Posner MI, Walker JA, Freidrich FJ, Rafal RD. Effects of parietal injury on covert orienting of attention. *Journal of Neuroscience* 1984; **4**: 1863–1874.
26 Posner MI, Walker JA, Freidrich FJ, Rafal RD. How do the parietal lobes direct covert attention? *Neuropsychologia* 1984; **25**: 135–145.
27 Rafal RD, Posner MI. Deficits in human visual spatial attention following thalamic lesions. *Proceedings of the National Academy of Sciences of the United States* 1987; **84**: 7349–7353.
28 Rafal R, Posner MI, Friedman JH, Inhoff AW, Bernstein E. Orienting of visual attention in progressive supranuclear palsy. *Brain* 1988; **111**: 276–280.
29 Posner MI, Rafal R, Choate LS, Vaughan J. Inhibition of return: Neural basis and function. *Journal of Cog Neuropsychology* 1985; **2**: 211–228.
30 Sapir A, Soroker N, Berger A, Henik A. Inhibition of return in spatial attention: evidence for collicular generation. *Nature Neuroscience* 1999; **12**: 1053–1054.
31 Kinsbourne M. Mechanisms of unilateral neglect. In: M Jeannerod (ed) *Neurophysiological and Neuropsychological Aspects of Unilateral Neglect*. Amsterdam: Elsevier Science, 1987; 69–86.
32 Anderson B. A mathematical model of line bisection behaviour in neglect. *Brain* 1996; **119**: 841–850.
33 Ring H, Feder M, Schwartz J, Samuels G. Functional measures of first stroke in patient rehabilitation: The use of the FIM total score with a clinical rationale. *Archives of Physical Medicine and Rehabilitation* 1997; **78**: 630–635.
34 Deouell LY, Sacher Y, Soroker N. A novel method for dynamic assessment of spatial attention after brain damage. Submitted for publication, 2004.
35 Marshall JC, Halligan PW, Robertson IH. Contemporary theories of unilateral neglect: a critical review. In: IH Robertson, JC Marshall (eds) *Unilateral Neglect: Clinical and Experimental Studies*. Hove: Lawrence Erlbaum, 1993; 311–329.
36 Teuber HL. Physiological Psychology. *Annual Review of Psychology* 1955; **9**: 267–296.
37 Shallice T. *From Neuropsychology to Mental Structure*. Cambridge: Cambridge University Press, 1988; 245–266.
38 Husain M, Rorden C. Non-spatially lateralized mechanisms in hemispatial neglect. *Nature Rev Neuroscencei* 2003; **4**: 26–36.
39 Bonneh Y, Pavlovskaya M, Ring H, Soroker N. Abnormal binocular rivalry in unilateral neglect: evidence for a non-spatial mechanism of extinction. *Neuroreport* 2004; **15**: 473–477.