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Recovery from Neglect after Right Hemisphere Stroke

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Abstract

Favourable outcome after cerebrovascular stroke is associated with early admission to rehabilitation, small lesion size and minor cognitive impairment. The aim of the present study was to explore factors associated with the amelioration of neglect after right hemisphere stroke. Twenty-one consecutive eligible right hemisphere stroke patients in one rehabilitation center were assessed and followed for 6 months. The neglect syndrome was assessed by the conventional subtests of the Behavioural Inattention Test (BIT) and by the Catherine Bergego Scale (CBS) before and after the 3-week rehabilitation and at 6-month follow-up. The manifestations of extinction, pusher syndrome and depression were evaluated. Recovery from neglect was strongly associated with early rehabilitation and the initial severity of neglect. Intensive treatment yielded recovery in severe or moderate visual neglect long after the first two to three months after stroke. Even chronic patients with sufficient cognitive and psychological capacity improved with intensive rehabilitation. Tactile extinction was common in these patients but was not associated with recovery. Manifestations of pusher syndrome hampered amelioration of visual neglect in acute and sub-acute stroke patients, whereas depression did not prevent recovery from neglect. Intensive rehabilitation promotes recovery from neglect in the acute phase after right hemisphere stroke. A comprehensive program later, in sub-acute or chronic phase, may also be effective especially in those patients who have not received intensive multi-professional rehabilitation soon after the stroke.

Keywords: Cerebrovascular diseases; Right hemisphere stroke; Neglect rehabilitation; Pusher syndrome; Extinction; Depression

Introduction

Stroke is today and will continue to be the most frequent cause of chronic disability in adults in the western world [1,2]. Nearly half of the stroke survivors display neuropsychological deficits acutely after stroke [3] and one in every three stroke patients is diagnosed with neglect. Although many patients recover from neglect spontaneously within the first months, ten percent of these individuals still show neglect three months after right hemisphere cerebral accident [4,5]. Neglect often predicts a poor functional outcome [6,7]. The aim of the present study was to search for the factors associated with recovery from neglect yet considering the heterogeneity of the syndrome.

Neglect, the right hemisphere syndrome, is a set of symptoms depending on the extent and localization of the lesion [8,9].The most frequent etiological causes of neglect are large infarctions in the right middle cerebral artery territory involving several cerebral lobes [10-12]. Patients with neglect typically have larger lesions than right hemisphere patients without neglect and they experience more motor and sensory impairments than patients without neglect. The syndrome is characterized by inattention to the contralateral hemispace. Mesulam et al. [13] has speculated that thalamus and cingulate cortex is essential in neglect, emphasizing aspects of regulation of arousal and motivation in the syndrome. Karnath and Dietrich [14] argued that superior temporal area, insula and temporoparietal junction form a multisensory area where also vestibular information is processed in relation to spatial orientation. These areas are integrative for vestibular, auditory and visual information coming from the surrounding space to form multimodal spatial representation. Further Karnath and Rorden [15] suggest that "the tight perisylvian anatomical connectivity between superior/middle temporal, inferior parietal and ventrolateral frontal cortices might explain, why lesions at these distant cortical sites around the sylvian fissure in the human right hemisphere can lead to the same egocentric bias of orienting behaviour, namely to spatial neglect."

Sensory impairments are not the cause of neglect, but they often occur with spatial deficits [16,17] and also visual field deficits are common [18]. Patients with only hemianopia learn to compensate for the field loss by eye movements to the blind hemifield, whereas patients with neglect fail to compensate for the deficit because of their inability to orient searching movements of eyes, head and body towards the contralesional side [19-24]. Thus patients with both hemianopia and neglect display left inattention in behaviour long after the visual neglect has ameliorated [25]. Extinction, unawareness of the lateralized stimuli in double simultaneous stimulation situations, is observed in vision, hearing or touch and even between elements in different sensory modalities [26-28]. Tactile extinction or inattention of the contralesional stimulus occurs in a competitive situation, where a patient is simultaneously touched on the contralesional and ipsilesional sides in hands, face or neck, symmetrically or asymmetrically. Anosognosia, unawareness of the illness, hemiparesis or neglect, can also co-occur with neglect but is often double-dissociated in such way that a patient shows unawareness of illness or neglect or hemiparesis but not necessarily all of these symptoms [29].

Hemispatial neglect has been characterized not only as inattention of stimuli on the contralesional side but also by hyperactive or magnetic orientation to the ipsilesional side [30-33]. Pusher syndrome can be classified as one of the positive/productive manifestations of neglect. Pusher syndrome is pathologically strong pushing with the healthy extremities to the ipsilesional side, and it contributes to the disturbed body balance [34,35]. Both pusher syndrome and neglect take longer to recover, when they occur together. Perseveration is often present in the acute phase after the stroke but may persist longer. In clinical

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practice, severe perseveration is a signal of executive problems and often is associated with slower recovery. Sandson and Albert [36,37] differentiated three distinct types of perseveration in neurological patients: (a) continuous perseveration implied compulsive repetition of a once initiated movement, (b) stuck-in-set perseveration as an inability to switch strategies, when task requirements changed and (c) recurrent perseveration. The recurrent perseverations were common in patients with left hemisphere damage and aphasia, whereas continuous perseveration was more frequent in patients with right hemisphere damage. Nys et al. [38] searched for anatomical correlates of perseveration and found out that lesions in caudate nucleus and lenticular nucleus were associated with perseverations.

Neglect has a negative effect on long-term outcome: these patients take longer to recover and they are left with more functional disabilities than patients with right hemisphere lesions without neglect [6,39-41]. Less than half of neglect patients recover spontaneously during the first weeks after stroke and less than 10% show complete recovery. Severe disabilities often lead to lack of co-operation acutely after stroke and dementia and attention deficits increase the probability of late failure in recovery [42]. Early admission to rehabilitation decreases long-term adverse outcomes [42]. Hemispatial neglect and depression are associated with an increased risk of low recovery as assessed in activities of daily living (ADL), but not on mobility. Previously stroke patients who improved most at one year follow-up were those with larger lesions and generalized cognitive impairment at baseline, however, aphasia and neglect were not influencing the long term recovery [3].

In the present study, neurological deficits, the amount and quality of rehabilitation and neuropsychological deficits in patients with neglect during the course of recovery were assessed. The role of hemianopia, extinction, pusher syndrome and depression were also analysed in the recovery from neglect. We searched for determinants of excellent or poor recovery from neglect.

Materials and Methods

Subjects

Forty-two patients, who were referred to a local rehabilitation centre for rehabilitation during three consecutive years, were screened for neglect. The subjects had to have a diagnosis of first single right hemisphere stroke. Since we were interested in the amelioration of neglect in different phases after stroke, specific inclusion criteria of neglect for acute, subacute and chronic patients were used. Acute patients entered the study after the first ten days after stroke, when they were able to transfer from acute hospital to rehabilitation unit, but less than three months from stroke. Subacute phase was defined from three to six months. The chronic phase started from one year after the stroke onset to clearly differentiate it from the subacute phase.

The criteria for acute neglect were defined as severe to exclude any transient symptoms. Left acute neglect was defined by at least two of the following conditions: a score of 100 or less on the Behavioural Inattention Test (BIT C) [43], at least two of the BIT conventional subtests under the cut-off points, or a Catherine Bergego Scale (CBS) occupational therapist evaluation score [44,45] of 10-30 points. The subacute phase criteria follow the traditional definitions of neglect in rehabilitation studies and the patients had to fulfil at least two of the following criteria: a score of less than 130 points in the BIT C subtests, at least one of the BIT C subtests under the cut-off point, or a CBS score of two points or more. In the chronic phase (≥ 1 y) the criteria were residual neglect or no neglect at all in the BIT C if neglect in behaviour was present: a score of 140 or less in the BIT C or the CBS score of 5 points or more.

Sixteen patients did not reach the inclusion criterion of neglect, two patients were not willing to participate in the trial, one patient was too tired to co-operate and two patients were excluded because of their left-handedness. A total of 21 patients met the criteria. The study was approved by the local institutional review board (North Savo Hospital District) and written informed consent was obtained prior to participation. The lesion location was based on CT or MRI assessed by a neuroradiologist. Acute and subacute patients were randomized into either Arm Activation training or Visual Scanning training using envelope concealment. All chronic patients were recruited in the order of admission. All 21 patients were followed up at 6 months.

Clinical assessment

Neurological examination: An extensive clinical examination was conducted for each patient before rehabilitation (pre-rehabilitation), after the 3 weeks of rehabilitation (post-rehabilitation) and six months after the rehabilitation (follow-up) by neurologist. On admission, patients' examination included the assessment of motor disability using the Modified Rankin Scale [46] and the confrontational assessment of visual fields. General functional status was assessed by a nurse with the Functional Independence Measure FIM; [47]. Motor functions were assessed by a physiotherapist. The Modified Motor Assessment Scale, MMAS [48], was used. A physiotherapist evaluated pusher syndrome using the Scale for Contraversive Pushing (SCP) [49]. It includes three domains assessed for both sitting and standing positions: posture, extension, and resistance. Patients are scored from 0-6 such that the higher the score, the greater the severity of pushing. Patients were identified as showing pusher syndrome if they scored >0 on any of the three domains as in Danells et al. [33]. For objective assessment of the changes in the affected hand motor performance, the structured Wolf Motor Function Test, WMFT [50], was used.

Neuropsychological assessment: The neuropsychological assessments were conducted by one research neuropsychologist and another neuropsychologist served as the rehabilitation neuropsychologist. Handedness was assessed by the Edinburgh Inventory [51] at baseline. All other tests were conducted at pre-rehabilitation, at post-rehabilitation and at follow-up, each time in a standard order. The pencil and paper tests were presented in the patient's midline as instructed.

Visual memory was assessed by the visual reproduction subtest (VR) of the WMS-R [52], the object memory test [53] and the Rey complex figure test [54]. The WMS-R visual reproduction subtest is commonly used test of visual memory and administered here according to the manual. The Rey figure is a test of planning, visuo-constructive abilities as well as of visuo-spatial memory and the left and the right side can be scored separately. The Corsi block test was used to assess the spatial working memory span; two successful trials were demanded for a span [54]. The List Learning Test [55] was included to test verbal memory. Four subtests of the Wechsler Adult Intelligence Scale–Revised WAIS-R; [56] were used to evaluate verbal and visuo-spatial abilities. Digit Span, Picture Completion, Similarities and Block design were presented according to the manual. The sum of correct answers was calculated in each subtest.

Perseveration was assessed by performance in the motor learning and fluency test, where the patient had to write the letter S alternating with a mirror image of S for three minutes [57]. The total number of letters, the number of perseveration errors from the left and the right side were scored. Tactile extinction was assessed by the double

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	Age	F/M	Education	Post onset months	Areas of lesion	Motor disability	Sensory impairment	VFD	TDSS	Pusher syndr.	Persev. errors left / right	EI
3	62	M	Elementary	0	F,TA,P	Moderate	No	No	1	1.0	0 / 22	89
5	62	M	Elementary	0	F,TA	Mod.severe	Severe	No	0	6.0		94
6	62	M	Vocational	1	F,P	Mod.severe	Severe	No	0	-	2 / 6	84
7	70	F	Graduated	3	Th	Mod.severe	Mild	No	2	4.75	0 / 0	84
9	56	F	Elementary	3	F,P	Moderate	Moderate	HH	2	2.75	7 / 8	95
10	45	F	College	6	F	Mod.severe	Severe	No	3	-	6 / 2	84
4	62	F	College	0	F,TA	Mod.severe	Mild	No	1	4.25	7 / 5	78
1	49	F	Elementary	1	F,TA,TP,P	Mod.severe	Moderate	HH	3	1.5	0 / 8	84
2	60	M	Elementary	2	F, TA	Slight	Mild	No	5	2.0	0 / 8	95
11	40	F	Vocational	3	F,TA,P	Mod.severe	Severe	HH	3	2.75	0 / 2	80
8	74	F	Elementary	5	TP, O	Mod.severe	Mild	HH	4	1.0	6 / 3	80
12	61	M	Elementary	5	F, BN	Moderate	No	No	4	-		95
17	54	M	Elementary	12	F,TA	Mod.severe	Moderate	No	0	0	3 / 5	86
14	59	F	Elementary	15	F,TA,P	Moderate	Severe	No	2	-		91
15	56	M	Elementary	48	BN	Moderate	Moderate	No	3	0	6 / 4	83
13	54	F	University	131	F,TA	Moderate	Mild	No	0	0.25	0 / 0	66
20	51	F	College	16	TP,BN	Slight	No	HH	0	0	1 / 0	80
21	58	M	Vocational	16	TP,O,Th	Slight	Moderate	Partial	0	0	2 / 4	82
22	59	M	College	24	F	Moderate	Mild	Partial	0	-	3 / 7	81
18	58	M	Vocational	24	TP	Mod.severe	Severe	HH	0	-	1 / 3	94
19	57	F	Elementary	47	F,TA,BN	Moderate	Mild	No	4	-	0 / 0	100

Areas of lesion: F = frontal, TA = temporal anterior, TP = temporal posterior, P = parietal, O = occipital, Th = thalamus, SC = subcortical, BN = basal nuclei. VFD = visual field deficits; HH = homonymous hemianopia. Tactile extinction was measured by the Tactile Double Simultaneous Stimulation test (TDSS) where 0 = severe extinction and 8 = no extinction. Pusher syndrome was measured by the SCP which is scored from 0 to 6: the higher the score, the greater the severity of pushing. EI = Edinburgh Inventory of handedness, 100 meaning totally right handed.

Table 1: Patient characteristics, neurological data and scores of tactile extinction, pusher syndrome, perseveration errors and handedness at baseline.

simultaneous stimulation test (TDSS, NIH stroke scale). Patients were blindfolded and touched from behind in the area of their head and neck. Four out of eight touches were unilateral and four were bilateral stimuli, in a random order. The bilateral stimuli were delivered in different locations on each side. Patients normally identified correctly all unilateral stimuli. If the left-sided stimulus in a bilateral trial was not reported, the score was 0. If the left-sided stimulus was reported at the same site with the right sided stimulus, the score was 1. If the patient reported both stimuli accurately, the score was 2. Severe tactile extinction was defined as 0-1 points, moderate as 2-4 points, mild as 5-7 points and no tactile extinction was defined as 8 points.

Patient characteristics, neurological data and scores of tactile extinction, pusher syndrome, perseverative errors and handedness of the patients at baseline are shown in Table 1 and the scores of cognitive tests are in Table 2.

Rehabilitation procedures

Arm Activation training patients received 20-30 h of modified arm activation training, which included voluntary shoulder motor training of the left arm using a simple push-pull equipment in the left hemispace about 50% of the training hours and 50% of passive arm activation. The passive arm activation consisted of multichannel functional electrical stimulation (FES) induced movement, sensory electrical stimulation of the left hand with a stimulating glove or movement aided by the therapist. All exercises were performed by the left arm in the left hemispace, leaving the right hand to rest at the right side. Visual Scanning training corresponded to the visual scanning training program first described by Pizzamiglio et al. [57]. Three different procedures were used at each training session: 1. visual scanning of pictures, facial expressions, words, numbers and calculations from a wide video screen (iReach™ rehabilitation program); 2. reading and copying written material and 3. copying drawings from a dot matrix. Patients received 10 h of visual scanning training during the 3 weeks of rehabilitation. Both groups recovered significantly and rather equally [58].

Individually Planned visual rehabilitation was designed together with the patient and the multiprofessional team to support the aims of 3 weeks of rehabilitation for four chronic patients who had only residual visual neglect.

The numbers of hours of previous rehabilitation, rehabilitation during and after the study until the follow-up are in Table 3.

Statistical analyses

Due to the lack of data normality, nonparametric tests were used. Correlations were analyzed using the Spearman's correlation (2-tailed). Because of the small and heterogeneous groups (acute, subacute and chronic cases in the study population) only correlations were investigated. It is clear that more comparisons would be preferable however, with very small groups we did not want to over interpret the data. Significance was set at $p<0.05$. The SPSS for Windows 14.0 was used in the calculations.

Results

The mean recovery rate of 21 patients in the BIT C was 15% of the maximum score (22.7, SD 34.3) by the follow-up at 6 months. More than 60% of the recovery had been achieved by the end of the rehabilitation. Seven patients showed remarkable improvements in visual neglect (>20 points) and most patients gained 10-20 points. Three patients deteriorated from the pre-rehabilitation to the follow-up. Neglect in behaviour observed by the CBS diminished markedly in three patients (decrease > 10 points) and most of the recovery was still present at the follow-up assessment (75%). Five patients failed to improve in the CBS (Table 4).

When recovery of visual neglect was analysed from the pre-

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Patient	Months from stroke	WAIS-R verbal Σ (%)	WAIS-R performance Σ (%)	15 words 4. trial	15 words delayed recall (% of immediate)	WMS-R, VR immediate	WMS-R, VR delayed (% of imm.)	Rey copy	Rey delayed (% of copy)
1	0	34 (55)	0 (0)	8	8 (100)	0	0	1	0 (0)
2	0	-	-	-	-	-	-		
3	1	37 (60)	15 (21)	7	3 (43)	20	0 (0)	31	4 (13)
4	3	38 (61)	22 (30)	10	3 (30)	16	0 (0)	29	0 (0)
5	3	21 (34)	13 (18)	9	6 (67)	28	0 (0)	17	11 (65)
6	6	41 (66)	29 (40)	10	8 (80)	34	12 (35)	22	6 (27)
7	0	44 (71)	14 (19)	11	10 (91)	27	13 (48)	7	0 (7)
8	1	40 (65)	14 (19)	8	0 (0)	4	0 (0)	8	4 (50)
9	2	48 (77)	19 (26)	7	2 (29)	33	8 (24)	21	3 (14)
10	3	38 (61)	23 (32)	4	0 (0)	13	0 (0)	9	3 (33)
11	5	13 (21)	10 (14)	11	9 (82)	9	0 (0)	11	0 (0)
12	5	43 (69)	28 (38)	11	6 (55)	36	0 (0)	28	20 (71)
13	12	32 (52)	15 (21)	7	2 (29)	26	0 (0)	9	0 (0)
14	15	35 (56)	22 (30)	7	6 (86)	34	0 (0)	26	12 (46)
15	48	36 (58)	25 (34)	8	0 (0)	25	12 (48)	24	0 (0)
16	131	38 (61)	15 (21)	12	11 (92)	30	5 (17)	32	13 (41)
17	16	37 (60)	25 (34)	7	6 (86)	25	12 (48)	20	9 (45)
18	16	37 (60)	13 (18)	9	8 (89)	12	3 (25)	12	0 (0)
19	24	25 (40)	15 (21)	11	7 (64)	-	-	16	4 (25)
20	24	39 (63)	22 (30)	12	13 (108)	28	21 (75)	25	10 (40)
21	47	40 (65)	14 (19)	8	6 (75)	20	5 (25)	22	0 (0)
Mean(SD)	17.2 (30)	35.8 (8)	17.7 (6)	8.9 (2)	5.7 (4)	22.1 (11)	4.8 (6)	18 (9)	4.9 (6)

Table 2: The sum of raw scores and percents of maximum raw scores in two verbal (number span, similarities, Σ = 62) and in two performance subtests (picture completion, block design, Σ= 73) of the WAIS-R and memory data of 21 patients with hemispatial neglect at baseline.

P	Post onset months	Earlier rehabilitation weeks	During the 3 week rehabilitation							During follow-up		
			AA	VS	PT	OT	Gr	NP	Σ	PT	OT	NP
1	0	3 anw	21		18	2	9		50	7	0	0
2	0	2,5 anw	21		18	0	9		48	29	5	0
3	1	4 anw	21		18	9	6	1	55	85	14	0
4	3	2 anw + 13 hc	30		10	5	2		47	36	0	0
5	3	11 mp	30		11	7	0		48	48	0	0
6	6	18 mp + 11 hc	30		10	6	2		48	48	24	0
7	0	3 anw		10	18	14	8		50	90	45	5
8	1	7 anw		9	18	9	9		45	50	0	0
9	2	8,5 mp		10	18	8	11		47	48	24	0
10	3	6 anw + 8 hc		10	18	9	8		45	100	21	8
11	5	7 anw + 16 hc		9	18	9	9		45	-	-	-
12	5	11 mp		9	16	10	13		48	48	0	0
13	12	20 mp + 9 hc	30		10	6	4	1	51	48	0	0
14	15	-	20		6	4	3		33	48	24	0
15	48	10 mp+ 2hc	30		3	1	7		41	48	0	0
16	131	Good acute rehabilitation	30		11	5	10		56	48	0	0
17	16	-			7	4	10	5	26	48	0	36
18	16	8 mp + 12 hc			11	7	6	14	38	-	-	-
19	24	12 mp			13	5	7	16	41	72	0	0
20	24	-			11	3	-	7	-	26	13	0
21	47	4 anw			6	4	0	5	15	48	0	0

P = patient number, earlier rehabilitation, ANW: Acute Neurology Ward, HC: Health Center; MP: Multi-Professional Stroke Unit;
PT: Physiotherapy, OT: Occupational Therapy, GT: Group Therapies, NP= Neuropsychological Rehabilitation

Table 3: Number of hours of rehabilitation before entering the study, during the study and during the follow-up period.

rehabilitation to the end of rehabilitation, good recovery in visual neglect was associated with less time from stroke, severe motor impairments and severe neglect at pre-rehabilitation assessment (Table 5). The presence of pusher syndrome at the pre-rehabilitation assessment correlated with less improvement in visual neglect during the rehabilitation.

The total amount of improvement in the BIT C from the pre-rehabilitation to the follow-up assessment was associated with the amount of multi-professional rehabilitation previously provided, i.e. subacute patients who had received intensive multiprofessional rehabilitation before entering the study improved less than those who received comprehensive rehabilitation only in the present study. Good

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P	Post onset months	Rehab Group	CBS OT 1	CBS OT 2	CBS OT 3	CBS OT 1-2	CBS OT 2-3	CBS OT 1-3	CBS P-CBS OT	CBS P-CBS OT	CBS P-CBS OT	BDI 1	BDI 3
1	0	AA	11	10	0	-1	-10	-11	3	7	0	7	0
2	0	AA	-	-	5	-	-	-	-	-	3	7	7
3	1	AA	10	2	1	-8	-1	-9	-2	0	-4	17	-
4	3	AA	11	8	6	-3	-2	-5	4	2	0	3	6
5	3	AA	6	4	4	-2	0	-2	4	-	1	3	0
6	6	AA	9	6	5	-3	-1	-4	-1	-3	-1	9	18
7	0	VS	-	8	5	-	-3	-	-	1	0	4	1
8	1	VS	23	17	12	-6	-5	-11	13	-	9	-	8
9	2	VS	17	12	5	-5	-7	-12	12	11	1	7	7
10	3	VS	11	8	3	-3	-5	-8	-2	-3	2	21	13
11	5	VS	14	8	11	-6	3	-3	-2	-3	3	17	9
12	5	VS	2	1	5	-1	4	3	-3	-5	0	6	6
13	12	AA	5	3	7	-3	5	2	-1	-2	3	8	6
14	15	AA	2	1	0	-1	-1	-2	-2	0	-1	13	11
15	48	AA	1	-	2	-	-	1	-2	-	-1	2	6
16	131	AA	2	2	4	0	2	2	-2	-	0	-	-
17	16	Indiv	13	13	5	0	-8	-8	5	-	-	-	-
18	16	Indiv	17	-	10	-	-	-7	3	-	-	7	10
19	24	Indiv	15	-	13	-	-	-3	12	-	9	-	20
20	24	Indiv	12	-	12	-	-	0	4	-	-	12	22
21	47	Indiv	6	-	6	-	-	0	-	-	-	26	16

Mean(SD) 9.8(6.0) 6.8(4.7) 5.7(3.9) -3.07(2.5) -1.9(4.4) -4.1(4.8)

Table 4: Behavioural neglect in the CBS at the baseline (1), at the post-rehabilitation (2) and at the follow-up (3) and the change in scores between the assessments. The anosognosia scores are included (CBS Patient - CBS OT).

	Recovery of visualneglect									Recovery of behaviouralneglect								
	BIT C 1-2 [1]			BIT C 2-3[2]			BIT C 1-3[1]			CBS OT 1-2[1]			CBSOT 2-3[2]			CBS OT 1-3[1]		
Significantlycorrelatingvariables	cc	p	n	cc	p	n	cc	p	n	cc	p	n	cc	p	n	cc	p	n
Monthsfromstroke	-.59	.01	21	-.67	.00	21	-.75	.00	21	.64	.01	14				.69	.00	19
Motor impairment	.45	.05	20				.49	.03	20	-.64	.01	14						
MMAS total							-.48	.04	19	.76	.00	13						
Pushertotal	.61	.03	13															
Wolf functionalitytotal										.54	.04	14						
FIM total							-.53	.02	18	.72	.00	14						
BIT C total	-.80	.00	21	-.57	.01	21	-.71	.00	21									
CBS OT total										-.57	.03	14	-.54	.04	15	-.72	.00	19
CBS patienttotal										-.62	.02	14						
CBS anosognosiascore													-.70	.02	11	-.46	.05	19
WMS-R, VR immediate																.51	.03	18
Reyfigure,copy				-.54	.02	20												
Reyfigure, delayedrecall										.59	.03	14						
CorsiBlockspan	-.68	.00	20				-.56	.01	20									
15 words, delayedrecall										.59	.03	14						
WAIS-R numberspan													-.66	.01	15	-.46	.05	19
Perseverations in motor fluency test							.55	.02	20									
Hours of therapy during rehabilitation							.53	.02	20									
Previous multiprofessional rehabilitation				-.62	.02	14							.64	.03	12	.63	.03	12

[1]= recovery is correlated with the baseline assessment, 2= recovery is correlated with the post-rehabilitation assessment, CC=Correlation Coefficient, p=level of significance, n=sample size.

Table 5: Significant correlations between recovery of visual and behavioural neglect and other assessed factors

recovery in visual neglect from the pre-rehabilitation to the follow-up assessment was also associated with the amount of rehabilitation. Lower overall functional independency in FIM and more perseveration errors in the motor fluency test pre-rehabilitation were associated with relatively more recovery. Not surprisingly, chronic patients who had received comprehensive acute and subacute rehabilitation and now attended the individually planned, not so intensive, rehabilitation, gained least.

The amount of amelioration in behavioural neglect from pre- to post-rehabilitation assessments was significantly associated with the time from stroke: improvement was better in the acute phase after the stroke. Furthermore, patients with better functional independence, minor motor impairment and better functioning of the affected arm also displayed milder neglect and showed less drastic recovery. The severity of neglect in behaviour was crucial: the more severe the neglect at pre-rehabilitation, the more opportunity for improvement. At the follow-up, better number span of the WAIS-R and good immediate visual recall were associated with good recovery. The lack of awareness of neglect in everyday situations at pre-rehabilitation significantly associated with more alleviation of neglect in behaviour. The lack of intensive rehabilitation before entering the study was clearly linked with more recovery of behavioural neglect after the rehabilitation. The severity of visual neglect in the BIT C was not significantly associated with the observed recovery in behavioural neglect.

Hemianopia was significantly associated with larger lesion size (r=.479, p=.028, n=21). At the pre-rehabilitation assessment, visual field deficits were linked with the severity of neglect in the CBS (r=.630, p=.004, n=19). At the six month follow-up, visual field deficit was associated with the severity of behavioural neglect (r=.511, p=.018, n=21), with anosognosia of neglect in behaviour in the CBS (r=.690, p =.001, n=19) and also with the severity of visual neglect in the BIT C (r=-.531, p=.013, n=21). Hemianopia was also negatively associated with the severity of tactile extinction, i.e. hemianopia was a negative predictor of tactile extinction (r=-.461, p=.036, n=21).

At pre-rehabilitation, 10 patients showed severe tactile extinction, 10 moderate and one patient displayed only mild extinction. Eleven patients failed to recover by the follow-up. Extinction scores were stable from one assessment to the next (measurement 1 to 2 r=.642, p=.002 and from measurement 1 to 3, r=.669, p=.001). In patients less than six months from stroke (n = 12) extinction was more severe. At the follow-up assessment, a failure of amelioration in extinction was associated with parietal lesion (r=-.454, p=.039, n=21). However, the severity of extinction was not associated with the overall recovery of neglect and it did not correlate with motor scores.

Pusher syndrome was present in all patients in acute and subacute phase at the pre-rehabilitation measurement (Table 1). At that stage, pusher was significantly associated with low score in the functional independence measure FIM (r=-.671, p=.012, n=13). Pusher syndrome disturbed most washing, dressing and managing in the toilet. Pusher syndrome was also linked with low motor functioning in the MMAS (r=-.787, p=.012, n=9) and with a better line bisection score in the BIT C (r=.795, p=.010, n=9). Pusher syndrome alleviated in most acute and subacute patients by the 6 month follow-up.

Depression was reported by 35% of 17 patients who filled the BDI: two patients reported moderate and four patients mild depression at the pre-rehabilitation assessment and depression was significantly associated with the number of lesioned brain areas (r=.576, p=.016, n=17); nearly all patients who reported depression had a lesion extending over at least three brain areas. In addition, patients who themselves evaluated that they were displaying more neglect in their everyday functioning (the CBS patient score) at pre-rehablitation, were more depressed (r=.688, p=.003). At follow-up, depression was significantly associated with more severe visual neglect (r=-.497, p=.036), especially in chronic patients (r=.550, p=.018). Instead, good verbal reasoning in the WAIS similarities subtest was linked with less depression (r=.522, p=.021).

Discussion

We searched for determinants of good or poor recovery in neglect by associating the total amount of recovery in the BIT C and in the CBS from pre- to post-rehabilitation and follow-up assessment with background variables and amount of rehabilitation. Patients, who had less time from stroke, lower functional capacity and more severe neglect at pre-rehabilitation gained most in their recovery scores. The significance of intensive acute rehabilitation was confirmed in our subacute and chronic patients who had received intensive acute rehabilitation in a multi-professional stroke unit previously and now showed relatively mild recovery. In chronic patients, the total amount of therapies provided during the rehabilitation was crucial for improvement: 30 h of arm activation treatment was more effective than the conventional individual program for chronic phase of neglect. These findings are in agreement with previous studies [40,59,60]. The severity of visual neglect was not significantly associated with the amelioration of behavioural neglect and vice versa. The presence of hemianopia explained partly the variation in recovery of visual and behavioural neglect as the combination of hemianopia and neglect lead to prolonged left inattention in activities of everyday life [25]. Instead, a general cognitive impairment (decreased delayed memory power and limited attention span) was associated with less recovery in behavioural neglect. Extinction was common in our patients and failure in recovery from extinction was associated with larger lesion size and parietal localization of lesion consistent with previous studies [26,27]. Pusher syndrome hampered amelioration of visual neglect in acute and subacute patients during the rehabilitation period. Patients with large lesions and severe handicaps reported more depressive symptoms. However, depression was not significantly linked with the failure of recovery of neglect in acute or subacute phase after stroke. Few individual patients, who suffered from depression, did regress.

In the present study, patients entered the rehabilitation at a minimum of 18 days after the stroke, when the most rapid spontaneous recovery had already passed [8], but their neglect still ameliorated significantly due to the rehabilitation though spontaneous recovery may still occur for several weeks. Our study confirms the previous findings that early admission to rehabilitation increases the likelihood for better outcome [42]. We also confirm that significant recovery in visual neglect is possible during 3-6 months or even later after the stroke especially in patients with severe neglect and insufficient acute rehabilitation.

Persistent neglect has been shown to associate with large and multifocal right hemisphere lesions, which cover three or more cortical and subcortical areas [12,15,42,61]. The lesion size in our study was rated on categorical scale rather than measured volumetrically. Patients who recovered most had lesions in several brain areas and would correspond to the persistent neglect mentioned in the previous studies. Based on our findings, a larger lesion size in chronic patients with mild or residual visual neglect was associated with poor recovery, whereas sufficient rehabilitation acutely after stroke induced a significant improvement also in patients with large lesions and more severe visual neglect. Jehkonen et al. [29] diagnosed visual neglect in 15 out of 57 right hemisphere stroke patients at ten days post stroke. Even though visual neglect soon disappeared in the paper and pencil tests, these patients reported residual neglect which clearly restricted their real life activities. In our data, all patients with only residual or subclinical visual neglect still displayed mild or even moderate behavioural neglect and 50% of the patients with mild visual neglect still had moderate behavioural neglect seen in the CBS at the pre-rehabilitation assessment [25]. In agreement with [29,45], neglect was evident in our data in the activities of daily living longer than it could be detected in the conventional paper and pencil tests for neglect. This was especially true in our patients with neglect and hemianopia.

Extinction is considered as a residual form of spatial neglect [27] and this is why the tactile extension test was included in our study. Even though neglect appears without extinction and vice versa, tactile extinction was present in most of our acute and subacute patients. It remained rather stable and was not significantly associated with the recovery of neglect in these patients. This supports the notionthat there are different mechanisms behind these two disorders [15,27,62]. Extinction and neglect may share the same cross modal disintegration reported by Frassinetti et al. [63] who found defective integration of sensory stimuli in patients with both neglect and hemianopia, but not in patients with either hemianopia or pure neglect.

In patients with neglect, pusher syndrome has been more severe than in patients without neglect [33-35]. All our acute or subacute patients displayed some degree of pusher syndrome at the pre-rehabilitation measurement. Pusher syndrome alleviated in most patients by the follow-up measurement. Our results confirm the close connection between neglect and pusher syndrome acutely after right hemisphere stroke.

Depression did not prevent neglect recovery in the acute or subacute phase after stroke, but depressive chronic patients did not recover as well as those with less extensive depressive symptoms. Paolucci et al. [41] showed that the presence of neglect and depression at baseline were associated with an increased risk of a low response on ADL. In our patients, depression was associated with more functional losses and less recovery in visual neglect, but there was no association between the recovery of behavioural neglect and depression. Furthermore, we did not detect correlation between depression and FIM scores or depression and recovery in FIM scores.

The current sample size, even after three years of gathering data, is small and this hinders a reliable analysis of determinants of recovery, i.e. our results are limited. Small and different numbers of chronic and subacute patients entering the study with heterogeneous histories thwarts strong statistical analysis.

In conclusion, intensive multiprofessional acute rehabilitation is essential, even though comprehensive program also later can be effective in rehabilitation of neglect, especially in patients who have not received proper rehabilitation in the acute phase. Recovery from neglect is strongly associated with the severity of neglect and with early rehabilitation. Intensive treatment can induce recovery in severe or moderate visual neglect also long after the first two or three months after stroke. Even chronic patients with visual neglect improve after intensive rehabilitation, if they have sufficient compensatory cognitive and psychological capacities. Behavioural neglect is often found when visual neglect has already ameliorated and it may be associated with hemianopia. The combination of neglect and hemianopia needs to receive special attention in the rehabilitation program. The presence of pusher syndrome hampers recovery of neglect acutely after stroke, whereas tactile extinction is not associated with recovery from neglect. Depression may be associated with more extensive lesions and severe neurological losses in chronic neglect patients and should be diagnosed and treated even years after the stroke to enhance recovery.

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