J Rehabil Med 2012; 44: 505–511

Included in the special issue:
CONSCIOUSNESS AND THE VEGETATIVE STATE: TODAY
J Rehabil Med 2012; 44: 481–516

ORIGINAL REPORT

RECOVERY OF COGNITIVE FUNCTION DURING COMPREHENSIVE REHABILITATION AFTER SEVERE TRAUMATIC BRAIN INJURY

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Objective: **To explore the course and timing of functional recovery in patients who have emerged from coma after undergoing severe traumatic brain injury.**
Methods: **An observational study involving 19 patients with traumatic brain injury recovered from coma who underwent holistic, intensive and multidisciplinary neurorehabilitation. Daily performance in each cognitive function (long-term memory, short-term memory, orientation, calculation, attention, mental control, automation, and planning) was clinically scored and compared at admission and discharge.**
Results: **The course of cognitive recovery after post-traumatic coma is not uniform, offering a curve with many ups, downs and plateaus. To achieve a good response and outcome nearing normalcy, a patient needs over 300 h of intensive rehabilitation.**
Conclusion: **The consolidation of functional recovery in patients with traumatic brain injury requires time and adequate training, and discharge is not recommended until cognitive improvement is established.**

Key words: cognitive functions; neuropsychological rehabilitation; neurorehabilitation; traumatic brain injury.

J Rehabil Med 2012; 44: 505–511

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Submitted September 27, 2011; accepted March 15, 2012

INTRODUCTION

Functional disorders affecting daily living activities are frequent in patients who emerge from coma after sustaining severe traumatic brain injury (TBI). These disorders usually result in impairment to memory, attention, reasoning, mental imagery, language, problem-solving abilities or executive functioning, as noted by León-Carrión (1), and require treatment to achieve functionality. Recent studies have proven the efficacy of functional rehabilitation for patients who have emerged from deep coma. As shown by Cicerone et al. (2), there is substantial evidence supporting interventions for attention, memory, social communication skills, and executive functioning, and for comprehensive neuropsychological rehabilitation after TBI, designed to help the person recover maximum functionality nearing pre-injury level. However, the timing and duration of these interventions has not been established. Prigatano (3) reports that "cognitive rehabilitation is labor intensive. Patients must spend hours at cognitive remediation tasks before any notable change can be achieved. No matter how well-randomized or designed, studies that employ less than 100 hours of cognitive rehabilitation will most likely be associated with minuscule results. This reality exists because we do not know how to deliver re-training activities systematically in a cost-efficient manner".

In the search for TBI treatment, insurance companies, healthcare professionals, families, and patients are concerned with the duration of neurorehabilitation and whether it will be worthwhile. Different systematic reviews, most notably Rohling et al.'s (4), have demonstrated that in-hospital cognitive rehabilitation for patients with moderate-to-severe TBI is more effective than at-home rehabilitation or no rehabilitation post-injury. Studies by Cicerone et al. (5) and Yu (6) have also shown that a certain degree of spontaneous recovery occurs during the first few weeks, and even months, after injury. A previous study by Leon-Carrion & Machuca-Murga (7) analysed the course of post-TBI cognitive deficits in patients who did not receive neuropsychological rehabilitation, and endeavoured to establish the point at which cognitive deficits ceased to present signs of spontaneous recovery. Our study involved 28 subjects with severe TBI who were neuropsychologically assessed at 8 months post-TBI and again, 19 months later. Results showed no significant differences between the two neuropsychological exams and no spontaneous recovery beyond the 8 month post-TBI. Neurocognitive deficits consequential to TBI appeared to be established within the first 8 months post-trauma.

The present study reports on the outcome of 19 adults with severe TBI in the post-acute phase after undergoing a holistic, intensive, and multidisciplinary programme in a highly specialized neurorehabilitation centre in Europe.

METHODS

Subjects

Nineteen patients with severe head trauma (3 female, 16 male; mean age 23.57 years) and a median Glasgow Coma Scale (GCS) score of 5 (interquartile range (IQR): 4 –7) at admission. Patients were recruited from the Center for Brain Injury Rehabilitation (C.RE.CER) in Seville, Spain. No control group was used in this descriptive study. Inclusion criteria included emergence from coma, a GCS score of ≤ 8 within 24 h post-TBI, and the presence of at least 3 impaired cognitive functions

 doi: 10.2340/16501977-0982
Journal Compilation © 2012 Foundation of Rehabilitation Information. ISSN 1650-1977

(deterioration of mental process involving symbolic operations, such as orientation, memory, attention, mental control, automation, and planning). All patients began the neurorehabilitation programme approximately 24 months post-injury. Patients' mean GCS score, mean time from brain injury to programme admission and demographic data are shown in Table I.

Treatment programme

Patients enrolled in a holistic, intensive and multidisciplinary rehabilitation programme at Center for Brain Injury Rehabilitation (7–11). Patients underwent daily 4-h rehabilitation, 4 days a week, for 6 months. Each rehabilitation session lasted 60 min, and was given by a specialized therapist (neuropsychologist, physical therapist, speech therapist, or occupational therapist) in accordance with the patient's needs. In general, patients received a combination of these rehabilitation sessions, which were specifically tailored to meet the physical, emotional, behavioural and cognitive needs of each patient, and could include pharmacological treatment, as reflected in previous studies by León-Carrión (1, 12, 13). Cognitive rehabilitation included exercises in orientation, memory, attention mechanisms (automation and mental control), calculation, planning and executive functioning (14) (Appendix I).

Outcome scoring system

Each cognitive function was clinically scored on a scale from 1 to 10 by the therapist who conducted the session. Baselines for cognitive functions were obtained at admission, using the CRECER Clinical Outcome Scale (CRECERCOS) and neuropsychological assessments prior to rehabilitation (Table II). Patients received a score of normalcy when performance achieved pre-morbid levels of functioning. This normalcy was clinically established through interviews with the patients' families and closest associates. A score of 1–2 was assigned to subjects with severe impairment (almost no response) in a specific function (10–20% normalcy); 3–4 indicated impaired, although inconsistent, response (30–40% normalcy); 5–6 showed consistent, but scarce, response (60% normalcy); 7 indicated a good response, but too scarce to be considered at normal level (70% normalcy); 8–9 reflected near normal response in quantity and quality, but not at pre-morbid levels (80–90% normalcy). A score of 10 was assigned when patient performance showed either his/her previous level of functioning (100%) or statistical normalcy.

Statistical and data analysis

The following analyses were carried out: comparison of initial scores with scores after discharge; mean number of sessions completed for each cognitive function; percentage of functional gain obtained after rehabilitation, and percentage of functionality at discharge compared with admission. The percentage of functional gain is calculated from the CRECERCOS baseline at admission and the final level of functionality obtained after neurorehabilitation, with a maximum score of 10. For example, a patient with a 6 on the CRECERCOS scale has a potential gain of 4 points to achieve the maximum score of 10. If the functional gain of this patient after treatment is 2 points, his/her percentage of functional gain is 50% (half of the potential 4 points). The equation used to determine the latter is as follows:

$$FG\% = \frac{MI - M0}{10 - M0} \times 100$$

Ml is the score obtained by the patient in the last month of rehabilitation. M0 represents the patient's score at admission. FG% is the percentage of functional gain for each specific function obtained in the final assessment. Statistical analyses were performed using SPSS 15.0 software for Windows, with alpha set at 0.05 for all tests. Fisher's exact test was applied to analyse categorical variables. Given the asymmetrical distribution of most of the variables, non-parametric analyses were performed. Means, standard deviations, medians and interquartiles are displayed in Tables I, III, IV and V. We applied the Mann-Whitney *U* tests to analyse independent samples and the Wilcoxon test for related samples. Correlation analysis was carried out using the Spearman's rank order correlation (rho). We used mean values and standard deviations (SD) to summarize our results due to their higher illustrative capacity for presenting and comparing our data.

Table I. *Patient demographic data: age, Glasgow Coma Score (GCS) score within 24-h post-traumatic brain injury (TBI) and time from injury to programme admission*

Patient data $n=19$	Mean (SD)	Median (IQR)
Age	23.57 (7.04)	23 (19–28)
GCS Score	5.37 (1.89)	5 (4–7)
Time from injury to programme admission, months	23.94 (58.62)	11 (4–17)

GCS: Glasgow Coma Scale; SD: standard deviation; IQR: interquartile range.

RESULTS

CRECERCOS score analyses

Table III displays patients' mean scores on the CRECERCOS scale at admission and discharge from the neurorehabilitation programme. At admission, the group mean for the different cognitive functions was 4.59. The lowest mean scores were for *automation* and *short-term memory*, while *orientation* received the highest score. At discharge, the group mean for all areas increased to 7.52, with *calculation* scoring the lowest, and *orientation* the highest mean score.

Functional gain increased in all areas. The global mean score reached 56.24%, with patients achieving the highest gains in *orientation* and *automation* and the least gain in *calculation* and *mental control*. Comparative analysis between areas showed the most significant gain in *orientation*, particularly compared with *calculation* and *mental control* ($p<0.01$). Significant differences were also found between short-term memory and calculation (Table III).

Statistical comparisons were carried out between number of rehabilitation sessions and cognitive function. Table IV illustrates the number of sessions (60 min per session) which patients underwent during the rehabilitation programme. The mean number of sessions was 43. *Planning* received the most rehabilitation sessions, whereas *mental control* received the

Table II. *Classification for Center for Brain Injury Rehabilitation Clinical Outcome Scale (CRECERCOS). The first column shows CRECERCOS scores; the second indicates percentage of cognitive functionality compared with pre-morbid levels of normalcy; the third shows level of impairment associated with each score*

CRECERCOS score	Impairment score, %	Specific function/s
1–2	10–20	Severe impairment (almost no response) in a specific function
3–4	30–40	Impaired, inconsistent response
5–6	50–60	Consistent response
7	70	Good response
8–9	80–90	Near normal response in quantity and quality, but not pre-morbid level
10	100	Previous functioning level

Table III. *Classification for Center for Brain Injury Rehabilitation Clinical Outcome Scale (CRECERCOS) scores at admission and discharge, and overall functional gain*

		CRECERCOS at admission		CRECERCOS at discharge		FG%		CRECERCOS Differences admission–discharge	FG% Differences between cognitive functions
Cognitive functions	*n*	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Wilcoxon (Z value)	Mann-Whitney U test
Long-term memory	19	4.27 (1.68)	4 (3–6)	7.7 (1.44)	8 6.75–8.625)	57.26 (24.4)	56.47 (33.33–72.32)	–3.73**	c*
Short-term memory	19	3.86 (1.97)	4 (2–5.5)	7.4 (61.16)	7.5 (7–8)	56.69 (18.03)	55.55 (47.77–71.4)	–3.82**	c*, d*
Orientation	15	7.45 (3.15)	8.5 (6.1–10)	9.47 (1.46)	10 (9.875–10)	88.33 (20.61)	100 (77.5–100)	–2.66**	a*, b*, d**, e*, f**, h*
Calculation	14	4.3 (1.77)	4.5 (3.75–5.35)	6.87 (1.61)	7 (7–7.75)	43.32 (20.06)	40 (31.78-58.33)	–3.18**	b*, c**
Attention	8	4.58 (1.60)	5 (4.12–5.8)	7 (1.64)	7 (5.75–7.87)	46.3 (25.69)	44.44 (26.25–56.25)	–2.52*	c*
Mental control	16	4.53 (1.73)	4.5 (4–6)	7.03 (1.71)	7.5 (6.12–8)	44.6 (30.54)	50 (22.72–66.66)	–3.24**	c**
Automation	8	3.28 (2.27)	4.5 (1–5)	7.28 (2.15)	7 (6–10)	60.43 (33.79)	66.66 (25–100)	–2.37*	
Planning	18	4.34 (1.46)	4.3 (3–5.5)	7.41 (1.43)	7.5 (7–8)	53.05 (24.76)	53.84 (37.5–72.5)	–3.77**	c*

a: significant differences for *long-term memory*; b: significant differences for *short-term memory*; c: significant differences for *orientation*; d: significant differences for *calculation*; e: significant differences for *attention*; f: significant differences for *mental control*; g: Significant differences for *automation*; h: significant differences for *planning*.
$*p<0.05$; $**p<0.01$.
SD: standard deviation; FG: functional gain; IQR: interquartile range.

least. The comparative study between cognitive functions showed significant differences between *calculation* and the following: *short-term memory* ($p<0.01$)*, orientation* ($p<0.05$), and *planning* ($p<0.01$). Significant differences were also found between number of sessions for *mental control* compared with *long-term memory, orientation, and planning (*$p<0.01$). Correlation analysis between functional gain and number of sessions was also performed for each cognitive function (see Table IV). Only *planning* showed a linear correlation between the two variables, as more sessions associated with greater functional gain (rho = 0.63, $p<0.01$).

Correlation analysis between patients' total functional gain and time from injury to programme admission was carried out for each cognitive function. The analysis revealed significant negative correlations between these variables for *long-term memory* (rho = –0.63) and *planning* (rho = –0.62). No other functions correlated with the time from injury to programme admission (Table IV).

To determine whether the initial state of a patient affected his/her subsequent rehabilitation, we relied on the GCS score at time of injury. We were able to obtain this information for 16 of the 19 patients in our study. All scores fell below 8 on

Table IV. *Number of sessions, time elapsed from brain injury to rehabilitation programme admission and functional gain (FG)*

	Sessions, *n*		Mann-Whitney U test Number of sessions Differences between cognitive functions	Spearman correlation (rho)	
Cognitive functions	Mean (SD)	Median (IQR)		Correlation FG%–number of sessions	Correlation FG%–time from injury to programme admission
Long-term memory	46.53 (26.44)	54 (23–70)	f**	–0.08	–0.63**
Short-term memory	50.16 (23.63)	58 (43–70)	d**	0.03	–0.29
Orientation	55.67 (31.05)	53 (22–88)	d*, f**	–0.48	–0.55
Calculation	28.29 (27.65)	14.5 (4–53.5)	b**, c*, h**	0.36	–0.13
Attention	37 (32.89)	25.5 (7.25–72)		0.38	–0.25
Mental control	23 (18.62)	13.5 (10.25–40.5)	a**, c**, h**	0.26	0.09
Automation	42.2 (33.97)	43 (5.75–76.5)		0.2	–0.16
Planning	69 (42.39)	53.5 (41.75–83.75)	d**, f**	0.63**	–0.62**

a: significant differences for *long-term memory*; b: significant differences for *short-term memory*; c: significant differences for *orientation*; d: significant differences for *calculation*; e: significant differences for *attention*; f: significant differences for *mental control*; g: Significant differences for *automation*; h: significant differences for *planning*.
$*p<0.05$; $**p<0.01$.
IQR: interquartile range: SD: standard deviation.

Table V. *Between-group comparison of lowest and highest GCS scores*

Patient demographic data	Low GCS score ($n=7$) Mean (SD)	Low GCS score ($n=7$) Median (IQR)	High GCS score ($n=9$) Mean (SD)	High GCS score ($n=9$) Median (IQR)	Between-group differences Mann-Whitney U test (z score)
Gender (M/F)	5/2		8/1		0.55[a]
Age, years	21.57 (4.81)	22(19–23)	22.89 (8.27)	25(16.5–28)	–0.48
GCS score	3.57 (0.53)	4 (3–4)	7.22 (1.92)	7 (5.5–8)	–3.38**
Time from injury to programme admission (months)	10.85 (8.39)	15 (1–16)	39 (84.72)	11 (3.5–21.5)	–0.42
Cognitive functions ($n_{low\ GCS}/n_{high\ GCS}$)	**Functional gain % Low GCS score ($n=7$) Mean (SD)**	**Median (IQR)**	**High GCS score ($n=9$) Mean (SD)**	**Median (IQR)**	**Between-group differences Mann-Whitney U test (z score)**
Long-term memory (7/9)	60.9 (27.80)	62.5 (33.3–85.07)	50.47 (19.68)	50 (29.16–69.04)	–0.79
Short-term memory (7/9)	58.78 (16.11)	58.33 (50–64.28)	58.52 (12.72)	55.55 (48.88–72.38)	–0.05
Orientation (4/4)	88.75 (13.14)	90 (76.25–100)	85 (30)	100 (55–100)	–0.33
Calculation (6/6)	47.45 (25.13)	50.86 (25.45–64.58)	35.79 (12.77)	36.92 (28.57–43.33)	–0.96
Attention (2/5)	54.16 (5.89)	54.1 (50–58.33)	42.41 (33.06)	30 (21.59–69.4)	–1.16
Mental control (6/8)	28.40 (28.94)	38.18 (–3.57 to 50.08)	59.56 (23.78)	58.33 (50–72.9)	–2.02*
Automation (5/2)	49.60 (33.49)	36.36 (22.5–83.33)	87.5 (17.67)	87.5 (75–100)	–1.37
Planning (7/9)	44.53 (33.30)	45.94 (33.33–75)	60.23 (14.24)	62.5 (49.65–69.58)	–1

[a]Fisher's exact test.
*$p < 0.05$; **$p < 0.01$.
GCS: Glasgow Coma Scale; SD: standard deviation; IQR: interquartile range; M: male; F: female.

the GCS. We divided these patients into two groups: the low GCS group ($n=7$), with scores ≤4, and the high GCS group ($n=9$), with scores >4. As shown in Table V, both groups had similar distributions of gender and age ($p>0.05$), as well as time from injury to programme admission ($p>0.05$). However, mean GCS scores between the two groups (3.57 for low GCS and 7.22 for high GCS) did show significant differences ($p<0.01$).

Table V displays the percentage of functional gain obtained by both GCS groups in each cognitive function throughout the rehabilitation programme. The low GCS group showed a mean functional gain of 53.09%, whereas the high GCS group mean reached 61.74%. The highest functional gain for both groups was in orientation. The lowest gain was found in *mental control* in the low GCS group and in *calculation* in the high GCS group. We also compared the mean functional gain of each group in these cognitive functions, as shown in Table V. Significant differences were found in *mental control* ($p<0.05$), with the highest gain shown by the high GCS group.

DISCUSSION

The main results of this study may be summed up as follows. Firstly, percentage of functional gain in all cognitive areas did not differ between low and high GCS score groups, with the exception of mental control. Secondly, cognitive functions improved significantly from rehabilitation admission to discharge. Thirdly, functional gain was related to the number of sessions the patient underwent during the course of rehabilitation. Fourthly, not all cognitive functions required the same number of sessions to recover statistic or clinical normalcy. Finally, total functional gain and time from injury to cognitive rehabilitation showed an inverse relationship between long-term memory and planning.

The first aim of this study was to ascertain whether the severity of the lesion at admission determined the severity of the cognitive sequelae observed as a consequence of the physical damage to the brain. To determine the severity of the lesion, we used the patient's worst GCS score during the first 24 h post-injury. The GCS score, since its introduction, has been considered one of the most important predictors of outcome after head injury, although different studies have demonstrated that a correlation does not always exist after brain trauma (15). Our results showed a partial correlation between severity of lesion (GCS) at admission and patients' cognitive functional gain. This correlation was only found in mental control. Our data did indicate that patients scoring higher within the GCS 5–8 range tended to achieve higher functional gain than those with lower scores, although a comparison of mean functional gain between groups in each cognitive function only showed significant differences in *mental control*. As a cognitive function, *mental control* is related to the part of executive functioning that engages and directs different mental activities (16). This function is directly related to an individual's capacity to be independent (17).

Our CRECERCOS analysis of scores at rehabilitation admission (4.59) and discharge (7.52) found significant differences between number of treatment sessions and the patient's cognitive functional gain. This functional gain is observed in all cognitive areas, with a global mean of 56.24%. Our results support those of other authors, who maintain that the period of cognitive rehabilitation may vary (18).The course of cognitive recovery after post-traumatic coma is irregular, with many ups, downs, and plateaus. Our results indicate that, to achieve a good response and outcome nearing normalcy, a patient needs over 300 h of intensive rehabilitation. This data supports and validates Prigatano's (3) earlier statement that the effects of cognitive rehabilitation are not observed in patients with TBI who receive less than 100 hours of treatment. Our data is also in accordance with Cicerone et al. (2), whose comprehensive review of the empirical literature on cognitive rehabilitation found evidence supporting this treatment and its advantages over conventional forms of rehabilitation.

It is important to note that patient scores increased and decreased throughout the treatment period. Progress during any rehabilitation programme, whether it is physical or cognitive, is not uniform. In our study, each cognitive function required a mean of 43 training sessions, with planning requiring the most (69), and mental control the fewest (23). Our results also indicate that not all cognitive functions require the same number of sessions to recover statistic normalcy. For example, long-term memory, orientation and planning differed in terms of time and effort needed to achieve recovery.

In a previous study, we found that consolidation after an initial gain required more rehabilitation time. Each achievement must be consolidated, and this takes time and repetition, which is reported to have significant physiological effects on learning and working memory (19). In clinical practice, we have observed that if the patient is discharged as soon as s/he obtains a score of 7 or 8, the possibility of a drop or regression persists. Time is also required for structural and functional reorganization in the brain. Training cannot be given all at once, although it should be consistent and progressive. Hence, we recommend that this rehabilitation period be scheduled as 4-h daily sessions, 4 days a week. Treatment should not be abandoned if for a short period of time the patient does not show improvement, or if s/he regresses somewhat. Nonetheless, if regression or stalls persist, their causes should be sought before continuing with the rehabilitation programme. Our results indicate that not all cognitive functions require the same type of treatment; some are more costly to recovery in terms of time and effort.

Another finding is of particular relevance to the planning and timing of TBI rehabilitation. We found that the sooner patients receive treatment after injury, the better their cognitive outcome, especially in long-term memory and planning. However, this treatment requires time, especially to consolidate recovery. Memory is a time-dependent process, as shown by McGaugh & James (20). Furthermore, the duration of post-traumatic memory problems, such as amnesia, has traditionally been a better predictor of cognitive outcome than admission GCS score, as shown by Miller et al. (21).

In conclusion, the rehabilitation of cognitive deficits in TBI patients who have emerged from deep coma is advisable when a holistic, intensive and multidisciplinary programme is applied. However, the course of cognitive recovery after TBI is not uniform, and depends on which cognitive functions are impaired, and on the severity of this impairment. Successful treatment of these deficits varies in terms of time and effort. The number of sessions needed to rehabilitate impaired cognitive functions differs from function to function. For example, our results showed that planning and memory require the highest number of rehabilitation sessions to achieve near normalcy. We should also note that cognitive functions are interrelated, and their rehabilitation must be structured to maximize outcome. Furthermore, the consolidation of cognitive gain also requires time, proper training, and well-programmed therapy. We suggest that patient discharge should occur only after cognitive improvements are consolidated. This study provides an approximation of recovery time after TBI. More studies, involving different technology and theoretical bases, could help expand our knowledge of effective post-TBI cognitive rehabilitation.

ACKNOWLEDGMENTS

This research has been funded by a contractual agreement between the Center for Brain Injury Rehabilitation (C.RE.CER) and the Human Neuropsychology Laboratory at the University of Seville, Spain. We would also like to extend our appreciation to Dr Fernando Machuca Murga for his assistance in collecting data, and Ignacio Solís Marcos for his contributions to data organization and analyses.

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Appendix I. *The Center for Brain Injury Rehabilitation integral, intensive and multidisciplinary model of rehabilitation for people with acquired brain injury*

Interdisciplinary holistic and intensive programmes

- involve brain damage specialists from different fields: neuropsychologists, speech therapists, neurologists, psychiatrists, neurosurgeons, physical therapists, etc.
- ecologically-valid
- divided into synchronized phases (aims, methods and professionals)

use quantitative and qualitative methods

each deficit is allotted the necessary time and dedication to provide best possible outcome

Basic operational requirements:

- rehabilitation treatment designed by specialized personnel, adapted to patient's needs

patient/specialist – at least one professional per three patients

- adequate installations, apparatus and rehabilitation techniques for efficient treatment

Multidisciplinary Programme Structure:

Neuropsychological Rehabilitation

- based on neurological evaluation of patient's cognitive capacities and emotional state
- outcome goals based on clinical and statistic results of this evaluation
- main goal: patients attains maximum degree of functional independence
- treatment sessions include individual (and family) psychotherapy – rehabilitation may continue when patient goes home

Speech rehabilitation

fluidity, auditory comprehension, denomination, reading, writing, repeating, automatic mechanisms, comprehension of written language and presence of paraphasic errors:

- fluency tasks: articulatory agility, length of phrases, verbal agility, etc.
- auditory tasks: differentiating, identifying/obeying orders
- denomination tasks: visual confrontation, free association, etc.
- deficits appearing in reading/writing process are re-taught

Physical rehabilitation

spasticity, posture control, balance, trembling, emotional reactivity

we use NeuroBird system of computerized muscular training as well as other physiotherapy techniques (e.g. Bobath)

Occupational therapy/functional therapy

focus on patient's environment, his/her interests and motivation, culture, values, beliefs and the role the patient plays in his/her surroundings

Efficiency of treatment

CRECER programmes undergo daily evaluation and progress control

- neurofunctional state of patient
- efficacy of methods applied