# **Cognitive Rehabilitation for Multiple Sclerosis Patients With Executive Dysfunction**

E P O R T

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Accumulating data suggest that Multiple Sclerosis (MS) patients suffer from various cognitive impairments (Amato, Ponziani, Pracucci, Bracco, Siracusa & Amaducci, 1995; Truelle, Palisson, Le Gall, Stip & Derouesne, 1987; Callanan, 1989; Maurelli, Marchioni, Cerretano, Bosone, Bergamaschi, Citterio, Martelli, Sibilla & Savoldi, 1992; Zakzanis, 2000). Yet, only a few studies have focused on intervention techniques that aim to improve the cognitive functioning of MS patients. Jonnsson (Jonnsson, Korfitzen, Heltberg, Ravnborg & Byskov-Ottosen, 1993) reported that although the effects of short-term (46 days) neuropsychological training on cognitive measures were not unequivocal, the results of the Beck Depression Inventory seemed to confirm the beneficial effects of the neuropsychological treatment. The present study reports the effects of cognitive rehabilitation over a period of six months, with approximately 24 therapeutic sessions. We focused our intervention on executive functions, since they are commonly reported as one of the cognitive impairments typical in MS patients.

Executive functions encompass cognitive processes, such as attention and working memory and also metacognitive control processes, such as the evaluation of a task's difficulty, planning and choosing the right strategies, anticipating results, and monitoring the ongoing process (Flavell, 1985). Thus, the metacognitive processes are essential for successful executive functions. Metacognitive dysfunction may be described as a decrease in the use of efficient processing strategies to select, discriminate, organize, and structure incoming information, as well as a reduced ability to access previous knowledge and to apply knowledge and skills flexibly to a variety of situations (Toglia, 1991).

These metacognitive control processes are considered to be associated with prefrontal cortex functions (Shallice, 1988; Shallice & Burgess, 1991). Hence, executive functions are typically assessed using neuropsychological tests that were found to be sensitive to the evaluation of frontal lobe functions, such as the Wisconsin Card Sorting Test (WCST) (Bryan & Luszcz, 2000). It has been demonstrated that MS patients fail to use an efficient strategy in the WCST (Beatty, Goodkin, Monson & Beatty, 1989; Arnett, Rao, Grafman, Bernardin, Luchetta, Binder, & Lobeck, 1997; Beatty & Monson, 1996; Arnett, Rao, Bernardin, Grafman, Yetkin & Lobeck, 1994; Foong, Rozewicz, Quaghebeur, Davie, Kartsounis, Thompson, Miller & Ron, 1997). MS patients were also found to be impaired on other executive function measures, including temporal-ordering, semantic encoding, the Tower of Hanoi test, and word fluency tasks (Amato et al, 1995; Beatty et al, 1989; Arnett et al, 1997; Archibald & Fisk 2000). A specific difficulty with applying an efficient working strategy in a verbal recognition task was also reported (Carroll, Gates & Roldan, 1984).

In a former study (Birnboim, 2004), we tested 76 MS patients using the Strategy Application Test (SAT), (Levine et al, 1998; Birnboim, 2004) which aims to measure the ability to apply and maintain a working strategy for efficient execution of tasks. Strategies are sequences of activities aimed towards reaching goals efficiently and effectively (Nickerson, Perkins & Smith, 1985). Ten of the MS patients with very poor results on the SAT who also were able to commit to six months of cognitive rehabilitation were selected for the current study. The aim of this study was to explore the effectiveness of cognitive rehabilitation for MS patients with executive function impairments.

The Metacognitive therapeutic approach was used in the neuro-rehabilitation (Birnboim, 1995) (see description in *Methods*). According to this approach, the final goal of the intervention is to improve the patient's functioning in his/her daily life. However, we cannot expect patients with cognitive impairments to transfer and incorporate the strategies learned in the clinic to daily life without the therapist's guidance and encouragement. Thus, the intervention must encompass the patient's relevant activities outside the clinic, and the main measure of the intervention's success should be the degree to which changes are incorporated in daily life. The two case reports illustrate the intervention principles and techniques.

### **Patients and Methods**

Ten MS patients volunteered to participate in this study. Inclusion criteria were as recently described (Birnboim & Miller, 2004). Demographic data of the patients are presented in Table 1.

All the participants were assigned 6 months of therapy, provided in weekly, one hour sessions by an occupational therapist with expertise in cognitive rehabilitation. A battery of pre- and post-intervention tests was administered. The battery included the following:

Attention test: The digit symbol of the WAIS-R; (Wechsler, 1981), Memory tests: The digit forward and backward of the WAIS-R (Wechsler, 1981) and the Rey Auditory Verbal Learning

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Table 1.Demographic data

Patient No.	Age (y)	Education (y)	Disease Duration (y)	Kurtzke EDSS Score	Type of MS
1	39	17	10	1	RR
2	54	16	13	4.5	RR
3	50	12	6	3	RR
4	44	10	1	4.5	SP
5	47	15	4	1	RR
6	51	17	19	4	SP
7	34	15	8	2	RR
8	51	12	11	5.5	SP
9	57	22	13	4	SP
10	28	12	5	4	SP
Mean	45.5	14.8	9	3.25	5 RR/5 SP
(s.d.)	(9.25)	(3.49)	(5.29)	(1.74)	

# Test (AVLT); (Lezak, 1995)

Executive function tests: The Strategy Application Test (SAT), (Levine, Stuss, Milberg, Alexander & Schwartz, 1998; Birnboim, 2004) the Wisconsin Card Sorting Test (WCST),(Lezak, 1995; Milner, 1963) the word fluency FAS (the letters 'R', 'S'; grocery and animal lists), (Milner, 1963; Benton & Hamsher, 1976) and the Key Search of the Behavioral Assessment of the Dysexecutive Syndrome (BADS) (Wilson, Alderman, Burgess, Emslie & Evans, 1996).

Additionally, depression was assessed by the short Zung test(Tucker, Ogle, Davison & Eilenberg,1987); fatigue was assessed by the Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash & Steinberg, 1989) and ADL was assessed by the OT FACT level II questionnaire (Smith, 1990).

# Cognitive intervention principles and techniques

The metacognitive therapeutic approach was used (Birnboim, 1995). According to this approach, specific attention is given to the metacognitive aspects of behavior. This approach assumes that the metacognitive aspects can and should be learned explicitly, using a process that includes the following phases. (I) *Understanding:* the patient has to recognize his/her specific metacognitive difficulties (e.g., not planning). This may be achieved by confronting various tasks in the clinic (e.g., computer games). This phase of the process leads to awareness. (2) *Practice* 

of efficient strategies: therapist and patient together identify specific strategies intended to facilitate task completion (e.g., setting priorities), and these strategies are learned and practiced; and (3) Learning *transfer* abilities: patient and therapist consider when and where to apply these strategies in real life situations.

A variety of computer-based strategy games from commercial software (e.g., 500 games - games for windows 95 by Quality Multimedia Solution) as well as pen-and-paper exercises were used for phases one and two of the rehabilitation process. We have demonstrated (Birnboim, 1995) how computer games can be utilized as efficient cognitive tools. Some specific exercises are described in the case reports.

# **Statistical Analysis**

Descriptive statistical analyses (means  $\pm$  S.D., median) were used to describe test results. The Wilcoxon Signed Ranks Test was used to compare pre- and post-intervention test results. The percent of improvement (delta -  $\Delta$ ) was calculated for each patient regarding each test, according to the equation:

 $\Delta = [(\text{post test} - \text{pre test}) / \text{pre test}] \times 100$ 

Spearman's rho was used to calculate the correlation of the  $\Delta$  with the demographic data.

Table 2.

Strategy Application Test results

Patient	SAT	SAT	SAT	
No.	Pre-intervention	Post- intervention	of change%	
	score	score		
1	61.68	95	53.97	
2	48.2	52.8	9.54	
3	51.35	52.5	2.24	
4	48.64	55.29	13.67	
5	50	75	50.00	
6	60	61.5	2.50	
7	48	78	62.50	
8	48.3	53	9.73	
9	55	69	25.45	
10	48	61.45	28.02	
Mean	51.9	65.4	25.76	
(s.d.)	(5.2)	(14.0)		

#### Results

Patients' SAT results, along with their percent of improvement ( $\Delta$ ) are presented in Table 2. A comparison between the percent of improvement on SAT's of RR and SP MS patients revealed that the RR patients improved by a mean of 35.65%, whereas the SP patients improved by a mean of 15.87%.

The pre- and post-intervention test results are presented in Table 3, along with the results of the Wilcoxon Signed Ranks Test that compared them.

As can be discerned from the means, there were improvements in all the test results, which reached 2-tailed significance rate on the SAT, digit-symbol, the Rey AVLT delayed, and the FAS, as well as on the occupational role part of the ADL questionnaire.

Spearman's rho correlations of the  $\Delta$  with demographic data regarding age, years of education, duration of disease, and EDSS enabled characterization of patients who benefited from the intervention.

*EDSS* had a weak inverse correlation with the SAT improvement (r= -.560, p= .046), and also with the key search scores improvement (r=.652, p. 021). Thus, the higher the EDSS score, the smaller were the improvements in the SAT and the Key Search.

*Disease duration* was inversely correlated with improvement of the digit symbol (r=-.626, p=. 026), the digit forward (r=-.837. p= .002) and the ADL self care (r=-.650, p. 021). Thus, long disease duration correlated with lower improvement rates on the digit symbol, digit forward, and the ADL self-care tests.

Age was inversely correlated with improvement on both the SAT (r=-6 14, p = .028) and the digit forward (r= -.623, p=. 028) tests. Thus, as patients' age increased, the percent of improvement on the SAT and the digit forward decreased.

*Years of education* was also inversely correlated with the percent of ADL self care improvement (r=-.617, p=.029). Thus, the higher the patient's education is, the smaller the improvement on the ADL self-care.

To describe the rehabilitation process, we describe two cases, of patients 1 and 6. Both patients were working women with 17

years of education. They both started with very low SAT results, of about 60/100 (SAT norms for ages 20-60 are at 85.97, s.d. 18.78). However, Patient 1 had an EDSS score of 1, while Patient 6 had an EDSS score of 4. They also differed in age and disease duration (see details in Table 1). Table 4 presents their test results.

As can be seen, Patient 1 benefited more from the intervention, specifically on the SAT and the digit-symbol the time for searching the key was reduced while the scores improved, and the ADL self care and occupational role scores also improved. Patient 6, in comparison to Patient 1, benefited mostly on the Rey AVLT, on recalling list A, on the delayed condition, on the  $\sim$ R' and on the grocery and animal lists of the FAS. Improvement was also noted on all the measures of the WCST: the number of categories doubled, while the number of errors and perseverative errors was reduced. There was also an improvement on the occupational role of the ADL. It must also be noted that in both cases, the patients' depression level was reduced (Patient 6 more than Patient 1); However, Patient 6 reported a higher level of fatigue after the 6 months of intervention, while fatigue was slightly reduced in Patient 1.

#### The therapeutic process —Two case studies

#### Patient 1

*A* is a 39 year old lawyer who owns a small law firm, and is married with 4 children. She was diagnosed 10 years ago with MS of the RR type. At the time of the intervention she had a minimal disability (EDSS was 1), and her main MS symptoms were fatigue and concentration difficulties. The three phases of her rehabilitation process will be briefly described.

#### *Phase 1 — understanding the metacognitive difficulties*

A's basic complaints (she was anxious to participate in this study, although it required a drive of more than 100km each way) were in the areas of organization pertaining to work (at home she had full-time help). She had tried to manage her office without help, but failed to do so efficiently. She was always tired, and felt that she could no longer keep up with her work. Indeed, her SAT results were very low in the pre-intervention test, as were the results of the key search part of the BADS, which was both very long and ineffective. However, her other test results were normal. Although capable of using categorization strategies (as was also apparent from her FAS and Rey AVLT results; see Table 3), she often neglected to apply these while performing tasks. Her main problems, as analyzed by the occupational therapist after observing As attempts to perform various tasks in the clinic, were being overly flexible, easily distracted, and failing to apply an efficient working strategy over time (i.e., monitoring and control processes were ineffective), despite "theoretical knowledge" of the proper way to approach a task. A was too meticulous; she paid too much attention to the smallest details, sometime loosing sight of the whole picture. She was also very unfocused in her talk, often associatively sidetracked from her main subject. A also reported high levels of fatigue, both in the clinic and in her daily life.

Test	Pre- inte	Pre- intervention results			ervention re	esults		
	Mean	S.D.	Median	Mean	S.D.	Median	Wilcoxon Z	Sig. (2-tailed)
SAT	51.9	5.2	49.3	65.4	14.0	61.5	-2.80	.005
Digit	39.6	13.1	45	50	15.3	50.5	-2.35	.019
Symbol								
Digit	5.6	1	5.5	5.9	1.2	6	-1.34	.180
Forward								
Digit	4.7	1.1	5.0	5.3	1.5	6	-1.90	.058
Backward								
ReyAVLT	12.9	2.4	13.5	13.9	1.9	15	-1.59	.112
List A								
ReyAVLT	11.0	4.5	14	12.1	4.4	14.5	-2.46	.014
Delayed								
ReyAVLT	47.8	3.3	49.0	48.4	1.8	48.6	736	.461
recognition								
FAS ~R'	12.2	5.1	13.5	12.9	5.4	11.5	769	.442
FAS ~S'	13.2	5.4	14	16.7	6.9	16.5	-2.536	.011
FAS	20.0	8.1	19	24.7	9.5	23	-2.196	.028
Grocery								
list								
FAS	19.9	8.6	19	22.5	9	19.5	-1.942	.052
Animal list								
Key search	43.9	28.5	30.5	40	28.1	39.5	178	.858
time (sec.)								
Keysearch	5.9	9.8	2	2.6	1.1	3	060	.52
score	0.9	2.0	2	2.0	1.1	5	.000	.02
Wisconsin	5.9	2.1	7	5.6	2.7	7	365	.715
	5.9	2.1	/	5.0	2.1	/	303	./13
Categories Wisconsin	10.7	0.0	15 5	18.2	10.3	13	631	570
	19.7	9.8	15.5	16.2	10.5	15	031	.528
no. errors	5 4	(7	2	2.0	5 1	5	046	244
Wisconsin	5.4	6.7	2	3.6	5.4	.5	946	.344
pers. errors	01.6		101		16		110	0.0.6
ADL	91.6	22.2	101	92	16	95.5	119	.906
Self care	<i></i>		~~					
ADL	62.4	15.8	68	74.5	19.3	78.5	-2.675	.007
occ. role								
ShortZung	53.8	9.1	52.5	51.5	9.4	51.3	870	.384
Fatigue	54.7	7.3	55	52.4	8.4	52.5	892	.372
scale								

 Table 3.

 Median, mean (s.d.) of test results and Wilcoxon Signed Ranks Test that compared the pre- and post intervention results

Phase 2 — practice of efficient working strategies

Various computer strategy games (for example, the computer game "Mastermind") were used to practice monitoring and control processes, focusing on the "mission" while setting priorities and inhibiting less relevant stimuli.

# Phase 3— transfer to daily life

Phase 2 was relatively short, because soon *A* started to openly describe real life situations in which she encountered difficulties. These situations were analyzed with the occupational therapist, the metacognitive aspects were identified, and real solutions were

generated and practiced both in the clinic and in her office. Gradually, she started to apply a more efficient filing system in her office, and found more efficient ways to collect and document relevant information. Priorities were set for her work, according to time limits and target dates.

# The outcomes

*A*'s post-intervention SAT results marked dramatic improvement in her ability to face non-routine situations, while being able to ignore distractions and remain focused on the task. Her depression and fatigue levels were slightly reduced, and she was very appreciative of the rehabilitation process, which had

Table 4.

Pre-test         Post-test $\Delta$ Pre-test           SAT         61.68         95         53.97         60           Digit         45         62         37.78         32           Symbol         Digit         6         6         0         5           Forward         -         -         3         32           Digit         5         6         20         3           Backward         -         -         3         3           ReyAVLT         15         15         0         12           List A         -         -         11         -           Pelayed         -         -         -         14           ReyAVLT         49         49         0         48           recognition         -         -         -         -           FAS -R'         15         10         -33.33         13         -           FAS S'2         22         25         13.64         15         -           FAS         33         40         21.21         14         -           Animal list         -         -         -         - <t< th=""><th>no. 6 (EDSS=4)</th><th></th></t<>	no. 6 (EDSS=4)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Post-test	$\Delta$
Symbol Digit6605ForwardDigit56203BackwardReyAVLT1515012List AReyAVLT14157.1411DelayedReyAVLT4949048recognitionFAS -R'1510-33.3313FAS 'S'222513.6415FAS334330.3019GrocerylistKey search7245-37.5031(sec.)*Wisconsin8803CategoriesWisconsin00015per err. *ADL92103.512.50105Self careADL869510.4773Occ. roleShortZung62.557.5-8.0052.5	61.5	2.50
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Forward Digit56203Backward1515012ReyAVLT1515012List A1415 $7.14$ 11Delayed711415 $7.14$ 11Delayed724949048recognition722513.6415FAS334330.3019Grocery1510 $-33.33$ 13FAS53222513.6415FAS334330.3019Grocery157245 $-37.50$ 31(sec.)*7245 $-37.50$ 31Key search7245 $-37.50$ 31Score*90025Wisconsin8803Categories910.4773Wisconsin0015per. err. *4DL92103.512.50105Self care34052.557.5 $-8.00$ 52.5		
$\begin{array}{c ccccc} \text{Digit} & 5 & 6 & 20 & 3 \\ \text{Backward} & & & & & & & \\ \text{ReyAVLT} & 15 & 15 & 0 & 12 \\ \text{List A} & & & & & & \\ \text{ReyAVLT} & 14 & 15 & 7.14 & 11 \\ \text{Delayed} & & & & & & \\ \text{ReyAVLT} & 49 & 49 & 0 & 48 \\ \text{recognition} & & & & & \\ \text{FAS ~R' & 15 & 10 & -33.33 & 13 \\ \text{FAS 'S' & 22 & 25 & 13.64 & 15 \\ \text{FAS & 33 & 43 & 30.30 & 19 \\ \text{Grocery} & & & & & \\ \text{Ist} & & & & & \\ \text{FAS & 33 & 40 & 21.21 & 14 \\ \text{Animal list} & & & & \\ \text{Key search & 72 & 45 & -37.50 & 31 \\ (sec.)^* & & & & \\ \text{Key search & 3 & 4 & 33.33 & 1 \\ \text{Score*} & & & & \\ \text{Wisconsin & 8 & 8 & 0 & 3 \\ \text{Categories} & & & & \\ \text{Wisconsin & 10 & 10 & 0 & 25 \\ \text{no. errors *} & & & & \\ \text{Wisconsin & 0 & 0 & 0 & 15 \\ \text{per. err. *} & & & & \\ \text{ADL & 92 & 103.5 & 12.50 & 105 \\ \text{Self care} & & & & \\ \text{ADL & 86 & 95 & 10.47 & 73 \\ \text{Occ. role} & & & & \\ \text{ShortZung & 62.5 & 57.5 & -8.00 & 52.5 \\ \end{array}$	4	-20
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Wisconsin       8       8       0       3         Categories       10       10       0       25         wisconsin       10       10       0       25         no. errors *	-	-
Categories       Visconsin       10       10       0       25         no. errors *       0       0       0       15         Wisconsin       0       0       0       15         per. err. *       0       0       105       105         Self care       0       0       105       1047       73         Occ. role       0       0       52.5       10.47       52.5	6	100
Wisconsin       10       10       0       25         no. errors *       0       0       0       15         Wisconsin       0       0       0       15         per. err. *       ADL       92       103.5       12.50       105         Self care       ADL       86       95       10.47       73         Occ. role       0       0       52.5       57.5       -8.00       52.5	Ũ	100
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per. err. * ADL 92 103.5 12.50 105 Self care ADL 86 95 10.47 73 Occ. role ShortZung 62.5 57.5 -8.00 52.5	3	-80.00
ADL         92         103.5         12.50         105           Self care	5	00.00
Self care         ADL         86         95         10.47         73           Occ. role         5000000000000000000000000000000000000	95	-9.52
ADL         86         95         10.47         73           0cc. role         -8.00         52.5	10	1.54
Occ. role         57.5         -8.00         52.5	84	15.07
ShortZung 62.5 57.5 -8.00 52.5	т	10.07
	42.2	-19.62
Fatigue 62 60 -3.23 38	42.2 51	34.21
-	51	34.21
scale On these measures, lower results mark improvement.		

Pre- and post-intervention test results and  $\Delta$  (% of change) of cases 1 and 6.

taught her to be more efficient in her work, to conserve her limited energy, and to focus on the essential matters.

# Patient 6

*B is* a 51 year old pharmacist, married with 2 children, working full time. She was diagnosed 19 years ago with MS of the SP type. Although encountering walking problems (EDSS =4), *B* was independent in her self-care ADL, while there was a reduction in her occupational role activities, both at home and in the community. Her rehabilitation process will be briefly described, according to the three phases of the process.

# $Phase \ l-understanding \ the \ metacognitive \ difficulties$

When describing her main problems, *B* focused on memory problems. However, looking at her memory test results (Table 3), these problems were only marginal. While performing various exercises, some other difficulties emerged: *B* was very slow in processing information (see also her digit-symbol and FAS results in Table 3), and indecisive. She was also extremely rigid, and lacked the ability to flexibly consider various solutions to the same problem (see also her WCST results in Table 3). She could not confront uncertainty and surprises, and relied heavily on routine and structured schemas. *B* had also a serious attention deficit: she could not relate to two or more stimuli in parallel,

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thus also making her performance slow and inefficient. In the rehabilitation process, these difficulties were gradually uncovered, and explained to her, thus leading to awareness. *B* also received explicit explanations of the theory of metacognitive skills and about the linkage between awareness to difficulties and behavioral change.

#### Phase 2 — practice of efficient working strategies

In the clinical setting, various exercises were suggested to *B*, and with each one the therapist explained the main metacognitive aspects that were being practiced. For example, a matrix with columns of fruits and rows of weights was structured. *B* first had to assign prices to each cell of the matrix, thus working on her indecisiveness. Then, she had to answer questions such as "what would 70g of almonds cost?" or "which item costs NIS 16?" (the answer being 100g of plums), thus attending to several aspects consecutively. Various exercises were devoted to enhance flexibility (e.g., B. had to formulate several different questions about a newspaper headline). While performing a "21 questions" exercise (discover a secret item with 21 questions), it became apparent that *B* did not use any categorization strategy. This impairment was also confronted and dealt with. Computer games served to practice planning and application abilities.

## Phase 3— transfer to daily life

Transfer to B's work scenario was extremely important, since as a pharmacist, she needed to consider several aspects of a prescription, to meet and react flexibly to emerging and unexpected problems, to patiently attend to customers' demands, etc. All these aspects of B's work were analyzed, and as she demonstrated a greater awareness of her job performance, she started to bring to the rehabilitation sessions difficulties that emerged in her work. These were analyzed, solutions were offered, and B tried to apply them in her daily life. Some changes in her work settings and responsibilities were also implemented.

#### The outcomes

After 6 months, *B*'s post-intervention test results marked distinct improvements in the FAS test, reflecting both faster naming and the application of an efficient categorization strategy. Her WCST improvement also supported these conclusions. Additionally, there was a reduction in her depression level, although increased fatigue was reported. Hut, unfortunately, her SAT results did not improve. Thus, although *B* benefited from the cognitive rehabilitation, she did not succeed in formulating efficient strategies for handling a new, non-routine situation. This was brought to her attention as well, and she was advised to stick to routine procedures at work, and avoid taking responsibilities that were beyond her abilities.

# Conclusions drawn from Case Reports

The two cases had almost opposite metacognitive difficulties. While Patient 1 was too flexible, Patient 6 was too rigid, thus illustrating that the therapeutic process needs to be individually tailored. Both patients had difficulties at work. However, while Patient 1 had relatively good awareness of her difficulties and needs, and openly discussed them with her therapist, Patient 6 was less aware, and at the beginning she was less keen to share her work difficulties with her occupational therapist; thus, it took longer to uncover her precise metacognitive difficulties. Both patients went through the same three-phase therapeutic process, although the specific content of the intervention was different. Both benefited from the rehabilitation process, and demonstrated better on-the-job functioning, which, as stated in the introduction, was the main goal of the process.

Another goal of this study was to characterize the profile of patients who are likely to benefit most from the cognitive approach to the rehabilitation process. As regards the two case studies, it would seem that Patient 1 benefited more. She was 12 years younger than the other patient, with disease duration shorter by almost 10 years, and an EDSS score of I. As both patients started with the same result on the SAT - 60/100, it is likely that EDSS, age, and disease duration affected the efficacy of the rehabilitation process. This observation supports the results of the statistical analyses, which found a negative correlation between percent of improvement on the SAT, the patient's age, and the EDSS score.

#### Discussion

The present study aimed to explore the efficacy of the cognitive rehabilitation process implemented with ten MS patients who demonstrated executive dysfunction. Both a quantitative analysis of the data and a qualitative description of the rehabilitation process were presented. Quantitatively, the percent of improvement between the pre- and the post-intervention tests indicated that there was an overall improvement, which was significant on the SAT, meaning that the patients succeeded in learning to apply efficient working strategies to a non-routine situation while inhibiting irrelevant stimuli. There was also improvement on the FAS, which is also considered an executive function measure (Bryan & Luszcz, 2000), indicating that the patients generated efficient searching strategies. Interestingly, while there were no specific exercises that directly addressed the areas of attention and memory, there were significant improvements on the digit symbol test, which is an attention test, and on the Rey AVLT delayed (naming list A after 20 minutes). Similarly, the significant improvement on the occupational role section of the ADL questionnaire might be related to the fact that the last stage of the intervention focused on transfer to daily life. All of these findings suggest that the intervention was effective and reached its goals.

Our results differ from those of Jonnsson et al.,(1993) who did not find significant differences between a group of MS patients that received specific cognitive treatment and a group of patients that received a non-specific mental stimulation. Several explanations can be offered: first, the Jonnsson et al (1993) intervention was short (46 days), while ours lasted six months, since it was already established that cognitive rehabilitation requires a long intervention process (Sbordone, 1988). Second, the therapeutic approaches were different in the two studies. Jonnsson et al (1993) administered a goal-directed cognitive training that employed common principles in cognitive rehabilitation programs: compensation, substitution, and direct

training. This traditional cognitive rehabilitation approach is guided by the assumption that cognition can be divided into distinct subskills (e.g., perception, attention, memory), and focuses on specific cognitive deficits (Averbuch & Katz, 1992). The metacognitive approach employed in our study investigates the underlying conditions and processing strategies that influence performance, and our treatment incorporates metacognitive aspects such as strategy training, awareness, and transfer to multiple daily situations (Toglia, 1992; Birnboim, 1995). Third, in the Jonnsson et al (1993) study, patients with mild to moderate cognitive and behavioral impairments associated with MS were randomized to the cognitive treatment, while in our study, patients were selected on the basis of having executive dysfunctions, as demonstrated by the SAT, while their other cognitive functions might have been within normal range (see Patient 1). All these factors together may have contributed to the success of the present intervention. The main success of Jonnsson et al (1993) was in reducing the levels of depression in the specific cognitive treatment group. In our study there was also a small reduction in the levels of depression and fatigue, but it did not reach statistical significance. It must be noted, however, that MS is a progressive disease in which functional deterioration, rather than improvement, is expected to be part of the natural history of the patient's disease course.

In trying to characterize the patients who benefited most from the cognitive rehabilitation, we calculated the correlation between the percent of change and the demographic data. It seems that patients with low EDSS (0-3) and also those who were of a young age, benefited more from the metacognitive rehabilitation approach. The case reports also confirmed this finding. Additionally, patients with shorter disease duration improved more on basic cognitive skills such as attention and working memory. Disease duration was inversely correlated to self-care ADL; thus, the longer the patient's disease course, the less the improvement demonstrated on the ADL self-care. These results are also reflected in the cases reports.

The correlation between the SAT percent of improvement and the EDSS requires some consideration. It is claimed that it is impossible to predict a patient's cognitive status from the degree of disability,(Beatty et al, 1990; Cobble, 1992; Maurelli et al, 1992) and, in fact, SAT results did not correlate with EDSS scores in our former study (Birnboim, 2004). It must be noted, however, that in the present study, the calculations were made with the A (percent of change) and not with the SAT results. It may be that MS patients with good EDSS might have low SAT results, but better ability for improvement (see for example cases 1, 5, and 7 in table 2). Thus, EDSS might not be a reliable measure for prediction of cognitive status, but it might be a useful predictor for anticipating the contribution of the neuro-rehabilitation intervention. In times when cost-effectiveness of intervention is a factor in selecting patients for different therapeutic activities, the present study offers a very simple criterion for predicting the efficacy of the metacognitive approach in neuro-rehabilitation.

The two case studies offer a qualitative description of the cognitive rehabilitation process according to the metacognitive approach. In this process, patients became aware of their thinking processes and learned to monitor and correct them if necessary. Most importantly, patients learned to apply the acquired metacognitive strategies to other relevant situations in their lives.

Since the metacognitive approach is only a general guidance for the process, there is much flexibility with its application. However, it might be less beneficial for people with extremely low cognitive performances, who are unable to understand and follow simple instructions. With these patients, a more functional approach would probably be the method of choice, rather than cognitive therapy.

In summary, the present study suggests that for MS patients with mild-to-moderate cognitive impairment and associated executive dysfunction, the metacognitive approach may serve as an effective interventional rehabilitation.

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