COGNITIVE AND AFFECTIVE CHANGES IN MULTIPLE SCLEROSIS, A NOVEL GROUP PSYCHOTHERAPY IN THE EARLY PHASE OF THE DISEASE

PhD thesis

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Introduction

Multiple sclerosis (MS), the most common chronic autoimmune neurological disease that causes disability in early life, does not only influence physical functioning but is also related to cognitive impairment, fatigue, depression, and anxiety and can significantly impact quality of life (QoL). Understanding the complex interplay between various factors concerning the nature of MS is of utmost importance in the management of MS. Adjustment to disease burden in different life domains creates challenges for both patients and their family members. The need for MS specific psychological interventions cannot be called into question. However, literature on the development of interventions based on the biopsychosocial model of the disease is missing and even less attention has been paid to interventions dedicated to young adults with MS.

Cognitive impairment affects 40-65% of MS patients, partly independent from the course and stage of the disease. Most frequently involved cognitive domains are information processing speed, learning and episodic memory with additional difficulties in executive functions, working memory, verbal fluency and word list generation, complex attention, and visuospatial skills. Social cognition has been demonstrated to be affected, as well, with a larger impact in theory of mind and in the recognition of negative facial emotional expressions.

Recently word-finding difficulty and multitasking deficit have been reported in early MS. Considering the life task of young adulthood (effectively managing multiple simultaneous aims), multitasking is more related to real-world functioning compared to monotasking.

A large interpatient variability can be seen in the pattern and severity of cognitive deficits in MS. Therefore a number of biological and psychological factors has been investigated in order to explain this phenomenon. Fatigue and depression has been shown to be the main correlates of cognitive impairment in MS with domain-specific associations.

Among individuals with MS, mental health comorbidities contribute to secondary disability and detract from QoL. A significant incidence and prevalence of psychological disorders in MS has been described. Depression is the predominant psychological disturbance. Anxiety is also frequent, occurs in newly diagnosed patients, and its co-morbidity with depression contributes to the increase of the rate of suicidal ideation. Other psychiatric illnesses, as bipolar affective disorder, pathological laughing and crying, or psychosis, occur less frequently in MS.

The prevalence of depression is higher in the population with MS than in general public or in many other chronic patient populations. In general, up to 50% of people with MS is reported to experience major depressive disorder in their lifetime. Aetiology of depression in MS is

multifactorial with a complex interplay between biological and psychosocial variables. MS patients could be predisposed for depression by several psychosocial risk factors such as insufficient social support or emotion-focused coping.

Psychological treatment may be beneficial for people with MS to gain skills to cope with emotions, thoughts and to adjust to MS diagnosis and symptoms. Apart from reducing depressive symptoms and anxiety, positive impacts may include outcomes such as prevention of new brain lesions in patients with MS, improvement in adherence to treatment, decrease in fatigue, and increase in mental and total health related QoL. A significant finding is that peers and peer support is an important component in rehabilitation from the perspective of individuals therefore group-based intervention might have an extra benefit. The importance of psychological support of MS patients including MS-specific considerations is justifiable. As the adjustment process including perceived disease burden starts with the diagnosis, the early stage of MS can be considered a good time for a psychological intervention.

Aims

Our aim was to understand the cognitive and psychobehavioural dimensions of multiple sclerosis, to reveal their complex interplay with the intention of designing a psychological preventive intervention program in the early phase of the disease.

First, we aimed to investigate the pattern of cognitive functioning and depression in benign MS (BMS) and relapsing remitting MS (RRMS) patients following them for two years.

Second, we intended to explore the differences in psychological characteristics between MS patients and healthy population.

Third, we aimed to design an integrative intervention group protocol for MS patients in the early stage to support the adjustment process and to prevent the development of severe psychological consequences.

Methods

Neuropsychological characteristics of BMS patients

Participants

The study was conducted based on the analysis of clinical data acquired from a registry of 400 MS outpatients from the year of 2014 at the Department of Neurology in Semmelweis University. Twenty-two patients were included in the BMS group based on a definite diagnosis of MS (according to 2010 McDonald diagnostic criteria) and a benign course defined as an EDSS score ≤ 3.0 after at least 10 years from the clinical onset of the disease. These patients

have never been treated with immunomodulatory drugs. They follow the natural course of the disease.

A comparison group of 22 RRMS patients was recruited. In the beginning of disease course, the disease activity was higher in this group compared to BMS group. Therefore each patient started drugs after their first relapse in the setting of everyday clinical practice (based on the legislation of National Health Insurance Fund of Hungary). Controlling for demographic and clinical characteristics, cases in the patient groups were matched in terms of age, gender, education and disease duration.

After a 2-year period patients were clinically re-evaluated. In both groups patients had the same disease course remaining in the same MS group. RRMS patients continued to receive the DMT. None of them were treated especially for cognitive impairment or depression. They were reassessed through the use of the same neuropsychological testing battery that had been initially administered.

Healthy volunteers matched with the sample for gender, age and education were also studied at baseline.

Neuropsychological assessment

Participants underwent a neuropsychological evaluation exploring the cognitive domains most frequently impaired in MS: complex attention [Paced Auditory Serial Attention Test 3 seconds (PASAT-3)]; visuo-spatial memory [Rey-Osterrieth Complex Figure Test (CFT)]; learning, verbal memory [Auditory-Verbal Learning Test (AVLT)]; working memory [Digit Span (DS)]; information processing speed [Wechsler's Digit Symbol Test (WDST)]; and executive function [Tower of Hanoi (TH)]. Depression was assessed using the Zung Self-Rating Depression Scale (SDS).

Statistical analysis

Demographic and clinical characteristics of the participants were summarized as mean ± SD. Data were tested for normal distribution using the Shapiro-Wilk test. Group differences in EDSS score were determined using non-parametric Mann-Whitney U-test. Differences in cognitive parameters and depression between groups were determined using the multivariate analysis of variance tests. At baseline, Kruskal-Wallis H test was applied in case the assumption of normal distribution failed. The Bonferroni correction adjusted multiple comparisons between groups. Analysing follow-up data, between group comparisons were assessed using the 2-tailed t-test for unpaired samples or the non-parametric Mann-Whitney U-test. The Wilcoxon test or 2-tailed t-test for paired samples was used for within group comparisons. Pearson's correlation was performed to evaluate the association between depression and the different cognitive

domains. All analyses were carried out using the SPSS software. In all cases p values < 0.05 were taken as significant.

Psychological characteristics of MS patients

Participants and study design

Patients attending regularly scheduled appointments at the Department of Neurology in Semmelweis University were asked to participate in the study. Sixty-eight RRMS patients were recruited consecutively. The battery required approximately one hour to complete and patients completed it by the end of their clinic appointment or returned it in a distributed envelope by mail. Sixty-six healthy volunteers matched with the sample for gender, age and education were recruited.

Measures

In addition to an initial page eliciting demographic and disease-related information, the battery included the following questionnaires and measures:

- Beck Depression Inventory (BDI) to measure the level of depression.
- Short Health Anxiety Inventory (SHAI) to assess the level of health anxiety.
- Modified Fatigue Impact Scale (MFIS) to assess the effects of fatigue.
- Ways of Coping to analyse the coping strategies.
- Dysfunctional Attitude Scale (DAS) to explore dysfunctional attitudes.
- Emotional Quotient Inventory (EQ-i) to assess emotional-social intelligence.
- Toronto Alexithymia Scale (TAS-20) to evaluate the level of alexithymia.

Statistical analysis

Demographic and clinical characteristics of the participants were summarized as mean (SD) or median (interquartile range). Data were tested for normal distribution using the Shapiro-Wilk / Kolmogorov-Smirnov normality test. Analysing data, between group comparisons were assessed using the 2-tailed t-test for unpaired samples or the non-parametric Mann-Whitney U-test. Correlation analyses (using Pearson's r for variables with a normal distribution or Spearman's rank correlation for non-parametric variables) were performed to evaluate the association between depression / anxiety / fatigue and the different psychosocial variables. Additionally, variables with a p-value below 0.20 in a bivariate analysis were selected for multivariate forward stepwise linear regression analysis to explain depressive symptoms. All analyses were carried out using the SPSS software. In all cases p values < 0.05 were taken as significant.

Patients and process

This pilot study was conducted at the Department of Neurology in Semmelweis University. The recruitment process intended to imitate clinical practice for identifying MS patients in the early stage who needed psychological counselling due to depressive symptoms or anxiety. After giving informed consent, patients were referred to a baseline evaluation conducted by a psychologist. Six patients were assigned to the group intervention therapy. They were reassessed at post-intervention (six months after pre-treatment evaluation) and six months after post-intervention including the same tests as in the baseline data collection.

Primary outcome measures were: (1) Beck Depression Inventory (BDI) to measure the level of depression; (2) Short Health Anxiety Inventory (SHAI) to assess the level of health anxiety; and (3) Modified Fatigue Impact Scale (MFIS) to assess the effects of fatigue. Secondary outcome measures were: (1) Emotional Quotient Inventory (EQ-i) to assess emotional-social intelligence; (2) Ways of Coping to analyse the coping strategies; and (3) Toronto Alexithymia Scale (TAS-20) to evaluate the level of alexithymia.

Feasibility of the designed integrative group intervention protocol was characterized by recruitment rate, number of cancellations, attrition rate, and potential adverse events.

Intervention

The intervention consisted of 20 group sessions administered on a weekly basis for 1.5 hour. The intervention group program was designed for people with MS based on the information gathered from previous studies, based on the results of our study on psychological characteristics of MS patients and based on the experience in relaxation and supportive group therapy for MS patients at the Department of Neurology, Semmelweis University. The goal was to introduce a combination of evidence-based therapies in order to better serve the needs of MS people in the early stage and to ease the adjustment difficulties associated with depression or anxiety.

The sessions involved an opening relaxation exercise, homework reflection and presentation, discussion and practice of a new topic involving new skills. Homework based on session topics was assigned to encourage the participants to practice new skills at home. They were asked to perform relaxation exercises every day.

Statistical analysis

Demographic and clinical characteristics of the participants were summarized using mean (SD) or median (IQR). Mean differences in outcome measures from baseline to 6-month follow-up were calculated. Descriptive statistics were used to analyse outcome variability.

Results

Neuropsychological characteristics of BMS patients

Demographic and clinical characteristics did not differ significantly between BMS and RRMS group. The mean level of depression was elevated in the BMS group compared to the RRMS group, however, significant differences were found only between BMS and healthy groups (p=0.008) (Table 1).

Table 1 Demographic and clinical characteristics of the study sample, baseline.

	BMS 1 n=22	RRMS 2 n=22	Control 3 n=22	*p*-value 1-2	1-3	2-3
Gender, n (men/women)	5/17	5/17	5/17	n.s.	n.s.	n.s.
Age, y, mean (SD)	44.9 (9.5)	45.1 (9.2)	44.9 (9.6)	n.s.	n.s.	n.s.
Education, y, mean (SD)	13.6 (2.1)	14.1 (2.2)	13.9 (2.5)	n.s.	n.s.	n.s.
Disease duration, y, mean (SD)	14.9 (6.1)	13.7 (6)	n.r.	n.s.	-	-
EDSS score, mean (SD)	1.2 (0.9)	1.7 (1.5)	n.r.	n.s.	-	-
Depression score, mean (SD)	43.4 (10.1)	39.4 (7.5)	35.9 (5.7)	n.s.	0.008	n.s.

Note. y: years, SD: standard deviation, EDSS: expanded disability status scale, Depression score measured by SDS, n.s.: not significant, n.r.: not relevant.

Non-significant differences between MS groups were noted in the measured cognitive domains at baseline (Table 2). In comparison with the healthy control group, there were significant differences in the BMS group in the following mean scores and domains: CFT (p=0.005) – visuo-spatial memory; AVLT-L (p=0.04) – auditory-verbal learning; and WDST (p=0.017) – information processing speed. In RRMS group significant differences were found compared to healthy group in terms of PASAT-3 (p=0.032) – complex attention; CFT (p=0.044) – visuo-spatial memory; and WDST (p=0.001) – information processing speed.

Table 2 Neuropsychological scores at baseline, comparison between groups.

Domain and test	BMS 1 n=22	RRMS 2 n=22	Control 3 n=22	*p*-value 1-2	1-3	2-3
Complex attention						
PASAT-3	40.09 (11.1)	35.55 (12.5)	45.82 (11.5)	n.s.	n.s.	0.015
Memory						
CFT	18.34 (5.3)	19.72 (5.7)	24.43 (7.5)	n.s.	0.005	0.044
AVLT-L	51.82 (8.8)	55.14 (8.8)	58.23 (8.4)	n.s.	0.04	n.s.
AVLT	10.73 (3.3)	11.41 (3.2)	12.36 (2.6)	n.s.	n.s.	n.s.
DS	12.05 (2.1)	12.27 (2.2)	12.18 (2.3)	n.s.	n.s.	n.s.

Domain and test	BMS 1 n=22	RRMS 2 n=22	Control 3 n=22	*p*-value 1-2	1-3	2-3
Information processing speed						
WDST	42.05 (10.5)	38.23 (13.2)	52.00 (10.8)	n.s.	0.017	0.001
Executive function						
TH*	26.86 (4.1)	29.23 (4.5)	28.00 (5.4)	n.s.	n.s.	n.s.

Note. Scores are mean (SD).

PASAT-3: Paced Auditorial Serial Attention Test 3 seconds; CFT: Rey-Osterrieth Complex Figure Test; AVLT-L: Auditory-Verbal Learning Test, learning; AVLT: Auditory-Verbal Learning Test, verbal memory; DS: Digit Span; WDST: Wechsler's Digit Symbol Test; TH: Tower of Hanoi, n.s.: not significant, *lower value means better performance.

The cognitive evaluation showed no significant differences between BMS patients and RRMS patients at two-year follow-up (Table 3). In BMS group, significantly higher mean scores were found on AVLT-L subtest (p=0.024) – auditory-verbal learning; and on WDST test (p=0.022) – information processing speed.

Table 3 Neuropsychological scores, 2-year follow-up, comparison within groups and between groups.

Domain and test	BMS 1(t_1) n=22	BMS 1(t_2) n=22	*p*	RRMS 2(t_1) n=22	RRMS 2(t_2) n=22	*p*	*p*-value 1(t_2)-2(t_2)
Complex attention							
PASAT-3	40.09 (11.1)	41.68 (10.8)	n.s.	35.55 (12.5)	39.23 (12.7)	n.s.	n.s.
Memory							
CFT	18.34 (5.3)	19.27 (6.5)	n.s.	19.72 (5.7)	19.43 (6.0)	n.s.	n.s.
AVLT-L	51.82 (8.8)	55.77 (10.1)	0.024	55.14 (8.8)	56.45 (9.4)	n.s.	n.s.
AVLT	10.73 (3.3)	11.23 (3.8)	n.s.	11.41 (3.2)	11.36 (3.3)	n.s.	n.s.
DS	12.05 (2.1)	11.45 (2.3)	n.s.	12.27 (2.2)	11.86 (2.4)	n.s.	n.s.
Information processing speed							
WDST	42.05 (10.5)	45.43 (12.0)	0.022	38.23 (13.2)	39.57 (14.5)	n.s.	n.s.
Executive function							
TH*	26.86 (4.1)	28.59 (5.1)	n.s.	29.23 (4.5)	29.73 (7.9)	n.s.	n.s.

Note. Scores are mean (SD).

PASAT-3: Paced Auditorial Serial Attention Test 3 seconds; CFT: Rey-Osterrieth Complex Figure Test; AVLT-L: Auditory-Verbal Learning Test, learning; AVLT: Auditory-Verbal Learning Test, verbal memory; DS: Digit Span; WDST: Wechsler's Digit Symbol Test; TH: Tower of Hanoi, t_1: baseline; t_2: 2-year follow-up, n.s.: not significant, *lower value means better performance.

Psychological characteristics of MS patients

Demographic and main clinical data of the subjects included in the study are shown in Table 4.

Table 4 Demographic and clinical characteristics of the study sample.

	RRMS n=68	Control n=66	*p*-value
Gender, n (men/women)	17/51	19/47	n.s.
Age, y, mean (SD)	36.4 (8.9)	35.5 (9.9)	n.s.
Education, y, mean (SD)	14.4 (2.1)	14.8 (1.9)	n.s.
Disease duration, y, mean (SD)	6.6 (5.3)	n.r.	n.r.
EDSS score, mean (SD)	1.2 (1.4)	n.r.	n.r.

Note. y: years, SD: standard deviation, EDSS: expanded disability status scale, IQR=interquartile range, DMT: disease modifying treatment, n.s.: not significant, n.r.: not relevant.

RRMS patients had a higher mean depression score (p=0.00), a higher mean health anxiety score (p=0.009) and a higher mean fatigue score (p=0.006) than controls (Table 5). In comparison with control group, RRMS patients used less problem-focused strategies (p=0.045), and support seeking strategy (p=0.017) and were more prone to use withdrawal strategy (p=0.001). They exhibited more elevated dysfunctional attitudes in the value systems of love (p=0.028), entitlement (p=0.025) and autonomy (p=0.002). Their mean EQ-i score was significantly lower (p value<0.000). Relative to controls, RRMS patients had a significantly higher mean global score of alexithymia (p=0.000).

Table 5 Comparison of psychological characteristics between RRMS patients and controls.

	RRMS n=68	Control n=66	*p*-value
BDI	11.57 (8.48)	5.74 (5.2)	**0.000**
SHAI	19 (8.89)	15.33 (6.61)	**0.009**
MFIS	29.75 (21.09)	19.67 (15.13)	**0.006**
Physical subscale	15.1 (11.3)	7.61 (6.45)	**0.000**
Cognitive subscale	11.9 (10.06)	10.33 (8.41)	0.530
Psychosocial subscale	2.75 (2.37)	1.73 (1.78)	**0.015**
Ways of Coping			
Problem-focused strategies	1.71 (0.54)	1.9 (0.53)	**0.045**
Problem analysing	1.91 (0.67)	2.18 (0.56)	0.072
Goal directed behaviour	1.51 (0.66)	1.62 (0.71)	0.456
Emotion-focused strategies	1.34 (0.33)	1.25 (0.4)	0.143
Emotion-centred behaviour	0.93 (0.63)	0.8 (0.55)	0.234
Adaptation	1.41 (0.54)	1.37 (0.52)	0.381
Support seeking	1.57 (0.67)	1.86 (0.8)	**0.017**

	RRMS n=68	Control n=66	*p*-value
Emotional balance seeking	1.29 (0.68)	1.11 (0.68)	0.082
Withdrawal	1.5 (0.64)	1.12 (0.67)	**0.001**
DAS			
Approval	0.69 (3.99)	-0.74 (3.51)	0.039
Love	0.97 (4.79)	-0.77 (4.31)	**0.028**
Achievement	-0.51 (6.22)	-2.44 (5.09)	0.051
Perfectionism	0.37 (4.86)	-0.89 (3.16)	0.141
Entitlement	3.33 (4.37)	1.86 (4.1)	**0.025**
Omnipotence	1.1 (4.58)	0.39 (3.69)	0.294
Autonomy	0.79 (4.11)	-1.44 (3.69)	**0.002**
EQ-i	418.28 (56.76)	457.95 (46.13)	**0.000**
1-Intrapersonal	120.24 (23.33)	134.92 (19.15)	**0.000**
2-Interpersonal	90.54 (12.4)	97.12 (9.86)	**0.001**
3-Stress Management	56.56 (8.91)	60.76 (8.21)	**0.005**
4-Adaptability	91.12 (11.79)	97.86 (11.26)	**0.001**
5-General Mood	91.12 (11.79)	97.86 (11.26)	**0.001**
TAS-20	48.57 (13.35)	40.12 (9.57)	**0.000**
DIF	13.56 (4.87)	10.45 (3.57)	**0.000**
DDF	16.35 (5.08)	11.92 (4.02)	**0.000**
EOT	19.26 (4.61)	17.65 (4.51)	**0.043**

Note. Scores are mean (SD).

BDI: Beck Depression Inventory, SD: standard deviation, SHAI: Short Health Anxiety Inventory, MFIS: Modified Fatigue Impact Scale, DAS: Dysfunctional Attitude Scale, EQ-i: Emotional Quotient Inventory, TAS-20: Toronto Alexithymia Scale, DIF: difficulty in identifying feelings, DDF: difficulty in describing feelings, EOT: externally oriented thinking.

The bold values indicate the P values of scales/subscales which their differences were significant.

Regression analysis showed that in MS group, 68.4 % of the variation in BDI score can be explained using EQ-i score, Cognitive subscale score of MFIS, Adaptability scale score of EQ-i, Emotion-centred behaviour score of Ways of Coping and DIF score of TAS-20 (r^2=0.684, p=0.000). In control group, 54.5 percent of the variation in BDI score can be explained using DDF score of TAS-20, Stress management scale score of EQ-i, Self-regard subscale score of EQ-i and SHAI score (r^2=0.545, p=0.000).

Integrative group therapy for people in early MS

Demographic and main clinical data of the subjects are shown in Table 6.

Table 6 Demographic and clinical characteristics of the patients.

	Intervention n=6
Gender, n (men/women)	2/4
Age, y, mean (SD)	31.7 (4.4)
Education, y, mean (SD)	16.5 (2.0)
Disease duration, y, median (IQR)	1 (0.875, 3.5)
EDSS score, median (IQR)	1.25 (0.75, 2.25)
Immunomodulatory treatment, n	4

Note. y: years, SD: standard deviation, IQR=interquartile range.

Patterns of change in the outcome measures across time are presented in Table 7. Improvement was detected in scores of all scales and this alteration remained at 6-month follow-up.

Table 7 Scores on outcome measures at assessment time points.

	Intervention Group (n=6)		
	Pre-treatment	Post-treatment	6-month follow-up
Depression			
BDI	9.33 (3.56)	5.5 (4.23)	4.67 (2.5)
Health Anxiety			
SHAI	22.17 (6.18)	14.17 (2.32)	13.0 (5.76)
Fatigue			
MFIS	17.5 (12.74)	15.5 (20.12)	12.83 (10.5)
Physical subscale	8.83 (8.98)	10.67 (12.71)	7.83 (6.34)
Cognitive subscale	6.5 (6.98)	4.00 (6.29)	4.17 (4.36)
Psychosocial subscale	2.17 (1.72	1.33 (2.34)	0.83 (0.98)
Emotional-social intelligence			
EQ-i	432.83 (36.71)	453.33 (28.18)	464.33 (43.14)
EQ-i-1	126.83 (11.58)	132.67 (12.68)	137.50 (15.63)
EQ-i-2	87.17 (6.97)	90.00 (6.32)	91.17 (7.88)
EQ-i-3	59.67 (9.4)	63.00 (3.74)	64.50 (7.23)
EQ-i-4	94.33 (13.02)	98.67 (8.78)	100.33 (11.83)
EQ-i-5	64.83 (7.81)	69.00 (7.07)	70.83 (8.26)
Coping			
Problem-focused strategies	1.74 (0.65)	1.81 (0.41)	2.16 (0.46)
Problem analysing	1.89 (0.81)	2.00 (0.3)	2.28 (0.44)
Goal directed behaviour	1.58 (0.47)	1.63 (0.44)	2.04 (0.49)
Emotion-focused strategies	1.22 (0.58)	1.22 (0.58)	1.3 (0.7)

	Intervention Group (n=6)		
	Pre-treatment	Post-treatment	6-month follow-up
Emotion-centred behaviour	0.96 (0.58)	0.79 (0.37)	0.88 (0.61)
Adaptation	1.17 (0.49)	1.00 (0.45)	1.21 (0.62)
Support seeking	1.58 (0.8)	1.42 (0.66)	1.75 (0.99)
Emotional balance seeking	1.08 (0.2)	1.63 (0.45)	1.33 (0.61)
Withdrawal	1.33 (0.63)	1.28 (0.68)	1.34 (0.52)
Alexithymia			
TAS-20	44.33 (4.37)	38.83 (4.54)	38.00 (8.20)
DIF	13.50 (1.88)	11.67 (2.34)	11.00 (2.61)
DDF	13.17 (3.31)	10.17 (2.79)	10.83 (2.32)
EOT	17.67 (3.93)	17.00 (3.58)	16.17 (6.24)

Note. Scores are mean (SD).

BDI: Beck Depression Inventory, SHAI: Short Health Anxiety Inventory, MFIS: Modified Fatigue Impact Scale, EQ-i: Emotional Quotient Inventory, EQ-i-1: Intrapersonal Scale, EQ-i-2: Interpersonal Scale, EQ-i-3: Stress Management Scale, EQ-i-4: Adaptability Scale, EQ-i-5: General Mood Scale, TAS-20: Toronto Alexithymia Scale, DIF: difficulty in identifying feelings, DDF: difficulty in describing feelings, EOT: externally oriented thinking.

During the three-month recruitment period eight potential participants were approached and six patients were included, giving an average recruitment rate of two persons/month. All patients finished the intervention group, giving a completion rate of 100 %. Patients demonstrated good compliance with the treatment and the follow-up session (the attrition rate was 0%). The average number of sessions attended was 19 (range 14-20 sessions). No adverse events were reported.

Conclusions

In our study we used a multidimensional approach to understand the cognitive and psychobehavioural dimensions of multiple sclerosis, to reveal their complex interplay with the intention of designing a psychological preventive intervention program to be included in the routine clinical practice.

The neuropsychological study represents to our knowledge the first attempt of evaluating cognitive functions of BMS patients never treated – following the natural course of the disease – compared to RRMS patients treated with disease modifying therapy. The results of our study confirm that cognitive functions and mood can be affected in MS independent of disease course. Therefore the “benign” label should be treated only as a reference to the physical status. Cognitive and psychological status should be assessed and managed irrespectively to MS

subtype, meaning the need for routine monitoring of non-motor symptoms in MS in order to detect clinically meaningful changes and to start a timely and effective treatment. Thus a younger patient age could be targeted, when compensatory abilities, brain plasticity, and cognitive reserve may be better exploited.

As previously reported, the prevalence of depression, anxiety, and fatigue is high in the MS population. Left untreated, they do not seem to improve spontaneously. With respect to the pathogenesis of depression in MS, a multifactorial aetiology can be supposed. Studying different psychological characteristics of MS patients, we can conclude that lower emotional and social intelligence, alexithymia, emotion-focused coping strategies are present in this population. Their attitude is driven by the desire for love, entitlement and less autonomy compared to general public. Therefore a different therapeutic approach is necessary in psychological interventions in MS.

We have identified lower level of emotional-social intelligence, cognitive fatigue, lack of competencies in change management, emotion-centred coping and difficulty in identifying emotions as predictors for the susceptibility of depression in MS. Therefore we can conclude that these psychological features might play an important role in the vulnerability to depression and they should be addressed in psychological intervention programs.

Implementing the findings of previous studies and our results, we aimed to design an integrative intervention group protocol for people at the early stage of MS to support the adjustment process and to avoid severe psychological complications. Preliminary findings show that our program might be beneficial for and accepted by MS patients, and it might reduce depressive symptoms, health anxiety and fatigue. Furthermore, it may reinforce social support, protective factors – such as emotional-social intelligence, change management – promote adaptive coping mechanism and reduce risk factors, i.e. alexithymia. A future effectiveness study could include outcome measures for cognitive functioning as well.

As stated in the introduction, considering the challenges imposed by MS in the early stage, delivering care and early interventions for this group can substantially reduce disease burden. These support strategies may improve cognitive, emotional, and social functioning, and enhance the adjustment process resulting in a positive spill-over effect on family and economic burdens.

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