

Metacognitive model of mindfulness can improve executive function in multiple sclerosis patients

MARZIEH NAZARIBADIE¹, ALI GHALEIHA^{1*}, MOHAMMAD AHMADPANA¹, MEHRDOKHT MAZDEH¹, NASRIN MATINNI², MOHAMMAD-KAZEM ZARABIAN¹

¹Research Center for Behavioral Disorders and Substance Abuse, Hamadan University of Medical Sciences, Hamadan, Iran.

²Nursing department, Hamedan branch, Islamic Azad University, Hamedan, Iran.

Corresponding author: * Ali Ghaleiha Full professor of psychiatry. Affiliation: Research Center for Behavioral Disorders and Substance Abuse, Hamadan University of Medical Sciences, Hamadan, Iran. Email: dralighaleiha@gmail.com

ABSTRACT

Background: The experience of executive dysfunctions is common among patients with multiple sclerosis (MS).

Objective: The present study aimed to evaluate the effect of the Metacognitive model of detached mindfulness (MDM) as an adjuvant treatment on executive functions in multiple sclerosis patients.

Methods: In this study, 27 patients with multiple sclerosis were recruited to the experimental group and 26 in the control group. The participants in the experimental group were trained based on the intervention program during eight weeks. The intervention encompassing the metacognitive model of detached mindfulness was conducted in group sessions once a week. However, the patients in the control group received the common treatment as usual. At the baseline and at the end of the intervention, patients completed the Wisconsin Card Sorting Test (WCST) of executive functions, Paced Auditory Serial Addition Test (PASAT) Hamilton Rating Scale for Anxiety (HRSA).

Results: At the end of treatment, the scores showed significant reduction in WCST (perseveration errors, and a number of errors), and HRSA in the experimental group compared to than in the control group.

Conclusions: The results prove the initial evidence that adjuvant MDM can improve executive functions and anxiety among the multiple sclerosis patients.

Keywords: metacognition, detached mindfulness; executive function; multiple sclerosis; randomized controlled study.

INTRODUCTION

Multiple sclerosis (MS) is a degeneration disease with unknown etiology [1]. Cognitive impairment (CI) and psychiatric symptoms are frequent in MS patients [2, 3]. Executive function is considered as one of the most important functions, impaired in MS patients[4]. It is defined as the capability to organize our behavior, flexibility, and ability to alter cognitive strategies in reaction to changing social demands [5]. Julian et al., 2009 in their study found that anxiety predicted performance on the index of executive function[3], and cognitive slowing related to anxiety MS patients [6].

Metacognition is closely related to executive functions, which involves monitoring and controlling information processing on voluntary actions [7]. Over the recent years, self-regulatory executive function (S-REF) model has been regarded as one of the most effective models for explaining mental disorders [8]. In this model, all psychiatric disorders can be related to an ineffective model of cognitive activity called "cognitive, attentional syndrome (CAS)", which is stored in the long-term memory and is regarded as a pattern of strategic processing activity set by metacognitive knowledge[8]. CAS involves self-focused attention and rigid thinking styles in thoughts that leads to difficulty in behavior [8]. Attentional ways can play a role in enhancing prolonged or repetitive disturbances in thinking which causes inconsistent behaviors [9]. In the protocol developed by Wells, it has been considered that the metacognitive-based detached mindfulness as the opposite and incompatible point of CAS[9], and techniques of detached mindfulness modify the ineffective model of cognitive activity called "cognitive, attentional syndrome"(CAS). Mindfulness is a kind of internal

consciousness regarding automated processes and unintentional processing of internal currents and events, especially in thoughts. In this situation, individuals learn to cognitively separate themselves from their thoughts. Mindfulness can regulate choice of diverse contemplate and behavioral ways, and further use of mindfulness strengthens the new design to regulate the cognitive function of the mind [10]. Generally, mindfulness is seeing of inner thoughts without answering and appraisal, for example this method helps us not to respond anxiously to a disturbing event in mind. In fact, it helps to accept events and allows them to be in the mind as an event without any additional processing [10].

Based on some recent non-pharmacological studies, the use of metacognitive strategies can improve cognitive functions [11-19]. Training mindfulness can improve unfocused and sustained attention, as well as some executive functions[20]. In addition, a number of studies reported that mindfulness practice results in enhancing cognitive functions such as executive function and sustained attention [21-23]. On the other hand, drug therapy such as Interferon beta (IFN β) is used as a method for treating MS patients, which can play an indirect effect on cognition. Since IFN β reduces immune-mediated inflammation and demyelination, it can result in maintaining function [24-31].

Many studies have used the mindfulness practices for the treatment of neuropsychological disorders. In recent years, psychologists have been implementing metacognitive therapy-based detached mindfulness (DM) in order to treat the psychiatric disorder such as depression and anxiety [32-35].

OBJECTIVES

Although the effectiveness of mindfulness has been confirmed in previous studies related to depression and anxiety, it has been less considered on cognitive functions such as executive function. Hence, the present study aimed to investigate the effect of detached mindfulness via an applied metacognitive model of detached mindfulness training as adjuvant pharmacological therapy on executive function in MS patients.

METHODS

Trial design and setting: This randomized controlled trial study was conducted on the outpatient clinic of Farshchian Hospital (Hamadan University of Medical Sciences) and Hamadan Multiple Sclerosis Association during December 2016-April 2018. The registration number of this study is: IRCT2016112728119N5.

Randomization: A ballot box containing 30 green and 30 yellow cards was provided for assigning the patients under the study conditions. Each color represented a study condition. The patients drew cards and were assigned in accordance with the study conditions.

Procedure: First, a total of 60 outpatients who were clinically diagnosed to have MS (ICD 10: G35) with executive dysfunction were selected based on the Wisconsin Card Sorting Test (WCST). The patients were between the age range of 18- 45 with EDSS (Expanded Disability Status Scale) ≤ 4, had no history of mental (psychosis), physical disorders and clinically not depressed, had diploma or higher education and had no absence for more than two sessions. The samples included 53 patients, among whom 27 were randomly selected as the experimental group and 26 were selected as the control group. Treatment was conducted in group sessions once a week. Group size varied from 5 to 7 participants. Before starting treatment sessions, a neuropsychological test was performed by a trained psychologist. The experimental group was treated by a group therapy based on the

metacognitive model of detached mindfulness during eight-week sessions (each session lasting one hour), and neuropsychological tests performed by a psychologist after 8 sessions. It is worth noting that the time taken to complete the neuropsychological tests for any participant of the experimental and control groups ranged from 30 to 45 minutes.

Instruments of the study

Wisconsin Card Sorting Test (WCST): WCST includes perseveration error, category, conception responses, total correct number, number of errors, other errors, and first trial category[36]. It is utilized to evaluate the capacity to form the abstract concept, shift and maintain set, and utilize feedback. The test was planned to assess abstraction capacity, and the aptitude to shift cognitive strategies in reply to altering environmental contingencies. Furthermore, it is a tool to evaluate executive function. The perseveration responses of this test disclose capability to turn over the old category for the new one, or the incapability to see a new probability. Category represents the early conceptualization, by reflecting the concentration of perseveration errors with respect to the total test performance [37]. The reliability of WCST and the test-retest is 0.83 and 0.74, respectively, and the reliability of this test in another study was reported to be 0.85[5].

3.2.2. Paced Auditory Serial Addition Test (PASAT): This test as a serial addition task is used to assess the rate of information processing, flexibility and attention [5] as well as executive function in the model of working memory[6]. The reliability of this test was 0.90, and the calculated Cronbach's alpha was 0.74 [38].

3.2.3. The Hamilton Rating Scale for Anxiety (HRSA) consists of 14 items, which assesses the mental and physical symptoms. Scores range from 0 to 56, which 0–13 represents the normal condition in the test, 14–17 (small), 18–24 (average) and ≥25 indicates severe condition [39].

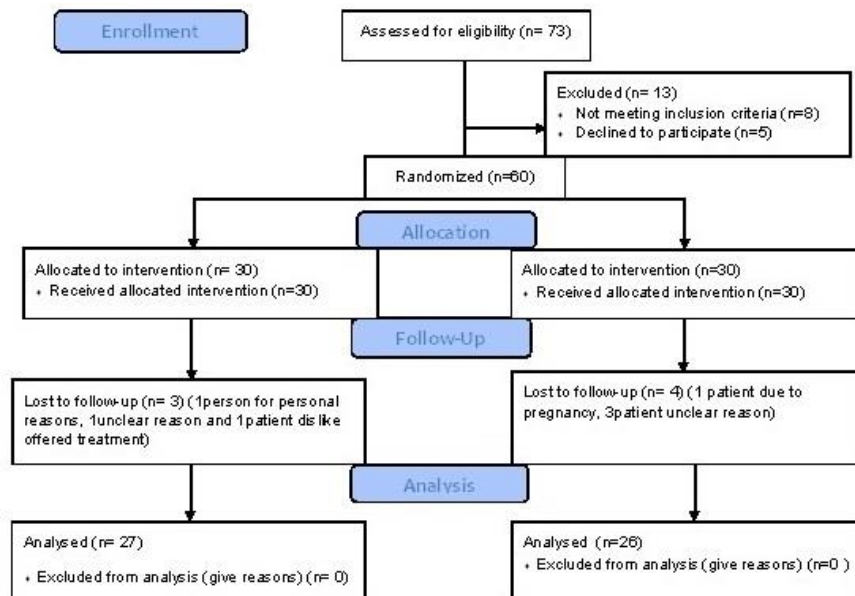


Figure 1: CONSORT flow diagram (Figure1).

Treatment

Pharmacological treatment: All patients received IFN β 1a (Avonex 30 mg, Cinnovex 30 mg or Actovex 30 mg) weekly.

Non-pharmacological treatment: Detached mindfulness is considered as a new theoretical and therapeutic advancement in research [33, 40]. In the present study, "mindfulness" refers to an observe consciousness of thought or belief, while "detachment" means the disconnection of reaction or activity in answer to the thought and separate the conscious experience of self from the thought. These factors consist of the individual becoming aware of being the perceiver of thought and separating themselves from their thoughts [9]. In this study, detached attention awareness techniques were used for reinforce scheduled cognitive control (improved executive control flexibility) among the patients.

Intervention was performed in group sessions by psychologists in 8 group sessions and 1 session per week for 60-70 minutes. Each group included 5-7 participants. Homework practice was a central component of the procedure of all sessions. In the present study, the explanation of the used protocol is summarized. As mentioned below, it has been thoroughly described by Wells in 2011 [9, 10].

Session 1: Introduction

Introducing members, goal of sessions, explanation intervention plan and metacognitive based on detached mindfulness therapy.

Session 2: Attention Program Task (APT)

The attention program task as a method is used to enhance meta-cognitive reviewing, prevent operations and decrease powerful perceptual activity. APT as a practice consists of three parts, including election, change and separation of attention.

Session 3: Metacognitive Guidance and Free Association techniques

Metacognitive Guidance: application of groups of queries when encountering to conditions. The purpose of this technique is increasing consciousness, defocusing, and separating of vigilance.

Free Association techniques: This technique is used to Facilitation of mindfulness, de-centering, attentional detachment, and low conceptual processing.

Session 4: suppression of anti-repression

Individual wants to get rid of annoying thoughts. This technique of mindfulness is applied to achieve this purpose. This session aimed to clarify that attempting to stop thoughts is a form of active engagement with thoughts.

Session 5: Tiger technique: Participants are motivated to passively look at different aspects of the image that they have imagined in their minds for the experience of mindfulness (detached of disturbing thoughts and images), after practicing with neutral image, this technique is used for disturbing image and thoughts.

Passing clouds: In this technique, individuals are motivated to see their thought as clouds in transition. The logic of this technique is for clients to look at feeling and thoughts like these transitional clouds, if seeing them

without attention, pass through the mind spontaneously like clouds.

Session 6: Verbal repeat and unruly child management techniques

Verbal Repeat, repeated presentation of thoughts through audio recording or verbal repeat reduce the prominent and semantic concept of those thoughts.

Unruly child management techniques: this technique helps clients in comprehending the distinction among and outcomes of involvement with confusing situations against an active observer.

Session 7: Looking at the thoughts just as a thought and detaching from those thoughts: In this technique, clients are learned that their perceptions of events reflect what we add to reality. Our thoughts are not real facts, even those who themselves claim to be real

Detached: see yourself: Detached involves freeing from control, intellectual processing, and experiencing thoughts or beliefs as an observer without judgment.

Session 8: Final sessions: summarizing and answer the final questions of patients.

Note: it is worth mentioning at the end of session homework and how to use techniques were taught to the client

Control condition: The patients in the control group were referred to the dedicated clinic to MS patients once a week. They received medical treatment and counseling about the complications related to illness, as well as coping with these complications and socio-therapeutic factors. The social communication with the patient was regularly kept in this group and this situation allowed them to keep social contact.

Statistical analysis: A series of repeated measure ANOVAs test was used by considering Time (pre-test, post-test), Group (experimental, control), and some dependent variables such as WCST scores, including category, perseveration, conception responses, total correct number, number of errors, other errors, first trial category, PASAT2", PASAT3" and AT scores. In addition, ANOVA tests were used to assess the effect of time based on group interaction on therapeutic effects. Post hoc analysis was applied after Bonferroni- Holm correction. Statistical tests were performed using Greenhouse- Geisser corrected df (degrees of freedom). In the present study, df were notified with related Greenhouse- Geisser epsilon value. The level of significance was set at $\alpha < 0.05$. Cohen's d's effect sizes were reported for the baseline and study completion change in the experimental group, MDM baseline, and study completion change in the control group, along with the differences between experimental and control groups. Statistical analysis was performed with SPSS 21.4.

RESULTS

Result indicated that no significant difference was observed between the two groups (including experimental and control groups) in age, gender, education, duration of illness, MS type, EDSS, sub tests of WCST, PASAT2", PASAT3" and AT in the baseline of the study (Table 1).

Table.1: Demographic characteristic

Demographic characteristics	Experimental group (M±SD)	Control group	F or X2	p
Age	33.48±8.59	31.42±6.58	2.10	0.15
Gender (%)				
Male (n %)	33.3%	46.2%	X2=2.28	0.13
Female	66.7%	53.8%		
MS type (%)				
Relapsing remitting	55.6%	57.7%	X2= 0.92	0.33
Secondary progressive	44.4%	42.3%		
EDSS	2.92±0.74	2.00±0.63	0.23	0.62
Education	13.37±2.33	13.615±2.38	0.14	0.70
Duration of illness	5.22±2.57	5.11±2.99	0.11	0.74
WCST (category)	2.07±1.75	2.15±1.43	0.033	0.85
WCST (perseveration)	9.33±5.29	9.88±5.06	0.15	0.70
WCST (conception responses)	2.49±2.80	2.00±2.26	0.40	0.52
WCST (total correct number)	27.92±8.19	28.76±7.51	0.15	0.68
WCST (number of errors)	30.70±9.52	30.80±7.18	0.002	0.96
WCST (other errors)	21.48±5.50	20.23±4.23	0.84	0.36
WCST (first trial category)	25.71±22.19	18.88±14.97	1.61	0.20
PASAT2"	27.25±13.12	26.88±10.81	0.13	0.91
PASAT3"	32.88±11.18	31.80±11.18	0.12	0.72
HRSA	17.00±4.42	15.96±6.31	0.48	0.49
MS: multiple sclerosis EDSS: Expanded Disability Status Scale WCST: Wisconsin Card sorting Test PASAT: Paced Auditory Serial Addition Test HRSA Score: Hamilton Anxiety Rating Score				

The results of Table 3 show the mean and standard deviation of variables in baseline and at the end study (Table2).

Table.2: Descriptive analysis of executive functions components (WCST), PASAT2", PASAT3" and HRSA in two groups (experimental and control groups) at baseline and end study.

WCST: Wisconsin Card sorting Test	Groups			
	Baseline		End study	
	Mean (SD)		Mean (SD)	
	Experimental group	Control group	Experimental group	Control group
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
WCST (category)	2.07(1.75)	2.15(1.43)	4.18(2.05)	3.53(2.02)
WCST(perseveration)	9.33(5.29)	9.88(5.06)	3.22(2.65)	8(5.45)
WCST (conception responses)	2.44(2.80)	2(2.26)	4.81(2.09)	3.92(2.72)
WCST (total correct number)	27.92(8.19)	28.76(7.51)	37.88(7.97)	31.69(10.07)
WCST (number of errors)	30.70(9.52)	30.80(7.18)	17.85(7.50)	25.26(9.61)
WCST (other errors)	21.48(5.50)	20.23(4.23)	13.96(6.22)	16.61(6.12)
WCST (first trial category)	25.51(22.19)	18.88(14.91)	9.88(8.81)	13.84(14.27)
PASAT2"	27.92(8.19)	28.76(7.51)	37.88(7.97)	31.69(10.07)
PASAT 3"	32.88(11.18)	31.80(11.18)	44.11(10.10)	33.61(14.75)
HRSA	17.00(4.42)	15.96(6.31)	6.44(4.06)	13.00(5.83)

Table.3: Inferential statistical of the WCST components, PASAT2", PASAT3" and HRSA with the factors Time (baseline and end study), Group (experimental vs. control) and Time x Group interaction

Factors				
WCST: Wisconsin Card sorting Test	time	group	Time x group interaction	Greenhouse-Geisser epsilon
	F partial eta ²	F partial eta ²	F partial eta ²	
WCST (category)	33.81 ^{***} , 0.39	0.47, 0.009	1.33, 0.026	0.56
WCST(perseveration)	23.60 ^{***} , 0.31	8.85, ^{**} 0.14	6.74 ^{**} , 0.11	0.58
WCST (conception responses)	81.38 ^{***} , 0.38	1.65, 0.031	0.35, 0.007	0.50
WCST (total correct number)	14.35 ^{***} , 0.22	3.25, 0.06	4.32 [*] , 0.077	0.53
WCST (number of errors)	27.66 ^{***} , 0.35	4.27 [*] , 0.077	4.10 [*] , 0.075	0.54
WCST (other errors)	21.91 ^{***} , 0.30	0.39, 0.08	2.66, 0.50	0.59
WCST (first trial category)	10.43 ^{***} , 0.17	0.073, 0.01	3.78 [*] , 0.069	0.53
PASAT2"	11.75 ^{***} , 0.18	0.017 [*] , 0.10	7.96 ^{**} , 0.13	0.60
PASAT 3"	28.92 ^{***} , 0.36	4.77 [*] , 0.086	15.34 ^{***} , 0.23	0.53
HRSA	171.61 ^{***} , 0.77	9.36 ^{**} , 0.15	60.76 ^{***} , 0.54	0.52

Degree of freedom: Time: (1.51), Group (1.51) and Time x Group- interaction. ^{*}p < 0.05; ^{**}p < 0.01 ^{***}p < 0.001.

The effect of WCST components based on time and group: All WCST components, PASAT2", PASAT3" and AT improved over time. In addition, the perseveration and the number of errors related to WCST, PASAT2", PASAT3" and AT significantly improved in the patients recruited the treatment by mindfulness. The considerable time based on group interaction indicated that perseveration, total correct number, number of errors, the first trial category of WCST, PASAT2", PASAT3" and HRSA improve significantly (Table3). Regarding the

single effect size scores at the baseline, the mean difference was small between the experimental and control group, while it was medium in most subtests of WCST, PASAT2", PASAT3" and AT at the end of the study. Further, the mean difference from pre to post assessment in the experimental group was medium in subtests of WCST, PASAT2", PASAT3"and Large in HRSA while it was small from baseline and end study assessment in control group (Table4).

Table.4: Effect sizes for mean comparisons for pre-to post-test within the groups (experimental and control groups) and between group at baseline and end study

Effect sizes: Cohen's d's				
WCST: Wisconsin Card sorting Test	Baseline-end study: experimental group	Baseline-end study: control group	Baseline experimental group vs. control	End study experimental vs. control
	Cohen's d (effect size)	Cohen's d (effect size)	Cohen's d (effect size)	Cohen's d (effect size)
WCST (category)	1.10(0.48)[M]	0.87(0.36) [S]	0.05((0.02) [S]	0.31(0.15) [S]
WCST(perseveration)	1.46(0.58) [M]	0.35(0.17) [S]	0.10(0.05) [S]	1.11(0.48) [M]
WCST (conception responses)	0.95(0.43) [M]	0.76(0.5) [S]	0.17(0.086) [S]	0.36(0.18) [S]
WCST (total correct number)	1.23(0.52) [M]	0.32(0.16) [S]	0.10(0.05) [S]	0.69(0.32) [S]
WCST (number of errors)	1.49(0.59) [M]	0.65(0.31) [S]	0.01(0.005) [S]	0.85(0.39) [M]
WCST (other errors)	1.28(0.53) [M]	0.68(0.32) [S]	0.25(0.12) [S]	0.42(0.20) [S]
WCST (first trial category)	0.92(0.42) [M]	0.34(0.17) [S]	0.35(0.17) [S]	0.36(0.18) [S]
PASAT2"	1.05(0.46) [M]	0.13(0.06) [S]	0.096(0.048) [S]	0.83(0.38) [S]
PASAT 3"	1.05(0.46) [M]	0.13(0.06) [S]	0.096(0.048) [S]	0.83(0.38) [S]
HRSA	2.48(0.77) [L]	0.48(0.23) [S]	0.19(0.095) [S]	1.30(0.54) [M]

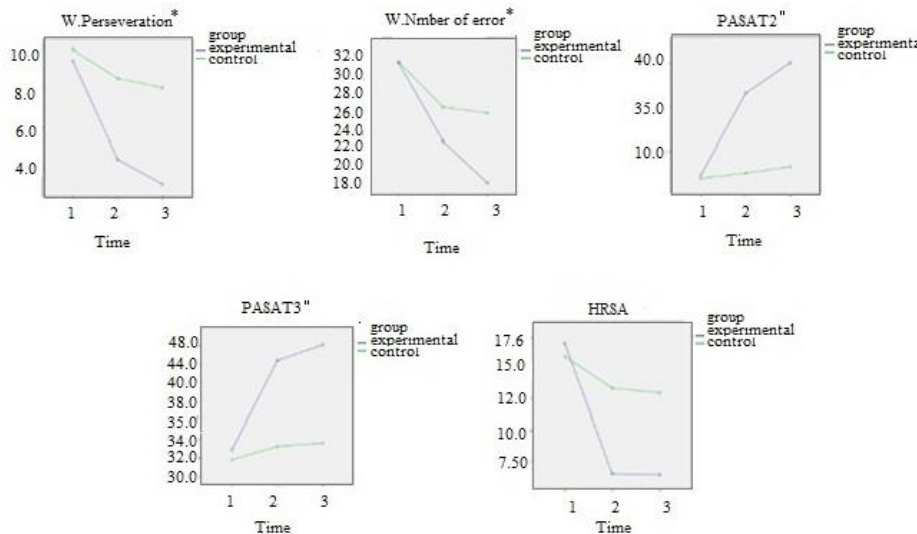


Figure2. Perseverative errors, number of error, PASAT2", PASAT3" and HRSA decreased significantly over time in the experimental group (Figure2).

DISCUSSION

In the present study, adjuvant treatment based on the metacognitive model of detached mindfulness was implemented on executive functions in MS patients. The structure manual of protocol was described fully by Wells[9]. In addition, Wisconsin Card Sorting Test (WCST) and PASAT tests was used to evaluate the executive function components among the patients[36, 41].

Based on the results, DM treatment affects the perseverative errors, number of errors, PASAT2",

PASAT3" and HRSA in the experimental group, compared to the control group (Table 3). Perseveration was considered as one of the most important components of executive function in WCST test. In this regard, MS patients made more perseverative errors and responses on the WCST significantly[42], and PASAT is one of most commonly used tests to evaluate the cognitive impairment in these patients [43]. In order to justify the findings, we can point out that Mindfulness-Based Interventions (MBIs) may cause changes in the brain that are important for emotional

self-regulation. It might be also associated with the raised cognitive reserve or recovering cognitive functions in MS patients [44]. Mindfulness techniques decreased anxiety and exhausting in patients with MS. Anxiety and exhausting are important components affecting information processing. [21]. Mindfulness can modulate mental state such as creating a balance between mental rest and fatigue [21]. Previous studies have shown that the capability to self-modulate emotions is the most important component to increase cognitive function [45]. As described before that cognitive slowing related to anxiety[6] and MBI has been shown to positively influence on anxiety in MS patients[46]. The finding of this study showed an improvement in the detached mindfulness on anxiety symptoms. This finding is consistent with the results of a previous study applied detached mindfulness for treating depression and anxiety [32].

This finding may be due to the target of detached mindfulness techniques which can upturn the attention and decrease "closed" self-centered functions[47] such as perseveration in this study. As it was already mentioned, the self-regulatory executive performance model is considered as one of the most important and effective models for explaining mental disorders during recent years[8]. In this model, all psychiatric disorders can be related to an ineffective model of cognitive activity called "cognitive attentional syndrome (CAS)". This syndrome is a pattern of strategic processing activity which is triggered by metacognitive knowledge stored in long-term memory[8], CAS plays a role in locking individual into long or repetitive troubles in thinking such as perseveration (important component of executive function in WCST), leading to incompatible behaviors[9]. According to the protocol developed by Wells, detached mindfulness improves the ineffective form of cognitive function (CAS) [9]. DM can improve a greater flexible control over the choice of various thinking and behavioral strategies, as well as the application of DM powered new plans for regulating cognitive activity, and can free-up resources for disconfirmatory functioning and repair of beliefs[10]. DM is alternative to the CAS and provides strategy to disengage or prevent full activation of the CAS in reaction to triggers [10]. This modification of processing improves thinking related to mental disorder such as anxiety, thus modifies emotion regulating and improve cognition engagement in executive function (planning, shifting and attentional syndrome).

Consistent with Wells and Matthews, "Patients should be encouraged to develop a higher metacognitive awareness and learn to process information in order not to trigger thorough self-regulatory executive function (S-REF) activity, which may be obtained by training self-observation and attentional control (PASAT), leading to the promotion of detached mindfulness". In the present study, Attention program task (APT) could support this objective[9]. The APT was first developed by Wells (2011) to decrease self-focus and upturn attentional and metacognitive control. However, it can disrupt the activation of specific styles and dimensions of thinking related to special disorders and facilitate the improvement of new knowledge for controlling processing [9]. The findings of the present study were consistent with those of other studies related to

mindfulness for different aspects of attention and executive functions, in which training mindfulness can improve unfocused, sustained, and especially selective attention[20]. Some executive functions like perseveration, appeared to be better among the people after training mindfulness or with higher levels of mindfulness disposition[20]. Further, the result was in line with those in another study aimed to compare the neuropsychological functioning related to executive function and attention in outpatients with depression following treatment metacognitive therapy or cognitive-behavior therapy. Based on the results, a significant improvement occurred in executive function among the participants in metacognitive group [12].

Furthermore, an improvement was reported in all components of WCSS for the experimental group regarding the effect sizes, compared to the control group (Table 4). The findings are congruent with those of previous studies [12, 15, 45]. Additionally, the results could expand our knowledge due to the improvements observed among MS with degenerative impairment. The findings are important, in spite of medium effect size, because they can motivate most psychologists and mental health groups to use this kind of treatment for this group of patients.

Despite the intriguing finding, the results of the present study cannot be generalized in all contexts due to some limitations. First, the sample size was small and the findings cannot be generalized to older adults, although they indicated acceptable effects on executive function. In addition, the review of Jankowski et al., (2014) reported that mindfulness can increase the level of executive function, although further studies should be conducted for more clarification [48], and other limitation of this study was that due to the fatigue of these patients we could not apply more tests, although we used two important and useful tests to measure neuropsychological functions and a psychological test (anxiety) in these patients.

In conclusion, the present study pioneered to evaluate the effect of adjuvant treatment based on the metacognitive model of detached mindfulness on executive function, though further research is needed to support the findings such as the evaluation of all subtypes of MS or other chronic disease like Alzheimer, and Parkinson disease in which executive function is impaired

CONCLUSION

Adjuvant metacognitive model of detached mindfulness improved executive function component (perseveration, attention) and anxiety in MS patients. Beneficial effects were observed in intervention completion, suggesting, therefore, that non-pharmacological treatment can be applied besides the pharmacological treatment in these patients.

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Ethical Approval: All procedures performed in the study were accordance with the 1964 Helsinki declaration and approved by Ethics Committee of Hamadan University of Medical Sciences with the number: IR.UMSHA.REC.1395.382.

Informed Consent: Informed consent was obtained from all outpatients participate in the study.

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