ORIGINAL ARTICLE

Effectiveness of detached mindfulness intervention on cognitive functions in multiple sclerosis patients, results from a randomized controlled study

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ABSTRACT

Background: The experience of cognitive deficit is prevalent in people with Multiple sclerosis (MS).
Objective: The present study aimed to evaluate the impact of the adjuvant metacognitive model of detached mindfulness (MDM) treatment on cognitive function in MS patients.
Methods: in this study, twenty-seven patients with multiple sclerosis were recruited to the mindfulness training group and twenty-six in the common treatment group. In the current study, the intervention was done in MDM group in eight weeks. Standard treatment for all patients consisted Interferon beta (IFNβ). Treatment consists of MDM conducted in weekly group meeting. Patients in the common treatment group received medical treatment and socio-therapeutic intervention. At the baseline and after intervention, patients completed the attention test, Visual-spatial memory test, working memory and anxiety test.
Results: Upon study completion scores of working memory, information processing on WAIS-R (Digit span), PASAT 3" and scores of Anxiety Test (AT) significantly increased in the MDM compared with those for the common treatment group ($p<0.05$) and There was no significant improvement on visual memory (RCFT) and information processing in sub tests of WAIS-R (Symbol Coding).
Conclusion: This study proves initial evidence that adjuvant detached mindfulness intervention improves cognitive function in the domain of working memory, information processing and attention in PASAT, sub tests of WAIS-R and Anxiety Test (AT) in the MS patients.
Key words: detached mindfulness; cognitive function; multiple sclerosis; randomized controlled study.

BACKGROUND

Cognitive deficit has been detected in all sub types of multiple sclerosis [1-4], and it is estimated that 40% to 65% of cognitive- decreasing-inflicted patients suffer some degree of cognitive difficulties [5-7] of which working memory, attention, visual memory and information processing speed are the most involved [1]. In addition, cognitive decreasing is related to motor task and anxiety in patients with multiple sclerosis [4, 8].

Pharmacologic and non-pharmacologic interventions may improve cognitive deficits in these patients [9]. Interferon beta (IFNβ), IFNβ can have an effect on cognition [10-13]. In recent years non-pharmacological studies have indicated that metacognitive strategies are applied for cognitive improvements [14-18]. And a limited amount of research has found that mindfulness practice improves cognitive functions [19-21]. A review of the results from studies relating to mindfulness and information processing proves that cognitive processes are involved in mindfulness [22].

Mindfulness is the understanding of what is happening within us as well as in the environment around us at the present time and without any judgment. Mindfulness is a tool that helps us manage our thoughts and feelings[22]. The contemplation that man makes on his mental processes, and the thinking about thinking, is called metacognition and neuropsychological experiment has shown that the neo-cortex plays an essential role in the higher processes of the mind[22]. The neo-cortex is thought to play a key role in cognitive control mechanisms [23]. The neo-cortex is part of the brain connects to cognitive function [24], as well as neo-cortex plays a crucial role in working memory[25, 26] and information processing[27].

Jankowski et al. (2014) constructed the concept of mindfulness within a meta-cognitive framework [22]. The neo-cortex has been shown to be associated with metacognition[22]. There is found literature demonstrating the impact of mindfulness techniques on neo-cortex[28]. In psychopathology of mental disorders such as anxiety and depression, excellent processes of the mind (memory and attention) play an important role[29]. Mindfulness training enhances working memory capacity, attention and information processing [15, 30, 31].

There have been several pathways leading to clinical implementations of mindfulness practices. In recent years, psychologists have been implementing metacognitive therapy-based detached mindfulness (MDM) in order to treat the psychiatric disorder such as depression and anxiety [32-35].

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 [36]. 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 [36].

OBJECTIVES

Although the effectiveness of MDM has been confirmed in the previous research on depression and anxiety, its effectiveness on cognitive functions such as working memory, visual memory, attention and information processing speed has not been investigated. In this study, our aim was to investigate to the effect of detached mindfulness via an applied metacognitive model of detached mindfulness (MDM) training as an adjuvant pharmacological therapy on cognitive functions in multiple sclerosis 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 multiple sclerosis (ICD 10: G35) with information processing dysfunction were selected based on the Paced Auditory Serial Addition Test (PASAT). the age range of patient was between 18- 45 with EDSS (Expanded Disability Status Scale) ≤ 4, had no history of mental (psychosis) and physical disorders and clinically were not depressed, had diploma or higher education and had no absence for more than two sessions. The samples included 53 patients, of whom 27 were randomly selected as the experimental group and 26 were related to the control group. Treatment was conducted in group sessions once a week. Group size varied from 5 to 7 participants. Before treatment sessions started, a neuropsychological test was performed by a trained psychologist. The experimental group was treated with a group therapy based on the metacognitive model of detached mindfulness during the eight-week sessions (each lasting one hour), and neuropsychological tests were performed by a psychologist after 8 sessions and the two-month follow- up. 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. The follow-up session was held after two months in the same place and conditions.

Instruments of the study

Wechsler Adult Intelligence Scale Revised(WAIS-R): Digit Span and coding of this tests were apply to assessment of working memory and cognitive processing [37]. Reliability of this test, is 0.90 [37].

Paced Auditory Serial Addition Test (PASAT): This test is apply to assessment of information processing and attention [38]. Reliability of this test is 0.90, and the calculated Cronbach's alpha is 0.74 [37].

Rey Complex Figure Test (RCFT): This test is composed of copy trials, immediate and delayed recall, as well as recognition. This test used to assess visual memory. The validity of this test was 0.50 and test-retest reliability of this test has been reported to be about 0/90 [39].

Anxiety Test (AT): The Hamilton anxiety scale 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.

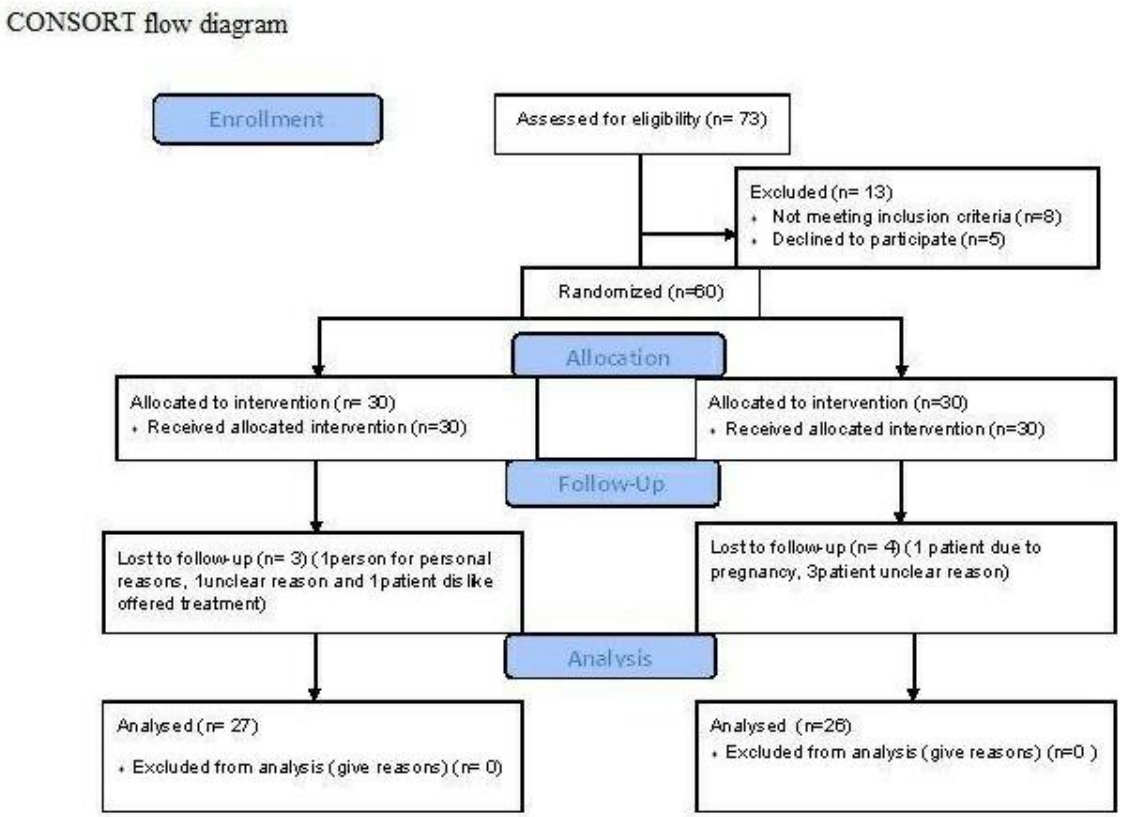

Figure1.CONSORT flow diagram, 73 MS patients were initially analyzed. 13 patients were excluded from the study due to lack of eligibility criteria. 60 patients (30 treatments and 30 controls) were randomly assigned to the groups and finally 27 patients in the treatment group and 26 patients in the control group were analyzed.

Treatment

Pharmacological treatment

All patients received IFNβ1a (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 [41]. In this study, detached attention, awareness techniques were used for reinforcing scheduled cognitive control 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. Table 1 indicates a summary of the contents for all sessions and thoroughly described by Wells in 2011[41].

Except for the first and final sessions, other sessions were the same as other techniques of detached attention awareness techniques

Table1. Content of the sessions of metacognitive model of detached mindfulness (detached attention awareness techniques) therapy

session	Content of session
1.	Introducing members, goal of sessions, explanation intervention plan, metacognitive based on detached mindfulness therapy, Brochure and homework practices
2.	Review homework of prior session, Attention program task(APT), explaining the logic of APT and its application, Brochure and homework practices
3.	Discussion of homework of prior session, training of metacognitive guidance and association techniques of detached attention, awareness and its application, Brochure and homework practices
4.	Discussion of homework of prior session, training of suppression of anti- repression and unruly child management techniques of detached attention awareness and its application, Brochure and homework practices
5.	Discussion of homework of prior session, training of the train station and imagery of passing clouds techniques of detached attention, awareness and its application, Brochure and homework practices
6.	Discussion of homework of prior session, training of verbal loop and detached: see yourself technique of detached attention, awareness and its application, brochure and homework practices
7.	Discussion of homework prior to session, training of imagination and looking at the thoughts using techniques of detached attention and awareness, Brochure and homework practices.
8.	Discussion of homework of prior session, summarizing and answer the final questions of patients

Control condition: The patients in the control condition referred to the outpatient clinic for multiple sclerosis 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 information processing and working memory test, visual-spatial memory test, attention and information processing and Anxiety Test. 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 by applying 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 demonstrated 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.

RESULTS

Results of table 2 indicate that experimental and control group statistically not different in age, genus, education, duration of illness, MS type, EDSS, sub tests of WAIS-R, RCFT, PASAT and AT test in a baseline of the study.

Table.2. Demographic characteristic in baseline

Demographic characteristics	MDM treatment (M±SD)	Common treatment	F or X^2	p
Age	33.48±8.59	31.42±6.58	2.10	0.15
Genus (%)				
Male (n%)	33.3%	46.2%	X^2=2.28	0.13
Female	66.7%	53.8%		
MS type (%)				
Relapsing remitting	55.6%	57.7%	X^2= 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
WAIS-R(Symbol coding)	44.03±7.77	45.03±10.03	0.16	0.68
WAIS-R (Digit span)	5.66±1.46	5.50±1.42	0.17	0.67
PASAT 3"	32.88±11.18	31.80±11.18	0.12	0.72
RCFT(copy)	35.85(0.53)	35.92(0.27)	0.92	0.35
RCFT(recall)	17.66(5.15)	19.26(5.11)	1.83	0.18
(AT)	17.00±4.42	15.96±6.31	0.48	0.49

MS: multiple sclerosis
EDSS: Expanded Disability Status Scale
WAIS-R: Wechsler Adult Intelligence Scale Revised
PASAT: Paced Auditory Serial Addition Test
Rey Complex Figure Test(RCFT)
Anxiety Test (AT)

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

Table.3. Descriptive analysis of working memory, information processing, attention, visual memory and anxiety in two groups (experimental and control groups) at baseline and end study

WAIS-R, PASAT, RCFT and AT	Groups			
	Baseline		End study	
	Mean (SD)		Mean (SD)	
	MDM treatment	Common treatment	MDM treatment	Common treatment
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
WAIS-R(Symbol coding)	44.03(7.77)	45.03(10.03)	50.40(9.26)	45.88(10.58)
WAIS-R (Digit span)	5.66(1.46)	5.50(1.42)	6.74(1.53)	5.38(1.20)
PASAT 3"	32.88(11.18)	31.80(11.18)	44.11(10.10)	33.61(14.75)
RCFT(copy)	35.85(0.53)	35.92(0.27)	36.00(0.00)	36.00(0.00)
RCFT(recall)	17.66(5.15)	19.26(5.11)	24.77(5.29)	22.80(3.28)
(AT)	17.00(4.42)	15.96(6.31)	6.44(4.06)	13.00(5.83)

All WAIS-R sub tests, PASAT 3", RCFT and AT improved over time. In addition, the WAIS-R (Digit span), PASAT3" and AT significantly improved in MDM treatment, and there is no improvement in RCFT and WAIS-R (Symbol coding) in MDM treatment compared to the common treatment group. The considerable time based on group interaction indicated that WAIS-R (Symbol coding), WAIS-R (Digit span), RCFT (recall) and PASAT 3"could improve significantly.

Table.4. RCFT, WAIS-R sub tests PASAT 3" and AT over Time between and within groups.

Factors				
WAIS-R, PASAT, RCFT and AT	**Tim**	**Group**	**Time × Group interaction**	
	F partial eta²	**F partial eta²**	**F partial eta²**	**Greenhouse-Geisser epsilon**
WAIS-R(Symbol coding)	21.02*** ,0.29	0.68, 0.013	12.24***, 0.19	0.63
WAIS-R(Digit span)	12.90***, 0.20	4.955**, 0.089	12.04***, 0.19	0.71
PASAT 3"	28.92***, 0.36	4.77**, 0.086	15.34***, 0.23	0.53
RCFT(copy)	3.69**,068	0.37, 007	0.37, 007	0.50
RCFT(recall)	67.88***, 0.57	00.0, 0,00	7.92, **0.13	0.58
(AT)	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 × Group- interaction.*$p < 0.05$; **$p < 0.01$*** $p < 0.001$.

Regarding the single effect size scores at the baseline, the mean difference was small between the MDM treatment and common treatment, while it was medium in most of the subtests at the end of the study. Further, the mean difference from Baseline to end study assessment in the MDM treatment was medium while it was small from Baseline to end study assessment in the common treatment.

Table.5. Baseline and end study effect sizes

Effect sizes: Cohen's d's				
WAIS-R, PASAT, RCFT and AT	**Baseline-end study: MDM treatment**	**Baseline-end study: common treatment**	**Baseline MDM vs. common**	**End study MDM vs. common**
	Cohen's d (effect size)	**Cohen's d (effect size)**	**Cohen's d (effect size)**	**Cohen's d (effect size)**
WAIS-R(Symbol coding)	0.74(0.34)[M]	0.082(0.041) [M]	0.11((0.05) [S]	0.45(0.22) [S]
WAIS-R (Digit span)	0.72(0.33))[M]	0.091(0.045) [S]	0.11(0.055) [S]	0.98(0.44) [M]
PASAT 3"	1.05(0.46))[M]	0.13(0.06) [S]	0.096(0.048) [S]	0.83(0.38) [M]
RCFT(copy)	0.40(0.19) [S]	0.41(0.20) [S]	0.16(0.08) [S]	Non
RCFT(recall)	1.36(0.56) [M]	0,73[M]	0.31(0.15) [S]	0.40(0.19) [S]
(AT)	2.48(0.77) [L]	0.48(0.23) [S]	0.19(0.095)) [S]	1.30(0.54) [M]

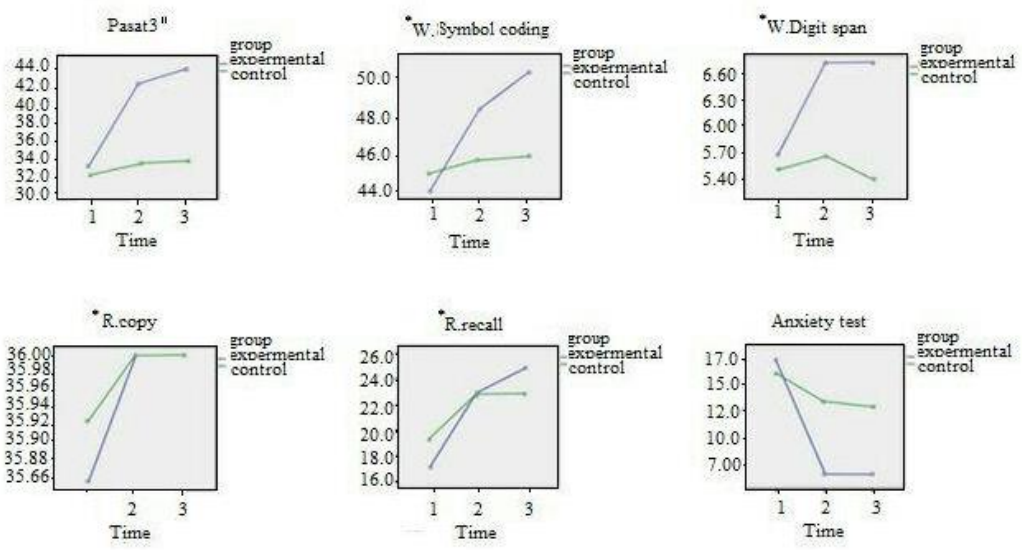

Figure 2. PASAT3", WAIS (digit span), WAIS (Symbol coding), RCFT (Recall), and AT decreased significantly over time in the MDM treatment (Figure2).

DISCUSSION

In the present study, adjuvant treatment based on the metacognitive model of detached mindfulness(MDM) was implemented on information processing, attention, working memory, visual memory and anxiety in multiple sclerosis patients. The structure manual of protocol was fully described by Wells [41]. In addition, (PASAT), (WAIS-R) test and (RCFT) were used to studies for evaluating of cognitive functions in these patients[9].

Based on the results, MDM treatment could influence the working memory, attention, information processing and anxiety on WAIS-R (Digit span), PASAT 3" and AT in the MDM treatment group, compared to the common treatment group (Table 4). Results from the Roberg et al, (2012) study showed that memory is impaired by anxiety and psychosis, and that information processing speed is slowed down by anxiety.[4] and we can point out that Mindfulness-Based Interventions (MBIs) may cause changes in the brain that self-regulate emotions and that might be linked to raised cognitive reserve or recover cognitive function in MS patients [42]. Mindfulness techniques decreased anxiety and exhausting in patients with MS. Anxiety and exhausting are important components affecting information processing.[19]. Mindfulness can modulate mental state such as creating a balance between mental rest and fatigue [19]. Previous studies have shown that the capability to self-modulate emotions is the most important component to increase cognitive function[43]. As described before that cognitive slowing related to anxiety[8] and MBI has been shown to positively influence on anxiety in MS patients[44] another finding of this study was to improve the detached mindfulness on anxiety symptoms. This finding is in line with the study applied detached mindfulness to treat 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[45] such as attention in this study. Self-regulatory executive performance model is considered as one of the most important and effective models for explaining mental disorders during recent years[46]. In this model, all mental disorders can be related to an ineffective model of cognitive activity called “cognitive attentional syndrome (CAS)”. This syndrome is a type of defective mental activity that occurs with metacognitive information that is in long-term memory.[46], CAS plays a role in locking people into prolonged or repetitive disturbances in thinking, leading to inconsistent behaviors[41]. According to Wells, the metacognitive-based detached mindfulness is regarded as the opposite and incompatible point of CAS[41]. Consistent with Wells and Matthews, "Patients need to learn to have better metacognitive processing and information processing and learn to process information in order not to trigger thorough self-regulatory executive function, which possible this problem is solved by training self-monitoring and control of attention, leading to the promotion of detached mindfulness". In the present study, Attention Program Trask (APT) could support this objective[41]. Wells (2011) developed APT to decrease self-focus and upturn attentional and metacognitive control. However, it can disrupts ways of thinking about specific disorders and improves control of cognitive function[41]. The findings of the present study were consistent with those of other studies related to mindfulness for different aspects of attention and working memory, in which training mindfulness can improve working memory, unfocused, sustained, and especially selective attention[30]. Further, the result was in line with those in another study aimed to compare the neuropsychological functioning related to working memory, information processing and attention in outpatient with depression following treatment metacognitive therapy or cognitive-behavior therapy. Based on the results, a significant improvement occurred in cognitive function among the participants in metacognitive group [15].

Another finding was that there was no significant improvement in WAIS-R (Symbol coding) and Rey Complex Figure Test (RCFT) in the MDM treatment group in comparison to the common treatment group. To explanation of this finding can point to that the multifaceted nature of Digit Symbol—Coding and Rey Complex Figure Test (RCFT) first is its strength and its most important weakness, because for good cognitive function we need multiple abilities, and this test is designed to measure psychological neurological dysfunction. Disruption in each of the multiple abilities will result in a low score.[47], motor task disability in this patient is prevalent and multiple sclerosis patient in motor performance perform slower than the healthy people and perceived cognitive deficit was linked to efficiency on motor activities [4, 48], the multifaceted performance (such as hand coordination and speed) is need to perform these test in versus the other neuropsychological test was used in this study can be one of the reason of this finding.

Furthermore, an improvement was reported in most components of cognition for the MDM treatment group regarding the effect sizes, compared to the common treatment group (Table 5). The findings are congruent with those of previous studies [15, 30, 31]. Additionally, the results could expand our knowledge due to the improvements observed among multiple sclerosis 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 cognitive function (working memory, information processing and attention) further studies should be conducted for more clarification.

In conclusion, the present study pioneered to evaluate the effect of adjuvant treatment based on the metacognitive model of detached mindfulness on cognitive function (working memory, visual memory,

information processing and attention), though further research is needed to support the findings such as the evaluation of all subtypes of multiple sclerosis or other chronic disease like Alzheimer, and Parkinson disease in which cognitive function is impaired

CONCLUSION

Adjuvant metacognitive model of detached mindfulness improved cognitive function (working memory, attention and information processing) in multiple sclerosis 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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Conflict of Interest: All authors declare that have no conflict of interest.

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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