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Effectiveness of Unified Transdiagnostic Protocol in psychosomatic symptoms in patients with Multiple Sclerosis: A randomized controlled trial

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ABSTRACT

Introduction: Psychologically-driven manifestations, including psychosomatic symptoms, are common in MS patients. Aims: The present study aimed to examine and develop the efficacy of the Unified Transdiagnostic Protocol (UTP) in psychologically driven and, more specifically, the psychosomatic symptoms of MS patients. Methods: The present randomized clinical trial was conducted at the Brain and Neurology Clinic of Mohebe Mehr Hospital, Tehran, Iran, in 2022. In total, 43 MS patients were entered into the study and randomly assigned to two groups: intervention (n=21) and control (n=22). We implemented UTP in 12 weekly online sessions (each session took 60 minutes). Fatigue Severity Scale (FSS), Pittsburgh Sleep Quality Index (PSQI), and Larson Sexual Satisfaction Questionnaire (LSSQ) were used to assess psychosomatic symptoms. Results: Based on multivariate tests, there was a significant difference between different stages of the study, as well as the interaction effect between groups in terms of fatigue, desire to have sex, sexual attitude, sex life quality, sexual compatibility, and sleep quality (P<0.001). Moreover, there was a considerable difference in the changes in psychological symptom scores in UTP groups compared to control groups during the measurement stages (P<0.001). The stability of the treatment effects has been confirmed over time (P<0.001). Conclusion: As evidenced by the obtained results, UTP had stable effects on the treatment of psychosomatic symptoms. These include fatigue, desire to have sex, sexual attitude, sex life quality, sexual compatibility, and sleep quality, in MS patients.

Keywords: Cognitive Behavioral Therapy Multiple Sclerosis, Psychosomatic, Unified Transdiagnostic Protocol Symptoms

1. INTRODUCTION

Multiple sclerosis (MS) is defined as a chronic, progressive, neurodegenerative disorder of the central nervous system (Feinstein et al., 2019). Due to the physiopathology and unpredictable course of MS, psychological disorders are also among the typical characteristics of the disease (Henry et al., 2019). The likelihood of experiencing the symptoms of psychological disorders in MS patients is higher than that in healthy people and those with other chronic conditions (Grech et al., 2019). Maladaptive coping strategies and emotional dysregulation among MS patients are the strongest and most accurate predictors of suicidal ideation, as much as 85% (Feinstein and Pavisian, 2017).

In addition, comorbidities have an excess adverse effect on the patient's mental health and are associated with an elevated risk of debilitating consequences, elevating the disease burden. For instance, risky behaviors in MS patients might expose them to various troublesome environmental agents (Hawkes and Boniface, 2014). Despite the high frequency of emotional disorders, comorbidities, and mental disorders in MS cases, these conditions are often overlooked, underdiagnosed, and undertreated (Skokou et al., 2012). Psychologically-driven manifestations, including psychosomatic symptoms, are common in MS patients and can lead to mental non-functionality over time (Nazari et al., 2020). MS patients have higher rates of psychologically-driven issues, resulting in numerous somatic complaints (i.e., sexual dysfunction, sexual dissatisfaction, sleep disorders, and fatigue) (Houtchens and Sadovnick, 2017; Nazari, 2020).

There could be multiple reasons behind this underdiagnosed condition. First of all, in the neurologic context, the evidence demonstrated that there are shortcomings concerning the application of DSM criteria (Strober and Arnett, 2015). The diverse complexity of the MS illness, as well as the possibility of mistaking specific physical complaints of MS, such as fatigue, sleep disorders, and sexual dissatisfaction, for depressive symptoms, might contribute to exaggerated underdiagnosis rates. Secondly, according to primary and secondary diagnoses, disorder-specific treatments are successful in complicated cases (Newby et al., 2015). Furthermore, when the clinical reality is intricately complex, and comorbidities are the norm, as is the case for a chronic somatic condition (e.g., MS), disorder-specific therapeutic measures might be hardly justifiable (Holmes et al., 2020). There are no established efficacious therapeutics for psychologically-driven problems in somatic diseases such as MS (Simpson et al., 2017).

Recent studies have indicated that Cognitive Behavioral Therapy (CBT) has been less effective than other psychological therapeutic approaches in the treatment of MS patients (Sesel et al., 2018). Integrated and transdiagnostic treatments have emerged as suggested ways for the treatment of a variety of coinciding psychosomatic issues since they guide a more efficient pathway in dealing with comorbidities (Clark et al., 2017; Norton and Paulus, 2016). The Unified Transdiagnostic Protocol (UTP) is a CBT transdiagnostic skill-based emotion-focused treatment (Barlow et al., 2017; Barlow et al., 2017b). The UTP has been detailed for the treatment of various psychologically driven symptoms, in which emotion dysregulation is the key component (Barlow et al., 2017). The results of many studies have confirmed the efficacy of UTP in the improvement of psychosomatic manifestations (i.e., sleep quality, sexual satisfaction, and fatigue) (Bullis et al., 2015). For psychosomatic symptoms, neuroticism has been a critical etiologic mechanism held in common by all emotional disorders (Brown and Barlow, 2009).

The UTP is deemed to be a gold-standard disorder-specific treatment approach for patients with comorbid emotional disorders (Barlow et al., 2017). The UTP, as a skill-based, emotion-focused interventional approach, could be of undeniable assistance given the high prevalence of psychologically-driven symptoms, increased comorbidities, recurring emotional problems, and the increased prevalence of risky behaviors in MS patients (Hawkes and Boniface, 2014). However, there is not enough practice-based data on the efficacy of UTP in the course of MS. Therefore, the present study aimed to examine and develop the efficacy of UTP in psychologically driven and, more specifically, the psychosomatic symptoms (fatigue, sleep disturbances, and sexual dysfunction) of MS patients.

2. METHOD

We conducted this randomized clinical trial on MS patients who were referred to the brain and neurology clinic of Imam Khomeini Hospital, Tehran, Iran, in 2022.

Inclusion and Exclusion Criteria

The inclusion criteria included a neurologist-confirmed diagnosis of the relapsing-remitting course of MS, an age range of at least 20 years, having a sexual relationship, proficiency in Persian language, stability in the type and dosage of the used medication three months before the commencement of the intervention, and participation in weekly appointments. On the other hand, the exclusion criteria entailed having severe psychiatric disorders (e.g., psychosis, bipolar disorder, substance abuse, severe depression or

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anxiety, serious suicidal thoughts requiring the use of psychiatric medications), having a concurrent severe or chronic physical illness, changing the type or dosage of drugs during the treatment period, receiving concurrent psychological treatments, changing the physical or mental conditions disturbing the therapy, a history of epilepsy or developmental disorder, a history of undergoing psychological treatments, changing the marital or sexual activity status, failure to participate in more than two treatment sessions, and unwillingness to continue treatment.

Study Design, Participants, and Data

A total of 43 patients with MS, who fulfilled the inclusion criteria and whose diagnosis was confirmed by a neurologist, were selected by targeted sampling method from all the MS patients referring to the brain and neurology clinic. A CONSORT 2010 Flow Diagram presents the sampling process (Figure 1). We gathered the participants' data, including baseline demographics, as well as all the data extracted from questionnaires regarding their psychosomatic symptoms (i.e., fatigue, sexual satisfaction, and sleep quality). Sexual satisfaction was further described by its components (desire to have sex, sexual attitude, sex life quality, and sexual compatibility).

The participants were assigned to two groups using a random allocation technique. In each stage - including the evaluation of the entry criteria and registration of participants, random allocation, and statistical data analysis - to avoid bias and administer blinding as much as possible, a different research assistant was asked for help. The groups remained unaware of each other's existence. The Unified Transdiagnostic Treatment protocol was then implemented in the intervention group for 12 60-minute weekly sessions. Both groups completed a set of questionnaires for post-test evaluation and follow-up at the end of the treatment period, as well as one and three months after that. The participants had a very high degree of adherence, the protocol was well tolerated, and patients in the UTP group completed the treatment sessions and all post-treatment measures.

Definitions

Unified Transdiagnostic Protocol is a cognitive-behavioral therapy with an emphasis on emotional regulation. The treatment protocol includes eight main sections that target critical aspects of the processing and regulating emotional experiences: 1. Increasing motivation to participate in treatment, 2. Psychological training and tracking of emotional experiences, 3. Training awareness of emotion, 4. Cognitive evaluation, 5. Avoiding destructive emotions and behaviors arising from them, 6. Awareness of bodily sensations and tolerance of them, 7. Facing internal and external emotional triggers, 8. Preventing recurrence (Barlow et al., 2017).

Fatigue (or lethargy) refers to a state of weakening or depletion of one's physical and/or mental resources, including a range of numbness caused by the over-activity of the muscles (Association, 1995). Sleep quality could be described by a wide spectrum of sleep-related measures, such as general sleep deficiency, delay in falling asleep, duration of decent sleep, sleep sufficiency, sleep disorders, the need for taking sleeping pills, feeling rested after sleep, and the morning performance after night sleep (Buysse et al., 1989). Sexual satisfaction could be defined by a variety of measures, including the desire for sexual relations, sexual attitude, quality of sex life, and sexual compatibility (Larson et al., 1998).

Data Collection Tools

Structured Clinical Interview for DSM-5 Disorders (SCID-5-CV)

DSM-5, is the most structured diagnostic tool used for the assessment of disorders. The evaluation of the validity and reliability of the clinical version of this tool showed that the percentage of favorable agreement between interview and clinical diagnosis was between 0.73 and 0.97, diagnostic sensitivity was 0.70, the rate of agreement between evaluators was above 0.75, and the Kappa level was 0.70 for most diagnoses (Osório et al., 2019). In a study conducted by the internal consistency, test-retest reliability, and the Kappa coefficient were 0.95-0.99, 0.60-0.79, and 0.57-0.72 for this instrument, respectively (Mohammadkhani et al., 2020). In the present study, this tool was used to evaluate the disorders mentioned in the exclusion criteria.



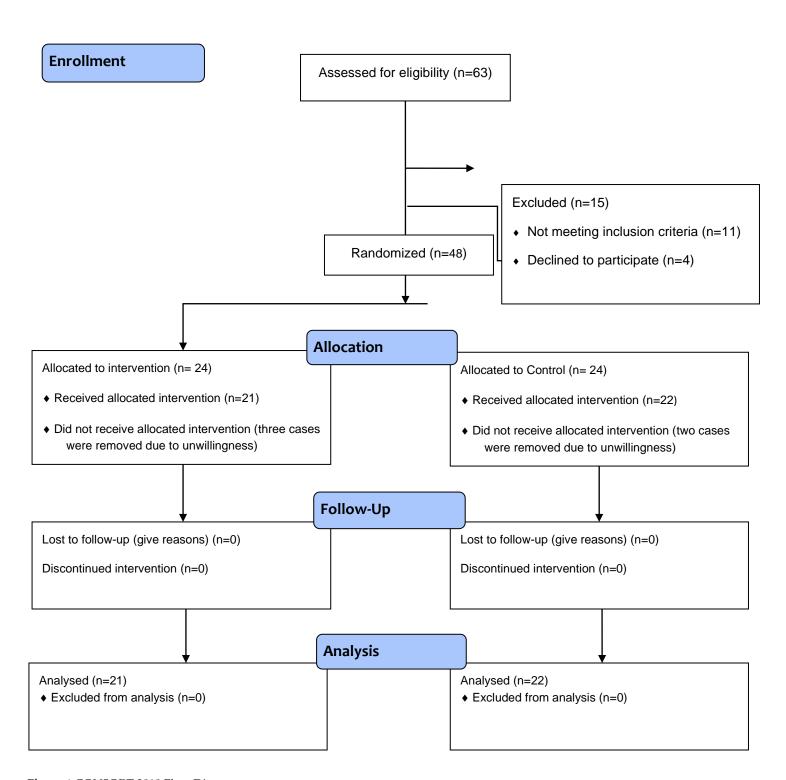


Figure 1 CONSORT 2010 Flow Diagram

Fatigue Severity Scale (FSS)

The FSS is a 9-item scale to measure fatigue severity in people with MS and lupus. It is the shortened form of the original 28-item fatigue intensity scale, which is graded from 1 (completely disagree) to 7 (completely agree), on a Likert scale. The scores of 9-18, 18-45, and >45 indicate low, moderate, and high fatigue levels, respectively. The designers confirmed the test-retest reliability and construct validity of the seven components: Scale, and Cronbach's alpha was reported to be 0.81 for MS patients (Krupp et al., 1989). In reviewing the Persian version of this scale, confirmed its internal consistency and reported a Cronbach's alpha coefficient of 0.96, which is very satisfactory (A'zimian et al., 2013). Salehpour et al., (2013) examined and confirmed the internal consistency, reliability, construct validity, as well as concurrent and predictive validity of this scale. The investigation of the predictive validity of this scale using multivariate regression showed that the scores obtained in this scale could predict the level of depression, anxiety, physical function, physical pain, and general health of patients (Salehpour et al., 2013).

Pittsburgh Sleep Quality Index (PSQI)

This index evaluates the subject's sleep quality over the past month according to seven components, including subjective sleep quality (the individual's experience of sleep quality), sleep latency (delay in falling asleep), sleep duration; getting enough sleep, sleep disturbances (night awakenings), the amount of sleep medication consumption, and finally, morning performance (problems caused by poor sleep during the day). The scoring of this index is from 0 (no problem) to 3 (severe problem) on a Likert scale. The minimum and maximum scores on this scale are 0 and 21. The scores 0, 1, 2, and 3 in each component indicate normal, mild, moderate, and severe sleep problems, respectively.

A total score of 6 or more signifies inadequate sleep. The researchers have investigated the clinical indicators of this index during 18 months in two populations of good sleepers (52 healthy samples) and bad sleepers (54 depressed patients and 62 patients with sleep disorders). Cronbach's alpha coefficient of 0.83 and validity and retest reliability of 0.85 confirmed the internal consistency of this index. It also obtained a total score of more than 5 with a kappa coefficient of 0.75, a specificity of 86.5%, and a diagnostic sensitivity of 89.6%, indicating its power for differentiating good sleepers from bad sleepers (Buysse et al., 1989). Different studies confirmed the reliability and validity of the Persian version of the index (Farahbakhsh and Dehghani, 2016; Shafaat et al., 2017).

Larson Sexual Satisfaction Questionnaire (LSSQ)

This 25-item questionnaire evaluates four components: the desire to have sex, sexual attitude, sex life quality, and sexual compatibility. The questionnaire is scored on a Likert scale from 1 (never) to 5 (always). The score ranges of 25-41, 42-84, and above 84 indicate low, moderate, and high sexual satisfaction, respectively. The Cronbach's alpha coefficient of 0.91 and test-retest reliability of 0.93 confirmed the internal consistency of this scale (Larson et al., 1998). Bahrami et al., (2016) investigated the 4-factor design of the Persian version of this questionnaire using confirmatory factor analysis. Cronbach's alpha coefficient of more than 0.70 confirmed the internal stability of the scale (Bahrami et al., 2016).

Statistical Analysis

We analyzed data using SPSS software (version 24) through student's t-test and two-way repeated measures analysis of variance (ANOVA). We used the Kruskal-Walli's and Mann-Whitney U tests to assess the variables with non-normal distribution. The ANOVA was conducted with a mixed model using both within-subject and between-subject designs to determine the impact of the UTP on all reported measures. We tested the homogeneity of variances, normal distribution of scores, and the sphericity using the Levene's test, the Kolmogorov-Smirnov test, and the Mauchly's test, respectively. The level of significance was less than 0.05 (P< 0.05).

Ethical considerations

The researchers registered the study in the Iranian Registry of Clinical Trials (IRCT20221230056986N1). Before the commencement of the study, the participants were informed of the study objectives and assured of data confidentiality. All participants signed the informed written consent. The Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (Ethics code: IR.SBMU.MSP.REC.1398.669) approved the study protocol.

3. RESULTS

A total of 43 MS patients participated in this study, of which 22 cases (51.2%) were in the intervention group and 21 others (48.8%) were in the control group. Patients in both groups were homogeneous in terms of demographic features, including age, gender, and education. Table 1 and Figure 2 present the mean scores of psychosomatic symptoms in three stages of measurement divided by study group. There was no significant change in the control group in the mean scores in the pre-test compared to the post-test and follow-up stages. In the experimental group, on the other hand, we observed a decrease in the mean scores in the post-test and follow-up stages compared to the pre-test stage. There was a significant difference, based on multivariate tests, between different stages of the study, the interaction effect between groups in terms of fatigue, desire to have sex, sexual attitude, sex life quality, sexual compatibility, and sleep quality, (P<0.001) (Table 1).



Figure 2 The mean scores of psychosomatic symptoms in three stages of measurement compared between the Control group and UTP group

Table 1 Mean of psychosomatic symptoms' scores in three stages of measurement divided by study group

Variables		Control			Intervention			
		Pre-test	Post-test	Follow-up	Pre-test	Post-test	Follow-up	
Fatigue		36.71 ± 2.85	37.62 ± 2.42	37.38 ± 1.96	37.09 ± 2.35	33.23 ± 2.18	33.68 ± 2.17	
Sexual Satisfaction	Desire to Have Sex	13.95 ± 2.73	14.52 ± 2.68	14.38 ± 2.52	14.23 ± 2.49	17.55 ± 2.99	16.91 ± 2.72	
	Sexual Attitude	15.14 ± 3.78	15.71 ± 3.51	15.43 ± 3.80	15.05 ± 3.68	18.73 ± 3.47	17.95 ± 3.40	
	Sex Life Quality	19.76 ± 2.74	20.07 ± 2.38	19.50 ± 2.72	20.41 ± 2.67	23.50 ± 3.00	22.99 ± 2.88	
	Sexual Compatibility	13.67 ± 3.65	13.70 ± 2.84	14.43 ± 3.64	14.55 ± 4.14	19.14 ± 4.04	18.12 ± 4.22	
	Total Sexual Satisfaction	65.52 ± 7.17	64.01 ± 6.83	63.74 ± 7.31	64.23 ± 8.25	78.91 ± 8.50	75.97 ± 8.69	
Sleep Quality		13.62 ± 2.44	13.14 ± 2.43	12.95 ± 2.48	13.55 ± 1.87	9.77 ± 1.66	10.27 ± 2.12	

The results of the univariate (within-subject effects) test for the comparison of psychosomatic symptoms in the control and UTP groups are presented in (Table 2). Our findings indicated that the F values associated with the interaction effects between groups and repeated measures for all psychological symptoms were significant at a significance level of 0.01 (P<0.01). The significance of the interaction effects highlights the fact that there are statistically considerable differences between the changes in psychological symptom scores reported for the groups of control and UTP during the measurement stages.

Table 2 The results of the univariable within-subject effects test to compare the psychosomatic symptoms of the control and UTP groups

The Course of Fifte 1		Repeate	ed Measure	2	Interaction between Groups and Repeated Measures		
The Source of Effe	F	P-value	Effect Size	F	P-value	Effect Size	
Fatigue	The Greenhouse-Geisser	8.947	0.001	0.179	21.832	0.001	0.347
	The Huynd-Feldt	8.947	0.001	0.179	21.832	0.001	0.347
Desire to Have Sex	Sphericity Assumed	39.208	0.001	0.489	19.851	0.001	0.326
	Lower-bound	39.208	0.001	0.489	19.851	0.001	0.326
Sexual Attitude	Sphericity Assumed	40.729	0.001	0.498	23.251	0.001	0.362
	Lower-bound	40.729	0.001	0.498	23.251	0.001	0.362
Sex Life Quality	The Greenhouse-Geisser	30.362	0.001	0.425	26.573	0.001	0.393
	The Huynd-Feldt	30.362	0.001	0.425	26.573	0.001	0.393
Sexual	Sphericity Assumed	23.392	0.001	0.363	18.377	0.001	0.309
Compatibility	Lower-bound	23.392	0.001	0.363	18.377	0.001	0.309
Sleep Quality	Sphericity Assumed	21.405	0.001	0.343	11.530	0.001	0.219
	Lower-bound	21.405	0.001	0.343	11.530	0.002	0.219

Furthermore, to compare the mean scores during the measurement stages, Bonferroni's post hoc test was used. The pairwise comparisons presented in Table 3 indicate the difference in the scores of psychosomatic symptoms during the treatment stages in the control and UTP groups. Considering the results obtained in the UTP group, the difference between the mean scores of the pretest stage and those obtained in the post-test and follow-up stages was statistically significant (P<0.05). The follow-up scores decreased significantly compared to the pre-test stage. The difference between the scores reported in the post-test and follow-up stages was not statistically significant (P<0.05), indicating the stability of the treatment effects over time.

There was no statistically significant difference in the control group between the scores of the pre-test stage and those in the post-test and follow-up stages. The difference between the scores of the post-test and follow-up stages was not statistically significant (P>0.05). A weak correlation has been reported between sexual satisfaction and quality sleep in MS patients (r=0.41, P=0.006). Fatigue had a reverse weak correlation with quality sexual satisfaction (r=-0.48, P=0.001) and a reverse moderate

correlation with quality sleep (r=-0.61, P<0.005) in MS patients. Logistic regression showed that quality of sleep was a predictor of fatigue (β =1.51; P=0.02), while sexual satisfaction could not predict the value of fatigue (β =0.94; P=0.76).

Table 3 Post hoc Bonferroni test

			UTP group			Control Group		
Variables	Proximal	Distal	The Difference	Standard	P-value	The Difference	Standard	P-
	Stage	Stage	of means	Error	r-value	of means	Error	value
Fatigue	Pre-test	Post-test	3.864	0.435	0.001	-0.905	0.445	0.145
		Follow-up	3.409	0.567	0.001	-0.667	0.580	0.772
	Post-test	Follow-up	-0.455	0.617	1	0.238	0.631	1
Desire to Have Sex	Pre-test	Post-test	-3.318	0.298	0.001	-0.571	0.305	0.204
		Follow-up	-2.682	0.349	0.001	-0.429	0.357	0.712
	Post-test	Follow-up	0.636	0.326	0.173	0.143s	0.333	1
	Pre-test	Post-test	-3.682	0.329	0.001	-0.571	0.337	0.293
Sexual Attitude		Follow-up	-2.909	0.377	0.001	-0.286	0.386	1
	Post-test	Follow-up	0.773	0.320	0.060	0.286	0.327	1
Sex Life Quality	Pre-test	Post-test	-3.091	0.352	0.001	-0.305	0.360	1
		Follow-up	-2.582	0.328	0.001	0.257	0.335	1
	Post-test	Follow-up	0.509	0.244	0.129	0.562	0.249	0.089
Sexual Compatibility	Pre-test	Post-test	-4.591	0.568	0.001	-0.038	0.581	1
		Follow-up	-3.573	0.559	0.001	-0.762	0.573	0.572
	Post-test	Follow-up	1.018	0.454	0.091	-0.724	0.465	0.381
Sleep Quality	Pre-test	Post-test	3.773	0.451	0.001	0.476	0.461	0.924
		Follow-up	3.273	0.513	0.001	0.667	0.525	0.633
	Post-test	Follow-up	-0.500	0.550	1	0.190	0.563	1

4. DISCUSSION

As evidenced by the results of this study, 12 60-minute weekly sessions of UTP had a statistically significant effect on fatigue, desire to have sex, sexual attitude, sex life quality, sexual compatibility, and sleep quality in MS patients. Different studies have confirmed the stability of the treatment effects of UTP over time. In this study, we followed the development of the emotion regulation mechanism outlined in the unified transdiagnostic protocol treatment framework, by which fundamental underlying factors aim to enhance the quality of care and life of patients with MS. We unveiled that MS patients with undergoing UTP experienced lower fatigue intensity, improved sleep quality, and more sexual satisfaction as a result of becoming more emotionally-regulated.

Nevertheless, we found no similar study assessing the effectiveness of UTP in psychosomatic symptoms, including fatigue, sexual dysfunction, and sleep quality, in MS patients to reject or confirm the present findings. The fatigue associated with MS is one of the most common symptoms of patients with this disease, particularly in its early stages (Krupp et al., 2010). Approximately 80% of patients with MS reported fatigue, and more than 55% of patients considered it the worst symptom of their condition (Iriarte et al., 2000). The studies have demonstrated that as the occurrence of fatigue elevates in MS patients, their overall disability increases and their physical and psychological quality of life decreases (Latimer-Cheung et al., 2013).

Fatigue has an association with depression, anxiety, sleep quality, and sexual dysfunction in patients with MS. Although some studies have recommended psychological interventions, including meditation and cognitive-behavioral therapy for the management of fatigue in these patients Asano and Finlayson, (2014), Chalah et al., (2019), Darija et al., (2015), Siengsukon et al., (2018), the supporting evidence has not been strong enough. The results of the present study pinpointed that the patients who received UTP treatment reported lower measures of physical fatigue. Studies confirmed an improvement in fatigue after transdiagnostic treatment (Ellard et al., 2012; Hara et al., 2018). However, none of these studies focused on patients with MS; therefore, future studies can provide more evidence in this respect.

Sleep disturbances are common in MS, and polysomnography studies indicate changes in the micro and macro structures of sleep-in patients with this disease (Neau et al., 2012). Sleep disturbances in MS can be secondary to multiple symptoms of the disease or have a primary cause. There are bidirectional relationships between sleep disturbance and the worsening of MS symptoms Fleming and Pollak, (2005) and also a bidirectional relationship between sleep disturbance and depression, which causes a decrease in the quality of life in MS patients (Trojan et al., 2012). Sleep disturbance is also associated with more fatigue in these patients (Braley and Boudreau, 2016). The evaluation of sleep quality can provide reliable prognostic information related to the relapsing-remitting course of MS. It has been suggested that integrated interventions in the treatment of patients with MS could help improve sleep disturbances (Harvey, 2009).

Therefore, these therapeutic measures should simultaneously target other areas, such as depression and anxiety, other than sleep quality, all of which could be targeted by UTP treatment. This signifies that UTP treatment for sleep disturbances in MS patients could fulfill such a goal (Buratti et al., 2019, De-la-Vega et al., 2019). Accordingly, our findings demonstrated that MS cases who received UTP treatment developed objectively higher quality of sleep during their treatment. The other results of the present study confirmed the role of UTP in improving sexual dysfunction in MS patients. Sexual dysfunction, as one of the other most common symptoms reported by MS patients, has been observed in about 40%-80% of them (Gromisch et al., 2016). In addition to cortical and spinal lesions associated with MS, psychological and social problems, and physical complications, such as excretion problems and convulsive states, could all lead to sexual dysfunction (Cordeau and Courtois, 2014; Fragalà et al., 2014, Sanders et al., 2000; Winder et al., 2016). In addition, sexual dysfunction is robustly associated with depression, anxiety, and sleep problems (Crayton et al., 2004; Young et al., 2017).

Despite the importance of sexual dysfunction in MS, these symptoms are often overlooked. This can worsen the number and severity of symptoms and affect multiple aspects of mental health and quality of life in these patients (Foley and Beier, 2006; Schairer et al., 2014). It is worth mentioning that psychological-based interventions, namely UTP, are capable of improving sexual dysfunction and subsequently increasing the quality of life for these patients (Schairer, 2015). Similarly, the present study demonstrated that MS patients treated with UTP had markedly lower rates of sexual dysfunction compared to their peers who did not receive UTP. In line with our study, based on the study conducted by De-Ornelas-Maia et al., (2017) sessions of UTP lead to marked improvements in one's quality of life, anxiety, and depression in those with mental disorders.

All in all, to understand why UTP drastically impacts somatic complaints in MS patients, one must notice that the occurrence of psychosomatic symptoms (i.e., fatigue, sleep disturbances, and sexual dysfunction) are all intricately intertwined with each other while also being closely interwoven with psychologic symptoms in MS patients. As previously mentioned, there have been multiple accounts of bidirectional correlations of MS severity with fatigue, depression, and sleep disturbances (Braley and Boudreau, 2016; Chalah et al., 2019; Fleming and Pollak, 2005; Trojan et al., 2012). Therefore, an integrated therapeutic measure that could influence all the components in this interlaced network of symptoms could substantially improve them and enhance the quality of life in MS patients; this is what the UTP treatment does.

5. CONCLUSION

It seems that 12 sessions of UTP had a stable effect on treating psychosomatic symptoms, including fatigue, desire to have sex, sexual attitude, sex life quality, sexual compatibility, and sleep quality in MS patients. The findings of this study supported the notion that the UTP could be an additional efficient therapeutic measure as a financially optimal transdiagnostic treatment of psychosomatic symptoms in adult MS patients. The UTP is as equally efficacious as gold-standard disorder-specific protocols in MS patients. Nonetheless, additional analysis is required to expand the findings obtained in this study. Transdiagnostic research can better present the clinical and scientific reality of psychosomatic problems and reflect the complexity and comorbidity that is the norm in clinical practice.

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Author Contributions

Amir Mahdi Katani (data collection and writing), Abbas Masjedi Arani (analysis), Reza Hajmanouchehri (Data collection), Banafsheh Mohajerin (Data collection)

Ethical approval

The Medical Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (Ethical approval code: IR.SBMU.MSP.REC.1398.669) approved the study protocol.

Informed consent

Before the start of the study, informed written Oral informed consent was obtained from all participants included in the study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

- Asano M, Finlayson ML. Meta-analysis of three different types of fatigue management interventions for people with multiple sclerosis: exercise, education, and medication. Mult Scler Int 2014; 2014;798285. doi: 10.1155/2014/798285
- Association AP. Association, AP Diagnostic and statistical manual of mental disorders. Arlington, VA, US. American Psychiatric Publishing, Inc 1995.
- A'zimian M, Fallah-pour M, Karimlou M. Evaluation of reliability and validity of the Persian version of Fatigue Severity Scale (FSS) among persons with multiple sclerosis. Arch Rehabil 2013; 13:84-91.
- Bahrami N, Yaghoob-Zadeh A, Sharifnia H, Soliemani MA, Haghdoost AA. Validity and reliability of the persian version of Larson sexual satisfaction questionnaire in couples. J Kerman Univ Med Sci 2016; 23:344-356.
- 5. Barlow DH, Farchione TJ, Bullis JR, Gallagher MW, Murray-Latin H, Sauer-Zavala S, Bentley KH, Thompson-Hollands J, Conklin LR, Boswell JF, Ametaj A, Carl JR, Boettcher HT, Cassiello-Robbins C. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders Compared with Diagnosis-Specific Protocols for Anxiety Disorders: A Randomized Clinical Trial. JAMA Psychiatry 2017; 74(9):875-884. doi: 10.1001/jamapsychiatry.2017.2164
- Barlow D, Farchione TJ, Sauer-Zavala S, Latin HM, Ellard KK, Bullis JR, Bentley KH, Boettcher HT, Cassiello-Robbins C. Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide, Oxford University Press 2017b.
- Braley TJ, Boudreau EA. Sleep disorders in multiple sclerosis. Curr Neurol Neurosci Rep 2016; 16(5):50. doi: 10.1 007/s11910-016-0649-2
- 8. Brown TA, Barlow DH. A proposal for a dimensional classification system based on the shared features of the

- DSM-IV anxiety and mood disorders: implications for assessment and treatment. Psychol Assess 2009; 21(3):256-71. doi: 10.1037/a0016608
- Bullis JR, Sauer-Zavala S, Bentley KH, Thompson-Hollands J, Carl JR, Barlow DH. The unified protocol for transdiagnostic treatment of emotional disorders: Preliminary exploration of effectiveness for group delivery. Behav Modif 2015; 39(2):295-321. doi: 10.1177/014544551455 3094
- Buratti L, Iacobucci D, Viticchi G, Falsetti L, Lattanzi S, Pulcini A, Silvestrini M. Sleep quality can influence the outcome of patients with multiple sclerosis. Sleep Med 2019; 58:56-60. doi: 10.1016/j.sleep.2019.02.020
- Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28(2):193-213. doi: 10.1016/0165-1781(89)90047-4
- 12. Chalah MA, Kauv P, Creange A, Hodel J, Lefaucheur J-P, Ayache SS. Neurophysiological, radiological and neuropsychological evaluation of fatigue in multiple sclerosis. Mult Scler Relat Disord 2019; 28:145-152. doi: 10.1 016/j.msard.2018.12.029
- 13. Clark LA, Cuthbert B, Lewis-Fernández R, Narrow WE, Reed GM. Three approaches to understanding and classifying mental disorder: ICD-11, DSM-5, and the National Institute of Mental Health's Research Domain Criteria (RDoC). Psychol Sci Public Interest 2017; 18:72-145.
- 14. Cordeau D, Courtois F. Sexual disorders in women with MS: assessment and management. Ann Phys Rehabil Med 2014; 57(5):337-347. doi: 10.1016/j.rehab.2014.05.008
- 15. Crayton H, Heyman RA, Rossman HS. A multimodal approach to managing the symptoms of multiple sclerosis.

- Neurology 2004; 63(11 Suppl 5):S12-8. doi: 10.1212/wnl.63.1 1_suppl_5.s12
- Darija K-T, Tatjana P, Goran T, Nebojsa S, Irena D, Sarlota M, Jelena D. Sexual dysfunction in multiple sclerosis: A 6-year follow-up study J Neurol Sci 2015; 358(1-2):317-23. doi: 10.1016/j.jns.2015.09.023
- 17. De-la-vega R, Miró J, Esteve R, Ramírez-Maestre C, López-Martínez AE, Jensen MP. Sleep disturbance in individuals with physical disabilities and chronic pain: The role of physical, emotional and cognitive factors. Disabil Health J 2019; 12(4):588-593. doi: 10.1016/j.dhjo.2019.04.001
- De-Ornelas-Maia ACC, Sanford J, Boettcher H, Nardi AE, Barlow D. Improvement in quality of life and sexual functioning in a comorbid sample after the unified protocol transdiagnostic group treatment. J Psychiatr Res 2017; 93:30-36. doi: 10.1016/j.jpsychires.2017.05.013
- Ellard KK, Deckersbach T, Sylvia LG, Nierenberg AA, Barlow DH. Transdiagnostic Treatment of Bipolar Disorder and Comorbid Anxiety with the Unified Protocol: A Clinical Replication Series Behav Modif 2012; 36(4):482-508. doi: 10.1 177/0145445512451272
- Farahbakhsh A, Dehghani F. Effectiveness of mindfulness therapy in sleep quality and mental health of women with insomnia disorder. J Torbat Heydariyeh Univ Med Sci 2016; 4(3):8-15.
- 21. Feinstein A, Pavisian B. Multiple sclerosis and suicide. Mult Scler 2017; 23(7):923-927. doi: 10.1177/1352458517702553
- 22. Feinstein A, Brochet B, Sumowski J. The cognitive effects of anxiety and depression in immune-mediated inflammatory diseases. Neurology 2019: 10.1212/WNL.0000000000006840. doi: 10.1212/WNL.0000000000006840
- 23. Fleming WE, Pollak CP. Sleep disorders in multiple sclerosis. Semin Neurol 2005; 25(1):64-8. doi: 10.1055/s-2005-867075
- 24. Foley FW, Beier M. Assessment and treatment of sexual dysfunction in multiple sclerosis. NMSS Clin Bull 2006; 8:1-11.
- 25. Fragala E, Privitera S, Giardina R, Di-Rosa A, Russo GI, Favilla V, Caramma A, Patti F, Cimino S, Morgia G. Determinants of sexual impairment in multiple sclerosis in male and female patients with lower urinary tract dysfunction: Results from an Italian cross-sectional study. J Sex Med 2014; 11(10):2406-13. doi: 10.1111/jsm.12635
- 26. Grech LB, Butler E, Stuckey S, Hester R. Neuroprotective benefits of antidepressants in multiple sclerosis: are we missing the mark? J Neuropsychiatry Clin Neurosci 2019; 31(4):289-297. doi: 10.1176/appi.neuropsych.18070164
- 27. Gromisch ES, Schairer LC, Pasternak E, Kim SH, Foley FW. Assessment and treatment of psychiatric distress, sexual dysfunction, sleep disturbances, and pain in multiple

- sclerosis: a survey of members of the Consortium of Multiple Sclerosis Centers. Int J MS Care 2016; 18(6):291-297. doi: 10.7224/1537-2073.2016-007
- 28. Hara KW, Borchgrevink PC, Jacobsen HB, Fimland MS, Rise MB, Gismervik S, Woodhouse A. Transdiagnostic group-based occupational rehabilitation for participants with chronic pain, chronic fatigue and common mental disorders. A feasibility study. Disabil Rehabil 2018; 40(21):2516-2526. doi: 10.1080/09638288.2017.1339298
- 29. Harvey AG. A transdiagnostic approach to treating sleep disturbance in psychiatric disorders. Cogn Behav Ther 2009; 38 Suppl 1:35-42. doi: 10.1080/16506070903033825
- 30. Hawkes CH, Boniface D. Risk associated behavior in premorbid multiple sclerosis: A case-control study. Mult Scler Relat Disord 2014; 3(1):40-7. doi: 10.1016/j.msard.2013. 05.002
- 31. Henry A, Tourbah A, Camus G, Deschamps R, Mailhan L, Castex C, Gout O, Montreuil M. Anxiety and depression in patients with multiple sclerosis: The mediating effects of perceived social support. Mult Scler Relat Disord 2019; 27:46 -51. doi: 10.1016/j.msard.2018.09.039
- 32. Holmes EA, O'connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, Ballard C, Christensen H, Silver RC, Everall I. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. Lancet Psychiatry 2020; 7(6):547-560. doi: 10.1016/S2215-0366(20)30 168-1
- 33. Houtchens MK, Sadovnick AD. Health issues in women with multiple sclerosis. Springer 2017.
- 34. Krupp LB, Larocca NG, Muir-nash J, Steinberg AD. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989; 46(10):1121-3. doi: 10.1001/archneur.1989.0052046011 5022
- 35. Krupp LB, Serafin DJ, Christodoulou C. Multiple sclerosisassociated fatigue. Expert Rev Neurother 2010; 10(9):1437-47. doi: 10.1586/ern.10.99
- 36. Larson JH, Anderson SM, Holman TB, Niemann BK. A longitudinal study of the effects of premarital communication, relationship stability, and self-esteem on sexual satisfaction in the first year of marriage. Sex Marital Ther 1998; 24(3):193-206. doi: 10.1080/00926239808404933
- 37. Latimer-Cheung AE, Pilutti LA, Hicks AL, Ginis KAM, Fenuta AM, Mackibbon KA, Motl RW. Effects of exercise training on fitness, mobility, fatigue, and health-related quality of life among adults with multiple sclerosis: a systematic review to inform guideline development. Arch Phys Med Rehabil 2013; 94(9):1800-1828.e3. doi: 10.1016/j.ap mr.2013.04.020

- 38. Lriarte J, Subirá ML, de-castro P. Modalities of fatigue in multiple sclerosis: correlation with clinical and biological factors. Mult Scler 2000; 6(2):124-30. doi: 10.1177/1352458500 00600212
- Mohammadkhani P, Forouzan AS, Hooshyari Z, Abasi I. Psychometric properties of Persian version of structured clinical interview for DSM-5-research version (SCID-5-RV): a diagnostic accuracy study. Iran J Psychiatry Behav Sci 2020; 14(2):e100930
- 40. Nazari N, Sadeghi M, Ghadampour E, Mirzaeefar D. 2020. Transdiagnostic treatment of emotional disorders in people with multiple sclerosis: randomized controlled trial. BMC Psychol 2020; 8(1):114. doi: 10.1186/s40359-020-00480-8
- 41. Neau J-P, Paquereau J, Auche V, Mathis S, Godeneche G, Ciron J, Moinot N, Bouche G, Des-Neurologuespoitou-Charentes G. Sleep disorders and multiple sclerosis: a clinical and polysomnography study. Eur Neurol 2012; 68 (1):8-15. doi: 10.1159/000335076
- 42. Newby JM, Mckinnon A, Kuyken W, Gilbody S, Dalgleish T. Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. Clin Psychol Rev 2015; 40:91-110. doi: 10.1016/j.cpr.2015.06.002
- 43. Norton PJ, Paulus DJ. Toward a unified treatment for emotional disorders: update on the science and practice. Behav Ther 2016; 47(6):854-868. doi: 10.1016/j.beth.2015.07.0
- 44. Osório FL, Loureiro SR, Hallak JEC, Machado-de-sousa JP, Ushirohira JM, Baes CV, Apolinario TD, Donadon MF, Bolsoni LM, Guimarães T, Fracon VS, Silva-Rodrigues APC, Pizeta FA, Souza RM, Sanches RF, Dos Santos RG, Martin-Santos R, Crippa JAS. Clinical validity and intrarater and test–retest reliability of the Structured Clinical Interview for DSM-5–Clinician Version (SCID-5-CV). Psychiatry Clin Neurosci 2019; 73(12):754-760. doi: 10.1111/pcn.12931
- 45. Salehpour GH, Rezai S, Hoseinizadeh M. Psychometric properties and validation of fatigue intensity scale in patients with multiple sclerosis. J Kerman Univ Med Sci 2013; 20(3):263-278.
- Sanders AS, Foley FW, Larocca NG, Zemon V. The multiple sclerosis intimacy and sexuality questionnaire-19 (MSISQ-19). Sex Disabil 2000; 18:3-26.
- 47. Schairer LC. Pilot Randomized Control Trial of a Brief Multidisciplinary Consultation Intervention for Treating Sexual Dysfunction in MS, Yeshiva University 2015.
- 48. Schairer LC, Foley FW, Zemon V, Tyry T, Campagnolo D, Marrie RA, Gromisch ES, Schairer D. The impact of sexual dysfunction on health-related quality of life in people with multiple sclerosis. Mult Scler 2014; 20(5):610-6. doi: 10.1177/1352458513503598

- 49. Sesel A-L, Sharpe L, Naismith SL. Efficacy of psychosocial interventions for people with multiple sclerosis: a meta-analysis of specific treatment effects. Psychother Psychosom 2018; 87(2):105-111. doi: 10.1159/000486806
- 50. Shafaat N, Makvand-Hosseini S, Rezaei AM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. J Clin Oncol 2005; 23(25):6083-96. doi: 10.1200/JCO.2005.09.548
- 51. Siengsukon CF, Alshehri M, Aldughmi M. Self-report sleep quality combined with sleep time variability distinguishes differences in fatigue, anxiety, and depression in individuals with multiple sclerosis: a secondary analysis. Mult Scler J Exp Transl Clin 2018; 4(4):2055217318815924. doi: 10.1177/2055217318815924
- 52. Simpson R, Mair FS, Mercer SW. Mindfulness-based stress reduction for people with multiple sclerosis—a feasibility randomised controlled trial. BMC Neurol 2017; 17(1):94. doi: 10.1186/s12883-017-0880-8
- 53. Skokou M, Soubasi E, Gourzis P. Depression in multiple sclerosis: a review of assessment and treatment approaches in adult and pediatric populations. ISRN Neurol 2012; 2012: 427102. doi: 10.5402/2012/427102
- 54. Strober LB, Arnett PA. Depression in multiple sclerosis: The utility of common self-report instruments and development of a disease-specific measure. J Clin Exp Neuropsychol 2015; 37(7):722-32. doi: 10.1080/13803395.2015.1063591
- 55. Trojan DA, Kaminska M, Bar-or A, Benedetti A, Lapierre Y, Da-costa D, Robinson A, Cardoso M, Schwartzman K, Kimoff RJ. Polysomnographic measures of disturbed sleep are associated with reduced quality of life in multiple sclerosis. J Neurol Sci 2012; 316(1-2):158-63. doi: 10.1016/j.jns.2011.12.013
- 56. Winder K, Linker RA, Seifert F, Deutsch M, Engelhorn T, Dörfler A, Lee DH, Hösl KM, Hilz MJ. Neuroanatomic correlates of female sexual dysfunction in multiple sclerosis. Ann Neurol 2016; 80(4):490-8. doi: 10.1002/ana.24746
- 57. Young CA, Tennant A, Group TS. Sexual functioning in multiple sclerosis: Relationships with depression, fatigue and physical function. Mult Scler 2017; 23(9):1268-1275. doi: 10.1177/1352458516675749