



ORIGINAL ARTICLE

Medicine Science 2020;9(4):837-43

The effects of physiotherapy methods combined with respiratory and relaxation exercises on patients with major depression

Elisa Calisgan¹, H Birgul Cumurcu², Burcu Talu³, Esra Porgali Zayman², Yusuf Aydin⁴

¹Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey

²Inonu University, Faculty of Medicine, Department of Psychiatry, Malatya, Turkey

³Inonu University, Faculty of Health Sciences, Malatya, Turkey

⁴Sanliurfa Balıkligol Public Hospital, Department of Psychiatry, Sanliurfa, Turkey

Received 17 April 2020; Accepted 20 July 2020

Available online 25.08.2020 with doi: 10.5455/medscience.2020.04.051

Abstract

This study aimed to evaluate the effects of physiotherapy methods combined with respiratory and relaxation exercises on patients with major depression. This randomized, controlled trial included 42 patients with a sedentary lifestyle, comprising 21 males and 21 females with a mean age of 37.78 ± 11.67 years (range, 20-60 years). The experimental (n:22) and control groups (n:20) were evaluated using the Beck Depression and Anxiety Score, Visual Analog Score, Patient Health Questionnaire-15, Generalized Anxiety Disorder 7-Items, and Patient Health Questionnaire-9. In both the experimental group and control group, a statistically significant difference was found in all parameters over time, with greater improvements made in the experimental group than in the control group in all the parameters. A rehabilitation program combined with respiratory and relaxation exercises applied in addition to standard treatment, can obtain more successful outcomes in major depression treatment.

Keywords: Major depression, physical exercises, respiratory, relaxation, antidepressant

Introduction

Depression is a common illness of mood disorders and an explicit public health problem [1]. According to some studies, it is frequently seen in females and individuals aged > 40 years [1, 2]. Depression is classified as major depression, dysthymic, premenstrual, atypical, and postpartum depression [3]. Major depression is the most common type of depression and is seen to last for at least two weeks [4]. The symptoms of major depression are insomnia, frequent feelings of sadness and anxiety, loss of energy, fatigue, sleep confusion, pain, lethargy, loss of appetite, psychomotor retardation, and hopelessness [5]. -How do exercises affect neurobiological and physiological mechanisms? Exercises affect the level of monoamine neurotransmitter content, which are serotonin, dopamine, glutamate, epinephrine, and norepinephrine, providing connection between neurons in the brain [6]. Moreover, exercises increasing blood circulation and body temperature, thereby affecting the hypothalamic-expectoration-adrenal structure.

These structures have a positive effect on motivation and parts of the brain such as the limbic system, amygdala, and hippocampus. Also, moderate exercise increases the level of B-endorphin, which is correlated with improved mood state [7, 11]. Thirty minutes of moderate to high-intensity physical exercise has been shown to increase urinary β -phenylacetic acid, which is a glutamatergic neuromodulator. Physical exercise also modulates the level of glutamate neurotransmission to the nucleus accumbens, which is the locus of pleasure and drug addiction [8, 11].

Respiratory exercises include isolated chest and abdominal breathing exercises, active breathing cycle, resistance band exercise, deep diaphragmatic exercise, and pursed-lip breathing. It can be explained as a technique that improves respiratory muscles and chest expansion [9]. Furthermore, walking exercises combined with respiratory exercise has been shown to provide more benefits than standard walking as there is a synchronized contraction of motor units and a decreased prevalence of depression [10].

Relaxation exercises that stimulate neurobiological and physiological mechanisms can be applied to treat depression types such as major depression as they stimulate complex body systems. Relaxation activities increase self-esteem and self-awareness as the activities have positive effects on depression disorder [11].

*Corresponding Author: Elisa Calisgan, Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey, E-mail: elisa.calisgan@inonu.edu.tr

According to researchers, the contraction-relaxation exercises used in these activities can prevent depression symptoms [12].

Selective serotonin reuptake inhibitors (SSRIs) are the most common type of antidepressant used in the standard treatment of depression. SSRIs improve neuron functions in the brain and regulate emotions, also inhibiting reuptake and so resulting in a greater supply of serotonin. According to previous studies, exercise alone is not sufficient to reduce the psychotic symptoms of depression [13]. The purpose of this study was to objectively evaluate the effects of physiotherapy methods combined with respiratory and relaxation exercises in patients with major depression.

Materials and Methods

Design

The study included patients aged 20-60 years, who were diagnosed with mild and moderate forms of major depression and prescribed SSRI drugs, then followed up in the Department of Psychiatry, Faculty of Medicine, Inonu University, between December 2018 and February 2019. The experimental group comprised 22 patients diagnosed with mild and moderate forms of major depression, who were treated with physiotherapy methods combined with respiratory and relaxation exercises in addition to the pharmacological treatment. A control group was formed of 20 patients with mild and moderate forms of major depression treated with the standard pharmacological treatment only.

Ethical Considerations

The experimental protocol was approved based on the ethical standards of the Declaration of Helsinki. To conduct this study, the required permission and consent was obtained from the Malatya Clinical Research Ethics Committee (Approval number: 2018/23-21, dated: 18/12/2018). The individual must be having at least 5 depression criteria of DSM-V (experienced most day and last for at least two weeks), having mild and moderate forms of major depression diagnosis, patients with major depression aged 20-60 years, using SSRI drugs with same effects for depression, would be able to adapt to the training program, to be involved in voluntary work and individuals who have been given their informed consent. Patients who agreed to participate in the study and met the inclusion criteria were selected with a randomized sampling method.

Patients who are not between the ages of 20-60, not diagnosed with mild and moderate forms of major depression, can not make mental evaluations, can not adapt to the education program, and refuse to participate in the study will not be included.

10 volunteers were excluded as they could not adapt to the treatment program.

Data collection tools

Before participation in the present study, all individuals provided written informed consent.

Visual Analog Scale (VAS)

The pain was assessed using VAS, which is a 10-point scale ranging from 0=no pain to 10=intolerable pain. Patients were instructed to

mark the scale according to the intensity of pain felt. The VAS scale is important and recommended for evaluation as it has proven high reliability [14].

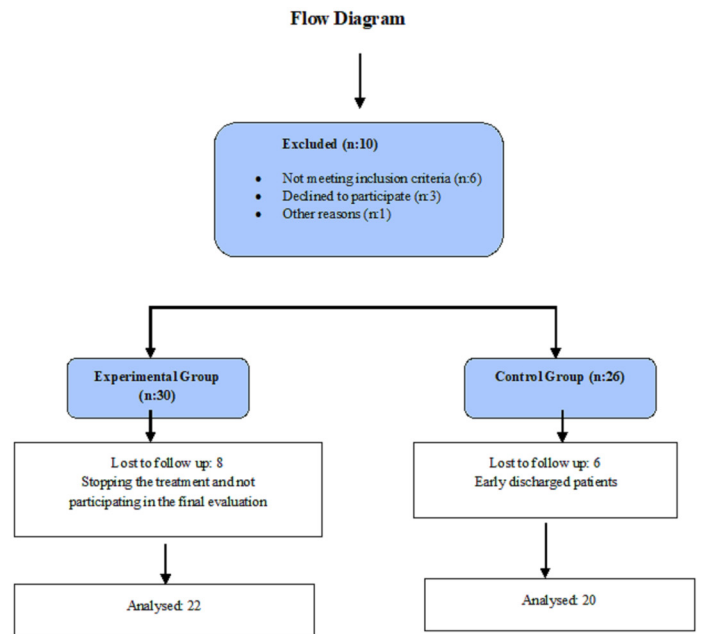


Figure 1. Flow Diagram

Beck Depression Inventory (BDI)

The BDI is a 21-item self-reported questionnaire that evaluates the severity of depression in adults. The items in the BDI refer to the cognitive, physiological, and emotional symptoms of depression. The total score can range from 0 to 63 points, with a total score of 0-9 points indicating minimal depression, 10-18 points mild, 19-29 points moderate, and 30-63 points severe depression [15].

Beck Anxiety Inventory (BAI)

The BAI is a 21-item self-report questionnaire that evaluates the severity of anxiety in adults. The items in the BAI refer to the cognitive, physiological, and emotional symptoms of anxiety. The total score can range from 0 to 63 points, with a score of 0-7 points indicating minimal anxiety, 8-15 points mild, 16-25 points moderate, and 26-63 points severe anxiety [15].

Patient Health Questionnaire-15(PHQ-15)

The PHQ-15 is a 15-item self-reported inventory that evaluates the severity of physical problems in adults such as abdominal or chest pain. The items in the PHQ-15 refer to the cognitive, physical, sexual, physiological, and emotional symptoms of anxiety and depression. The total score of the PHQ-15 can range from 0 to 30 points, with a score of 0 classified as minimal and 30 as maximal and severe level [16].

Generalized Anxiety Disorder 7-Items (GAD-7)

The GAD-7 is a 7-item self-reported questionnaire, developed Swinson et al. to evaluate the severity of psychological problems in adults such as the severity of anxiety. The items in the GAD-

7 refer to the cognitive, physical, sexual, physiological, and emotional symptoms of anxiety. The total score can range from 0 to 21 points, with 0 classified as minimal, 5 mild, 10 moderate, 15 severe, and 21 maximal and severe anxiety [17].

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9, developed by Kroenke et al. (2001), is the depression module of the diagnostic instrument for common mental disorders such as depression [18]. A total score of 0-4 points indicates minimal depression, 5-9 points mild, 10-14 points moderate, 15-19 points moderately severe, and 20-27 points a severe level of depression [18, 19].

Procedure

The SSRI drugs used by both the experimental and control groups had the same effects on depression. Depending on the symptoms, the antidepressant drugs used were sertraline 50 mg/day in 16 patients (38.0%), paroxetine 20 mg/day in 11 patients (26.1%), and escitalopram 10 mg/day in 15 patients (35.7%). On the second visit, if required by the clinical condition of the patient, sertraline was increased to 100 mg/day, paroxetine to 40 mg/day, and escitalopram to 20 mg/day.

The experimental group of 22 patients diagnosed with major depression, were treated with respiratory and relaxation exercises in addition to the pharmacological treatment by psychiatrists. The physiotherapist applied the physiotherapy program to the experimental group. The exercises comprised upper and lower extremity muscle relaxation, pursed-lip, chest, and abdominal breathing exercises, moderate-intensity strengthening exercises for the upper trapezius muscle, abdominal and pectoral muscles, core stabilization muscles, upper and lower muscles using a Theraband™ and soft weight ball. Cervical extensor muscle strength (dynamic isometric exercises using a Theraband) and stretching exercises were combined with respiratory exercises in sitting and standing positions, and home exercises were given (including walking, respiratory and relaxation exercises) to be performed as 3 sets of 10 repetitions 3 days a week for 6 weeks. The duration of on physiotherapy sessions of the experimental group was 60 minutes. Jacobson's technique (progressive muscle relaxation) was used for upper and lower extremity relaxation in the cephalocaudal direction. Patients were instructed to tense the muscle for 5 seconds then relax for 10 seconds, and to perform 10 repetitions. Breathing exercises included pursed-lip, diaphragmatic, and chest breathing. Patients were instructed to inhale for 2 seconds then exhale for 4 seconds, and to perform 10 repetitions in sitting and lying positions. The number of repetitions was increased progressively or the exercises were made more difficult over time with weights, such as a sandbag. The control group consisted of 20 patients with major depression who were treated with SSRI drugs only by psychiatrists. Evaluations of all the patients were made before the treatment and after 6 weeks of the exercise program.

Data analysis

Data obtained in the study were analyzed using IBM-SPSS Statistics 22.0 software. The results were stated as mean ± standard

deviation values. Pearson's Chi-Square Test and Fisher's Final Test were used to evaluating categorical variables. The Mann-Whitney U test was used for the comparison of the significance of data that did not meet parametric conditions. To compare pre and post-treatment values in two dependent groups of variables not showing normal distribution, the Wilcoxon signed-rank test was applied. A value of $p < 0.05$ was accepted as statistically significant.

Results

The evaluation was made of 42 participants with mild or moderate forms of major depression and a sedentary lifestyle, comprising 21 males and 21 females with a mean age of 37.78 ± 11.67 years (range, 20-60 years). The mean body mass index (BMI) of the participants was 26.67 ± 3.97 kg/m². All participants were evaluated in respect of the level of depression and anxiety, pain, and the severity of physical problems.

No statistically significant difference was determined between the groups in respect of age, gender, BMI, level of education, medical history, occupation, habits, socioeconomic status, family history, and comorbidity ($p > 0.05$) (Table 1).

The average pain values at rest, during activity, and at night pre and post-treatment are shown in Table 2. Comparisons were made within and between the groups. No difference was determined between the groups before treatment ($p > 0.05$), and a statistically significant difference was determined between the groups post-treatment ($p < 0.05$). For all three measurements of pain at rest, during activity, and at night, there was a greater improvement in the patients in the experimental group than in the control group ($p < 0.05$).

In both groups, there was a statistically significant decrease in the pain scores at rest, during activity, and at night post-treatment compared to the pre-treatment values ($p < 0.05$) (Table 2).

In terms of the level of depression and anxiety, no statistically significant difference was determined between the groups pre-treatment ($p > 0.05$), and there was a statistically significant difference post-treatment ($p < 0.05$) (Table 3). The change in the level of depression and anxiety in the experimental group patients was statistically better than in the control group ($p < 0.05$) (Table 3).

In both groups, there was a statistically significant change in the level of depression and anxiety post-treatment compared to the pre-treatment values ($p < 0.05$) (Table 3).

The results of the patient health status (PHQ-15, PHQ-9, GAD-7) and generalized anxiety pre and post-treatment are shown in Table 4. There was no significant difference between the two groups pre-treatment in any of these scales ($p > 0.05$). The post-treatment results of the PHQ-15, PHQ-9, GAD-7 were statistically significantly better in the experimental group than in the control group ($p < 0.05$) (Table 4).

A statistically significant improvement was found in all three scores in both groups in the comparison of pre and post-treatment results ($p < 0.05$) (Table 4).

Table 1. Comparison of demographic characteristics of groups

		Experimental (n=22)	Control (n=20)	Total (n=42)	p
Age (year)		38.09±12.47	37.45±11.03	37.78±11.67	0.861 ^a
Sex	Female	9 (%40.9)	12 (%59.1)	21 (%50.0)	0.217 ^b
	Male	13 (%60.0)	8 (%40.0)	21 (%50.0)	
BMI (kg/m ²)		26.68±4.48	26.66±3.45	26.67±3.97	0.985 ^a
Education Status	Preschool	7(%31.8)	6(%30.0)	13(%31)	0.863 ^b
	Highschool	10(%45.5)	8(%40.0)	18(%42.9)	
	University	5(%22.7)	6(%30.0)	11(%26.2)	
Medical History	Yes	7 (%31.8)	8 (%40.0)	15(%35.7)	0.749 ^c
	No	15 (%68.2)	12 (%60.0)	27 (%64.3)	
Career	Yes	11 (%50.0)	9(%45.0)	5 (%10.0)	0.767 ^c
	No	11 (%50.0)	11(%55.0)	45 (%90.0)	
Habits	Yes	4 (%18.2)	8 (%40.0)	12(%28.6)	0.175 ^c
	No	18 (%81.8)	12 (%60.0)	30(%71.4)	
Socioeconomic Status	Low	4(%18.2)	8 (%40.0)	12(%28.6)	0.140 ^b
	Medium	18 (%81.8)	11(%55.0)	29(%69)	
	High	0 (%0.0)	1 (%5.0)	1(%2.4)	
Family History	Yes	7 (%31.8)	8 (%40.0)	15(%35.7)	0.749 ^c
	No	15(%68.2)	12 (%60.0)	27 (%64.3)	
Comorbidity	Yes	2 (%9.1)	1 (%5.0)	39 (%92.9)	1.000 ^c
	No	20 (%90.9)	19 (%95.0)	30 (%7.1)	

a: Independent Samples t-test b: Pearson ki-square test c: Fisher's exact test

Table 2. Comparison of pain values between groups and intra-groups

		Experimental (n=22)	Control (n=20)	P ^a
Resting Pain Score	Pre-Treatment	5.00 (4.00-8.00)	5.00 (3.00-10.00)	0.411
	Post-Treatment	2.00 (1.00-3.00)	5.00 (2.00-8.00)	<0.001
	P ^b	<0.001	0.009	
Active Pain Score	Pre-Treatment	7.00 (6.00-9.00)	6.50 (5.00-10.00)	0.103
	Post-Treatment	2.00 (2.00-4.00)	6.00 (4.00-9.00)	<0.001
	P ^b	<0.001	0.001	
Night Pain Score	Pre-Treatment	6.00 (4.00-8.00)	5.00 (2.00-10.00)	0.060
	Post-Treatment	2.00 (0.00-3.00)	5.00 (2.00-9.00)	<0.001
	P ^b	<0.001	0.015	

a: Mann-Whitney U test b: Wilcoxon test

Table 3. Comparison of changes in depression and anxiety levels between groups and intra-groups

		Experimental (n=22)		Control (n=20)		p ^a
		Mean±SD	Median (Min, Max)	Mean±SD	Median (Min, Max)	
Beck Depression Inventory	Pre-Treatment	26.27±3.11	27.00 (17.00-29.00)	25.20±2.37	25.00 (20.00-29.00)	0.070
	Post-Treatment	12.00±2.76	12.00(7.00-17.00)	17.70±4.82	19.00 (10.00-25.00)	<0.001
	p ^b	<0.001		<0.001		
Beck Anxiety Inventory	Pre-Treatment	22.36±2.70	22.50 (17.00-27.00)	22.70±4.11	23.50 (15.00-29.00)	0.703
	Post-Treatment	10.70±3.74	10.00 (6.00-19.00)	20.50±4.01	20.00 (12.00-29.00)	<0.001
	p ^b	<0.001		<0.001		

a: Mann-Whitney U test b: Wilcoxon test

Table 4. Comparison of patients' health status and generalized anxiety among groups and intra-groups

		Experimental (n=22)		Control (n=20)		p ^a
		Mean±SD	Median (Min,Max)	Mean±SD	Median (Min, Max)	
PHQ15	Pre-Treatment	21.13±4.30	22.00 (12.00-27.00)	25.20±2.37	22.50 (20.00-26.00)	0.364
	Post-Treatment	8.77±2.75	10.00 (4.00-14.00)	21.45±2.28	22.00 (18.00-26.00)	<0.001
	p ^b	<0.001		<0.001		
PHQ9	Pre-Treatment	19.36±4.63	19.50 (11.00-27.00)	17.75±3.94	17.00 (12.00-25.00)	0.156
	Post-Treatment	10.70±3.74	7.59±3.08	16.50±4.01	15.50 (12.00-22.00)	<0.001
	p ^b	<0.001		0.003		
GAD7	Pre-Treatment	15.27±3.29	16.00 (9.00-21.00)	14.50±2.91	14.50 (9.00-19.00)	0.360
	Post-Treatment	6.09±1.63	6.00 (2.00-9.00)	12.90±3.55	14.00 (6.00-19.00)	<0.001
	p ^b	<0.001		0.003		

a: Mann-Whitney U test b: Wilcoxon test

Discussion

This study investigated the effects of physiotherapy methods combined with respiratory and relaxation exercises on patients with major depression. The results demonstrated that physiotherapy methods combined with respiratory and relaxation exercises in addition to the standard method are a more effective treatment method than standard treatment methods alone in patients with major depression.

To the best of our knowledge, this is the first study to compare the standard method and physiotherapy methods combined with respiratory and relaxation exercises in addition to the standard treatment method in patients with major depression.

Previous studies have evaluated the relationship between the amount of aerobic exercise and depression threshold, and a negative correlation has been reported [20]. According to the results of the current study, physiotherapy methods combined with relaxation and respiratory exercises have a positive effect on major

depression.

Hemat et al. (2012) claimed that the treatment of depression needs a multidisciplinary approach and should include pharmacological and psychological treatments and regular exercise [21]. In the current study, patients in the experimental group were treated with pharmacological therapy and regular exercise, while the control group received pharmacological treatment only. After the treatment, greater improvements in all parameters were seen in the experimental group than in the control group.

Silveira et al (2013) compared the effect of short-term aerobic exercise and standard treatment combined with physical and relaxation exercise for 8 weeks. The standard treatment was found to be no more effective than aerobic treatment, but patients treated with aerobic exercise improved in terms of depression [22]. This conclusion was in contrast to the conclusion of the current study in terms of the effect on the level of depression of standard treatment mixed with physical and relaxation exercise.

Some researchers have found that the duration of exercise is also important, and have emphasized that the length of the exercise program was more effective than age, or gender and a program of at least 9 weeks resulted in the maximum decrease of depression. Also, when the effects of psychotherapy and pharmacotherapy were compared with the effects of exercise on depression, exercise was found to have a much greater impact on patients with depression compared to other treatments [23]. In the current study, it was recommended that the exercises combined with relaxation and respiratory exercises were performed as 3 sets of 10 repetitions for one hour 3 days a week for 6 weeks.

It has been shown that routine exercises increase the levels of serotonin, dopamine, and noradrenaline, providing neurogenesis of the prefrontal cortex and caudate nucleus, increasing white matter of the anterior corpus callosum, resulting in greater hippocampal volume and improved memory function [24]. According to Philips et al. (2014), especially consistent moderate high-intensity aerobic exercises increase the number of neurotrophic factors (BDNF (brain-derived neurotrophic factor), VEGF (vascular endothelial growth factor) and IGF-1 (growth factor) which can cross the blood-brain barrier and promote blood vessel formation in the brain, increase gray matter volume of the prefrontal cortex, anterior cingulate cortex, cerebellum, nucleus accumbens, and hippocampus. These neurotrophic factors increase phenylethylamine concentrations, signaling through tropomyosin receptor kinase B and tyrosine kinase, hippocampal neurogenesis, and synaptic plasticity. Therefore, consistent (over several months) aerobic exercises improve mood, the opioid system, attention control, stress coping, cognitive control of motor behavior, the speed of information processing, cognitive flexibility, inhibitory control and working memory [25]. Thus it can be considered that the neurobiological and physiological mechanisms of exercise improve the opioid system, mood, stress coping, working memory, motor control, and increase the effect of SSRI drugs which inhibit the activity of monoamine oxidase enzyme. Neuroimaging methods can be used to evaluate the stimulated side of the brain.

Dunn et. al (2005) studied the dose-response relation of exercise and reduction in depressive symptoms in patients with major depression. They found that those who exercised according to the public health recommendations, for one hour 3-5 times a week with a weekly energy expenditure of 17.5 kcal/kg/week, had significantly larger reductions in depression compared to those who exercised with low intensity and weekly energy expenditure of 7 kcal/kg/week. The latter had results comparable to a placebo condition with stretching and flexibility exercise (non-aerobic) [26]. This study investigated the acute effect of moderate-intensity exercises combined with respiratory and relaxation exercises for one hour 3-5 times a week with a weekly. It is not evaluated the effect of energy expenditure on depressive symptoms.

Limitations

There were some limitations to this study, primarily that the scales used were self-reported questionnaires. The use of more objective scales such as the Montgomery-Asberg Depression Rating Scale (MADRS) and the Hamilton Rating Scale for Depression (HRSD) according to the clinical status of the patients would provide more reliable results.

Conclusion

The findings of this study demonstrate that physiotherapy methods combined with respiratory and relaxation exercises in addition to standard treatment provide a reduction in pain and improved mood in patients with major depression compared to standard treatment alone. Therefore, the implementation of these methods should be considered in addition to standard treatment for the successful treatment of major depression.

Implications for Practice

Psychiatric nurses should investigate the pharmacological and physical treatment effects on patients with major depression and the associated physiological function changes in the brain mechanism. Improved treatments can be developed with further research into how physical therapy contributes to psychological health. Major depressive disorders can be treated more easily with physical therapy combined with pharmacological therapy. The quality of life of patients can be improved with collaboration between psychiatric nurses and physiotherapists.

Conflict of interests

The authors have no conflicts of interest to declare.

Financial Disclosure

All authors declare no financial support.

Ethical approval

The experimental protocol was approved based on the ethical standards of the Declaration of Helsinki. To conduct this study, the required permission and consent was obtained from the Malatya Clinical Research Ethics Committee (Approval number: 2018/23-21, dated: 18/12/2018).

References

1. Kroenke K, Sitzer RL, Williams JB. Anxiety disorders in primary care: prevalence, impairment, comorbidity and detection. *Ann Intern Med.* 2007;146:317-25.
2. Lawlor DA, Hopker SW. The effectiveness of exercise as an intervention in the management of depression: Systematic review and meta-regression analysis of randomized controlled trials. *Br Med J.* 2001;322:763-7.
3. Stubbs B, Rosenbaum S, Vancampfort D, et al. Exercise improves cardiorespiratory fitness in people with depression: A meta-analysis of randomized control trials. *J Affect Disord.* 2016;190:249-53.
4. Kaur J, Masaun M, Bhatia MS. Role of physiotherapy in Mental Health Disorders. *Delhi Psych J.* 2013;16:404-8.
5. Koroğlu E. Depresyon Bozuklukları. In: DSM-5 Tanı Ölçütleri Başvuru El Kitabı. Ed: E. Koroğlu. Ankara, Hekimler Yayın Birliği, 2014.
6. Cai X, Kallarackal AJ, Kvarita MD, et al. Local potentiation of excitatory synapses by serotonin and its alteration in rodent models of depression. *Nature neuroscience.* 2013;16:464-72.
7. Brosse AL, Sheets ES, Lett HS, et al. Exercise and the treatment of clinical depression in adults: recent findings and future directions. *Sports Med.* 2002;32:741-60.
8. Kim TK, Park JY, Han PL. Physiological parameters in the blood of a murine stress-induced depression model before and after repeated passive exercise. *Endocrinol Metabol.* 2015;30:371-80.
9. Martinsen EW. Effect of aerobic exercise on depression: a control study. *Br*

- Med J (Clin Res Ed). 1985;291:109.
10. Jang WS. Exercise and Depression. *Endocrinol Metab.* 2015;30:270-1.
 11. Egil WM. Exercise and Depression. *Int J Sport Exe Psych.* 2005;3:469-83.
 12. Dimeo F, Bauer M, Varahram I, et al. Benefits from aerobic exercise in patients with major depression: A pilot study. *Br J Sports Med.* 2001;35:114-7.
 13. Stahl SM. *Essential Psychopharmacology. Neuroscientific Basis and Practical Applications.* Mens Sana Monogr. 2010;8:146-50.
 14. Ströhle A. Physical activity, exercise, depression and anxiety disorder. *J Neural Transm.* 2009;116:777-84.
 15. Beck AT, Steer RA, Garbin MG. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. *Clin Psychol Rev.* 1988;8:77-100.
 16. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med.* 2002;64:258-66.
 17. Swinson RP. The GAD-7 scale was accurate for diagnosing generalised anxiety disorder. *Evid Based Med.* 2006;11:184.
 18. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606-13.
 19. Haddad M, Walters P, Phillips R. Detecting depression in patients with coronary heart disease: a diagnostic evaluation of the PHQ-9 and HADS-D in primary care, findings from the UPBEAT-UK study. *PLoS One.* 2013;8.
 20. Pinto-Meza A, Serrano-Blanco A, Penarrubia MT. Assessing depression in primary care with the PHQ-9: can it be carried out over the telephone? *J Gen Intern Med.* 2005;20:738-42.
 21. Hemat FA, Shahsawari A, Mousavi SR. Effects of selected aerobic exercises on depression and concentrations of plasma serotonin in the depressed female students aged 18 to. *J App Res.* 2012;12:47-52.
 22. Silveira H, Moraes H, Oliveira N, et al. Physical exercise and clinically depressed patients: a systematic review and meta-analysis. *Neuropsychobiology.* 2013;67: 61-8.
 23. Szuhany KL, Bugatti M, Otto MW. A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *J Psychiatr Res.* 2015;60:56-64.
 24. Erickson KI, Leckie RL, Weinstein AM. "Physical activity, fitness, and gray matter volume". *Neurobiol. Aging.* 2014;35:520-8.
 25. Phillips C, Baktir MA, Srivatsan M, et al. "Neuroprotective effects of physical activity on the brain: a closer look at trophic factor signaling". *Front Cell Neurosci.* 2014;8:170.
 26. Dunn AI, Trivedi MH, Kampert JB, et al. Exercise treatment for depression. Efficacy and dose response. *Americ J Prevent Med.* 2005;28:1-8.