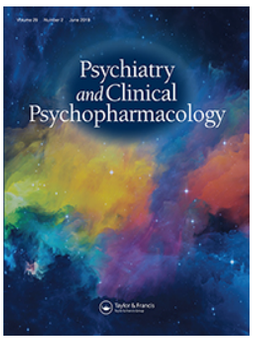

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Effect of exercise on therapeutic response in depression treatment

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ABSTRACT

OBJECTIVES: The aim of this study is to investigate the effect of exercise on therapeutic response in depression treatment.

METHODS: Thirty-three patients admitted to the Psychiatry Department of Firat University Hospital and diagnosed with major depressive disorder according to DSM-IV criteria and met the study criteria were included in the study. The patients in Group 1 were treated with antidepressant medication and were asked for brisk walking for at least 30 minutes a day, at least 4 days a week, for 12 weeks. Only antidepressant medication was given to the patients in Group 2. The Hamilton Depression Rating Scale, the Hamilton Anxiety Rating Scale, and the Clinical Global Impression Scale were applied to both groups at baseline and at the end of 6 weeks and 12 weeks.

RESULTS: Anxiety and depression levels decreased in both groups. The decrease in anxiety and depression scores with antidepressant use is an expected outcome. However, there was a statistically more decrease in the average-scaled scores in the Group treated with antidepressant and exercise than the Group treated with only antidepressant.

CONCLUSIONS: Exercise had a positive effect on the therapeutic response in depression treatment. However, long-term studies in larger sample groups are needed.

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KEYWORDS
Depression; exercise; therapeutic response

Introduction

Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behaviour, feelings, and physical well-being. Depression is a syndrome with symptoms, a feeling or a state of depression in the deep gloom of thought, slowdown and recession on speech and movements, worthlessness, smallness, weakness, reluctance, pessimism, slowdown on thoughts, and feelings with physiological functions [1]. Depression is a serious individual and community health problem because it is the most common mental disorder in this century, has a high rate of chronicity and recurrence, is a significant risk factor for suicide, and causes workforce loss [2]. Exercise is defined as repetitive physical activity that is produced as a result of the contraction of skeletal muscles and requires energy expenditure above basal metabolic rate. It is a planned, structured, and voluntary action that is aimed at improving the components of physical fitness [3]. Regular physical activity reduces the morbidity and mortality, provides a person to be socio-economically more efficient, and increases the quality of life depending on the preservation and continuity of cognitive functions [4]. It is known that regular exercise has positive effects on both physical and mental health. While there are many studies on the effects of exercise on physical health, there are not enough studies on its effects on mental health [5]. Exercise can be used as both a direct or complementary treatment in the treatment of mild and moderate symptoms of depression, which is one of the most common diseases throughout the world today. It is thought that it may be an important intervention method in terms of controlling or preventing depression [6,7].

Depression has negative effects on the quality of life of millions of people around the world [8]. Complementary and alternative therapies such as exercise, meditation, tai chi, qigong, and yoga are investigated in the treatment of depression and anxiety. It has been reported that they can be tried as alternatives to standard pharmacological and psychotherapeutic treatment approaches and that they can give positive results when used as complementary therapies with these standard treatment approaches [9,10]. Some studies have reported that exercise may be as effective as psychological interventions and drug therapy in depression treatment [11,12]. It has been thought that physical activity can be used as a very effective treatment method especially in people who cannot use drugs, in pregnant women and in children because of low cost and low side effect compared to drug treatment [13,14]. Exercise in the treatment of depression did not show any drug side effects such as withdrawal symptoms and weight gain, dry mouth, or insomnia

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[15]. However, it is strongly recommended that exercise is used as adjunctive therapy, when considering that it has potential health benefits such as weight loss [16]. Many studies in the systematic review conducted by Mammen have reported that exercise can have great potential in protection as well as treatment and that there is increasing evidence on this issue. Moreover, it has been suggested that active individuals should maintain their physical activity habits and that inactive individuals should begin a physically active lifestyle. Therefore, it has been reported that the introduction of physical activity at the population level can be a strategy to improve mental health of the population as well as their physical health [17]. New findings demonstrate that exercise can be recommended as an adjunct to use of medications in the first-line treatment for mild to moderate depression [18], as an alternative to cognitive behavioural therapy [10] and in the prevention of depression in healthy populations [19,20].

The aim of this study is to investigate the effect of exercise on therapeutic response in depression treatment.

Methods

Thirty-three patients, who were admitted to the Psychiatry Department of Firat University Hospital and were diagnosed with major depressive disorder (MDD) according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and met the study's criteria, were included in the study. After verbal and written information about the purpose and method of the study were given to the patients, written consent was obtained from them. This study was approved by the Ethics Committee of Firat University Faculty of Medicine.

Inclusion Criteria for Study: Being between 18 and 65 years of age, no another Axis I disorder except for MDD, no mental retardation, no history of alcohol and substance abuse or addiction within the last 6 months, EF (ejection fraction) >50%, as determined by a cardiology consultation, no history of heart disease (those with stable hypertension can be included), no arrhythmia, no significant physical pathology or disease that would affect the distribution of psychiatric symptoms present in the patient and obtaining the signed informed consent form.

Exclusion Criteria for Study: Being under 18 years old and over 65 years old, another Axis I disorder except for MDD, mental retardation, EF <50%, history of heart disease, arrhythmia, history of alcohol and substance abuse or addiction within the last 6 months, any significant physical pathology or disease that would affect the distribution of psychiatric symptoms present in the patient, not obtaining the signed informed consent form.

Implementation

A detailed medical history was taken from the patients enrolled in the study. General medical condition and past medical and family history as well as sociodemographic data, such as age, gender, educational status, were recorded in the prepared forms. The SCID-I was applied to the patients. The patients were divided into two groups. The patients in Group 1 were treated with antidepressant medication and were asked for brisk walking for at least 30 minutes a day, at least 4 days a week, for 12 weeks. Only antidepressant medication was given to the patients in Group 2. The Hamilton Depression Rating Scale (HDRS), the Hamilton Anxiety Rating Scale (HARS), and the Clinical Global Impression (CGI) Scale were applied to both groups at baseline and at the end of 6 weeks and 12 weeks. During the study period, there were 32 patients in Group 1 and 24 patients in Group 2. 15 patients in Group 1 were excluded from the study because they did not walk regularly or they left drug treatment. 8 patients in Group 2 were excluded from the study because they left drug treatment. 17 patients in Group 1 and 16 patients in Group 2 were able to complete the study.

Scales used in study

1. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

Axis I diagnosis was detected by applying the SCID-I. The SCID-I is a structured clinical interview that was developed for major DSM-IV Axis I disorders by the American Psychiatric Association in 1997. The validity and reliability studies for Turkish adaptation of the SCID-I were previously performed by Çorapçıoğlu et al. [21].

2. The Sociodemographic and Clinical Data Form (SCDF)

The sociodemographic and clinical data form, which was prepared in accordance with the clinical experience and the information obtained from the screened sources in the patients and by taking into account the objectives of the study, was used. This form is a semi-structured form that contains the sociodemographic information such as age, gender, marital status, educational status, occupation, place of residence, family structure and the clinical data such as use of alcohol, cigarettes and substance, history of physical or mental illness, disease duration, type of treatment, psychiatric medication history.

3. The Hamilton Depression Rating Scale (HDRS)

This scale is applied by the clinician, measures level of depression and change in severity of depression. It consists of the structured questions. Each question is scored on a scale of 0–4. A total score 0–13 indicates no depression, 14–27 mild depression, 28–41 moderate depression, 42–53 severe depression. The scale which was developed by Hamilton and Williams [22]. The Turkish validity and reliability study was made by Akdemir et al. [23].

4. The Hamilton Anxiety Rating Scale (HARS)

This scale is used to determine anxiety level and symptom distribution, contains a total of 14 questions, including sub-dimensions questioning both psychic and somatic symptoms. It is a five-point Likert-type scale. The total score is calculated by the sum of the scores obtained from each item [24]. It was developed by Hamilton. The reliability and the validity of the Turkish version were analysed by Yazıcı et al. [25].

5. The Clinical Global Impression (CGI) Scale

This scale was developed to assess patients in clinical trials and to observe changes that occur with treatment during the follow-up period. It is an observer-rated scale. The CGI Scale is composed of three parts, including severity of illness, improvement, and severity of side effects [26].

6. The Informed Consent Form

It was created as a form informing about the study that the patients agreed to participate in.

Statistical analysis

The current data were evaluated in the light of the literature. "SPSS (Statistical Package for Social Sciences) for Windows 21.0" computer package program was used in the evaluation of the data. The *t*-test was used in binary comparisons, the Chi-square test was used in categorical comparisons and ANOVA was used in cofactor comparisons.

Results

There was no significant difference in the sociodemographic data between Group 1 and Group 2 (Table 1). There was no significant difference between the two groups in terms of HAS-1, HDS-1, and CGI-1 at baseline. It was determined that both groups had major anxiety and moderate depression according to HAS-1 and HDS-1 and had moderate disease according to CGI-1. Both groups had major anxiety according to HAS-2 at the end of 6 weeks. The mean score for Group 1 was significantly lower than the mean score for Group 2 ($p = 0.005$). According to HDS-2 at the end of 6 weeks, Group 1 had mild depression but Group 2 had moderate depression ($p = 0.007$). According to the CGI severity subscale (CGI-S2), Group 1 had limited disease but Group 2 had mild disease ($p = 0.014$). According to the CGI improvement subscale (CGI-I2), Group 1 had marked improvement but Group 2 had mild improvement ($p = 0.043$). No side effects were also seen in both groups according to the CGI tolerability subscale (CGI-T2) ($p = 0.724$). Both groups had major anxiety according to HAS-3 at the end of 12 weeks. The mean score for Group 1 was significantly lower than the mean score for Group 2 ($p = 0.01$). According to HDS-3 at the end of 12 weeks, Group 1 had no depression but Group 2 had mild

Table 1. The Sociodemographic Characteristics of the Patients in Group 1 and Group 2.

	Group 1	Group 2	*p*
Age	37.24 ± 7.926	39.81 ± 8.352	0.37
Gender (F/M)	14/3	14/2	0.68
Educational status			0.888
Literate	0	1	
Primary school	7	6	
Secondary school	2	2	
High school	6	5	
University	2	2	
Marital status			0.541
Single	3	1	
Married	10	12	
Divorced	3	3	
Widow	1	0	
Occupation			0.5
Housewife	10	11	
Student	2	0	
Officer	1	2	
Worker	3	1	
Private occupation	1	1	
Unemployed	0	1	
Smoking			0.393
Yes	6	8	
No	11	8	
History of physical illnesses			0.776
Yes	5	4	
No	12	12	
History of mental illnesses			0.598
Yes	8	9	
No	9	7	
Use of psychiatric medication			0.201
No	6	4	
Tricyclic antidepressant	1	0	
Selective Serotonin Reuptake Inhibitor	9	6	
Serotonin Norepinephrine Reuptake Inhibitor	1	3	
Others	0	3	
Treatment modality			0.133
Outpatient clinic	17	14	
Hospitalization	0	2	
Past medical history			0.325
Admission for first time	7	4	
Continuing treatment for a while	10	12	
Place of residence			0.446
Village	1	2	
District	0	1	
City	16	13	
Family type			0.866
Core	9	8	
Wide	8	8	

depression ($p = 0.006$). According to the CGI severity subscale (CGI-S3), Group 1 had no disease but Group 2 had mild disease ($p = 0.007$). According to the CGI improvement subscale (CGI-I3), Group 1 had marked improvement but Group 2 had moderate improvement ($p = 0.01$). No side effects were also seen in both groups according to the CGI tolerability subscale (CGI-T3) ($p = 0.675$) (Table 2).

Discussion

Exercise may be recommended for people with depressive disorder in any demographic group, regardless of socioeconomic status. However, it has been reported that it has a stronger effect in people over the age of 40, with mild to moderate depression, and with obesity [27,28].

In our study, there was no significant difference between the two groups in terms of the sociodemographic characteristics such as mean age, gender, marital status, place of residence, occupation, and family type. Most of the patients in both groups were women. For this reason, it was seen that none of the patients had alcohol and substance abuse and that cigarette smoking was lower than the general population. Most of the patients in both groups consisted of those who were admitted to the outpatient clinic, those who continued treatment for a while, and those who had previously received psychiatric medication.

In our study, it was found that anxiety and depression levels decreased in both groups. The decrease in anxiety and depression scores with standard pharmacological treatment is an expected outcome. However, this decline occurred at a higher level in the group treated with antidepressant and exercise than the group treated with only antidepressant.

Lindwall et al. investigated the reciprocal nature of the physical activity-depressive symptoms relationship in 17,593 older adults from 11 European countries' older adults across 2-year follow-up. They revealed that regular physical activity may be a valuable tool in the prevention of future depressive symptoms in older adults, and depressive symptoms may also prevent older adults from engaging in regular physical activity [29].

Similarly, Oeland et al. showed that physical exercise was useful in mild to moderate depression and anxiety disorders in 27 patients and 21 controls [30].

Exercise seems to have both protective and therapeutic effects in the course of depression, but the underlying mechanisms are not fully understood. It has been reported that the effect of exercise in the modulation of depression may be dependent on neurophysiological, neurodevelopmental, and psychological factors [31]. The protective effects of exercise against stress have been focussed on hippocampus with potential mediators such as exercise-induced neurogenesis [32] and growth factor expression [33], which have been suggested [34]. Other suggested mechanisms include exercise-induced changes in the hypothalamic–pituitary–adrenal axis that regulates the stress response [35] and activity alterations in serotonergic neurons within the dorsal raphe nucleus that plays a mediating role in learned helplessness behaviours [36]. Exercise enhances synaptic plasticity by directly affecting synaptic structure and potentiating synaptic strength, and by strengthening the underlying systems that support plasticity including neurogenesis, metabolism, and vascular function. Such structural and functional changes induced by exercise have been documented in various brain regions, but the hippocampus is the best-studied brain structure [37]. In an exercise study conducted on rats, Eldomiaty et al. reported that serum and hippocampal brain-derived neurotrophic factor (BDNF), macrophage migration inhibitory factor (MIF) and hippocampal vascular endothelial growth factor (VEGF) levels increased significantly but serum interleukin-6 (IL-6) levels decreased significantly. He reported a significant reduction in degenerative neurons in the hippocampal region and an increase in healthy neurons in the upper part of the dentate gyrus. This study has shown that there may be a correlation between serum and hippocampal myokin levels and development or improvement of depression [38]. In another review, Ranjbar et al. [39] reported that exercise increased the level of peripheral norepinephrine, reduced the levels of mediators such as TNFα, IL1β, IL6, decreased the level of ACTH in the central nervous system, and increased the levels of endocannabinoids, endorphins, BDNF.

Several theories that explain exercise-induced benefits with psychological reasons have been put forward. It has been reported that exercise can be useful in reducing stress and anxiety as well as in improving body image, elevating self-concept, self-efficacy, self-esteem, self-confidence, and preventing negative thoughts. Consequently, exercise plays an important role in improving well-being, satisfying life, improving conceptual functions, and increasing general health condition [40].

Table 2. The Scale Scores of the Patients in Group 1 and Group 2.

	Group 1	Group 2	*p*
HAS-1	39.94 ± 6.94	43.25 ± 7.523	0.198
HDS-1	18.88 ± 5.036	22.50 ± 7.554	0.114
CGI-S1	4.06 ± 0.899	4.63 ± 1.147	0.124
HAS-2	21.18 ± 13.97	34.38 ± 11.039	0.005
HDS-2	7.06 ± 7.909	15.94 ± 9.855	0.007
CGI-S2	2.18 ± 1.286	3.44 ± 1.504	0.014
CGI-I2	1.94 ± 1.144	2.81 ± 1.223	0.043
CGI-T2	1.06 ± 0.243	1.00 ± 0.632	0.724
HAS-3	18.41 ± 14.62	31.13 ± 11.949	0.01
HDS-3	5.76 ± 6.61	14.13 ± 9.57	0.006
CGI-S3	1.76 ± 1.091	3.19 ± 1.682	0.007
CGI-I3	1.65 ± 1.115	2.81 ± 1.328	0.01
CGI-T3	1.06 ± 0.243	1.00 ± 0.516	0.675

Although many studies show that exercise has a supportive effect in depression treatment, there is not enough evidence about a standard exercise programme (type, frequency, and severity) to be applied in depression treatment [41]. It has been reported that although the dose and area of physical activity are different in review studies, even a low dose of physical activity can be protective against depression [42]. In a review where Lök and Lök investigated the effects of physical exercise in chronic psychiatric patients, it was concluded that physical activity programmes should last approximately 40–50 minutes (warming up for 5 minutes and cooling for 5 minutes), at least 3 days a week [43]. In the systematic review conducted by Stanton, it was reported that exercise which is effective in depression treatment should be at least 30–40 minutes a day, 3–4 times a week, at least 9 weeks [44]. In the study of Aylaz et al. [45], 24 patients were asked to aerobically walk for 60 minutes a day, 5 days a week, for 10 weeks. It was determined that depression scores decreased significantly in the group treated with antidepressant and exercise compared to the group treated with only antidepressant. In a recent review, Janssen and LeBlanc [46] reported that a 8–12-week exercise programme had a positive effect on at least one symptom of depression.

Although most studies have used walking or running programmes, there are also studies showing the effectiveness of non-aerobic exercise [47]. The need for more physical space, financial investment, and qualified denomination for non-aerobic exercises allows that aerobic exercise is used as an easier option [27]. For example, walking as an aerobic exercise can be an effective option in terms of cost in depression treatment, but a stationary bike or a treadmill is other alternatives [48,49]. Kara et al. [50] demonstrated that aerobic exercises and clinical pilates exercises in MS patients led to moderate changes in cognitive, physical performance, balance, depression, and fatigue levels.

It may be difficult to motivate depressed patients to perform physical activity [51]. Group exercises or supervised exercise programmes may be useful for motivating patients [10]. The success rate of exercise therapy is also related to staying in the exercise programme. To increase the motivation of the patients in the exercise group, music or games and recreational activities may be useful as a strategy [52]. In addition, behavioural techniques such as keeping a daily exercise note can make it easy to comply home exercise programmes [53]. Other forms of communication, including telephone calls, brochures, and oral expressions, can be implemented by the intervention team [54]. Motivational methods such as telephone call (once a week for each patient in Group 1), keeping daily exercise notes, and oral expression were used in our study.

Consequently, after depressed patients completed a 12-week brisk walking programme lasting for at least 30 minutes a day, at least 4 days a week, their depressive symptoms, anxiety levels, and disease severities were found to be decreased. The decrease in anxiety and depression scores with antidepressant use is an expected outcome. However, there was a statistically more decrease in the average-scaled scores in the Group treated with antidepressant and exercise than the Group treated with only antidepressant. Accordingly, it is thought that physical exercise is a supporting method in depression treatment.

There are some limitations in our study. The number of male patients is lower than that of female patients. Moreover, the relative smallness of the sample limits the significance of the findings in the study. On the other hand, the information on whether the recommended exercises were performed at the desired amount and level are based on patient statements and this is a limitation. However, there is a need for long-term studies that would be performed in larger groups and include supervised exercise programmes and that would be accompanied by biological variables such as neurohormonal and brain imaging.

Disclosure statement

No potential conflict of interest was reported by the authors.

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