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The significance of physical activity in the prevention of depressive disorders

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Summary

Owing to the complex etiology of depression taking into account the psychosocial and biological interactions in its formation and course, a comprehensive and integrated approach to this health issue is essential, one that would take into account additional forms of therapeutic interventions besides traditional methods, and increase in physical activity as one of them.

The objective of the present paper is to present the significance of physical activity in the prevention and treatment of depressive disorders, based on the results of research carried out in 2014–2019. The review of empirical works indicates that physical activity adjusted to the individual's needs and health situation can play a role in the prevention and complementary treatment of depressive disorders, including those that occur in the course of somatic diseases. It should be noted that hasty recommendation of physical training to the patients with a severe form of the disorder may cause provocative thoughts, their guilt because of the inability to face the challenge or suicidal behavior.

Key words: depression, prevention, physical activity

Introduction

WHO estimates indicate that 322 million people worldwide suffer from depression, which is 4.4% of the total population, with the illness more often affecting women (5.1%) than men (3.6%). In Europe, symptoms typical of this disorder occur in approximately 4.9% of women and 2.8% of men, while in Poland they are diagnosed in 8.2% of the general population – twice as often in women than men [1]. In adulthood, depression is one of the most frequently diagnosed mental disorders, and by 2020 it will be diagnosed as the second most common cause for deterioration of health [2].

Depression is believed to be one of the main factors implicating disability in people around the world and it significantly increases the risk of developing various somatic diseases [3].

The American DSM-5 classification defines depressive disorders as major depression, while its European and Polish counterparts use the similar term of 'depressive episode' (F.32), included in the ICD-10 classification. However, it should be pointed out that although the meaning ranges of the terms referred to above are similar, they are not fully synonymous and these were coined for different purposes [4–7].

The clinical picture of the disorder differs significantly from the occasional mood fluctuations and short-term emotional reactions to challenges encountered in everyday life activities. Many people with depression suffer from anxiety symptoms, they can also report a number of somatic complaints that are difficult to explain. It should also be emphasized that a chronic moderate or chronic severe course of the illness is seen as a serious threat to life [3]. It has been reported that suicides committed in the course of depressive disorders constitute nearly 1.5% of deaths worldwide and are the second most common cause of death for people aged 15 to 29 years [1, 3].

Depression is a heterogeneous disorder with only partially known pathomechanism in which chronic exposure to stress and its physiological effects play a very important role because it disrupts the functioning of many neurotransmitter systems [8–10]. Neuroimaging studies have shown the disappearance of some brain structures, in particular the prefrontal cortex and the hippocampus area, which is responsible for regulating emotions, mood and cognitive functions [11, 12]. Numerous reports indicate a reduction in the expression of brain growth factors, including brain-derived neurotrophic factor (BNDF) [13–16]. The co-occurrence of chronic stress and recurrent depression is well explained by the phenomenon of hypothalamic-pituitary-adrenal axis (HPA) activation. Its activation in chronic stress leads to increased secretion of endogenous glucocorticoids triggering a development of receptor resistance to cortisol due to its constant production [17]. High level of cortisol causes activation of microglia and secretion of pro-inflammatory cytokines in the central nervous system, which may be responsible for the development of oxidative stress and neurodegeneration demonstrated within the hippocampus structures [18–20]. It is worth mentioning that microglia damage impedes the regulation of BNDF secretion, while the activation of inflammatory phenomena further reduces the sensitivity of BNDF receptors [21]. Increased levels of various pro-inflammatory cytokines have also been found in the serum of people suffering from depression in numerous clinical studies [22]. Pharmacological antidepressant treatment by reducing the symptoms of depression also reduces the content of pro-inflammatory cytokines in blood serum [23].

One of the hypotheses of pathophysiological depression concerns the disruption of tryptophan metabolism and related disturbances in signal transmission in the glutamatergic and serotonergic systems. Tryptophan is not only an essential exogenous amino acid used for protein synthesis, but it also serves as a substrate for the production of compounds of neuroactive substances. One of them is serotonin (5-hydroxy-

tryptamine), which is an important neurotransmitter involved in the control of central nervous system processes directly related to mood, anxiety and cognitive processes [24, 25]. Serotonin can be converted into N-acetyl serotonin and then into melatonin. Each of these neurotransmitters is responsible for controlling the circadian rhythm. At the same time, tryptophan is degraded by kynurenine transformations, which generates a number of intermediate metabolites with high biological activity with regard to glutamatergic receptors, such as kynurenine, quinolinic acid and kynurenic acid [26]. They are involved not only in the phenomena of neuroprotection and neurodegeneration, but also many of them affect the regulation of inflammatory processes, immune tolerance, skeletal muscle metabolism, and protection of gastrointestinal mucous membranes [27–29]. Since enzymes of the kynurenine pathway have been identified in many tissues, it is currently believed that the transformations take place both in the brain and in peripheral tissues – mainly in the liver, immune cells, gastrointestinal tract and skeletal muscles [30]. The kynurenine pathway of tryptophan degradation is overactivated in chronic stress/depressive disorders via pro-inflammatory cytokines [31–34]. In patients suffering from endogenous depression the reduced tryptophan levels in blood serum have been found with simultaneous increase in the pro-inflammatory mediators: interleukin 6 (IL-6), interferon (IFN-γ) and acute phase protein [35]. The mechanism of indoleamine 2,3-dioxygenase activation by IL-6 is mainly postulated. It is one of two key enzymes that incorporate tryptophan into kynurenine metabolism in addition to tryptophan 2,3-dioxygenase [36, 37].

The concept of gut microbiome disorders as a cause in psychosomatic disorders and depression is being intensively developed. Marin et al. [38] found that mice with behavioral disturbances under chronic stress conditions exhibit low colonization with the *Lactobacillus* strain and high circulating kynurenine levels. In the same work it was reported that the intestinal reconstruction of the *Lactobacillus* population is sufficient to reduce the kynurenine concentration and at the same time to alleviate the behavioral symptoms of depression. According to other authors [39], this should be associated with the production of oxygen-releasing molecules (ROS) by *Lactobacillus* bacteria, which are the inhibitor of indoleamine 2,3-dioxygenase [39].

Due to the complex etiology of depressive disorders, their treatment is usually long-lasting. It is also characterized by varied prognosis. The basic methods used in this process are pharmacotherapy and psychotherapy. In most patients, the most beneficial effects are achieved through their combination. Moreover, chromotherapy, phototherapy and various relaxation techniques are used as complementary treatment [25, 40, 41]. In the case of pharmacological treatment, properly chosen drugs, usually after 10 to 28 days after the first dose bring a significant improvement in mental health in most patients [42–44]. The results of the meta-analyzes confirm their considerable effectiveness [45].

It should also be added that regardless of the recommended form of pharmacotherapy, it is not always possible to achieve satisfactory results. In approximately two-thirds of patients the use of the first drug does not lead to improvement of their

clinical condition, and in more than 30% of patients drug-resistant depression is diagnosed, which requires modification of the treatment [46]. Clinical studies indicate that the effectiveness of pharmacotherapy can be increased by increasing the dose of the prescribed drug, combining several antidepressants, or adding an antipsychotic drug, e.g., olanzapine, quetiapine, aripiprazole or risperidone [47–49].

As already mentioned, psychotherapy plays a significant role in the treatment of depressive disorders [50]. It is conducted based on different paradigms, however, the empirical meta-analyzes of randomized placebo-controlled studies confirm the effectiveness of CBT (cognitive behavioral therapy). Its essence is a short-term, structured and focused on specific goals and problems psychotherapist's cooperation with the patient [40, 51–54].

There is also empirical evidence suggesting that a significant role in primary prevention and complementary role in therapy based on recognized and traditional methods of treating depressive disorders may be played by other forms of interactions that are perceived as helpful in this process. These include physical activity, understood as any type of body movement caused by working muscles and leading to energy expenditure exceeding the level of resting energy [3, 55–60].

Paradoxically, in the course of some depressive syndromes, especially in the severe form of the illness, any movement can cause patients' suffering or patients may not even be able to perform the simplest activities, therefore there is a significant risk that motivating them to undertake physical activity will imply a sense of guilt because of the inability to implement this type of action, provoking suicidal thoughts and intentions [1, 3, 61,62]. Moreover, there are – although relatively few – empirical works showing inefficiency or confirming the low importance of physical activity in reducing depressive symptoms [63–66]. It has also been demonstrated that physical activity characterized by excessive frequency and intensity, i.e., one that exceeds the needs and capabilities of the body, may be associated with an increase in oxidative stress, which leads to many different disorders, including depression [67, 68]. Therefore, it seems reasonable to try to answer the question: what is the role of physical activity in the prevention and treatment of depressive disorders?

Aim

The aim of the present paper is to present the significance of physical activity in the prevention and therapy of depressive disorders, based on the results of research carried out in 2014–2019.

Physical activity and the risk of depressive disorders

Research focused on the analysis of relationships between physical activity and mental health confirm that higher levels of physical exercise are associated with a lower risk of depressive symptoms, especially in the case of younger people [15, 69, 70].

There is much empirical evidence that exposure to chronic childhood stress can lead to behavioral and neuronal deficits in adulthood that are associated with increased levels of anxiety and depression. Based on the animal model, it was proven that regular physical activity is a protective factor against the harmful effects that chronic distress has on the prefrontal cortex structure. Moreover, aerobic training has a positive morphological effect on neurons in the prefrontal cortex in animals not exposed to chronic stressors. These observations provided important evidence that pre-puberty exercise protects against these neuronal and behavioral disorders that are a consequence of distress [71].

In addition, it was proven that aerobic training can modify the volume of the hippocampus, which is lower in patients with depressive disorders than in healthy people. Numerous evidence indicate that the experienced stress inhibits the signaling of neuronal remodeling processes associated with the production and activity of BDNF, which consequently weakens structural plasticity, including neurogenesis and dendritic remodeling within the hippocampus [15, 69, 72]. There are also indications that increased and prolonged release of cortisol in response to psychological stress can cause permanent neuronal damage to the hippocampus in its structures responsible for the operation of the feedback mechanism that controls the functioning of the hypothalamic-pituitary-adrenal axis. Excessive activation of this axis leads to cognitive disorders and it intensifies the symptoms of depression, while the cycle of biochemical changes activated under the influence of skeletal muscle activity prevents the negative effects of stress by increasing the production of BNDF [15, 69, 72, 73]. It was proven that BNDF stimulates cell differentiation and repair processes, and supports the activity of neurons as well as the formation of memory pathways, which has a positive effect on affective and cognitive functioning as well as daily activities of a patient [74, 75]. Furthermore, there were significant relationships between the abnormal BDNF levels, Trk-B receptor dysfunction, the lack of BDNF–Trk-B signaling and the occurrence of not only depression, but also schizophrenia, epilepsy and Alzheimer's and Huntington's diseases [76]. Based on the animal model, it was confirmed that BDNF expression stimulated by physical exercise plays a protective role against the occurrence of behavioral symptoms of affective disorders [13], while some empirical papers emphasize that the desired effects of physical activity on mental health depend on its type and weekly frequency [77, 78]. The meta-analysis conducted by Beserra et al. [78] demonstrates that aerobic exercises performed five times a week are the most effective [78].

Research aimed at verifying whether the relationships between physical activity, hippocampus volume and mood are already noticeable in the development phase preceding puberty, carried out on a sample of 4,191 children aged 9 to 11 years, demonstrated that regardless of sex, practicing sports correlated positively with the volume of the hippocampus, whereas in boys the volume of the hippocampus correlated with mood and acted as a mediator of the relationship between physical activity and mood [15]. Regardless of gender, the importance of physical exercise in the primary prevention of depressive disorders was also confirmed in a representative population of 6,497 children born in the years 2000–2002 in Great Britain. It should be added, however,

that intervention that included a combination of moderate and intense 60-minute daily physical exercises, during the five-year observation period brought the desired effects only to 10% of the respondents [63, 79]. In turn, a meta-analysis of random effects devoted to the assessment of the impact of physical activity taken in childhood and adolescence on the risk of symptoms characteristic of depressive disorders, in which data from 89,894 persons were analyzed, demonstrated that aerobic training plays a protective role against the occurrence of depressive symptoms in the future, and also alleviates the course of the current disorder [80].

The prophylactic effect of physical activity was also confirmed in studies on the prevention of postpartum mood disorders. Their aim was to verify whether physical activity undertaken during pregnancy can act as a protective factor against their occurrence in the postnatal period. The conducted meta-analysis included the results of empirical studies that assessed the impact of any type of physical activity during pregnancy on the occurrence of symptoms of depression in the first year after giving birth. Seventeen studies conducted in a total population of 93,676 women were subjected to analysis. The meta-analysis of random effects demonstrated a significantly lower severity of symptoms of postpartum depression in women who were physically active during pregnancy, as compared to subjects who did not perform any aerobic exercise, and the obtained relationship was the strongest in the case of women participating in programs involving physical activity [81]. Comparable conclusions were also drawn from the research conducted on a sample of 15,538 women, whose aim was to estimate the risk factors of postpartum depression. Participants were examined using *the Pregnancy Physical Activity Questionnaire* (PPAQ), *the Beck Depression Inventory* (BDI) and the Postnatal Depression Scale. In the adjusted predictive models, lower levels of activity in the household and a sedentary lifestyle in the third trimester of pregnancy were associated with an increased probability of occurrence of symptoms of postpartum depression, while in the first trimester of pregnancy there were no significant relationships between physical activity and depressive disorders [82].

The significance of physical activity in depressive disorder treatment

Numerous research works highlight the important role of physical activity in the treatment of depressive disorders [83–85]. The beneficial effect of 24-week interval training in the reduction of mild depressive symptoms (examined using *the Beck Depression Inventory-I*) was observed in a population of 36 women who were not treated for any somatic disorders. In addition, it was observed that the anxiety of the respondents, understood as a transient and situational condition, was reduced. However, it has not been shown that the intervention contributed to reducing the trait-anxiety of the subjects that, as a relatively stable feature of intrapsychic human functioning, is not subject to dynamic changes over such a relatively short period of time. The above-mentioned dimensions of anxiety were measured using the STAI [64, 86]. Furthermore, Gerber et al. [87] conducted research focused on three goals. First of all, they aimed at

determining whether the initial levels and the change in objectively assessed cardiorespiratory fitness and subjectively perceived efficiency resulting from the implemented intervention explain the severity of depressive symptoms, well-being and the quality of sleep. The second goal of the researchers was to verify whether exercise modality – interval training compared to aerobic training – predicts the severity of depressive symptoms, mood and sleep quality, and the third – to check whether affective reactions during and after physical exercise condition the severity of depressive symptoms, mood and sleep quality. The research subjects were a sample of hospitalized patients diagnosed with major depressive disorder. The studied population consisted of 53 adults with a diagnosis of depression, who were randomly assigned to two groups. The first one participated in interval training, and the second in aerobic training. The tests were carried out before the program and after four weeks of physical exercise. Regression analyzes demonstrated that an improvement in cardiorespiratory fitness following the intervention was associated with fewer depressive symptoms and better well-being. In addition and regardless of the form of the training, the improvement in perceived fitness was associated with a better sleep quality and improved mental condition, and positive changes in cardiorespiratory fitness and perceived physical fitness co-occurred with favorable changes in the severity of depressive symptoms, well-being and sleep quality [87].

Comparable effectiveness of interval and physical exercises in the prevention of depressive disorders was also confirmed in other studies carried out on an adult population diagnosed with major depression. Patients were randomly assigned to two 25-person groups, which then participated in 12 training sessions. The first group was subjected to interval training and the second group was subjected to aerobic training. The comparative analyzes demonstrated that the analyzed groups of patients in question did not differ in terms of desired changes (assessed as differences between measurements carried out prior to and after the program) regarding motivation for physical activity, affective states, circulatory and respiratory efficiency, and the severity of depressive symptoms. This observation seems to be important for patients who, based on personal preferences on the type and intensity of exercise, will be able to make free choices between different methods of physical activity [77], which is particularly important in the case of men diagnosed with depressive disorders who, in comparison with women, exhibit lower motivation to undertake actions conducive to reducing the symptoms of distress and symptoms typical of depression [88].

In the context of the analyzed issues, evaluation studies of a 12-week program stimulating physical activity implemented in the adult population treated with pharmacological treatment for depressive disorders are also interesting. The intervention allowed beneficial changes in the thickness of the anterior cingulate cortex, which is the structure of the limbic system responsible for the regulation of behaviors and some emotional states, as well as an area important for memorizing and motivational processes. It was observed that the group of patients treated pharmacologically and completing supervised aerobic training benefited more than those receiving only

medication. The conducted exploratory analyses confirmed the relationship between improvement in efficiency and the increase in cortical thickness in the anterior cingulate cortex of the patients and at the same time allowed researchers to conclude that – regardless of the age of patients – the combination of pharmacological treatment and physical activity brings the desired neuronal benefits in the brain area responsible for mood [83]. Comparable effects were observed in the population of people aged over 60 years. Research conducted among 2,604 participants found that involvement in moderate or intense, but also sufficient (150 minutes/week) physical activity is a factor protecting against symptoms of depression and weakening of cognitive processes and acts as a mediator of relation between depressive disorders and cognitive functions [84].

Furthermore, in the studies evaluating the effectiveness of physical exercise and cognitive behavioral psychotherapy in the treatment of symptoms of acute depression in hospitalized persons, it was proved that a 30-minute walk combined with individual psychotherapy brings greater benefits than standard psychotherapeutic treatment [89]. However, this is not fully confirmed by the research results of Knapen et al. [90], which indicate that in the course of mild and moderate depressive disorders, the effect of physical exercise is comparable to pharmacological treatment and psychological therapy, and in the case of an acute depressive episode, physical activity promotes better treatment results [90]. The significant efficacy of aerobic exercises in the treatment of affective disorders was also positively verified in studies aimed at determining whether a 24-week treatment of depressive disorders with small doses of sertraline (50 mg daily), supplemented with physical activity will result in higher therapeutic results than standard pharmacotherapy. The researchers searched for answers to the research question in data collected in three groups of primary healthcare patients (aged 60 and over) suffering from severe depression. The first group underwent treatment with the aforementioned drug and a 24-week intensive aerobic training, the second group received sertraline and was involved in moderate exercise for the same period, while the third group of participants of the program was treated only pharmacologically. The results of 121 patients were included in the analyzes. After completing the study, 81.0% of the subjects from the group treated pharmacologically and participating in intense aerobic training, 75.0% of people in the group using sertraline and performing moderate physical exercise and 45% of participants in the group taking only sertraline achieved remission, with depressive symptoms resolving quicker in the group of patients treated pharmacologically and participating in intense aerobic training than in those treated with sertraline, and thus confirming that physical exercise is an effective supplement to the antidepressant therapy of seniors [91].

Another research on the major depression therapy in the elderly was focused on determining factors moderating the effectiveness of a 24-week treatment of disorders by means of sertraline and aerobic training. Patients received small doses of sertraline (50 mg daily) and were involved in physical activity. The highest probability of achieving remission was related to age – from 75 years upwards (effect size 0.32), multi-drug treatment of other disorders (effect size 0.35), normal cardiorespiratory fitness (effect

size 0.48), psychomotor condition (effect size 0.49), as well as low anxiety (effect size 0.30). The acquired data show that in this age group the integrated form of therapy for major depressive disorders, based on pharmacological treatment and physical activity, which is adapted to specific clinical features of patients, is highly effective [92].

Significant improvement of the mood after intervention in the form of physical exercises is also confirmed by the results of a meta-analysis aimed at assessing the role of aerobic exercises in the treatment of postpartum depressive disorders. The acquired data show that both supervised and group physical exercises, physical activities selected by the patients themselves, aerobic training combined with interventions motivating to undertake physical effort, as well as traditional methods of treatment – pharmacotherapy and psychotherapy, proved to be comparably effective. In addition, regardless of sociodemographic factors, the effectiveness of physical exercise in reducing symptoms was high [93]. The effectiveness of the completed exercise cycle (Qigong training) was also confirmed in the population of women experiencing intimate partner violence. The research involved 136 participants of the 22-week program and 135 women who qualified for the next intervention cycle. These persons were simultaneously part of the control group. Based on the conducted analyzes, it was found that after six weeks of the program both the perceived level of stress and the severity of depressive symptoms were significantly lower in the intervention group than in the control group [94], which seems to coincide with the conclusions from the meta-analysis by Guo et al. [95], which demonstrates that Qigong exercises used in the therapy of depressive disorders bring significant benefits. Used both as an independent form of treatment and one integrated with other methods of treatment, they reduce the severity of symptoms of depression as well as the risk of subsequent episode of the disorder [95]. It was also proved that in addition to improving mental health, they alleviate the course of various psychosomatic disorders and minimize the risk of their occurrence. The results of the meta-analysis conducted jointly on a sample of 1,282 seniors with symptoms of depressive disorders indicate that the applied exercises reduced their severity and also contributed to the improvement of the physical fitness of the respondents [96].

The obtained data seem to be of particular importance in the health prophylaxis addressed to the elderly because this period of life is associated with an increased risk of many health issues [97], including depressive disorders. On the other hand, undiagnosed or incorrectly treated depression reduces life expectancy, exacerbates the course of many somatic diseases, and also generates higher healthcare costs. It should also be emphasized that in the case of elderly people depressive disorders are the main cause of suicide [2, 98–100]. The key factors determining the genesis and course of depression of people over 60 include sedentary lifestyle and poor eating habits, and in particular a diet low in omega-3 fatty acids [2, 101, 102]. The results of the meta-analysis of Farioli Vecchioli et al. [2] confirmed the effectiveness of interventions promoting physical activity combined with a diet containing the optimal dose of these acids in the treatment of seniors' depression.

The significance of physical activity in the therapy of depressive disorders in the course of somatic diseases

Studies aimed at assessing the relationships between moderately intense aerobic exercise and mood disorder coexisting with mild cognitive impairment in the elderly demonstrated that, as a result of the intervention, participants have achieved significant improvements in the functioning of cognitive processes and quality of their life related to health. It was also noticed that the completed training cycle with the mediation of cognitive functioning brought the expected benefits in the form of reduction of the symptoms of depression and improvement in the sleep quality, which also underlined the mediating role of the aerobic exercise program in relation to the cognitive and affective areas of the analyzed population [103].

Furthermore, it was demonstrated that in a group of oncological patients after treatment with chemotherapy, the use of which may contribute to cognitive decline and the occurrence of depressive symptoms, moderate and intense aerobic training reduces the risk of this type of disorders [104] and, apart from psychotherapy, forms an effective method of non-pharmacological treatment of depressive symptoms in this group of patients [105]. The obtained data seem to be particularly important in the context of the health situation of oncological patients, as they are usually less physically fit than their peers already before the treatment, and during chemotherapy and up to five years after the end of their treatment their physical activity is below the reference levels, which is often associated with the occurrence of depressive disorders that can make physical exercise to be perceived as requiring considerable effort and very exhausting, which in turn may reduce the probability of their regular undertaking. This type of dependence was confirmed in the studies of women following breast cancer surgery, and in particular in the case of patients demonstrating the increased severity of depressive symptoms. Compared to women who did not show any symptoms characteristic of depressive disorders, patients diagnosed with major depression demonstrated a greater increase in physical strain (assessed using *the Borg Scale*), while no significant differences in the heart rate ranges were recorded [106].

The benefits of physical activity for mental health are also confirmed by observational studies on a population of adolescents treated for multiple sclerosis. Four-year observations of 182 people confirmed that systematic physical activity is inversely related to the severity of depressive symptoms experienced by young people and the level of fatigue resulting from the disease [107]. The results of the meta-analysis by Herring et al. also lead to similar conclusions, suggesting that aerobic training is conducive to reducing the severity of depressive symptoms in adults treated for multiple sclerosis. It was also proved that the obtained effect depends on the level of fatigue experienced during the exercises. Excessive levels of fatigue decreased the positive effect of physical exercise on the mental health of the patients [108]. However, in the group of patients treated for epilepsy, the use of aerobic training interventions contributed to achieving the desired effects in reducing the level of perceived symptoms of depressive disorders, but no significant changes in the frequency of seizures and

perceived quality of life resulting from the disease [109]. In turn, in a population of 52 patients over 80 years, diagnosed with early stage Parkinson's disease, a linear regression analysis corrected for variables such as gender, age and level of education showed that the daily physical activity of seniors measured with the accelerometer was at a very low level and was not associated with the severity of symptoms characteristic of depressive disorders [65]. The desired effects in reducing the severity of depressive symptoms were also not confirmed in the meta-analysis which included the results of studies of 121 people diagnosed with Huntington's disease who participated in the interventions involving a combination of supervised and independent physical activity in the period from 8 to 16 weeks [66].

In the context of the analyzed issues, the results of the randomized pilot study carried out after the completion of the cardiological support program which was directed to patients with ischemic heart disease also seem interesting. The intervention was carried out via text messages sent to participants' mobile phones four times a week for six months. Its task was to maintain the motivation of patients for regular physical activity and education concerning healthy lifestyle. The evaluation carried out after six months showed that the severity of depressive symptoms (as examined using *the Patient Health Questionnaire*-9 – PHQ-9) was lower in the population of people participating in the project than in the control group, with the frequency of the analyzed symptoms in the intervention group amounting to 6.3% in total, compared to 24.6% in the control group [110].

The high efficiency of aerobic training in the treatment of depressive disorders of people diagnosed with various somatic disorders is also emphasized by the results of a meta-analysis which included data from 24 studies conducted on a total of 4,111 patients. Its aim was to verify whether physical exercise allows to achieve higher therapeutic effects in relieving depressive symptoms than standard medical procedures. The analyses included, comparable in number, patients with a clinical diagnosis of mild and moderate depression, as well as people who reported the occurrence of single symptoms characteristic of depressive disorders. Based on the obtained data, it was found that aerobic training contributed to reducing the symptoms of depression to a greater extent than traditional methods of treatment, and the observed effect was particularly pronounced in cardiac patients [111].

Furthermore, the effectiveness of interventions based on physical activity was positively verified during the evaluation of the program addressed to overweight or obese women treated for polycystic ovary syndrome, where the correct body mass is essential for treatment. Training interventions combined with a properly balanced diet took place in outpatient centers of clinical trials, and lasted 2 to 8 months, depending on the individual needs of the participants. After the end of the program, the results were compared with measurements taken prior to the start of it, proving that 63% of the participants reduced their body mass, and the recorded levels of depressive symptoms were also lower [112].

Discussion

Estimated data indicate that only one-third of people who display symptoms typical of this nosological unit of classification use pharmacotherapy and psychotherapy. This justifies the need to search for new methods of prevention and treatment of depressive symptoms. The wise use of physical activity raises some hope. Despite the fact that its positive impact, not only on the mental health, was grounded in the scientific literature [96, 113–115], one should also refer to the results of the research from which slightly different conclusions were drawn [63–66].

Terashi et al. [65] observed no relationship between physical activity and the severity of senior depressive symptoms in early Parkinson's disease. These observations seem to be understandable in the light of the results confirming that the daily physical activity of the subjects was classified as insufficient in relation to WHO recommendations, which could at the same time significantly limit its preventive role [60, 65]. It is interesting, then, whether interventions based on a cycle of supervised and adapted to these patients' health physical exercises would lead to the opposite conclusions.

The need to include this type of recommendations in the training program is also indicated by the authors of the meta-analysis including data from five randomized and controlled studies carried out in the group of people suffering from Huntington's disease, in which no beneficial effect of physical activity on the mental functioning of patients has been demonstrated [66].

The positive effects of physical exercises were observed especially in groups of people at risk of cardiac disorders, chronic musculoskeletal pain, diabetes, obesity, cognitive impairment, multiple sclerosis, Parkinson's disease, and cancer. Regular physical exercises reduce distress and stimulate brain neuroplasticity [116, 117].

Many contemporary authors agree that this effect is best explained by the physiological mechanism consisting in re-tuning the kynurenine pathway under the influence of muscle activity [29, 30, 55, 118–122]. The activity of transaminases that transform neurotoxic kynurenine into neuroprotective kynurenine acid, i.e., kynurenine transaminases, is stimulated by an increased skeletal muscle activity. The mechanism of this enzymatic stimulation has been shown to be mediated by the protein PGC-1α1 (peroxisome proliferator-activated receptor gamma coactivator 1-alpha), whose expression increases under the influence of muscle activity [123]. It is a transcriptional coactivator that plays a key role in stimulating mitochondrial biogenesis, fatty acid oxidation and angiogenesis within muscles, which prevents their disappearance [124]. Physical exercises, especially endurance exercises, increase the PGC-1α1 expression, supporting skeletal muscle adaptation to exercise [125, 126].

It should be emphasized, however, that empirical research indicates significant individual differences in this respect, which means that there are people who 'respond' and 'do not respond' to the same type of physical training [79]. This factor might have been one of the leading reasons for achieving the desired effects of the exercise cycle in the primary prevention of depressive disorders in only one-tenth of the examined

children [63]. Therefore, the question arises, which variables should be taken into account so that the planned intervention actually has a preventive role?

It has been observed that aerobic training brings the desired neural changes only when the exercises are adapted to the needs of the trainees in terms of form, intensity, duration, and frequency, i.e., to the level of their cardiorespiratory capacity and general health. Therefore, the recommendations for this type of preventive training programs should be individualized, which in turn will result in maximizing their benefits and minimizing potential health loss [79].

This seems to be particularly important in the context of the research confirming that excessive and intense physical activity may lead to oxidative stress, which is associated with overproduction of free radicals. Consequently, free radicals can cause damage to many internal organs, and also cause chronic fatigue as well as reduced immunity and disorders of the body's homeostasis. A direct consequence of the disturbed balance between reactive oxygen species (ROS) and antioxidants is also the increased risk of developing many diseases, e.g., cardiovascular diseases, gastrointestinal tract diseases, cancer, Parkinson's and Alzheimer's disease, as well as depressive disorders [67, 68]. Should one take physical activity in spite of the significant health risk?

In response to this question, it is worth referring to the studies confirming that optimal physical effort results in an increase in the body's antioxidant potential. It has been proven that the body's defense against free radicals is higher in people doing sports than in the inactive ones. In addition, oxidative stress caused by exercise is lower in physically active people than in those who lead a sedentary lifestyle because training stimulates the body's adaptation to the effects of free radicals and thus counteracts their negative consequences. This indicates that physical activity – if adequately adapted to the individual health condition – is a factor conducive to maintaining a balance between oxidants and the body's antioxidant capabilities, which is also beneficial for people who reveal symptoms typical of depressive disorders [67, 68, 127, 128].

In the absence of specific medical conditions for this group of patients, WHO recommends physical activity three times a week for about forty-five minutes [3, 60]. It is important, however, to emphasize the fact that not all patients (and in particular those with a severe form of depression) will be able to take it. A patient with a mild depressive episode will have moderate difficulties in functioning at work and carrying out various types of activities, but most likely he/she will not completely withdraw from them. In contrast, the essence of a severe depressive episode, except in a few cases, is the complete exclusion of a person from previous activities [3], which is why hasty motivation of patients to take physical activity can have extremely negative effects associated with a risk of increased guilt, which can activate suicidal thoughts and behaviors [1, 3, 61, 62].

It should also be emphasized that physical activity in the case of depression can only be a complementary method to pharmacotherapy and psychotherapy, while for healthy people it is an effective form of primary prevention of many somatic diseases as well as depressive disorders. The desired effects of physical exercise were noted in

various age groups, which suggests that it is advisable to consider including them, in a form adapted to the participants' state of health, in the intervention programs being developed [96, 113].

Conclusions

The analysis of the contemporary empirical work allows the following conclusions to be drawn:

- in the absence of health contraindications, regular exercise may be a form of prevention of depression;
- systematic physical exercises should be treated as a complementary technique to pharmacological treatment and psychotherapy of depressive disorders, including those occurring in the course of somatic diseases;
- when recommending physical activity to people suffering from depression, it is necessary to take into account that the hasty motivation of patients with a severe course of the disorder can activate a sense of guilt, suicidal thoughts and behaviors;
- physical activity, both as a form of primary prevention and as a complementary method to pharmacotherapy and psychotherapy, in terms of intensity, duration and frequency should be adapted to the individual capabilities and health of the trainees.

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