24. Depression

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Summary

Physical activity has a positive effect in depression with respect to both preventing depressive episodes, and acute and long-term treatment of episodes that do occur. The physical training is beneficial when conducted parallel to customary treatment with drugs and therapy. Although many studies have methodological problems and there is still a shortage of long-term studies, there is clear scientific support for using physical training in the acute treatment of mild and moderate depression and as a means to reduce the risk of relapse. A preventive effect has been shown in epidemiological studies and long-term studies followed up to 10 years. Other health effects of physical activity are also of importance, as depression often covariates with physical diseases. Physical activity holds great benefit both for the individual and for society.

Definition

Major depression is common and becoming more prevalent. The lifetime prevalence in different countries and different studies ranges between 6 and 20 per cent. One Norwegian study, published by Kringlen and colleagues in 2001, found a lifetime prevalence of 17.8 per cent (1). In 2000, WHO ranked depressive disorders as the fourth largest health problem in the world. A significant difference exists between the genders, with depression in women ranking fourth in total disease burden, and only seventh in men (2).

Diagnostic criteria

From a diagnostic standpoint, depression belongs to the group of mental illnesses called mood disorders and is divided into two main groups: unipolar affective disorders with only depressive episodes, and bipolar affective disorders with both depressive episodes and hypomanic and/or manic episodes. In comparison to unipolar disease, bipolar disease is rare and will not be discussed here. Research is in general lacking when it comes to physical activity and bipolar disease. Dysthymia is a milder form of depression but the condition is often chronic, lasting two years or more, and is not addressed here either.

Depression demonstrates a significant comorbidity with other psychiatric disorders, above all anxiety disorders, as well as physical diseases where cardiovascular disease is prominent.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV, which is used world-wide, the following criteria apply to *major depression*:

A: Five or more of the following symptoms have been present during the same 2-week period and represent a change in the person's condition. At least one of the symptoms, 1) depressed mood or 2) loss of interest, must be present.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g. feel sad or empty) or observation made by others (e.g. appears tearful).
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day, as indicated by either subjective account or observation made by others.
3. Significant weight loss (when not dieting) or weight gain (e.g. a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
4. Sleeping disturbance (insomnia or hypersomnia nearly every night).
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Feeling of fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (as indicated either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or have a specific plan for committing suicide.

The symptoms are not better explained by other psychiatric conditions and must cause clinically significant suffering or impaired function at work, in social situations or in other important respects.

Diagnostic procedure

DSM IV and ICD 10, with similar criteria are used in diagnostics in Norway and Sweden. The diagnosis is based on these criteria, which are descriptive. The rating scales are used mainly to measure the severity of the depression. There are no biomarkers for the disease.

Cause and risk factors

There is no simple causal relationship and genetic predisposition in not particularly strong. One frequently used model is that of stress and susceptibility. For the individual, negative stress causes depression, but individual susceptibility varies. Risk factors that can produce increased vulnerability include separation in childhood, psychological trauma, abuse and a number of somatic factors. Losses of varying nature are common as a precipitating factor. How lifestyle, for example, physical inactivity, affects depression is discussed in studies that are presented below.

Pathophysiology

There is no single pathophysiology. In some cases, a pathological increase in hypothalamic-pituitary-adrenocortical axis activity can be found as a sign of stress in ongoing depression. A normalising usually occurs with recovery. Because antidepressant drugs improve the function of neurotransmitters such as serotonin, noradrenaline and dopamine, one theory is that depression is caused by disturbances in these systems. New research has shown cell death in certain parts of the brain, especially the hippocampus, in depression.

What does the disease lead to?

Depression produces considerable suffering for the person affected and others close to him or her. It also leads to reduced levels of function at work and socially. Depression is a dominating diagnosis when it comes to sick leave and sick pay for mental illness, and is the major cause of completed suicide.

Treatment principles

Pharmacological treatment with modern antidepressant drugs and several forms of psychotherapy, including cognitive therapy and interpersonal therapy, have a documented effect. To prevent repeat episodes, antidepressant drugs and treatment with lithium are used. Improvement of the patient's condition is not always complete and a combination of different drugs as well as the use of electroconvulsive therapy (ECT) may be needed in severe cases. The use of light therapy for winter depression is widespread in Sweden and Norway but there are different opinions on the scientific basis for this.

As with other disease conditions, non-specific treatment options such as psychosocial support and rehabilitation measures are often needed.

Effects of physical activity

Acute effects

As early as 1905, Franz and Hamilton published the first report describing how moderate physical activity led to significant improvement in the cognitive, physical and emotional conditions of two patients with severe depression (3). In 1984, McCann and Holmes (4) showed that running had a significantly better effect than relaxation and no treatment at all in a group of students with mild to moderate depression. A few years later, Martinsen and colleagues at the Modum Bad centre in Norway published results in which they found that depressed patients admitted to hospital had significantly better effects from physical training three times a week for nine weeks, than from occupational therapy for the same amount of time (5, 6).

In recent years, a number of important studies have verified earlier findings of a positive acute effect from physical training in depression. In 1999, Blumenthal and colleagues published a study in which 156 patients aged 50–77 years were randomly divided into three treatment groups. The trial lasted for four months. Group 1 was treated with sertraline (Zoloft), 50–200 mg per day. The second group received exercise training in the form of 30 minutes of walking and jogging, 3 times a week. The third group received both sertraline and exercise training. They found no significant difference in treatment effect between the three groups, and all showed a good effect from the treatment (7).

In 2005, Dunn and colleagues published a long-awaited dose-response study (8). Eight patients were assigned to one of four groups. Group 1 received exercise treatment with an energy expenditure of 7 kcal/kg body weight/week, 3 times a week; Group 2 – an expenditure of 7 kcal/kg body weight/week, 5 times a week; Group 3 – 17.5 kcal/kg body weight/week, 3 times a week; Group 4 – 17.5 kcal/kg body weight/week, 5 times a week; and Group 5 – stretching, 3 times a week, as a placebo. Groups 3 and 4 received the exercise intensity commonly given in public health recommendations, while groups 1 and 2 received low intensity exercise treatment. The treatment lasted for 12 weeks.

They found that the depression score (according to the Hamilton Depression Rating Scale, HDRS) fell by 47 per cent in groups 3 and 4, but by only 30 per cent in groups 1 and 2, and by 29 per cent in Group 5. The conclusion was that the exercise intensity usually recommended had an obvious therapeutic effect in mild to moderate depression, while lower intensity was equivalent in effect to the placebo (8). In 2006, Trivedi and colleagues published an article in which 17 patients who had not become well with antidepressant drugs received exercise training for 12 weeks, continuing with the same medication during that time. The patients included in the study showed a strong positive effect with greatly reduced depression scores (9). This pilot study shows the possibility of using exercise to increase the effect of antidepressant drugs in depression. In a randomised controlled study the same year, Knubben and colleagues showed that relatively strenuous daily jogging for 10 days, up to 80 per cent of maximal heart rate, yielded significantly better therapeutic effect than placebo (stretching and relaxation) in a group of admitted patients with moderate to deep depression (10).

Long-term effects

When following up the above-mentioned patients from Blumenthal and colleagues' study, Babyak and colleagues found that, after an additional 6 months, those who received only exercise training had a significantly lower risk of further depressive episodes than those who received only sertraline. A significantly higher percentage of those who received the exercise training were also in full remission at 10 months after the study start (11).

There are also a number of studies with longer follow-up periods. Three recently published prospective studies show a link between physical activity and depression. Harris and colleagues followed 424 depressed patients for a period of 10 years. They found that more physical activity was associated with less depression and counteracted the effect of physical illnesses and negative stress factors on the depressive symptoms (12).

Meta-analyses

In a meta-analysis from 1998, Craft and Landers looked at 37 articles and found that exercise was better than no treatment at all for depression. No difference was found between different types of exercising. The effect was, however, better if the treatment lasted more than 9 weeks, compared to less than 8 weeks. According to the authors, the best effect was found for moderate to severe depression (13). In a meta-analysis published in 2001, Lawlor and Hopker found 14 studies whose methodologies merited inclusion, though, according to the authors, all of which also did have methodological weaknesses. However, they found a total effect of 1.1, which is satisfactory. The conclusion was nevertheless that it was not possible to say with certainty whether exercise had an antidepressant effect (14). In an article from the same year, Dunn and colleagues conducted a review of 18 studies. Eight of these found a 50 per cent reduction in depressive symptoms during the acute phase. In seven studies with follow-up periods ranging from 3 to 21 months, they were able to demonstrate that the effect was retained with continued exercise. These authors also draw attention to methodological problems, and call for a controlled dose-response study, which they later conduct themselves (see above) (15).

Meta-analysis makes it possible to draw conclusions from a larger group of patients than provided by individual studies. A disadvantage is that, if demands with respect to the quality of the included studies are high, a lot of data from somewhat smaller, well-conducted studies gets left out.

Epidemiological studies

As early as 1988, using data from Canada and the US, Stephens found that a high level of physical activity correlated to a low level of anxiety and depressive symptoms (16). In a German population group, Weyerer found that those who reported no physical activity ran three times the risk of developing moderate to severe depression as those who reported being physically active (17). Three Finnish studies also found similar results (18–20). A well-known study is that of Paffenbarger and colleagues from 1994, in which they followed Harvard students for a period of 23–27 years, retrospectively, and compared the amount

of physical activity and exercise to depressive illness. The conclusion was that those who engaged in regular physical exercise had a lower risk of developing depression. The effect was clearly dose-dependent (21). There are also studies that show no link between physical activity and reduced depression. One such study is a study published by Cooper-Patrick and colleagues with a 15-year follow-up (22).

Wiles and colleagues show in a 2007 report from the Caerphilly Study in Wales that there is a relation between a high level of physical activity in leisure time and at work, and reduced incidence of mental disorders (mainly depression and anxiety), at a 5-year follow-up but not after 10 years (23). An interesting study from Japan by Yoshiuchi and colleagues measured the physical activity of 184 individuals, aged 65–85 years, with an accelerometer and pedometer, for one year. They found a significant negative relation between physical activity and depressive symptoms (24).

There are obvious weaknesses in these types of studies, both regarding the validity of the data and the causal relationships, especially in cross-section studies. Is it the physical inactivity that leads to depressive symptoms or is it the depression that leads to inactivity. There may also be a third factor that explains the relationship. In longitudinal studies, a population is followed over time. In this case, one can start with healthy individuals, identify those who become ill, and observe whether there is a link between the level of physical activity and disease tendency. In these studies, the causal relationships are clearer. A weakness of such studies, however, is the selection phenomenon. It is possible that people who are physically active have more resources and that they would fare best regardless of whether or not they were physically active. In order to control this phenomenon, randomised controlled intervention studies are required.

Plausible hypotheses of functional mechanisms

Physical activity involves a change in behaviour, a behaviour modification. In depression, a person's behaviour is often characterised by passiveness, withdrawal and isolation. Changing behaviour can affect thoughts and emotions, and in doing so contribute to reversing depression (25). Cognitive behaviour therapy has also been shown to produce a positive effect in the treatment of depression. Physical exercise has been shown to encourage positive thoughts and emotions, increased confidence in coping, and increased self-confidence and capacity for self-control. Salmon (26) discusses another possible psychological mechanism. His hypothesis is that one becomes more resistant to stress through physical exercise. This could be linked to reduced activity in the hypothalamus-pituitary-adrenocortical axis, whose function is often pathologically increased in depression.

Another possibility is that it is the improved physical functional capacity gained through exercise that is the mechanism of action. However, there does not appear to be clear connection between the improvement in physical capacity and reduction of depression in depressed patients (27). Physical activity improves synthesis and metabolism of the neurotransmitters noradrenaline, serotonin and dopamine in test animals (28). Definite proof that this is the case in humans is not available yet, however, though it is a plausible hypothesis of an important underlying mechanism. A popular hypothesis is that the effect

of exercise is due to an increased concentration of endorphins, that is, the body's own morphine. Both rat and human trials support this hypothesis (29, 30), but more research is needed on the effect of endorphins in the brain of patients being treated with physical exercise.

An exciting possibility is also that exercise dramatically helps in cell regeneration in some parts of the brain, especially the hippocampus, which is important for learning and memory. Researchers have found a lower hippocampal volume in depressed individuals (31), and that treatment with antidepressant drugs yields regeneration of cells there (32). A research group at Karolinska Institutet have recently found that the antidepressive effect seen in depressed rats that were allowed to run is linked to hippocampal cell proliferation, and that the cell proliferation when they run is as high as when being treated with antidepressant drugs (33).

Indications

1. Physical activity and exercise can be used to reduce the risk of developing depression.
2. Exercise training can be used as a treatment for clinical depressive disorders. The training is conducted parallel to other antidepressant treatment such as medication and/or psychotherapy.
3. Exercise training can be used to reduce the risk of further depressive episodes both during the first year and later on.

Prescription

Type of training	Intensity	Frequency (times/week)	Duration (min.)
Aerobic training Minimum of 9 weeks	Moderate to high (13–15; Borg RPE scale)	2–3	30–45
Strength training Minimum of 9 weeks	8–10 exercises 1–3 sets of 8–12 reps	2–3	30–60

* RM = Repetition Maximum. 1 RM corresponds to the maximum weight that can be lifted through the entire exercise movement one time.

Functional tests/Need for health check-ups

A pilot project on exercising against depression (in Swedish "Motion mot depression") has been conducted for a total of four semesters in cooperation with the Psychiatric Care Team from northwest and central Stockholm and the Swedish School of Sport and Health Sciences (Gymnastik och idrottshögskolan, GIH).

The following tests and instruments were used:

- Depression-rating using MADRS (34) or PHQ-9 questionnaire (35).
- Fitness/endurance tests using Åstrand's exercise bike test (36) or the 6-minute walk test (37).
- Abdominal and hip flexor muscle test (38) and back-lift endurance test (39).
- Leg strength test and shoulder musculature test.
- Health survey from GIH on perceived health and lifestyle habits such as physical activity, diet, smoking, alcohol, sleep, and time for recreation.

The severity of the depression should be rated before and after treatment using an appropriate rating scale. If possible, the and endurance tests should be performed before and after completed treatment.

Interactions with drug therapy

One experience from treatment with older antidepressant drugs, so-called tricyclic antidepressants, is that they can make exercising more difficult due to their side-effects, above all in the form of increased heart rate, dry mouth and sweating. Modern antidepressant drugs have a lot fewer side-effects and are judged to affect exercise to a very small degree.

Contraindications

Underweight patients with diagnosed eating disorders should not be prescribed exercise for depression.

Risks

As with other indications, there are risks with certain somatic disorders.

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