

Therapeutic Impact of Exercise on Psychiatric Diseases

Guidelines for Exercise Testing and Prescription

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Abstract

Aerobic exercise seems to be effective in improving general mood and symptoms of depression and anxiety in healthy individuals and psychiatric patients. This effect is not limited to aerobic forms of exercise. There are almost no contraindications for psychiatric patients to participate in exercise programmes, provided they are free from cardiovascular and acute infectious diseases. However, very little is known about the effects of exercise in psychiatric disease other than those in depression and anxiety disorders. A few reports indicate the need for controlled investigations in psychotic and personality disorders.

Unfortunately, no general concept for a therapeutic application of physical activity has been developed so far. Reliance on submaximal measures is highly recommended for fitness assessment. Monitoring of exercise intensity during training sessions is most easily done by measuring the heart rate using portable devices (whereas controlling the exact workload may be preferable for scientific purposes). Appropriate pre- and post-training testing is emphasised to enable adequate determinations of fitness gains and to eventually allow positive feedback to be given to patients in clinical settings.

Cross-sectional^[1-8] as well as longitudinal studies^[9-17] in healthy individuals suggest a favourable influence of physical training on different aspects of human mood. However, so far there is no convincing evidence for the causality of exercise for these improvements, for example, a large influence of suggestive information on the outcome of training trials was demonstrated.^[18] The biochemical 'link' – that is the neurotransmitter actions or hormonal influences – is still lacking.

Much less is known about the clinical effectiveness of physical training in patients with manifest psychiatric disorders. A few studies^[19-30] suggest a beneficial effect of exercise on the clinical course of anxiety and depressive disorders, but very little is known about the impact of regular physical activity on psychotic diseases (schizophrenia, bipolar disorder) and personality disorders.

There are indications that, in theory, most psychiatric patients would experience beneficial effects from regular training because a low fitness level seems to be common in these patients and this may be the reason for the development of a 'sense of mastery' through training. On the other hand, the neurobiological effects of exercise might directly result from neurotransmitter metabolism which seems to be dysregulated in a number of psychiatric disorders.

Most of the results being published rely on endurance training as the principal mode of exercise. The reason for this choice lies in the sufficient access to necessary testing equipment, the ease of carrying out training sessions and the well established formulas for prescribing endurance training. Therefore, this review will focus on endurance training studies; some reference will be given to resistance training or other modes of exercise only where appropriate. This does not necessarily imply that alternative ways of training are inferior to endurance conditioning.

In addition to a summary of therapeutic trials, this review includes recommendations on how exercise testing should be carried out and how endurance training should be prescribed considering the special requirements for patients with psychiatric

disorders. This article focuses on the practical aspects of exercise treatment in a clinical setting, thus a discussion of methodological issues (e.g. psychometric tools) and biochemical mediators is beyond the scope of this review. These aspects have been extensively covered in other reviews.^[31,32] The selection of literature presented in this article is based on search results from the MEDLINE data bank. Additionally, the references of all selected papers were screened for other relevant publications.

1. General Considerations about Exercise in Psychiatric Patients

In principal, psychiatric patients can participate in training programmes in the same manner as healthy individuals provided they have no cardiovascular or acute infectious diseases. However, many patients with psychiatric disorders have a low fitness level^[33-37] (fig. 1) which influences the choice of exercise testing and training methods.

Most psychiatric patients have no experience with endurance training.^[36-38] Patients with anxiety disorders might fear that training may provoke symptoms such as dyspnoea, tachycardia or dizziness. A slow increase in the volume of training may therefore be advisable, and for the first session, the support of an experienced trainer/therapist is necessary. Our practical experiences show that patients often quickly adapt to the training stimulus and soon learn that it will not be harmful to their health.

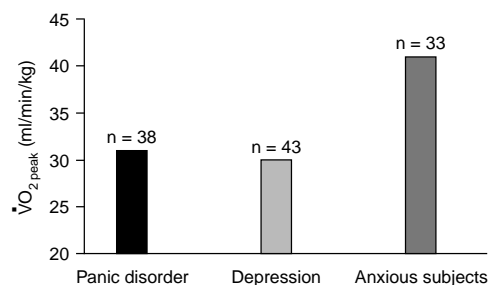


Fig. 1. Peak oxygen uptake ($\dot{V}O_{2peak}$) in patients with panic disorder,^[37] depressed patients^[22] and anxious individuals from a normal population.^[17]

2. Clinical Trials in Psychiatric Disease

Only a few clinical studies assessing the effects of exercise have been conducted in defined psychiatric populations and these mainly concentrate on depressive and anxiety disorders. Because of the small number of available investigations, criteria for their election were not too strict – particularly for the use of adequate control conditions.

2.1 Depression

The classical study is from Greist et al.^[19,39] who compared 10 weeks of endurance training with 2 forms of psychotherapy (time-limited and -unlimited) in 28 clinically depressed patients. This research group did not detect any significant differences in the clinical effects between treatments using a depression symptom check list. Endurance training was carried out in the form of jogging at a comfortable pace without strict intensity guidelines, and the amount of organised group exercise was reduced in favour of home training. Dropout rates were comparable between the treatment groups. However, the initial paper^[39] does not fulfil modern-day requirements for publication, thus making it difficult to accurately assess the reported findings. Nevertheless, this study represents the first controlled trial of exercise therapy in psychiatric patients.

In a study in 4 severely depressed women, Doyne et al.^[40] showed improvements in depressive symptoms and cognitive function after 6 weeks' training on a cycle ergometer for 30 minutes 4 times a week. However, the small sample size makes it difficult to draw further conclusions from this study.

Inspired by these results, McCann and Holmes^[20] tested 49 moderately depressed women [Beck Depression Inventory (BDI) score > 11] for the clinical effects of endurance training (10 weeks duration). Relaxation techniques and a waiting list condition (inactivity) were used for comparison. The antidepressant effects of training were significantly greater than those of the 2 control groups. The authors tried to control for the expectations of the participants by questioning patients before training; no differ-

ences in expectations were detected between the aerobic training and relaxation techniques. The necessity of employing a waiting list condition was emphasised because the authors documented the occurrence of 'spontaneous' improvements in this group of patients. These latter changes may have resulted from the 'transparent' nature of the questionnaire (BDI) used in this study.

Martinsen et al. in 1985^[22] and 1989^[21] conducted 2 training studies in depressed patients without psychotic symptoms. In the first investigation,^[22] 9 weeks of aerobic endurance training was compared with occupational therapy, both administered with concomitant psychotherapy and drug treatment in 49 patients. Both groups of patients showed clinical improvement, but, because of the accompanying therapy, no conclusive statement can be made as to whether exercise alone was responsible for the antidepressant effects. Similar results were reported from a trial in 99 depressed or dysthymic patients who trained for 8 weeks with high or low intensity exercises.^[21] No graduating influence of fitness gains, and thus no dose-response pattern, was reported in either trial.^[21,22] This is in some contrast to the causal role of exercise for antidepressant effects.

Doyne et al.^[23] trained 40 women with different forms of depression. The exercise programme lasted 2 months and was carried out 4 times per week. Aerobic training elicited the same positive effects on depressive symptoms as resistance exercise, and both were superior to inactivity (waiting list).

Over 3 months, MacMahon and Gross^[41] tested 2 modes of endurance training, based on the intensity level, in young delinquent males whose mood ranged from not at all to severely depressed. The more strenuous programme (long-distance running, basketball) resulted in greater improvements in mood than did less strenuous training, yet, psychological improvements showed no correlation to endurance gains.

Pappas et al.^[24] compared 32 moderately depressed women who either danced or played racquetball (similar to squash), with 19 depressed participants of a psychology course (BDI > 12 in both groups

of patients). Both forms of exercise resulted in decreases in BDI scores whereas merely taking part in the 'inactive' course showed clearly smaller effects. Dancing was slightly more effective at relieving depressive symptoms than was racquetball. The authors suggest that the amount of aerobic impact was the main cause (hypothetical) of the changes in BDI scores. However, no appropriate ergometric measurements were conducted.

Williams and Getty^[25] selected 41 students from a group of 900 on the basis of elevated depression scores [Profile of Mood States (POMS)]. Patients either exercised 3 times per week on a high intensity level or twice on a lower level. No significant differences in antidepressive effects were observed between the 2 training schedules. Similar mood improvements to those observed in both groups of patients undertaking exercise were found in the control group who took part in psychology or chemistry courses and did not undertake any physical activity. This argues against a causal role of exercise *per se* for antidepressive effects. Instead, solely the influence of any kind of organised group activity might be responsible for the changes detected by the authors. To correctly interpret these results it should be noted that all participants were able to choose their favourite course instead of being randomly assigned the procedure, may have made favourable outcomes for all courses more likely.

In summary, the above studies suggest a moderate antidepressive potential for regular endurance training. The most seriously depressed patients may experience the greatest benefits. However, the causal role of exercise remains unproven, and other non-specific factors may be responsible for at least part of these effects.

2.2 Anxiety

Preliminary indications for a therapeutic effect of physical training on anxiety states stem from 3 case reports^[26-28] in which an attenuating role of short term exercise on phobic anxiety was observed. Exhausting runs were performed shortly before the exposition to a phobically feared situation in two cases,^[26,27] and a decrease in the anxiety level was

noted afterwards. McDaniel^[27] observed that phases of lowered training volume led to an increased need for benzodiazepines in a patient with panic disorder and exercise-induced panic attacks.

In a group of 52 patients with 'anxiety neurosis' or minor depression, Sexton et al.^[29] induced a reduction in anxiety with 8 weeks of walking or jogging. No nonactive control group, which could have controlled for nonspecific effects from other types of activity (including nonsports), was included. Analogous to the aforementioned literature, the 2 modes of exercise showed no differences in the therapeutic effect that was induced, despite larger fitness gains with jogging. At follow-up after 6 months, the best results were reported in those patients who had the highest fitness levels. However, the dropout rate was remarkably higher in the jogging group which led the investigators to recommend low intensity exercise for training programmes aimed at anxiety reduction.

In a more recent study, Brooks et al.^[30] investigated a group of 45 patients with panic disorder. Endurance training (jogging) was compared with standard drug therapy (clomipramine 112.5 mg/day) and placebo. Clinical evaluations over 10 weeks revealed that exercise was significantly superior to placebo in terms of symptom severity. However, the therapeutic effects of clomipramine occurred earlier and were slightly greater than those of endurance training (fig. 2). One strength of this investigation was the exclusive application of endurance training, that is, without concomitant therapy. Therefore, a specific positive effect of physical activity on panic disorder could be documented. It has been shown that maximal exercise testing represents no danger to patients with panic disorder.^[42] Thus, these investigators were able to carry out appropriate ergometric tests which demonstrated relatively small endurance gains in the exercise group which did not correlate to a clinical improvement.^[37]

2.3 Addiction

Very few scientific studies of exercise therapy have been conducted in patients with alcohol or drug dependency. Sinyor et al.^[43] observed a lower

relapse rate in 58 abstinent alcoholics after 5 weeks of a mixed fitness programme than in alcoholic patients not undergoing exercise. These results were attributed to lower depression and anxiety in alcoholic patients. However, causality could not be adequately addressed because there was no qualification of such mood changes. Furthermore, control groups were not strictly paralleled to the treatment group in that different individuals served as the control group for clinical (abstinence) and ergometric results.

In another study, Weber^[44] compared 4 months of additional endurance training with routine therapy alone in 26 alcoholic patients. Comparable decreases in trait anxiety but stronger positive effects on stress and anxiety were observed in the group undertaking exercise. It was emphasised by the author that most of the therapeutic effects were detected during the first half of the programme. Unfortunately, no ergometric results were reported which prevents correlative calculations to better describe cause and effect relationships. The relatively modest differences between treatment and control groups might suggest that a routine therapeutic programme alone elicits greater effects than endurance training alone.

2.4 Other Psychiatric Diseases

Psychotic diseases have rarely been investigated in therapeutic training trials. In a case report, Adams^[45] described findings from a training programme in a male patient with schizophrenia. The activity stimulus induced contradictory findings regarding mood and other psychometric items. Nevertheless, the author concludes that an exercise programme may be of benefit in severe mental illnesses in improving fitness, self-confidence and body image.

Based on his clinical experience Martinsen^[46] considers exercise to be of limited value in patients with psychotic or melancholic features.

The only substantial evidence for the beneficial effects of exercise in psychotic disorders stems from Hannaford and Harrell^[47] who applied running training 3 times per week to a group of 25 outpatients

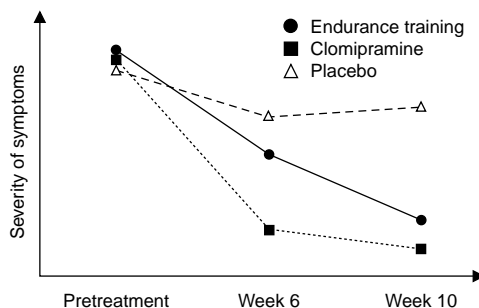


Fig. 2. Schematic representation (several psychometric scales) of the clinical course in patients with panic disorder during 10 weeks of treatment with endurance training, clomipramine (112.5 mg/day) or placebo.^[28] Higher values on the y-axis represent more severe symptoms.

with schizophrenia, major depression or bipolar disorder. Improvements in depressive mood and physical fitness compared with a waiting list control group and a group practising lower intensity exercises were reported. No subgroup analysis was performed to elucidate the differential effects on schizophrenia and depressive disorders.

Recently, an interventional exercise study was carried out in patients with chronic fatigue syndrome (CFS),^[48] which showed a beneficial influence of exercise on the clinical course of CFS. This syndrome is characterised by generalised 'somatic' fatigue accompanied by a deterioration of mood. Fulcher and White^[48] demonstrated that improvements in the self-rated clinical global impression of 59 patients with CFS were significantly greater with 12 weeks of aerobic exercise than with flexibility training. The amount of placebo effect from the programme could not be assessed because a resting control group was not included. Participants were randomized into the 2 groups, and cross-over was allowed to the flexibility group members. Initial findings were confirmed in follow-up measurements conducted 3 and 12 months after the end of the programme. No correlational analysis was carried out to elucidate the relationship between fitness gains and clinical improvement.

2.5 Summary of Findings

Aerobic exercise seems to be effective in improving general mood and depressive and anxiety symptoms in selected psychiatric patients. This effect is not limited to aerobic forms of exercise.^[23] However, there is still no conclusive evidence for a causal role of exercise *per se*. Some of the reported psychological improvements must be attributed to either patient expectations or association without a causal link. Furthermore, the large influence of suggestive information on the psychological outcome of exercise trials in healthy individuals has been shown,^[18] and it is expected that this factor may play an even larger role in psychiatric patients.

There are almost no contraindications for psychiatric patients to participate in exercise programmes provided they are free from cardiovascular and acute infectious diseases. Very little is known about the effects of exercise in psychiatric disease other than that in patients with depression and anxiety disorders. However, a few reports have indicated the need for controlled investigations in patients with psychotic and personality disorders.^[45,47]

3. Exercise Testing

A validated method of exercise testing is necessary to document the actual fitness level of a patient and the longitudinal fitness gains. A prescription for a training schedule is most accurately done on the basis of an initial test.

3.1 Choice of Testing Mode

For routine purposes there are 2 applicable testing modes which are carried out under common laboratory conditions: treadmill and bicycle ergometry. The correct choice of test depends on the intended training as well as on the diagnostic information to be derived from the test. Training recommendations are optimal if the training mode matches the testing mode. Treadmill testing is the preferable testing method for jogging. Endurance gains from jogging will also be most likely detected on a treadmill. On the other hand, bicycle ergometry may be

more useful when a simultaneous assessment of cardiovascular health is intended because the ECG is of a better quality, and parallel measurements of blood pressure are possible, using this testing mode.

3.2 Choice of Testing Protocol

Practical considerations usually lead to the application of incrementally-graded testing protocols which enable observations to be made of the reaction of the cardiorespiratory system to different workloads independent of the maximal stage reached. Some general guidelines should be followed. A minimum of 4 completed stages is a reasonable target, if possible, to get an impression of the individuals reaction to exercise conditions. This means a minimum duration of 12 minutes for 3-minute stages (preferable for lactate measurements) or 8 minutes for 2-minute stages (minimum for steady heart rates). The initial stage and the increment in workload may be chosen according to this goal. Alternatively, if the determination of ventilatory thresholds and maximal oxygen uptake ($\dot{V}O_{2max}$) is the main goal, ramp-like protocols of the same length may be more appropriate.^[49]

4. Determination of Fitness and Adequate Training Intensity

The directly measured $\dot{V}O_{2max}$ represents the classic parameter to assess endurance capacity, and many investigators and clinicians make their intensity recommendations as percentages of this value.^[21,50-53] However, several objections have been raised against this procedure.^[54-57] The most important objection in patients not having previously undergone training is the dependence on a sufficient degree of effort. As these unaccustomed patients often have difficulties reaching their physical limits it is sometimes impossible to obtain an accurate $\dot{V}O_{2max}$. In addition, intensity determinations in terms of percentages of this parameter have been criticised fundamentally for other reasons.^[54-56] Indeed, it is unclear what a particular percentage of the $\dot{V}O_{2max}$ relates to in terms of metabolic output for an individual patient'. If one feels that reference to $\dot{V}O_{2max}$ is warranted, it may be advisable to use intensities

of around 50 to 60% of the $\dot{V}O_{2\max}$ which probably represent 'easy' exercise in the aerobic domain.

The same problems arise with percentages of the maximal heart rate^[12,13,47,58] which can only be accurately determined when reaching maximal test intensities. Estimations using formulas that depend on the age of the individuals may be useful for clinical purposes but lack the precision necessary for scientific investigations. A well chosen aerobic training intensity for running can be described by a heart rate of 200 minus the age of the patient (in years) and for cycling by a rate of 180 minus age.^[59] Intensity determinations become even more complicated with percentages of heart rate reserve^[60] because it is often impossible to obtain accurate resting values under testing conditions in psychiatric patients.

Thus, methods relying on submaximal measurements seem preferable for psychiatric patients and other patients who have not undergone previous training. Reliable results can be expected from lactate measurements accompanying exercise testing.^[61-64] These determinations can be easily made from capillary blood obtained from the fingertip or the hyperaemised earlobe. This procedure is generally well tolerated by even the most anxious individuals. In contrast, the need for a face mask and possibly an additional nose clamp by the patient during spiroergometry can cause discomfort and may be an anxiety-inducing procedure in rare instances in patients with psychiatric disease. Under such conditions Broocks et al.^[36] observed full-blown panic attacks in 2 of 45 patients with panic disorder. Other investigators reported 1 such attack in 35 patients being tested at very high intensities.^[42]

A few models are available with which reference points on the lactate-workload plot can be determined and these can be roughly divided into 2 categories: those describing the first rise of blood lactate levels above baseline values and those representing the highest workload that can be maintained during endurance exercises of long duration. Both may be valuable in guiding psychiatric patients through their training sessions.

Several methods – some of them computer-aided and/or using spirometric tools – have been developed to detect the first rise in blood lactate levels to above baseline values.^[65-69] This point can usually be reliably found using spiroergometry.^[70,71] The corresponding workload represents a training intensity in the lower range, and this level of intensity can be maintained over at least 20 to 30 minutes by almost all individuals with sufficient motivation.^[72,73]

The other lactate 'thresholds' represent a much higher individual training intensity, and about 80% of the corresponding workload can be regarded as adequate for the psychiatric population. A more detailed description of the models used to determine these thresholds is beyond the scope of this review and can be obtained from the cited literature.^[70,74-78]

If the target is monitoring training by subjective measures like the rate of perceived exertion scale (RPE),^[79] it is advisable to obtain such measures during the incremental test already. This procedure enables test results to be related to training intensity. However, considerable interindividual variability has to be taken into account when applying RPE values without adequate pre-training testing.^[80,81] The above recommended intensities in the range of the first rise in blood lactate values, represent average RPE values of 12 to 14,^[82] which obviously does not preclude single outliers.

5. How to Monitor Training

There are only a few reliable methods to monitor training intensity. If one has prescribed an intensity derived from the above (see sections 3.1 and 3.2) discussed exercise tests, the best parameter for monitoring purposes is the workload. Thus, a specific velocity should be given for jogging, and the workload should be given in Watts for ergometer cycling. Usually, reliance on secondary parameters is unavoidable because jogging is seldom done on measured tracks by psychiatric patients and cycling is often done outside the home.

Heart rate is usually easily and accurately measured by portable devices and well reflects the cardiovascular load.^[83] Manual measuring proce-

dures can be taught to patients if these devices are not available. In most instances, a heart rate range of about 10 beats per minute for endurance workouts will be met without too many difficulties by psychiatric patients.

An alternative approach to heart rate measurements might be to use subjective measures like RPE.^[84,85] Particularly for psychiatric patients, the observed relationships to state anxiety and body awareness^[86] argue in favour of considering RPE for monitoring purposes. If prescribing intensity via RPE, an individual 'calibration' during pre-training testing is highly recommended because of the considerable interindividual variability.^[80,81] Finally, the physician/investigator must be aware that the application of RPE monitoring is not equivalent to using heart rate measurements;^[87] subjective measures of exertion include a mixture of information. In contrast, heart rate primarily reflects sympathetic tone and thus cardiovascular load.

6. Other Issues for Exercise Prescription

Several issues related to the choice of exercise intensity must be taken into account when determining the exercise regimen to be prescribed. Firstly, the duration of endurance sessions must become shorter with increasing intensity. For moderate endurance training in young psychiatric patients, a total duration of 30 minutes can be regarded as adequate. From our experience longer but slower (less intensive) workouts are preferable because they may interrupt depressive thoughts more effectively. Secondly, the frequency of training limits the choice of intensity; training intensity has to be lower with increasing frequency. Usually, for training regimens that aim to improve the endurance capacity of individuals who have not undergone previous training, exercising 2 to 4 times per week will be satisfactory when the above suggested intensities (see section 4) are applied.^[11,13,22,88]

Breaks should be allowed as needed during training sessions in the first weeks to ensure patient compliance. Easier forms of physical activity, such as walking, can be performed during these breaks, and

a reduction of the number and duration of breaks should be enforced during the exercise programme.

Programme length is an important factor to ensure endurance gains go beyond short term habituation effects. Four weeks may represent the lower time limit for patients to adopt new activity patterns, and after about 15 weeks individuals should be able to organise their own home-based training. Many studies use programmes of 8 to 14 weeks' duration.^[12,17,18,21,23,24,29,30,47,52]

To adequately prescribe endurance exercise and assess its effects, one has to consider the nonendurance tasks that are being carried out regularly by patients. Resistance training has been shown to elicit endurance gains,^[89] and some daily life activities may also have an aerobic impact on psychiatric patients not having undergone previous training. Thus, an activity diary or an accurate sport history is warranted.

7. Conclusion

A considerable number of studies have been published indicating that endurance training is beneficial for patients with psychiatric diseases. Unfortunately, no general concept for the therapeutic application of physical activity has been developed so far. For fitness assessment, reliance on submaximal measures is highly recommended. Monitoring of exercise intensity during training sessions is most easily done by measuring the heart rate using portable devices (whereas controlling the exact workload may be preferable for scientific purposes). Appropriate pre- and post-training testing has been emphasised to enable adequate determination of fitness gains and eventually allow positive feedback to be given to patients in the clinical setting.

An applicable schedule for the initiation of a therapeutic endurance programme includes:

- Screening for cardiovascular diseases
- Appropriate choice of the intended exercise mode for training (factors to be considered include disease, gender, age, exercise experiences and location-specific exercise circumstances)
- Appropriate choice of exercise testing method and protocol (based on the desired clinical/car-

- diovascular information required, chosen exercise mode for training, intended method for exercise prescription)
- Exercise testing and derivation of exercise prescription (consider availability of lactate analysis, experience with prescription models, need for accuracy)
 - Initiation of training programme (monitoring of intensity, registration of other activities with endurance effects). Avoid initial overdemand
 - Accompanying clinical control investigations with exercise testing to adjust prescription to increased fitness level (recommended for longer programmes)
 - Post-training testing (should be identical mode and protocol to pre-training testing), evaluation of clinical improvement after 10 to 12 weeks, decision concerning continuation of exercise programme
 - Home-based exercise programme (follow-up testing).

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