

Aerobic exercise in the adjunctive treatment of depression: a randomized controlled trial

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Summary

Two clinical trials have been conducted in a sample of depressed patients to determine whether the addition of an aerobic exercise programme to their usual treatment improved outcome after 12 weeks. In the first trial, an aerobic exercise group had a superior outcome compared with a control group in terms of trait anxiety and a standard psychiatric interview. A second trial was then conducted to compare an aerobic exercise programme with low intensity exercise. Both groups showed improvement but there were no significant differences between the groups. In neither trial was there any correlation between the extent of change in the subjects' physical fitness due to aerobic exercise and the extent of the improvement of psychiatric scores.

Introduction

'Exercise therapy' has a theoretical scientific basis with a number of possible biochemical, physiological, and psychological mechanisms as mediating pathways for the psychological effects of exercise¹. There have been a few controlled trials in the United States and Norway to determine the effect of exercise in depression²⁻⁹. The studies reported aerobic exercise to be as effective as psychotherapy and superior to an inactive control period in the treatment of unipolar depression of mild to moderate severity. It was hoped to improve on previous studies by increasing the number of subjects and using objective standardized assessments.

The first aim of the present study was to determine whether adding aerobic exercise to the treatment of patients suffering from depression produced additional benefit. This was investigated by a single blind clinical trial in which depressed patients currently receiving standard treatment were randomly allocated to either an aerobic exercise group or to a control group which had no extra intervention. The second aim was to determine whether the therapeutic component of the exercise programme was because of the improvement in the aerobic fitness. This second aim was investigated by a clinical trial in which depressed patients were allocated to either an aerobic exercise group or to a low intensity exercise group.

Methods

The inclusion criteria for entry into the trial were based on the Clinical Interview Schedule (CIS)¹⁰. All subjects had to have: (i) a total weighted score of 17 or greater and (ii) a depression severity score of 2 or more. Subjects could be of either sex but had to be aged between 18 and 60. Concurrent treatment with psychotropic medication, psychotherapy or other social interventions were not a bar to entry.

Subjects were assessed at baseline with the CIS¹⁰, the Social Supports and Stresses Interview¹¹. They completed the Beck depression inventory¹², and the State-Trait anxiety inventory¹³. Aerobic fitness was characterized by the maximum oxygen uptake which was predicted from the heart rate attained after 6 min exercising on a bicycle ergometer¹⁴. The same assessment measures were repeated at 12 weeks.

In the first trial subjects were randomly allocated in the ratio of 3:2 to one of two groups, an aerobic exercise group or a control group who received no extra intervention, until the estimated group size required had been obtained. In the second trial, subjects were randomly allocated in the ratio of 1:2 to either an aerobic exercise group or a low intensity exercise group. The data from the patients in the aerobic exercise group in the first trial were combined with the data from the aerobic exercise group in the second trial for the purposes of statistical analysis. This amalgamation was necessary to reduce the risk of a type 2 error and was carried out on the bases that: (a) the patients were being referred from the same sources, (b) the second trial began immediately after the end of the first trial, (c) the aerobic group from the first trial did not differ from the aerobic group in the second trial on any variables at baseline of the trial or at week 12.

In study 1, the aerobic exercise group was offered three supervised sessions per week for 12 weeks in groups. Each session consisted of a warm-up routine and stretching exercises, followed by a running programme. No extra treatment was offered to the control group who were asked to attend at requested intervals for assessment.

The aerobic exercise programme in study 2 was the same as in study 1. The low intensity exercise programme consisted of three supervised sessions per week for 12 weeks in groups. The session consisted of relaxation, stretching exercises and yoga. The statistical analysis consisted of 2 tail *t*-tests and Chi-square tests.

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Results

The population recruited consisted of 124 subjects over a period of 2 years. The mean age was 35.5 years (range 19-58). Thirty-six per cent of the subjects were male, and 64% female. At the time of the first assessment 33% were prescribed anti-depressants; 24% were taking benzodiazepines. Patients in both groups continued to receive the usual psychiatric treatment as provided by their referring agencies which included supportive psychotherapy. This did not include any other structured activities such as occupational therapy.

Study 1

A total of 83 subjects were entered into the first trial - 48 subjects were allocated to the aerobic exercise group and 35 to the control group. There were 12 drop-outs (25%) in the aerobic exercise group - 10 subjects were lost to follow-up and two were withdrawn due to illness. In the control group six subjects (17.2%) were lost to follow-up. There was no statistical difference between the drop-outs from the aerobic and the control group. The total of 18 drop-outs did not significantly differ from the 65 remaining subjects except the drop-outs had a significantly higher score on the CIS (mean=40.05, SE=1.81) compared with the remainder (mean=35.56, SE=0.97) ($P<0.038$). There were no significant differences between the aerobic exercise group or the control group at baseline in any of the variables except one - the control group was more depressed on the Beck depression inventory (Table 3). There was no statistical difference between the percentage of patients prescribed anti-depressants (34% in the control group and 45% in the aerobic exercise group) at baseline.

A significant difference was found between the group means at week 12 in favour of the aerobic exercise group for the total weighted score on the CIS (Table 1) and trait anxiety (Table 2). No significant difference was found between the groups at week 12 for the Beck depression inventory (Table 3) although

Table 1. Total weighted score (clinical interview schedule): study 1

	Control group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	35	37.57	1.49	48	35.87	1.07
12 weeks	28	26.39*	2.50	36	16.80*	2.06
Change at 12 weeks	-7	-11.18		-12	-19.07	

* $P<0.005$ between groups

Table 2. Spielberger trait anxiety: study 1

	Control group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	35	65.20	1.63	48	61.79	1.31
12 weeks	29	57.82*	2.48	36	49.22*	2.54
Change at 12 weeks	-6	-7.38		-12	-12.57	

* $P<0.018$ between groups

Table 3. Beck depression inventory: study 1

	Control group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	35	26.66*	1.52	48	22.91*	1.1
12 weeks	29	17.79	1.89	36	13.94	2.13
Change at 12 weeks	-6	-8.87		-12	-8.97	

* $P<0.05$ between groups

the control group was significantly more depressed at the beginning of the trial. A significant difference was found for the changes in the maximum oxygen uptake *within* the aerobic exercise group (mean +0.28 l/m, SE 0.07, $P<0.001$) but not within the control group by week 12. There were no differences for the changes in aerobic fitness *between* the groups. There was no statistical difference between the percentage of patients prescribed anti-depressants (24% in the control group and 44% in the aerobic exercise group) at week 12.

The Pearson correlation coefficient between the change in the total weighted score and the change in the estimated maximum oxygen uptake between the baseline and week 12 was 0.02 ($n=27$, $P<0.46$) in the control group and 0.15 ($n=36$, $P<0.18$) in the aerobic exercise group. This implies that there was no relationship between change in aerobic fitness measured and change in observed ratings of mental state.

Study 2

Forty-one new subjects were recruited for this study in which an aerobic exercise group was compared to a low intensity exercise group. Fifteen further subjects were allocated to the aerobic group of the first trial and 26 subjects to the new low intensity group. Nine subjects were lost to follow-up at 12 weeks.

The aerobic exercise group in study two was created by the amalgamation of the data from the aerobic exercise group in study one with the 15 new recruits. To justify this, two comparisons were made.

(a) The baseline data of the 48 subjects from study 1 was compared with those of the 15 new recruits from study 2. There were no significant differences except that the percentage of males in the aerobic exercise group was 50% in the first trial and 13.3% in the second trial (Chi-square=4.91, 1 d.f., $P<0.026$). This was thought unlikely to be relevant. (b) The changes of all measures between the baseline and 12 weeks were compared for the 48 subjects in study 1 and the 15 in study 2. The two groups had responded to the experimental exercise intervention similarly.

The number of subjects in the combined aerobic exercise group was 63 and 17 subjects were lost to follow-up (26.9%). The number of subjects in the low intensity group remained at 26 and 4 were lost to follow-up (15.8%). There was no significant difference in the number of drop-outs between the two groups by a chi-square test. The total of 21 drop-outs did not significantly differ from the remaining subjects.

The group means of the combined aerobic exercise group were then compared with the low intensity group by a two tail *t*-test. There were no significant differences between the groups at baseline in any of the variables except that (i) the low intensity group

Table 4. Total weighted score (clinical interview schedule): study 2

	Low intensity group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	26	32.92	1.81	63	35.85	0.94
12 weeks	21	18.0	2.78	46	17.87	1.81
Change at 12 weeks	-5	-14.92		-17	-16.98	

Table 5. Spielberger trait anxiety: study 2

	Low intensity group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	26	60.73	2.06	60	61.61	1.33
12 weeks	19	54.31	3.47	46	50.52	2.26
Change at 12 weeks	-7	-6.42		-14	-11.09	

Table 6. Beck depression inventory: study 2

	Low intensity group			Aerobic exercise group		
	n	Mean	SE	n	Mean	SE
Baseline	6	22	1.37	62	23	1.08
12 weeks	22	13.31	1.86	46	14.96	1.80
Change at 12 weeks	-4	-8.69		-16	-8.04	

was older (mean 39.2 years, SE=2.03) than the aerobic exercise group (mean 34.4 years, SE=1.15) ($t=2.05$, $P<0.046$). (ii) More of the patients in the aerobic exercise group were prescribed antidepressants at the time of the assessment (41.2%) than in the low intensity group (11.5%) (Chi-square=6.11, $P<0.013$).

No significant differences were found between the groups at week 12 on the CIS (Table 4), trait anxiety (Table 5), Beck depression (Table 6), or aerobic fitness; or the percentage of patients prescribed antidepressants (41% in control group and 42% in aerobic exercise).

For the purpose of comparison, the aerobic exercise group was divided into two subgroups according to the degree of compliance to the aerobic exercise programme in study 1 and 2. The first was formed by combining data from subjects who never exercised with those who attended on average less than once a week. The second was formed by combining the data from subjects who exercised on average between once and twice a week with those who attended on average three times a week. At week 12 there was no significant difference between the two groups in terms of the total weighted score on the CIS, Beck depression score and Spielberger trait anxiety score, or the maximum oxygen uptake.

Discussion

This study has shown that it is possible to recruit and enter depressed patients into an aerobic exercise

programme - only 29% of subjects refused or never attended the exercise programme. Given the nature of the demands of the procedure on the patient this would seem encouraging.

The aim of the first trial was to determine whether adding aerobic exercise to the usual treatment provided for depressed patients produced additional benefit. This seemed to be the case as justified by the symptom score and trait anxiety showing greater improvement in the aerobic group. This finding seemed to apply even though a significant number in the exercise programme did not fully comply with the supervised programme.

The results of the second study suggest that the therapeutically effective component of the exercise programme was not the improvement in aerobic fitness. Further, no correlation was found between the changes in the CIS and the measure of aerobic fitness, nor was there any significant difference in maximum oxygen uptake between the two groups in the first trial, and lastly there was no difference in outcome between those who attended less than once a week and those who attended between one and three times a week.

In study 1, there was a bias at randomization as the control was significantly more depressed on the Beck depression inventory before any intervention. However these differences were not reflected in the CIS. The differences had disappeared after 12 weeks mirroring the changes in the other outcome variables. In study 2 the number of subjects prescribed antidepressants was significantly greater in the aerobic group. There may therefore have been a bias in favour of the aerobic group.

In study 1 and study 2 there were no significant differences between the groups in terms of the maximum oxygen uptake at 12 weeks. The lack of difference between the groups at 12 weeks may have occurred because: (a) the error in estimating maximum oxygen uptake from sub-maximal measurements may be up to 10%, and (b) not all the subjects in the aerobic group complied with the full exercise programme.

The results of study 1 are broadly similar to Martinsen *et al.*⁸ and Sexton *et al.*⁹ which are the only other studies that used aerobic exercise as an adjunct to the usual treatment of depression. The therapeutically effective components of both exercise programmes in this study may therefore be:

- (i) the social interaction and support of a group which met at regular intervals;
- (ii) the extra attention and special interest of a health professional received by the subjects;
- (iii) a structured programme of activity which may be important in counteracting the lack of motivation and lethargy that is characteristically found in depression;
- (iv) the reduction in muscle tension which may contribute to the reduction in trait anxiety.

Further research will be required to determine the therapeutic effective component in an exercise programme by recruiting a larger number of subjects to compare different types of exercise.

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