Physical activity dose-response effects on outcomes of depression and anxiety

ANDREA L. DUNN, MADHUKAR H. TRIVEDI, and HEATHER A. O'NEAL

The Cooper Institute, Dallas, TX; and University of Texas Southwestern Medical Center, Dallas, TX

ABSTRACT

DUNN, A. L., M. H. TRIVEDI, and H. A. O'NEAL. Physical activity dose-response effects on outcomes of depression and anxiety. *Med. Sci. Sports Exerc.*, Vol. 33, No. 6, Suppl., 2001, pp. S587–S597. **Purpose:** The purpose of this study was to examine the scientific evidence for a dose-response relation of physical activity with depressive and anxiety disorders. **Methods:** Computer database searches of MEDLINE, PsychLit, and Internet and personal retrieval systems to locate population studies, randomized controlled trials (RCTs), observational studies, and consensus panel judgments were conducted. **Results:** Observational studies demonstrate that greater amounts of occupational and leisure time physical activity are generally associated with reduced symptoms of depression. Quasi-experimental studies show that light-, moderate-, and vigorous-intensity exercise can reduce symptoms of depression. However, no RCTs have varied frequency or duration of exercise and controlled for total energy expenditure in studies of depression or anxiety. Quasi-experimental and RCTs demonstrate that both resistance training and aerobic exercise can reduce symptoms of depression. Finally, the relation of exercise dose to changes in cardiorespiratory fitness is equivocal with some studies showing that fitness is associated with reduction of symptoms and others that have demonstrated reduction in symptoms without increases in fitness. **Conclusion:** All evidence for dose-response effects of physical activity and exercise come from B and C levels of evidence. There is little evidence for dose-response effects, though this is largely because of a lack of studies rather than a lack of evidence. A dose-response relation does, however, remain plausible. **Key Words:** MAJOR DEPRESSIVE DISORDER (MDD), ANXIETY, TREATMENT, EFFICACY, PHYSICAL ACTIVITY, EXERCISE, REVIEW

Understanding the dose-response relation of physical activity to depression and anxiety requires consideration of several conceptual issues. Haskell concisely summarized these issues for the 1992 Second International Consensus Conference on Physical Activity, Fitness, and Health (22), and they are of considerable importance to the topic of depression and anxiety. Their consideration, described below, provides a framework to focus the content of this review and to identify future research directions.

ISSUES RELATED TO THE SPECIFICITY OF THE RESPONSE

Defining depression and anxiety. The first issue that should be considered before undertaking a review of depression and anxiety is specifically defining the response. Just as the dose-response varies for different health outcomes, it is also likely to differ depending on how one defines the desired outcomes, in this case, depression and anxiety. Experimental and quasi-experimental studies have examined effects of exercise training using various outcome measures. The participants studied have ranged from healthy individuals with few or no symptoms of depression or anxiety to individuals experiencing a clinically diagnosed disorder that could be classified as severe. Furthermore, many studies have examined the acute effects of exercise on symptoms, but such effects do not reflect the true nature of these disorders, as these illnesses are considered to be chronic and not responsive to acute treatment. Not surprisingly, this wide variation in disease severity or diagnostic criteria leads to a wide variation in responses. Consequently, for the purpose of this review, we have chosen to use standardized and specific diagnoses of depressive and anxiety disorders as outlined by *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) (1). Furthermore, we have chosen to specify depression and anxiety outcomes that are likely to be ameliorated by exercise or physical activity. For example, Bipolar Disorder is thought to have a particularly strong genetic linkage that increases susceptibility to the disorder compared with other depression subtypes (20). Because of this stronger genetic link, it is unlikely that exercise alone could be an effective treatment for this disorder. Similarly, many anxiety disorders such as phobias and Posttraumatic Stress Disorder are linked to specific situations or cues (1). These disorders can be effectively treated with psychotherapy alone, and it seems unlikely that exercise could be a plausible single treatment modality. The specific definitions of depression and anxiety that have been chosen for evaluating dose-response effects should be limited to those disorders where exercise is biologically plausible.

0195-9131/01/3306-0587/$3.00/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

Submitted for publication January 2001.
Accepted for publication March 2001.
Proceedings for this symposium held October 11–15, 2000, Ontario, Canada.

Criteria for diagnoses. Depression and anxiety will be defined according to the DSM-IV and the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) and ICD-10 criteria (1). Depression will include Major Depressive Disorder (MDD) (Code 296.2 or 296.3) (0–6), Dysthymic Disorder (300.4), and Depressive Disorder Not Otherwise Specified (311), but will not include Bipolar Disorder, Cyclothymia, Mood Disorder Due to a General Medical Condition, or Substance-Induced Mood Disorder. Anxiety will include Panic Disorder without Agoraphobia (300.01), Generalized Anxiety Disorder (300.02), or Anxiety Disorder Not Otherwise Specified (300.00). Other anxiety disorders such as Posttraumatic Stress Disorder, Social Phobia, Acute Stress Disorder, Agoraphobia, Obsessive Compulsive Disorder, Specific Phobias, Anxiety Disorder Due to a General Medical Condition, or Substance-Induced Anxiety Disorder will not be included.

Only studies that have evaluated the specific symptoms linked to these illnesses and include gradations of symptoms that would include at least mild to moderate levels of depression or anxiety disorders will be included in this review. Furthermore, randomized control trials (RCTs) and quasi-experimental studies will only be included if the study population has been diagnosed with the depression or anxiety disorders specified above. Depression also can be secondary to other illnesses such as cardiovascular disease, stroke, cancer, and diabetes. Similarly, other complications can arise from untreated depression such as substance abuse and alcoholism (24). These associations with other illnesses are likely to involve different or additional mechanisms that further complicate the dose-response question. To clarify issues of dose-response, it will be judicious to only review studies where depression and anxiety are the primary disorder and are not secondary to other illnesses or psychopathology.

Criteria for clinical outcomes. Another issue that is related to the specificity of the response is the way one defines the treatment response. A dose-response study of exercise as a treatment for depression or anxiety should use similar criteria to those used for established treatments of pharmacotherapy and psychotherapy. In this literature, treatment plans are linked to five key clinical outcomes. They are: 1) response and 2) remission, goals of acute phase treatment; 3) prevention of relapse and 4) recovery, goals of continuation phase treatment; and 5) prevention of recurrence, the goal during maintenance phase treatment (28,43). Response is generally operationalized and defined by clinical practice guidelines as a 50% reduction in symptoms during the acute phase of treatment. Often this acute phase of treatment lasts from 6–12 wk. There are two key points in this particular guideline that are related to dose-response. First, studies that demonstrate a statistical improvement in depressive or anxious symptoms may not always meet the accepted criterion for a treatment response. We believe this stricter criterion of a 50% reduction in symptoms should be used in establishing dose-response effects, since an improvement that is less than 50%, although statistically significant, is unlikely to be clinically relevant. Second, it is clear that amelioration of symptoms takes 6–12 wk and may not be well sustained when it occurs after a short bout of medication, psychotherapy, or exercise.

Potential etiological mechanisms. Depression and anxiety have been linked to multiple etiologies including psychological trauma and chronic stress, faulty neurotransmitter systems such as norepinephrine (NE) and serotonin (5-HT), and hypothalamic-pituitary-adrenocortical (HPA) dysfunction (11,14,34). It is highly likely that depression, like high blood pressure, has multiple etiologies, and that exercise, acting on multiple biological and psychological systems, could lead to synergistic adaptations that effectively reduce symptoms of these disorders. At the present time, the exact etiology of depression and anxiety is unknown. However, the recently released Surgeon General's Report on Mental Health documents an evolving understanding that both depression and anxiety have a biochemical basis that is found in the brain (52). For this reason, dose-response effects of exercise are biologically plausible. In fact, well-designed RCTs of nonpharmacological treatments such as psychotherapy have been shown to relieve symptoms of depression, and symptom relief is associated with neurobiological changes among treatment responders (52).

METHODS

Selection of articles for this review. A computer search of MEDLINE, PsychLit, and the Internet was conducted using combinations of the following keywords: depressive disorder, depression, anxiety, anxiety disorder, physical activity, and exercise. Next we reviewed reference lists from review articles, book chapters, and meta-analyses on exercise and depression, exercise and anxiety, and exercise and mental health. In addition, we searched our personal files and identified more than 1000 potential articles for inclusion. Articles that did not specify methods of measurement of depression or anxiety for study outcomes and that did not measure effects of exercise in depressed and/or anxious participants were excluded. Also, studies that only measured acute effects of exercise on symptoms of depression or anxiety or that measured depression secondary to other comorbid conditions and review articles were excluded. We also excluded all current meta-analyses on depression and anxiety, because the overwhelming number of studies included in the analyses of effect sizes have been performed in populations that are asymptomatic. For example, one of the most complete meta-analyses on the acute and chronic effects of exercise on anxiety included more than 100 studies. Out of these 100-plus studies, 7 were conducted in patient populations with broadly defined psychopathology, and the remainder were conducted in asymptomatic, normal populations (41). After all exclusions, the final yield was 37 articles.

TABLE 1. Cross-sectional epidemiologic studies of physical activity and depression.

Study	Population	Design/Methods	Results	Conclusion
Stephens, 1988 (49)	Four population surveys: 6913 individuals (age 25–74 yr), 23,791 individuals (age ≥15 yr), 3025 individuals (age 20–64 yr), 22,250 individuals (age ≥10 yr)	Four surveys with measures of physical activity categories (much, moderate, little/no) and depressive symptoms	CES-D depression score by amount of leisure exercise Men <40 yr: much 6.41, moderate 6.40, little/no 9.05 ($P < 0.001$) Women < 40 yr: much 9.49, moderate 9.22, little/no 12.89 ($P < 0.001$) Men ≥40 yr: much 7.56, moderate 6.91, little/no 7.38 ($P = 0.09$) Women ≥40 yr: much 8.62, moderate 8.89, little/no 11.31 ($P < 0.001$)[a]	Level of physical activity was positively associated with fewer depressive symptoms in the U.S. and Canadian populations.
Kivelä and Pahkala, 1991 (25)	Random sample of 618 men and 911 women in Finland (age ≥60 yr)	Structured interview assessing depressive symptoms, social and socioeconomic status, health, functional capacity, health behavior and losses	All: no regular exercise and depressive symptoms OR = 1.5; Men: no regular exercise and depressive symptoms OR = 1.4; Women: no regular exercise and depressive symptoms OR = 1.5	Lack of physical exercise was associated with depressive symptoms in both women and men.
Weyerer, 1992 (54)	Representative sample of 1536 males and females in Upper Bavaria (age ≥15 yr)	Structured interview assessing psychiatric disorders (Clinical Interview Schedule) Physical activity categories (regular, occasional, no)	No exercise and depression OR = 3.15 (95% CI, 1.84–5.38) Regular exercise and depression OR = 1.00 Occasional exercise and depression OR = 1.55 (0.82–2.92)	Subjects who reported no physical activity were more likely to have depressive symptoms compared with regular exercisers.
Krause et al., 1993 (27)	Random sample of 1351 males and females in Japan (mean age 68.7 yr)	Structured interview assessing physical health problems, financial strain, emotional support, negative interaction, physical exercise, depressive symptoms (CES-D)	Exercise frequency and depressive symptoms: ($\beta = -0.16$; $P < .01$)	More frequent exercise was associated with fewer depressive symptoms.
Rajala et al., 1994 (42)	Random sample of 345 males and 435 females in Finland (age 55 yr)	Postal questionnaire, interviews, and clinical examinations; depressive symptoms (Zung Self-Rating Depression Scale) and exercise categories (little, moderate, much)	Risk of depression by exercise: Men, little vs much exercise RR = 2.0 (0.7–5.8) Men, moderate vs much exercise RR = 0.7 (0.2–1.9) Women, little vs much exercise RR = 1.1 (0.4–2.9) Women, moderate vs much exercise RR = 0.9 (0.5–1.5)	Respondents who reported little or moderate amounts of exercise were not at increased risk for depression compared with individuals reporting much exercise.
Ruuskanen and Ruoppila, 1995 (44)	Representative sample of 1600 males and females in Finland born 1904–13 (age 65–84 yr) and 1914–23 (age 65–74 yr)	Structured interview assessing demographic status, social network, health status, physical activity, depressive symptoms	Intensive and regular activity was significantly associated with fewer depressive symptoms in the two youngest (65–69 and 70–75 yr) age groups	Intensive activity was related to better self-rated health, fewer depressive symptoms, and self-rated meaningfulness of life.
Penninx et al., 1999 (40)	Cohort of 6247 males and females (age ≥65 yr)	CES-D, physical disability Physical activity categories (low, moderate, high) at 4 time points Baseline data from 6-yr prospective study	Percentage of respondents who were not depressed by level of physical activity: low, 7.1%; moderate, 45.4%; high, 47.5% Percentage of respondents who were depressed by level of physical activity: low, 14.4%; moderate, 50.8%; high, 35.7% High activity: not depressed vs depressed $P < 0.001$	Respondents who reported high levels of physical activity were less likely to be depressed at baseline.
Bhui and Fletcher, 2000 (5)	Sample from the Health and Lifestyle Survey	Questionnaire measuring anxiety and depression Physical activity (minutes per day)	92–161 min·d^{-1}: OR = 0.57 (0.37–0.87), $P < 0.01$ 162–554 min·d^{-1}: OR = 0.65 (0.43–0.97), $P < 0.05$	Men who exercised at least 92 min·d^{-1} had less common depression and anxiety states. No effect was found for women.
Hassmen et al., 2000 (23)	Random sample of 3403 males (1547) and females (1856) in Finland (age 25–64 yr)	Beck Depression Inventory (BDI) Frequency of exercise (daily, 2–3×/wk, 1×/wk, 2–3×/mo, a few times per year, cannot exercise)	Exercise frequency was associated with depressive symptoms ($F = 8.5$, $P < 0.001$)	Individuals reporting less frequent exercise had more depressive symptoms.

[a] Reporting only CES-D data from the NHANES I survey. Analyses from other surveys using less accepted measures of depression were consistent with these results.

TABLE 2. Prospective epidemiologic studies examining physical activity and depression.

Study	Population	Design/Methods	Results	Conclusion
Farmer et al., 1988 (49)	Representative sample of 1900 healthy men and women in U.S. (age 25–77 yr)	Cross-sectional and prospective (8-yr follow-up): CES-D Self-report recreational and nonrecreational physical activity categories (little/no, moderate/much)	*Depressive symptoms at baseline*: Little/no vs moderate/much recreational activity: white men OR = 2.2 (95% CI, 1.2–4.2); black men OR = 16.5 (2.1–128); white women OR = 1.7 (1.1–2.5); black women OR = 1.2 (0.3–4.1) Little/no vs moderate/much nonrecreational activity: white men OR = 1.1 (0.4–2.7); white women OR = 2.1 (1.1–4.0); black women OR = 19.2 (2.3–160). *Depressive symptoms at follow-up by baseline depression*: Little/no vs moderate/much recreational activity: white men w/few symptoms OR = 1.3 (0.5–3.1); white men w/more symptoms OR = 12.9 (1.7–98.9); white women w/few symptoms OR = 1.9 (1.1–3.2); white women w/more symptoms OR = 2.0 (0.8–14.5)	White respondents who reported little or no recreational activity had twice the odds of depressive symptoms at baseline. White women with few symptoms at baseline who engaged in recreational activity were less likely to have depressive symptoms at follow-up. Small sample size and lack of follow-up data limit conclusions regarding effects of activity on depressive symptoms for black men and women.
Camacho et al., 1991 (54)	Selected sample of 1799 men and women (age ≥20 yr)	Cross-sectional and prospective (18-yr follow-up) Self-report of depressive symptoms and physical activity categories (low, moderate, high)	*Depression by activity in 1974*: low vs high activity OR = 4.22 (3.17–5.62), moderate vs high activity OR = 2.14 (1.61–2.86) *Depression in 1974 by activity in 1965*: men, low vs high activity OR = 1.76 (1.06–2.92); men, moderate vs high activity OR = 1.46 (0.91–2.34); women, low vs high activity OR = 1.7 (1.06–2.7); women, moderate vs high activity OR = 1.0 (0.63–1.59)	Low activity levels at baseline were associated with increased risk for depression at follow-up. Respondents who were inactive in 1965 but reported increased activity in 1974 were not at higher risk for depression compared with respondents who were active in 1965 and 1974.
Stewart et al., 1994 (51)	Cohort of 1758 males and females with chronic medical conditions (mean age 56.1 yr)	Prospective (2 yr follow-up) Self-report physical activity, other health behaviors, functioning and well-being, and disease and comorbidity	At 2-yr follow-up, depression was associated with perceived activity level, total time spent exercising, and total time spent walking ($P < 0.05$)	Increased physical activity was associated with better health.
Paffenbarger et al., 1994 (39)	Cohort of 21,596 college alumni (age 35–74 yr in 1962 or 1966)	Prospective (23–27 yr follow-up) Self-report physical activity (estimated kcal·wk^{-1}) Self-report physician-diagnosed depression	Physical activity index in 1962 or 1968 and risk of depression in 1988: <1000 kcal·wk^{-1} RR = 1.00; 1000–2499 kcal·wk^{-1} RR = 0.83; 2500+ kcal·wk^{-1} RR = 0.72 ($P = 0.008$)	Risk of depression was lower for individuals reporting higher levels of physical activity.
Foreyt et al., 1995 (18)	Sample of 381 normal-weight and obese men and women (mean age 44.1 yr)	Prospective (4-yr follow-up): CES-D, Eating Self-Efficacy Scale, General Well-Being Schedule Self-reported recreational activity and perceived importance of activity at 2 time points	Change in physical activity and depression for normal weight respondents ($P \leq 0.05$): lowest quartile (decreased exercise) 3.1; 2nd quartile (decreased exercise) 0.8; 3rd quartile (increased exercise) –0.9; highest quartile (increased exercise) –0.3. Correlation between change in depression and change in physical activity: normal weight –0.17 ($P \leq 0.05$), obese 0.11 (NS)	Normal weight respondents who reported an increase in physical activity exhibited fewer depressive symptoms at follow-up.
Mobily et al., 1996 (36)	Cohort of 2084 males and females (age ≥65 or older)	Cross-sectional and prospective (3-yr follow-up): modified CES-D Self-report of walking frequency (daily walking vs less frequent walking)	Baseline depression by walking status: walkers vs nonwalkers OR = 0.825 (0.64–1.06) Follow-up depression by walking status and baseline depression: few depression symptoms and daily walking OR = 1.11 (0.77–1.6); more depression symptoms and daily walking OR = 0.38 (0.18–0.79)	For individuals reporting more depressive symptoms at baseline, daily walkers were more likely to improve their scores at year 3.
Cooper-Patrick et al., 1997 (10)	Cohort of 690 male and 62 female medical students (classes of 1948–1964)	Prospective (15-yr follow-up) Self-report physical activity (change in activity, number of sweats per week) Self-report of clinical depression and review of medical records, and psychiatric distress (General Health Questionnaire)	Cumulative incidence of depression 6.4% at follow-up; risk of depression through 1993 by physical activity in 1978: *Number of sweats per week*: 0×/wk vs 3×/wk RR = 1.18 (0.53–2.64); 1–2×/wk vs 3+×/wk RR = 1.08 (0.48–2.45) *Change in activity from medical school*: Inactive vs remained RR = 0.86 (0.33–2.24); became vs remained RR = 0.66 (0.27–1.65)	Individuals who reported little or no exercise were not at increased risk for depression compared with those who reported exercising to a sweat at least 3 times per week. No increased risk for depression for those who were inactive or who became active relative to those who remained active.

TABLE 2. *Continued*

Study	Population	Design/Methods	Results	Conclusion
Morgan and Bath, 1998 (37)	Representative cohort of 1042 men and women in U.K. (age ≥65 yr)	Prospective (8-yr follow-up): depressive symptoms measured by Symptoms of Anxiety and Depression (SAD) scale, measured physical activity, general health, and social activity (BASE) at 4 time points	Outdoor/leisure activity at baseline and depression at 4-yr follow-up: OR = 0.92 (0.85–0.99)	Baseline level of outdoor/leisure physical activity was associated with a slight reduction in risk for depression at follow-up.
Lampinen et al., 2000 (29)	Cohort of 663 older men and women from Finland (age ≥65 yr)	Prospective (8-yr follow-up): RBDI (modified version of Beck's depression scale) Physical activity categories by increased, maintained, or decreased intensity (necessary chores, regular walking, strenuous exercise)	Change in physical activity type and depressive symptoms at 8-yr follow-up by baseline activity level: necessary chores (remained vs increased) OR = 0.96 (0.25–3.7); regular walking (decreased vs increased) OR = 10.56 (2.35–47.4); regular walking (remained vs increased) OR = 2.21 (0.53–9.3); strenuous exercise (decreased vs increased) OR = 1.23 (0.32–5.03)	Low levels of physical activity predicted depressive symptoms especially for those who reduced their intensity of activity type. Levels of physical activity at baseline predicted depression after adjusting for SES and physical function.

RESULTS

Dose-response effects of total amount of leisure-time and occupational physical activity effects on symptoms of depression and anxiety (Evidence Category C). There are nine cross-sectional and nine prospective studies (Tables 1 and 2) that examined the relation of varying amounts of leisure-time and occupational physical activity on levels of depression and anxiety, and these yield similar results across cultures. In a North American sample, Stephens (49) conducted cross-sectional analyses of data combined from surveys conducted in the United States and Canada and found that higher levels of physical activity were associated with little or no symptoms of anxiety and depression. In individuals performing moderate amounts of physical activity, there was a decrease in depressive symptoms, and this was particularly true for women and older populations. Similarly, cross-sectional analyses in a German sample (54) of 1536 men and women found those who reported no physical exercise were 3.15 times more likely to have moderate to severe depression. The odds ratio (OR) for those who reported occasional exercise was also elevated (1.55), but this was not statistically significant. Kivelä and Pahkala (25) and more recently Ruuskanen and Ruoppila (44) found similar results in a population of older adults in Finland. Even though the results of cross-sectional studies are generally consistent, the findings for men and women sometimes differ. Also, it is not clear from these analyses whether physical inactivity leads to depressive symptoms, whether depressive symptoms lead to inactivity, or whether it is a third factor such as social support that might mediate this relation. Prospective studies can help determine the direction of this relation by examining whether low levels of physical activity predict development of depressive symptoms or whether increasing physical activity can reduce depressive symptoms.

Several prospective studies have examined the temporal relation between physical activity and depression to determine if low levels of activity predict future depression. Farmer et al. (16), using survey data from the National Health and Nutrition Examination Survey (NHANES I), found low levels of leisure activity at baseline did predict depression 8 yr later in white women despite depressive symptoms being low at the time of the baseline examination. These findings remained after adjusting for age, other chronic illness, education, employment, and income. The same relation did not hold for men with few symptoms of depression at baseline; however, low levels of physical activity did predict depression in men who had depressive symptoms at the baseline examination. The Alameda County study (8) showed a similar inverse relation. Comparing active to inactive respondents at follow-up and adjusting for sex, health, and age, the ORs for depression were 1.8 for men and 1.7 for women. However, a German study did not find low baseline physical activity to be a risk factor for developing depression at 2 yr (54). A later study of male and

TABLE 3. Quasi-experimental and experimental studies examining the efficacy of exercise as a treatment for depression.

Study	Study Design and Sample	Treatment and Comparison Group	Diagnosis Type and Instrument	Depression and/or Anxiety and Fitness Treatment Outcome	50% Decrease in Symptoms
Morgan et al., 1970 (38)	Pre-post between-group design; 6 wk treatment in one of five treatment groups (circuit, jog, swim, lab, control). $N = 101$ men (age, 26–55 yr) APT	AT 3×/wk, 85% HRmax AT1 30–45 min ($N = 18$); AT2 30–45 min ($N = 23$), AT3 30–45 min ($N = 27$), AT4 10–20 min ($N = 17$), WLC Sole	Zung Self-Rating Depression Scale (SDS) score ≥ 50 indicating depression; 11 subjects scored ≥50 at pre-test	Participants who were depressed at the onset of study experienced a decrease in depressive symptoms after 6 wk of physical activity (SDS 51.45–44.45, $P < 0.01$).	No
Greist et al., 1978 (21)	Repeated measures design (12 wk treatment; 3-wk follow-up); random assignment, $N = 28$ men and women (age, 18–30 yr) APT/FUP	AT 3×/wk ($N = 10$) vs time-limited PSY ($N = 6$) and time-unlimited PSY ($N = 12$) Sole	Minor depression as determined by Symptom Checklist-90 (SCL-90) score ≥50 and Research Diagnostic Criteria (RDC) (49)	Running was as effective in reducing symptoms as both PSY. At 12 wk, running and time-limited PSY showed a greater reduction in symptoms than time-unlimited therapy PSY. 3-wk follow-up showed continued reduction in symptoms in AT.	Yes
Conroy et al., 1982 (9)	Repeated measures design; 6-wk treatment, $N = 17$ men (mean age, 25.5 yr) APT	AT 3×/wk ($N = 9$) vs AT ≤1×/wk ($N = 8$) Adjunct	Beck Depression Inventory (BDI), Self-Assessment Scales	Participants in the 3×/wk exercise group had a reduction in depressive symptoms (BDI 19.9–13.9) compared with ≤1×/wk exercise group (BDI 19.9–20.7).	No
Doyne et al., 1983 (12)	Multiple baseline design across subjects; 6-wk treatment; $N = 4$ women grouped in 2 pairs (age, 19–24 yr) APT	Multiple baseline measures were attention placebo 3×/wk until one pair group in treatment showed improvement; active treatment was 4×/wk interval training sessions for 30 min for 6 wk Sole	Major depression as measured by 2 raters according to RDC obtained by using Schedule for Affective Disorders and Schizophrenia interview (15)	Exercise decreased symptoms of depression as measured by BDI (mean change scores from baseline to treatment of 14, 16.9, 15.2, 11.3) and Depression Adjective Check List (DACL). Treatment gains maintained at 3-mo follow-up.	Yes
Martinsen et al., 1985 (32)	Repeated measures design for 9 wk in men and women (age, 17–60 yr) APT	AT (50–70% max. aerobic capacity) 1 hr/3×/wk + PSY ($N = 28$; 9 on PHM) vs PSY ($N = 21$; 14 on PHM) Adjunct	DSM-III criteria for major depression (1) Level of depression assessed by Comprehensive Psychological Rating Scale (CPRS) (2) and BDI (4)	Both groups significantly decreased depression scores, and exercise training group had significantly larger effect. Also, increase in aerobic power inversely correlated with reduction of symptoms. A later report (31) showed 50% in exercise group continued to exercise and had significantly fewer depressive symptoms.	Yes
Klein et al., 1985 (26)	Pre-post between-group design; 12 wk of treatment with follow-up to 9 mo; random assignment of men and women (mean age, 30 yr) APT/FUP	AT 45 min/2×/wk ($N = 27$) and PSY ($N = 24$) vs PHM ($N = 23$) Sole	Diagnosis of major or minor depression and receiving no other treatment (RDC) and SCL-90 (15)	All groups significantly reduced symptoms at 12 wk. There was no difference between groups at 12 wk. Symptoms were still reduced at 9 mo.	Yes
Sime and Sanstead, 1987 (46)	Multiple baseline with repeated measures design; 4 wk baseline, 10 wk treatment; men and women (age, 26–53 yr) APT/FUP	AT 4×/wk for 21 mo ($N = 15$) Sole	Moderate depression assessed by BDI (4)	Significantly decreased at 6 and 21 mo follow-up; 13 participants completed follow-up measures (9 of 13 reported continuing exercise).	No
Doyne et al., 1987 (13)	Repeated measures design (baseline, 1 mo, 7 mo, and 12 mo); 8 wk treatment; $N = 40$ women matched on baseline BDI and randomly assigned to 1 of 3 groups (age, 18–35 yr) APT/FUP	AT 4×/wk using ACSM guidelines and RT 4×/wk below 50–60% max HR vs WLC for 8 wk Sole	Diagnosis using RDC criteria, measured BDI, DACL, Hamilton Rating Scale for Depression (HRSD), and fitness	Significant decrease in depression in two exercise groups compared with wait list control measured by BDI, HRSD, and DACL. Symptoms were still reduced at 1 mo, 7 mo, and 12 mo. Neither exercise group increased fitness. There was no significant difference in attrition.	Yes
Fremont and Craighead, 1987 (19)	Repeated measures (10 wk treatment; 2 mo follow-up) random assignment of men and women (age, 19–62 yr) APT/FUP	AT 20 min 3×/wk ($N = 15$); PSY ($N = 16$) vs AT 20 min/3×/wk and PSY ($N = 18$) Sole	BDI score between 9 and 30	All groups significantly improved by the 5th week and improvement was maintained during 2-mo follow-up BDI baseline walk/run 17 ± 6.2, counseling 19 ± 7.8, combined 18 ± 7.5; Wk five 7 ± 5.7, 9 ± 6.6, 13 ± 8.8; 2 mo 6 ± 7.0, 7 ± 6.6, 6 ± 6.5; No difference for more severe symptoms.	Yes
Martinsen et al., 1989 (30)	Pre-post randomized block by gender (38 men, 61 women); 8 wk treatment (mean age, 41 yr) APT	AT (70% $\dot{V}O_{2max}$) for 1 hr/3×/wk ($N = 51$) and RT (strength, flexibility, and relaxation at low intensity for equivalent time) Adjunct	DSM-III criteria for major depression, dysthymia, depressive disorder not otherwise specified (49 patients also had diagnosed anxiety disorder) (1); BDI > 9	Both groups had significant reductions in depression scores and increase in fitness was not correlated with increase in cardiorespiratory fitness; 90 of 99 completed the study (only 2 withdrew due to exercise).	No
Sexton et al., 1989 (45)	Repeated measures design (8 wk treatment, 6 mo follow-up) men and women ($N = 52$) randomly assigned (age, 19–60 yr) APT/FUP	AT (jog, 70% predicted HRmax) 30 min/3–4×/wk vs AT (walk, comfortable speed) 30 min/3–4×/wk Sole	Nonpsychotic DSM-III diagnosis, Symptom Checklist, State-Trait Anxiety Inventory, BDI, Global Assessment Scale	Both groups showed a similar reduction in anxiety and depression scores *Walkers*: baseline BDI 22.4 ± 7.1, 8 wk BDI 11.9 ± 10.7, 6 mo BDI 12.2 ± 9.5 *Joggers*: baseline BDI 23.0 ± 9.3, 8 wk BDI 9.8 ± 10.8, 6 mo BDI 10.2 ± 11.6 Reductions were maintained at the 6-mo follow-up. Those with greater aerobic fitness had significantly lower anxiety at follow-up.	Yes

TABLE 3. *Continued*

Study	Study Design and Sample	Treatment and Comparison Group	Diagnosis Type and Instrument	Depression and/or Anxiety and Fitness Treatment Outcome	50% Decrease in Symptoms
Steptoe et al., 1989 (50)	Pre-post between-group design matched on age, sex, body weight, activity level, and initial anxiety level; 28 women and 5 men randomly assigned to 1 of 2 treatment conditions for 10 wk; (age, 20–60 yr) APT	AT (60–65% HR_{max}) 30 min/4×/wk vs flexibility, mobility, and strength (50% HR_{max}) 30 min/4×/wk Sole	Score of 8–10 or ≥11 on the Hospital Anxiety and Depression Scale (HAD) and/or score on the tension-anxiety scale of the Profile of Moods States (POMS)	Participants in the aerobic exercise group had a decrease in tension-anxiety and depression scores on the POMS. Tension-anxiety (9.6–6.6), depression (0.77–0.58)	No
McNeil et al., 1991 (33)	Pre-post between-group design; participants randomly assigned to 1 of 3 treatments for 6 wk; (mean age, 72.5 yr) APT	AT 20–40 min (2 supervised; 1 unsupervised visits·wk^{-1}); social contact (2 visits·wk^{-1}) vs WLC Sole	BDI score within moderate range of 12–24	Both exercise and social contact decreased depressive symptoms significantly compared with wait list control (BDI exercise 16.6 ± 3.1 to 11.1 ± 3.0; social contact 16.0 ± 3.6 to 11.8 ± 4.0; wait list 15.2 ± 2.4 to 14.7 ± 3.7). Greater decrease in somatic symptoms in exercise group than social contact and wait list.	No
Veale et al., 1992 (53)	Pre-post between-group design (2 studies); 12 wk treatment; $N = 83$ (study 1) and $N = 89$ (study 2) men and women randomly assigned (age, 18–60 yr) APT	Study 1: AT 3×/wk vs control Study 2: AT 3×/wk vs low-intensity exercise (relaxation, stretching, yoga) 3×/wk Sole/Adjunct	Clinical Interview Schedule (CIS) >17 and depression severity score >2; also BDI; not all patients receiving PSY or PHM	*Study 1*: AT decreased depressive symptoms on CIS but not BDI when compared with control (no fitness improvement). *Study 2*: no difference between intensity groups; both improved on CIS and BDI.	No
Singh et al., 1997 (47)	Pre-post between-group design; men ($N = 12$) and women ($N = 20$) randomized to 1 of 2 groups for 10 wk (mean age, 71 yr) APT	High-intensity RT 3×/wk vs interactive EDC for 2×/wk Excluded if mini-mental state <23 (17) Sole	DSM-IV diagnosis of minor, major depressive disorder (mild to moderate) or dysthymia; also BDI, HRSD, and Geriatric Depression Scale (GDS) (56)	Resistance-trained group significantly reduced all depressive symptoms on all measures compared with health education controls (BDI 21.3 ± 1.8 to 9.8 ± 2.4 vs controls 18.4 ± 1.7 to 13.8 ± 2, $P = 0.002$). The intensity of training was a significant independent predictor of decrease in depression scores.	Yes
Broocks et al., 1998 (7)	Pre-post between-group design; men ($N = 23$) and women ($N = 23$) were randomized to 1 of 3 treatment conditions for 10 wk (age, 18–50 yr) APT	AT 3–4×/wk, PHM, and PHM placebo Sole	DSM-III-R diagnosis of panic disorder and agoraphobia and ICD-10 criteria	Exercise had a significant effect over placebo at 8 wk. When comparing exercise and clomipramine, clomipramine was more effective. Hamilton Anxiety Scale: Exercise 14 vs clomipramine 9.	No
Meyer et al., 1998 (35)	Repeated measures design, matched on age; men ($N = 36$) and women ($N = 37$), 1 of 3 treatment conditions for 10 wk APT	AT 45–60 min/3×/wk (panic patients), AT 45–60 min/3×/wk (controls), PHM, and PHM placebo Sole	Bandelow Panic Agoraphobia Scale self rating 25.0 SD 7.6, observer rating 25.4 SD 7.9. Hamilton Anxiety Scale 22.6 SD 7.6, Clinical Global Impression 4.4 SD 0.8	At 10 wk, exercise group (panic patients) showed significant improvement in all 4 clinical efficacy criteria compared with placebo treatment. At 4 wk, clomipramine was more effective than exercise but at 8 wk this effect almost diminished. BPAS 10 wk: exercise 15 vs clomipramine 10. Hamilton 10 wk: exercise 10 vs clomipramine 10.	Yes
Blumenthal et al., 1999 (6)	Repeated measures design; men ($N = 43$) and women ($N = 113$) randomized to 1 of 3 groups for 16 wk (age ≥ 50 yr) APT	AT 3×/wk at 70–85% HR_{max}; PHM (sertraline); AT and PHM (sertraline) Sole and Adjunct	DSM-IV diagnosis of major depressive disorder and HRSD ≥13, BDI	All treatment groups reduced depressive symptoms. HRSD baseline Exercise 17, Medication 18, Combination 17 vs 16 wk post Exercise 8, Medication 7, Combination 9. BDI baseline 20, 22, 22 vs 16 wk post 9, 8, 10 for Exercise, Medication, and Combined, respectively (numbers interpreted from graph)	Yes
Babyak et al., 2000 (3)	Repeated measures design; $N = 133$ of the original 156 participants available for assessment at 10 mo (age ≥ 50 yr) FUP	AT 3×/wk at 70–85% HR_{max}; PHM (sertraline); AT and PHM (sertraline) Sole and Adjunct	DSM-IV diagnosis of major depressive disorder and HRSD, BDI	6 months after conclusion of the treatment program BDI scores did not differ between groups: Exercise 8.9, Medication 11.0, Combination 10.6. Participants in Exercise (30%) had lower rates of depression compared with Medication (52%) or Combination (55%), with depression defined as DSM-IV diagnosis or HRSD >7.	Yes

RT, resistance training; AT, aerobic training; PSY, psychotherapy; PHM, pharmacotherapy; WLC, wait list control; EDC, education control; APT, acute phase treatment; FUP, follow-up; Sole, exercise treatment only; Adjunct, exercise and psychotherapy and/or pharmacotherapy.

female medical students also did not find an increased risk of depression attributable to being inactive at baseline or becoming inactive at a 15-yr follow-up (10).

Five prospective analyses also report whether increases in physical activity lead to reductions in depression. For example, improvements in depression scores come from observations of the Iowa 65+ Rural Health Study (36). A logistic regression analysis of 2084 men and women found those who reported more depressive symptoms at baseline and who walked every day were one third (OR, 0.38) as likely to report high a number of depressive symptoms at follow-up compared with those who did not walk. In the group who reported no depressive symptoms at baseline and who walked every day, there was no change in depressive symptoms (e.g., their depressive symptoms remained low). Paffenbarger et al. (39) also found an inverse relation between physical activity and subsequent risk of depression in the Harvard Alumni study. Men who expended 1000–2499 $kcal \cdot wk^{-1}$ in walking, stair climbing, and sports play were at 17% less risk of developing clinical depression than their less active peers. Men who expended 2500 or more $kcal \cdot wk^{-1}$ were 28% less likely to develop clinical depression. This is the only prospective study that demonstrates a dose-response gradient between amounts of physical activity and reduction in diagnosed depression. Other prospective studies examining effects of increasing physical activity on symptom reduction did not analyze any dose-response relation.

Exercise training studies: characterizing the dose in terms of intensity, duration, and frequency on depression and anxiety (Evidence Category B). Table 3 shows consistency across studies in demonstrating a reduction in symptoms of depression and anxiety with aerobic and resistance training protocols. Eight of 18 studies indicate a 50% reduction in symptoms during the acute phase treatment. Furthermore, in the seven studies that also included a follow-up or maintenance phase, this response was maintained for periods of 3–21 months. Although the results of these studies are consistent, there are limitations and design flaws in many of these studies including lack of adequate control groups, mixing of treatments (e.g., exercise is combined with pharmacotherapy or psychotherapy), and small sample sizes. Also, we were able to locate only two studies examining these effects in patients diagnosed with anxiety disorders.

We were not able to locate a single published study that has examined the combined effect of varying intensity, duration, and frequency of exercise, although some studies have compared different intensities or different frequencies. With regard to intensity, Sexton et al. (45) examined reductions in depressive symptoms and anxiety in "neurotic" inpatients assigned to either a walking treatment or a more vigorous jogging treatment. Both groups showed equal reduction in their symptoms of anxiety and depression, but the jogging group had significantly more dropouts. Veale et al. (53), who compared aerobic exercise of low intensity with higher intensity, found similar results. Both groups decreased their depressive symptoms, but there was no significant difference between groups.

In addition to the issue of exercise intensity, one study has examined the effects of two different frequencies of aerobic training on depressive symptoms. Conroy and colleagues (9) examined the effects of exercise 1 $d \cdot wk^{-1}$ versus 3 $d \cdot wk^{-1}$ over a 6-wk period and found the 3-$d \cdot wk^{-1}$ treatment had greater effects than the 1-$d \cdot wk^{-1}$ treatment. We were unable to locate any published studies in depressed patients that have examined differing durations of exercise. Future studies that examine the dose of exercise will also need to take into account total energy expenditure, because the intensity, frequency, and duration sum to total energy expenditure.

Aerobic versus resistance training and reduction of symptoms of depression and anxiety (Evidence Category B). Sixteen of the 19 studies in Table 3 used only aerobic exercise as the exercise treatment modality. Of the remaining three studies, two compared aerobic exercise with resistance training (13,30), and one examined the effects of resistance training compared with a health education control (47). Each of these three studies examining the effects of resistance training showed significant effects in reducing depressive symptoms among different aged populations.

Fitness and treatment response (Evidence Category B). Only 25% of the studies in Table 3 and none of the studies in Tables 1 and 2 measured whether improvements in cardiorespiratory fitness were associated with changes in depression. Studies that did measure changes in fitness are equivocal. For example, the first study by Martinsen et al. (32) indicated the decrease in depression was significantly correlated with the increase in cardiorespiratory fitness, whereas the later study comparing aerobic fitness and weight training exercise did not replicate this finding (30).

SUMMARY

First, with regard to the question of whether the amounts of occupational and leisure time physical activity are linked to reductions in symptoms of depression and anxiety: This evidence is generally consistent for both cross-sectional and prospective studies and findings are similar across cultures; however, these studies are only observational. Also, only two of these observational studies presented data on anxiety symptoms. Second, with regard to the question of whether varying the intensity, frequency, and duration of the exercise prescription has a dose-response effect on depression and anxiety, there is evidence to suggest that both moderate and vigorous exercise can reduce symptoms of depression. No studies have varied frequency or duration or controlled for total energy expenditure. Third, with respect to resistance and aerobic exercise, there is evidence that both can reduce symptoms of depression. However, in the studies that compared aerobic versus resistance training, it is unknown if total energy expenditure was equivalent. Fourth, it is also not clear from the exercise training

studies whether or not increases in cardiorespiratory fitness are necessary to reduce symptoms of depression. Also, with respect to all of these questions, there are more data examining depression disorders compared with anxiety disorders.

RESEARCH RECOMMENDATIONS

The questions posed for this review suggest several lines of research to understand dose-response effects of exercise and physical activity on the treatment and management of depression and anxiety disorders. In all of these future research efforts, studies should follow criteria established for treatment studies in terms of adequately diagnosing patients and using outcome measures with appropriately defined treatment standards. Until this becomes the accepted practice, rather than the exception, little progress will be made with regard to understanding exercise as a treatment modality for either depression or anxiety. Furthermore, future studies should carefully document the exercise dose and examine the relation of treatment outcomes with cardiorespiratory and/or muscular fitness.

1. Prospective observational studies should be conducted to determine whether increasing the frequency, intensity, or duration of physical activity is associated with symptom reduction of depression and anxiety. Furthermore, it will be important to compare various subgroups in these analyses (e.g., comparing older with middle-aged and younger persons, comparing men with women, and comparing different ethnicities).
2. Prospective observational studies also are needed to examine the relation between cardiorespiratory fitness and symptoms of depression. Again, it will be important to examine the influence of age, gender, and ethnic subgroups.
3. RCTs are needed to examine the effect of types of exercise as well as frequency, intensity, and duration on various subtypes of depression and anxiety. Future trials also should examine whether different doses of exercise can be a sole treatment or should be implemented as an adjunct treatment depending on depression or anxiety severity and subtype.
4. To clarify issues related to intensity of exercise and physical activity, it will be important to examine effort sense (rating of perceived exertion) for both relative and absolute exercise intensities in patients with different subtypes of depression and anxiety.
5. RCTs examining biological and psychological mechanisms in relation to exercise dose and treatment effects need to be conducted. Examples of mechanisms to be investigated include brain imaging studies similar to those conducted for antidepressant drug studies, effects on HPA axis function, or neurotransmitter regulation.
6. Because both resistance training and aerobic exercise have demonstrated similar effects, it will be important to explore possible mechanisms that these different types of exercise share (e.g., changes in vagal tone or neurotransmitter modulation), and the relation to possible treatment effects.
7. Dose of exercise also needs to be examined with respect to the other phases of the illness, in addition to the acute phase treatment. For example, how many weeks of exercise are needed for a full remission? Can different types of physical activity and/or exercise prevent recurrence?
8. Finally, exercise may have its greatest impact on prevention of depression. Population studies are needed to evaluate this question. Also, RCTs should be conducted to examine the effects of exercise on recurrence of depression or anxiety disorders, particularly during continuation or maintenance phase treatment.

CONCLUSION

All evidence for dose-response effects of physical activity and exercise comes from Evidence Category B and C levels. Cross-sectional data from observational studies consistently demonstrate that physical activity is associated with reduced symptoms of depression, but there is less evidence for reduced symptoms of anxiety. Data from prospective studies are more equivocal. Furthermore, there is only one prospective study that has examined the dose-response question with respect to depression. Clearly, more observational studies are needed to evaluate the potential for prevention of clinical illness. Evidence from quasi-experimental studies and RCTs also consistently demonstrates a reduction in symptoms of depression attributable to both aerobic and resistance exercise. Again, there are fewer quasi-experimental studies and RCTs in patients diagnosed with anxiety disorder. Additional RCTs are needed to examine dose-response of exercise as both a sole and adjunct treatment in different subtypes of depression and anxiety and in various subgroups. Also, RCTs are needed to explore the possible underlying biological and psychological mechanisms of treatment effects. At this point the evidence is suggestive but not convincing.

We thank Heather Kitzman, Melba Morrow, and Stephanie Parker for their assistance in preparing this manuscript.

Address for correspondence: Andrea L. Dunn, Ph.D., The Cooper Institute, 12330 Preston Road, Dallas, TX 75230; E-mail: adunn@cooperinst.org.

REFERENCES

1. AMERICAN PSYCHIATRIC ASSOCIATION. *Diagnostic and Statistical Manual of Mental Disorders*, 4th Ed. Washington, DC: American Psychiatric Association, 1994.
2. ASBERG, M., C. PERRIS, D. SCHALLING, and G. SEDVALL. The CPRS—development, and applications of a psychiatric rating scale. *Acta Psychiatr. Scand. Suppl.* 271:1–27, 1978.

3. BABYAK, M., J. A. BLUMENTHAL, S. HERMAN, et al. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. *Psychosom. Med.* 62:633–638, 2000.
4. BECK, A. T., C. H. WARD, M. MENDELSON, J. MOCK, and J. ERGAUGH. An inventory for measuring depression. *Arch. Gen. Psychiatry* 4:561–571, 1961.
5. BHUI, K., and A. FLETCHER. Common mood and anxiety states: gender differences in the protective effect of physical activity. *Soc. Psychiatry Psychiatr. Epidemiol.* 35:28–35, 2000.
6. BLUMENTHAL, J. A., M. A. BABYAK, K. A. MOORE, et al. Effects of exercise training on older patients with major depression. *Arch. Intern. Med.* 159:2349–2356, 1999.
7. BROOCKS, A., B. BANDELOW, G. PEKRUN, et al. Comparison of aerobic exercise, clomipramine, and placebo in the treatment of panic disorder. *Am. J. Psychiatry* 155:603–609, 1998.
8. CAMACHO, T. C., R. E. ROBERTS, N. B. LAZARUS, G. A. KAPLAN, and R. D. COHEN. Physical activity and depression: evidence from the Alameda County Study. *Am. J. Epidemiol.* 134:220–231, 1991.
9. CONROY, R. W., K. SMITH, and A. R. FELTHOUS. The value of exercise on a psychiatric hospital unit. *Hosp. Community Psychiatry* 33:641–645, 1982.
10. COOPER-PATRICK, L., D. E. FORD, L. A. MEAD, P. P. CHANG, and M. J. KLAG. Exercise and depression in midlife: a prospective study. *Am. J. Public Health* 87:670–673, 1997.
11. DEMITRACK, M. A., J. K. DALE, S. E. STRAUS, et al. Evidence for impaired activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. *J. Clin. Endocrinol. Metab.* 73:1224–1234, 1991.
12. DOYNE, E. J., D. L. CHAMBLESS, and L. E. BEUTLER. Aerobic exercise as a treatment for depression in women. *Behav. Ther.* 14:434–440, 1983.
13. DOYNE, E. J., D. J. OSSIP-KLEIN, E. D. BOWMAN, K. M. OSBORN, I. B. MCDOUGALL-WILSON, and R. A. NEIMEYER. Running versus weight lifting in the treatment of depression. *J. Consult. Clin. Psychol.* 55:748–754, 1987.
14. DUNN, A. L., and R. K. DISHMAN. Exercise and the neurobiology of depression. *Exerc. Sport Sci. Rev.* 19:41–98, 1991.
15. ENDICOTT, J., and R. L. SPITZER. A diagnostic interview: the schedule for affective disorders and schizophrenia. *Arch. Gen. Psychiatry* 35:837–844, 1978.
16. FARMER, M. E., B. Z. LOCKE, E. K. MOSCICKI, A. L. DANNENBERG, D. B. LARSON, and L. S. RADLOFF. Physical activity and depressive symptoms: the NHANES I Epidemiologic Follow-up Study. *Am. J. Epidemiol.* 128:1340–1351, 1988.
17. FOLSTEIN, M. F., S. E. FOLSTEIN, and P. R. MCHUGH. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12:189–198, 1975.
18. FOREYT, J. P., R. L. BRUNNER, G. K. GOODRICK, S. T. ST. JOER, and G. D. MILLER. Psychological correlates of reported physical activity in normal-weight and obese adults: the Reno diet-heart study. *Int. J. Obes. Relat. Metab. Disord.* 19:S69–S72, 1995.
19. FREMONT, J., and L. W. CRAIGHEAD. Aerobic exercise and cognitive therapy in the treatment of dysphoric moods. *Cognitive Ther. Res.* 11:241–251, 1987.
20. GERSHON, E. S. Bipolar illness and schizophrenia as oligogenic diseases: implications for the future. *Biol. Psychiatry* 47:240–244, 2000.
21. GREIST, J. H., M. H. KLEIN, R. R. EISCHENS, J. FARIS, A. S. GURMAN, and W. P. MORGAN. Running through your mind. *J. Psychosom. Res.* 22:259–294, 1978.
22. HASKELL, W. L. Dose-response issues from a biological perspective. In: *Physical Activity, Fitness, and Health*, C. Bouchard, R. Shephard, and T. Stephens (Eds.). Champaign, IL: Human Kinetics, 1994, pp. 1030–1039.
23. HASSMEN, P., N. KOIVULA, and A. UUTELA. Physical exercise and psychological well-being: a population study in Finland. *Prev. Med.* 30:17–25, 2000.
24. KHANTZIAN, E. J. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am. J. Psychiatry* 42:1259–1264, 1985.
25. KIVELA, S.-L., and K. PAHKALA. Relationships between health behaviour and depression in the aged. *Aging (Milano)* 3:153–159, 1991.
26. KLEIN, M. H., J. H. GREIST, A. S. GURMAN, et al. A comparative outcome study group psychotherapy vs. exercise treatments for depression. *Int. J. Ment. Health* 13:148–177, 1985.
27. KRAUSE, N., L. GOLDENHAR, J. LIANG, G. JAY, and D. MAEDA. Stress and exercise among the Japanese elderly. *Soc. Sci. Med.* 36:1429–1441, 1993.
28. KUPFER, D. J. Recurrent depression: challenges and solutions. *J. Clin. Psychiatry* 52:28–34, 1991.
29. LAMPINEN, P., R.-L. HEIKKINEN, and I. RUOPPILA. Changes in intensity of physical exercise as predictors of depressive symptoms among older adults: an eight-year follow-up. *Prev. Med.* 30:371–380, 2000.
30. MARTINSEN, E. W., A. HOFFART, and O. Y. SOLBERG. Aerobic and non-aerobic forms of exercise in the treatment of anxiety disorders. *Stress Med.* 5:115–120, 1989.
31. MARTINSEN, E. W., and A. MEDHUS. Adherence to exercise and patients' evaluation of physical exercise in a comprehensive treatment programme for depression. *Nord. Psykiatr. Tidsskr.* 43:411–415, 1989.
32. MARTINSEN, E. W., A. MEDHUS, and L. SANDVIK. Effects of aerobic exercise on depression: a controlled study. *Br. Med. J. (Clin. Res. Ed.)* 291:109, 1985.
33. MCNEIL, J. K., E. M. LEBLANC, and M. JOYNER. The effect of exercise on depressive symptoms in the moderately depressed elderly. *Psychol. Aging* 6:487–488, 1991.
34. MEADOR-WOODRUFF, J. H., J. F. GREDEN, L. GRUNHAUS, and R. F. HASKETT. Severity of depression and hypothalamic-pituitary-adrenal axis dysregulation: identification of contributing factors. *Acta Psychiatr. Scand.* 81:364–371, 1990.
35. MEYER, T., A. BROOCKS, B. BANDELOW, U. HILLMER-VOGEL, and E. RÜTHER. Endurance training in panic patients: spiroergometric and clinical effects. *Int. J. Sports Med.* 19:496–502, 1998.
36. MOBILY, K. E., L. M. RUBENSTEIN, J. H. LEMKE, M. W. O'HARA, and R. B. WALLACE. Walking and depression in a cohort of older adults: the Iowa 65+ Rural Health Study. *J. Aging Phys. Act.* 4:119–135, 1996.
37. MORGAN, K., and P. A. BATH. Customary physical activity and psychological wellbeing: a longitudinal study. *Age Ageing* 27:35–40, 1998.
38. MORGAN, W. P., J. A. ROBERTS, F. R. BRAND, and A. D. FEINERMAN. Psychological effect of chronic physical activity. *Med. Sci. Sports* 2:213–217, 1970.
39. PAFFENBARGER, R. S., JR., I.-M. LEE, and R. LEUNG. Physical activity and personal characteristics associated with depression and suicide in American college men. *Acta Psychiatr. Scand.* 377:16–22, 1994.
40. PENNINX, B. W. J. H., S. LEVEILLE, L. FERRUCCI, J. T. M. VAN EIJK, and J. M. GURALNIK. Exploring the effect of depression on physical disability: longitudinal evidence from the established populations for epidemiologic studies of the elderly. *Am. J. Public Health* 89:1346–1352, 1999.
41. PETRUZZELLO, S. J., D. M. LANDERS, D. B. HATFIELD, K. A. KUBITZ, and W. SALAZAR. A meta-analysis on the anxiety reducing effects of acute and chronic exercise: outcomes and mechanisms. *Sports Med.* 11:142–182, 1991.
42. RAJALA, U., A. UUSIMAKI, S. KEINAMEN-KIUKAANNIEMI, and S.-L. KIVELA. Prevalence of depression in a 55-year-old Finnish population. *Soc. Psychiatry Psychiatr. Epidemiol.* 29:126–130, 1994.
43. RUSH, A. J., M. TRIVEDI, D. SCHRIGER, and F. PETTY. The development of clinical practice guidelines for the diagnosis and treatment of depression. *Gen. Hosp. Psychiatry* 14:230–236, 1992.
44. RUUSKANEN, J. M., and I. RUOPPILA. Physical activity and psychological well-being among people aged 65 to 84 years. *Age Ageing* 24:292–296, 1995.
45. SEXTON, H., A. MAERE, and N. H. DAHL. Exercise intensity and reduction of neurotic symptoms: a controlled follow-up study. *Acta Psychiatr. Scand.* 80:231–235, 1989.
46. SIME, W. E. Exercise in the prevention and treatment of depression. In: *Exercise and Mental Health*, S. E. Golston (Ed.). Washington, DC: Hemisphere Publishing Corporation, 1987, pp. 145–152.

47. SINGH, N. A., K. M. CLEMENTS, and M. A. FIATARONE. A randomized controlled trial of progressive resistance training in depressed elders. *J. Gerontol. A Biol. Sci. Med. Sci.* 52:M27–M35, 1997.
48. SPITZER, R. L., J. ENDICOTT, and E. ROBINS. Research diagnostic criteria: rationale and reliability. *Arch. Gen. Psychiatry* 35:773–782, 1978.
49. STEPHENS, T. Physical activity and mental health in the United States and Canada: evidence from four population surveys. *Prev. Med.* 17:35–47, 1988.
50. STEPTOE, A., S. EDWARDS, J. MOSES, and A. MATHEWS. The effects of exercise training on mood and perceived coping ability in anxious adults from the general population. *J. Psychosom. Res.* 33:537–547, 1989.
51. STEWART, A. L., R. D. HAYS, K. B. WELLS, W. H. ROGERS, K. L. SPRITZER, and S. GREENFIELD. Long-term functioning and well-being outcomes associated with physical activity and exercise in patients with chronic conditions in the Medical Outcomes Study. *J. Clin. Epidemiol.* 47:719–730, 1994.
52. U.S. DEPARTMENT OF HEALTH, AND HUMAN SERVICES. *Mental Health: A Report of the Surgeon General.* Rockville, MD: U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, National Institutes of Health, National Institute of Mental Health, 1999, pp. 1–278.
53. VEALE, D., K. LE FEVRE, C. PANTELIS, V. DE SOUZA, A. MANN, and A. SARGEANT. Aerobic exercise in the adjunctive treatment of depression: a randomized controlled trial. *J. R. Soc. Med.* 85:541–544, 1992.
54. WEYERER, S. Physical inactivity and depression in the community. Evidence from the Upper Bavarian Field Study. *Int. J. Sports Med.* 13:492–496, 1992.
55. YESAVAGE, J. A., and T. L. BRINK. Development and validation of a geriatric depression screening scale: a preliminary report. *J. Psychiatr. Res.* 17:37–49, 1983.