34 Exercise for Substance Use Disorders

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Contents

Abstract

This chapter provides an overview of the rationale and evidence for exercise as a treatment intervention for substance use disorders. The benefits of exercise on physical health, including weight management and cardiovascular outcomes, are well documented. Research has also demonstrated positive effects of exercise in reducing depression and anxiety and improving sleep and cognitive function. Negative affect states, such as depression and anxiety, are commonly associated with substance use and are risk factors for relapse. Exercise may facilitate abstinence by ameliorating negative affect via effects on the endogenous opioid system and potentiation of dopaminergic transmission. Recent clinical trials have demonstrated benefits of exercise as a treatment intervention for methamphetamine, alcohol, and other substance use disorders. Engagement in activities such as exercise

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may provide a reinforcing alternative behavior that is complementary to other treatment interventions while promoting health and facilitating treatment goals.

Keywords

Exercise · Substance use disorders · Treatment · Methamphetamine · Depression · Anxiety

34.1 Exercise Is Effective for Medical Conditions and Symptoms

The U.S. Department of Health and Human Services' updated *Physical Activity Guidelines for Americans* [91] provide a comprehensive review of the literature and document strong evidence for the general health benefits of physical activity. For adults, improvements ensuing from regular exercise at moderate levels include lower risk of early death, heart disease, stroke, diabetes, high blood pressure, adverse blood lipid profile, metabolic syndrome, and colon and breast cancers. Exercise is helpful for the prevention of weight gain and weight loss, particularly when combined with a lower caloric diet, and is also associated with improved cardiorespiratory and muscular fitness, reduced depression and anxiety risk, and better sleep and cognitive function.

Exercise has been shown to reduce fatigue in individuals with multiple medical conditions, including fibromyalgia [36] and ankylosing spondylitis [25]. The benefits of exercise in reducing chronic pain have also been extensively documented in the literature [29], including reductions in lower back pain and functional improvements from prescribed aerobic [55] and resistance [81] exercise programs. Although the overall quality of evidence is low due to sample sizes and issues with study design, improvements have been demonstrated in chronic pain severity, physical function, and quality of life [29].

34.2 Exercise Is Effective for Psychiatric Conditions and Symptoms

Substance use disorders (SUDs) are associated with elevated rates of comorbid psychiatric disorders, particularly depressive and anxiety disorders (e.g., [31, 40]). Severity of psychiatric symptoms has been associated with poorer treatment outcomes in multiple prior studies (e.g., [15, 30]). Upon cessation of substance use, withdrawal and abstinence syndromes comprising prominent psychiatric features may emerge (e.g., [56]). Syndromes may be characterized by drug cravings, coupled with marked depressive symptoms, including anhedonia, dysphoria, irritability, poor concentration, hypersomnia, low energy, and even suicidality [60]. The contribution of emotional stress to drug use and relapse has been well documented (e.g., [27, 83, 87]), and considerable evidence is accumulating to suggest that substance users exhibit deficits in their ability to process and regulate such stress.

Aerobic and resistance exercise interventions are useful for a wide range of psychiatric conditions, including anxiety and depression [79, 93]. The majority of studies have demonstrated efficacy of exercise in reducing symptoms of depression in both inpatient [54] and outpatient (e.g., [58]) settings; favorable results have been highlighted in several review articles (e.g., [6, 53]) and meta-analyses [20, 65]. Exercise has been shown to reduce depressive symptoms in medically compromised populations, including cardiac [69] and cancer [57] patients. The benefits of exercise relative to psychotropic medication [8] and psychotherapy [28, 33, 42] have also been investigated; equivalent benefits have been found comparing exercise with medication, time-limited or time-unlimited psychotherapy, group therapy, and cognitive–behavioral therapy.

State anxiety has been shown to acutely diminish after individual episodes of exercise [73], and aerobic exercise may confer significant benefit in the treatment of adults with moderate to severe panic disorder [12, 85] and obsessive–compulsive disorder [1]. The majority of studies have suggested efficacy of exercise in mitigating stress-related symptoms across a variety of study populations, including nonclinical [5, 9, 47], clinical [1], and medically compromised [72] adults. In a study of adults with significant anxiety sensitivity, a 2-week exercise intervention significantly reduced anxiety sensitivity relative to a no-treatment control [84], an effect that mediated the benefits of exercise on negative affect states, including anxious and depressed mood.

34.3 Exercise Improves Cognition

Cognitive deficits have been observed in long-term users of various substances. Chronic opioid use, for example, is associated with deficits in attention, processing speed, working memory, and executive functions [61], which can negatively impact methadone treatment response [21]. Methamphetamine users suffer from cognitive impairments during initial months of abstinence, including working memory, selective attention [82], learning [32], and decision making (e.g., [7, 68]). Deficits in multiple cognitive domains have been observed in alcohol-dependent individuals, including impairment in visuospatial and perceptuomotor functions, executive functions, and short-term memory, in addition to dementia and Korsakoff syndrome [43].

Meta-analyses of randomized, controlled trials confirm that normal and cognitively impaired adults derive cognitive benefits from physical exercise [4, 17, 26, 38]. Improvements are the greatest for executive control processes (e.g., planning, scheduling, working memory, dealing with distraction, multitasking), for participants in combined strength and aerobic training regimens, and when exercise duration is greater than 30 minutes [17]. Angevaren et al. [4] found the largest effects of aerobic exercise on motor and auditory function, and moderate effects on cognitive speed and visual attention. Executive and other cognitive functions have been shown to improve after acute bouts of resistance exercise in middle-aged adults [16].

34.4 Exercise and Substance Use Disorders

34.4.1 Neurobiology of Exercise and Substance Use Disorders

Exercise may hasten or improve recovery from SUDs by modifying underlying neurobiological processes, such as dopamine activity [77]. A study demonstrated reversal of methamphetamine-induced striatal dopamine transporter and tyrosine hydroxylase damage after exercise in rodents [67]. In addition, neurotrophic proteins may be regulated in part by exercise and play an important role in regulating neuronal function in the brain and help to sustain normal cognitive, emotional, and behavioral functioning. Brain-derived neurotrophic factor (BDNF), the most widely expressed neurotrophin in the brain, supports synaptic plasticity, facilitates neurogenesis, and modulates neurotransmission [22].

An emerging literature suggests that BDNF may have a role in the pathogenesis of addictive disorders [37]. Treatment interventions that affect BDNF production may mediate synaptic plasticity and neuroprotection, which could, in turn, ameliorate negative affective symptoms, impulsivity, and other cognitive deficits associated with ongoing drug use and relapse risk. Exercise, for example, has been shown in preclinical [78, 80] and human [70] studies to enhance the BDNF release in the brain. This is potentially significant because of the purported benefits of exercise on cognitive functioning [64]; cognitive deficits have been observed in chronic substance users as evidenced by poor performance on memory, attention tasks, and learning deficits [74]. Substance use disorders are also associated with poor impulse control and selective processing [49]. In addition, exercise has been shown to ameliorate negative mood states that may contribute to substance relapse, and prior literature has suggested that low BDNF levels in individuals with SUDs may predispose individuals to higher rates of psychiatric comorbidity [3].

34.4.2 Exercise for Reducing Substance Use and Preventing Relapse

An emerging literature on exercise-based interventions for SUDs provides preliminary evidence in support of this approach. In a study of cocaine-addicted rodents, rats given access to aerobic activity demonstrated reduction in cocaine-seeking, relative to those that did not have access to such activity [50]. The majority of clinical research has focused on aerobic exercise as a potential intervention to aid smoking cessation and has shown mixed effects of exercise on smoking abstinence [90]; more consistent positive effects on cigarette cravings, withdrawal symptoms, and smoking-related behaviors after exercise sessions have been demonstrated [88]. In an investigation of women enrolled in a 12-week cognitive–behavioral smoking-cessation program, subjects were randomized to receive either vigorous aerobic exercise or health education three times a week [10]. Those who participated in the exercise group evidenced significant reductions in cigarette craving, negative affect, and nicotine withdrawal during most weeks of the program.

More recent studies have suggested a preliminary positive effect of exercise in facilitating alcohol use reduction in individuals with alcohol use disorder [51] and in reducing substance use in both treatment-engaged substance users [13] and in non-treatment-seeking cannabis users [14]. In the treatment-engaged population, it was noted that substance use outcomes were significantly better among substance users who attended at least 75% of exercise sessions [13]. An 8- to 9-week structured exercise program has also demonstrated efficacy in adolescents enrolled in drug-treatment programs; adolescents who improved in self-concept, anxiety, and depression risk factors reported reduced substance use relative to those who did not improve on similar measures [18]. Similarly, a prospective investigation of more than 4000 twins revealed lower rates of illicit drug use and alcohol-use consequences in adulthood among physically active adolescents, supporting prior work suggesting a relationship between low physical activity in adolescents and drug use [44].

There have been a number of recent reviews and meta-analyses on the role of exercise in treating patients with SUDs. Hallgren et al. [35] reviewed 22 studies on the efficacy of exercise to reduce alcohol use. Although the evidence did not support the efficacy of exercise to directly reduce alcohol use, exercise did provide benefits in reducing symptoms of depression and improving physical fitness. These conclusions were supported by Stoutenberg et al. [86], who emphasized that while exercise appeared to produce significant positive benefits to individuals in treatment for alcohol use disorders (e.g., reduced anxiety, depression, and impulsivity, and improved self-efficacy), the evidence for exercise in reducing alcohol use was very limited. Linke and colleagues [46] reviewed the impact of exercise on a heterogeneous set of patients with SUDs. Although they concluded that exercise might be a potentially useful intervention that warranted further research, they noted that in many trials, adherence to exercise protocols is poor and, therefore, results are difficult to interpret. Finally, Morris et al. [62] reviewed the literature on the role of exercise in improving outcomes and quality of life for individuals who had been previous users of methamphetamine. The results from this literature review support other findings that exercise can reduce anxiety and depression and improve numerous medical measures and quality of life in this population of former drug users.

34.5 Study of Exercise as an Intervention for Methamphetamine Use Disorder

A multisite study was conducted in the United States by the Clinical Trials Network (CTN), funded by the National Institute on Drug Abuse (NIDA), investigating the benefits of an exercise component added to residential programs addressing stimulant use disorders. The Stimulant Reduction Intervention using Dosed Exercise (STRIDE) study was a randomized controlled trial that tested the effectiveness of the addition of exercise versus the addition of health education to treatment as usual in improving drug treatment outcomes in 302 participants with diagnostic and statistical manual of mental disorders, fourth edition (*DSM-IV*)-diagnosed stimulant abuse or dependence (e.g., cocaine, methamphetamine, and amphetamine) and receiving treatment initially in residential settings and then transitioning to outpatient settings; participants were randomized to receive either a dosed exercise intervention plus usual care or a health education intervention control plus usual care. Although the primary outcome of percentage of abstinent days did not show a significant treatment effect between groups, post hoc analyses controlling for treatment adherence and baseline stimulant use demonstrated greater stimulant abstinence rates among exercise-adherent participants [89].

From 2010 to 2015, the chapter authors (Mooney and Rawson) led a research team in conducting a NIDA-funded evaluation of exercise as a therapeutic intervention for methamphetamine users in early abstinence. The study examined the utility and efficacy of an 8-week, evidence-based aerobic and resistance exercise intervention to promote improved treatment outcomes for a sample of 150 individuals in residential treatment for methamphetamine use disorder. The study examined medical, psychiatric, neurocognitive, and behavioral benefits that may accrue during participation in an 8-week exercise intervention, as well as possible sustained beneficial impacts on drug use following completion of the exercise protocol and discharge from the residential treatment program. The project also included a brain imaging component to collect data leading to an improved understanding of the mechanisms that may underlie observed effects on treatment outcomes and symptom remediation associated with the exercise intervention.

DSM-IV-diagnosed methamphetamine-dependent individuals were screened to determine eligibility, and those randomized to the exercise intervention participated in supervised progressive endurance and resistance training three times per week for 8 weeks (24 sessions), consistent with current guidelines for comprehensive exercise programs (American College of Sports Medicine [ACSM], [2]). Each session consisted of a 5-minute warm-up, 30 minutes of aerobic activity on a treadmill, 15 minutes of resistance training, and a 5-minute cool-down with stretching and light calisthenics. The goal of the aerobic training was to accumulate at least 30 minutes of continuous aerobic exercise at a target intensity set by data derived from maximal incremental exercise testing (XT), as described later. Information derived from the incremental testing was also used to define a safe ceiling for exercise intensity for each participant. The goal of the resistance training was to develop adaptations in muscle strength and body composition to complement the aerobic training program. A total of nine exercises involving the major muscle groups were performed each day.

Participants randomized to the control condition participated in a health and wellness education session three times a week for 45 minutes. A counselor provided informational materials, facilitated discussion of educational content, monitored attendance, and documented participants' involvement. Sessions consisted of an integrated multimedia educational program addressing a variety of health, wellness, and lifestyle topics such as nutrition, dental care, acupressure, sleep hygiene, and health screening, adapted from a previously implemented wellness manual used by Kinnunen et al. [41].

All study participants completed a maximal incremental exercise test (XT) on a treadmill ergometer using a symptom-limited incremental protocol with linear increases in the work rate with respect to time [19]. This test occurred three times during participation—at baseline, study week 5, and immediately following the intervention phase or upon intervention termination. Aerobic capacity ($\dot{V}O_2$ max), and the metabolic or lactate threshold ($\dot{V}O_2\,\theta$), which is the level of oxygen uptake that defines one's ability to perform prolonged work, were measured using indirect calorimetry with an automated metabolic measurement system. The $\dot{V}O_2$ max and $\dot{V}O_2\,\theta$ were used as baseline markers of aerobic fitness as well as for objective indices of each individual's tailored aerobic exercise intervention.

Participants underwent further fitness assessments to determine baseline body composition (skinfolds), muscle strength by 1-repetition maximum (1-RM) for leg press and chest press, and muscle endurance (repetitions to failure using 85% of their leg press and chest press 1-RM values). The 1-RM represents the maximum weight that can be lifted only once through a complete range of motion. The 1-RM and muscle endurance test data were used to establish baseline values of muscle strength and endurance in the study population and to help guide the development of the individually tailored resistance training exercise program (National Strength and Conditioning Association [NSCA], [63]). This test was administered at baseline, week 5, and upon intervention termination. Data obtained from the body composition analysis enabled tracking of changes in fat mass and, importantly, changes in the fat-free mass and skeletal muscle mass. These data were obtained using standard skinfold and girth measurement techniques [48] and calculated using the Jackson and Pollack equation [39] and magnetic resonance imaging (MRI)-validated equations, respectively [45].

A subset of consenting participants (15 from each condition) underwent two positron emission tomography (PET) sessions and two magnetic resonance imaging (MRI) sessions before commencement of the experimental condition and again after the 8 weeks of intervention. Brain region volumes were determined for subcortical regions, including the caudate, putamen, and nucleus accumbens. Dopamine D_2/D_3 receptor availability was calculated as binding potential (BP_{ND}) using the D2/D3 ligand [(18)F] fallypride. The MRI scan was used to confirm the absence of structural brain lesions and to aid in localization of volumes of interest.

34.5.1 Results from the Exercise Study

Methamphetamine users over the course of the 8-week trial were able to safely engage in exercise and derived significant health benefits over a short period. Data from the first 29 study completers, randomized to either exercise (EX, $n = 15$) or health education (ED, $n = 14$), were analyzed to evaluate exercise-related physical outcomes, including aerobic fitness, body composition, and muscle strength. EX subjects significantly improved maximum oxygen uptake by 0.63 ± 0.22 L/min (21%), leg press (LP) strength improved by 24.4 ± 5.6 kg (40%), and chest press (CP) strength by 20.6 ± 5.7 kg (49%). For EX subjects, LP and CP endurance improved by ten repetitions (120%) and seven repetitions (96%), respectively, and these changes were significantly greater than those seen in the ED group. Changes in body composition for EX subjects included significant reductions in body weight (average 1.7 ± 2.4 kg, 2%), percentage of relative body fat (2.8 ± 1.3%, 15%), and fat weight (2.8 ± 1.8 kg, 18%). None of these variables changed significantly in participants receiving ED [24].

Preliminary data collected from 50 study participants revealed diminished heart-rate variability (HRV) relative to age-matched, drug-free controls. HRV reflects the ability of the autonomic nervous system (ANS) to adapt quickly to stress and changes in the environment [23]. At the end of the 8-week study, HRV increased in individuals who participated in the exercise program, but no significant change was observed relative to baseline in individuals randomized to the health education control group, suggesting that physical activity improved balance in autonomic tone in MA users. In addition, results from the PET and MRI neuroimaging examination of a subset of participants suggest improvement in striatal dopamine receptor binding after participation in the exercise program. Study participants in the EX condition ($n = 10$) demonstrated improvement in striatal D2/D3 binding after 8 weeks of exercise according to analysis of PET (using ^{18}F-fallypride), whereas those in the ED condition ($n = 9$) did not [77], suggesting that exercise is an intervention that may ameliorate dopaminergic deficits in individuals with methamphetamine use disorder.

Although differences in relapse rates post discharge from residential treatment did not differ between 135 individuals randomized to the 8-week EX condition versus ED at 1, 3, and

6 months, when groups were analyzed based on the severity of methamphetamine use at baseline, a significant difference in relapse rates was observed in the lower severity users (as defined by use up to 18 days in the month prior to admission). Lower severity users (45.2% of the sample) were less likely to relapse to methamphetamine use at all three time points than higher severity users (54.8% of the sample), as measured by self-report and urine drug screen results [76]. Participants randomized to the EX intervention were more likely to experience reduction in depression and anxiety symptom severity than those in the ED group, and a dose effect was observed whereby attending more EX sessions was associated with greater reduction in symptoms [75]; furthermore, those with more severe medical, psychiatric, and SUDs were most likely to derive benefit in reduction of depressive symptoms from the EX intervention [34].

34.6 Summary/Conclusion

Exercise may be a useful approach to aiding individuals with SUDs in their efforts to avoid relapse after they have achieved abstinence via treatment. The addition of a new, non-drug-related activity could provide a reinforcing alternative behavior that may be effective in facilitating abstinence by enhancing positive mood states via the effects of exercise on the endogenous opioid system and potentiation of dopaminergic transmission [59]. Prior literature demonstrates that exercise can improve anxiety and depression, symptoms that are often associated with initial phases of abstinence after cessation of drug use. Such conditions predispose individuals to relapse and predict poorer treatment outcomes (e.g., [66, 71]). Exercise also improves sleep [92] and performance on cognitive tasks, which may be impaired in chronic substance users. In light of the documented associations between stress, negative affect, and substance relapse in addicted populations [11, 52], together with evidence demonstrating stress regulation deficits in substance users, the development of interventions to ameliorate symptoms of depression and anxiety and improve affect regulation may help to reduce relapse risk in this population. Relief of distressing psychological symptoms may serve to complement relapse prevention skills taught in common therapy approaches for substance users and to promote health and positive behavioral changes consistent with treatment goals.

Key Points

- Exercise is associated with numerous physical health benefits, including improved strength, cardiovascular fitness, weight management, and cognitive function.
- Emerging evidence demonstrates improvements in mental health symptoms associated with exercise, including reduction in depression and anxiety and improved sleep.
- Emerging evidence suggests beneficial effects of exercise as a treatment intervention for substance use disorders.
- Negative affects states, such as anxiety and depression, are common effects of substance use and are risk factors for relapse.
- Exercise may facilitate abstinence from substances by ameliorating negative affect via effects on the endogenous opioid system and dopaminergic transmission.

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