Clinical Exercise Considerations for Opioid Addiction Recovery

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ABSTRACT

According to the American Psychiatric Association, in 2018, approximately 2 million Americans were suffering from a substance abuse disorder, defined as substance abuse and dependence (1), related to opioids that were prescribed for pain management (2), while worldwide, it is estimated this approaches 16 million (3). Consequently, exercise clinicians will be increasingly exposed to individuals who have been affected by opioids and should therefore know how these drugs affect physiological functioning and how exercise can play a role in opioid addiction recovery. This review article is intended to provide some of this information. *Journal of Clinical Exercise Physiology*. 2021;10(3):117–125.

INTRODUCTION

The common comorbidities of opioid addiction include diabetes, obesity, osteopenia, and osteoporosis (4,5). Individuals also experience cardiopulmonary abnormalities, such as cardiac arrhythmias or valvular heart disease (VHD) (6). Exercise for opioid addiction recovery has the potential to contribute many physiological benefits as well as psychological because, during exercise, the body releases endogenous peptides which elicit a state of euphoria, like opioids. This has the potential to create a dependence to the euphoria from exercise, rather than with opioid consumption (7,8), and act as an adjuvant to the opioid agonist medications in helping treat and maintain recovery. However, currently, no specific exercise testing nor explicit exercise prescription guidelines exist for individuals recovering from opioid addiction. Interestingly, animal studies have demonstrated that aerobic and resistance training provide benefits to opioid addiction recovery, providing evidence that these benefits may also be seen in humans (9,10).

PATHOPHYSIOLOGY OF OPIOID ADDICTION

Opioid addiction transpires when an individual is physically and psychologically dependent and tolerant to opioids (11). Opioid addiction is more prevalent in poor socioeconomic locations (12) and in individuals who are younger (17–30 years), who typically experience opioid addiction from heroin, and older (>65 years), who are more likely to abuse opioids from prescriptions (13). While females are more often prescribed opioids, they are less likely to abuse opioids than males (7). Furthermore, individuals are more at risk for development of opioid addiction if they have a history of mental disorders, history of self or family substance abuse, and have the experience of injury or surgery with prescribed pain medications (8,14).

Opioid addiction involves several opioid receptors which regulate significant functions in the human body such as pain, stress, temperature, respiration, gastrointestinal and endocrine activity, and mood (15). These functions are often altered with individuals who are addicted to or in recovery from opioid abuse, with particular effects on pain perception (16). Opioids bind to these receptors for release of regulatory peptides (15). For example, morphine intake inhibits gamma-aminobutyric acid (GABA) release, which serves to prevent dopamine release. However, if GABA is inhibited from opioid intake, dopamine release freely occurs, resulting in euphoric feelings (17). Constant dopamine release from the brain can eventually lead to addiction from the desire to receive the euphoric sensation time and time again.

These actions involve the reward centers of the brain and mimic the pleasurable feelings stemming from everyday

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activities such as eating. However, when an individual ingests opioids in the absence of pain, the memory centers of the brain record this activity and link the pleasurable feelings to opioid intake, causing the individual to continue consumption, which can lead to dependence (18). Typically, drug dependence causes an increase in opioid consumption to achieve a euphoric mental state, which is not possible because the individual becomes tolerant from decreased opioid receptor sensitivity. Once consumption of opioids stops, the individual can experience withdrawal symptoms including dysphoria, anxiety, and panic attacks (18). After the individual is in withdrawal, they can return to a normal mental state over time; however, they can also relapse. Relapse rates vary widely, with factors such as greater rate of drug use before treatment, younger age, and low treatment uptake playing a role in the likelihood of relapse (19). The initial "high" will never be achieved with repetitive opioid consumption, and when individuals relapse, they experience a greater dysphoric mental state than the initial opioid consumption period (18). Figure 1 demonstrates the typical mental patterns or states that occur with opioid intake, withdrawal, and relapse.

CARE AND MANAGEMENT OF OPIOID ADDICTION AND RECOVERY

Providing care to individuals in recovery from opioid addiction is multifaceted because this population will face barriers including poor health and mental status. Clinicians working with this population will face difficulty in retaining an individual's attendance in recovery. Various treatments exist for those in recovery from opioid addiction including psychological counseling and behavioral therapy, pharmacologic treatment, nutrition, and exercise.

Psychological and Counseling Therapy

Chronic opioid addiction results in more severe pain and lower tolerance for pain sensations, called *opioid-induced hyperalgesia* (20). Researchers have suggested that psychological and behavioral therapy such as pain coping skills and counseling can suppress opioid craving, use, and abuse (21). Currently, not enough evidence demonstrates that psychological counseling alone benefits individuals recovering from opioid addiction. However, in conjunction with pharmacologic treatment, a slight advantage in prevention of relapse exists (22).

Pharmacologic Treatment

Most if not all individuals recovering from opioid addiction will be prescribed an opioid agonist (23) to aid recovery and reduce the risk of relapse. Methadone and buprenorphine are the 2 most common opioid agonists which work by suppressing withdrawal symptoms and attenuating the psychological effects of opioids (23). Methadone has the most

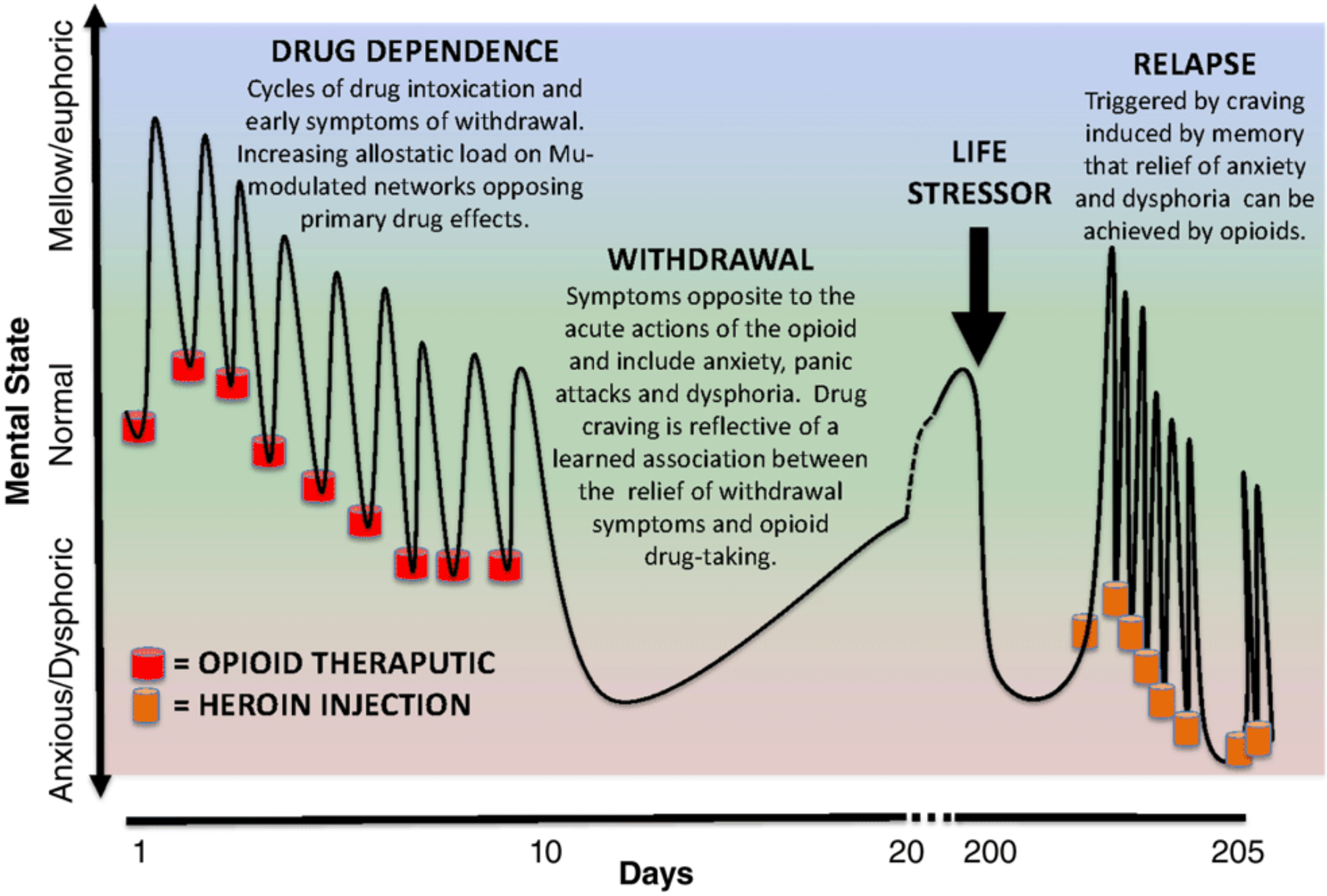

FIGURE 1. Manifestation of opioid addiction. ©Evans and Cahill (18). Used with permission by CC 4.0.

influential effect on opioid addiction recovery, likely because it fully binds to opioid receptors without creating mental euphoria, can eliminate typical withdrawal symptoms, and minimizes the possibility of relapse (24). Unlike methadone, buprenorphine effects the brain by mimicking the "problem" opioid and thus avoiding withdrawal symptoms and cravings (25). However, buprenorphine has a "ceiling effect" and cannot stimulate opioid receptors as strongly as methadone (26). While opioid dependence is an independent factor for premature mortality risk, pharmacological treatment reduces this risk. Specifically, buprenorphine reduces all-cause mortality compared with methadone within the first 4 weeks of the pharmacological opioid treatment therapy, after which minimal variation between the 2 exists. However, during the first 4 weeks out of treatment, drug-related overdose deaths are lower in individuals being treated with methadone than buprenorphine (27), potentially due to higher relapse rates with buprenorphine treatment (28).

Nutrition

Opioid addiction and recovery have disparate effects on the nutritional health of individuals. While opioid addiction itself results in poor nutritional habits (28) and underweight characterization, opioid recovery and the use of opioid agonists causes weight gain (29) and substandard body composition changes. During recovery, most individuals are likely to be overweight or obese and have prediabetes (30), with females typically having a greater weight gain than males (29). This weight gain is associated with the use of methadone. This is likely because the intake of opioids mimics the reward pathway of consuming foods (31). Therefore, integration of nutritional therapy is a critical component to a successful outcome of substance abuse treatments (32).

Exercise

An increasingly popular treatment being explored is exercise and physical activity (33). However, data from methadone-maintained persons showed that only 38% of participants meet the current US physical activity guidelines (34). While no exercise prescription guidelines exist targeting opioid addiction recovery, the American College of Sports Medicine guidelines (35) can be used to treat the commonly associated comorbidities, such as diabetes and obesity. Currently, there is a paucity of human research with a few clinical trials in progress. However, animal research lends significant insight into the effects of exercise on opioid use.

EFFECT OF OPIOID ADDICTION ON EXERCISE PHYSIOLOGY

Chronic opioid addiction can substantially alter physiological functioning of primarily the pulmonary, cardiovascular, musculoskeletal, and metabolic systems, with influence on the acute and chronic exercise responses during the recovery process.

Pulmonary

Opioid consumption results in respiratory depression, both from acute and chronic use. This is thought to be a result of reduction in central perception of dyspnea, decreased oxygen consumption, and a decrease in sensitivity to hypercapnia (36). Individuals on methadone treatment are known to have a decreased sensitivity to hypercapnia (37) and decreased oxygen saturation immediately after administration of maintenance doses (38). Additionally, opioid use can cause bronchoconstriction and worsen asthma symptoms (39) and may also result in the development of asthma (39). Taken together, authors of these studies demonstrate a need to monitor pulmonary system of individuals in recovery partaking in exercise.

Cardiovascular

The cardiovascular system is compromised by opioid use in multiple ways, primarily through the development of arrhythmias, endocarditis, and VHD. Acute opioid use can cause intermittent and severe bradycardia (37), while opioid addiction causes an increased risk of arrhythmias, specifically atrial fibrillation (40). Chronic opioid abuse can also lead to prolonged corrected QT interval (QTc). High-dosage methadone consumption, which is an effective treatment (41), leads to development of prolonged QTc and torsade de pointes (42). Interestingly, buprenorphine decreases the likelihood of QTc prolongation compared with methadone (43).

In addition to electrophysiological changes, opioid consumption and abuse can lead to structural complications. Intravenous (IV) drug use can lead to infective endocarditis from bacteria entering the bloodstream from contaminated needles (44). If untreated, infective endocarditis has the potential to damage heart valves causing VHD, further increasing the risk of congestive heart failure development and myocardial abscesses (45) and increasing mortality (46). Also, a risk of myocardial injury exists with further potential negative effects on the response to exercise (47).

Musculoskeletal

Opioid addiction or dependence may lead to decreased bone strength and bone mineral density, particularly in women, where it has been found that as many as 34% with opioid dependence have osteopenia or osteoporosis (4). The degree of bone loss and quality of bone is highly correlated with the duration of drug intake (48). Muscular fitness may also be affected, including low muscular strength and endurance from low physical activity and/or sedentary lifestyle because of addiction (49). However, little published data exist on fitness levels of opioid users.

Metabolic

The abuse of opioids results in metabolic system complications, such as type 2 diabetes and altered gastrointestinal function. Opioid intake results in a delayed insulin response to food, as well as increased resting insulin concentrations (50,51) that coexist with sedentary behavior and lower insulin sensitivity. Moreover, methadone treatment can delay and inhibit insulin response to food ingestion (52) and decrease the levels of key glycolytic enzymes hexokinase and phosphofructokinase (53). If this occurs, a risk of hyperglycemia exists. However, evidence suggests buprenorphine-naloxone lowers glycated hemoglobin levels like metformin or sulfonylureas (5).

Gastrointestinal system function can be altered when individuals chronically abuse opioids, causing decreased gastrointestinal motility and slower gastric emptying rates. This is most likely to occur when consuming high-carbohydrate foods (54). Additionally, when opioids, including maintenance drugs like methadone, are consumed in chronic amounts, an induction of constipation further leads to bowel dysfunction rooted from opioids (55).

BENEFITS OF EXERCISE FOR PEOPLE LIVING WITH SUBSTANCE USE DISORDER

For individuals in recovery from opioid addiction, exercise has potential benefits that may lessen the possibility of relapse (33) and create a more manageable recovery process. Significant evidence exists of psychological benefits of exercise in opioid addiction recovery, including improved abstinence and withdrawal and decreased depression and anxiety (56). Indeed, in methadone-maintained individuals, those with higher levels of physical activity report a greater belief that exercise can decrease relapse rates and improve mood (34). However, a dearth of human evidence exists on the physiological benefits of exercise during recovery. The following section reviews the effect of exercise on the physical and mental benefits to individuals in recovery from opioid addiction, specifically by decreasing cardiovascular disease risk via improved aerobic capacity and self-efficacy (57), while also decreasing substance use (33). Unfortunately, significant barriers to exercise participation exist in those recovering from opioid addiction, including lack of motivation to begin, altered pain sensing, and body consciousness (i.e., excessive sweating) that must not be overlooked and will be discussed further.

Aerobic Exercise

Unfortunately, most researchers using aerobic exercise interventions for opioid disuse do not quantify changes in physical fitness levels, as their studies are primarily designed to investigate changes in mental state and recovery management. However, a few human studies on the effect of aerobic exercise exist. Authors of a pilot study of drug addicts (not specific to opioid disuse) showed unstructured aerobic exercise, such as cycling and weight training, significantly improved aerobic capacity during a step test by 3.2 $mL \cdot kg^{-1} \cdot min^{-1}$ (58). Authors of another study indicate that exercise such as walking for 30 minutes per day, 3 days per week can improve serotonin and dopamine levels, body fat percentage, muscular endurance, and flexibility (49). These improved levels of dopamine and serotonin indicate that, during aerobic exercise, the brain uses the same reward pathways as with opioid consumption. Indeed, this has been shown in healthy nonopioid-using individuals during moderate-intensity exercise, but not high-intensity exercise (59). In fact, high-intensity exercise in healthy men resulted in exhaustion, low energy, and irritation compared with moderate-intensity exercise (59). However, high-intensity circuit training in a small cohort of persons suffering from substance abuse (not specific to opioid disuse) improved aerobic capacity 15 ± 7% (60), though the authors did not measure psychological effects of exercise. Additionally, meta-analytical data suggest high-intensity exercise is effective for treating anxiety (61). The differences may in part be due to variations in intensities of exercise, with lower intensity (80%–95% $\dot{V}o_2$max) causing fewer mental perturbations than higher intensities (all-out efforts). This indicates that those in recovery from opioid addiction may want to avoid all-out effort, high-intensity exercise (i.e., repeated Wingate sprints) to prevent anxiety or fatigue and instead participate in shorter high-intensity training with appropriate rest or moderate-intensity exercise, which produces satisfaction and euphoria.

In terms of abstinence from substance use, authors of a pilot study of 16 individuals participating in alcohol and drug treatment investigated the use of aerobic exercise in recovery (33). Individuals were prescribed a 12-week exercise intervention consisting of aerobic exercise 3 days per week at 55%–69% of age-predicted maximal heart rate for 20 minutes (progressing up to 40 minutes by week 12). The authors reported a significant increase of 0.5 metabolic equivalent (MET) as well a 43-second increase in exercise test duration from baseline through treatment. Furthermore, significant increases existed in percent of days where individuals abstained from alcohol and drug use in the exercise group versus control. Those that were compliant with ≥75% of the exercise sessions had less substance use and lower relapse rates than those who did not (33). Authors of the previously mentioned pilot study (n = 17) also found an 18% decrease in the desire to use drugs in those participating in unstructured exercise (58). Though more research is needed, it is noted that similar findings are reported with mice, where 11 and 30 days of aerobic exercise decreased self-administration of morphine (9).

To understand how exercise can improve quality of life in opioid addiction recovery, Huang et al. (62) studied heroin-addicted individuals for 6 months, during which half the participants walked or jogged 3 days per week at 50%–60% of the maximal oxygen consumption ($\dot{V}o_2$max) for 40–60 minutes. The individuals in the exercise group showed improved withdrawal, anxiety, and depression scores, with greater improvements the longer the training went on. Unfortunately, these authors did not report changes in physical fitness levels.

Taken together, consistent evidence shows that moderate aerobic exercise has positive effects on mental state in opioid addiction recovery. It is reasonably likely that moderate-intensity aerobic exercise training improves physical health as well.

Resistance Training

Unfortunately, to date, no human intervention studies regarding resistance training and opioid addiction exist; however, animal studies lend insight into the potential benefits. In rats who were trained to climb a ladder with a weighted vest carrying 70%–100% of their body weight, 6 days per week for 5 weeks, heroin self-administration significantly decreased (10). This is like findings of aerobic exercise and indicates that resistance training may possibly have a positive influence on withdrawal and abstinence from opioids.

Mindful Movement Exercise

Yoga is a complimentary medicine technique that is often used in substance abuse treatment, in part because it decreases anxiety and increases GABA levels (63). Participation in yoga 5 days per week at an intensity of 2.5–3.0 METs for approximately 50 minutes per session (64) improved mood status and quality of life of heroin-addicted females compared with those in the control group (64).

Tai Chi can similarly be used as a complimentary treatment for substance abuse, in part because it encompasses both physical activity and encourages mindfulness, both which may help with relapse prevention in opioid recovery. Li et al. (65) found the use of Tai Chi 3–4 days per week for 60 minutes at an intensity of 3 METs decreased feelings of guilt, depressed mood, and heroin withdrawal symptoms.

BARRIERS TO EXERCISE

Perhaps the most important barrier to exercise is that chronic opioid abuse can lead to increased levels of anxiety and depression, as well as distorted pain perception (66). Indeed, those on methadone maintenance with chronic pain and higher levels of depression are less likely to participate in exercise than those without (67). Additionally, if an individual has distorted pain perception, they may be hesitant to progress during training due to muscle soreness. Furthermore, individuals in this population face psychological barriers with motivation to begin and remain in exercise. Specifically, lacking motivation to start exercise and a lack of perceived energy to participate in exercise are noted as the largest barriers in methadone-maintained persons (34). Additionally, a recent qualitative study of individuals living with substance use disorder indicates methadone maintenance symptomology, such as excessive sweating and mood swings. These participants also noted they lacked motivation to exercise because they did not want to be seen outside by members of the community, as they were embarrassed by their past criminal behavior (68).

Moreover, individuals in this population may be overweight or obese and significantly deconditioned (29), which may inhibit the use of some modalities and may require shorter exercise sessions to avoid exhaustion. Comorbidities including diabetes, osteoporosis, osteopenia, and gastrointestinal dysfunction should also be monitored. If an individual has diabetes, the need exists to monitor their blood glucose before, during, and after exercise to ensure avoidance of adverse events (35). Regarding osteoporosis or osteopenia, fall risk and risk of injury with falls should be assessed using a tool such as the Hendrick II Fall Risk Model, which can predict falls in acute care and community settings (69). Electrocardiographic supervision is warranted during exercise testing and initial exercise sessions to monitor development of arrhythmias (6).

EXERCISE TESTING

For clinical exercise physiologists, it is important to consider the best prescription for everyone and approach every client as a new case, in which every individual may have a variety of different limitations or risks during exercise. In addition to providing baseline values for goal setting and to evaluate improvements, exercise testing allows individuals to become familiar with exercise equipment and permits the opportunity to identify how the individual responds to exercise, both physiologically and psychologically.

Body Composition

Ideally, body composition should be assessed with dual energy x-ray absorptiometry (DEXA) to assess lean mass, fat mass, and bone density. However, lack of access may dictate the use of bioelectrical impedance analysis (BIA) if all pre-assessment guidelines are followed. Typical outcomes expected for body composition for individuals in recovery from opioid addiction include low bone mineral density (48), normal to high body weight and fat mass (29), and normal to low fat free mass (49). Bone mineral density has been shown to improve with resistance training in individuals with a substance abuse disorder (70). Therefore, it is likely that exercise intervention in persons living with opioid abuse disorder will also improve.

Cardiorespiratory Fitness

Due to altered pain sensing and potential for early test termination, cardiorespiratory fitness should be assessed using submaximal testing, such as a perceptually regulated treadmill test. This test is commonly performed using rating of perceived exertion (RPE) scales to anchor exercise intensity during the test, slowly increasing to the next RPE level as the test progresses. The test allows individuals to control the intensity of the exercise, even changing during each stage, so long as it elicits the correct RPE value (71). $\dot{V}o_2$max can then be estimated to create an exercise prescription. Alternatively, the modified Naughton protocol may be used due to its slow and steady incremental exercise intensity (72). The outcomes compared with the healthy population for this component would be presumed poor, as those with substance abuse disorder have been shown to have a 15%–25% lower $\dot{V}o_2$max than healthy controls (60). However, data specific to opioid disuse in the literature are lacking.

Muscular Fitness

Muscular fitness is presumed to be poor in this population due to lack of activity and muscle atrophy from opioid abuse. During the recovery phase, values are expected to improve.

REVIEW

An appropriate muscular fitness test would be an estimated 1 repetition-max of upper body and lower body using 3–5 repetitions of each exercise. The expected outcome from this exercise test is presumed poor as data on persons with a substance abuse disorder demonstrate a 30%–33% reduction in 1-repetition maximum squat compared with healthy individuals (60). In people living with substance use disorder, resistance training programs have improved 1-repetition max squat by 70%–88% (70,73). However, data specific to opioid disuse are lacking.

Flexibility

Flexibility has not been commonly assessed in this population. While the expected outcomes from a sit-and-reach or back-scratch test can be inferred as below average or poor due to the history of physical inactivity, authors of 1 study demonstrated average flexibility on a sit-and-reach test in men aged 20–30 (49).

EXERCISE PRESCRIPTION

As stated above, many exercise interventions are appropriate for individuals undergoing recovery from opioid addiction. Below, we highlight our suggestions for basic exercise prescription in this population including cardiorespiratory, resistance, flexibility, and mindfulness training (summarized in Table 1). In a cohort of those in recovery from substance abuse (n = 97), interest in participating in targeted structured exercise training as part of recovery is high (94%) (74), indicating a desire to use exercise as a tool for recovery. However, the retention rates of participants from this special population require high attention. Therefore, it is important to find activities that the individual enjoys, perhaps in an outdoor environment and with a buddy, to promote activity engagement. In addition, journaling and maintaining a log of activity may be a way to promote retention through higher self-efficacy (75).

Cardiorespiratory Training

Following the American College of Sports Medicine exercise prescription guidelines, aerobic exercise should occur most, if not all days of the week for 20–60 minutes (35). Due to the nature of the condition with increased presence of arrhythmias and altered pain sensing, RPE is the preferred mode for monitoring intensity. Individuals should begin with walking or cycling and possibly progress to jogging or running; however, exercise intensity should be maintained at a moderate level (12–14 Borg RPE) to avoid the negative effect associated with high-intensity exercise (76). It would be ideal to begin with exercise in 5- to 10-minute increments with rest breaks, progressing slowly by adding duration. If the individual can perform the proposed aerobic endurance exercise prescription, increase the duration to two 15-minute bouts and progressively increase RPE intensity along with duration. Circuit training may also be a plausible alternative to continuous training, as it has been demonstrated to successfully help improve aerobic capacity in substance abuse disorders (not specifically opioid abuse). However, the intensity should remain below all-out effort, as this can cause negative affect in sedentary people (77), and long-term adherence is low (78).

Resistance Training

Resistance training can occur 2–3 days per week of 8–12 exercises using large muscle groups; body weight exercises or machines may be safer until individuals are educated and conditioned for free-weight exercises. Data indicate maximal resistance training of hack squat exercise of 4 sets, 4–5 repetitions at 80%–90% is well tolerated and improves squat performance and rate of force development (73). Avoiding high-intensity eccentric work that may result in myalgias and increase the likelihood of dropout is imperative.

Flexibility and Mindfulness Training

Participation in yoga or Tai Chi is strongly encouraged to provide both physical and mental benefits such as improved mood, reduced anxiety, and relapse prevention (64,65). Flexibility or mindfulness training should occur 3–5 days per week at a light to moderate intensity (2–4 METs) for at least 30 minutes and progressing to 60 minutes.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Exercise training, regardless of type, appears to be beneficial for opioid addiction recovery, not only for physiological parameters but also mental health and long-term

TABLE 1. FITT-P exercise prescription.

	Frequency	Intensity	Time	Type	Progression
Aerobic	5–7 d/wk	12–14 RPE (Borg scale; 40%–60% $\dot{V}o_2$max)	Minimum 30 min/d, may be in 3–6 bouts of 5–15 min	Walking, cycling	Aim for 30 continuous min, progressing to 60 min
Resistance	2–3 d/wk	40%–60% 1 RM (or estimated 1 RM)	1–2 sets; 8–12 reps	Body weights to begin, progress to free weights	Increase sets, then increase resistance up to 80% 1 RM
Flexibility	3–5 d/wk	2–4 METS	30 min	Yoga, Tai Chi (fluid movements)	Up until 60 min per session

FITT-P = frequency, intensity, time, and type-progression; RPE = rating of perceived exertion; MET = metabolic equivalent of task; RM = repetition-maximum; REPS = repetitions quality of life. However, clinical exercise professionals should be aware of the physiological consequences of opioid addiction and possibly avoid using all-out intensity protocols that might lead to a negative effect and discourage adherence to exercise programs. Tailoring exercise programs specifically for individuals recovering from substance abuse, specifically by collaborating with them on what they would like to participate in, may be one of the ways to ensure successful exercise adherence. Additional practical strategies to improve adherence include setting specific, measurable, achievable, relevant, and time-based (SMART) goals and empowering the person living with opioid use disorder to self-monitor their progress.

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REVIEW