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Exercise as an Adjunct Treatment for Opiate Agonist Treatment: Review of the Current Research and Implementation Strategies

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Abstract

Opiate dependence is a significant public health concern linked to poor quality of life, co-morbid psychiatric disorders, and high costs to society. Current opiate agonist treatments are an effective but limited intervention. Adjunctive interventions could improve and augment opiate agonist treatment outcomes, including drug abstinence, quality of life, and physical health. This article reviews exercise as an adjunctive intervention for opiate agonist treatment, especially in regards to improving mood and overall quality of life, while reducing other substance use. Poor adherence and dropout frequently prevent many individuals from garnering the many physical and mental health benefits of exercise. Strategies for implementing an exercise intervention, including safety considerations, are discussed.

Keywords

exercise; opiate agonist treatment; adjunctive interventions; contingency management

Opiate dependence is associated with many health problems and social complications that make recovery difficult. Individuals with opiate addiction frequently are unemployed, homeless, and/or involved in drug-related criminal activities. Moreover, costs to society in terms of medical care, lost productivity, crime, and social welfare of this disorder are estimated to be in the billions of dollars¹. The treatment of opiate dependence using opiate agonists, such as methadone, has been shown to be safe and effective since the late 1960s. Specifically, methadone maintenance therapy (MMT), and more recently other opiate agonists, such as buprenorphine, relieves craving for narcotic drugs, temporarily suppresses symptoms of withdrawal, and blocks the euphoric effects of opiates². However, while opiate agonist patients show reductions in HIV-risk behaviors and improved social integration and psychosocial functioning³, many continue to suffer from a variety of psychiatric and medical ailments, including Hepatitis B and C viruses, HIV, major depression, other substance use disorders (SUD), and poor quality of life^{4–6}.

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Although MMT is considered to be the “gold standard” of opioid dependence treatment, its use and success is limited⁷. The average retention rate ranges from approximately 40% to 55%^{8, 9} at 1-year follow up. Frequently, MMT programs implement rules and criteria which often lead to a high drop-out rate by patients⁷. In addition, treatments which simply replace one drug with another have led to longer durations in programs and decreased chances of retention and overall success¹⁰. In order to improve mental and physical health and overall quality of life and to reduce substance use among opiate agonist patients, adjunctive interventions are needed^{9, 11}. Adjunctive treatments are supplementary services and activities for therapeutic or medical gain. For example, adjunctive treatments for SUDs range from acupuncture and substance abuse education to self-help groups (e.g., Narcotics Anonymous⁹).

One promising adjunctive treatment for opiate agonist programs that could address many of its limitations is exercise. Exercise is defined as moderate to vigorous physical activity. In this paper, we propose a model which suggests exercise as a potentially beneficial adjunct treatment for opiate dependence. Exercise has many physical and mental health benefits, which have been demonstrated across various populations. We propose that based on the guidelines suggested by the American College of Sports Medicine (ACSM) and the American Heart Association for adults aged 18–65 years, individuals with opiate dependence disorders can reap the many benefits of adding exercise to a treatment program. The overall goal of adjunctive exercise interventions should be to gradually build over time exercise activity that is in accordance with these guidelines.

First, we will discuss the benefits of exercise in physical and mental health domains and possible mechanisms of action. We will also propose an intervention to increase adherence to an exercise program. Finally, we will discuss other concerns and considerations for treatment of opiate dependent population. A comprehensive literature search was conducted on the PsychINFO and MedLine databases for the period of 1900 to 2011. Key search terms were (in alphabetical order): contingency management, exercise, methadone, opiate agonist treatment, physical activity, and substance use disorders.

Benefits of Exercise

Exercise has demonstrated substantial benefits in terms of mental and physical health with improvements in cardiovascular health and health-related quality of life, and reduction in the risks for various chronic diseases (e.g., type-2 diabetes mellitus, coronary heart disease, obesity¹²). Exercise also has well-established beneficial effects on reducing symptoms of anxiety, lowering the risk of major depression relapse^{13, 14} decreasing urges to drink alcohol¹⁵, lessening nicotine withdrawal and cannabis and cigarette cravings^{16, 17}. Additionally, exercise has greater benefits as a means of coping and managing depression than other substance-free activities with effect sizes ranging from moderate to large ($d = 0.39$ to 0.50)¹⁸. Similar effect size estimates are noted for the impact of exercise on anxiety¹⁹. The benefits of exercise are numerous for mental and physical health, which is why exercise is recommended as an adjunctive treatment over other activities.

The mental and physical benefits of exercise make physical activity a unique strategy that may help individuals with opiate dependence cope with stressors. Many opiate agonist patients rely upon avoidant coping strategies, which can lead to more frequent substance use and greater substance-related problems when compared to opiate agonist patients who engage in active coping^{20, 21}. The detrimental effects of an avoidant coping style, in comparison to an active coping style, are numerous in terms of psychological and physical well-being across a wide spectrum of behaviors and problems^{22, 23}. Coping styles are typically assessed via self-report measures²⁴. Given that exercise has been shown to help individuals cope with stress ($d = 0.56$ to 1.42)²⁵ and induce positive affect, it is hypothesized that exercise will also be an effective adjunct intervention for patients who are using substances as a means of avoidant coping.

Potential Mechanisms of Action

Given the benefits noted above, exercise has garnered attention as a potential adjunct to SUD treatment^{26, 27}. A basic premise of 12-step, cognitive-behavioral, community reinforcement, and contingency management (CM) therapies is to assist patients in developing rewarding and enjoyable activities that do not revolve around drug use. Exercise can serve as a healthy substitute behavior^{28, 29}. Theories of how exercise bestows its beneficial effects are numerous and unclear at this time. Possible mechanisms of action include increased socialization³⁰, improved emotion regulation³¹, decreased anxiety sensitivity³², and improved stress management³³. It is hypothesized that these mechanisms of action mediate the effect that engagement in exercise has upon clinical outcomes, such as abstinence, problem severity, quality of life, and depression.

Both emotion regulation and anxiety sensitivity, which is fearfulness of anxiety itself, are risk factors for the development and maintenance of substance use disorders^{34, 35}. Individuals potentially use substances to self medicate or avoid the aversive stimuli that are hallmarks of poor emotion regulation and anxiety sensitivity. In the case of anxiety sensitivity, exercise provides exposure to the anxiety sensitivity sensations such as racing heart beat, fast breathing, and perspiration. Exposure to these symptoms without the induction of anxiety lessens reactivity to these sensations³⁶. Reductions in anxiety sensitivity may lead to reductions in substance use to self medicate these aversive feelings. Exercise aids emotion regulation by inducing positive affect and relieving stress.

Perceived stress leads to a psychological and biological response that can have a range of outcomes, both positive and negative. Maladaptive responses to stress in individuals with SUD potentially include using substances to relieve stress. Stress management interventions typically focus on reducing stressors and development of adaptive responses to stress, including modification of cognitive appraisals of the perceived stress, and coping behaviors. Stress management is important for individuals with substance use disorders as they often experience greater stress³⁷ and are likely to handle it less effectively than the general population³⁸ by turning to substances for relief. Not only do these individuals experience more stress, but the continued use of alcohol and drugs continuously activates the stress axes, impairing the body's natural response mechanism. Repeated use of these substances causes dysregulation of the stress response system, leaving individuals more prone to and

experiencing stress³⁹. Research has demonstrated that stress is a strong predictor of drug and alcohol use and subsequent relapse^{40, 41}.

Exercise has the ability to improve the regulation of the stress axes by maintaining homeostasis and improves the body's response to stress. Exercise is consistently associated with positive mood by increasing feelings of vigor and reducing tension, fatigue, and confusion⁴². Moreover, exercise can increase positive affect and decrease negative affect, which is consistent with many SUD treatment models. For example, drugs operate by positively reinforcing the patient with feelings of euphoria. The individual's mood rises above the normal set point when the drug is administered, decreases below normal, and then returns to the set point⁴³. Over time, the set point continues to be placed lower and lower. This results in the patient needing more of the drug to reach the old "normal" level. Koob and Le Moal's dependence theory of addiction⁴³ operates on the basis that individuals who experience withdrawal symptoms (i.e., negative affect, depression) alleviate these symptoms by using more of the substance, which in turn continues the cycle of substance use and dependence⁴⁴. In behavioral terms, substance use and dependence is maintained by a negative reinforcement schedule (i.e., withdrawal symptoms promote more substance use to alleviate the negative symptoms) and the cycle can be broken by positive reinforcement, such as exercise. Therefore, exercise may have the potential to help "reset" the stress reactivity for substance users in treatment, and subsequently reduce the risk of relapse.

Another theory is the manner in which the brain is involved during physical activity itself. Opiate drugs impact the brain's natural reward system by releasing powerful neurotransmitters which elicit feelings of euphoria⁴⁵. Likewise, exercise also has the ability to release endogenous opioids, in the peripheral and central nervous system^{46, 47} which can result in a positive mood⁴⁸. In fact, studies suggest opioid levels play a role in the "runner's high" phenomenon^{49, 50}. Endogenous opioids have chemical properties similar to that of opiates such as heroin and morphine⁴⁵ which potentially makes exercise a compatible substitute for drug use. Other neurobiological mechanisms of action of physical activity's impact upon psychological functioning also potentially include serotonin⁵¹. Researchers should assess these possible mechanisms to ascertain if any mediate outcome in relation to exercise engagement.

Experimental Studies Involving Exercise

As discussed earlier, substance use can be conceptualized as a goal directed behavior that is governed by the principles of reinforcement. Animal studies repeatedly demonstrate that rates of substance self-administration vary inversely with the availability of substance-free reinforcers such as food, wheel-running, and social environments⁵². In human studies, data are emerging that suggest substance use often occurs at the expense of other, substance-free activities^{53, 54}. Experimental studies have investigated the efficacy of increasing alternative substance-free behaviors as a means to decrease substance use. For example, Murphy, Pagano, and Marlatt⁵⁵ in a randomized clinical trial with 60 heavy drinking college students found that exercise demonstrated the greatest reductions in alcohol consumption in comparison to a meditation intervention and a no-treatment control group. Reductions were significantly greater than the no-treatment control group ($d = 0.97$ to 1.19) and were

primarily related to reductions in weekday drinking and a moderate effect size was found for exercise in comparison to the meditation group ($d = 0.56$ to 0.71). Despite problems with attrition ($> 30\%$), this study provides preliminary evidence that increasing a specific substance-free activity (i.e., exercise) can decrease drinking.

In addition to a reduction in drinking behavior, quasi-experimental studies have found evidence of physical health benefits in other SUD populations. Sinyor and colleagues⁵⁶ evaluated 58 alcohol dependent patients who participated in 6 week tailored exercise program. In addition to receiving the physical health benefits of exercise (e.g., decreases in body fat), individuals who exercised had the best alcohol outcomes post-treatment and throughout an 18-month follow-up period relative to two comparison groups of alcohol dependent patients who did not exercise. More recently, Brown and colleagues⁵⁷ in a sample of SUD patients from a partial-hospitalization program found that those who adhered (62.5%) to a moderate intensity exercise intervention were less likely to relapse to substance use and had improved physical fitness outcomes. Overall, these studies demonstrate that exercise can decrease substance use and increase physical health.

Gaps in our knowledge about the potential beneficial effects of exercise remain. Greater specificity in our knowledge regarding exercise as an adjunct intervention for SUD is needed. Currently, empirically-based guidelines regarding the exercise prescription required to produce reductions in substance use and affect improvements in SUD populations is unknown. Future studies investigating the frequency, intensity, and type of exercise that produce beneficial outcomes are warranted. To increase the rigor and validity of future randomized controlled trials of exercise in SUD samples careful measurement and quantification of exercise is suggested. Exercise can be quantified in terms of frequency, intensity, time and type (FITT). We recommend assessing and reporting intensity of physical activity terms metabolic equivalents of a task (METs)⁵⁸. Additionally, testing the potential of mechanisms of action discussed previously remains.

Exercise Guidelines and Safety Considerations

Intensity of exercise occurs along a continuum from light, to moderate, to vigorous. Vigorous intensity exercise is not recommended for substance use populations due to the more intensive pre-participation screening and monitoring/supervision of the exercise itself. Therefore, moderate intensity exercise is preferred as the risk of injury or other adverse events is less, monitoring and supervision required is also significantly less, and is more cost efficient. If a moderate intensity exercise program were to be adopted in an opiate agonist clinic, we recommend using the ACSM's exercise pre-participation screening guidelines⁵⁹. These empirically-supported guidelines provide a risk categorization scheme that determines whether or not individuals need to consult with a medical professional prior to beginning an exercise program.

The ACSM and the American Heart Association have published physical activity recommendations for adults aged 18–65 years⁶⁰. These recommendations include the following components: (1) aerobic exercise a minimum of 5 times per week for a duration of approximately 30 minutes per session at moderate intensity (i.e., noticeably increases

breathing and heart rate), or vigorous intensity (i.e., substantial increases in breathing and heart rate) aerobic exercise for 20 minutes 3 days per week; (2) a strength/resistance program 2 to 3 times per week with 1 to 3 sets of 8–15 repetitions of the major muscle groups; and (3) a flexibility or stretching program of the major muscle groups 2 to 3 times per week. In addition, the U.S. Department of Health and Human Services' *2008 Physical Activity Guidelines for Americans* provides recommendations for all adults⁶¹. These guidelines suggest for substantial health benefits, adults should complete at least 150 minutes of moderate intensity aerobic exercise or 75 minutes of vigorous intensity aerobic activity per week. In addition, muscular strength or resistance exercise (moderate to high intensity) should be completed involving all major muscle groups at least two days each week⁶¹. The overall goal of adjunctive exercise interventions should be to gradually build over time exercise activity that is in accordance with these guidelines.

Many patients are likely to be sedentary. In fact, most adults are not active enough to reap the benefits of physical exercise. Only 30% of individuals in the U.S. engage in a significant amount of exercise each week⁶². For some, their regular amount of activity falls below the recommended guidelines. The risks of failing to exercise according to recommended guidelines are significant. Sedentary individuals are at increased risk for obesity, metabolic syndrome, diabetes mellitus, and certain types of cancers, which in turn is associated with increase morbidity and mortality⁶³. Even individuals that do engage in minimal amounts of exercise are not getting the sufficient dosage of exercise needed to see the mental and physical health benefits. However, moderate intensity exercise is beneficial for all individuals indicating that the risk-benefit profile is favorable⁶⁴.

Consultation with a physician may be necessary to ensure safety and to monitor any current or past health concerns. Perez-Moreno and colleagues⁶⁵ engaged HIV/Hepatitis C co-infected MMT prison inmates in a supervised aerobic and resistance training program. After four months, participants randomized to the exercise condition evidenced improved physical fitness, muscle strength, and overall quality of life in comparison to a control condition. In addition, no adverse events were reported for any exercise participants, suggesting exercise is safe even in medically compromised opiate agonist patients. Unfortunately, no substance use data were collected and potential mechanisms of action were unexplored.

All individuals can benefit from regular physical activity, however, we advocate exercise in opiate agonist patients because of the unique circumstances which MMT programs offer. Methadone only lasts for 24 hours, which means it must be administered once a day to avoid withdrawal symptoms⁴⁴. Daily visits over a sustained period of time provide a prime opportunity in which health care and treatment providers can intervene and offer adjunctive therapies, such as exercise.

Designing an Appropriate Exercise Program

Due to the way in which many exercise programs are implemented, most individuals do not adhere to or sustain a regular physical activity schedule. A commonly cited statistic is that approximately 50% drop-out or do not adhere with the exercise regimen⁶⁶. Common causes of dropout and barriers to adherence are poor social support for exercise, low exercise self-

efficacy, time pressures, low motivation to exercise, and unrealistic and vigorous intensity physical activity prescriptions^{67–69}. Additionally, some exercise programs do not prescribe a sufficient amount of exercise for an individual to gain its many benefits.

For example, in Walker et al.⁷⁰, an exercise program was established in an outpatient methamphetamine treatment program offering classes twice a week. Initially, exercise groups were poorly attended and staff had difficulties following administrative policies related to the groups. Because of the inadequacy of program execution, we advocate for the utilization of contingency management (CM) to reinforce exercise participation, as it is an effective behavioral strategy that increases adherence to various observable behaviors. Contingency management is a behavioral intervention in which tangible reinforcement is provided when a target behavior is completed and objectively verified. Through experimental studies and real-world applications, behavioral reinforcement programs have been used both effectively and ineffectively as an intervention for increasing exercise adherence. It appears that physical activity can be most effectively modified *if* it is monitored frequently with immediate, desirable rewards are offered, *and* reinforcement is withdrawn in instances of non-adherence.

We suggest a CM for exercise intervention as it incorporates personalized attention, utilizes frequent monitoring of exercise behaviors, offers high magnitude rewards that escalate for continued completion of exercise behaviors, and enforces a reset contingency when exercise behaviors are not completed. The combination of these factors is likely to improve initiation and adherence to an exercise regimen in opiate agonist patients.

While few investigations focus on exercise in opiate agonist patients⁶⁵, numerous studies examine methods for initiating and adhering to an exercise program in various other populations, including those with obesity, diabetes mellitus, cardiac disease, and mood disorders^{71–73}. Overall, these studies demonstrate the difficulty of initiating and maintaining an exercise program, as many participants discontinue exercising prior to realizing its many potential benefits.

Conversely, several factors are associated with successfully initiating and maintaining an exercise program. Moderate intensity exercise has greater adherence rates in comparison to vigorous intensity exercise⁶⁷. Other factors include social support, self-efficacy, motivation, having physical activity choices, goal setting and behavioral contracts, positive reinforcement, and feedback⁶⁸. Additionally, studies have found that extrinsic motivation may be important for initiating exercise⁶⁹ while intrinsic motivation is necessary for long-term adaption.

We believe a CM intervention will demonstrate a strong effect in terms of increasing exercise, as it does for other target behaviors⁷⁴. Whether these effects will be maintained after a CM intervention has ended is a significant empirical question. Theoretically, over time individuals will experience other positive effects of exercise besides the incentives provided, and these effects may become motivating for continued adherence. CM studies for drug abstinence find that longest duration of abstinence during the CM intervention is one of

the strongest predictors of abstinence at long-term follow-up^{75, 76}. Therefore, these factors need to be considered when designing and implementing exercise interventions.

Contingency Management for Exercise

Contingency management, an empirically supported treatment for SUD^{74, 77}, could easily be adapted for exercise and would adequately incorporate the above referenced factors and address difficulties associated with initiating and sustaining an exercise program. As a SUD intervention, CM patients are typically reinforced with vouchers, exchangeable for retail goods and services, when objective evidence confirms abstinence from drugs. Contingency management is efficacious in a variety of SUD populations and settings, including methadone maintenance clinics⁷⁸. Consistently, in these and other studies, CM increases retention in treatment and engenders longer durations of drug abstinence^{74, 77}.

Currently, two empirically supported CM protocols exist: voucher-based and prize-based. Voucher-based CM protocols operate on a fixed-ratio schedule of reinforcement with a pre-determined magnitude of reinforcement provided each time the target behavior is demonstrated. Meanwhile, prize-based CM protocols operate on a variable-ratio schedule of reinforcement. Individuals earn draws from a prize bowl each time the target behavior is demonstrated. The prize bowl contains a set number of slips of paper, 50% are associated with winning a prize (i.e., reinforcement). Typically, prize-based CM protocols are less expensive than voucher-based CM protocols. In head-to-head studies, prize-based CM was as efficacious as voucher-based CM even when arranged dollar amount of reinforcement was lower⁷⁹.

Contingency management has been adopted, with much success, to reinforce other behaviors, including medication adherence, completion of therapy related-goals, and treatment attendance. Common to all these applications of CM are three central tenets: (1) the environment is arranged such that target behaviors are frequently and easily monitored, (2) tangible reinforcers are provided whenever the target behavior is demonstrated, and (3) when the target behavior does not occur, rewards are systematically withheld (and sometimes a slight punisher may also be delivered). In fact, Lussier and colleagues⁷⁷ found that immediacy and magnitude of rewards were significant moderators of CM effect sizes with more immediate access to large reinforcement increasing the effect size.

While CM can alter a variety of behaviors, few studies have utilized CM procedures for exercise. Several physical activity interventions utilizing contingent incentives have shown modest effects, while others have been ineffective. These differences in outcome appear to be related to the implementation of and adherence to CM principles. For example, Jeffery and colleagues⁸⁰, offered incentives (ranging from \$1–\$3, paid out *monthly*) for one specific exercise activity: attending a structured walking session in obese adults. Those receiving the incentives along with a personal trainer had better attendance at the walks than any other condition. Thus, incentives and personalized attention appear to positively impact the target behavior; however, the intervention did not impact overall exercise engagement or weight loss, probably because incentives were not offered for those specific target behaviors. Other

contingent incentive studies demonstrating limited efficacy provided minimal reinforcement that was delayed⁸¹.

In a real-world clinical setting, contingency management for increasing exercise adherence can be effective, but the method in which it is implemented is important. For instance, Walker and colleagues⁷⁰ investigated different settings in which CM for exercise was used. Attendance at exercise classes fluctuated across the weeks, which the authors attributed to problems in implementation by the clinic staff. Therefore, it is important to reinforce with a desirable incentive as soon as possible after the behavior. Petry⁸² recommends administering this type of reinforcement on a daily basis. In contrast, studies showing more pronounced effects for incentives on physical activity are those that engage in frequent monitoring of the target behavior, offer tangible and immediate reinforcement, and withhold reinforcement when the behavior was not completed^{83, 84}. In other studies that provided immediate positive rewards for physical activity (i.e., pedometer counts), participants were more physically active⁸⁵. In comparison to other SUD populations, MMT patients are prime candidates for CM protocols due to their daily visits to the methadone clinic.

One potential barrier that has hampered the dissemination and utilization of contingency management for behavior change is the financial costs associated with implementing the program. A commonly stated question is, “who pays for the incentives?”⁸⁶. Due to its efficacy and subsequent reductions in other healthcare costs (i.e., cost-effectiveness)⁸⁷ some government agencies, such as the Veterans Administration, and large insurance corporations have assumed the costs and begun widespread implementation. Others have noted that with the introduction of contingency management insurance reimbursement increases due to increased retention in treatment such that the contingency management program is self-sustaining via the increased reimbursement. For example, Lott and Jenicus⁸⁸ found that individuals were retained an additional two days in an outpatient community drug treatment program.

Considerations and Conclusions

Generalizability of a CM intervention for exercise is already demonstrated in that positive reinforcement systems for health behavior change are already being implemented in the healthcare field. For example, Blue Shield of California and IBM provide monetary rewards for engaging in physical activity and completing health risk assessments⁸⁹. Other considerations for increasing participation in physical activity in the real world may be to build a gym within the opiate agonist facility. Easy access to exercise equipment may increase participation and adherence. Providing pedometers and/or heart rate monitors may also be advantageous. Self-monitoring can be a potent motivator for behavioral change⁹⁰. Behavior monitoring from others (e.g., insurance companies) can motivate adherence and devices such as pedometers can serve as “proof” that the individual completed the activity. Some fitness facilities have incorporated fitness equipment that is programmable and tracks and individuals’ workout within session and over time. These machines, which consist of a USB port/card on the exercise equipment, are commercially available (TechnoGym USA Corporation, Seattle, WA). The possibilities for incorporating contingency management into the real world are reasonable and promising.

In summary, opiate dependence is a significant public health concern. While opiate agonists are an effective intervention for opiate dependence, room for improvement exists as many opiate agonists patients continue to use other substances, have co-morbid psychiatric problems, and experience poor quality of life. Engaging in alternative substance-free activities appears to be associated with reductions in substance use, although it remains to be rigorously tested in an opiate agonist population. Evidence from one small trial with opiate agonist prison inmates highlights the potential of exercise as a substance-free activity⁶⁵. However, initiating and maintaining an exercise regimen consistent with health benefits is problematic due to low adherence and dropout. Contingency management is a behavioral intervention that can aid in overcoming the many obstacles confronting those who desire to start and maintain an exercise program. In conclusion, with proper precautions exercise can be a safe and beneficial adjunctive treatment in opiate agonist populations.

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