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A pilot randomized trial of exercise as adjunct therapy in a heroin-assisted treatment setting

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ABSTRACT

Background: Although the potential of exercise as an adjunct treatment for substance dependence is persuasive in theory, few controlled trials have assessed its effectiveness. Existing research has also largely focused on individuals aiming towards, or having already achieved, abstinence. This study employed a randomized design in a pilot trial to assess the feasibility, acceptance, and effects of an exercise intervention for individuals receiving outpatient heroin-assisted treatment.
Method: 50 individuals receiving heroin-assisted treatment at a clinic in Switzerland were invited to take part in the trial. Participants were randomized to 12 weeks of exercise twice per week, or a corresponding duration of non-exercise group activities in a comparison condition. Data on attendance, compliance, and numerous psychological and physiological parameters were gathered.
Results: 24 individuals were willing to take part in the study. 92.3% of the exercise condition ($n = 13$) were compliant or semi-compliant with the protocol; by contrast, only 54.6% of participants in the comparison condition ($n = 11$) were compliant or semi-compliant ($\chi_2 = 7.049$; $p = 0.029$). Participants in the exercise condition significantly increased the number of minutes spent exercising at a high intensity level ($F(2,44) = 3.794$; $p = 0.046$; $\eta^2 = 0.159$). No other significant interaction effects were observed.
Conclusions: An exercise intervention is a feasible and accepted supplementary therapy to heroin-assisted treatment. Participation rates were high, particularly given the outpatient setting. No evidence regarding the potential mechanisms of exercise as a therapy modality could be identified. Patients in heroin-assisted treatment may require a longer-term exercise programme, specifically targeting particular health parameters, before measurable improvements can be observed.

1. Introduction

The recognition that exercise is a fundamental aspect of good human health, which may not only prevent many diseases, but also be therapeutically effective, has grown rapidly in the last two decades. Numerous studies have reported the positive influence of an exercise regimen for a range of illnesses, especially cardiovascular and metabolic diseases (Pattyn, Cornelissen, Eshghi, & Vanhees, 2013; Taylor et al., 2004). In particular, there has been an increased interest in the potential of exercise as an adjunct treatment for mental disorders (Richardson et al., 2005; Rosenbaum, Tiedemann, Sherrington, Curtis, & Ward, 2014). The strongest evidence exists for the treatment of depression (Blumenthal et al., 2007; Cooney et al., 2013), with certain beneficial effects for anxiety disorders and schizophrenia (Callaghan, 2004), although evidence from methodologically robust studies is sparse, and often less promising than from studies without control conditions (Zschucke, Gaudlitz, & Ströhle, 2013).

Substance dependence is a mental disorder frequently accompanied by comorbidities such as depression, anxiety disorders and personality disorders (Volkow, 2001). It is treated with pharmaceutical and therapeutic modalities (in some cases encompassing a withdrawal period) in ways similar to those employed for other mental disorders (Kleber et al., 2006). To date, studies assessing the potential of exercise as an adjunct treatment for substance use disorders have varied considerably in primary outcomes, and in quality.

Evidence from preclinical studies suggests that, with the exception of alcohol, undertaking exercise reduces drug self-administration, escalation, and reinstatement. A number of mechanisms have been posited, most importantly the rewarding properties of exercise due to activation of the mesolimbic pathway, the amelioration of striatal dopamine receptor deficits (Robertson et al., 2015), and the concurrent reduction of comorbidities which may perpetuate the substance use cycle (Lynch, Peterson, Sanchez, Abel, & Smith, 2013). Some authors have

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suggested that the caloric content of alcohol, and the route of administration, may account for the inconsistency of studies involving ethanol (Bardo & Compton, 2015; Lynch et al., 2013). Though purely speculative, we suggest that dopamine release and, possibly, receptor availability, following alcohol administration may differ from other substances to such a degree that this could also contribute to the findings summarised above (Nutt, Lingford-Highes, Erritzoe, & Stokes, 2015).

Evidence from clinical trials, although promising, remains in the early stages. A recent literature review reports on eight studies examining exercise as an adjunct treatment for substance use, which showed weak evidence for positive effects on a variety of outcome variables (Zschucke, Heinz, & Strohle, 2012) such as increases in days of abstinence (Brown et al., 2010; Burling, Seidner, Robbins-Sisco, Krinsky, & Hanser, 1992; Collingwood, Reynolds, Kohl, Smith, & Sloan, 1991), decreased heroin withdrawal symptoms (Li, Chen, & Mo, 2002), and reduced craving (Buchowski et al., 2011; Roessler, 2010). The review also speculates that in clinical populations, numerous social, behavioural and neurophysiological mechanisms may be implicated in the effects of exercise interventions, although no study has examined these in detail. A wide variety of exercise forms, including strength training, Qi Gong, aerobic training using circuits, exercise bikes and treadmills, softball games, volleyball, and in some cases several of these combined, has been employed, with frequencies varying from one to five times per week.

Since that review, a pilot randomized controlled trial with 29 individuals currently receiving methadone treatment has demonstrated that a video-game based intervention, involving 25 min of a combination of aerobic training, strength training, and flexibility exercises undertaken individually, is a feasible and acceptable method of exercise participation for this population. Participants also significantly reduced their cocaine and opioid use, and experienced improved mental wellbeing, although there was no difference between the exercise or control group (Cutter et al., 2014). In a study by Dolezal et al. (2013), 39 individuals following inpatient treatment for methamphetamine dependence were randomized to an exercise intervention involving three hour-long sessions of treadmill running and strength circuits, or a control condition. As well as showing the feasibility of the intervention, the exercise group significantly improved VO2max (the maximum volume of oxygen that an individual can use during exercise) (Hawkins, Raven, Snell, Stray-Gundersen, & Levine, 2007) and muscle strength (Dolezal et al., 2013). In a subsequent study in this population, with the same exercise protocol, heart rate variability improved following eight weeks of training (Dolezal et al., 2014).

Although not a clinical trial, Weiss and colleagues report, based on interviews with recovered or relapsed heroin addicts, that participating in exercise, amongst other activities, can be helpful in achieving abstinence (Weiss et al., 2014). Further research is also currently in development; Mooney and colleagues are developing an aerobic and resistance training programme, to be supervised thrice weekly over an 8-week period following residential treatment for methamphetamine dependence, while Trivedi and colleagues have designed a 12-week programme of thrice weekly treadmill-training, followed by 6 months of once-weekly supervised sessions for individuals undertaking residential treatment for stimulant abuse. Both studies focus on days of abstinence following residential care as the primary outcome (Mooney et al., 2014; Trivedi et al., 2011).

While these studies have shown tentatively promising results, Zschucke et al. (2012) and colleagues note that many have been plagued by issues, such as small sample sizes and high drop-out rates, which limit their statistical power (Zschucke et al., 2012). Furthermore, to date, all but one of the studies have been carried out with individuals already abstinent and not receiving opioid substitution therapy, and aiming towards long-term abstinence. It remains to be seen whether an exercise programme is feasible, acceptable and effective for individuals for whom abstinence is not a current realistic possibility, and who are not in a setting (such as inpatient care), in which regular structured exercise can be relatively easily carried out.

In Switzerland, and a small number of other countries, heroin-assisted treatment (HAT) is offered for opioid-addicted individuals who have failed to respond to conventional treatment, such as methadone substitution or abstinence-oriented treatment (Bundesamt für Gesundheit, 2015). Patients are prescribed a dose of clinical-standard heroin (diacetylmorphine), which they inject or ingest within the clinic once or twice per day. The principal aim of HAT is to provide patients with a treatment modality which will enable them to stabilise their lives, and avoid the illegal behaviour which opioid consumption otherwise frequently necessitates (Bundesamt für Gesundheit, 2000). A review of studies of HAT in Canada, Switzerland, Germany, the Netherlands, and the United Kingdom, found the treatment to be safe, effective in reducing delinquent behaviour and illicit opioid consumption, and a valuable, if "last-resort" treatment option (Fischer et al., 2007). The Swiss Department of Health lists overall health, and specifically exercise promotion amongst the mid-term aims of HAT (Bundesamt für Gesundheit, 2000). To date, however, the feasibility of integrating an exercise programme into this treatment form has not been investigated.

The aim of the present randomized pilot study was to test the feasibility, acceptability and psychological and physiological health effects of an exercise programme in an out-patient HAT setting, for opioid-addicted individuals not aiming towards abstinence at the time of the study. In order to minimise the potential confounding effects of the intervention being associated with contact time with new team leaders, access to prohibitively expensive environments, and a financial reward, a comparison condition was used in this study. In this way, it is hoped that patient attitudes to sport specifically can be disentangled from patient attitudes to new activities and study participation in general. In contrast with the majority of other studies in this field, in which abstinence was a central outcome, relevant outcomes for individuals in HAT should be seen as potential harm reduction measures, such as reduced illicit drug consumption. Four research questions were formulated in line with this aim:

1.1 Can HAT patients be recruited to participate in a randomized trial of exercise as an adjunct treatment modality?
2.1 Will the exercise group comply with the study protocol?
3.1 Will the comparison group comply with the study protocol?
4.1 Will an exercise programme lead to any alterations or improvements in the above-mentioned variables, and will these differences also be found in the comparison group?

2. Methods

The study took place between November 2014 and February 2015, and was part of larger study into exercise as feasible treatment in outpatient opiate substitution therapy.

2.1. Participants and procedures

Participants were recruited from a HAT clinic, treating 150 patients, in Basel, Switzerland. Participants were recruited via face-to-face contact with study or clinic personnel, and informative posters and flyers in the clinic. The sole exclusion criterion was any psychological or physical impairment precluding participation in light exercise, a decision made solely by the treatment staff of the clinic. In total, 50 patients were deemed capable of taking part, and were invited to join the study. Patients who agreed to participate were randomized to either an exercise or comparison condition through a blinded process of identical sealed envelopes, stipulating one of the two conditions. Patients were informed verbally and in writing that, if they were in the comparison group, they would also receive 12 weeks of exercise training immediately upon completion of the study. All patients were informed that in addition to drinks and snacks following training, they would receive a sports T-shirt, and 100 Swiss francs as reward for participation. Patients were informed that if they missed more than five training sessions, this

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