Effects of Acute Exercise on Opiate and Cigarette Craving in Methadone Patients

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Abstract: Acute aerobic exercise has been shown to reduce craving for cigarettes in smokers. Over 80% of patients enrolled in methadone maintenance treatment (MMT) programs for opiate addiction are smokers and 29% suffer from diabetes. Many MMT counselors believe that regular physical exercise helps their patients to be successful in the program; however, there have been no previous studies demonstrating that increased physical activity positively impacts MMT patients.

Purpose: To determine if acute aerobic exercise changes opiate and cigarette craving in MMT patients.

Methods: 9 MMT patients (Age = 45±2 years; BMI=27.5±1.9) completed 3 randomly applied experimental trials immediately before receiving their daily methadone dose. The experimental trials consisted of 20 minutes of rest, moderate exercise (65% predicted maximal heart rate), or vigorous exercise (80% predicted maximal heart rate). Craving for opiates, cigarettes, and sweets was recorded before, immediately after (IPE), and 10 minute after exercise (10 Post). Subjects also completed the Subjective Opiate Withdrawal Scale (SOWS) before and 10 minutes after exercise.

Results: Craving for opiates was reduced ($p<0.05$) as a result of vigorous exercise at IPE (-26.8$\pm$6.9%) and 10 Post (-5.5$\pm$0.5%); however, craving for opiates was unchanged following moderate exercise. Craving for cigarettes was reduced ($p<0.05$) following both moderate (IPE=-37.9$\pm$6.1%; 10 Post=-13.1$\pm$9.1%) and vigorous (IPE=-37.1 $\pm$7.1%; 10 Post=-8.8$\pm$9.2% exercise. Craving for sweets and the SOWS was unchanged as a result of exercise.

Conclusion: The results of this investigation suggest that craving for opiates and cigarettes in patients participating in a MMT program may be influenced acute aerobic exercise.

Keywords: Methadone, exercise, craving, smoking.

INTRODUCTION

In the United States and Europe, 1-2 % of adults report using heroin or other opiates (oxycontin, dilaudid, and hydrocodone) during their lifetime [1]. It is estimated that 1 in 4 people who use opiates become dependent [2]. Once addicted, people may use opiates for decades interspersed by periods of abstinence, treatment, and incarceration [3]. Oral methadone maintenance treatment (MMT) is one of the most common ways to treat opiate addiction. Once enrolled in a MMT program, patients typically receive treatment for at least a year and may receive treatment for years or decades [4]. Regular aerobic exercise has been theorized to be beneficial in the treatment for addiction because of its potential ability to attenuate the physiological responses to stress experienced during withdrawal and positive impact on depression and mood [5,6].

While MMT treatment is effective at protecting these patients from the risks associated with opiate addiction, it appears that they are at increased risk for other diseases and health behaviors that continue to increase their risk for premature death. One of the most prevalent negative health behaviors of MMT patients is smoking. The rate of cigarette smoking in MMT patients is typically reported to be 80% or nearly 4 times higher than the rate in the US (20%) [7]. MMT patients are also heavy smokers consuming approximately 2 packs per day [8]. While most MMT smokers express an interest in quitting smoking (~75%), the quit ratio (12%) (proportion of former to ever smokers) is 4 times less than that seen in US population (50%) [8]. There is some concern that larger methadone doses may actually increase smoking behavior [9,10]. Acute exercise has been shown to reduce cigarette craving in normal smokers [11] and may be effective means to positively influence smoking behavior in MMT patients.

The frequency of diabetes mellitus (DM) in MMT patients is very high. Fareed and colleagues report that 28% of MMT patients suffer from DM, a rate much higher than that seen in the general population (6.2%) [12]. These authors also found that 86% of premature deaths in MMT participants occurred in patients with DM [12]. The exact mechanisms underlying the increased frequency of DM in MMT

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patients is unclear; however, MMT patients have been reported to consume and crave sweets at a much higher level as compared to controls [13,14]. There is some limited evidence that acute moderate exercise can reduce the urge to consume chocolate in regular chocolate eaters [15]. As a consequence, it may be possible that exercise could be effectively used to moderate sweet consumption and craving in MMT patients.

MMT patients are typically advised to increase their physical activity by counselors; however, there have been no prior studies investigating the impact of increased physical activity on MMT patients. The purpose of this investigation was to determine if acute aerobic exercise changes opiate and cigarette craving in MMT patients.

METHODS

Participants

Nine patients (5 men, 4 women; Age = 45±2 years; Body Mass Index=27.5±1.9) enrolled in a Methadone Maintenance Treatment (MMT) program participated in this investigation. Prior to participating in this investigation all subjects read and signed an informed consent form approved by the University's Institutional Review Board (IRB) for Protection of Human Subjects in Research and were screened by a physician. Patients with significant risk of cardiovascular, metabolic, or orthopedic disease were excluded from the investigation. All subjects had been enrolled in MMT for more than 6 months and had been found to be completely compliant with the program for at least 30 days before participation. None of the subjects in this investigation participated in regular physical activity (one time per week) for at least 6 months prior participation in this investigation. All subjects were currently smoking between 15 and 30 cigarettes per day.

Experimental Trials

For each experimental trial subjects reported to the testing area between 7 and 8 am and 24 hours after their previous methadone dose. After waking, subjects abstained from food consumption, caffeine intake, and smoking until after completion of the experimental trial. Subjects then completed 3 experimental trials consisting of rest (REST), moderate exercise (MOD), or vigorous exercise (VIG). During REST subjects sat in a quiet room with no visual or auditory stimulation. During MOD (65% predicted maximal heart rate) and VIG (80% predicted maximal heart rate) subjects exercised on a Monark 828 cycle ergometer at 50 RPMs for 20 minutes [16]. Heart rate was continually monitored during the first 5 minutes of each exercise session and workload was appropriately adjusted to facilitate the desired heart rate response. In an effort to minimize order effects experimental trials were administered using a repeated 3X3 Latin Square Design [17]. Temporary cessation of smoking was confirmed by measurement of carbon monoxide in expired air (<10 ppm) using a Mirco^{+} Smokelyzer (Bedfont Scientific Inc, Rochester, Kent, UK).

Instrumentation

During each trial heart rate (HR), blood pressure (BP), and RPE were recorded before, every ten minutes during exercise, and 10 minutes after exercise. HR was measured using a Polar heart rate monitor. BP was measured using traditional auscultatory techniques. RPE was monitored using the Borg 0-10 scale [18].

Table 1. Physiologic (Heart Rate, SBP:Systolic Blood Pressure, DBP:Diastolic Blood Pressure) and Perceptual (RPE:Rating of Perceived Exertion) Responses to Moderate (MOD, 65% Predicted Maximal Heart Rate) and Vigorous (VIG, 80% Predicted Maximal Heart Rate) Exercise in MMT Patients

Time	Pre	10 min	20 min	Post 10 min
Heart Rate				
Rest	73 ± 5	73±4	69±2	68±3
MOD	74±2	113±2*	112±4*	82±5*
VIG	75±5	130±7$^{*,\#}$	134±8$^{*,\#}$	89±7*
SBP				
Rest	120±9	121±8	119±9	119±8
MOD	126±9	149±12*	148±13*	120±10
VIG	124±10	166±12$^{*,\#}$	171±15$^{*,\#}$	121±17
DBP				
Rest	72±5	70±4	72±5	73±6
MOD	73±5	76±7	78±8	76±6
VIG	74±8	70±6	73±5	71±9
RPE				
Rest	n/a	n/a	n/a	n/a
MOD	n/a	4±1	5±2	n/a
VIG	n/a	7±2$^{\#}$	8±1$^{\#}$	n/a

*Indicates difference from Rest, $^{\#}$ Indicates difference from MOD.

Craving for Opiates, Cigarettes, & Sweets

Craving for opiates, cigarettes, and sweets was measured before, immediately after, and 10 minutes after exercise by a visual analog scale (VAS) using 100 mm line anchored on the left with "No Craving" and the right with "Extreme Craving". Single item assessment of craving assessment using a VAS has been reliable and response for a variety of substances [19,20]. Subjects were asked to make a mark on the line that represents their perception of their current state of craving for the substance. Similarly, the Subjective Opiate Withdrawal Scale (SOWS) [21] was used to measure symptoms of opiate withdrawal. The SOWS is a 16-item self-report scale. Responses to each item are made using a 5-point Likert-type scale (ranging from 0 = 'Not At All' to 5 = 'Extremely').

Data Analyses

A 2-way (Time x Condition) multivariate analysis of variance (MANOVA) was conducted to determine if there were any differences across the different exercise conditions. Significance was set a priori at the $p < 0.05$ level. When significant main effects were observed a Newman-Keuls Multiple-Comparison Test was performed. For all values, means $\pm$ SE are reported in the text or presented in a table or figure. All statistical analyses were completed using Number Crunchers Statistical Software (NCSS; Version 07.1.19; Kaysville, UT).

RESULTS

Physiologic and perceptual responses to exercise are described in Table **1**.

Craving for opiates and cigarettes was impacted by exercise conditions. MANOVA demonstrated a significant across exercise conditions across opiates ($F_{2,48}$=4.99, p=0.017) and cigarettes ($F_{2,48}$=13.95, p<0.001). Specifically, craving for opiates was reduced immediately after exercise and 10 minutes after exercise only during VIG exercise condition (Fig. **1**). In contrast, craving for cigarettes was reduced at these same time points during both the MOD and VIG exercise conditions (Fig. **2**). Craving for sweets did not change from rest (Rest=22$\pm$9 mm; MOD=38$\pm$7 mm; VIG=34$\pm$6 mm) to immediately after exercise (Rest=29$\pm$12 mm; MOD=30$\pm$9 mm; VIG=25$\pm$10 mm) to 10 minutes after exercise (Rest=35$\pm$5 mm; MOD=24$\pm$7 mm; VIG=38$\pm$9 mm)

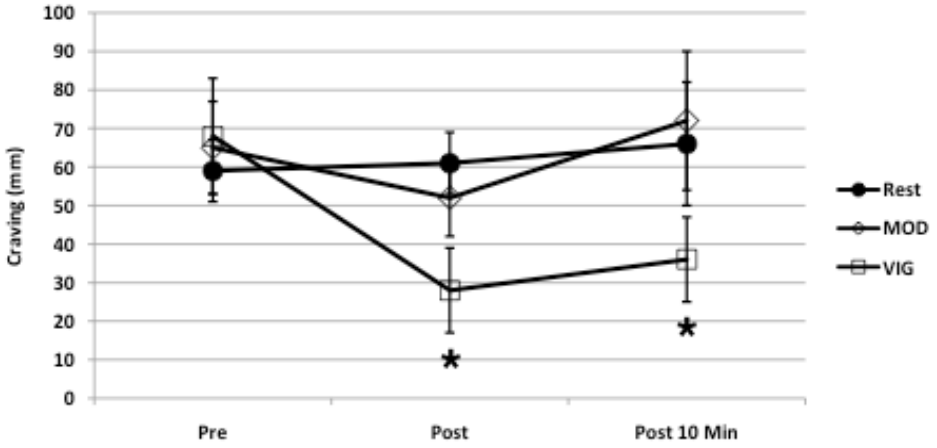

Fig. (1). Impact of acute exercise on opiate craving in MMT patients.
*Indicates difference from rest & MOD in VIG (p<0.05).

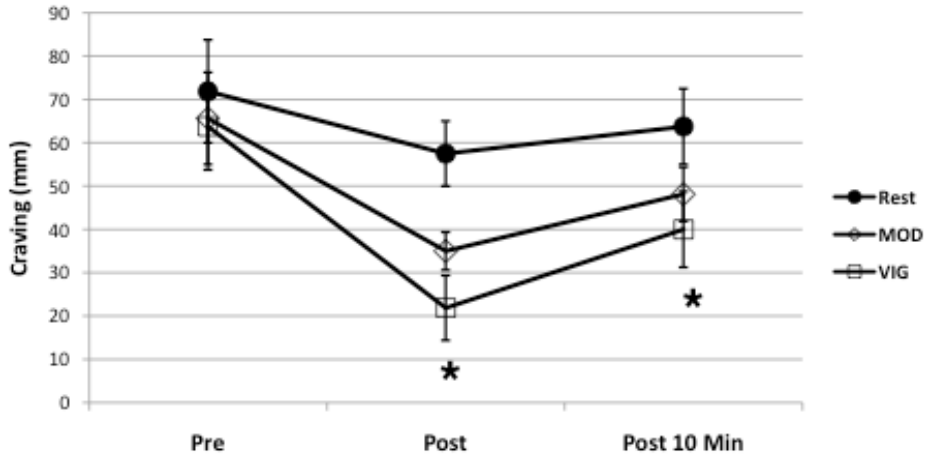

Fig. (2). Impact of acute exercise on craving for cigarettes in MMT patients.
*Indicates difference from rest in MOD & VIG (p<0.05).

under any condition ($F_{2,48}$=1.54, p=0.231). Similarly, the SOWS did not change from pre (Rest=6.6±1.8; MOD=6.0±2.1; VIG=7.4±1.2) to 10 minutes after exercise (Rest=6.0±2.7; MOD=8.4±1.2; VIG=7.2±1.9) under any condition ($F_{2,48}$=1.78, p=0.202).

DISCUSSION

Acute exercise reduced cravings for cigarettes in MMT patients immediately after exercise and the changes were maintained 10 minutes after exercise. These findings are similar in direction and magnitude to those described by many investigators in "normal" smokers [11]. The mechanisms underlying these positive changes are unclear; however, it is possible that acute exercise reduced craving for cigarettes by distraction, reducing stress, and/or some undetermined neurophysiological mechanism.

There have been few investigations that have explored the effects of varying exercise intensities on cigarette craving in smokers. In this investigation, exercise at 80% of predicted maximal heart rate was no more effective at reducing craving for cigarettes than exercise at 65%. These findings are similar to those described by Pomerleau and colleagues [22] (30% versus 80% VO_2max), Everson and colleagues [23,24] (44% versus 55% age-predicted maximal heart rate and 40-59% versus 60-84% heart rate reserve), and Scerbo and colleagues [25]. Taken together these findings suggest that the change in craving for cigarettes following exercise in MMT patients is similar to that typically observed in "normal" smokers. While the mechanisms underlying these changes remain unclear, it seems important to recognize that exercise intensity does not appear to have a varying effect on craving to smoke. It is somewhat challenging to interpret the impact of exercise intensity on smoking craving in this and other investigations because of the methodologies used to establish exercise intensity. Affective responses to exercise above ventilatory threshold (VT) tend to be negative and tend to be positive to exercise below VT [26]. It seem very possible that at least some of the subjects exercising at the higher intensities used in the investigations described above were exercising above VT causing a more varied and possibly negative affective response to exercise. In the future, it may be appropriate to develop experimental designs where all exercise intensities are made relative to VT. Despite these concerns, it seems reasonable to conclude that acute exercise of any intensity may be a valuable strategy to modify smoking behavior in MMT patients.

Acute exercise has also been shown to reduce smoking behavior. Information about the impact of acute exercise in MMT patients on smoking behavior (e.g. time to *ad libitum* smoking) was not collected in this investigation and should be included in future investigations. Future investigations in this population should also observe these measures and measures of cigarette craving for longer periods of time after exercise (>10 minutes) than used in this investigation. This information would be valuable when developing strategies to use acute exercise to modify smoking behavior in MMT patients.

Craving for opiates in MMT patients was reduced as a consequence of vigorous exercise and was unchanged as a result of moderate exercise. As far as we are aware, this is the first investigation that has described changes in opiate craving as a result of exercise in people suffering from opiate addiction. The only similar finding, was described by Mclachlan and colleagues [27]. These authors found that voluntary exogenous opiate consumption was lower in exercising versus sedentary rats. Potential mechanisms underlying the positive effect of acute exercise on opiate craving are unknown. Some have speculated that it might be possible that exercise could replace or mimic some of the neurophysiologic events associated with exogenous opiate consumption and reduce the craving for exogenous opiates. This hypothesis is purely conjecture at this point and significant work needs to be done to describe the neurophysiologic events associated with exercise in the opiate addiction environment. It seems just as plausible that the psychological mechanisms proposed for changes in cigarette craving after acute exercise (i.e. distraction and stress reduction) are playing a role in changes in opiate craving.

No changes in cravings for sweets or symptoms of opiate withdraw were observed as a consequence of acute exercise. There have been some limited reports of increased sweet intake and preference towards sweets in MMT patients compared to controls [13, 14]; however, this investigation provides no evidence to suggest that acute exercise could influence consumption of sweets in this population. These findings are somewhat in contrast to those of Taylor and Oliver [15] who found cravings for chocolate to be reduced in regular chocolate users following a 15 minute brisk walk. These investigators introduced a strong cue (opening a wrapped chocolate bar) before assessing craving and it is possible that the more passive nature of this investigation was not able to detect changes in sweet cravings. More importantly, the lack of changes in sweet cravings along with the changes in smoking and opiate cravings suggest that acute exercise does not have a global impact of craving for consumption of all substances. The baseline cravings for sweets were low compared to the baseline cravings for cigarettes and opiates. Perhaps acute exercise is only valuable in altering cravings for the most desirable substances for the individual. Similarly, the baseline SOWS measures in this investigation were low. These low baseline measures suggest that, in this chronically treated and stable MMT population, a 24 hour period following the previous methadone dose was not long enough to precipitate significant withdraw symptoms. Use of the SOWS in an acute exercise environment to measure symptoms withdraw is also problematic because interpretation of several of the items by the subject could be influenced by physical activity.

CONCLUSIONS

Acute exercise apparently reduced cravings for opiates and cigarettes in MMT patients for a short period of time. The mechanisms that precipitated this response are unclear and should be investigated in the future. Acute aerobic exercise may be beneficial to MMT patients to reduce cigarette smoking and the risk illicit opiate consumption.

CONFLICTS OF INTEREST

None declared.

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None declared.

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