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Voluntary Wheel Running Induces Exercise-Seeking Behavior in Male Rats: A Behavioral Study

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Abstract

Background: Research evidence shows that exercise is associated with positive physical and mental health. Moreover, exercise and wheel running in rats activate overlapping neural systems and reward system. The most commonly used models for the study of rewarding and aversive effects of exercise involve using treadmill and wheel running paradigms in mice or rats. The purpose of our experiment was to study the influence of continuous voluntary exercise on exercise-seeking behavior.

Methods: In this experimental study, we used 24 adult male Sprague–Dawley rats weighing 275–300 g on average. Rats were divided into 3 experimental groups for 4 weeks of voluntary wheel running. Each rat ran in the cage equipped with a wheel during 24 hours. A within-subject repeated measure design was employed to evaluate the trend of running and running rates.

Results: We found that time and higher levels of exercise will increase exercise tendency. Our results also show that the interaction of exercise within 4 weeks and different levels of exercise can significantly promote rats' exercise-seeking behavior ($F = 5.440$; $df = 2.08$; $P < 0.001$).

Conclusion: Our data suggest that voluntary wheel running can increase the likelihood of extreme and obsessive exercising which is a form of non-drug addiction.

Keywords: Exercise, Non-drug addiction, Rats, Running wheels

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Introduction

Physical activity or exercise is generally associated with positive mental and physical health outcomes.[1] Despite this general viewpoint, it has been found that in humans, extreme exercise can lead to addiction to such activities.[2] Some studies have speculated that exercise dependency can also occur in animals and that this dependency can lead to the development of other types of addiction through sensitization of dopaminergic pathways.[3] There is a robust correlation between dopamine and all behavioral dimensions that involve motor activity and it has been shown that physical activity increases the synthesis and release of dopamine, leads to an increase in neuroplasticity of the brain and promotes feelings of well-being.[4,5]

Exercise addiction, belonging to a group of behavioral addictions, is a state described by increasing amounts of exercise, tolerance (need for significantly increased amounts of exercise to achieve the desired effect) and withdrawal symptoms (revealed by anxiety and fatigue when the amount of exercise decreases), impaired control over behavior, excessive time spent in physical activities and continuing intensive exercise despite adverse consequences on the lives of patients and their relatives, social/occupational conflicts and knowledge of physical problems caused by exercise.[2,6-10] Exercise addiction is not classified as a psychiatric disorder but has been shown to be correlated with mood disorders,[11] eating disorders[12] and other behavioral addictions.[9,13] The prevalence of exercise addiction has been estimated to be 3% in general population[14] and 3% to 29% in different sport cultures.[9] Interestingly, runners are more susceptible to the addictive properties of exercise. This issue may help to understand why runners often report "addictive-like" symptoms such as feeling of elation after exercising; increasing the amount of exercise to achieve the sense of well-being; difficulties in job performance and social interactions; and the onset of withdrawal symptoms such as irritability and depression when inhibited from running.[6,15-17]

Much of the related research literature appears to be focused on the brain's reward system. A well-known opinion is that natural rewards can induce an addiction-like state.[18] Shared genetic vulnerabilities,[19] common

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neuropsychological characteristics[20] and the same reward circuits are implicated in the development of both substance and behavioral addictions (e.g. exercise addiction).[19] Moreover, Fontes-Ribeiro et al[4] assert that exercise and drugs of abuse activate overlapping neural systems, suggesting that intensive exercise (e.g. running) shares similarities with drug taking and seeking behaviors. It has been found that wheel running activates a reward system, implying that the after-effect of wheel running would be rewarding. More specifically, wheel running has a reinforcing effect[21] because it occurs spontaneously and tends to increase with experience. Thus, in an instrumental learning situation, it can serve as a reinforcer.[21] Using wheel running as a measuring indicator of activity levels in animals has a long history and is valid and repeatable.[22] Although there are methodological issues that have to be surmounted (e.g. wheel surface, size, length of measurement), wheel-running, unlike compulsory treadmill exercise, has been applied as the most demanded and appropriate model of human voluntary exercise and produces brain neurotransmitter changes similar to those seen in humans.[23] The behavioral effects of chronic and voluntary wheel running, unlike acute or forced exercise, may more accurately represent neurobiological changes that are stable and not confounded with stress or exercise withdrawal symptoms.[24]

Therefore, it is of utmost importance to understand how and why exercise addiction or exercise seeking behaviors develop as well as to identify strategies to prevent this phenomenon. In the present study, we explore a research hypothesis; time period (4 weeks) and different levels of exercise have a significant influence on promoting exercise seeking behavior.

Materials and Methods

Experimental Animals

Adult male Sprague–Dawley rats (weighing 250 to 275 g, 2 months old, n = 24), were provided by the Center of Comparative and Experimental Medicine (Shiraz University of Medical Sciences, Iran). The rats were individually housed under standard conditions (at a temperature of 22.0 ± 2ºC and a 12L: 12D light schedule; lights off at 7:00 AM and lights on at 7:00 PM) and had access to food and water *ad libitum*. All testing took place during the light phase. The procedure involving rats and their care was confirmed by Shiraz University of Medical Sciences, Animal Care and Use Committee. Additionally, care was taken to use the minimum number of rats possible.

Apparatus

The rats (n = 24) were individually housed in polycarbonate activity wheel cages (43 × 23 × 15 cm) with running wheels circumference of 1.07 m as a modified model. The cages were equipped with custom-made wheel interfaced with a digital micro-switch counter to record the number of wheel revolutions, which were manually recorded twice a day.

Prolonged Daily Voluntary Running

In the first 5 days of experiment, all rats were given training trials and had continuous access to wheels set up in their cages. During this phase, we observed that they had different levels of activity and accordingly, we categorized them in low, medium and high exercise groups. To be more specific, rats were divided based on the number of wheel rotations per day (the number of wheel revolutions for each rat was registered twice a day). Rats designated in the low exercise group ran in a range of 0–80 rev/day (38.466 m/d), those in the medium exercise group ran 80 to 160 (107.59 m/d) and those in the high exercise group ran more than 160 rev/day (1601.94 m/d). Voluntary exercise was administered in a 4-week program of wheel running. In the course of the study, we lost one of the rats in high exercise group. The entire phases of the experiment procedure are delineated in Figure 1.

Results

Running Rates and Wheel Running Trend

Exercising rats ran an average distance of 839.18 m/d, ranging from 11.77 to 10832 m/d.

Table 1 presents the descriptive statistics including mean and standard deviation for running in the three different groups of exercises (low, medium and severe levels of exercise) in 4 consecutive weeks.

Table 1 and Figure 2 demonstrate the upward trend of mean running scores in experimental groups. Data presented in the table shows that the total mean score of running was 2233.11 in the first week, 2677.76 in the second week, 2940.96 in the third week, and 5105.70 in the last week. Also, the running mean scores obtained

Figure 1. The Entire Phases of Experiment Procedure.

Table 1. Total and Categorized Mean and SD for Running in the 4-Week Experiment (m/d)

Week	Exercise	Mean (m/d)	SD	N
1st	Low	216.81	282.637	8
	Medium	498.25	306.992	8
	Severe	6520.14	13976.435	7
	Total	2233.11	7858.162	23
2nd	Low	223.50	304.243	8
	Medium	813.06	339.657	8
	Severe	6713.71	15286.123	7
	Total	2677.76	8660.249	23
3rd	Low	448.88	208.834	8
	Medium	627.63	114.671	8
	Severe	8432.86	16811.178	7
	Total	2940.96	9533.944	23
4th	Low	426.62	230.060	8
	Medium	1054.38	429.599	8
	Severe	15083.29	23392.935	7
	Total	5105.70	13961.571	23

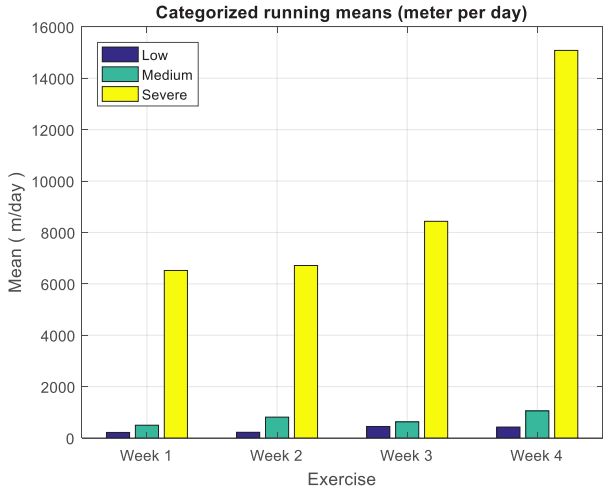

Figure 2. Categorized Mean for Running (m/d).

by rats in 2 groups (low and severe levels of exercise) increased through time so that the mean running score for rats in the low exercise group was 216.81 in the first week, 223.50 in the second week, 448.88 in the third week and 426.62 in the last week of experiment; mean score for rats with severe exercise level was even higher; 6520.14, 6713.71, 8432.86 and 15083.29 in weeks 1 to 4, respectively. In the medium exercise group, the mean scores were 498.25, 813.06, 627.63 and 1054.38 through four weeks of experiment. As it can be seen, there is a decrement in mean score of the third week. However, the overall results, so far, suggest that over time, rats are more willing to run on the wheel, and voluntary exercise promotes rats' tendency towards exercise.

A within-subject repeated measure design was employed to evaluate the trend of running and running rates. Before performing repeated measures analysis to test the hypothesis, 2 assumptions were tested to validate the analysis. We administered the test of equality of variance matrices and Mauchly's test of sphericity. The results of both tested assumptions indicate that our data violate the assumptions of equality and sphericity, because the tests were not statistically significant ($P < 0.11$). Since it is not uncommon to find these assumptions to be violated, we used Greenhouse-Geisser correction which relies on estimating sphericity. The results of Greenhouse-Geisser show that there is significant difference between weeks regarding rats' tendency toward exercise ($F = 7.104$; $df = 1.04$; $P < 0.001$); more interestingly, it shows that the interaction of exercise in time period (4-week) and different levels of exercise significantly promote the rats' exercise seeking behavior ($F = 5.440$; $df = 2.08$; $P < 0.001$). Figure 3 illustrates the upward trend of exercise seeking behavior in different groups of exercise.

According to Figure 3, within the time limit of a 4-week experiment, rats in the high exercise level group showed the highest exercise seeking behavior in comparison with rats in the low and medium exercise groups. More specifically, exercise tendency continued to increase gradually in the first three weeks and reached its peak in the last week of the experiment. This finding shows that severe levels of exercise have a positive effect on promoting exercise-seeking behavior in rats.

Discussion

The principal finding of this study was that time has a significant influence on promoting exercise-seeking behavior; implying that over the period of a 4-week experiment, rats were more willing to run, and voluntary exercise increased the likelihood of exercise-seeking behavior. This study also found that higher levels of exercise will increase exercise tendency, suggesting that intensive exercise has a positive effect on promoting "addictive-like" behaviors in rats. This study also highlighted the significant effect of consistent physical activity during the time as well as different levels of exercise on promoting exercise tendency in rats.

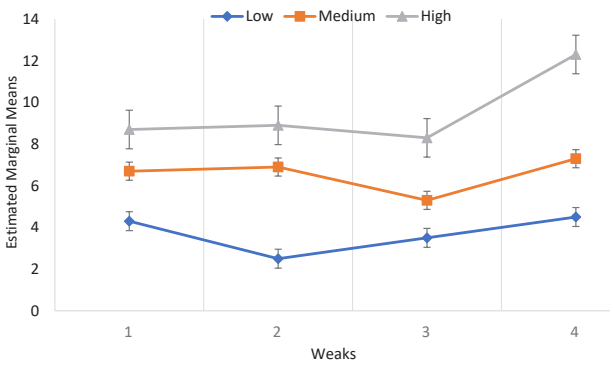

Figure 3. Four Weeks Upward Trend of Exercise Seeking in Different Levels of Exercise.

Emerging evidence is in agreement with our findings regarding exercise addiction[3,9,25] and the addictive feature of excessive exercise.[17,26-30] There are several theoretically important implications of these findings. First, although exercise is good for health, when taken to extreme, it can transit into an "addictive like" behavior. Second, behavioral addictions, including exercise addiction, constitute a situation in which individuals get addicted to the benefits and rewards of their own activities.[31] Because exercise provokes positive emotions and energy, enhanced sense of well-being and self-esteem, the behavior may develop into an addictive pattern.[9] Third, running and drugs activate similar neural pathways and the rewarding features of both are associated with the activation of the dopaminergic reward pathways.[32-34] Moreover, wheel running augments the levels of ΔFosB in nucleus accumbens, and overexpression of ΔFosB in striatal dynorphin neurons increases running.[34] The results reported by Werme et al[34] draw attention to the rewarding consequences of exercise through direct and indirect activation of dopamine pathways. In indirect activation, β-endorphin increases following exercise, activates the endogenous opioid system, and consequently stimulates dopaminergic activity.[17] Furthermore, exercise, by stimulating the sympathetic nervous system, increases the concentration of many neurotransmitters such as serotonin, norepinephrine, and dopamine. On a related note, contemporaries highlight the critical role of dopamine in motor function and the robust association between serotonergic activity and pain/ fatigue, which leads to the sense of well-being. Prolonged exercise not only activates the synthesis of serotonin but also activates the serotonin metabolism in cerebral cortex.[35] Previous studies used trained animals to investigate the effect of acute and prolonged exercise on both dopamine and serotonin synthesis and metabolism.[35-37] According to these authors, following exercise (e.g. running), dopamine metabolism and serotonin level were increased in the whole brain of rats. In this regard, Meeusen and De Meileir[35] assert that dopamine level in nucleus accumbens is the marker for the running speed of rats, suggesting that dopamine level in different parts of brain has a close link with the rewarding system.

Previous studies have found a strong association between participation in sport and developing drug abuse.[1,26,38] Such a condition is recognized in literature suggesting that the presence of drug abuse in sports contexts poses heightened risk of addiction for those who are vulnerable due to various reasons such as a biological vulnerability, family history, the existence of other predisposing behaviors, psychological features, circumstances and peer pressure.[26] Therefore, we can characterize them as more distressed individuals who are at risk of negative outcomes associated with behavioral addictions. There are some similarities between the effects of exercise and substance abuse. An evidence worthy of note is that in previous experiments, trained rats gave operant responses to find access to both drugs,[39] and running wheel,[40] and this represents the rewarding properties of exercise and drugs of abuse. These results demonstrate that exercise can be a substitute for drug-seeking behavior because rats running in wheels used smaller amounts of drugs than those housed in standard cages.[17,41-43]

Although our findings are not intended to be generalized to all individuals, because not all athletes exposed to sport environments will develop addiction, it is hoped that the insight into this phenomenon may resonate with, and provide us with a better understanding of how exercise may contribute to the development of exercise addiction. What is meanwhile important is that in the context of sports culture, some individuals are more vulnerable to the development of addictive behaviors, including exercise addiction, and this may be promoting the need for better support and also medication. Given that exercise addiction, which involves high amounts of exercise and distorted exercise attitudes, is correlated with mental disorders,[9] we suggest further investigation of related problems and specific strategies. The findings from the present study yield straightforward implications for sport context. It is recommended to do some global assessments before encouraging individuals to do professional sports. However, it is worth noting that the animal sample of this study limits generalizability to human samples; thus, there is a growing demand for human research to investigate the effects of exercise on addiction and exercise addiction and mental disorders, the results of which would be beneficial for treatment of addicted patients or preventing addiction in athletes.

Authors' Contribution

MN: study design and concept, acquisition of data, statistical analysis and interpretation of data; SFS: drafting the manuscript; MRZ: study supervisor.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

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