CARDIORESPIRATORY FITNESS PREDICTS HIGHER INHIBITORY CONTROL IN PATIENTS WITH SUBSTANCE USE DISORDER

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Abstract

Background: Impaired inhibitory control has been shown in individuals with substance use disorder (SUD). Cardiorespiratory fitness has been described as a potential factor to improve inhibitory control, however, the benefits in individual with SUD are unclear. **Aims:** To investigate the relationship between cardiorespiratory fitness with general and drug-specific inhibitory control in individuals with SUD. **Methods:** Sixty-two male participants under treatment for SUD performed a general and drug-specific inhibitory control test (Go/NoGo) and a cardiorespiratory fitness test. **Results:** Cardiorespiratory fitness, age and years of drug use were inversely associated with reaction time for both general and drug-specific inhibitory control. In addition, regression models show that cardiorespiratory fitness predicts general and drug-specific inhibitory control adjusted for age and time of drug use. However, cardiorespiratory fitness predicts equally both general and drug-specific inhibitory control. **Conclusions:** These findings suggest that increasing cardiorespiratory fitness could provide benefits in inhibitory function of individuals with SUD.

Keywords: Drug addiction, aerobic exercise, alternative therapies, inhibitory control, cognition.

1. Introduction

Chronic drug misuse is a worldwide public health problem. The Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-V 2013) classifies drug addiction as Substance Use Disorders (SUD) and Addictive Disorders. Several harmful consequences of SUD have been shown, including biological, mental, social, and financial problems (Beck & Heinz, 2013; Blanco-Gandía et al., 2015). In addition, SUD is also associated with metabolic and cardiovascular dysfunctions (Vongpatanasin, Taylor, & Victor, 2004; Whitman et al., 2017), increased risk of death (Fischbach, 2017) and harmful consequences to others including harassment, vandalism, physical aggression, and family problems (Nayak, Patterson, Wilsnack, Karriker-Jaffe, & Greenfield, 2019). The main neural mechanism associated with the persistent use of psychoactive substances is the release of dopamine neurotransmitter from the ventral tegmental area throughout the others areas in the reward system (i.e., nucleus accumbens, prefrontal cortex, striatum, and hippocampus) that leads to increased feelings of pleasure (Leshner, 1997). Repetitive drug use results in a decreased concentration of dopamine receptors (D2) in the reward system areas, leading to greater drug tolerance, abstinence, negative affect and craving feelings while provoking the urge to take higher doses (N. D. Volkow, Fowler, Wang, Baler, & Telang, 2009; Zorrilla & Koob, 2019). Chronically, this drug misuse also yields lower metabolic activity in the prefrontal cortex (PFC), while impairing higher order cognitive processes (i.e. executive functions) (Badre & Nee, 2018) and loss of control over drug seeking and behaviors (Goldstein & Volkow, 2011).

Inhibitory cognitive control is one component of executive functioning and can be defined as the ability to inhibit habitual impulses or behaviors according to advantageous future consequences (Feil et al., 2010). When it comes to addictive behaviors, poorer performance in inhibitory control is related to impulsiveness, and may lead to further harmful consequences (Brewer & and Potenza, 2008). On the other hand, greater performance on the inhibitory control may favor reduced impulsiveness (Bechara, 2005a) and improve decision making related to drug-seeking behaviors (Bechara, 2005b; Shenoy & Yu, 2011). Furthermore, poorer response inhibition in individuals with SUD is associated with difficulties in resisting the consumption of drug substances especially when exposed to higher salient substance-related cues (Robinson & Berridge, 2008; Strickland et al., 2018; Weafer & Fillmore, 2012) increasing drug-seeking and drug-taking behaviors (Fillmore & Rush, 2002; Fu et al., 2008; Luijten, Littel, & Franken, 2011; Rubio et al., 2008; Smith, Mattick, Jamadar, & Iredale, 2014; Volkow, Koob, & McLellan, 2016). Inhibitory control training have been suggested as a method to improve inhibitory control towards addictive behaviors (Bos et al., 2019), however, its efficacy is still under investigation.

In fact, different strategies have been proposed to treat drug addiction, such as pharmacotherapy, cognitive behavioral therapy and social support groups (Volkow & Li, 2005). However, it has been described a rate of 60% of relapse chances after treatment (Maisto, Pollock, Cornelius, Lynch, & Martin, 2003). Thus, new strategies are necessary to help the treatment of individuals with SUD. Regularly-performed physical exercise (defined as planned and structured activity to cardiorespiratory fitness) (Caspersen, Powell, & Christenson, 1985) has been shown to induce several benefits on the human body and has been considered an important complementary tool to treat different pathologies, including those associated with the neural functioning (Pedersen & Saltin, 2015; Sallis, 2009). The practice of physical exercise may improve cardiorespiratory fitness (Garber et al., 2011), which is associated with reduced all causes mortality risk (Lee et al., 2011; Blair, Kohl III, Barlow, 1995) and lower risk of poorer health development (Blair, Cheng, & Holder, 2001). Physical exercise have already been suggested to benefit the treatment of patients with SUD by decreasing drug related behaviors, such as abstinence, consumption and craving (Buchowski et al., 2011; Wang, Wang, Wang, Li, & Zhou, 2014). However, few studies have investigated the benefits of physical exercise in cognitive functions using neurobiological markers in individuals with SUD. Crucially, this is important to develop physical activity treatment strategies aiming to improve cognitive function (Costa, Cabral, Hohl, & Fontes, 2019).

For instance, previous research have demonstrated that acute exercise can decrease craving levels and abstinence feelings while improving inhibitory control (Wang, Zhou, & Chang, 2015; Wang, Zhou, Zhao, Wu, & Chang, 2016). Corroborating with this idea, we have also demonstrated that one single session of cycling exercise decreased drug craving feelings and increased PFC oxygenation in individuals with SUD, which was associated to higher inhibitory control performance (Grandjean da Costa et al., 2017). Recently, we have showed that greater cardiorespiratory fitness predicted better cardiac autonomic activity in response to an induced stressful situation in individuals with SUD (Cabral et al., 2019) while a 3-month running exercise program (3 times/week) improved PFC oxygenation, cardiac autonomic regulation, and inhibitory control in an alcoholic patient under treatment (Cabral et al., 2017). However, all of these studies have used general inhibitory cognitive measurements without drug cues (e.g., Color-Matching Stroop task), which might not trigger the psychophysiological responses related to drug cue-reactivity (i.e., increased heart rate and blood pressure, elevated cortisol and dopamine levels) (Papachristou, Nederkoorn, Havermans, Van Der Horst, & Jansen, 2012). To our knowledge, only two studies showed the benefits of aerobic exercise on an inhibitory cognitive task using drug-specific pictures (i.e., drug-specific inhibitory control) (Wang et al., 2015; Wang, Zhu, Zhou, & Chang, 2017a). However, these studies did not measure cardiorespiratory fitness, which make it difficult to infer any associations between the chronic exercise adaptations and cognitive response to drug-specific inhibition. Thus, we believe that, by improving the understanding of the link between cardiorespiratory fitness and drug-specific inhibitory control, we may bring new insights regarding the treatment of individuals with SUD.

Here we investigate the relationship between cardiorespiratory fitness and cognitive performance on a general and drug-specific inhibitory control task in individuals with SUD. We hypothesize that cardiorespiratory fitness would be associated with enhanced inhibitory control in individuals with SUD. We further predict that this association will be higher with drug-specific inhibitory control.

Methods

2.1 Participants

The study initially composed of 76 male adults under treatment for substance use disorder at five different rehabilitation community settings that are free of medications on their routine rehabilitation practice. To be eligible in this study, participants had to score the minimum of 24 points on the MMSE (Batista, Klauss, Fregni, Nitsche, & Nakamura-Palacios, 2015) and be approved on the physical activity screening questionnaire (PAR-Q) (Roy J, 1988) by answering "No" to all questions. There were no exclusion criteria for a specific substance. Sixty-two volunteers were used in the final sample. 14 individuals were excluded since they did not reached minimum score of 24 points on Mini-Mental State Examination (MMSE) and/or were not approved on the cardiac risk screening questionnaire (PAR-Q) (Roy J, 1988). The preferred substances of each participant (alcohol, nicotine, marijuana, cocaine/crack, LSD, amphetamines, hypnotic sedatives, and ecstasy) were defined by applying the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Henrique, Iara Ferraz Silva; Micheli, De Lacerda, De Lacerda, & Formigoni, 2008). Among the participants, 33 were multiple drug users (25 alcohol/crack, 4 crack/marijuana, 2 Alcohol/Marijuana, 2 Crack/Marijuana/Alcohol) and 15 were crack/cocaine users, 3 were marijuana users, 11 were alcohol users. All participants met at least two criteria for Substance Use Disorder from the DSM-V (Hasin et al., 2013). The study followed the Declaration of Helsinki standards and all participants signed the informed consent approved by the local ethics committee

2.2 Experimental Design

This cross-sectional study was performed in three visits at different rehabilitation community settings with a minimum interval of 48 hours between each visit. On the first visit, patients attended a lecture describing the harmful effects of drugs on the brain and the benefits of physical exercise. At the end, the study purposes and procedures were presented. On the second visit, the patients that agreed to participate in our study completed questionnaires for psychosocial state assessment, physical activity readiness (PARQ) and drug-specific risk status. On the third visit, the participants completed the general and drug-specific inhibitory task followed by the cardiorespiratory fitness test.

2.3 Measurements

2.3.1 Psychosocial Questionnaire

Psychosocial questionnaire for stress, anxiety and depression (DASS-21) was administered to the participants (Ribeiro, Honrado, & Leal, 2004). The DASS-21 consists of three scales of seven items each (total of 21 items). Each item consists of a phrase or statement referring to negative emotional symptoms. For each sentence there is a choice of four possible responses, presented on a Likert scale (e.g., 0 Did not apply to me at all; 1 Applied to me to some degree, or some of the time; 2 Applied to me to a considerable degree or a good part of time; 3 Applied to me very much or most of the time. The participants carried out the test in a quiet environment and in a reserved room. The DASS-21 score was quantified through three scales: depression, anxiety and stress, deriving scores for depression – dysphoria (two items); Discouragement, (two items); Life devaluation (two items); Auto depreciation (two items); Lack of interest or involvement (two items); Anhedonia (two items); Inertia (two items). Anxiety – excitation of the autonomous system (five items); Skeletal muscle effects (two items); Situational anxiety (three items); Subjective experiences of anxiety (four items). Stress – Difficulty in relaxing (three items); Nervous excitation (two items); Easily agitated/upset (three items); Irritable/exaggerated reaction (three items); Impatience (three items).

2.3.2 ASSIST Questionnaire

This questionnaire, developed by the World Health Organization (Group, 2002), assesses the risks and problems related to the use of alcohol, marijuana, cocaine/crack, LSD, sedatives, hallucinogens, heroin, Inhalants, opioids, and other drugs. The questionnaire consists of seven questions that include a score and classifies the individual as being without the need for intervention (< 3 pts), needing a brief intervention (> 4 pts), or a need of immediate intervention (> 27 pts) according to the preferred drug. In this study, the ASSIST was used to identify the drug of preference, since all volunteers were on a regimented treatment.

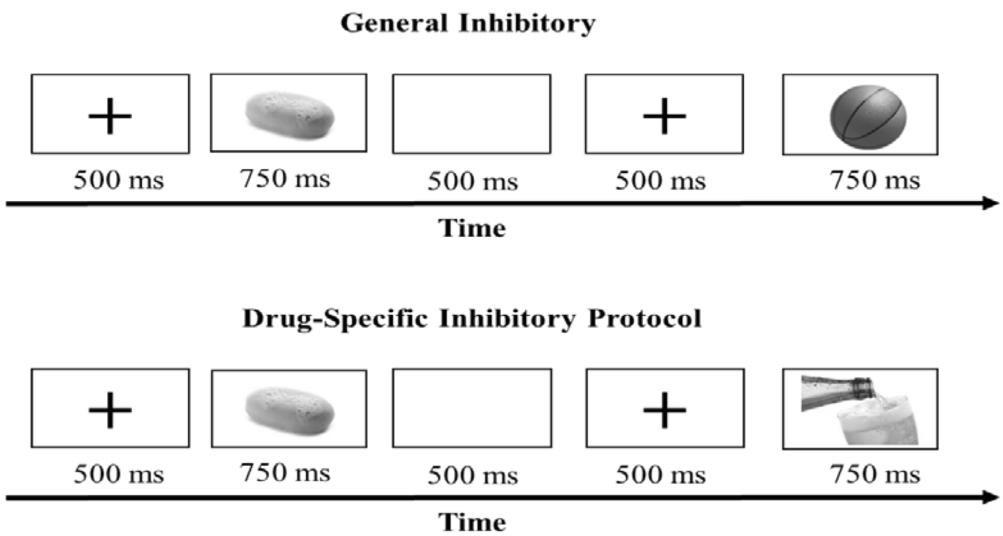
2.3.3 Cardiorespiratory Fitness Test

The participants initially had their weight and height assessed followed by the multistage 20-m shuttle run (a progressive effort test) proposed by Leger (1988). This test has been demonstrated to indirectly predict the VO_2max. A Meta-analysis showed that this test has been validated and has good reliability predicting VO_2max (Mayorga-Vega, Aguilar-Soto, & Viciana, 2015 (Léger, Mercier, Gadoury, & Lambert, 1988). In this test, the participants are asked to run from one cone to another cone with a fixed distance of 20m between them, and reversing the direction at each cone, thus returning to the opposite one. The running pace should occur according to the sound signals emitted by an audio recording specifically for this test. Initial speed was 8.5 km/h, with an increasing of 0.5 km/h each minute. An exception was given at the first minute, with an increase of 1 km/h. As the test speed increases, the interval between the sound signals decreases. The test was finished when the participant interrupted its displacement by voluntary exhaustion (ratings of perceived exertion = 10 on CR-10 Borg Scale) (Borg, G., Linderholm, 1970) or had not been at least 2m apart from the cone at the sound signal for two times, not necessarily consecutive times. The estimative of maximum oxygen consumption (VO_2max) was calculated (VO_2 =(Y) = -24.4) + [(6.0*X)] (*Y* = ml/kg/min*; X = velocity in km/h at the stage reached).*

2.3.4 Go/no-go inhibitory control task

An adapted go/no-go inhibitory control task was developed based on previous study with food related images (Price, Lee, & Higgs, 2016). For the drug-specific trials, images of marijuana, crack, cocaine and alcoholic beverages were used as no-go images. For the neutral trials, sports images were used as no-go images. In both cases, the go images were bathroom objects. All drug specific images were taken from the database “addiction pics” for experimental researchers (https://pixabay.com/pt/photos/addiction/). Images with other objects were taken from the BOSS normative database of photographs of objects (Brodeur, Dionne-Dostie, Montreuil, & Lepage, 2010). Images were randomly presented on a computer screen with a ratio of 20% (No Go) and 80% (Go). The presentation order of the drug-specific task and neutral task was counterbalanced. The individuals were told to press the space key button as fast as possible whenever they see a bathroom object (Go) and to not press the space key when the image was drug-cue or sports (neutral) images as relevant (No Go). Two hundred images were presented in total. Each image was shown on the screen for 750ms. Intercalating each image, a blank screen (500ms) and another screen with a "+" (fixing point for 500ms) were presented (Figure 1). Between each drug image and sports images, bathroom images were randomly inserted (3, 4 or 5 between every cue picture). The total test lasted approximately 7 minutes. Inhibitory control was evaluated by the number of times the space bar was pressed incorrectly in no-go trials (commission errors) and by reaction times (ms) on Go trials. Instructions were standardized and comprehension and willingness of the participants were assured by a short preceding practice trial. Drugs images were selected according to the drug preference of each subject. For example, if an individual was considered as a cocaine and alcohol user (multiple drug user), images of both drugs would be used during the, No Go trials.

Figure 1. General and drug-specific cognitive inhibitory task.



2.4 Statistical analysis

The Shapiro-wilk test was used to verify data normality and Levene's test was performed to check data homogeneity. Parametric data are described as mean ± standard deviation and non-parametric variables as median (confidence interval) (see table 1). Initial Spearman correlations were conducted for the variables of interest (commission errors and reaction time of go no/go task, VO_2max). Potential covariables (age, time of drug use, body mass index (BMI), days in abstinence, and DASS-21 scores) were also included on the correlation analysis. Significant covariables were included in the main regression analysis. Multiple linear regression analyses were applied to investigate the independent contribution of VO_2max to the variance in inhibitory control parameters. Assumptions of equality of variance, independence, linearity and normality were plotted, inspected, and verified using Studentized residuals. Multicollinearity was not observed among any of the independent variables. Statistical significance was set at $p<0.05$ and was used bootstrapping power analysis values are described in CI (Banjanovic & Osborne, 2016). We used the software SPSS® 22.0 for Windows (SPSS, Inc., Chicago, IL).

2. Results

Bivariate correlations (2-tailed) showed that cardiorespiratory fitness (VO_2max) was inversely associated with age ($r = -.46$, $p<.001$), time of drug use ($r = -.52$, $p<.001$) and reaction time for general ($r = -.43$, $p<.001$), and drug-specific inhibitory control ($r = -.47$, $p<.001$). No associations were found between VO_2max with BMI ($r = -.04$, $p<.709$), days in abstinence ($r = -.02$, $p<.851$), and DASS-21 scores (stress: $r = -.02$, p<.832; anxiety: r = -.11, p<.360; depression: r = -.13, p<.286). In addition, no association was found between commission errors and cardiorespiratory fitness (general inhibitory control errors (r = -.16, p<.189), and drug-specific inhibitory control errors (r = -.07, p<.580). Therefore, two multiple regression analyses were run for predicting reaction time on the general and drug-specific trials of the go/no-go task (see Table 2). Results show that cardiorespiratory fitness (VO_2max) predicts the reaction time for general [$F_{(6; 3)}$); (t = -3.0; β = -.41; p = .003] and drug-specific inhibitory control [$F_{(8; 3)}$); t = -3.2; β = -.42; p < .002] when we adjusted the analyses for age and time of drug use.

Sample general characteristics	
	Median (CI) (n=62)
Age	34 (31.9 – 36.4)
BMI (kg/m^2) #	24.6 ± 2.9
VO^2_{max} (ml/kg/min)	39 (38.4 – 42)
Time of drug use (yrs)	13 (12.9 – 18.3)
DSM-V (pts)	5.7 (5.2 – 6.2)
Abstinence use (days)	105 (103 – 173.6)
Anxiety (a.u)	28.5 (24.7 – 37.2)
Depression (a.u)	23.8 (22.3 – 33.8)
Stress (a.u)	23.8 (23.8 – 34.6)
Commission errors (general)	2 (1.7 - 2.8)
Commission errors (specific)	1 (1.2 - 2.1)
RT (general) (ms) #	482.5 ± 56.3
RT (specific) (ms) #	498.9 ± 61.5

Drug preferences	**N (%)**
Crack/Cocaine	15 (24.1)
Marijuana	3 (4.8)
Alcohol	11 (17.7)
Crack/Alcohol	25 (40.3)
Crack/Marijuana	4 (6.4)
Alcohol/Marijuana	2 (3.2)
Crack/Marijuana/Alcohol	2 (3.2)

Table I. *Describes the sample general characteristics and cognitive performance on the go/no-go task.*

Legend. RT (Reaction time) #Mean and standard deviation; BMI: body mass index; DSM-V: Substance Use Disorders.

Table 2. *Regression analyses between cardiorespiratory fitness and reaction time of general and specific inhibitory control adjusted by age and time of drug use.*

Predictors	Reaction time (General)		Reaction time (Drug-specific)	
	β (CI)	ΔR^2	β (CI)	ΔR^2
Model 1		.13		.16
Age	.34* (09 – 54)		.43** (15 – 60)	
Time of Drug use	.03 (04 – 49)		.00 (03 – 54)	
Model 2		.25		.27
Age	.23 (09 – 54)		.32 (15 – 60)	
Time of Drug use	-.10 (04 – 49)		-.13 (03 – 54)	
VO_2max	-.41** (- 62 – - 19)		-.42** (- 66 – - 23)	

*p<0.05; **p<0.01

Discussion

The present study sought to investigate whether cardiorespiratory fitness was associated with performance on a general and drug-specific inhibitory control task in individuals with SUD. We found that higher cardiorespiratory fitness predicted better performance on the cognitive test when controlling for age and length of time using the drug. However, cardiorespiratory fitness was not associated with stress, depression or anxiety scores and we could not find differences between general and specific inhibitory control performance predicted by cardiorespiratory fitness. Nevertheless, our results indicate the importance of cardiorespiratory fitness in cognitive control deficits in individuals with SUD.

Physical exercise is fundamentally important in the evolutionary history of human beings (Bramble and Lieberman, 2004), aiding survival in hunter-gatherer societies. Findings have demonstrated that levels of cardiorespiratory fitness during human evolution are correlated with increases in brain size, with the PFC being the most developed neural area when compared to any other primates (Raichlen & Polk, 2012). The cognitive functions of the PFC have been suggested to play role in exercise tolerance and performance (Robertson & Marino, 2016), with a cohort study revealing a preventive effect of exercise on drug use. In fact, McElrath and colleagues showed that individuals that performed physical exercise regularly were less likely to consume alcohol, cigarettes, and marijuana (McElrath, O'Malley, & Johnston, 2011). Thus, we speculate that our results showing that individuals with higher cardiorespiratory fitness have better inhibitory control may be related to these preventive effects on drug use. Individuals with SUD have been shown to display impairments of inhibitory control and PFC function during exercise (Grandjean da Costa et al., 2017), which could hamper exercise adherence and, consequently, the development of cardiorespiratory fitness. Previous research has also shown that exercise practice can be an effective complementary treatment for SUD rehabilitation (Weinstock, Farney, Elrod, Henderson, & Weiss, 2018). To date, most of the research that has analyzed the effects of physical exercise on behavioral outcomes in drug addiction, have not attempted to explore the mechanism of change (Wang et al., 2015; Wang, Zhu, Zhou, & Chang, 2017a). We have shown that cardiorespiratory fitness is related to inhibitory control in individuals with SUD, suggesting that the benefits of physical exercise in improving cardiorespiratory fitness may be related to improvements in inhibitory control. However, due to the cross-sectional nature of this study we cannot establish causality and longitudinal research is needed to confirm this assumption.

Typically, the commission errors during Go/No go tasks are the main parameter for inhibitory control performance. In our study, few commission errors were made, and may have induced a floor effect whereas the recorded data was unable to discriminate among the participants´ cognitive performance (Catts, Petscher, Schatschneider, Bridges, & Mendoza, 2009). Thus, we believe that this may help to explain why we did not find associations between cardiorespiratory fitness and commission errors. However, we did find an association between cardiorespiratory fitness and reaction times, which has also been indicated as a parameter of cognitive performance (Papachristou et al., 2012). In go/no-go tasks, slower reaction time in the go trials can indicate increased difficulty in inhibiting the response on the no go trials via a speed-accuracy trade-off (Bogacz, Wagenmakers, Forstmann, & Nieuwenhuis, 2010). In fact, previous studies used mean reaction time on the go condition as measure of inhibitory control performance (Smith et al., 2011; Wang, Zhu, Zhou, & Chang, 2017b). Thus, reaction time can also be used as an efficiency index of cognitive performance (Hirose et al., 2012), and we infer that better inhibitory control in individuals with higher cardiorespiratory fitness, as they performed the same amount of correct answers while having faster reaction time.

Few studies have investigated the relationship between physical exercise with general and drug-specific inhibitory control in individuals with SUD. Our results found that cardiorespiratory fitness independently predicts reaction time for general and drug-specific inhibitory control, which indicates the possible benefits of having higher cardiorespiratory fitness on cognition of individuals with SUD. Several studies have demonstrated the benefits of cardiorespiratory fitness on cognition in different populations (Colcumbe et al., 2006; Hillman, Erickson, & Kramer, 2008; Kramer, 2009). These benefits might also be transposed to SUD individuals as shown in our study. These findings have been discussed in terms of the effects of exercise on neuroplasticity in the prefrontal cortex, which may enhance executive functions (Maass et al., 2016). Therefore, we highlight the importance of investigating the effects of exercise on cognition in individuals with SUD to provide further understanding of the rehabilitation alternative methods.

However, we could not find differences between the associations of cardiorespiratory fitness and performances on the general and drug-specific inhibitory control. One possible explanation for this finding could be that the VO_2 max measurement in our study is an indirect measure and may not be a reliable indicator of cardiovascular fitness in individuals SUD. It may be the case that the drug-specific inhibitory control test is only sensitive to laboratory-based tests of VO_2max. Moreover, despite we have used specific images of drug cues for the drug preference of each individual, we speculate that these cues did not produce a physiological cue-reactivity response in order to difficult the inhibition process. Further studies measuring physiological markers (i.e. Heart rate variability, skin conductance, electrocortical activity) could help to evaluate such responses. For instance, studies have shown that cue-reactivity responses induce feelings of cravings that activate brain frontal areas and predict relapse in individuals with SUD (Wilson, Sayette, & Fiez, 2004). On the other hand, randomized control trials have failed to translate inhibitory control training to changes in addictive behaviors interventions (Bos et al., 2019; Jones et al., 2018). Thus, further studies are necessary to test if there is a difference in physiological and behaviors responses between drug-specific inhibitory and general inhibitory control in the drug-specific go/no-go task proposed in our study.

We do acknowledge that our study is potentially limited by the heterogeneity of the sample in terms of preferred drug and the small sample for each subgroup of drug use (cocaine/crack, alcohol, marijuana). This may have affected the cue-reactive responses during the drug-specific inhibitory control due to the different action mechanisms promoted by the drugs. However, studies have shown that all of these drugs impair PFC function and inhibitory control performance (Herbsleb et al., 2013; Luijten et al., 2014; Nora D. Volkow et al., 2016), which was the investigative focus of the present study. In this preliminary research study, we also did not have a healthy control group, which could have helped to further compare the benefits of cardiorespiratory fitness in inhibitory control. However, we believe that our findings are useful to guide future research in this area. We also did not use any neurobiological measurement (e.g., MRI, EEG), which could have masked some cerebral differences between the two inhibitory tasks. Future research should try to replicate our study but using some neural instrument. Based on our findings, further longitudinal studies with specific samples of SUD are necessary to test the efficacy of the drug-specific go/no-go task used in this study as an indicator of cognitive changes associated to improvements in cardiorespiratory fitness.

Clinical Implications

Our results suggest that improved cardiorespiratory fitness might be beneficial to inhibitory control in individuals with SUD. However, to date, there is no specific exercise prescription for patients with SUD. Thus, we suggest that professionals from therapeutic community settings apply the prescription based on the American College of Sports Medicine (ACSM) guidelines (Garber et al., 2011) which includes light to moderate intensity exercise for 150 minutes or more per week. Moreover, we believe that the PFC impairments in individuals with SUD might have a disadvantage on internal exercise regulatory process that may impact the adherence to exercise programs (Grandjean da Costa et al, 2019). We suggest that activities that promote higher distraction from internal cues, such as adding music, outdoors environment and group training might be important strategies to increase affective feelings while exercising. As a complement to the training program, future research could use the drug-specific cognitive task to understand the changes induced by long term exposure to chronic exercise programs.

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