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Executive functions improvement in individuals with substance use disorder: the role of high-intensity interval functional training

Melhora das funções executivas em pessoas com transtorno por uso de substâncias: o papel do treinamento funcional intervalado de alta intensidade

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Abstract

Objective

Individuals with substance use disorder exhibit a hampered cognitive capacity due to the impairment of their executive functions. This study evaluated the effects of high-intensity functional exercises on the executive functions of individuals with such a disorder.

Method

Forty patients were allocated to two groups: Intervention ($N = 22$) and Control ($N = 18$). They were evaluated before and after an acute session of high-intensity functional training (Intervention group) or a period of rest (Control group).

Results

The Intervention group improved cognitive capacity, performance in mental flexibility, inhibitory control, working memory, and showed positive perceptual responses to effort and affection (“Clear the Mind”, “Facilitate the Walk”) compared to the Control group.

Conclusion

The outcome suggests that high-intensity functional exercise can be an accessible, functional, and emotionally positive therapeutic alternative for individuals with substance use disorder.

Keywords: Drug addiction; Drug users; Executive function; Exercise training; Physical exercise.



Resumo

Objetivo

Pessoas com transtorno de uso de substâncias apresentam capacidade cognitiva comprometida pelos prejuízos nas funções executivas. Vinte minutos de exercício aeróbico moderado ou de força promoveu melhora na capacidade cognitiva dessas pessoas, contudo, não há uma padronização de tipo, programa, intensidade, duração e frequência. Este estudo avaliou o exercício funcional de alta intensidade sobre as funções executivas de pessoas com tal transtorno.

Método

Quarenta pacientes foram alocados nos grupos: Intervenção (N = 22) e Controle (N = 18), e, avaliados, antes e após uma sessão aguda de treinamento funcional de alta intensidade ou de um período de repouso, respectivamente.

Resultados

O grupo Intervenção melhorou: capacidade cognitiva, desempenho na flexibilidade mental, controle inibitório, memória de trabalho e respostas perceptuais positivas para esforço e afeto (“Clarear a Mente”, “Facilitar a Caminhada”) em comparação com o grupo Controle. Os resultados sugerem que esta intervenção pode ser uma alternativa terapêutica acessível, funcional e afetivamente positiva.

Palavras-chave: Transtornos relacionados ao uso de substâncias; Usuários de drogas; Funções executivas; Treinamento físico; Exercício físico.

The use of psychotropic drugs is a global public health problem that bears an impact on different economic, social and safety aspects, as well as on morbidity and mortality and costs for the health systems. It is estimated that 35 million people suffer from disorders associated with the use of psychotropic drugs (cannabis, opioids, alcohol, nicotine, among others), while only one in seven receives adequate support and treatment (United Nations Office on Drugs and Crime, 2022).

These substances exhibit specific pharmacodynamics, with their effects mediated by the rate of brain dopamine release reward system (Feltenstein et al., 2021). Dopaminergic neurons can trigger abruptly and transiently depending on their use, which is positively associated with different organic dysfunctions, but “immediately”, brain homeostasis is affected, with a high risk of temporary or permanent damage to higher functions such as cognitive, emotional, metabolic, psychomotor and behavioral responses (Olds & Milner, 1954; Solinas et al., 2019). This scenario adds to the risks of cardiovascular, pulmonary, liver and kidney disorders, sexually transmitted infections, severe poisoning and other behavioral consequences, such as violence and accidents (Volkow et al., 2019).

The Substance Use Disorder (SUD) *continuum* occurs as a cycle, with three characteristic phases: 1) repeated compulsion or intoxication, which produces learning and associative memories; 2) withdrawal or negative effect, related to an increase in the stress response resulting from negative emotions; and, 3) concern or anticipation (craving), a state in which changes in the prefrontal cortex, more specifically in the Executive Functions (EF), impair decision-making capabilities, Mental Flexibility (MF) and attribution of value to behavioral actions, thus weakening the ability to resist the urge to use the substance (Volkow & Blanco, 2023; Zhang & Volkow, 2019).

Among the EFs, one of the most affected is Inhibitory Control (IC), which consists of the ability to control attention to overcome a strong internal predisposition to make decisions based on impulsivity or desire, even knowing the relevant mistakes and their consequences. On the other hand Working Memory (WM), which consists of the ability to store and manipulate information simultaneously with the performance of other cognitive activities (Cristofori et al., 2019; Lezak et al., 2004) can be hampered by the use of the substances.

People with Substance Use Disorder (PSUD) exhibit functional and structural damage (reduced metabolism, morphological changes in dendrites in frontal areas, especially in the orbitofrontal cortex which results in impairment of EF, specifically in the IC, presenting greater

difficulty in coordinating mnemonic information and inhibiting behavioral actions (Friedman & Robbins, 2022). These changes jeopardize decision-making processes, leading to the option for more attractive solutions and immediate gains, to the detriment of more complex analyses related to the judgment consequences and the behavioral attitudes arising therefrom (Hobkirk et al., 2019; Matumoto & Rossini, 2013).

Physical Exercises (PE) are powerful reducers of organic, peripheral and central disorders due to some reduction of the pro-inflammatory cytokines, the recovery of the signaling capacity of growth factors and neural repair, when those exercises are performed according to the appropriate type, intensity and duration (Bechara et al., 2000; Merege Filho et al., 2014). Several factors are associated with PE such as: BDNF (brain-derived neurotrophic factor), VEGF (vascular endothelial growth factor), IGF1 (insulin-like growth factor 1) and myokines, such as irisin, released by the most active muscles during PE, and which stimulates the nervous system (Ben-Zeev & Okun, 2021; Severinsen & Pedersen, 2020).

PE can be a complementary strategy in the treatment of PSUD, and therefore understanding its physiological bases is of great interest. Its inclusion in the therapy in a safe and individualized way is capable of reducing thinking and compulsion, and acting positively on mood states, cognitive capacity, stress levels and socio-affective difficulties resulting from SUD, as well as reducing the negative emotional symptoms commonly present in the withdrawal syndrome (Brown et al., 2010; Ferreira et al., 2017; Huang et al., 2020; Linke et al., 2019). However, to date, there is no consensus on the type, program, intensity, duration, and frequency of PE that are appropriate or efficient in promoting PSUD's general health and cognitive capacity, or in improving adherence rates and treatment success (Ferreira et al., 2017).

In this connection, this study set the hypothesis that High-intensity Interval Functional Training (HIFT) is capable of inducing positive effects on the PSUD's EF, as it is a sport modality with a psychomotor strategy that induces neuroendocrine integration, cardiovascular and respiratory activation and recruitment of biomotor capacities (balance, motor coordination, agility, strength, flexibility and resistance, for example), which can be performed using only the practitioner's body mass or with the association of accessories and equipment, in movement patterns and serial repetition. Thus, we sought to evaluate the effects of a single HIFT session on EF (MF, IC and WM), and on the perceptual responses in relation to the physical effort of PSUD, comparing it to a control group.

Method

The study protocol was approved by the Research Ethics Committees of the Universidade Federal do Triângulo Mineiro (UFTM, Federal University of Triângulo Mineiro) (CAAE: 14878619.4.1001.5154) and the *Hospital Geral de Goiás* (HGG, General Hospital of Goiás) (CAAE: 24719019.3.0000.0035). It was also submitted and approved by the Research Department of the *Centro Estadual de Referência e Excelência em Dependência Química* (CREDEQ, Reference and Excellence State Center in Chemical Dependency), and presented to the team of health professionals of the institution, with the objective of socializing the information, as well as to clarify possible doubts and obtain support and engagement for the stages of the study, including its ethical aspects.

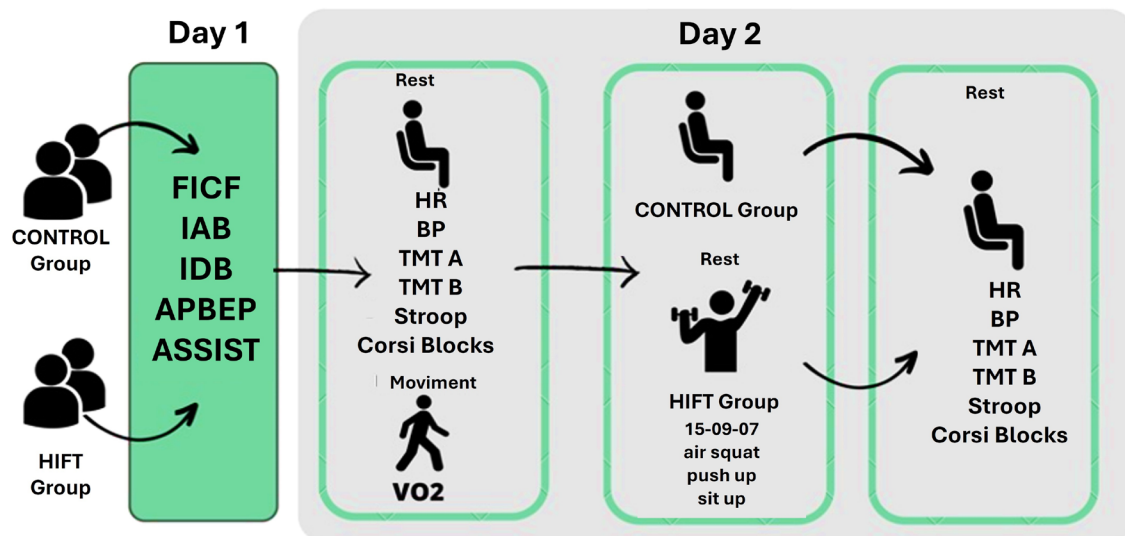
Participants

Individuals with disabilities admitted for treatment during the research period, who were diagnosed with or met diagnostic criteria for SUD (alcohol, tobacco, cocaine, opioids, cannabis

and/or other substances), who were male, over 18 years of age, who did not present absolute contraindications for performing HIFT, with informed and voluntary participation in the study were included. Male individuals with disabilities included in the sample were those who were literate, able to perform the tests to assess EF and to walk on a treadmill for 8 minutes; they had to be over 18 years of age, able and authorized by the medical team to perform the proposed HIFT, with a reception period between 8 and 15 days, and who had not participated in PE programs in the last 15 days. Individuals with mental disorders or disabilities that prevented them from measuring their EF using the proposed tests, or with physical impairments that prevented them from performing the proposed HIFT, who had a history of traumatic brain injury, presence of neurological diseases such as epilepsy, stroke, Parkinson's disease and/or Alzheimer's disease; those who abandoned the institution's shelter or were not cooperative with the study procedures were not admitted in the sample. A total of 120 individuals with substance use disorder were initially selected, of which 40 completed the study protocol and were allocated to the Control (Ctl-G, $N = 18$) and Intervention (HIFT-G, $N = 22$) groups. Dropouts were attributed to factors such as voluntary withdrawal, abandonment of treatment, difficulties in reading and numerical comprehension, or vision problems due to the absence of corrective glasses (Figure 1).

Figure 1

Flowchart of the two-day protocol of a study comparing a control group and a high-intensity functional interval training (HIFT) group



Note: Day 1 includes consent and baseline assessments (surveys): free and informed consent form (FICF), Associação Brasileira de Empresas de Pesquisa (ABEP, Brazilian Association of Research Companies), Alcohol, Smoking and Substance Involvement Screening Test (ASSIST); Day 2 shows the resting activity, executive function tests, heart rate (HR), blood pressure (BP), Trail Making Test A (TMT A), Trail Making Test B (TMT B), rest for the control group and physical exercise for the High-intensity Functional Interval Training (HIFT) group and post-activity assessments for both groups.

Instruments

Registration and Free and Informed Consent Form (FICF): Collection of general information about the participants' profile, such as name, age, number of times they had been admitted, time of current admission, type and time of use or abuse of psychotropic drugs. For the Economic Classification Standard, the questionnaire proposed by the Associação Brasileira de Empresas de

Pesquisa (ABEP, Brazilian Association of Research Companies) was used, which classifies by score, in Economic Classes A1, A2, B1, B2, C, D and E. (Associação Brasileira de Empresas de Pesquisa, 2020). The pattern of psychotropic drug use was verified using the Brazilian version of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Henrique et al., 2004).

Anthropometry: Body mass was measured on a digital scale (New Bk-50FAN, Balmak Ltda, Santa Barbara do Oeste, SP, Brazil) and height, using a stadiometer (Norgan, 1988).

Body Composition: Body Mass Index (BMI) was calculated and classified as indicated by the WHO.

Physiological Assessment: Heart rate (HR) and blood pressure (BP) were measured at rest using a digital sphygmomanometer (NS HBP-1100, Omron healthcare Brazil, São Paulo, SP, Brazil).

Perception of effort and affective response to physical effort: Were assessed by the participant's indication, during physical effort, on a 1 x 1 meter colored banner, using: 1) Borg Effort Scale from 6 to 20, in which 6 represents "no effort" and 20 "maximum effort" (Arney et al., 2019; Tibana et al., 2018). 2) Affective Valence Scale, which has a scale from -5 to +5, representing the affective extremes "very bad" and "very good", with intermediate indicators, namely: +3 = good, +1 = reasonably good, 0 = neutral, -1 = reasonably bad, -3 = bad (Hardy & Rejeski, 1989).

Maximum Oxygen Consumption (VO_{2max}): Estimated using the Ebbeling protocol for individuals with an average level of cardiovascular fitness, with the estimate depending on two stages: 4 minutes at a speed of 3.2 to 7.2 km/h, variation necessary for organic adjustments for physical effort between 50% and 70% of the maximum HR predicted for age, followed by 4 minutes at the speed achieved and addition of 5° of positive inclination, with the HR measured at the end of the effort for the purposes of estimation calculations (Ebbeling et al., 1991).

The tests were performed on a treadmill (Amazon 3.0, Athletic Way Comércio de Equipamentos para Ginástica e Fisioterapia Ltda., Joinville, SC, Brazil) and HR monitored by cardiac transmitter (H10 Polar, Polar Electro Brasil, São Paulo, SP, Brazil).

Assessment of Emotional and Motivational States: The assessment of emotional states and motivation was performed using standardized instruments, validated for specific psychological screenings: Beck Depression Inventory, composed of 21 items with the objective of measuring depressive symptoms, with scores suggesting minimal (0–13), mild (14–19), moderate (20–28) and severe (29–63) depressive symptoms (Gomes-Oliveira et al., 2012). The Beck Anxiety Inventory, with 21 items related to the most frequent anxiety symptoms, with suggested classification as minimal (0–10), mild (11–19), moderate (20–30) and severe (31–63) (Karino & Laros, 2014).

Inhibitory Control (IC): was assessed using the Victoria version of the Stroop Test, when three white cards with 24 stimuli organized in six rows and four columns are presented. Each card exhibits 24 rectangles printed in the colors green, pink, blue and brown. Cards 1 and 2 are similar except for the stimulus, since in card number 2 the rectangles are replaced by the words "each, never, today" written in green, blue, pink and brown capital letters. The task consists of naming the colors on these cards as quickly as possible, ignoring the words written on card number 2. On the third card, called the interference card, individuals should name as quickly as possible the colors in which the words are printed, ignoring the actual word (example: the written word "blue", printed in pink). Performance was measured according to the time needed to complete the task and the errors made on each card (Periñez et al., 2021).

Mental Flexibility (MF): Was assessed using the Trail Making Test (TMT), which is a manual instrument divided into two stages: A and B. In stage A, the proband must connect, in ascending order, the numbers randomly distributed on a sheet of paper, and in stage B, he must connect the numbers (1 to 13) to the letters (A to M), alternating in ascending order, between numbers and letters, for example: 1 - A - 2 - B - 3 - C and so on. Test performance was measured according to the time in seconds to perform the task.

Working Memory (WM): was assessed by the visuospatial sketch of the WM, using the Corsi Block Test, with performance obtained by the number of blocks correctly pointed out, in increasing sequence and direct order (Kessels et al., 2000; Siddi et al., 2020).

High Intensity Functional Training (HIFT): a training method with constantly varied functional movements performed at high intensity, including series of movements that use the practitioner's body mass or accessories and equipment. The modality uses Olympic lifting exercises, such as squats, snatches, cleans and presses; predominantly aerobic exercises such as rowing, running and cycling, and gymnastic movements such as handstands, parallel bars, rings and barbells (Schlegel, 2020).

To meet the objectives of the proposed protocol, the HIFT performed by the participants used movements with body mass, respecting the general vulnerabilities and individual conditions, especially the participants' psychomotor capacity. The HIFT was applied in a single session and organized into 4 moments, namely: 1) Presentation (5 min): the evaluator explained the dynamics on a whiteboard, demonstrating technically how the movements should be performed; 2) Warm-up (8 min, 8 sets, 20 s of stimulus with 10 s of interval), performed at lower intensity and complexity levels, in order to activate the autonomic and functional mechanisms; 3) Motor skills (10 min, 3 sets, 5 repetitions with 45 s interval), used to work on familiarization and learning the technical execution of the movements to be performed in the next stage, with the movements selected being: air squat (squat with body weight), push up (push-ups on the ground) and sit up (complete abdominal); 4) "Workout of the Day" (WOD), characterized by the performance of the movements learned in step 3, at high intensity. The movements were performed in the following order: air squat, push up and sit up, obeying the 15/15/15, 09/09/09 and 07/07/07 number of repetitions, with up to 6 min to perform the 3 proposed series. The evaluator offered guidance and verbal encouragement during the WOD, in order to ensure obtainment of the desired physical effort intensity.

At the end of the session, the perceptual responses to the effort performed and the affective response that was promoted were measured. HR was monitored before, during, 5, 10 and 15 minutes after the physical effort.

Procedures

The sample was selected according to the reception flow at the research site. After completing the initial detoxification period, which lasted until the 8th day after reception, participants were referred to the investigators by the clinical team and were invited to participate in the study. Data collection occurred between the 8th and 15th day, according to previously established criteria. After presentation of the protocol, answering questions and after collecting the signed FICF, anamnesis and cognitive screening were performed to further the other procedures. This process continued throughout the data collection period, with the participants being randomly distributed into the study groups. The procedures were performed in 2 meetings, always between 9:00 and 10:00 and lasted approximately 60 minutes with a 24-hour interval. The first meeting was intended for the invitation, presentation, signature of the informed consent form, anamnesis and

other characterizations and screenings. In the second meeting, participants underwent physiological monitoring, EF assessment (MF, IC and WM or TMT, Stroop Test and Corsi Blocks); the physiological variables were measured at rest and the test to estimate oxygen consumption was performed. After HR returned to resting levels, the Ctl-G was instructed to remain in a quiet place intended for rest and the HIFT-G was subjected to physical effort. Approximately 15 min after completion of the effort protocol, participants were again subjected to EF assessment.

Results

The Control and Intervention groups were not different from each other in relation to the clinical, social and physiological characterization variables. The data are presented in Table 1.

Table 1

Characterization of volunteers admitted at Goiás Reference and Excellence State Center in Chemical Dependency with substance use disorder, comparing control and experimental groups after high-intensity interval functional training

| Clinical variables | Ctl-G (N = 18) | HIFT-G (N = 22) | p |
|--------------------------------|----------------|-----------------|------|
| | M ± SD | M ± SD | |
| Age (years) | 37.2 ± 9.6 | 34.0 ± 7.6 | 0.24 |
| Consumption time (years) | 16.9 ± 8.2 | 14.0 ± 5.9 | 0.22 |
| Hospitalization time (days) | 10.4 ± 2.1 | 12.0 ± 2.6 | 0.07 |
| Weight (kilograms) | 69.2 ± 16.0 | 76.0 ± 18.2 | 0.17 |
| Height (centimeters) | 172.5 ± 6.6 | 176.0 ± 8.1 | 0.12 |
| BMI | 23.2 ± 4.8 | 24.0 ± 4.2 | 0.36 |
| Resting HR (bpm) | 75.9 ± 13.1 | 74.0 ± 14.6 | 0.73 |
| Systolic BP (mmHg) | 122.0 ± 13.0 | 120.0 ± 16.0 | 0.70 |
| Diastolic BP (mmHg) | 73.0 ± 11.0 | 76.0 ± 11.0 | 0.37 |
| VO _{2max} (ml/kg/min) | 33.5 ± 5.5 | 36.0 ± 6.8 | 0.25 |

Note: Comparisons were made using independent sample t-test, with significance level set at $p < 0.05$. BMI: Body Mass Index; BP: Systolic and Diastolic Blood Pressure; Ctl-G: Control Group; HIFT-G: Experimental Group; HR: Resting Heart Rate; VO_{2max}: Maximum Oxygen Consumption.

The sample showed that the participants belonged to the different ABEP socioeconomic strata, with no statistically significant differences between them: class A (10.6%), B1 (8.5%), B2 (12.8%), C1 (21.3%), C2 (29.8%) and D/E (17.0%) ($p = 0.65$). Regarding the level of education, 5% of the participants had completed higher education, 77.5% went to high school (complete or incomplete), and 17.5% had completed elementary school ($p = 0.60$). No significant differences were observed in the pattern of substance use ($p = 0.70$), with a predominance of multi-drug users in the total sample (83%), followed by smoking cocaine (crack) (11%), alcohol (6.4%) and snorted cocaine (powder) (4.3%). No isolated case of Substance Use Disorder (SUD) related to cannabis or tobacco use was identified. Regarding the level of anxiety, the participants were classified as: 61.7% with low anxiety, 23.4% normal, 10.6% with moderate and 4.3% with severe anxiety ($p = 0.58$). Regarding the level of depression, 12.8% of the participants had no depression, 38.3% were classified with mild depression, 36.2% with moderate and 12.8% with severe depression; no significant differences were observed between the groups in any assessment ($p = 0.62$).

As for the neuropsychological tests for assessing MF, the Ctl-G did not show significant changes in any of the parameters evaluated, while the HIFT-G group showed significant outcome in all assessments. The data are presented in Table 2.

Table 2

Effects of high-intensity interval functional training on mental flexibility in individuals with substance use disorder at Goiás Reference and Excellence State Center in Chemical Dependency

| TIME | Ctl-G | | | | HIFT-G | | | | HIFT x Ctl-G | |
|-------|--------------|---------------|-----|-------|--------------|---------------|---------|-------|--------------|--------|
| | Pre (N = 18) | Post (N = 18) | p | Δ% | Pre (N = 22) | Post (N = 22) | p | Δ% | Pre | Post |
| | M ± SD | M ± SD | | | M ± SD | M ± SD | | | p | p |
| TMT A | 46.5 ± 11.8 | 39.4 ± 9.9 | 0.7 | -14.5 | 53 ± 35 | 35 ± 19 | 0.0001* | -33.3 | 0.36 | 0.56 |
| TMT B | 141 ± 38 | 134 ± 40 | 0.4 | -5.2 | 135 ± 68 | 102 ± 60 | 0.009* | -24.5 | 0.39 | 0.05** |

Note: *Significant pre-post difference in HIFT-G ($p \leq 0.05$). **Difference between HIFT-G post and Ctl-G post ($p \leq 0.05$). Statistical analyses: TMT A [$F(1.38) = 178.9$; $\eta^2 = 0.825$; $p < 0.0001$], TMT B [$F(1.38) = 221.6$; $\eta^2 = 0.85$; $p < 0.0001$]. Trail Making Test results (TMT A and TMT B) expressed as mean ± standard deviation (time in seconds). Groups: Ctl-G (Control) and HIFT-G (Experimental). p: Statistical significance. Δ%: Percentage change.

For Inhibitory Control, no significant differences were observed for any of the parameters in Ctl-G, while in HIFT-G, the three cards presented significant results for the time and interference parameters. However, for the error variable, no card showed a result below the set significance level; the relevant data are displayed in Table 3.

Regarding working memory assessed by Corsi Blocks, the groups showed significant differences between the Pre and Post time points. The data are shown in Table 4.

Table 3

Inhibitory Control of volunteers with substance use disorder admitted to the Goiás Reference and Excellence State Center in Chemical Dependency, distributed between the groups: Control and Experimental who underwent a high-intensity interval functional training

| Stroop Test Variables | Ctl-G | | | | HIFT-G | | | | HIFT-G x Ctl-G | |
|-----------------------|--------------|---------------|------|-------|--------------|---------------|---------|--------|----------------|---------|
| | Pre (N = 18) | Post (N = 18) | p | Δ% | Pre (N = 22) | Post (N = 22) | p | Δ% | Pre | Post |
| | M ± SD | M ± SD | | | M ± SD | M ± SD | | | p | p |
| Time (S) | | | | | | | | | | |
| Color | 16.6 ± 2.9 | 15.9 ± 3.8 | 0.55 | -0.5 | 17.9 ± 5.1 | 14.6 ± 3.4 | 0.0001* | -18.5 | 0.10 | 0.49 |
| Word | 21.9 ± 4.2 | 20.6 ± 4.8 | 0.13 | -5.9 | 21.0 ± 7.1 | 16.3 ± 3.7 | 0.0001* | -22.1 | 0.56 | 0.002** |
| Color & Word | 34.9 ± 14.3 | 33.2 ± 8.5 | 0.36 | -4.9 | 31.2 ± 11.3 | 23.8 ± 6.0 | 0.001* | -23.7 | 0.33 | 0.01** |
| Error (N) | | | | | | | | | | |
| Color | 0.2 ± 0.5 | 0.1 ± 0.3 | 0.21 | -33.3 | 0.1 ± 0.5 | 0.1 ± 0.3 | 0.57 | -33.3 | 0.81 | 0.78 |
| Word | 0.1 ± 0.2 | 0.1 ± 0.3 | 0.52 | 100.0 | 0.1 ± 0.5 | 0 ± 0 | 0.16 | -100.0 | 0.45 | 0.29 |
| Color & Word | 2.3 ± 3.7 | 1.3 ± 1.5 | 0.18 | -43.2 | 1.8 ± 3.14 | 0.7 ± 1.6 | 0.10 | -60.0 | 0.64 | 0.48 |
| Interference | | | | | | | | | | |
| | 17.3 ± 12.7 | 15.2 ± 5.3 | 0.31 | -12.0 | 12.3 ± 7.9 | 9.0 ± 4.0 | 0.12 | -27.0 | 0.07 | 0.02** |

Note: p: Level of statistical significance; *Significant difference pre-post in HIFT-G ($p \leq 0.05$); **Significant difference between HIFT-G post and Ctl-G post ($p \leq 0.05$). Stroop Test results, representing inhibitory control and selective attention, expressed as mean ± standard deviation. S: Reaction time in seconds; N: Number of errors. Groups: Ctl-G (Control) and HIFT-G (Experimental). Effect sizes for the variables Stroop Color (Time: $F(1.38) = 833.6$; $\eta^2 = 0.96$; $p < 0.0001$; Error: $F(1.38) = 4.01$; $\eta^2 = 0.10$; $p = 0.053$), Stroop Word (Time: $F(1.38) = 687.7$; $\eta^2 = 0.95$; $p < 0.0001$; Error: $F(1.38) = 3.8$; $\eta^2 = 0.09$; $p = 0.06$), Stroop Color and Word (Time: $F(1.38) = 423.3$; $\eta^2 = 0.92$; $p < 0.0001$; Error: $F(1.38) = 17.2$; $\eta^2 = 0.31$; $p < 0.0002$), and Stroop Interference ($F(1.38) = 166.6$; $\eta^2 = 0.81$; $p < 0.0001$).

Table 4

Performance in the Corsi block test in volunteers with substance use disorder in Goiás Reference and Excellence State Center in Chemical Dependence after Intervention with high-intensity interval functional training

| Corsi Blocks | Ctl-G | | | HIFT-G | | | Ctl-G x HIFT-G | |
|--------------|-----------|-----------|-------|-----------|-----------|---------|----------------|----------|
| | Pre | Post | p | Pre | Post | p | Pre | Post |
| | M ± SD | M ± SD | | M ± SD | M ± SD | | p | p |
| Hits | 2.2 ± 0.9 | 2.7 ± 0.9 | 0.03* | 3.1 ± 0.8 | 4.3 ± 0.6 | 0.0001* | 0.17 | 0.0001** |

Note: Results of the Corsi Block Test for assessing visuospatial working memory. Data are presented as mean ± standard deviation for the number of correct answers. p: Statistical significance for pre-post comparisons within groups ($p \leq 0.05$) and between groups in the post-test ($**p \leq 0.05$). Analysis of variance demonstrated a substantial effect size for the interaction between group and time [$F(1.32) = 625.4$; $\eta^2 = 0.95$; $p < 0.0001$]. Ctl-G: Control Group, HIFT-G: Experimental Group, before and after intervention with high-intensity interval functional training.

As to the physical effort performed and perceived in the HIFT-G, a post-PE heart rate of 162 ± 20 BPM was observed, thus reaching 90% of the BPM predicted for age; perception of effort on the Borg scale was 15.6 ± 2.9 points and positive affective response 4.2 ± 1.1 .

Discussion

Substance Use Disorder (SUD) is a global health concern which requires diverse approaches. Although several strategies have been proposed, they often are unsuccessful due to the difficulty many people have in maintaining abstinence and resuming a healthy lifestyle. This study was designed for a sample of individuals affected by SUD who were undergoing treatment at a referral center associated with the public health system in Brazil. When applying a single session of HIFT as an intervention, a clinically relevant benefit was observed in cognitive functions associated with reduced desire and improved decision-making for substance use.

The sample assessed reflected important characteristics of the general population with SUD. The control and the intervention groups shared demographic and socioeconomic characteristics (such as age, income and education) as well as duration of substance abuse, BMI and physiological parameters (HR, BP, VO_{2max}). It is noteworthy that, despite the predominance of cocaine and its derivatives as drugs of choice, a significant portion of the sample revealed the profile of multi-drug users (83%), which characterizes the simultaneous or sequential use of multiple substances. This practice is commonly adopted with the aim of enhancing the desired effects or mitigating adverse effects and withdrawal (Connor et al., 2014; Liu et al., 2019).

Compared to the general population, individuals with SUD often present cognitive impairments in EF; neuropsychological assessments, such as the TMT and the Stroop test can provide valuable information to help guide the treatment (Broyd et al., 2016; Connor et al., 2014; Liu et al., 2019). In our study, the HIFT session played a promising role in activating EF, particularly considering the visuomotor function, sustained attention, mental flexibility, and inhibitory control.

There was an improvement after the intervention, as evidenced in the TMTA and TMTB tests, and the data obtained indicate a component of task learning and mental flexibility, with greater emphasis on cognitive flexibility, especially in the group that underwent the HIFT. Although both groups showed some improvement, the control group presented a smaller delta, without statistical significance, which suggests a slight effect of familiarization with the test. On the other hand, the group submitted to the HIFT had a significantly greater improvement, indicating that the exercise directly impacted the ability to switch between different rules and patterns, reflecting an improvement in mental flexibility. This finding is in line with studies that show the positive effect of physical exercise on the EF, such as the study by Wilke (2020) which, although conducted with older adults, obtained improvements in the processing speed obtained by the TMT in cognitive function after the intervention with HIFT, which may point to a convergent direction between the studies.

Thus, these clinical results support HIFT as a strategy capable of improving mental flexibility, which may be promoted due to the increase in blood flow mediated by physical exercise, which directs greater circulation to the prefrontal cortex, notably in the dorsolateral and ventrolateral cortices, as observed in previous studies (Khandekar et al., 2022; Park & Schott, 2022). However, it is worth noting that association between HIFT and brain activation is not consistent universally and may be influenced by the time of assessment and the context in which the exercise is performed (Chang et al., 2012), as discussed below.

The present study also revealed statistically significant improvements in the Stroop Test performance after the HIFT intervention. This result suggests a potentially beneficial association between exercise and the improvement of the cognitive functions linked to attention and IC. In addition, the physiological explanation associated with the increase in blood flow described above for the TMT also benefits cognitive processing in the Stroop Test by aiming to activate brain areas, which may have contributed to the participants' ability to filter irrelevant responses and focus on the specific task demands (Khandekar et al., 2022; Park & Schott, 2022). Biochemically, the hypothesis of the involvement of growth factors, such as BDNF, in the outcome was set up.

An increase in BDNF concentrations was observed in response to exercises like HIFT, when inhibitory control was assessed (Novkovic et al., 2015; Tsai et al., 2014). Here we add the data that enhance the BDNF's participation obtained by Vaughan and collaborators (Vaughan et al., 2014) who showed significant improvements in EF and increased BDNF concentrations in healthy elderly women undergoing HIFT, compared to a control group.

It is worth noting that, despite fast metabolization of the BDNF molecule, the activation of its signaling pathways impacts the production of intracellular messengers such as CREB (CAMP response element-binding protein), which promotes the expression of genes involved in neuronal survival and growth, as well as synaptic plasticity, effects that last longer than the lifetime of the BDNF molecule itself (Sharma et al., 2023; Xue et al., 2022). Thus, it is feasible to propose that the physiological stimulation induced by HIFT has as one of the biochemical elements the increase in the supply of BDNF, which through short and long-term mechanisms modify the neuronal response of PSUD. The coherence of these results with other previous investigations enhances the relevance of HIFT as a promising means to stimulate brain plasticity and to optimize cognitive aspects (Gilson et al., 2023; Yin et al., 2022).

In addition, the TMT assessment data revealed a significant 38% increase in post-intervention performance. This increase, in line with research data in diverse groups, including older adults and individuals with SUD, highlights the positive influence of HIFT on EF.

Thus, similar to what has previously been described, the improvement in TMT provided by HIFT can also be attributed to fast-acting factors such as increased cerebral blood flow, release of catecholamines and neurotrophins (such as BDNF), as well as stimulation of neuroplasticity, in a more extended outlook. Another factor that ought to be included in the discussion stems from the study by Da Costa et al. (2017) who observed, in individuals with SUD, improvements in cognitive flexibility after three months of running practice, highlighting the relationship between cognition and increased VO_{2max} . The results of studies using near infrared spectrometry and electroencephalogram confirmed greater blood flow, oxygenation and electrical activity of the prefrontal cortex, correlating with improvements in EF in the Stroop Test (D. Cabral et al., 2018; D. A. Cabral et al., 2017).

Despite the extensive documentation in the literature on the benefits of moderate-intensity aerobic PE on EF (Tian et al., 2023), a more ambiguous picture emerges when it comes to high-intensity PE, such as HIFT. This scenario is marked by both positive and negative evidence regarding cognition (Ai et al., 2021; Gilson et al., 2023), including the idea that the maximal anaerobic pathway may induce a state of central fatigue, leading to a potential decline in cognitive ability, outlining a correlation with the "inverted U" model (D. A. Cabral et al., 2017). However, Wilke (Wilke, 2020) compared three groups of healthy adults, namely: HIFT, walking and control group; they showed that HIFT is more effective than walking in improving EF.

In this connection, PE intensity emerges as a controversial topic when considering particularly the potential acute and chronic effects of PE on EF. Most traditional studies have

adopted predefined PE protocols, such as the use of treadmill or cycle ergometer, performing cognitive assessments during or immediately after the exercise (Teixeira et al., 2020). In contrast, Chang et al. (2012) proposed a differentiated temporal approach for the application of cognitive tasks after PE, considering hypofrontality in regions not directly associated with PE, aiming to provide recovery of the areas most directly involved. They observed a subsequent reduction in EF performance during vigorous aerobic PE, highlighting the importance of a recovery interval for brain physiological processes, particularly in the prefrontal cortex (Wang et al., 2016). These findings suggest a theoretical physiological model that emphasizes the need for a time interval between the end of PE and the beginning of cognitive assessment.

It is worth mentioning that most studies with high-intensity stimuli that lasted more than 30 minutes used a treadmill or cycle ergometer, which is an equipment associated with monotony and displeasure, in addition to the difficulty in maintaining the stimulus (Wilke, 2020). However, HIFT exhibits a more positive relationship with EF, attributed to the complexity of the motor tasks involved (D. A. Cabral et al., 2017; Ferreira et al., 2017; Wilke, 2020). Recently, considerable uptake of HIFT has been observed, both for recreational and competition purposes, including in rehabilitation contexts (Ben-Zeev et al., 2020; Feito et al., 2018). HIFT relevance is such that the American College of Sports Medicine points to it as a sports trend that will become more established in the coming years. Nevertheless, the body of knowledge regarding the effects of HIFT is still insufficient, especially with regard to its impacts on cognitive capacity, notably on the EFs.

Some recent studies have highlighted the relevance of HIFT in relation to EF, although there are still nuances to be elucidated (Vaughan et al., 2012; Wilke, 2020). In this connection, our study focuses on the improvement of cognition and EF through HIFT, exploring HIFT's potential physiological mechanisms and addressing methodological considerations and limitations in its use with PSUD.

The complexity of the motor tasks involved in the protocol of the present study may have induced greater cortical activation compared to simpler tasks, as suggested by studies exploring perfusion, cerebral oxygenation and BDNF during PE. Furthermore, the increase in heart rate, related to HIFT perceived effort and intensity, demanded greater attention to the execution of movements. This evidence supports the hypothesis that HIFT may have positive effects potentially superior to other forms of physical activities, such as walking, running or the use of cycle ergometers in PSUD.

Although our study yields contributions, some limitations are worth mentioning. The absence of direct comparison with classic models of treadmill or cycle ergometer EF and the lack of robust conclusions about the modality, intensity and recovery time for optimizing EF in PSUD require further investigation. The selected sample has also its limitations, as well as the frequency and intervals of data collection. The need for replication of the study considering intervening variables and the influence of the treatment offered to the participants deserves attention. However, despite these limitations, the improvement in EF observed after an acute HIFT session suggests a promising potential to promote brain plasticity and optimize cognitive aspects, which should be verified in further studies.

Finally, the positive perceptions of participants regarding HIFT, expressed by terms such as "Clears the Mind" and "Makes Walking Easier", enhances accessibility, motivation and affective aspects of this approach. Although there is a long way to go to comprehensively understand the underlying mechanisms and the methodological considerations, the results of this study add to the scientific literature the perspective that HIFT can be an effective tool to optimize the EF of individuals with SUD, providing potential benefits to their cognition and quality of life.

Conclusion

The improvement in executive functions observed after a HIFT session suggests a promising potential to promote brain plasticity and optimize cognitive aspects. Although this study has limitations, it paves the way for future investigations that can further explore these effects and elucidate the mechanisms underlying these cognitive changes. Finally, the positive perceptions of participants regarding HIFT, expressed by terms such as 'Clears the Mind' and 'Makes Walking Easier', enhance accessibility, motivation and affective aspects of this approach. Although there is a long way for the comprehensive understanding of the underlying mechanisms and the methodological considerations, the results of this study add to the scientific literature the perspective that HIFT can be an effective tool to optimize the EF of individuals with SUD, providing potential benefits to their cognition and quality of life.

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