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THE RELATIONSHIP BETWEEN THE USE OF PSYCHOACTIVE DRUGS AND COGNITIVE FUNCTIONS MODULATED BY THE PREFRONTAL CORTEX OF YOUNG UNIVERSITY STUDENTS

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ABSTRACT

The prefrontal cortex is an associative brain area that is fundamental for cognitive functions such as decision-making, planning, selective attention, and working memory. During adolescence, the prefrontal cortex undergoes significant changes, which are influenced by the use of psychoactive drugs. This study related the use of psychoactive drugs to variations in inhibitory control, selective attention, planning and decision-making in 50 young university students, through the categorization of groups based on the consumption of psychoactive substances and the application of the Stroop Color and Word Test, Iowa Gambling Task and Mini Mental State Examination. The group without significant consumption of psychoactive substances had better performance in inhibitory control and selective attention compared to the group with consumption.

Keywords: Attention. Inhibitory Control. Cognitive Neuroscience. Neuropsychological Tests. Decision Making.

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INTRODUCTION

The present project addresses the neurobiology of cortical development, with emphasis on cognitive functions related to the human prefrontal cortex – such as decision-making or planning, selective attention and working memory – and the relationship of the behavior of these elements to different levels of exposure to psychoactive drugs.

The human brain, in general, is considered a major protagonist of the central nervous system, corresponding to 80% of the total brain mass (Azevedo et al., 2009). It is divided into white matter and gray matter, the latter being the region where the nerve cells that form the cerebral cortex are located. The cortex is a thin layer composed of cell bodies and dendrites of neurons, subdivided into several areas responsible for functions such as language, perception, decision-making, and motor planning (Cadwell et al., 2019).

The ability of the prefrontal cortex to simultaneously maintain several fragments of information, presented subsequently, in order to be able to retrieve this information when necessary, is what can explain brain functions such as the elaboration of thought and the performance of intellectual functions associated with this region (Guyton, 2017). Thus, the cerebral cortex is primarily associated with the ability to plan complex cognitive behavior, combining thoughts and actions to achieve a goal. This attributes the psychological term "executive function" to the activities performed in this cortex. In addition to decision-making and working memory, it includes personality expression, moderation of social behavior, logic, and rationality (Rodrigues, 2022).

With regard to the neurobiology of brain development, it is during adolescence that significant changes and modifications occur in the cerebral cortex. The maturation process of the cerebral cortex is a neurophysiological phenomenon that extends from child development to 20 to 22 years of age (Andrade et. al, 2018).

In this way, the adolescence period becomes crucial, as it is when emotional and neuropsychological development and brain maturation occur (Cunha, 2019). It is precisely in this phase that the individual presents mood swings due to changes in affective modulation and impulsivity control, resulting from neuronal changes, especially those inherent to the prefrontal cortex. These changes in behavior, emotions, and thoughts are characteristic of adolescents (Greydanus & Patel, 2005; Paus, 2005). The need for discovery, combined with the lack of awareness of the real consequences of their actions, means that adolescents, at this stage, tend to develop behaviors that place them in vulnerable positions, such as risky activities and abuse of licit drugs, such as alcohol and

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tobacco, or illicit drugs, such as marijuana, cocaine, ecstasy, LSD, among others (Cunha, 2019).

In this sense, when the use of psychoactive drugs and the maturation of the prefrontal cortex is related, it is also identified that both influence each other in a mutual way, so that the delay in the maturation of the cerebral cortex, which matures on average after the age of 20, reflects on the capacity of critical judgment of an adolescent and makes him more vulnerable to drug consumption. Similarly, the toxic effects of drugs can affect the maturation of the prefrontal cortex and impair the development of enhanced abilities in this area of the brain (Biajoni & Uehara, 2021). The aim of this study was to relate the use of psychoactive drugs to variations in cognitive patterns modulated by the prefrontal cortex in young university students.

METHOD

This is a quantitative, descriptive research, with a cross-sectional design, involving the collection of primary data, through the application of cognitive tests. This study was developed at the Magalhães Barata School of Nursing (CCBS - Campus IV), located at Av. José Bonifácio, 1289 – Guamá – 66065-362- Belém-PA, and at the Center for Biological and Health Sciences (CCBS - Campus II), at Tv. Perebebuí, 2623 – Marco – 66087-662, Belém - PA, of the State University of Pará (UEPA).

This study was in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of the Marco School Health Center, of the State University of Pará (Certificate of Presentation of Ethical Appreciation No. 72716123.5.0000.8767). The processes of collecting, evaluating, and analyzing data from the participants were carried out from March 2024 to October 2024.

PARTICIPANTS

This study was carried out with 50 university students regularly enrolled at the University of the State of Pará; who were aged between 18-25 years; of both sexes. Individuals with physical (mobility and strength in the upper limbs) or cognitive restrictions were excluded; participants with clinical diagnoses that could compromise their cognitive functions (such as autism, depression, ADHD, etc.); those who used any psychoactive drug less than 48 hours before data collection; students who were interested, but did not attend the data collection; those who used psychotropic medications to treat chronic diseases;

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those who did not perform all the proposed cognitive tests and participants who already had prior knowledge about the Iowa Gambling Task, as this could influence their performance in a way unrelated to the prefrontal cortex.

Participation in the study followed the following flow: initially, a general approach was made in university classes for presentation and invitation to those interested in participating. Then, the interested parties were scheduled to perform the study procedures, which took place individually and in a reserved place.

Participants were divided into 2 groups: Group 1 - Significant Consumption (CS) and Group 2 - Non-Significant Consumption (CNS).

To divide the participants into these groups, the aspects related to their profile of consumption of psychoactive substances were considered, and for the composition of Group 1 - CS, those who, regarding the form of use and the relationship established with the drug and its possible consequences, pointed out the following behaviors alone or in combination: harmful use, binge, tolerance and controlled use; and/or who, regarding the frequency of consumption, classified it alone or in combination as frequent use and recent use or in the month; in addition to those that indicated the presentation of symptoms related to their consumption pattern, such as: strong desire or compulsion to consume drugs; lack of progressive interest in other pleasures and interests in favor of drug use; insistence on the use of the substance, despite harmful manifestations proven to result from this use; difficulties in controlling use, whether in terms of start, end or level of consumption; physiological state of abstinence; Evidence of tolerance, when the individual requires higher doses of substance to achieve the effects previously obtained with lower doses.

On the other hand, to categorize the participants for the composition of Group 2 - CNS, those who, in terms of the form of use and the relationship established with the drug and its possible consequences, pointed out the following behaviors in isolation or in combination: experimental use, occasional use, or that did not apply; and/or who, regarding the frequency of consumption, classified it in isolation or combination as use in the year, use in life, or that it did not apply; in addition to those who did not indicate the presentation of symptoms related to their consumption pattern.

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INSTRUMENTS

The cognitive tests used in this study were: *Stroop Color and Word Test* (SCWT), *Iowa Gambling Task* (IGT) and Mini Mental State Examination (MMSE) (Bechara et al., 1994; Scarpina and Tagini, 2017; Costa, et al., 2021).

The SCWT, developed by John Ridley Stroop in 1935, assesses inhibitory control and attention processes (Brandelero & Tonil, 2017). This test is based on the evidence that it takes longer to name colors than to read color names; just as it takes longer to name the printing color and/or read color names, when they are printed in an ink color different from the color they name. This phenomenon is related to the ability to inhibit cognitive interference, which occurs when the processing of one characteristic of the stimulus affects the simultaneous processing of another characteristic of the same stimulus, a phenomenon known as the Stroop Effect (Duncan, 2006).

In the most common version of the SCWT, originally proposed by Stroop in 1935, participants must read three (3) different tables as quickly as possible, the first two representing congruent conditions, in which participants must read color names (words) printed in black ink (W), and then name different color patches (C). The third table, called the word color condition (WC), represents an incongruent condition, where words of colors printed in an inconsistent color ink (for example, the word "red" printed in green ink) will be arranged), and it is up to the participant to describe the color of the word, and not the word itself (Scarpina & Tagini, 2017).

The IGT is a cognitive test developed by Bechara et al. (1994) that studies the process of planning and decision-making through a card game. The participant has 100 possibilities to choose from and must select a card from four decks (A, B, C and D) arranged in front of him. With each attempt, he can win or lose play money depending on the card chosen. The test was created to assess problems in patients with impairments in the ventromedial prefrontal cortex, a region of the brain involved in processing risk, fear, emotion and decision-making.

The MMSE is an instrument developed to provide a rapid, standardised and practical assessment in the clinical context. Recommended by the Ministry of Health and validated in Brazil, the MMSE works as a screening tool, assessing aspects such as orientation, immediate and recall memory, planning, language, concentration, and spatial skills. The maximum score is 30 points, adjusted according to the participant's education level (Costa et al., 2021).

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PROCEDURES

The analyses of the cognitive tests were performed according to the peculiarities of each test, as follows: IGT according to the frequency with which people decide on "high risk" (A/B) or "low risk" (C/D) decks; the SCWT according to the number of correct answers in each stage of the test – within the fixed time of 45 seconds for each phase – as well as by obtaining an individual interference score for each participant; the MMSE, according to the procedures established for the test, which include filling out a form according to the participants' response to the commands made by the evaluators/members of the research team.

The SCWT was initially evaluated according to the scoring method proposed by Golden (1978), in which the number of correctly named items is calculated in 45 seconds in each condition (W, C and WC), and the predicted WC score (Pcw) is calculated using the following formula: Pcw = (W x C) / (W + C). Afterwards, the Pcw value is subtracted from the actual number of correctly named items in the third step (IG = CW − Pcw), in order to obtain an interference score based on the participant's performance in the congruent steps (W and C). Thus, the positive score represents a favorable result that the individual was able to adequately inhibit the automatic response, and the negative score presumes that he or she did not inhibit the incongruent stimulus as expected.

For the analysis of the IGT, the global calculation was taken into account, which consists of subtracting the number of cards drawn from the disadvantageous decks from the number of cards drawn from the advantageous decks: [(C+D)-(A+B)], an interpretation widely used in the literature. From it, the participant obtains a score that, according to a binomial distribution adopted by Denburg et al. (2006), classifies him as: impaired (if score below -18), borderline (if score between -18 and +18) and adapted (if score above +18).

The tabulation of the collected data was carried out from the Google Forms survey management application, which is capable of creating forms, through spreadsheets in Google Drive, enabling the control and security of survey data, in parallel with the provision of quantitative results in a more practical and organized way.

For statistical analysis, the Student's t-test was used, considering 5% ($p<0.05$) as the significance level.

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RESULTS

Taking into account the objective of this study, which was to relate the use of psychoactive drugs to variations in cognitive patterns modulated by the prefrontal cortex in young university students, a comparison was established between two groups: young university students with significant consumption of psychoactive substances and young university students without this consumption.

The total number of participants in this study comprised 50 individuals, of whom 24 (48%) were categorized in Group 1, corresponding to individuals who have a significant pattern of psychoactive substance consumption, while 26 (52%) were categorized in Group 2, referring to individuals who do not have a significant consumption profile, according to the established parameters.

Regarding the composition of participants in Group 1 - Significant Consumption (SC), of the 24 participants that make up this group, 10 (41.67%) were classified based on their form of use, 21 (87.5%) based on their frequency of use, and 10 (41.7%) on the presentation of symptoms related to their pattern of consumption of psychoactive substances (see Table I).

Table 1 - Consumption Profile of Group 1 - Significant Consumption (CS).

	N	%
How to use		
Controlled use	8	41,67
Harmful use; tolerance	1	
Binge use	2	
	10	
Frequency		
Recent or monthly usage	14	87,5
Frequent use	7	
	21	
Signs and symptoms		
Strong desire or compulsion to consume drugs	2	41,7
Lack of progressive interest in other pleasures	2	
Insistence on the use of the substance	4	
Difficulties in controlling use	3	
Physiological state of withdrawal	1	
Evidence of tolerance	3	
	10	
Total	24	100

Source: The author

Regarding the composition of participants in Group 2 - Non-Significant Consumption (SNC), of the 26 participants that make up this group, 22 (84.62%) were classified based

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on their form of use and 21 (80.77%) based on their frequency of consumption of psychoactive substances (see Table II).

Table 2 - Consumption Profile of Group 2 - Non-Significant Consumption (CNS)

	N	%
How to use		
Experimental use	9	84,62
Occasional use	5	
Not applicable	8	
	22	
Frequency		
Year Usage	7	80,77
Use in life	5	
Not applicable	9	
	21	
	26	100

Source: The author

The results of the cognitive tests applied are described below, providing detailed information on the abilities assessed and the performance of the participants in each of the tests.

STROOP COLOR AND WORD TEST (SCWT)

Regarding the results obtained by the participants in the SCWT, we sought to evaluate parameters associated with inhibitory control, which is related to the capacity for selective attention and the performance of the prefrontal cortex.

Variations in the performance of the groups analyzed were identified, considering the results obtained from the individual Interference Score (GA) of each participant. Group 1 had a GA variation between -6.5 and 19.53, while group 2 had a GA variation between 0.11 and 29.32. These parameters indicate differences in performance between the groups, with group 2 showing greater variability in inhibitory control in positive performance values in the test, compared to group 1, which may reflect a difference in the capacity for selective attention among the participants. Figure 1 illustrates the variation in GI among the groups analyzed.

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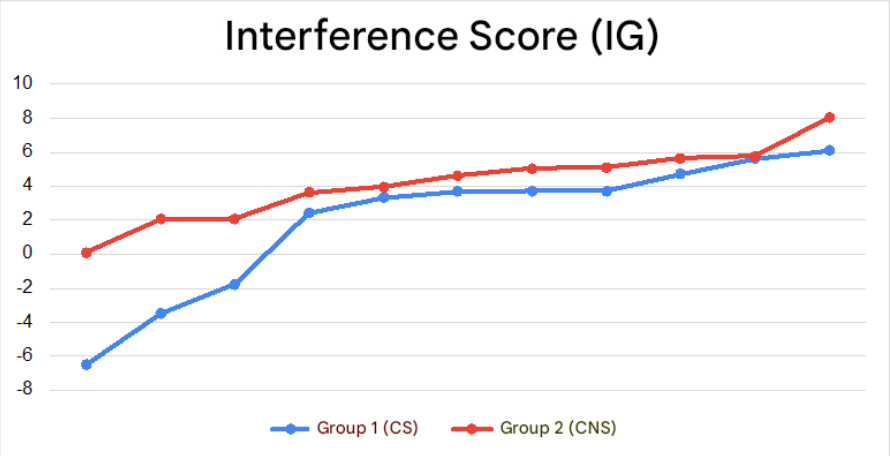
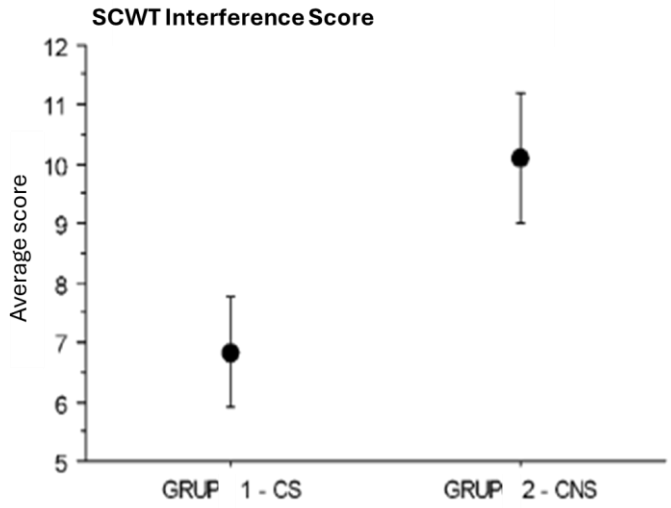
Figure 1 - Interference Score (GA)



Source: The author

There were significant differences between the means of the groups in the SCWT tasks. The results showed that group 1 - CS obtained a lower mean score than group 2 - CNS, with a significant difference (p=0.0301), indicating a better performance in selective care and inhibitory control in the group without significant drug use (see Figure 2).

Figure 2 - Performance Graph - SCWT



Source: The author

IOWA GAMBLING TASK (IGT)

Observing the results obtained by the participants in the IGT, we sought to evaluate parameters related to decision-making and planning capacity, domains also associated with the performance of the prefrontal cortex. However, no significant differences were found between the means of the groups in the IGT tasks. The mean difference was -0.256

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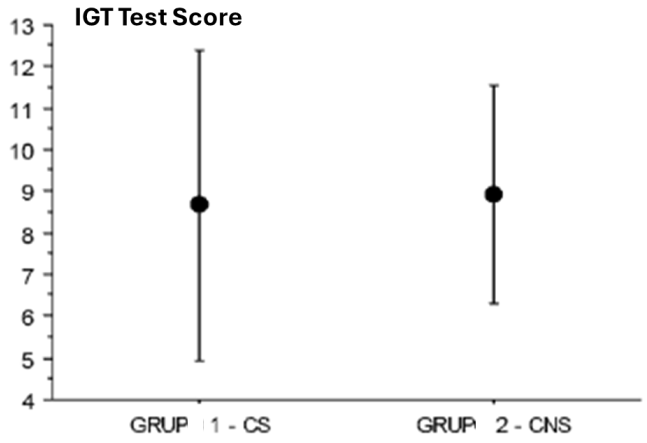
(p = 0.9549), indicating that the probability of this difference being due to chance is very high, which suggests that there is insufficient evidence to conclude that the groups differ in their performance (see Figure 3).

Figure 3 - Performance Graph - IGT

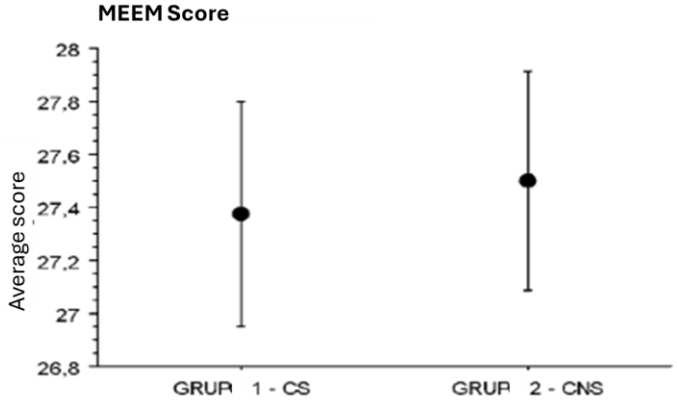


Source: The author

MINI MENTAL STATE EXAMINATION (MMSE)

Regarding the results achieved by the participants in the MMSE, we sought to analyze the parameter of the test related to the assessment of memory, cognitive function also associated with the prefrontal cortex. However, no significant differences were found between the means of the groups. The mean difference was -0.125 (p = 0.8337), indicating that the observed difference is not statistically significant (see Figure 4).

Figure 4 - Performance Graph - MMSE



Source: The author

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DISCUSSION

The present study showed a significant difference in the performance of the participants in relation to selective attention and inhibitory control, highlighting the relationship between the use of psychoactive drugs and cognitive functions modulated by the prefrontal cortex in young university students. On the other hand, in the evaluation of decision-making, using the IGT, and in the analysis of general cognitive functions, with emphasis on working memory, using the MMSE, no significant variations were observed between the groups.

In this sense, the superior performance in inhibitory control of the group that does not consume psychoactive substances in a significant way, compared to the group that does, reinforces the hypothesis that the expressive use of these substances influences the development of the prefrontal cortex and, consequently, the unfavorable expression of this cognitive function.

This difference could also be observed in the study by Barreto, Acosta and Arias (2018), which compared executive functions and family history of alcoholism in adolescents with and without a personal history of alcohol abuse, where skills such as working memory, verbal fluency, cognitive flexibility and decision-making were evaluated, with the lowest performance associated with the group adjacent to substance use, especially among adolescents with a personal and family history of alcohol abuse.

In addition, lower performance in inhibitory control was associated with predisposition to alcohol use, as well as impaired inhibitory control and cognitive flexibility were also related to cigarette use by adolescents (Assis, Junho & Campos, 2019).

On the other hand, another study investigated whether the consumption of psychoactive substances negatively impacts cognitive and executive functioning, comparing the levels of Montreal Cognitive Assessment (MoCA) and the Frontal Assessment Battery (FAB) with cognitive performance in the Stroop Test. Thus, Miranda (2019) evidenced differences in Stroop results between the clinical and normative groups, with higher levels of MoCA and FAB in the group that obtained above-average results in Stroop. These results indicated that, although significant differences were observed between the groups in the FAB, suggesting a greater impairment of executive functions in the clinical group, this same difference was not observed in the inhibitory control.

Regarding the cognitive domain related to decision-making, although the present study did not identify significant differences in performance between the different groups

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evaluated, this may indicate that additional factors may influence decision-making skills. However, as identified by Assis, Junho & Campos (2019), the predisposition to alcohol use was associated with negative performances in the decision-making process in adolescents, assessed by the IGT; On the other hand, decision-making performance did not show a significant predictive association with cigarette use.

Although heavy alcohol consumption among young people is associated with an increase in maladaptive decisions, a study by Michelini, Acuña & Godoy (2016) evaluated decision-making in young moderate and excessive alcohol users and found no significant differences in IGT performance, pointing to a possible lack of sensitivity of the test to detect deficits in decision-making. depending on the type of alcohol consumption.

With regard to selective attention, another cognitive function related to the prefrontal cortex, the absence of significant differences between the groups in the MMSE may be associated with the low specificity of the test for the analysis of this domain in young people. This is especially relevant considering the high applicability of the MMSE in studies that assess psychometric functions in older people. The usability of the MMSE in this study consisted of an experimental strategy to potentially detect differences between the groups analyzed, using as reference the parameters guided by Brucki (2003), who establishes 29 points as a cut-off score for individuals with more than eleven years of schooling.

Other studies involving the MMSE with a focus on the young population have not focused specifically on young university students, but have included, for example, patients who use drugs in treatment. Carvalho, Oliveira & Pinto (2021) evidenced evidence of cognitive deterioration among these users, with only 13.24% of the patients presenting adequate results in the MMSE, with memory standing out as the cognitive function with the worst performance.

It is noteworthy that the phase of youth is marked by a significant neuroplasticity of the prefrontal circuits, which are fundamental for the improvement of skills such as abstract reasoning, concentration and learning. This region of the brain is responsible for controlling impulses and anticipating the consequences of our actions during decision-making. This phenomenon contributes to cognitive immaturity, the desire for new experiences, and the impulsivity typical of adolescence, factors that can increase the predisposition to alcohol consumption (Kindler et al., 2015).

Similarly, while the extended time for maturation of the prefrontal cortex compromises the inhibitory control of young people and makes them more vulnerable to

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drug use, the toxic effects of drug use affect the development of the prefrontal cortex and, consequently, the improvement of skills that correspond to this area of the brain (Biajoni; Uehara, 2021).

Therefore, the immaturity of inhibitory control may be a reflection of the delay in the maturation of the prefrontal cortex, a process influenced by several factors, such as the toxic effects of psychoactive substances, which can be potentiated by the family situation, by permissive relationships in relation to the use of substances and by the association with peers who use drugs (Biajoni & Uehara, 2021).

Considering adolescence as a critical period for the development of the prefrontal cortex and as the time of greatest vulnerability to the consumption of licit and illicit substances, it is important to highlight that the long-term effects of these substances may be associated with different cognitive expressions and performances. The neural development that occurs in this phase can be considered a crucial window both for the improvement of cognitive skills and for the emergence of vulnerabilities. These vulnerabilities may be associated with behavioral patterns typical of this phase of human development, such as cognitive impulsivity, emotional lability, and danger seeking (Ernst, 2014).

The balance of the neurobiological development cascade is the factor that gives the brain its neoplastic characteristics, which will define the individual's cognitive behavior patterns, as sensitive windows change, contract or expand during the different points of neurophysiological development (Lee et al., 2014).

Thus, the relevance of neuropsychological assessment studies is highlighted, especially those that identify deficits related to chemical dependencies. There is a consensus among these studies about the impairment of executive functions, linked to the prefrontal cortex, caused by the consumption of psychoactive substances, regardless of their nature. These deficits result in significant impairments, such as executive dysfunction and decision-making problems, which correspond to the main cognitive and emotional problems associated with drug addicts (Verdejo-Garcia et al., 2006).

CONCLUSION

The results of this study indicate that significant consumption of psychoactive substances among university students is associated with changes in inhibitory control, as evidenced by lower performance in the Stroop Color and Word Test in Group 1 (Significant

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Consumption). On the other hand, no statistically significant differences were observed between the groups in the assessments of decision-making and planning (Iowa Gambling Task) and memory (Mini Mental State Examination). These findings suggest that the intense use of psychoactive substances can selectively impact cognitive functions related to inhibitory control, without affecting other cognitive areas evaluated. It is important to consider that the university environment, with its demands and pressures, can influence the behavior of students in relation to the use of psychoactive substances.

The development of basic research involving animal models and biomolecular analyses is necessary to affirm a cause-and-consequence relationship between drug use and the cognitive impacts found in this work. In addition, prevention and intervention strategies should be directed to mitigate the risks associated with the consumption of these substances and preserve the cognitive health of university students.

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CONTRIBUTION

Daniel Pinto dos Santos contributed to the conception and development of the research project, in processes of data collection, evaluation and analysis and was responsible for writing the article. Naomi Aimèe dos Reis Melo contributed to the conception and development of the research project, participated in the data collection, evaluation and analysis processes, and wrote the article. Vanessa Novaes Barros contributed to the design and development of the research project as an advisor, was present in the processes of data collection, evaluation and analysis; made the final corrections to the project, submitted the project for approval to the Ethics Committee, sought funding for the project, and submitted the work to the journal.

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