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Exploring the use of cognitive enhancement substances among Portuguese university students

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ABSTRACT

Background: Prescription drug use and the consumption of substances to enhance college students' cognitive performance, described as pharmacological cognitive enhancement (PCE), is a known phenomenon potentially impacting individuals' health. University and college students are two specific subpopulations noted to use PCE (up to 17%, on average). To our knowledge, no data have been published on the use of PCE drugs among university students at a national level in Portugal and the factors that might be associated with this usage.

Objective: The main objective was to estimate the prevalence of PCE use by Portuguese university students and to identify the PCE substances commonly used by university students, i.e., those classified as prescription drugs and other legal and nonprescribed substances, including food supplements.

Methods: The study followed a cross-sectional exploratory, descriptive design and pursued a convenience sample of students from Portuguese public and private universities (22 higher education institutions).

Results: From a sample of 745 university students, 32% indicated the use of prescribed and nonprescribed substances. The most consumed substances were food supplements with CNS stimulants being the most frequent prescription-only drugs but not necessarily accessed through a medical prescription. A significant statistical association was found between substance consumption and the field of study. Health science students reported more food supplements and drug intake, allegedly under prescribed regimens, compared to humanities and exact sciences students. The study discusses the need to better understand the competitive societies that produce and support young students' outputs and the perceived 'need' for performance-enhancing substances.

Conclusions: One-third of the university students aimed to improve their performance by pharmacological cognitive enhancement, with a preference for food supplements dispensed in pharmacies. PCE substance consumption in higher education is thus non-negligible. The study suggests the need to improve regulations on potential inequalities in academic rankings and success and an observant attitude concerning implications that negatively affect health in the long run.

1. Background

Human pharmaceutical enhancement has received significant attention from researchers and scholars in recent decades, comprising the improvement of cognitive, mood, and physical activities. Examples of perceived pharmaceutical enhancement include using cognitive-enhancing drugs for recreational and academic purposes, such as improving memory and concentration, gaining a competitive edge over others (though this is debated in the literature),[1] becoming a better version of oneself, enhancing personal achievement, improving well-being, and sensation seeking. The reasons for such aims are rooted in family perceptions and family and faculty endorsement, perceived prevalence of use among friends, financial stress, improvement in self-efficacy, and promotion of personal and public safety.[2–7] In the media, pharmaceuticals used for enhancement purposes have been described with favorable terms, such as 'cognitive enhancers,' 'neuroenhancers,' 'smart pills,' 'smart drugs,' and 'study drugs',[8] which are words that might give the user reasons to believe that he or she will be smarter when using these drugs.

Pharmacological cognitive enhancement (PCE) is defined as the use of any psychoactive substance by normal, healthy individuals with the primary aim of augmenting mental and cognitive brain functions, such as attention, concentration, or memory.[9,10] These substances are also known as nootropics and comprise the intake of over-the-counter drugs (e.g., caffeine-based medicines and *Ginkgo biloba*), as well as the off-label use of prescription drugs (also entitled nonmedical prescription drug use (NMPDU)) approved for the treatment of cognitive disabilities. These

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prescription drugs include psychostimulants to treat attention-deficit and hyperactivity disorder (ADHD) (e.g., methylphenidate or amphetamines), drugs used for sleep disorders (e.g., modafinil), and drugs used to treat Alzheimer's disease (e.g., acetylcholinesterase inhibitors). Illicit stimulants, such as some amphetamines (e.g., "speed," "ecstasy," and "crystal meth"), have also been used for this purpose.[10]

1.1. Cognitive enhancement in higher education

The use of PCE substances among adolescents and young adults is commonly known.[11] Nonmedical prescription drug usage is the second most common form of illicit drug use among precollege students, only behind recent nicotine vaping and marijuana use.[12] Studies have reported prevalence rates from 1 to 20%.[10,13] Although nonmedical use of PCE substances may affect a larger population,[5,14] university and college students are two specific subpopulations especially noted to use PCE substances (up to 17%, on average).[11,15] DeSantis et al. (2009) reported that out of 333 fraternity members at a public southeastern US research university, 55% reported using ADHD stimulants for nonmedical purposes (DeSantis et al., 2009).[16] In another US-based study, Bavarian et al. (2014) described how almost 11% of college students, in their multicampus sample, had used stimulants in the past year.[17] Additionally, studies from Australia and New Zealand[18,19] and European countries (e.g., Germany, Iceland, Denmark, and Switzerland) have focused on university students' use of PCE substances.[20,21] In the UK, a newspaper's informal survey revealed that 16% of 662 students had used modafinil and other 'study drugs' or 'smart drugs' without a prescription.[22] Dietz et al. (2013), who studied 2569 students from Germany, estimated the 12-month prevalence of cognitive-enhancing drug use to be 20%. In this study, prevalence varied by sex (male 23.7%, female 17.0%), field of study (highest in sports-related studies, 25.4%), and semester (first semester 24.3%, beyond the first semester 16.7%).[23]

Again, some of the reasons for PCE substance use in the higher education population have been to enhance cognitive performance, lose weight, counteract the effects of other drugs, match the perception of peer use, and get high.[24–26] PCE in higher education is frequently associated with other high-risk behaviors, such as alcohol intake, drug abuse, and illicit drug consumption.[21,27–32] In addition, the use of PCE substances is associated with a wide range of adverse effects, particularly with CNS stimulants.[33] For example, the two most commonly used substances, methylphenidate and modafinil, are associated with drug dependence, overdose, and suicide attempts[34] and with psychiatric disorders, cardiovascular symptoms, and severe skin and multiorgan hypersensitivity reactions, respectively; moreover, 49% of adverse events were related to off-label use of these substances.[35] Among healthy medical students, there are reports of methylphenidate usage (16% on average), with most individuals initiating its use after university admission.[36] In Portugal, a recent study (2021) found a low off-label consumption of PCE substances among medical undergraduates (5%), although higher among licensing exam applicants (14%), with nootropics mainly being consumed rather than CNS stimulants (e.g., caffeine and food supplements).[37]

Portugal is a country with successful policies on controlling the use of illicit psychoactive substances acquired through unauthorized channels.[38,39] Since 2001, the acquisition, possession, and consumption of such substances for 'individual' usage has not been a crime. Controlled substances and medications are accessible through community pharmacies as prescription-only or pharmacist-only medicines. Community pharmacies dispense other cognitive stimulating products (e.g., food supplements), which are also available at supermarkets and high street health-related outlets. Regarding the Portuguese higher education system, it is part of the European higher education area and observes the Bologna process, with shared principles and practices, such as a first three-year graduation cycle followed by two years for masters degrees.[40]

In Portugal, the phenomenon of PCE substance use among higher education students has also been described. One of the few systematic studies on the topic, undertaken in Portugal, reported a prevalence of 5.1% PCE substance use among students from the University of Lisbon (UL).[41] UL is located in Portugal's capital city, with implicit pressure for academic success and greater competition regarding job positions and access to the labor market. According to Silva et al. (2012), UL students reported how bad mood and emotional state, especially anxiety and stress related to academic performance demands and, to a lesser extent, feelings of sadness and depression correlated with loneliness, were associated with PCE substance use.[41]

1.2. Study objectives

In most Western countries, mapping and researching young people's prescription drugs for enhancement purposes is a societal concern.[42] According to previous studies,[43] initiating PCE seems more frequent among college students than among equivalent-aged populations. Research has shown that PCE substance use in this population is prevalent and increasing.[8] The emergence of PCE substance use in universities was confirmed by a recent review that found differences in countries according to legal, social, and ethical factors.[44] Moreover, differences between professions' acceptability of PCE have also been found, potentially influencing higher education students as future professionals.[45] At the same time, the European Union is concerned about performance-enhancing drugs in the workplace from occupational safety and health perspectives.[46]

To our knowledge, no data have been published, however, on the use of PCE drugs among university students at a national level in Portugal and the factors that might be associated with this usage. Therefore, this study's primary purpose was to estimate the prevalence of PCE substance use by Portuguese university students and identify the PCE substances commonly used by Portuguese university students, i.e., those classified as prescription drugs and other legal and nonprescribed substances, including food supplements. The secondary objectives comprised investigating the type of substances mostly used, reasons for usage, acquisition channels, and main perceived side effects, as proxies for the pharmacist's intervention.

2. Methods

The study followed a cross-sectional exploratory, descriptive design and pursued a convenience sample of students from Portuguese public and private universities. The study's primary research question addressed the general profile of PCE substance use among higher education students in Portugal, including the main study fields, type of PCE substances used, and reasons for their use.

2.1. Survey instrument

The online survey was developed as a closed and anonymous questionnaire written in Portuguese, based on a survey from the Brazilian Secretariat for Drug Policies (SENAD)[47] and on a study by Kaloyanides et al. (2007).[48] These previous studies aimed to examine the consumption of prescription-based stimulants, alcohol, and other drugs among college students from Brazil and the United States. The present study aimed to investigate the medical and nonmedical use of legal substances, including drugs that are not marketed in Portugal but are legal in other countries, such as methamphetamine or dextroamphetamine. The list of potential PCE substances was divided into four main groups:

a) CNS stimulants (e.g., methylphenidate, modafinil, and amphetamine);
b) N-Methyl-D-Aspartate (NMDA) receptor antagonists (memantine);
c) A heterogeneous group of nootropics marketed as legal medicines available from pharmacies (e.g., *G. biloba*, citicoline, piracetam, synthetic derivatives of amino acids, idebenone, deanol, and vinburnine);
d) Usual food supplements available from pharmacies and other outlets (i.e., outside the drug-regulated market, e.g., caffeine, vitamins, and proteins).

All substances shared the common feature of being administered through a pharmaceutical dosage form, with stimulants taken as food (e.g., coffee and tea) not being considered. Knowing that the products listed in d) are similar to natural or 'endogenous' substances, the analysis of findings primed 'exogenous' PCE substances with a higher harmful potential.

The questionnaire comprised three sections. Part A included seven questions concerning sociodemographic data. Part B incorporated an initial screening question, separating university students who self-reported using a substance recognized as a PCE substance from those with no experience, including usage in the highly demanding last secondary school or exam year. The former students were invited to select which substances they might have used before entering or during their higher education from the previous substance list. Respondents were also asked to provide details on the substance mainly used, including the date of first utilization, the general intended purpose, how it was used, the possible side effects and interactions, and the means of accessing the reported substance. The product items described in the questionnaire included brand and generic drug names and applicable jargon to increase the response rate (e.g., "crystals" for methamphetamine). In Part C, respondents were asked about their motivation to start PCE or experiment with other PCE substances and recommend these substances.

Before survey dissemination, a pilot study with ten pharmacy students was conducted to assess questionnaire readability, web design, and completion time. Minor changes were made following the pilot feedback, particularly those related to wording and item sequences. No further validation steps were undertaken, assuming the exploratory nature of the study.

2.2. Population, sampling, and participation

All higher education students in Portugal were eligible to participate in the study if they were less than 35 years old, assumed to be the threshold for completing a higher education degree according to the Europe 2020 Strategy (https://ec.europa.eu/eu2020/pdf). The higher education student inclusion criterion encompassed all students enrolled in an undergraduate or postgraduate program from a public or private university in Portugal, independent of holding national or foreign citizenship. Although no statistical representativeness was expected, a total of 384 participants was estimated as the initial expected number of respondents, using a 95% confidence interval and an error margin of 5% (https://www.qualtrics.com/blog/calculating-sample-size/),[49] from a total population of 361,943 individuals considering all 116 higher education institutions (HEIs) in the country (2017 data from PORDATA database, https://www.pordata.pt/).

After contacting all students' unions via e-mail, cooperation was obtained from all public sector HEIs (14) and eight private HEIs (primarily located in the Lisbon region). In Portugal, students' unions are undergraduate associations established by a university, school, or course, representing all students enrolled (and alumni) within the HEI. Usually, unions have comprehensive e-mail lists of all registered students in each HEI, managed by a local contact responsible for sending the invitation with the survey link. Not all contact persons replied after requesting the total number of registered students at each HEI, making it impossible to estimate a response rate later. Tailored e-messages with the survey website link, both in Portuguese and English, explaining and inviting the students to participate in the study, were sent to the contact persons for dissemination using Mailchimp (https://mailchimp.com/) software. Random contacts were made with known students to verify if the e-mail was received. The questionnaire link was active for two months, starting in October 2017. The survey was administered using a dedicated e-platform (https://www.typeform.com/). Responding students voluntarily completed an anonymous web survey. Data were held in a secured and restricted access folder. The National Commission for Data Protection (Ref. 27.959.645, from 15 October 2017) approved the study protocol.

2.3. Data analysis

Statistical analysis was carried out using the IBM Statistical Package for the Social Sciences (SPSS), version 25. Descriptive statistics were reported, comprising frequencies (in percentages), means and standard deviations, and the chi-square and Fisher's exact statistical tests were used as the standard measures of significance of the association between categorical variables, such as the reported PCE substance use by 'university' and 'field of study.' The significance level was set to $p < 0.05$, and only significant associations are reported in the Results.

3. Results

A total of 745 surveys were completed, 17% of which were conducted by international students attending Portuguese universities. The sample mean age was 22.6 years (SD = 3.4), with 73.2% being females. Most respondents were students from public universities (70.9%), particularly from the University of Lisbon (54.5%), while 37.3% were attending postgraduate studies (4.5% in Bologna 3rd cycles). In total, 32.5% ($n = 242$) of respondents reported using a PCE substance at least once.

Of all respondents, 31.1% reported using a PCE substance at least once in the period considered, with a majority (17.1%) having consumed such substances while at the university and 14.0% reporting preuniversity usage. Of that 31.1%, 28% reported the intake of food supplements before college and 33% during college. No significant association was found between the year of studies and the use of PCE substances. The most common frequency of use was up to ten times (16.8%), although an intake higher than ten and up to 40 (plus) times was mentioned by 14.6% of respondents; 21.7% of the last group referred to a daily PCE substance intake. Additionally, a significant association between females (34.9%) and PCE substance usage was found (Fisher's $p = 0.02$). Table 1 shows the study respondents' academic backgrounds and their replies to the question about the consumption of stimulant medications, prescribed or not.

More than one-third of the health sciences (HS) students (37.6%) self-reported using cognitive stimulants at some point in their university-related trajectory. The use of PCE substances seems significantly associated with the field of study, being higher for HS than humanities (Hm) ($Chi^2 = 11.741$, $p = 0.03$) (Fig. 1).

The reported last consumption showed that the most used substances overall were heterogeneous marketed drugs for cognitive function symptomatic treatment or nootropics (14.4%) and products available as food supplements (16.8%). The data also showed a tendency toward consuming CNS stimulants among Hm students compared with respondents from other study fields (Fig. 2).

Popular PCE substance options for CNS stimulants, such as methylphenidate and modafinil, are well-known drugs usually used in Portugal and abroad under medical surveillance. These substances share several side effects, namely, anxiety, agitation, and sleep problems. Table 2 details the results for both substances, which presented a relevant consumption, with methylphenidate reaching an almost significant association with study area.

Table 3 presents the main reasons for PCE substance use according to the study area. The responses indicate that the main reasons for use were that 'It helps me concentrate' (19.7%), 'It helps me study' (14.5%), and 'It helps increase my alertness' (1.7%). HS students were more likely to report these reasons than exact/natural science students or humanities students.

The most frequent reasons for using PCE substances were cross tabulated with the group substances (Table 4), knowing the possible differences in the awareness of risks according to the stimulant's nature. It was observed that food supplements were not significantly associated with experimentation. In contrast, CNS stimulants were statistically associated with the desire to increase concentration and focus or a medical prescription to treat a health condition.

Only 3.0% (25 respondents) of the PCE substance users reported experiencing at least one drug side effect, with the most frequent side effects being loss of appetite ($n = 13$), disturbed sleep pattern ($n = 10$),

Table 1
Usage of PCE substances at any time according to the field of study in the prior year and at university ($n = 745$).

	Humanities (%)	Exact & Natural Sciences (%)	Health Sciences (%)	Total (%)
No	168 (76.1%)	99 (67.8%)	236 (62.4%)	503 (67.5%)
Yes	53 (23.9%)	47 (32.2%)	142 (37.6%)	242 (32.5%)
Total	221 (100%)	146 (100%)	378 (100%)	745 (100%)

$Chi^2 = 11.74$, $p = 0.003$.

increased heart rate ($n = 6$), anxiety ($n = 4$) and/or agitation (n = 4). Five respondents planned to continue taking their reported PCE substances, but none indicated they would recommend these drugs to others. No respondents answered that they were likely to experiment with other stimulatory drugs.

The study respondents were also asked what channels they had used for accessing PCE substances. The top channel by far was through pharmacy staff recommendation (17.5%), although friends (3.4%) and online shopping (2.9%) were also mentioned. Only 6.9% of respondents indicated that the product was prescribed to them. Doctor prescription was associated with the use of CNS stimulants such as methylphenidate and amphetamine (Fisher's $p < 0.001$ and $p = 0.013$, respectively). Friends were associated with accessing methylphenidate and food supplements (Fisher's $p < 0.01$), while pharmacists were associated with accessing food supplements, including vitamins (Fisher's $p < 0.001$). Online shopping was used for acquiring methamphetamine (Fisher's $p = 0.47$) as well as for food supplements (Fisher's $p < 0.001$). Among students, 61% of HS students using PCE substances chose their products with pharmacists' advice, while PCE substance users from the exact and natural sciences (ENS) preferred online acquisition (45.5%).

4. Discussion

The present study aimed to assess the consumption of PCE substances by young adults in a higher education context, including the type of substances, main motivations, and overall experience from acquisition to adverse events. Almost one-third of all respondents reported using substances to enhance their cognitive performance, which might include repeated or simultaneous usage of different stimulants, raising questions related to individual health and safety, and issues of academic fairness.

4.1. PCE pattern among Portuguese undergraduates

The findings indicate that PCE substance usage was significantly associated with female students in this sample. This was not the trend in earlier studies of other populations,[23] although female Portuguese medical students and residents also prefer food supplements as cognitive stimulating substances.[37] This preference indicates a safety orientation in terms of pharmaceutical enhancement choices. The present findings also indicate the overall consumption of natural or 'endogenous' substances and nootropics as the predominant options, which are relatively safe products and mostly freely accessible from pharmacies and other outlets. Few respondents (6.9%) reported accessing PCE substances with a medical prescription, although only 2.5% were prescribed PCE substances to treat a medical condition. Pino et al. found that 10.2% of their respondents (2466 students at a large university) used prescription stimulants with their physician's approval, and 4.4% used prescription benzodiazepines with the support of their physician.[30]

A previous Portuguese study used a sample of university students and young workers and found that 17.7% to 25.3% consumed pharmaceuticals and natural products for mental concentration purposes.[50] Although not directly comparable, our study shows a higher frequency of PCE substance use based on data collected from university students in 2017. Additionally, approximately 20% of those reporting these substances also reported daily consumption, reinforcing the concerns raised by other authors regarding addiction and other health risks.[10,51,52]

Portuguese university students' use of 'study drugs' seems to follow a cautious pattern, with higher consumption of food-based substances and respecting the use of other stimulants according to health care professionals' prescription or advice. Nevertheless, less controlled use of CNS stimulants, including approximately 8% mentioning methylphenidate, and a non-negligible use of a heterogeneous group of other psychoactive substances were detected. This situation seems to reflect a global pattern, leading to concerns about the increasing prescription of methylphenidate over the past decades for young people diagnosed with ADHD, especially in the US.[14,53] Other authors who have documented methylphenidate use in a higher education context have interpreted its popularity concerning its perceived safety and low side effect profile,[54,55] features that might also underlie Portuguese and other European students' behavior.[56]

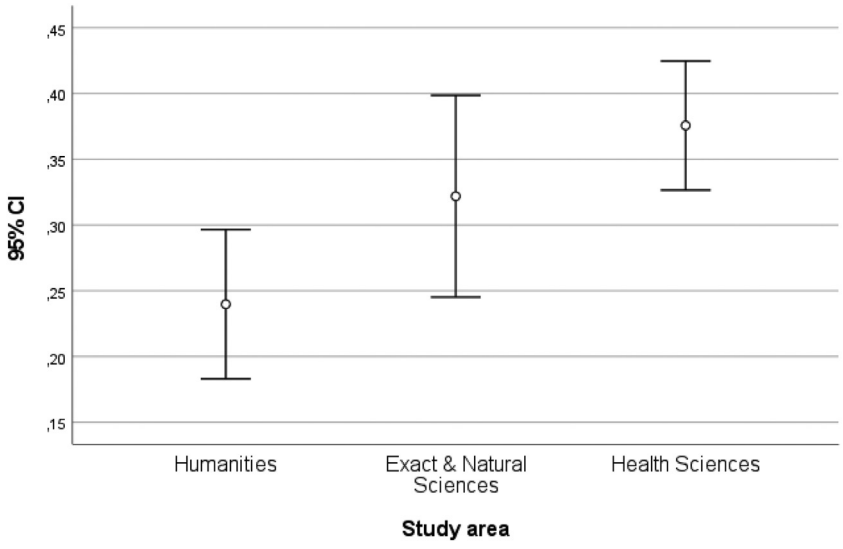

Fig. 1. Overall self-reported of single or repeated consumption of cognitive stimulant substances.

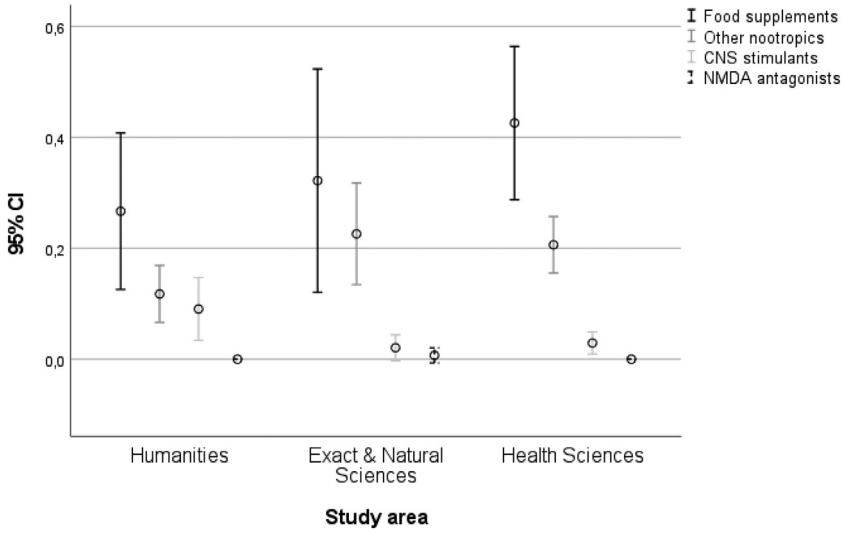

Fig. 2. Self-reported consumption of the types of cognitive stimulant substances according to field of study.

Portuguese higher education students appear to openly accept the use of substances for cognitive/mental performance,[50] while some have reported a willingness to experiment with PCE substances to determine their effects. Respondents infrequently reported their use 'to get high' or 'for fun,' suggesting a pragmatic approach to using PCE substances. Previous studies have shown that the overall perception of cognitive benefits outweighing short-term risks strengthens the ethical implications of PCE substance use, beyond their application in possible neuropsychiatric disorders and brain injury,[57] toward societal implications.

4.2. Interplay between types of stimulants and study areas

The findings in the present study show a statistical association between the field of study and PCE substance use. HS students were the largest consumers overall, mainly using food supplements and other stimulants, followed by ENS students. It was not determined whether this could be explained by a perceived sense of control over therapeutic substances by future health care professionals or because it is linked to their university program demands. Time pressure might be more challenging for HS students, explaining these students' higher use of PCE substances. A recent study by Krøll based on 28 in-depth qualitative interviews with young adults (age 20–30) enrolled at universities or colleges in Denmark describes how a majority of the students associate their nonmedical drug use with situations in which they experience urgency and a crisis of temporal agency due to their inability to pursue perceived necessary rhythms of studying or resting.[4]

When comparing the four groups of substances, i.e., CNS stimulants, NMDA antagonists, other nootropics, and food supplements, between respondents from different study areas, our findings show that Hm respondents consume significantly more CNS stimulants, such as methylphenidate and modafinil, compared to the highest overall consumption from HS respondents. These data suggest that humanities students might prefer drugs with described and manifest effects, possibly looking for higher stimuli and creativity levels. Nevertheless, the high levels of competition and related stress seem relevant in affecting PCE substance use, as experienced by medical students.[58,59] This was not the case in our study, and the underlying reasons might be the greater awareness by medical students of the implications of using CNS stimulants, although further research is needed to determine the motivational and behavioral reasonings for each field of study.

Table 2
Consumption of methylphenidate and modafinil according to the field of study (n = 745).

	Humanities (%)	Exact & Natural Sciences (%)	Health Sciences (%)	Total (%)
Methylphenidate[1]				
No	211 (95.5%)	145 (99.3%)	370 (97.9%)	726 (97.4%)
Yes	10 (4.5%)	1 (0.7%)	8 (2.1%)	19 (2.6%)
Total	221 (100%)	146 (100%)	378 (100%)	745 (100%)
Modafinil[2]				
No	211 (95.5%)	145 (99.3%)	370 (97.9%)	726 (97.4%)
Yes	10 (4.5%)	1 (0.7%)	8 (2.1%)	19 (2.6%)
Total	221 (100%)	146 (100%)	378 (100%)	745 (100%)

[1] $Chi^2 = 6.0, p = 0.05$.
[2] $Chi^2 = 5.30, p = 0.061$.

4.3. Motivations and implications of PCE substance use

When asked about their motivations for PCE substance use, respondents chiefly referred to the expected improved academic performance mainly associated with better memory, more clarity, and focus. Other reasons included prescribed treatments for health conditions, such as ADHD in adults, and experimentation. Obtaining a high, just using for fun, or improving physical condition (e.g., losing weight) had residual responses. This finding is aligned with previous findings on personal awareness, including the need to avoid addiction risks.[51,60] Nevertheless, it should be noted that the reported side effects might have been perceived as less severe, and counteracted by the perceived benefits of PCE substance use. Concerning the transition to an active labor situation, the year of study completed, and associated adulthood development, were all independent of PCE substance use in this sample.

Inside and outside tertiary education, there have been concerns beyond medical safety and involving coercion and fairness. The latter includes issues on equality of opportunity, honesty, and authenticity, expressed by users and nonusers, with nonusers displaying more societal concerns than users,[9] even if academic compensation is not necessarily established.[1] Nevertheless, the social prescription, summing to a personality disposition for exceedingly high-performance standards, has shown a positive contribution to university students' intake of cognitive enhancers, intended to boost their academic performance.[61] The writings by Martin (2000) on how the individual has become a site of investment: the self, a portfolio of assets, which must be continually managed and improved; and how the self is increasingly responsible for its abilities and possibilities with the diminishing role that social institutions in contemporary Western society play for life support, might be echoed in the present sample.[62]

The growing number of years spent at university and students' approach to the real world of job demands should increase PCE substance use.[43]

Table 3
Main reasons for PCE substance use by study area (n = 745).

		Humanities (%)	Exact & Natural Sciences (%)	Health Sciences (%)	Total (%)
It helps me concentrate*[1]	No	192	120	286	598
	Yes	29 (3.9%)	26 (3.5%)	92 (12.3%)	147 (19.7%)
It helps me study*[2]	No	201	128	308	637
	Yes	20 (2.7%)	18 (2.4%)	70 (9.4%)	108 (14.5%)
It helps increase my alertness*[3]	No	208	133	320	661
	Yes	13 (1.7%)	13 (1.7%)	58 (7.8%)	84 (11.3%)
To experiment/try[4]	No	215	137	364	716
	Yes	6 (0.8%)	9 (1.2%)	14 (1.9%)	29 (3.9%)
It helps me to stay sharp[5]	No	215	138	367	720
	Yes	6 (0.8%)	8 (1.1%)	11 (1.5%)	25 (3.4%)
It was prescribed for my health condition[6]	No	217	142	367	726
	Yes	4 (0.5%)	4 (0.5%)	11 (1.5%)	19 (2.5%)

* Significant associations.
[1] $Chi^2 = 11.50$, $p = 0.003$.
[2] $Chi^2 = 10.77$, $p = 0.005$.
[3] $Chi^2 = 13.5$, $p = 0.001$.
[4] $Chi^2 = 2.87$, $p = 0.238$.
[5] $Chi^2 = 3.0$, $p = 0.223$.
[6] $Chi^2 = 0.71$, $p = 0.703$.

Recent results from a US-based dataset of 1121 undergraduate and graduate students indicated that the latter are twice as likely to report nonmedical prescription stimulant use than undergraduate students.[63] However, the present study did not find a significant association between the number of years spent at the university and reported PCE substance use. Summing to preuniversity usage, the usage pattern thus seems to remain individually stable, also influenced by the lower societal acceptance and stigmatization of using psychoactive substances.[64,65]

Health care professionals, including pharmacists, should play a role in PCE substance use. On the one hand, pharmacies were the top channel for acquiring stimulants, probably those in the nootropics and food supplements groups, thus indicating young people's trust in pharmacy staff counseling for performance enhancement substance use.[66,67] Previous studies have described different channels and associated motivations, such as friends, family members, black-market vendors, and clinicians' prescriptions.[68] In addition to friends, other sources of medication were not found in our sample. Contrary to other products used by young populations,[69] online acquisition was not (yet) the predominant channel, knowing that internet purchase and mail delivery is not a legal channel for acquiring medicine in Portugal. Nevertheless, critical issues may arise with the growing internet purchase of medicine.[70,71]

4.4. Where to go from here?

On the one hand, the urgency of a new policy or regulatory response to PCE substance use is not apparent.[72] Evidence suggests that regulatory changes are not imperative, knowing that use is not particularly widespread at a population level (UK data), and the current enhancers available are not considered particularly dangerous. However, considering that movements exist toward a natural, drug-free, or abstinent society in many Western countries, current regulatory methods do not appear to inhibit PCE substance use since studies continually show a small (albeit significant and growing) market for the substances. On the other hand, community pharmacists are primary care professionals involved in dispensing stimulating substances and pharmacovigilance duties. In line with their sentinel role regarding active substance abuse, these professionals should not lose sight of young adults who use prescribed and nonprescribed substances to enhance their cognitive performance.

A literature review by Abelman (2017) suggested alternative harm reduction and addiction science initiatives for how academia can deal with, foresee, and/or prevent PCE substance use.[73] One suggestion is to provide systems that reduce peer pressure and stigma by encouraging students with ADHD to share their medication experiences. Another suggestion is to run campaigns for improving students' confidence and making the course work more enjoyable. Universities might also include general and introductory educational sessions on the dangers of PCE substance use, risk factors, and options to obtain help. Increased public discussion about pro- and anti-drug websites is another suggestion worthwhile pursuing. For instance, Duke University introduced a screening test (DAST-10), enabling the university to predict students at risk of using PCE substances in the future.[73]

In addition, subsequent fruitful studies on PCE substance use might be based on so-called assemblage theory since these studies typically pay at-

Table 4
Main reasons for PCE substance use according to group of substances ($n = 744$)[§].

		Food supplements	Other nootropics	CNS stimulants	Total (%)
It helps me concentrate	No	49	50	8	107
	Yes	79 (10.7%)*	59 (7.9%)*	16 (2.1%)*	154 (20.7%)
It helps me study	No	77	59	13	149
	Yes	51 (6.8%)*	50 (6.7%)*	11 (1.5%)	112 (15%)
It helps increase my alertness	No	86	70	20	176
	Yes	42 (5.6%)*	39 (5.3%)*	4 (0.5%)	85 (11.4%)
To experiment/try	No	114	97	22	233
	Yes	14 (1.9%)	12 (1.6%)*	2 (0.3%)	28 (3.8%)
It helps me to stay sharp	No	115	96	22	233
	Yes	13 (1.7%)*	13 (1.7%)*	2 (0.2%)	28 (3.7%)
It was prescribed for my health condition	No	118	98	21	237
	Yes	10 (1.3%)*	11 (1.5%)*	3 (0.4%)*	24 (3.2%)

[§] NMDA antagonists are not reported ($n = 1$).
* Significant associations.

tention to the *time* and *place* of drug use, as Duff showed in his case study of the social context of methamphetamine use in Melbourne.[74] Duff showed how drug use could be explained not only from the perspective of a *person's* choices and experiences but also from an *assemblage* of forces that shape and frame both the drug use and the context in which it exists.[20] Last but not least, following other researchers, we would also argue for the value of policy responses that acknowledge and respond to a broader range of enhancement practices, including different user groups.[72]

4.5. Study limitations and strengths

The primary study limitation is the time lag between data collection and the dissemination of findings under the unique pandemic circumstances. The present data collection could provide different findings, particularly after the restrictive measures adopted by countries such as Portugal in 2020 that might have increased in-house drug abuse, including cognitive enhancers and new psychoactive substances.[75]

Methodological obstacles, such as underreporting, can occur using online surveys, as well as uncertainty related to breaches in data confidentiality when disclosing socially sensitive issues such as drug usage. The convenience sampling might have missed segments of the university student population (e.g., self-selection and nonresponse bias), and private university students may have been underrepresented, although they accounted only for 19.6% of the potential respondents. Gender skewed the distribution, with a 19.2% higher participation of females compared to the college population, which also illustrates sampling issues, although this exploratory study did not follow power calculations for statistical representation purposes. Additionally, web-based surveys have been extensively used and seem to provide equivalent accounts for socially sensitive issues compared with direct questionnaires in university populations.[76]

Another limitation is related to the definition of PCE being related to the use by 'normal' healthy individuals of any psychoactive substance with the primary aim of augmenting mental and cognitive brain functions, such as attention, concentration, or memory. It was not known if our survey respondents were 'healthy' because the survey used did not include assessing the health status of the students surveyed. A respondent might have had a diagnosed health condition (e.g., diagnosis of ADHD) that they were not asked to disclose, or had a health condition that has not yet been diagnosed.

No construct, content, or reliability validation of the survey tool was carried out. For instance, the instrument was not tested regarding memory bias when reporting last consumption. This also fits the limitation related to the use of international nonproprietary names for substances. We aimed to assess individual stimulants quantitatively, but no guarantee existed regarding respondents' bias for the substances they might be using. We tried to control this issue by using examples of Portuguese brand names and well-known international brands (e.g., Ritalina™ and Concerta™ for methylphenidate).

One major strength is the study's national scope, involving several public and private universities, even though there were varying response rates. It was also a first attempt to survey many different stimulants, including both substances considered food supplements and prescribed drugs.

5. Conclusion

This study described the prevalence, types, and main reasons for PCE substance use among university students in Portugal. One-third of the surveyed university students aimed to improve their academic performance through pharmacological cognitive enhancement, with a preference for food supplements dispensed in pharmacies. PCE drug consumption in higher education is non-negligible in Western societies and is a novel public health issue. In any case, it is necessary to improve the regulations on potential inequalities in academic rankings and success and adopt an observant attitude concerning the negative health implications in the long run.

It is recommended that universities and other stakeholders consider individual and public health measures, such as information and education campaigns and random screenings, after a robust debate and consensus among all involved. Further research should engage universities' social and medical services, as well as other members of the higher education ecosystem, to ensure that higher education students avoid the misuse of cognitive enhancement drugs. Also, a more exhaustive assemblage analysis of forces that shape and frame PCE substance use and the context in which it exists is recommended.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix

PCE substance usage among higher education students in Portugal.

Part A.

1. In which country were you born?
2. What is your age?
3. What is your gender?
4. What is your field of study?
5. What is the highest level of education you have completed?
6. Where do you study?
7. Do you have a financial income?

Part B.

8. Considering the preuniversity year (*12° year*) and while at the university, have you ever consumed stimulant substances, prescribed or not, to increase your cognitive performance?
9. Ok, since you answered {yes {answer_8}}, please mark all that you have used at least once:

- Methylphenidate (Ritalin or Rubifen)
- Methamphetamine (Crystals)
- Amphetamine (Adderall)
- Fish oil plus vitamins (e.g., Juvamine)
- Protein and vitamin supplements (e.g., Nutrex, Energy bars, Ovofull, or Muscle Pharm)
- Neurozan
- Dextroamphetamine (Dexedrine)
- Opiate-type (codeine, morphine, Demerol, Vicodin, Darvon, Percocet, or Percodan)
- Modafinil ("Smart Drug")
- Phosphatidylcholine/Acetylcholine Supplements (Cerebrum)
- Memantine (Axura)
- L-carnitine
- Aspartate Arginine (Asparten or Sargenor)
- *G. biloba* (Gincoben or Biloban)
- Diphosphate-choline (Hipercol or Somazine)
- Piracetam (Noostan or Acetar)
- Racetam
- Pyritinol (Cerbon-6)
- Vincamine
- Sulbutiamine (Arcalion)
- Riluzole
- Other substances, which?

10. Choose the ONE from {{answer_9}} that you most frequently use or have used.
11. When did you first start using {{answer_9}}?
12. Regarding the last occasion you used the substance {{answer_9}}: how have you used, {{answer_9}}, i.e., how many units (e.g., X pill(s), Y mL, Z gram(s)) per a given period (e.g., day, week, month)?
13. How do you use it?

- Orally (e.g., pill, tablet, or capsule)
- Intranasally (e.g., spray or drops)
- Injecting (e.g., IV/IM preparations)
- Other routes, which?

14. Why have you used the substance {answer_9}} (mark all apply)?

- It helps me concentrate
- It helps me to stay sharp
- It improves my physical performance
- It helps increase my alertness
- It gives me a high
- Just for fun
- It was prescribed for my health condition
- It counteracts the effects of other drugs
- It helps me study
- It helps me lose weight
- To experiment/try
- I am addicted
- Other reasons, which
- Rather not say

15. Regarding {{answer_9}}, were you able to feel any of the following substances' side effects (mark all apply)?

- Disturbed sleep patterns
- Nausea
- Loss of appetite
- Hallucinations, hyperexcitability, or irritability
- Panic and obsession (psychopathic behavior)
- Impulsive behavior
- Increased heart rate, blood pressure, or body temperature
- Respiratory (breathing) problems
- Depression
- Hyperactivity
- Bizarre, erratic, sometimes violent behavior
- Dilation of pupils
- Other side effects, which

16. Did you feel any warning sign of drug interactions with other drugs or food (mark all apply)?

- Drowsiness
- Hypertension (high blood pressure)
- Arrhythmias (increased heart rate)
- Depression
- Anxiety
- Agitation
- Other signs, which

17. How have you obtained the substance?

- Prescribed by a doctor
- Recommended by a pharmacist
- Online
- Through friends
- Street dealer
- Gym
- Para-pharmacy
- Other outlets, which

18. How likely are you to continue taking {{answer_9}}?

Likert scale: 1 – Not at all, 10 – Totally.

19. How likely are you to recommend {{answer_9}} to others?

Likert scale: 1 – Not at all, 10 – Totally.

Part C.

20. Are you willing to try another stimulant substance in the future?

- I am not interested in trying new one(s)
- I am interested in trying the following (mark all that apply)

  - o Methylphenidate (Ritalin or Rubifen)
  - o Methamphetamine (Crystals)
  - o Amphetamine (Adderall)
  - o Fish oil plus vitamins (e.g., Juvamine)
  - o Protein and vitamin supplements (e.g., Nutrex, Energy bars, Ovofull, or Muscle Pharm)
  - o Neurozan
  - o Dextroamphetamine (Dexedrine)
  - o Opiate-type (codeine, morphine, Demerol, Vicodin, Darvon, Percocet, or Percodan)
  - o Modafinil (“Smart Drug”)
  - o Phosphatidylcholine/Acetylcholine Supplements (Cerebrum)
  - o Memantine (Axura)
  - o L-carnitine
  - o Aspartate Arginine (Asparten or Sargenor)
  - o *G. biloba* (Gincoben or Biloban)
  - o Diphosphate-choline (Hipercol or Somazine)
  - o Piracetam (Noostan or Acetar)
  - o Racetam
  - o Pyritinol (Cerbon-6)
  - o Vincamine
  - o Sulbutiamine (Arcalion)
  - o Riluzole
  - o Other substances, which?

21. How likely are you to recommend stimulant substances to a friend or a colleague?

Likert scale: 1 – Not at all, 10 – Totally.

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