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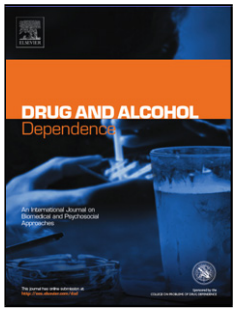

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The Importance of Stress, Self-Efficacy, and Self-Medication for Pharmacological Neuroenhancement among Employees and Students

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ABSTRACT

Objectives: This study examined the relationship between stress, self-efficacy, self-medication, and pharmacological neuroenhancement (PNE) in the Swiss general population. *Methods:* Using the largest Swiss Internet panel, a sample of 10,171 employees and students (unweighted N = 10,084) aged 15 to 74 years was recruited and asked to complete a self-administered online survey. The data were weighted for age, sex, and language region to provide results that were representative of the Swiss population. Multinomial logistic regression models were conducted to identify predictors of pharmacological cognitive enhancement (PCE) and pharmacological mood enhancement (PME) over the past year. Two self-medication models and an overall model were determined. *Results:* Current medical treatment for a mental disorder was the best predictor of both PCE and PME use as serious self-medication. The overall model revealed that cannabis use, frequent stress, and long-term stress were predictors of both PCE and PME, whereas negative stressors and time pressure at work did not remain in the final model. Furthermore, past-year PCE with and without PME was associated with being male, being a student, and using illegal drugs other than cannabis, whereas being female and having low self-efficacy predicted past-year PME only. *Conclusions:* Consideration of the predictor variables identified in this study may help to identify the potential PCE and PME users for whom measures to prevent drug abuse and manage stress are most appropriate. More specifically, the use of PCE and PME as self-medication to enhance performance at work or while studying needs further consideration in the neuroenhancement debate.

KEYWORDS: Neuroenhancement, cognitive enhancement, mood enhancement, self-medication, illegal drug use, mental health

1. INTRODUCTION

Pharmacological neuroenhancement (PNE) refers to the nonmedical use of prescription drugs, alcohol, and illegal drugs for the purpose of enhancing cognition, mood, or pro-social behavior to improve performance at work or while studying (de Jongh et al., 2008; Maier and Schaub, 2015). Nonmedical use of prescription drugs is defined as use without having a prescription or use for another purpose than prescribed (Maier and Schaub, 2015). More specifically, some people with a mental disorder use their medication in higher doses or through a different route of administration than prescribed for the purpose of enhanced cognitive performance (Arria et al., 2008; Maier et al., 2013).

However, the literature most likely focuses on healthy individuals' nonmedical use of prescription stimulants for pharmacological cognitive enhancement (PCE). For the most part, the discussions are limited to the question whether the drugs used for PCE affect the cognitive processes in users without considering altered emotion sufficiently (Vrecko, 2013). Nevertheless, stimulants' effects are not purely cognitive, but also affective and the motivational effects are significantly involved in performance outcomes (Ilieva and Farah, 2013; Vrecko, 2013). Stimulants' effect on enhanced motivation might also explain why healthy users still perceived an enhanced cognitive function, when no objective cognitive enhancing effects were found (Ilieva et al., 2013). Furthermore, potential motivational enhancing drug effects are also relevant when considering pharmacological mood enhancement (PME) or substance use to cope with stress (de Jongh et al., 2008; Maier and Schaub, 2015).

However, an increasing number of media reports on PNE might generate the misperception that PNE is an acceptable means of coping with stress and overwhelming demands at work or school (Schleim, 2014; Wolff and Brand, 2013). Lazarus described stress as a feeling that arises when professional or academic requirements exceed the personal and

social resources that an individual is able to mobilize at a given time (Lazarus, 1989). A comprehensive study among German students supported this theory and found an association between performance pressure and PNE (Middendorff et al., 2012). A further interesting study finding was that one quarter of students experienced with PNE reported cannabis use to cope with the study demands (Middendorff et al., 2012).

Notwithstanding, responses to stress can vary greatly among individuals; the use of prescription and recreational drugs for PNE represents only one of many possible pharmacological coping strategies (Maier and Schaub, 2015; Park and Iacocca, 2014). Moreover, PNE with stimulants is strongly associated with risky health behaviors such as illegal drug use (Arria et al., 2008; McCabe et al., 2005). Insufficient coping skills and substance abuse in the face of chronic stress might cause mental health problems, and vice versa (Mohr et al., 2014). Additionally, individual and situation-specific differences in the perception of stress and in coping strategies are related to decisions about whether to engage in PNE (Sattler et al., 2014).

Self-efficacy is the ability to initiate and use successful stress coping strategies (Bandura, 1977) and mediates the path from stress to illness (Sawatzky et al., 2012). In addition, a study found that students with high achievement goals and high self-efficacy performed better than their counterparts (Cheng and Chiou, 2010). These findings refer to Bandura's (1986) social cognitive theory, which states that attainable goals, self-motivation, and controllable outcomes are crucial for self-efficacy and personal development. Once the individuals in these studies experienced PNE, they showed lower levels of avoidance self-efficacy because they could no longer avoid using illicit stimulants in highly stressful situations (Bavarian et al., 2013). In other words, they were not confident in their own abilities and the functional use of drugs for enhancement purposes even further diminished self-efficacy when performance was attributed to the drug effects rather than to one’s own abilities.

Responsible self-medication with indicated over-the-counter drugs for self-recognized conditions is an important element of self-care that reduces the burden on health care systems (WHO, 1998). However, Khantzians' (1997) self-medication hypothesis of addictive disorders claims that addicts use alcohol or illegal drugs to change the painful affect states that can result in addiction. The nonmedical use of prescription drugs or alcohol and illegal drugs for PCE or PME to treat an undesired physical or mental condition represents a form of *self-medication* that falls in the middle of the range between healthy self-care and addiction. However, the terms nonmedical use or misuse are preferred in the scientific literature, and definitions that contain the term "enhancement" arise from the bioethical debate (Racine and Forlini, 2008). These technical and optimistic terms increase good performers' fear of inadequacy and distract from the issue of *serious self-medication* among individuals with a mental disorder who use drugs to diminish certain higher-order capacities that cause specific symptoms of a disorder (Earp et al., 2014). An example provided by Earpand colleagues (2014) is the diminishment of memory to reduce traumatic memories. Another example might be diminishment of a certain brain function to reduce rumination in patients suffering from depression. Consequently, it often remains unclear whether drug use for cognitive enhancement in individuals with an undiagnosed mental disorder, such as ADHD, is self-treatment or misuse (Peterkin et al., 2011; Rabiner et al., 2009a). Both PCE and PME might be considered *self-medication* when healthy individuals use drugs to maintain good performance when few resources are available or to improve performance from good to excellent or from pathological to normal. Thus, PCE and PME are means of achieving specific health or performance goals (Wolff et al., 2014). For the most part, studies of academic PCE have focused on PCE as *moderate self-medication* in terms of the self-optimization of healthy individuals who suffer from stress (Singh et al., 2014; Wolff and Brand, 2013). Research has often excluded individuals with mental disorders to avoid the

discussion of where treatment ends and enhancement begins (Barrett et al., 2008; Maslen et al., 2014). The use of PCE and PME as *serious self-medication* to combat symptoms of mental disorders or the adverse side effects of medical treatment is prevalent (Kasten, 1999) but has not yet been investigated in the neuroenhancement literature. Therefore, the current study aimed to investigate factors associated with the use of both *moderate self-medication* and *serious self-medication* to enhance performance at work or while studying.

1.1.Current study

The current study is the first to perform an in-depth analysis of the predictors of two different forms of neuroenhancement, namely PCE and PME, based on representative national-level estimates. Mental disorders and their associated medical treatments as well as different forms of stress and self-efficacy were considered as possible predictors of PCE and PME. Taking into account the abovementioned theoretical work, stress and insufficient stress coping, other illegal drug use, and impaired mental health were assumed to predict both PCE and PME. Moreover, it was assumed that different enhancement intentions are related to different predictors. PME with the intention to increase psychological well-being differs from the rather competitive intention of PCE (Maier and Schaub, 2015; Schleim, 2014). Finally, the following hypotheses were made in terms of a *moderate self-medication*:

- past-year PCE and PME are both associated with higher levels of past-year stress and long-term stress
- past-year PCE is associated with time pressure and other negative professional or academic stressors in the past year
- past-year PCE and PME are both associated with illegal drug use in the past year
- past-year PME is associated with low self-efficacy

In addition, the following *serious self-medication* hypothesis was made:

- past-year PCE and PME are both associated with current medical treatment for underlying mental disorders

The understanding of the predictors of PCE and PME derived from this cross-sectional study has important implications for preventive measures and future longitudinal research that aims to disentangle the relationships among stress, self-efficacy, mental health, and PCE and PME.

2. METHODS

2.1.Enrollment procedure and study sample

Participants were recruited through a national Internet panel. The Internet panel of the LINK institute for market and social research in Switzerland includes more than 130,000 people living in Switzerland who consented to be contacted about online public opinion surveys during computer-assisted telephone interviews. The panelists were representative of the 15- to 74-year-old population in Switzerland that uses the Internet at least once per week for private purposes and is able to answer a questionnaire in German, French, or Italian. In March 2013, the LINK institute invited 39,996 panelists to participate in a study about health and stress at work and in education, and 18,094 panelists took the survey. Following screening for exclusion criteria (currently unemployed and not in education = 3,535), quota overflow (n = 2,155), and dropouts (n = 2,320), the final sample size was 10,084. The data were weighted for age, sex and language region (weighted N = 10,171). Informed consent was obtained from all of the participants who were included in the study.

2.2.Measures

A self-administered online survey was used to investigate PCE and PME in Switzerland (for survey details see Maier et al., in press). For the present study, only variables containing current and past-year indicators of stress, health, and health behaviors were considered.

2.3.Pharmacological neuroenhancement (PNE)

Two principal questions assessed past-year PNE. First, participants who indicated having ever used prescription drugs or recreational drugs for cognitive enhancement (PCE) at work or while studying were asked, whether use also occurred in the past 12 months. Second, participants who indicated having ever used prescription drugs or recreational drugs for mood enhancement (PME) at work or while studying were asked whether use also occurred in the past 12 months. The following four groups were specified: 1) no PNE in the past 12 months; 2) past-year PME only; 3) past-year PCE; and 4) both past-year PME and PCE. To provide sufficient statistical power for logistic regression analyses performed, groups 3 and 4 were merged to one group containing all PCE users with and without additional PCE use.

2.4.Stress measures

2.4.1. Frequency of stress. To determine the participants' frequency of stress experiences in the past 12 months, they were asked the following question: "During the past 12 months, how often have you felt stressed – never, rarely, sometimes, often, or very often?" This variable was modeled using the original Likert format.

2.4.2. Long-term stress at work or in education. To determine whether the participants had experienced long-term stress at work or in education, they were asked the following question: "Have you experienced stress at work or in education that persisted over several months? (Eurofound, 2010)" The answer format was dichotomous (yes or no).

2.4.3. Time pressure and negative aspects at work or in education. The participants answered seven questions about current stress at work or in education that were analyzed by an exploratory factor analysis. The factor analysis revealed two stress scales, which were used as potential predictors of PCE and PME. The first scale included two items ($\alpha = .76$) asking for frequency of working or learning at a fast pace and under tight deadlines (Eurofound, 2010; Grebner et al., 2010). The items were answered on a 6-point scale (almost never, approximately one-quarter of the time, approximately half of the time, approximately three-

quarters of the time, almost always, and always). The second stress scale included five items (α = .67) that measured time-independent negative conditions of the participants' current work and education situations that might be related to adverse health outcomes and PNE. Those items asked about the frequency of unclear instructions from supervisors and lecturers, the occurrence of unnecessary breaks at work or while studying, the feeling of a lack of control at work or while studying, competitive pressure, and the need to show inauthentic feelings at work or at school (Eurofound, 2010; Grebner et al., 2010). Each of the five items was coded on a 5-point scale (never, rarely, sometimes, often, or very often).

2.5. Other predictor variables

2.5.1. Socio-demographic characteristics. The following demographic variables were included in the analyses: sex, age (15-24, 25-34, 35-44, 45-54, and 55-74 years), professional activity (student, employed full-time, and employed part-time), relationship (none/temporary and stable), and the presence of children (< 18 years of age) at home (yes or no).

2.5.2. Mental health and health behavior. The participants indicated their current health status in response to the first question of the 12-Item Short Form Health Survey SF-12 (poor, fair, good, very good, and excellent), a survey often used by physicians determine patients' health. Moreover, participants were asked about past and current diagnoses of mental health disorders (ADHD, narcolepsy, depression, anxiety disorder, and substance use disorder) that are known to be treated with medications that the scientific literature often refers to as neuroenhancement drugs (Rabiner et al., 2009b; Sattler et al., 2014). A dichotomous variable was used in the analysis to represent the current use of a prescription drug to treat at least one of the aforementioned mental disorders (yes or no). Participants who reported undergoing medical treatment for a past or current mental disorder were asked whether they had ever used their prescribed medication in a manner other than prescribed (e.g., at a higher dose or via a different route of administration). Past-year psychoactive substance use was assessed

dichotomously for tobacco, alcohol, cannabis, and other illegal drugs (cocaine, MDMA, amphetamine, ketamine, and GHB/GBL).

2.5.3. Self-efficacy. The Generalized Self-Efficacy Scale (GSES) was used to assess the strength of the participants' belief in their ability to respond to novel or difficult situations and to cope with a variety of stressors (not at all true, barely true, moderately true, and very true). The psychometric characteristics of the GSES are satisfactory when implemented online (Schwarzer et al., 1999), and the present study revealed good internal consistency ($\alpha = .86$).

2.6. Logistic Regression Models

To evaluate each variable's ability to predict the outcome (PME or PCE with and without PME), initial separate multinomial logistic regression analyses were performed (subsequently termed 'univariate analyses'). Past-year non-users were the reference group for the dependent variable. First, all significant univariate socio-demographic predictors were entered in the preliminary multivariate model (model 1). Non-significant variables were removed from the overall model one at a time. Nagelkerke's R-square was calculated as a goodness-of-fit measure for the multivariate multinomial logistic regression model. In a second model, the demographics, stress, and self-efficacy were entered as predictors of PME and PCE with and without PME (*moderate self-medication*, model 2). In model 3 (*serious self-medication*), the demographics and current medical treatment for a mental disorder were entered. Finally, in an overall multivariate multinomial logistic regression model all remaining significant predictors were included to predict PME and PCE with and without PME (model 4). All quantitative analyses were conducted using IBM SPSS Statistics Version 22 (SPSS, Inc., Chicago, IL, USA), and $p < .05$ was set as the significance level.

3. RESULTS

Of the study participants, 2.1% ($n = 215$) reported past-year PNE. Two-thirds of the past-year PNE users (69.2%) felt frequently or very frequently stressed in the past 12 months,

compared with 35.5% of the non-users. Four out of five past-year PNE users (80.7%) reported long-term stress at work or in education, whereas half of the non-users (49.3%) reported such long-term stress. Whereas the non-users who said they experienced long-term stress reported that they were rarely unable to cope with their stress (7.6%), one-quarter of the PNE users (22.9%) were never or almost never able to cope with stress at work or in education. To further specify the groups of interest, 1.4% (n = 146) reported past-year PME and 0.7% (n = 69) reported past-year PCE with or without PME.

The characteristics of the study sample used in the analysis of the two different types of past-year PNE are depicted in Table 1. All variables except past-year alcohol use were univariate predictors of either past-year PME or past-year PCE with and without PME (Table 1).

Results from models 1 – 3 are depicted in Table 2. The demographic predictors (model 1) explained 14% of the variance (Nagelkerke's R^2). The *moderate self-medication* model, which included demographics, stress, and self-efficacy (model 2) explained 19% of the variance. Frequent stress in the past 12 months and long-term stress at work or in education were good predictors of PME and PCE with and without PME, but time pressure at work and negative stressors at work were excluded from the model. Self-efficacy predicted past-year PME. Finally, the *serious self-medication* model which included both the demographic predictors and current medical treatment for a mental health problem (model 3) explained 30%.

The overall prediction model resulting from the multinomial logistic regression (R^2 = .33) is presented in Table 3. Current medical treatment was the strongest predictor of both PME and PCE with and without PME. Past-year cannabis use and frequent and long-term stress were also predictors of both PME and PCE with and without PME. The past-year use of other illegal drugs, being male, being a student, being in a relationship, and living without minor

children at home were predictors of PCE with and without PME. Being female and having low self-efficacy were predictors of PME only.

Table 4 presents the prevalence mental disorders according to self-report data of non-users, PME users, and PCE users with and without PME. The majority of the PME users reported being diagnosed with depression, and half of them reported undergoing current medical treatment for their disorder. Only a small number of the participants with a mental disorder reported that they had ever misused their medication for a purpose other than that for which it was prescribed.

4. DISCUSSION

This study aimed to identify the predictors of PCE and PME separately to determine different user groups using two explanation models that focused on self-medication. The first *moderate self-medication* hypothesis stating that frequent and long-term stress predicts PCE and PME was confirmed.

Surprisingly, the second *moderate self-medication* hypothesis, that time pressure and work-related negative stressors would increase the likelihood of PCE, was rejected. In particular, no direct link was found between acute work- or study-related environmental stressors and PCE. These stressors seemed manageable and were not predictors of PCE and PME, whereas frequent and long-term stress and currently impaired mental health were more likely to predict drug use for PCE and PME. No matter whether PCE is considered as a coping strategy for stress or as part of a certain planning strategy of users, PCE use seems to occur most likely when no other effective alternative is promising for lasting changes of a somehow uncomfortable situation. As intermittent stress is sometimes resolved automatically, it might be less associated with finding new strategies to cope with, such as PCE, or with changing the planning behavior. However, our data rely on self-report and perceived stress can vary strongly between individuals depending on the cognitive appraisal of stress (Lazarus,

1984). Moreover, PCE might be perceived as a short-term solution to reduce long-term stress in people with insufficient personal and social resources required to meet certain demands in the long-term. This is in line with the finding that students who reported having used drugs to improve performance while studying had difficulties to meet the study demands and perceived persistently high performance pressure (Maier et al., 2013; Middendorff et al., 2012). Moreover, pronounced procrastination and high cognitive test anxiety, both characteristics that support chronic stress, increased the willingness to use drugs for PCE among students (Sattler et al., 2014).

Consistent with previous studies, the present findings support the third *moderate self-medication* hypothesis that PCE and PME are associated with illegal drug use (Arria et al., 2008; McCabe et al., 2005). Cannabis users were three times more likely to report PCE and five times more likely to report PME. A recent longitudinal study showed the strong link between cannabis use and mood disorders and suggested that cannabis was used as *self-medication*, similar to the definition of PME in the present study (Feingold et al., 2014). The use of illegal drugs other than cannabis was positively associated with PCE but not with PME. This finding might be explained by the presence of male participants with high levels of sensation seeking in the group (Rabiner et al., 2009a). Additionally, individuals with a history of illegal drug use might be less afraid of the unknown effects and side effects of prescription drugs used for PCE because they are generally used to deal with the uncertainty regarding effects and side effects. However, they might even be more likely to use illegal drugs they usually use recreationally also for cognitive or mood enhancement. This would then question the inclusion of past-year illegal substance use as predictor variable in our model. Nevertheless, when considering the low number of illegal drug users reported having ever used the illegal drug for direct cognitive or mood enhancement (Table 6 in Maier et al., in press), the inclusion is supposed to be accurate. Importantly, alcohol and cannabis use to relax

after stress at work or in education was far more prevalent (Maier et al., in press). This is consistent with the finding of Middendorff and colleagues (2012) whose study revealed that one quarter of PNE users used cannabis to cope with the study demands. However, cannabis users in the present study had most likely not thought about cannabis as a drug used for PNE.

The present findings supported the most specific *moderate self-medication* hypothesis that low self-efficacy would predict PME. Being female and having low self-efficacy were predictors of PME.

Furthermore, the *serious self-medication hypothesis* was confirmed in the analysis, and current medical treatment for a mental disorder, particularly depression and/or an anxiety disorder, was the strongest predictor of both PCE and PME. However, misuse of the treatment medication among patients was rare, and they used illicit substances for PCE or PME in addition to the existing medications to cope with stress and other psychological consequences of their disorders. Medical treatment might be perceived as helpful and effective for coping with the symptoms of the underlying disorder. Hence, the patients might have learned that drugs influence their health outcomes in a positive way, consequently engaging in *serious self-medication* to enhance their performance at work or while studying.

The present findings are in line with Lazarus' (1989) stress theory; PCE and PME are suggested to be stress management strategies for coping with high levels of stress. Consistent with previous research, insufficient coping is assumed to be associated with mental health problems despite or as a consequence of *moderate self-medication* in healthy individuals (Mohr et al., 2014). Moreover, the fact that PCE and PME were frequently used as *serious self-medication* in addition to current medical treatment provides a new perspective on the biomedical ethics debate about PNE. If the target group are not solely healthy people aiming to enhance their performance at work or while studying but also people with mental deficits aiming to perform normal, the impact of PNE on inequalities might differ. In particular,

inequality concerns and questions about the possible exacerbation of existing socio-economic inequalities have been raised (Maslen et al., 2014). However, what if people with a mental disorder engage in PNE to reduce the stress and symptoms associated with their disorder and thus enable themselves to perform at a level equal to that of their healthy counterparts? Given that no safe, effective, and highly priced drug for PNE enters the market, the drugs currently discussed as neuroenhancers are available relatively equally to all socio-economic groups. Earp and colleagues (2014) argued that diminishment can be seen as a form of enhancement. Therefore, drug use to diminish certain higher-order capacities that cause the symptoms of a mental disorder can be classified as PNE and is a *serious self-medication* unless it is recommended by a physician. Inevitably, normative questions would need to be used to define a cut-off point on the continuum between health and disease. However, such a cut-off point does not exist and would not be able to sufficiently take into consideration cultural differences in the concept of health and illness across and even within countries (Laungani, 2007). The absence of this clear cut-off point (Maslen et al., 2014), the individual differences in responses to drugs used for PNE (de Jongh et al., 2008), and the fact that people might obtain the desired prescription or illegal drug from physicians, friends, or via the Internet makes it difficult to legally regulate drug use for enhancement purposes. Maslen and colleagues (2014) suggest that no unambiguous differentiation between treatment and enhancement exists in the vast majority of cases. Therefore, *self-medication* with PCE and PME is also an unsolved issue that needs further consideration. If the bioethical debate is to be moved forward, a better understanding of the strong link between mental health and the non-competitive interests of PCE and PME users needs to be developed.

The few healthy PCE users who were identified showed self-efficacy scale values that were similar to or even higher than those of non-users. For those users, PCE seems to be a lifestyle choice, as Racine and Forlini suggest (2008). PCE users appear to be conscious of

their abilities and, in line with the drug instrumentalization theory (Wolff and Brand, 2013), they use the desirable functionalities of psychoactive substances as an additional resource.

Returning to the hypothesis that was posed at the beginning of the study, the findings revealed that both PCE and PME were associated with stress. An unanticipated finding was that time pressure and negative work aspects were not predictors of PCE and PME in the overall model. Only long-term stress and frequent stress predicted PCE and PME. Furthermore, the high prevalence of past-year cannabis use in the PCE and PME users demonstrated that such drug use is likely to be their stress management strategy and a form of *moderate self-medication*.

First, this study is one of the largest studies of pharmacological neuroenhancement, and the weighting procedures used ensured that the results were representative of the Swiss population. Second, participants with a current or past diagnosis of a mental disorder were included in the study, whereas many previous studies only focused on healthy individuals (Barrett et al., 2008). The important mechanism of s*elf-medication* in both healthy and PCE and PME users with mental disorders was unique and progressive. Given that the healthy PCE users in most previous studies were almost all students, the present investigation was the first to consider deficits in PME users in the general population.

The main limitation of the current study is its cross-sectional design, which did not allow the causal associations between the predictors to be conclusively examined. However, the *self-medication* hypothesis was supported, which allowed the interpretation of the findings. A further limitation is that the PCE users and the participants who reported both PCE and PME were modeled within one single group to increase the statistical power and strengthen the prediction models. However, the PCE group is the most commonly studied group (Maier and Schaub, 2015; Maslen et al., 2014); therefore, this grouping seems acceptable. Furthermore, regular PCE users show a very specific personality profile (Maier et al., 2015), hence it makes

sense to compare this group with nonusers and PME users only. The present study assessed stress at work and in education as possible predictors of PNE. Because of the length of the questionnaire, only single items (no validated scales) were used to assess stress to prevent participant dropouts. Retrospectively, the inclusion of at least one validated stress scale may have increased the predictive power of the overall model.

The understanding of PCE and PME as s*elf-medication* and as functional means of achieving certain ends related to performance or health, as Wolff et al. (2014) suggest, has important implications for further research and policy. The findings of the present study indicate a large gap between healthy, self-confident PNE users experiencing temporary stress and unconfident PNE users with persistently low self-efficacy and high stress or even pathological symptoms. Consistent with previous Swiss studies of PNE, only a small number of healthy people who reported PNE and recreational drug use as a lifestyle choice were found (Maier et al., 2013). Thus, future research should focus on complex problems in disadvantaged individuals (e.g., those with low self-efficacy, insufficient coping strategies, or mental disorders) who self-medicate without or beyond an indicated prescription. A careful diagnosis of mental health disorders, dialogue about treatment options, and investigation of social pressure to perform (e.g., in accordance with the perceived averages of healthy colleagues) might prevent PCE and PME among patients. The communication of risks and medication interactions is strongly recommended to achieve beneficial treatment outcomes regarding the absence of additional *serious self-medication*.

Various predictor variables for PCE and PME were identified in this study. Consideration of these variables may help identifying potential PCE and PME users for whom measures to prevent drug abuse and manage stress are most appropriate. Furthermore, causal theories concerning engagement in PCE and PME might be examined in longitudinal studies taking into account the identified predictors. Especially *serious self-medication* but also moderate

self-medication seem to be suitable candidates for disentangling causal explanations for engagement in PCE and PME and thus advancing the neuroenhancement debate.

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Table 1

Characteristics of the study population with and without current PNE (12 months) and the univariate multinomial associations of each variable with PME only and PCE with or without PME (reference group: no PCE/PME during the past 12 months [no current PNE])

	No current PNE	PME only, 12 months		PCE with and without PME, 12 months	
	n = 9,956	*n* = 146	OR (95%CI)	*n* = 69	OR (95%CI)
Sex					
Male (Ref.)	98.2% (5,335)	1.0% (56)		0.8% (42)	
Female	97.5% (4,621)	1.9% (90)	1.86 (1.33-2.60)**	0.6% (27)	0.74 (0.46-1.21)
Age in years					
15-24 (Ref.)	96.7% (1,814)	1.8% (33)		1.6% (30)	
25-34	98.1% (2,104)	1.2% (25)	0.66 (0.39-1.12)	0.7% (15)	0.42 (0.23-0.79)**
35-44	98.0% (2,206)	1.6% (37)	0.92 (0.57-1.47)	0.4% (8)	0.22 (0.10-0.48)**
45-54	98.2% (2,377)	1.4% (34)	0.79 (0.49-1.28)	0.4% (9)	0.24 (0.12-0.50)**
55-74	98.4% (1,454)	1.1% (17)	0.64 (0.35-1.15)	0.5% (7)	0.30 (0.13-0.68)**
Professional activity					
Student (Ref.)	96.1% (1,321)	1.8% (25)		2.1% (28)	
Full-time work ≥ 90%	98.4% (5,456)	1.2% (67)	0.64 (0.41-1.02)	0.4% (21)	0.18 (0.10-0.31)**
Part-time work < 90%	97.7% (3,169)	1.7% (54)	0.90 (0.56-1.45)	0.6% (19)	0.28 (0.16-0.50)**
Relationship					
None / temporary (Ref.)	97.0% (2,703)	2.2% (62)		0.8% (23)	
Stable	98.2% (7,252)	1.1% (85)	0.51 (0.37-0.71)**	0.6% (46)	0.75 (0.46-1.25)
Children in the household					
None (Ref.)	97.5% (6,371)	1.6% (105)		0.9% (58)	
At least one <18 years old	98.6% (3,585)	1.1% (41)	0.69 (0.48-1.00)*	0.3% (11)	0.32 (0.17-0.62)**
Drug use past 12 months					
No tobacco (Ref.)	98.4% (6,799)	1.1% (78)		0.4% (30)	
Tobacco	96.7% (3,157)	2.1% (68)	1.89 (1.36-2.62)**	1.2% (39)	2.77 (1.71-4.47)**
No alcohol (Ref.)	97.7% (966)	1.4% (13)		0.9% (9)	
Alcohol	97.9% (8,990)	1.4% (133)	1.07 (0.61-1.88)	0.6% (59)	0.69 (0.34-1.38)
No cannabis (Ref.)	98.3% (9,248)	1.2% (114)		0.5% (47)	
Cannabis	92.9% (708)	4.2% (32)	3.68 (2.47-5.48)**	2.9% (22)	6.12 (3.66-10.21)**
No other illegal drugs (Ref.)	98.0% (9,848)	1.4% (142)		0.5% (54)	
Other illegal drugs [a]	85.1% (108)	3.3% (4)	2.69 (1.00-	11.6% (15)	24.84 (13.53-

			7.25)**		45.60)**
Stress					
Not long-term (Ref.)	99.2% (5,049)	0.5% (26)		0.3% (16)	
Long-term	96.6% (4,907)	2.4% (120)	4.81 (3.14-7.37)**	1.0% (53)	3.45 (1.97-6.06)**
Frequency 12 months scale 1-5	3.2 (0.9)	4.1 (0.9)	2.89 (2.38-3.51)**	3.9 (1.0)	2.12 (1.63-2.76)**
Time pressure scale 1-6	3.2 (1.2)	3.6 (1.2)	1.30 (1.14-1.48)**	3.5 (1.2)	1.21 (1.00-1.46)*
Negative aspects scale 1-5	2.4 (0.6)	2.7 (0.7)	2.16 (1.70-2.73)**	2.6 (0.7)	1.90 (1.34-2.69)**
Self-efficacy scale 10-40	30.0 (4.1)	27.0 (0.7)	0.86 (0.83-0.89)**	28.1 (5.9)	0.90 (0.86-0.95)**
Perceived health scale 1-5	3.5 (0.8)	2.8 (0.9)	0.33 (0.27-0.41)**	3.0 (0.9)	0.45 (0.33-0.61)**
Current medical treatment for a mental disorder [b]					
No	98.9% (9,665)	0.7% (65)		0.4% (39)	
Yes	72.4% (291)	20.3% (81)	41.71 (29.49-58.99)**	7.4% (30)	25.06 (15.33-40.96)**

Note. Data are % (n) or mean (*SD*). PCE = pharmacological cognitive enhancement; PME = pharmacological mood enhancement; PNE = pharmacological neuroenhancement.

[a] Cocaine, ecstasy (MDMA), amphetamines (speed), ketamine, GHB/GBL
[b] ADHD, narcolepsy, depression, anxiety disorder, dependency

* $p < 0.05$; ** $p < 0.01$

Table 2

Multiple prediction models for PME and PCE with and without PME in the past 12 months (reference group: no PME/PCE in the past 12 months)

	PME only, 12 months *n* = 146 OR (95%CI)	PCE with and without PME, 12 months *n* = 69 OR (95%CI)
Model 1 (socio-demographic data)		
Sex		
Male (Ref.)		
Female	1.69 (1.17-2.45)**	0.52 (0.30-0.89)*
Professional activity		
Student (Ref.)		
Full-time work ≥ 90%	1.15 (0.67-1.97)	0.37 (0.19-0.71)**
Part-time work < 90%	0.99 (0.59-1.64)	0.14 (0.07-0.27)**
Relationship		
None/temporary (Ref.)		
Stable	0.61 (0.42-0.87)**	1.99 (1.12-3.54)*
Children in the household		
None (Ref.)		
At least one <18 years old	0.91 (0.61-1.34)	0.41 (0.20-0.83)*
Drug use past 12 months		
No cannabis (Ref.)		
Cannabis	3.54 (2.28-5.49)**	1.94 (1.02-3.70)*
No other illegal drugs (Ref.)		
Other illegal drugs [a]	1.14 (0.40-3.24)	15.47 (7.26-33.00)**
Perceived health scale 1-5	0.34 (0.28-0.43)**	0.42 (0.31-0.58)**
Model 2 (*moderate self-medication*)		
Socio-demographic data (model 1)		
Stress		
Not long-term (Ref.)		
Long-term	2.00 (1.24-3.19)**	1.98 (1.04-3.76)*
Frequency 12 months, scale 1-5	1.81 (1.45-2.27)**	1.54 (1.13-2.11)**
Self-efficacy, scale 10-40	0.92 (0.88-0.95)**	0.96 (0.90-1.02)
Model 3 (*serious self-medication*)		
Socio-demographic data (model 1)		
Current medical treatment for a mental disorder [b]		
No		
Yes	32.77 (22.20-48.38)**	24.91 (13.76-45.09)**

Note. N = 10,171. Model 1 R^2 = .03 (Cox & Snell), .14 (Nagelkerke). Model χ^2 (16) = 296.898, p < .001; Model 2 R^2 = .04 (Cox & Snell), .19 (Nagelkerke). Model χ^2 (22) = 409.561, p < .001; Model 3 R^2 = .06 (Cox & Snell), .30 (Nagelkerke). Model χ^2 (18) = 656.208, p < .001; PCE = pharmacological cognitive enhancement; PME = pharmacological mood enhancement.

[a] Cocaine, ecstasy (MDMA), amphetamines (speed), ketamine, GHB/GBL
[b] ADHD, narcolepsy, depression, anxiety disorder, dependency

* p < 0.05; **p < 0.01

Table 3

Overall multiple prediction model for PME and PCE with and without PME in the past 12 months (reference group: no PME/PCE in the past 12 months)

	PME only, 12 months *n* = 146 OR (95%CI)	PCE with and without PME, 12months *n* = 69 OR (95%CI)
Sex		
Male (Ref.)		
Female	1.58 (1.06-2.36)*	0.51 (0.29-0.89)*
Professional activity		
Student (Ref.)		
Full-time work ≥ 90%	1.17 (0.68-2.01)	0.16 (0.08-0.32)**
Part-time work < 90%	0.95 (0.53-1.71)	0.28 (0.13-0.57)**
Relationship		
None/temporary (Ref.)		
Stable	0.71 (0.47-1.05)	2.30 (1.26-4.17)**
Children in the household		
None (Ref.)		
At least one <18 years old	0.89 (0.58-1.36)	0.38 (0.19-0.78)**
Drug use 12 months		
No cannabis (Ref.)		
Cannabis	4.73 (2.89-7.23)**	2.86 (1.48-5.52)**
No other illegal drugs (Ref.)		
Other illegal drugs [a]	1.01 (0.33-3.12)	11.99 (5.48-26.22)**
Stress		
Not long-term (Ref.)		
Long-term	2.03 (1.24-3.31)**	2.12 (1.10-4.07)*
Frequency 12 months, scale 1-5	1.61 (1.28-2.02)**	1.43 (1.06-1.94)*
Self-efficacy, scale 10-40	0.93 (0.90-0.97)**	0.98 (0.93-1.04)
Current medical treatment for a mental disorder [b]		
No		
Yes	27.64 (18.78-40.68)**	23.17 (12.91-41.58)**

Note. N = 10,171. R^2 = .07 (Cox & Snell), .33 (Nagelkerke). Model χ^2 (22) = 708.669, $p < .001$; PCE = pharmacological cognitive enhancement; PME = pharmacological mood enhancement; PNE = pharmacological neuroenhancement.

[a] Cocaine, ecstasy (MDMA), amphetamines (speed), ketamine, GHB/GBL
[b] ADHD, narcolepsy, depression, anxiety disorder, dependency

* $p < 0.05$; ** $p < 0.01$

Table 4

Lifetime prevalence of specified mental disorders and associated medical treatment and medication misuse across study groups

	No current PNE *n* = 9,956	PME only, 12 months *n* = 146	PCE with and without PME, 12 months *n* = 69
Depression			
Lifetime diagnosis	12.0% (1,194)	72.2% (106)	55.1% (38)
Received medical treatment	8.0% (796)	70.4% (103)	44.4% (31)
Current medical treatment	2.2% (221)	51.9% (76)	29.6% (20)
Ever misused	0.3% (33)	6.2% (9)	10.9% (7)
ADHD			
Lifetime diagnosis	1.7% (174)	6.0% (9)	28.6% (20)
Received medical treatment	0.6% (62)	2.6% (4)	19.1% (13)
Current medical treatment	0.2% (22)	0	15.9% (11)
Ever misused	0.1% (7)	0.9% (1)	4.4% (3)
Anxiety disorder			
Lifetime diagnosis	8.3% (822)	42.7% (62)	24.4% (17)
Received medical treatment	3.4% (338)	31.8% (46)	9.7% (7)
Current medical treatment	0.8% (82)	20.7% (30)	6.9% (5)
Ever misused	0.2% (17)	5.3% (8)	2.9% (2)
Substance use disorder			
Lifetime diagnosis	3.7% (372)	8.3% (12)	19.8% (14)
Received medical treatment	0.4% (36)	4.0% (6)	5.6% (4)
Current medical treatment	0.1% (9)	0.8% (1)	1.6% (1)
Ever misused	0.1% (7)	0.8% (1)	2.9% (2)
Narcolepsy			
Lifetime diagnosis	1.0% (100)	4.0% (6)	5.2% (4)
Received medical treatment	0.3% (34)	1.9% (3)	5.2% (4)
Current medical treatment	0.1% (10)	0.6% (1)	2.0% (1)
Ever misused	0.03% (3)	0.7% (1)	0

Note. PCE = pharmacological cognitive enhancement; PME = pharmacological mood enhancement; PNE = pharmacological neuroenhancement.

Highlights

• Pharmacological neuroenhancement (PNE) as self-medication in health and disease.

• Representative data of employees and students (>10,000) to identify predictors of PNE.

• Drug use for mood enhancement is more prevalent than for cognitive enhancement.

• Mental health, illegal drug use, and stress are important predictors of PNE.

Contributors

MPS and LJM designed the study based on the findings of their previous feasibility study on pharmacological neuroenhancement in Switzerland. MPS and LJM collaborated with the LINK institute to implement, pilot, and validate the online survey, and to collect the data. LJM analyzed and interpreted the data. SH and MPS provided support for the data analysis. LJM has drafted the manuscript and all authors contributed to revisions and approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

Author disclosures

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