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Research Paper

Pharmacological cognitive enhancement among non-ADHD individuals—A cross-sectional study in 15 countries

Larissa J. Maier[a,*], Jason A. Ferris[b], Adam R. Winstock[c,d]

[a] Department of Psychiatry, University of California, San Francisco, USA
[b] Institute for Social Science Research, The University of Queensland, Australia
[c] Institute of Epidemiology & Health Care, Faculty of Population Health Sciences, University College London
[d] Global Drug Survey Ltd, London, UK

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ABSTRACT

Background: Psychoactive substance use aiming at increased performance at work or while studying, usually referred to as pharmacological cognitive enhancement (PCE), has been extensively researched in recent years. While large scale national studies have tried to assess the prevalence of PCE among the general population, cross-cultural comparisons have been hampered by the different definitions and designs included. In addition, the non-medical use of prescription drugs indicated to treat the symptoms of the Attention Deficit Hyperactivity Disorder (ADHD) has been the focus of discussion, yet no study has addressed the association between ADHD rates, prescribing behaviour and PCE yet.

Methods: The Global Drug Survey is an annually conducted anonymous web survey on substance use. Two data sets from male and female Global Drug Survey (GDS) participants aged 16 to 65 years with no previous ADHD diagnosis were analysed to assess12-month PCE in 15 countries. GDS2015 (n = 79,640) examined the patterns of and motives for stimulant PCE, while GDS2017 (n = 29,758) focused on both the use of stimulant and sedative drugs for PCE

Results: When comparing the study samples 2015 and 2017, PCE with prescription and illegal stimulants and modafinil increased across all countries. People who used stimulant drugs and modafinil for PCE rated the perceived effect on cognitive performance most beneficial, while alcohol was the substance with the most adverse effect.

Conclusion: The analysis of data on stimulant use for PCE in the largest global sample highlights relatively low-risk PCE use patterns except for participants with illegal stimulant use for PCE. The globalisation of ADHD, physicians' prescribing behaviour and changes in drug policy are likely to influence the country-specific rate of PCE among non-ADHD individuals what calls for further investigation.

Background

Pharmacological cognitive enhancement (PCE), refers to the use of prescription drugs, alcohol and illegal drugs for the purpose of improved performance at work or while studying and has become an increasing area of debate and research (Maier & Schaub, 2015; Maslen, Faulmüller, & Savulescu, 2014). Media articles portrayed PCE among healthy students as common and increasing (Partridge, Bell, Lucke, Yeates, & Hall, 2011), while scientific evidence for such an increase remained weak, (Maier & Schaub, 2015). Although the prevalence of PCE has been addressed in several large scale surveys, cross-cultural comparisons have been hampered by the different definitions used in these studies (Maier, Haug, & Schaub, 2016; Maier & Schaub, 2015; Mazanov, Dunn, Connor, & Fielding, 2013). For example, the lifetime prevalence of the non-medical use of prescription stimulants in the United States varied from 5% to 35% (Wilens et al., 2008), without specifying the purpose. German studies found lower prevalence rates, starting from 0.8% (Franke et al., 2011) and 2.0% of university students (Mache, Eickenhorst, Vitzthum, Klapp, & Groneberg, 2012).

Methylphenidate, a prescription stimulant indicated for the treatment of attention deficit hyperactivity disorder (ADHD), is the prescription stimulant most commonly used nonmedically for PCE among European students (Mache et al., 2012; Maier, Liechti, Herzig, & Schaub, 2013; Maier & Schaub, 2015; Singh, Bard, & Jackson, 2014). However, regular methylphenidate use among non-ADHD individuals who presumably benefit from PCE use is rare (Maier et al., 2015). The

* Corresponding author.
E-mail addresses: larissa.maier@ucsf.edu (L.J. Maier), j.ferris@uq.edu.au (J.A. Ferris), adam@globaldrugsurvey.com (A.R. Winstock).

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few regular non-ADHD individuals with PCE experience showed high trait impulsivity (Maier et al., 2015) and were about seven times more likely to be symptomatic for ADHD when compared to the control group (Peterkin, Crone, Sheridan, & Wise, 2011). Substance use can be a form of self-medication to address psychological problems and sleep deprivation (Khantzian, 1997). Hence, it often remains unclear where treatment ends and where enhancement begins (Maslen et al., 2014). In particular, stimulant medications have a high potential for non-medical use and diversion (Wilens et al., 2008). Approximately five million U.S. adults had used prescription stimulants nonmedically without developing a disorder (Compton, Han, Blanco, Johnson, & Jones, 2018). Moreover, the faster-than-predicted growth of the global market for ADHD medications as a consequence of increased use in the United States, in Canada and in Australia (Scheffler, Hinshaw, Modrek, & Levine, 2007) had also influenced European policies. Indeed, the globalisation of ADHD, the rise of stimulant use for PCE, and the high disparity between national ADHD prevalence rates have raised concerns about the validity of ADHD diagnoses and the ethics of prescribing stimulants in general (Singh, Filipe, Bard, Bergey, & Baker, 2013). The disparity can be partially explained by different diagnostic thresholds and treatment expectations of clinicians, health care providers, teachers, parents, and treatment seeking patients themselves (Hamed, Kauer, & Stevens, 2015; Singh et al., 2013). A recent systematic review and meta-regression found no evidence for an actual increase in the number of children who meet the ADHD criteria (Polanczyk, Willcutt, Salum, Kieling, & Rohde, 2014). Nevertheless, country differences exist. For example, ADHD is diagnosed frequently among children in the United States (10.1% among 5–17 years old, National Center for Health Statistics, 2015) and seen as a biological disorder with indicated stimulant drug treatment. In France, ADHD diagnoses are less prevalent (3.5%–5.6%, Lecendreux, Konofal, & Faraone, 2011) and although ADHD is identified as medical condition the primary treatment modality is psychosocial rather than pharmacological (Conrad & Bergey, 2014; Wedge, 2015). The unequal institutional values of national health departments are linked to differences in approval for specific prescription drugs and also to the physicians' prescribing behaviour (Banjo, Nadler, & Reiner, 2010; Hotze, Shah, Anderson, & Wynia, 2011; Ott, Lenk, Miller, Neuhaus Bühler, & Biller-Andorno, 2012) and the accessibility for prescription stimulants in general (Varga, 2012). For example, Adderall™ is approved for the treatment of ADHD symptoms in the U.S. and non-medical use among American students is prevalent (Varga, 2012). In most European countries, the medication is not approved due to potential harmful side effects of nonmedical use. While the drug might in fact increase alertness and wakefulness in non-ADHD individuals, creativity might be impaired (Farah, Haimm, Sankoorikal, Smith, & Chatterjee, 2009). As with other stimulant drugs, the effects are highly dose-dependent (Husain & Mehta, 2011).

Modafinil was shown to have cognitive enhancing properties in healthy individuals (Esposito et al., 2013; Repantis, Schlattmann, Laisney, & Heuser, 2010), more than methylphenidate, yet with potential adverse effects on emotion processing (Schmidt et al., 2018). While modafinil was rarely used as cognitive enhancer in Switzerland (Maier et al., 2016, 2013), the substance was the most commonly used prescription drug for PCE among UK students (Singh et al., 2014). Notwithstanding, beta-blockers and psychoactive substances with generally sedative effects, such as alcohol, cannabis and benzodiazepines are also used for direct or indirect cognitive enhancement, to reduce nervousness and test anxiety previous to exams or presentations as well as to increase relaxation after school or work to perform better the next day (Liakoni, Schaub, Maier, Glauser, & Liechti, 2015; Maier et al., 2016, 2013; Middendorff, Poskowsky, & Becker, 2015; Middendorff, Poskowsky, & Isserstedt, 2012). Although prescription stimulants and modafinil were included in most PCE studies, a reliable cross-country comparison of recent use (12 months) has been lacking so far. Therefore, the present study aimed to explore a) the extent of stimulant and other substance use for cognitive enhancement per country among participants of the Global Drug Survey (GDS) as well as b) the fluctuations in PCE per country between the two successive measurements.

Equally

Overall, people with a history of illegal drug use showed higher rates of non-medical prescription drug use and PCE (Maier et al., 2016, 2013; McCabe, 2008). A representative study of the Swiss general population revealed that participants who had used cannabis were twice as likely to report PCE; the lifetime prevalence of cannabis use was 52% among people with PCE experience versus 31% among those unexperienced (Maier et al., 2016). Lifetime use of cocaine, MDMA, illegal amphetamine, GHB/GBL, and ketamine were even better predictors for PCE since participants who had used any of these drugs were six up to twenty times more likely to report PCE (Maier et al., 2016). Due to the recruitment strategy of the GDS, GDS datasets consist of participants who have ever used at least one drug (Barratt et al., 2017). Thus, we hypothesized that, for the whole sample, the percentage of stimulant use for PCE among non-ADHD participants will be higher than the percentages observed in published studies: current studies suggest that the 12-month PCE rates vary between 1% to 20% among students (Dietz et al., 2013; Eickenhorst, Vitzthum, Klapp, Groneberg, & Mache, 2012; Franke et al., 2011; Maier et al., 2013; Singh et al., 2014) and 3% to 7% for employees (Compton et al., 2018; Kordt, 2009, 2015; Maier et al., 2016).

By country, we also hypothesized that the percentage of PCE use among non-ADHD participants is greater in countries with higher prevalence of ADHD given the common diversion of prescription stimulants (Benson, Flory, Humphreys, & Lee, 2015; Kaye & Darke, 2012; Wilens et al., 2008). Furthermore, we assumed that illegal stimulants, such as amphetamine and cocaine, are the main stimulant drugs used for PCE in countries such as France, where stimulant treatment for ADHD is less popular (Conrad & Bergey, 2014; Wedge, 2015). Finally, we explored predictors for the non-medical use of prescription stimulants, modafinil and illegal stimulants for PCE, since this behaviour bears the highest health risks due to unknown quality and quantity of the drugs used.

Methods

The global drug survey (GDS)

The GDS is a cross-sectional anonymous web survey on substance use behaviour widely promoted by a range of media partners including national newspapers, magazines, websites, and social media (Barratt et al., 2017). Each year between November and January the following year, GDS recruits a non-probability sample of respondents, 16 years and over, who have recreationally used legal and/or illegal drugs. The core questionnaire consists of an extensive substance use screen assessing patterns of use, motives for use and harms associated with using drugs. Substance use for cognitive enhancement was first introduced in GDS2015 and again, a subsection of questions were repeated in GDS2017. The GDS surveys have been translated into 10 languages (Barratt et al., 2017). Analysis of the data were based on participants aged 16 to 65 years, who indicated being male or female (transgendered persons were excluded from analysis), with no self-reported ADHD history for reasons of comparison of previous data and, to allow for country comparisons, where at least 1000 responses per country (in the GDS 2015 data) where captured (15 countries in total; n = 79,640). Data from GDS2017 included all respondents, from the 15 countries identified from GDS 2015 following the same inclusion criteria (n = 29,758) The second sample size is remarkably smaller because the module on substance use for cognitive enhancement has only been temporary included for the first month of the GDS2017 and then been cut in order to reduce survey length.

Specific module on substance use for cognitive enhancement

GDS2015 introduced a specific module on stimulant drug use for cognitive enhancement. Participants were asked whether they had ever used any prescription or illegal stimulant to increase performance at work or while studying. If so, they had to indicate lifetime, last year, and last month non-medical use of methylphenidate, modafinil, dexamphetamine (Adderall™), cocaine, illegal amphetamine, and illegal methamphetamine for cognitive enhancement purposes. Participants who reported last year use of at least one of these substances for the purpose of cognitive enhancement at work or while studying were then asked about the specific patterns of use of the drug most commonly used for PCE. Participants were asked to indicate their primary motivation of use (to improve performance at work, to improve performance while studying, or to socialise and to be intoxicated). They were asked to rate the perceived efficacy of the stimulant drugs used for PCE by choosing one of four categories (more than expected, as expected, less than expected, or much less than expected). Participants were asked how they obtained the stimulants when used in the last 12 months (prescribed by a physician, given by a family member who had a prescription, given by a friend, bought from a dealer, or bought on the internet. If a respondent indicated a physician had prescribed a script they were asked whether the physician had discussed the potential risks and side effects of the medication with them beforehand. Finally, participants who indicated stimulant use for PCE in the last 12 months were asked whether they would like to use less drugs for PCE in the next 12 months and whether they would like to seek help to reduce their stimulant use for cognitive enhancement.

The GDS2017 aimed to assess substance use for cognitive enhancement in the last 12 months more quickly and included additional substances – sedatives – as previous research had shown that students and employees use sedative substances to improve sleep and relaxation to increase cognitive performance the next day (Maier et al., 2016, 2013; Middendorff et al., 2015). Thus, participants were asked had they used prescription stimulants (e.g., methylphenidate, dexamphetamine), modafinil, beta-blockers, benzodiazepines or prescription sleeping pills, alcohol, cannabis, or illegal stimulants (e.g., amphetamine, cocaine), in the last 12 months, to increase their cognitive performance at work or while studying without having a medical indication to do so. For the substances used for cognitive enhancement in the last 12 months, participants had to indicate whether their cognitive performance under the influence of the substance was perceived as decreased or increased or remained the same.

Statistical analyses

Descriptive statistics were used to describe the distribution for the answer categories of the socio-demographic variables such as age in years (also categorised as 16–17, 18–30, and 31–65 years of age), sex (female and male), country of residence (Austria, Australia, Belgium, Brazil, Canada, France, Germany, Hungary, Ireland, New Zealand, Portugal, Switzerland, The Netherlands, The United Kingdom, and The United States of America), the 12-month use of illegal drugs (cannabis, cocaine, MDMA, illegal amphetamine, illegal methamphetamine, ketamine, LSD, and psilocybin), and current student status. As the sample was opportunistic, analyses focused on exploring relationships between demographics, stimulant use for cognitive enhancement and other variables of interest at the individual respondent level. Proportions were compared using Pearson's $c2$ test. For group comparisons, $p < .050$ was set as the significance level. In addition, logistic regression modelling was used to identify and quantify the strength of associations between these independent variables and the use of prescription stimulants, modafinil and/or illegal stimulants for PCE. All analyses were undertaken in IBM SPSS version 24.

Table 1
Sample characteristics of non-ADHD individuals who participated in GDS2015 (N = 79,640) and GDS2017 (N = 29,758) and answered at least the first question of the module on substance use for cognitive enhancement.

		GDS2015 (N = 79,640)		GDS2017 (N = 29,758)	
		N	%	*N*	%
Sex	Male	47,952	60,2%	20,475	68,8%
	Female	31,688	39,8%	9283	31,2%
Age	16–17 years	3387	4,3%	1341	4,5%
	18–30 years	50,793	63,8%	16,195	54,4%
	31–65 years	25,460	32,0%	12,222	41,1%
Student[a]	No	44,293	56,6%	17,941	64,7%
	Yes	33,935	43,4%	9795	35,3%
Illegal drug use	No, never	15,801	19,8%	4141	13,9%
	Yes, but not in the last 12m	16,116	20,2%	5512	18,5%
	Yes, in the last 12m	47,723	59,9%	20,105	67,6%
Country	Australia	3341	4,2%	1830	6,1%
	Austria	1539	1,9%	2046	6,9%
	Belgium	1681	2,1%	249	0,8%
	Brazil	4741	6,0%	977	3,3%
	Canada	1091	1,4%	2355	7,9%
	France	7701	9,7%	173	0,6%
	Germany	28,824	36,2%	10,142	34,1%
	Hungary	4156	5,2%	1221	4,1%
	Ireland	2146	2,7%	149	0,5%
	The Netherlands	4751	6,0%	733	2,5%
	New Zealand	2956	3,7%	1599	5,4%
	Portugal	1144	1,4%	343	1,2%
	Switzerland	5218	6,6%	2457	8,3%
	UK	5617	7,1%	1914	6,4%
	USA	4734	5,9%	3570	12,0%

[a] 1412 And 2019 missing values, percent reported are valid percent.

Results

Sample characteristics

The sample characteristics, by GDS year, are provided in Table 1. Across both years, there were more male than female respondents. The mean age of the sample from 15 countries for GDS 2015 was 29 years (SD = 10.6) and for GDS 2017 was 31 years (SD = 11.9). Roughly one third of the sample from either GDS year were from Germany, the distribution of the sample from other countries ranged between 0.6% (France, GDS 2017) and 12.0% (USA, GDS 2017). From the GDS 2015 sample, two fifths of participants were students; from the GDS 2017 sample one-third were students. Roughly 60% (or more) of all participants from either year had used at least one illegal drug in the last year (Table 1).

Non-medical prescription stimulant use for PCE (12m)

Overall, 3.2% of the GDS2015 and 6.6% of the GDS2017 participants reported the use of prescription stimulants for PCE in the last 12 months. The 12-month rates of PCE with prescription stimulants ranged from 0.8% among Austrian to 18.7% for U.S. participants and from 1.6% among Hungarian to 21.6% among U.S. participants (Table 2a). Prescription stimulant PCE was most common among US, Canadian, Dutch and Belgium non-ADHD individuals with a social interest in illegal drug use (Table 2a). The increase between the two measurements was not significantly different for Irish and Portuguese participants (Table 2a).

Table 2a
Rates of 12-month non-medical prescription stimulant PCE (e.g., methylphenidate, dexamphetamine) among participants of the GDS2015 and GDS2017 and comparison of the two rates in total and by country.

	Pr. stimulant PCE GDS2015[a]		Pr. stimulant PCE GDS2017[b]			
	N	%	*N*	%	$\chi 2$	*p*
Total	2517	3,2%	1975	6,6%	664,910	< .001
Australia	124	3,7%	124	6,8%	24,319	< .001
Austria	12	0,8%	48	2,3%	13,094	< .001
Belgium	60	3,6%	31	12,4%	38,069	< .001
Brazil	149	3,1%	56	5,7%	15,709	< .001
Canada	95	8,7%	295	12,5%	10,834	< .001
France	45	0,6%	8	4,6%	41,305	< .001
Germany	437	1,5%	305	3,0%	89,309	< .001
Hungary	6	0,1%	20	1,6%	43,753	< .001
Ireland	51	2,4%	5	3,4%	0,561	0.408
The Netherlands	391	8,2%	99	13,5%	21,727	< .001
New Zealand	55	1,9%	47	2,9%	5516	< .050
Portugal	13	1,1%	6	1,7%	0,786	0.410
Switzerland	94	1,8%	63	2,6%	4849	< .050
UK	98	1,7%	97	5,1%	62,506	< .001
USA	887	18,7%	771	21,6%	10,417	< .010

[a] Participants who indicated having ever used any prescription or illegal stimulant drug to increase performance at work or while studying reported the use of methylphenidate and/or dexamphetamine for PCE in the last 12 months.
[b] Participants were asked directly, whether they had used a prescription stimulant (e.g., methylphenidate, dexamphetamine) non-medically in the last 12 months to increase cognitive performance while studying or at work.

Table 2b
Rates of 12-month non-medical Modafinil PCE among participants of the GDS2015 and GDS2017 and comparison of the two rates in total and by country.

	Modafinil PCE GDS2015[a]		Modafinil PCE GDS2017[b]			
	N	%	*N*	%	$\chi 2$	*p*
Total	477	0,6%	720	2,4%	663,491	< .001
Australia	71	2,1%	100	5,5%	41,235	< .001
Austria	2	0,1%	20	1,0%	10,345	< .010
Belgium	4	0,2%	7	2,8%	25,342	< .001
Brazil	22	0,5%	9	0,9%	3140	0.200
Canada	9	0,8%	64	2,7%	12,881	< .001
France	10	0,1%	4	2,3%	45,401	< .010
Germany	66	0,2%	115	1,1%	132,875	< .001
Hungary	3	0,1%	14	1,1%	34,567	< .001
Ireland	11	0,5%	3	2,0%	5176	0.058
The Netherlands	12	0,3%	18	2,5%	56,652	< .001
New Zealand	5	0,2%	8	0,5%	3999	0.076
Portugal	2	0,2%	2	0,6%	1,64	0.229
Switzerland	12	0,2%	19	0,8%	12,258	< .010
UK	182	3,2%	191	10,0%	137,715	< .001
USA	66	1,4%	146	4,1%	59,437	< .001

[a] Participants who indicated having ever used any prescription or illegal stimulant drug to increase performance at work or while studying reported the use of modafinil for PCE in the last 12 months.
[b] Participants were asked directly, whether they had used modafinil in the last 12 months to increase cognitive performance while studying or at work.

Non-medical modafinil use for PCE (12m)

PCE with modafinil in the last 12 months was relatively low with 0.6% in GDS2015 where only people who indicated ever use of prescription or illegal drugs for PCE were directed to the substance question and 2.4% in GDS2017 when all people were asked the question. Modafinil use for PCE was most common among UK, Australian and Canadian participants (Table 2b). The increase between the two points of data collection was not significantly different for Brazilian, Irish, New Zealand and Portuguese participants (Table 2b).

Table 2c
Rates of 12-month illegal stimulant PCE (e,g., cocaine, amphetamine or methamphetamine) among participants of the GDS2015 and GDS2017 and comparison of the two rates in total and by country.

	Illegal stimulant PCE GDS2015[a]		Illegal stimulant PCE GDS2017[b]			
	N	%	*N*	%	$\chi 2$	*p*
Total	1681	2,1%	2484	8,3%	2300,760	< .001
Australia	71	2,1%	132	7,2%	81,156	< .001
Austria	23	1,5%	138	6,7%	56,449	< .001
Belgium	46	2,7%	27	10,8%	39,165	< .001
Brazil	86	1,8%	63	6,4%	68,552	< .001
Canada	36	3,3%	291	12,4%	71,209	< .001
France	174	2,3%	22	12,7%	76,230h	< .001
Germany	494	1,7%	556	5,5%	406,297	< .001
Hungary	116	2,8%	131	10,7%	135,679	< .001
Ireland	20	0,9%	24	16,1%	170,629	< .001
The Netherlands	198	4,2%	103	14,1%	119,600	< .001
New Zealand	22	0,7%	53	3,3%	42,333	< .001
Portugal	12	1,0%	20	5,8%	28,657	< .001
Switzerland	71	1,4%	146	5,9%	127,622	< .001
UK	104	1,9%	254	13,3%	411,131	< .001
USA	208	4,4%	524	14,7%	267,791	< .001

[a] Participants who indicated having ever used any prescription or illegal stimulant drug to increase performance at work or while studying reported the use of cocaine, amphetamine, and/or methamphetamine for PCE in the last 12 months.
[b] Participants were asked directly, whether they had used an illegal stimulant (e.g., cocaine, amphetamine) in the last 12 months to increase cognitive performance while studying or at work.

Illegal stimulant use for PCE (12m)

In GDS2015, only 2.1% of the sample indicated the use of illegal stimulants for PCE in the last 12 months. This rate increased to 8.3% in GDS2017 when illegal drug use explicitly for cognitive enhancement purposes was asked directly. The lowest rates were found among participants from New Zealand, Portugal and the three German-speaking European countries (Table 2c). Importantly, 7.1% ($n = 94$) of GDS2015 participants who used mainly illegal stimulants for PCE reported daily use in the last year and 30.3% ($n = 400$) reported use at least once a week.

Patterns of and motives for PCE

The patterns of and motives for PCE with stimulant drugs or modafinil are described in Table 3 and compared by sex. The patterns of use did not differ significantly between male and female participants with PCE experience, yet the motives did. Overall, female participants engaging in PCE were more likely to use the substances as study aid, to increase stamina, to reduce fatigue, to cope with stress and to lose weight, while males were more likely to use the drugs additionally to get high or to increase their sexual performance (Table 3). About a quarter of people who used substances for PCE in the last 12 months would like to reduce PCE in the next year, but less than 3% would like to seek help (Table 3). Daily stimulant use for PCE was uncommon. Two third of those engaged in PCE reported up to 10 occasions in the last year (Table 3). The most common pattern of PCE use among non-ADHD individuals was the use for a period of one or two weeks before and during exams or a very busy period at work once or twice a year (Table 3). According to the findings of GDS2015, the main source of supply for stimulant drugs for non-ADHD participants was the circle of friends (47.8%). One in ten indicated that a dealer or the internet were

Table 3
Patterns of PCE use in the last 12 months, primary motivation for PCE and willingness to reduce use among GDS2015 participants who reported the use of prescription stimulants, modafinil or illegal stimulants for cognitive enhancement in the last 12 months.

		Male PCE 12 m		Female PCE 12 m			
		N	%	*N*	%	$\chi 2$	*p*
PCE occasions last 12 m (n = 3699)	Once	347	15,3%	251	17,6%	7613	0.107
	2–10x	1069	47,0%	688	48,3%		
	11–50x	595	26,2%	326	22,9%		
	51–100x	151	6,6%	97	6,8%		
	100x	112	13,5%	63	4,4%		
PCE frequency last 12 m (n = 3665)	(Almost) Daily	111	4,9%	65	4,6%	14,978	< .060
	3–4 days per week	147	6,5%	79	5,6%		
	1–2 days per week	282	12,5%	168	11,9%		
	Once a month	283	12,5%	153	10,9%		
	For a period of 1–2 weeks before and during exams or busy period 1–2x/year	514	22,8%	371	26,3%		
	For a period of 1–2 weeks before and during exams or a busy period min. 3x/year	233	10,3%	174	12,3%		
	For a period of 3–4 weeks before and during exams or busy period 1–2x/year	120	5,3%	60	4,3%		
	For a period of 3–4 weeks before and during exams or busy period min. 3x/year	107	4,7%	54	3,8%		
	Less than once a month	459	20,3%	285	20,2%		
Primary motivation (n = 3669)	Improve performance at work	530	23,6%	278	19,5%	9660	< .010
	Improve performance while studying	1191	53,0%	817	57,5%		
	Improve socialising	526	23,4%	327	23,0%		
Motives for use (n = 3731)	Concentration	1776	77,4%	1124	78,2%	0,326	0,572
	Help me study	1376	60,0%	933	64,9%	9157	< .010
	Stamina	1132	49,3%	796	55,4%	12,938	< .001
	Fatigue/tiredness	1043	45,5%	721	50,2%	7855	< .010
	Help me work	951	41,5%	580	40,4%	0,437	0,516
	Getting high	717	31,3%	329	22,9%	30,610	< .001
	Socialising	566	24,7%	317	22,1%	3340	0,069
	Boredom	397	17,3%	197	13,7%	8539	< .010
	Coping	295	12,9%	295	20,5%	39,036	< .001
	Emotional distress	240	10,5%	224	15,6%	21,319	< .001
	Relaxation	225	9,8%	123	8,6%	1629	0,224
	Sexual performance	216	9,4%	63	4,4%	32,332	< .001
	Weight loss	181	7,9%	294	20,5%	125,634	< .001
	Medical condition	118	5,1%	88	6,1%	1627	0,211
	Withdrawal	92	4,0%	59	4,1%	0,021	0,932
PCE in the next 12 months (n = 2523)	Would like to use less	427	28,3%	281	27,7%	0,120	0,752
	Would like to seek help	38	2,5%	29	2,9%	0,265	0,615
	Plan to seek help	19	1,3%	14	1,4%	0,074	0,859

their main source (11.8% and 9.1%, respectively). Family members with a prescription (6.1%) and the physician (3.8%) were less common sources for stimulant drugs used for PCE. Notably, a quarter of the non-ADHD participants who had received the stimulants from a physician reported that the physician missed to inform them about the risks and potential side effects of stimulant use.

Associations with recent PCE 12m

The overall prediction model resulting from hierarchical logistic regression ($R^2 = 0.39$) is presented in Table 4 and revealed that the following variables were associated positively with prescription stimulant, modafinil, and/or illegal stimulant use for PCE in the last 12 months Being a student, having used illegal drugs in the last 12 months, in particular illegal stimulants, and having taken the second survey GDS2017 were also positively associated with PCE in the last 12 months and so was country (Table 4).

Increase in recent PCE use (12m) across time

In GDS2015, 4.9% of the sample reported the use of methylphenidate, modafinil, Aderall, cocaine, illegal amphetamine, and/or illegal methamphetamine, while the 12-month use questions were only shown to those who indicated ever use of prescription or illegal drugs for PCE in general. In GDS2017, where all participants were asked whether they had used prescription stimulants, modafinil or illegal stimulants non-medically and explicitly aiming to enhance performance at work or while studying, every seventh participant (13.7%) reported so, which is an increase of 180% (Fig. 1). Interestingly, the relative increase to the findings between the two measurement periods was lowest among U.S. participants who showed the highest rates for PCE for both measurements when compared to participants from other countries (Fig. 1). Similarly, Dutch and Canadian participants with high PCE rates in GDS2015, were below the average increase. The increase in recent PCE among the self-selected samples from France, Ireland, Austria, UK and Hungary was more than 300% (Fig. 1).

Sedative substance use for PCE (12m)

Almost a quarter of the GDS2017 sample indicated last year use of cannabis explicitly to enhance performance at work or while studying (Table 5). This also includes substance use for increased relaxation if it aims at increased work- or study-related performance the next day. Cannabis use for PCE was highest among U.S. and Canadian participants and lowest among those from the three German-speaking countries, New Zealand and Australia (Table 5). Alcohol was placed second and recent use explicitly for PCE ranged from 10.3% of German to 29.4% of Hungarian survey participants (Table 5). Benzodiazepine use

Table 4
Odds ratios (OR) for the overall model of the multivariable associations (fully adjusted results) between participant characteristics and PCE with prescription stimulants, modafinil and/or illegal stimulants in the last 12 months among non-ADHD individuals.

		OR (95%CI)	*p*
Age	Age in years	0,81 (0,75–0,87)	< .001
	Age2	1,01 (1,00–1,01)	< .001
	Age3	1,00 (1,00–1,00)	< .001
Student	No		
	Yes	1,32 (1,25–1,41)	< .001
Illegal drug use 12 m	Cannabis	1,43 (1,34–1,53)	< .001
	MDMA pills	1,54 (1,43–1,66)	< .001
	MDMA powder	1,29 (1,20–1,39)	< .001
	Cocaine	2,48 (2,33–2,65)	< .001
	Amphetamine	3,09 (2,87–3,32)	< .001
	Methamphetamine	2,71 (2,36–3,11)	< .001
	Ketamine	1,20 (1,10–1,30)	< .001
	LSD	1,51 (1,41–1,62)	< .001
	Magic Mushrooms	1,23 (1.14–1,31)	< .001
Country	Australia		
	Austria	0,35 (0,29–0,42)	< .001
	Belgium	0,73 (0,59–0,91)	< .010
	Brazil	0,93 (0,79–1,10)	0.390
	Canada	1,35 (1,16–1,57)	< .001
	France	0,24 (0,20–0,28)	< .001
	Germany	0,39 (0,35–0,45)	< .001
	Hungary	0,49 (0,41–0,58)	< .001
	Ireland	0,35 (0,28–0,45)	< .001
	The Netherlands	0,77 (0,66–0,89)	< .001
	New Zealand	0,61 (0,49–0,75)	< .001
	Portugal	0,54 (0,39–0,74)	< .001
	Switzerland	0,55 (0,47–0,65)	< .001
	UK	0,60 (0,52–0,70)	< .001
	USA	3,06 (2,70–3,48)	< .001
Survey year	GDS2015		
	GDS2017	2,22 (2,09–2,35)	< .001

$N = 105{,}963$. $R^2 = 0.13$ (Cox & Snell), 0.32 (Nagelkerke). Model $\chi^2(28) = 14672.867$, $p < .001$.

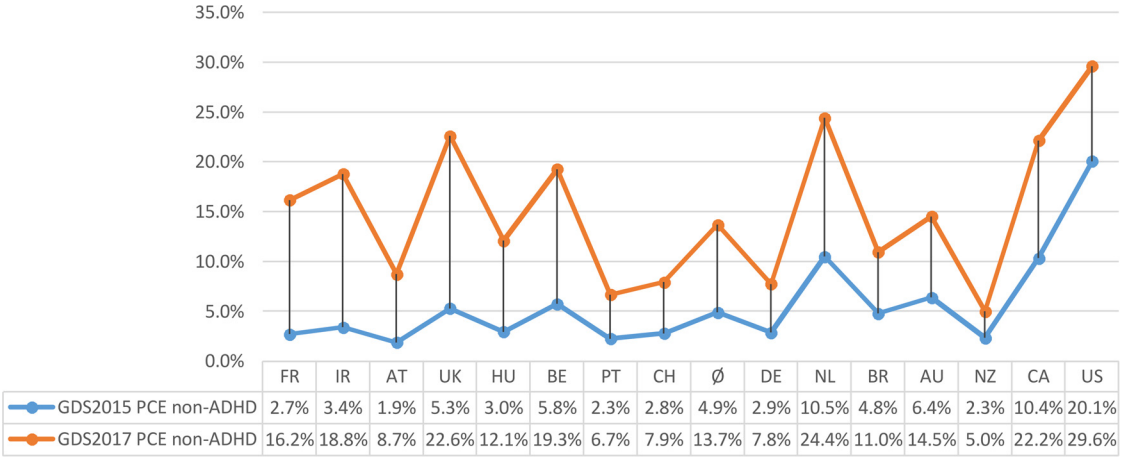
for PCE was least common among participants from the three German-speaking countries and Hungary, while more than 10% of U.S. and Brazil participants had recently used Benzodiazepines for enhancement purposes (Table 5). Only few reported the use of beta-blockers for PCE in the last year (Table 5).

Perceived effect on cognitive performance

In GDS2015, one in five participants who engaged in PCE last year (21.6%) reported that the stimulant substance(s) used for PCE could not meet the expectations, while half of were satisfied (50.4%) and a quarter rated the effects as more than expected (28.2%). Fig. 2 shows the perceived effect of the use of single substance (categories) on cognitive performance. When alcohol or benzodiazepines were used to directly or indirectly enhance cognitive performance at work or while studying, only few perceived an actual increase while half and a third, respectively, reported decreased performance following the use (Fig. 2). According to the provided self-reports, modafinil and prescription stimulants had the best effect profile (Fig. 2). Moreover, two third of participants who used illegal drugs for PCE in the last 12 months perceived an increase following the substance use (Fig. 2).

Discussion

This is the largest study on PCE that has ever been conducted. Data from more than 100,000 participants from 15 countries were collected as part of Global Drug Survey 2015 and 2017. Overall, 4.9% and 13.7% of the global sample reported the 12-month use of prescription or illegal stimulants and/or modafinil to improve the performance at work or while studying. This is on average an increase of 180% that can not only be explained by the self-selection of the sample and the different wording of the questions. Interestingly, U.S. participants showed the lowest relative increase of PCE rate between the two years while reporting highest PCE rates in both years. Similar patterns can be observed for Canada and the Netherlands. In all the three countries, recent efforts aimed to decriminalize use and possession of cannabis. Future drug policy research could thus evaluate how changes in cannabis policies affect other substance use. The current debate mainly focuses on the risks of cannabis use and trends in the frequency of use of adolescents as well as on problematic patterns of use. If cannabis policy changes were found to decrease other substance use that equally poses risk to health, such as illegal stimulant use for either recreational and/or enhancement purposes, the discussion would develop a new dimension. PCE use among non-ADHD individuals was relatively rare and, for the most part, limited to stressful periods at work or exam preparation periods. Despite investigating PCE in a sample of people predominantly experienced with illegal drug use, the rates of PCE were not higher than in previous research among European or American



	FR	IR	AT	UK	HU	BE	PT	CH	Ø	DE	NL	BR	AU	NZ	CA	US
GDS2015 PCE non-ADHD	2.7%	3.4%	1.9%	5.3%	3.0%	5.8%	2.3%	2.8%	4.9%	2.9%	10.5%	4.8%	6.4%	2.3%	10.4%	20.1%
GDS2017 PCE non-ADHD	16.2%	18.8%	8.7%	22.6%	12.1%	19.3%	6.7%	7.9%	13.7%	7.8%	24.4%	11.0%	14.5%	5.0%	22.2%	29.6%

Fig. 1. Self-reported rates of 12-month PCE with prescription stimulants, modafinil and/or illegal stimulants among non-ADHD individuals who participated in GDS2015 ($N = 79{,}640$) and GDS2017 ($N = 29{,}758$), respectively. The countries in the graph are ordered from left to right based on the highest to lowest increase between the two measurement periods as described in the legend.
AT = Austria (+358%); AU = Australia (+127%); BE = Belgium (+233%); BR = Brazil (+129%); CA = Canada (+113%); CH = Switzerland (+182%); DE = Germany (+169%); FR = France (+500%); HU = Hungary (+303%); IE = Ireland (+452%); NL = The Netherlands (+132%); NZ = New Zealand (+117%); PT = Portugal (+191%); UK = United Kingdom (+326%); US = United States (+47%).

Table 5
Rates of 12-month use of cannabis, alcohol, benzodiazepines and beta-blockers for PCE among participants in the GDS2017 in total and by country.

	Cannabis PCE		Alcohol PCE		Benzodiazepines PCE[a]		Beta-blockers PCE[a]	
	N	%	*N*	%	*N*	%	*N*	%
Total	6612	22,9%	4530	15,7%	1647	5,7%	333	1,2%
Australia	309	17,4%	270	15,2%	161	9,1%	33	1,9%
Austria	349	17,6%	319	16,1%	53	2,7%	13	0,7%
Belgium	63	26,1%	45	18,5%	11	4,5%	3	1,3%
Brazil	227	23,7%	204	21,4%	110	11,5%	19	2,0%
Canada	967	42,5%	511	22,7%	189	8,4%	29	1,3%
France	49	29,7%	38	22,8%	5	3,0%	1	0,6%
Germany	1086	11,0%	1018	10,3%	188	1,9%	53	0,5%
Hungary	303	25,4%	352	29,4%	35	2,9%	9	0,8%
Ireland	51	34,9%	28	20,0%	12	8,5%	2	1,4%
The Netherlands	156	22,5%	113	16,3%	43	6,2%	7	1,0%
New Zealand	229	14,6%	251	16,0%	103	6,6%	25	1,6%
Portugal	100	30,1%	51	15,3%	30	9,0%	11	3,3%
Switzerland	357	15,1%	331	14,0%	69	2,9%	29	1,2%
UK	550	29,6%	287	15,6%	164	8,9%	31	1,7%
USA	1816	52,5%	712	20,9%	474	14,0%	68	2,0%

[a] Non-medical use (without a medical indication).

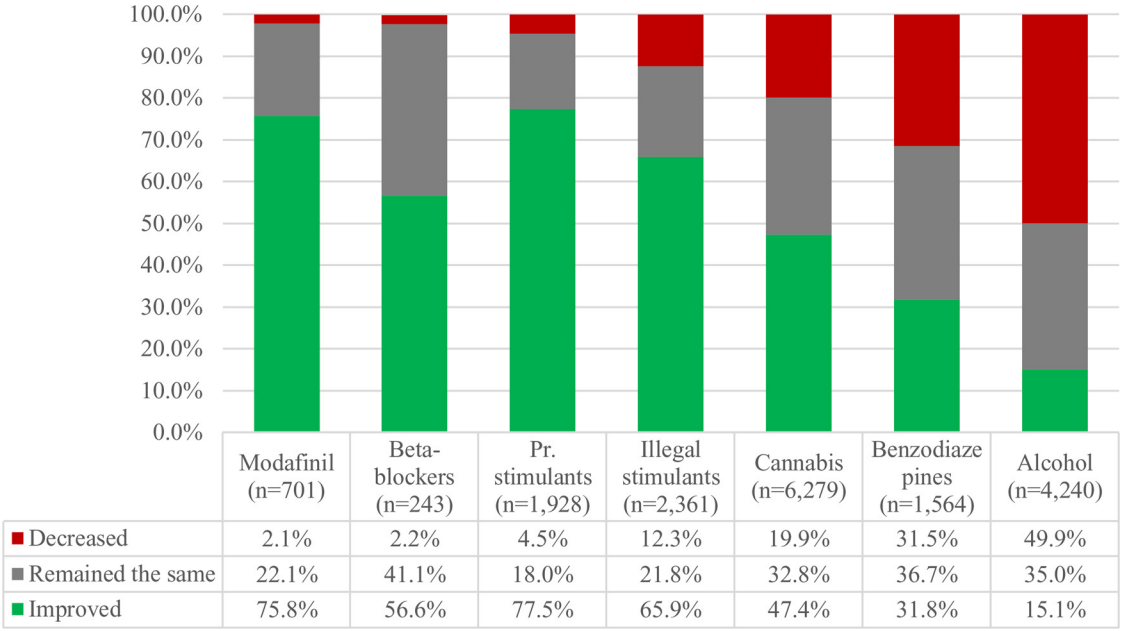


Fig. 2. Perceived effect of substance use for cognitive enhancement among GDS2017 participants who indicated having used the substance(s) for PCE in the last 12 months and provided an answer to the question. The substances in the graph are ordered from left to right based on the lowest to highest perceived decrease of cognitive performance following the substance use originally aimed at enhancement.

student populations (Arria et al., 2008; Maier et al., 2016; Maier & Schaub, 2015; Rabiner et al., 2009).

Amongst our sample, the PCE rates varied from 1.9% to 29.6%. These wide variations in both country-specific rates of substance use for PCE and ADHD are likely to reflect differences in drug policies, ADHD diagnostic frameworks and treatment guidelines (Singh et al., 2013). Future research is needed to assess the relative influences of these factors on physicians' diagnostic and prescribing behaviour (Hotze et al., 2011; Ott et al., 2012). The number of legitimate prescriptions of ADHD medications, such as dexamphetamine (Adderall™), in the United States makes stimulants there more accessible than in other countries (Varga, 2012). It appears that the globalization of ADHD has been strongly influenced by American-based psychiatry and the shift from ICD to DSM diagnostic criteria (Conrad & Bergey, 2014). The higher rates of prescription stimulant use for PCE among GDS participants residing in the United States, Canada, and Australia when compared to other Western countries correspond well with the recent growth in the use of ADHD medication in just the same countries (Scheffler et al., 2007). Again, the relative increase by year will most likely slow down once the PCE rate is high already. On the other end, we see French participants presenting with the highest relative increase of PCE although reporting one of the lowest rates in GDS2015. This can be partially explained by the considerable delay (more than 10 years) in approving stimulant treatment for ADHD and the limited range stimulant medications approved when compared to the United States (Conrad & Bergey, 2014). Moreover, a multinational study found low prevalence of ADHD in Hungarian and French individuals with substance use disorders when compared to Nordic countries (van de Glind et al., 2014). While drug policies in France and Hungary can be described as strict and restrictive, mainly promoting sobriety and abstinence, the three German-speaking countries have more progressive and evidence-based approaches of harm reduction strategies that serve as models for international drug policy. Similar successful models of professional acceptance of drug use were developed in the Netherlands

and in Belgium (de Jong & Weber, 1999). The access to drug information centres, substitution treatment, drug checking services and broad workplace health promotion facilities might influence the decision to use prescription stimulants for PCE to estimate quantity and quality of the drug used reliably. Nevertheless, stimulant drugs have only weak positive and sometimes even impairing effects on cognition of individuals without an underlying mental disorder (Repantis et al., 2010; Wood et al., 2014). Yet, individuals without ADHD-diagnosis who present with personality traits similar to ADHD symptoms, such as impulsiveness, are most likely to benefit from non-medical stimulant use for PCE (Maier et al., 2015; Peterkin et al., 2011). Moreover, impulsiveness is negatively correlated with self-control and stimulant use for PCE is assumed to be associated with a lack of self-control (Englert & Wolff, 2015). The motivational effect of stimulants used for PCE can help to increase self-control and make repeated use for PCE more likely (Englert & Wolff, 2015). According to the strength model of self-control, non-ADHD individuals use stimulants as functional means to improve performance (Englert & Wolff, 2015; Wolff, Brand, Baumgarten, Lösel, & Ziegler, 2014). The study revealed that the use of sedative drugs, especially cannabis and alcohol, is also common among people who take part in a drug survey. This is not surprising as people are likely to experiment with substances they had previously used, when it comes to PCE. The numbers are lowest for the German-speaking countries, New Zealand and Australia, which again can be an indicator of successfully applied drug policies and/or quality of education and health literacy (among participants) in these countries.

Policy implications

The findings of the current study have important implications for developing international policy responses on the globalisation of ADHD, associated increases in stimulant prescriptions and related increases in stimulant diversion and PCE among individuals without ADHD. The critical question in PCE prevention policy is whether we still aim at developing a better understanding of stimulant use as continuum from treatment to enhancement (Maslen et al., 2014) or whether we rather shift our attention away from the substance itself and more towards the underlying stressors and motives for psychoactive substance use. This is closely related to the decision on whether global drug policies follow a health-based approach and are self-control oriented, by understanding functional psychoactive substance use as means to reach a certain aim (Wolff et al., 2014). In particular, a professional acceptance of drug use (de Jong & Weber, 1999) facilitates the structure of resource-oriented prevention and intervention approaches for both problematic substance use for PCE and overtreatment of ADHD symptoms. Equally, studies comparing the effects of different similar acting substances on their potential for cognitive enhancement (Schmidt et al., 2018) are highly important to understand how these drugs affect the brain in the short- and long-term. This becomes especially important when focusing on the developing brain (Urban & Gao, 2017). Finally, the evidence from the present study suggests a strong relationship between national ideas and concepts of mental health issues, existing treatment options, and substance use behaviour in the general population. Therefore, governments, medical professionals and research should account for the possible, low-risk PCE use and focus on providing solutions for individuals with problematic use patterns and lack of resources or lack of motivation to implement desired changes in patterns of PCE use.

Limitations

Finally, a number of limitations need to be considered. The first two and most important limitations of the study are the self-selection of GDS survey participants and the use of self-report data. Since the sample is self-selected and the substance use for PCE consists of self-report data, the actual extent of PCE in the participating countries is not accurately known. The sample should not be considered representative of any country general population. GDS was purposefully designed to be answered by people who use legal and/or illegal psychoactive substances. A third limitation is that the GDS2015 questions on last year substance use for PCE were limited to stimulant drugs. Although stimulants are seen as the most common and most direct form of substance use for PCE, studies investigating the use of prescription sedatives and beta-blockers as well as alcohol and cannabis showed the importance of these substances for both direct and indirect PCE (Maier et al., 2016; Maier & Schaub, 2015). Furthermore, the impact of recall bias or deliberate misreporting on results has to be considered. Finally, due to the anonymous web survey instrument, the same individual might have completed the GDS2015 multiple times. However, $< 1\%$ of the sample provided identical response sets across demographics and key variables used in these analyses.

Conclusion

The analysis of stimulant use for PCE in the largest global sample shows relatively low-risk PCE use patterns except for participants who recently used illegal stimulants for PCE with no or insufficient access to prescription stimulants. The globalisation of ADHD and related medical treatment (Singh et al., 2013) is likely to influence the country-specific rate of PCE among non-ADHD individuals and needs further investigation. Policy-makers should utilize the best available scientific evidence to inform policy responses to stimulant drug use for PCE and related health issues. Providing sufficient and adequate treatment for ADHD and other mental disorders will increase global mental health and might, at the same time, decrease the subjectively perceived need for additional self-medication. One of the most significant findings to emerge from this study is that one third of people who use drugs for PCE would like to reduce their use without actually planning to seek help. More interdisciplinary and transnational research in the field of functional substance use for PCE is needed to identify problematic psychoactive substance use patterns and to address prevention of stimulant drug use for PCE to individuals with low self-control. Finally, it is worth investigating the impact of current and changing drug policies on national and state level regarding substance use for both recreation and enhancement. Future research could thus examine, whether the low-frequent, low-dose responsible use of psychoactive substances for cognitive enhancement is likely to change recreational substance use behaviour.

Conflict of interest

ARW is the founder and owner of Global Drug Survey. LJM and JAF are part of the Global Drug Survey Core Research Team but have no conflict of interest.

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