International Journal of Drug Policy 58 (2018) 104–112

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research Paper

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

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ARTICLE INFO

Keywords:
Cognitive enhancement
Stimulants
ADHD
Illegal drug use
Non-medical use

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

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https://doi.org/10.1016/j.drugpo.2018.05.009
Received 10 April 2016; Received in revised form 17 April 2018; Accepted 18 May 2018

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.