Tampere University

ALEKSI HUPLI

Smarter with Drugs?

Sociology of cognitive enhancement drugs from user's perspectives

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Sociology of cognitive enhancement drugs from user's perspectives

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Dedication

I wish to dedicate this dissertation to my late grandmother Alli Hupli, a pharmacist, and my late great uncle Veikko Hupli, a psychiatrist, both of whom directly and indirectly inspired my academic interest towards medication use.

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This dissertation would not have been possible without you.

ABSTRACT

This article-based dissertation focuses on the sociology of cognitive enhancement drugs from mainly student users' perspectives. The research material consists of qualitative interview data, a patient case study, a general review of available prevalence data on stimulants and a netnographic study on Youtube (Hupli et al. 2016; 2019ab; Hupli 2018a; 2020a).

Two interview studies (Hupli et al. 2016; 2019b, see Table 1) using 'crowded theory' to analyse separate qualitative data sets (N=35) and an online survey (N=113) showed that young students in the Netherlands and Lithuania had experienced a variety of positive and negative effects from using several legalised and illegalised drugs considered as "cognitive enhancers" in order to improve their life situations. The experiences and motivations of both self-reportedly diagnosed and those who did not report a psychiatric diagnosis did not differentiate to a large extent, empirically showcasing how the line between therapeutic and enhancement use is often blurred. Unrepresentative data sample and reliance on self-reports in terms of psychiatric diagnostics and drug effects limits the generalisability of the empirical findings and call for further study in this area in different country contexts.

By comparing statistical data from Finland and the Netherlands (Hupli 2020a) - using available data sets from international, European and national sources in relation to both medical and extra-medical use of stimulants among young people - a general review study revealed differentiating stimulant use trends between the countries. However, the full scope of these differences is challenging to evaluate especially in relation to cognitive enhancement drug use, as there is a chronic lack of research data, or even policy discussion in Finland compared to the Netherlands on this particular user practice.

To track new drug trends among young people by applying novel digital methods, a netnographic study on Youtube™ focused on a user practice called microdosing psychedelics (Hupli et al. 2019a). While the positive effects and dosing regimens mentioned in the six most viewed videos that were analysed require further critical evaluation, contrary to how typical users of illegalised drugs are often portrayed in the general media and science, these videos revolved around themes such as experiments, self-monitoring and the imperative of sharing research results. As microdosing psychedelics is seemingly a growing drug trend according to increasing Youtube video content and other media publications as well as scientific research, part of this PhD summary article will provide an update on microdosing psychedelics research especially in relation to cognitive enhancement. Cannabis as a potential cognitive enhancer is also briefly discussed.

Psychedelics and cannabinoids are rarely discussed in the pharmacological neuroenhancement literature, and therapeutic research into these compounds has been severely restricted until recently. One of the studies in this dissertation (Hupli 2018a) includes the first medical sociological patient case study of a male patient living in Finland with Attention Deficit/Hyperactivity Disorder (ADHD) who was prescribed cannabinoid therapeutics (Bedrocan®, Bediol®) to treat his ADHD as the primary indication. The case study partly confirmed increasing research into the potential of cannabinoid therapeutics for treatment-resistant conditions, including adults suffering from ADHD, although further studies and health policy reform are required in the rapidly growing field of cannabinoids in medicine.

The findings of this dissertation raise several bioethical and drug policy questions about the blurred line between pharmacological therapy and neuroenhancement, as well as the political and social dichotomy between prohibited versus promoted drugs. Using Science and Technology Studies (STS), critical drug studies and Anthropology of Pharmaceuticals literature, the author theoretically frames all classes of drugs as 'pharmacological neurotechnologies' in order to move beyond these dichotomies and to further develop sociology of technology and drugs. The sociological concepts

of medicalisation and especially pharmaceuticalisation are discussed with a focus on the parallel development of the diagnosis of ADHD and the use of pharmacology in its treatment. The last chapter offers research and policy recommendations for evidence-based drug policy making and presents some *politicogenic drug effects* of current drug policing.

TIIVISTELMÄ

Tässä artikkelipohjaisessa väitöskirjassa keskitytään kognitioon vaikuttavien psykoaktiivisten aineiden sosiologiaan käyttäjien näkökulmasta, varsinkin opiskelijoiden. Tutkimusmateriaali koostuu kvalitatiivisista haastatteluista, potilastapaustutkimuksesta, katsauksesta stimulanttien käytön yleisyyteen Suomessa ja Hollannissa sekä netnograafiseen videoainestoon Youtubessa (Hupli et al. 2016; 2019ab; Hupli 2018a; 2020a).

Kaksi julkaistua haastattelututkimusta (Hupli et al. 2016; 2019b, ks. Taulukko 1), joissa käytettiin Crowded-teoriaa erillisten kvalitatiivisten aineistojen (N=35 ja kyselyaineiston (N=113) analysoimiseksi, osoittivat, että nuorilla aikuisilla Hollannissa ja Liettuassa on ollut erilaisia myönteisiä ja kielteisiä kokemuksia useiden laillisten ja laittomien aineiden käytöstä. Kognition tehostajilla pyrittiin parantamaan yleisesti eri elämäntilanteita niin opiskelussa kuin töissä. Sekä itse diagnosoitujen että diagnosoimattomien opiskelijoiden kokemukset ja motivaatiot eivät eronneet suuressa määrin, mikä empiirisesti osoittaa, kuinka terapian ja tehostamisen välinen rajapinta on usein häilyvä. Tilastollisesti ei-edustava aineisto ja nojaaminen itseraportointiin psykiatrisen diagnoosin ja aineiden vaikutusten suhteen rajoittavat empiiristen havaintojen yleistettävyyttä ja vaativat lisätutkimusta aiheen parissa eri maissa.

Kansainvälisten, eurooppalaisten ja kansallisten aineistojen välinen vertailu Suomen ja Hollannin välillä – keskittyen stimulanttien lääketieteelliseen ja ei-lääketieteelliseen käyttöön nuorten keskuudessa – osoitti erilaisia käyttötrendejä maiden välillä (Hupli 2020a). Näiden trendien eroja on kuitenkin haastavaa kattavasti arvioida erityisesti kognition tehostamisen suhteen, sillä tutkimustietoa ei Suomesta juuri ole verrattuna Hollantiin. Myöskään päihdepoliittinen keskustelu liittyen

farmakologiseen neurotehostamiseen ei ole vielä alkanut Suomessa, toisin kuin osittain Hollannissa.

Yhdessä osajulkaisussa kehitettiin digitaalista menetelmää uusien huumetrendien tavoittamiseksi (Hupli et al. 2019a). Youtubeen keskittyvässä netnograafisessa verkkotutkimuksessa tarkasteltiin psykedeelien mikroannosteluksi kutsuttua käyttötapaa. Vaikka analysoiduissa videoissa mainitut positiiviset vaikutukset ja annostelu käytännöt edellyttävät kriittistä lisäarviointia, toisin kuin laittomien huumeiden tyypillisiä käyttäjiä kuvataan yleisesti mediassa ja tutkimuksissa, analysoidut videot sisälsivät teemoja liittyen kokeelliseen menetelmään, itseseurantaan ja tutkimustulosten jakamisen tärkeyteen. Psykedeelien mikroannostelu on näennäisesti nouseva huumetrendi lisääntyneiden Youtube-videoiden sekä muiden mediasisältöjen ja kasvavan tieteellisen tutkimuksen perusteella. Tämän takia yksi tämän yhteenvetoartikkelin luvuista tarjoaa päivitetyn katsauksen psykedeelien mikroannosteluun ja siihen liittyviin tutkimushankkeisiin erityisesti kognitiivisen tehostamisen kannalta. Kannabiksesta kognitiivisena tehostajana keskustellaan myös lyhyesti.

Psykedeelejä ja kannabinoideja käsitellään harvoin farmakologisessa neurotehostamiskirjallisuudessa, ja jopa näiden yhdisteiden terapeuttista tutkimusta on voimakkaasti rajoitettu. Yksi tämän väitöskirjan osajulkaisuista (Hupli 2018) sisältää ensimmäisen terveyssosiologisen potilastutkimuksen Suomessa asuvasta ADHD potilaasta, jolle määrättiin kannabinoiditerapiaa (Bedrocan®, Bediol®) aikuisiän ADHD:n hoitoon. Tapaustutkimus osittain vahvistaa kannabinoiditerapian potentiaalin hoitoresistenttien sairauksien hoidossa. Lisätutkimusten ja terveyspolitiikan uudistamisen tarve on kuitenkin ilmeinen tällä nopeasti kasvavalla lääkekannabinoidien alalla.

Tämän väitöskirjan tulokset nostavat useita bioeettisiä ja päihdepoliittisia kysymyksiä farmakologisen hoidon ja tehostamisen välisestä hämärtyneestä rajapinnasta sekä laittomiksi luokiteltujen huumeiden ja laillisiksi määriteltyjen lääkkeiden välisestä poliittisesta ja sosiaalisesta kahtiajaosta. Tässä

yhteenvetoartikkelissa kehitetään teoreettista viitekehystä, jonka mukaan kaikki psykoaktiiviset aineet voidaan luokitella ”farmakologisiksi neuroteknologioiksi”. Tarkoituksena on teoreettisesti päästä huume/lääke dikotomian yli tukeutuen tieteen- ja teknologiatutkimuksen (STS), kriittisen päihdetutkimuksen ja lääketieteellisen antropologian parissa kehitettyyn kirjallisuuteen. Myös medikalisaation ja erityisesti farmaseutikalisaation käsitteistä keskustellaan tarkasteltaessa ADHD- diagnoosin ja sen farmakologisen hoidon rinnakkaista kehittymistä. Viimeinen luku tarjoaa lisätutkimus ehdotuksia ja suosituksia tutkimusnäyttöön perustuvalle päihdepolitiikalle sekä esittelee nykyisen huumepolitiikan *politogeenisiä* vaikutuksia.

CONTENTS

1 Introduction 17
1.1 Narrowing the focus 17
1.2 Smart drugs? 20
1.3 Pragmatic positioning as a researcher 25
1.4 What are these 'things' called 'drugs'? 26
1.5 The social life-cycle of drugs 29

2 Research questions, methods and key findings 35
2.1 Research questions 35
2.2 General considerations on methods and data 35
2.3 Research ethics 37
2.4 Brief summary of main findings 38

3 Developing a theoretical framework 44
3.1 Drugs as pharmacological neurotechnologies 45
3.2 Drugs as non-human actors 48
3.3 Pharmaceuticalisation of attention? 51

4 Pharmacological Neuroenhancement Studies (PNS) 57
4.1 Definitions of pharmacological neuroenhancement 57
4.2 Bioethical discussion - brief overview 59
4.3 Efficacy & safety 61
4.4 Prevalence of stimulants as cognitive enhancement drugs 65
4.5 Qualitative approach to cognitive enhancement drug use 67

5 Betterment of the well – with psychedelics and cannabis 70
5.1 Cannabis as a 'cognitive enhancer'? 70
5.2 Psychedelics beyond therapy 73
5.3 Microdosing psychedelics – a form of neuroenhancement? 76

6 Discussion and research recommendations 82
6.1 The imperative to consider user perspectives 83
6.2 Focus on country-context 85

6.3 Moving beyond therapy vs. enhancement 87
6.4 Politicogenic drug effects 91
6.5 Evidence-based drug policymaking? 93
6.6 Towards smarter drug policies? 94

7 Concluding remarks 97

8 References: 100
8.1 Media references and links: 119

9 Publications 121

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Publication I Hupli, Aleksi; Didžiokaite, Gabija & Marte Ydema (2016). Towards the smart use of smart drugs: Perceptions and experiences of university students in the Netherlands and Lithuania. *Contemporary Drug Problems* Vol. 43, No. 3, pp. 242-257. https://doi.org/10.1177/0091450916660143

Publication II Hupli, Aleksi (2018). Medical Cannabis for Adult Attention Deficit Hyperactivity Disorder: Sociological Patient Case Report of Cannabinoid Therapeutics in Finland. *Medical Cannabis & Cannabinoids* Vol. 1, No. 2, pp. 112–118 https://doi.org/10.1159/000495307

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Publication IV Hupli, Aleksi; Didžiokaite, Gabija & Marte Ydema (2019b). Beyond treatment vs. enhancement: A qualitative study of pharmacological neuro-enhancement among Dutch and Lithuanian university students. *Contemporary Drug Problems*. Vol. 46, No. 4, pp. 379–399. https://doi.org/10.1177/0091450919884777

Publication V Hupli, Aleksi (2020). Cognitive enhancement with licit and illicit stimulants in the Netherlands and Finland: what is the evidence? *Drugs and Alcohol Today*, Vol. 20 No. 1, pp. 62-73. https://doi.org/10.1108/DAT-07-2019-002

1 INTRODUCTION

1.1 Narrowing the focus

So-called "human enhancement technologies" (HET) incorporate several technological devices that augment human brain and body functions and which have been initially designed to treat diseases. These technologies include genetic modification, 'non-invasive' brain devices like transcranial magnetic stimulation (TMS) and more 'invasive' deep brain stimulation (DBS) involving the use of neurosurgery and related brain-implant devices (Shah-Basak & Hamilton 2017; Attiah 2017; Warso et al. 2019).

The focus of this PhD research is on what the author refers to as pharmacological neurotechnologies (Hupli 2020b; Chapter 3), which when used for so-called enhancement, are sometimes referred elsewhere as human enhancement drugs (HEDs) (Chatwin et al. 2017; van de Ven, Mulrooney & McVeigh eds. 2019). As described in more detail below, the term 'human enhancement drugs' is difficult to define as both the term 'enhancement' and the term 'drugs' are contested categories. For example, HEDs include drugs for both physical enhancement (e.g. anabolic steroids), as well as the use of various psychoactive drugs aimed at enhancing mood, memory and pro-social behaviour (De Jongh et al. 2008; Maier & Schaub 2015). However, this thesis focuses on so-called cognitive enhancement drugs (CEDs), and especially from the perspectives of young users themselves.

These drugs are part of a practice called 'pharmacological neuroenhancement' (PNE) which is used by the author to refer to the use of psychoactive drugs, legalised or illegalised, with the intention of improving one's cognition, mood and/or memory as well as pro-social behaviour and even 'spirituality' (Maier & Schaub 2015; Tully et al. 2019; see Chapter 4.1.). It is important to note that this intention for neuroenhancement does not mean that drugs safely and reliably do enhance cognitive functions as discussed in more detail below. Nonetheless, academic literature concerning the use of drugs to make us smarter - meaning for example improved cognitive skills, mental agility/sharpness and increased ability to focus - has proliferated in the last 35 years (Murray et al. 1984; Parens ed. 1998; Schermer et

al. 2009; Maier & Schaub 2015; Jotterand & Dubljevic ed. 2016; Ter Meulen, Mohamed & Hall eds. 2017; van de Ven, Mulrooney & McVeigh eds. 2019; Coveney & Bjønness 2019). So far this academic discussion has to a large extent taken place in the fields of bio- and neuroethics, both of which have developed into their own respective academic areas of ethical expertise (DeVries & Subedi eds. 1998).

Partly due to this increasing amount of bioethical and sociological literature on the topic, there is a plethora of terms that have been used to research cognitive enhancement drug use, from 'smart drugs' (Rose 2002; Singh, Bard & Jackson 2014) and 'study drugs' (Vrecko 2013) to 'scholastic steroids' (Linton 2012) and nonmedical (ab)use/misuse of prescription drugs (Arria & Wish 2006). These terms often reflect various research and ethical paradigms and make defining the phenomena challenging (e.g. Coveney & Bjønness 2019). As shown below, also the term 'cognitive enhancement drugs' can be problematic as the line between therapeutic and neuroenhancement drug use is often blurred, and in general, users aim to enhance not just their cognition, but their emotions and motivation in various life situations (Hupli et al. 2016; 2019b; see also Vrecko 2013; Hildt, Lieb & Franke 2014; Petersen et al. 2015ab). This fine line between therapy and neuroenhancement is discussed in more detail below. This thesis work seeks to provide a sociological account of this blurred line between correcting deficits and improving 'normality' with the help of psychoactive drugs (Hupli et al. 2019b; Rose 2007).

However, what is often missing from the literature is the acknowledgement of the on-going situation of the war on drug users, "which is responsible for thousands of deaths a year globally, and the social and political death or exclusion of thousands more" (Zigon 2015; see Bublitz 2016 in relation to cognitive enhancement). The general literature about human enhancement through drugs rarely discusses this even though throughout the twentieth century, and continuing into the twenty-first century, the use of some drugs for anything other than medical and scientific reasons has aroused strong moral, political and social reactions, especially when used by certain, often minority, members of the community (Alexander 2010; Hart 2014; Hari 2015).

According to the Global Commission on Drug Policy (2017, p. 6) "For too long, drugs have been considered as substances that must be avoided at all cost; people who use drugs have been rejected by society and perceived as asocial, depraved or deviant." In relation to cognitive enhancement drugs, Coveney et al. (2011, p. 388, italics in original) also state that "Consumption of medical technology for purposes other than healing was regularly thought of as an abuse of medicine rather than enhancement and medical control of the substance via prescription was envisaged

as an effective mechanism to ensure benefits of the drug would be available to those that were in need of them, whilst protecting other individuals and society from the potential harms that unrestricted access to the drug could lead to."

This arguably remains the situation not only in the UK, to which Coveney et al. referred to a decade ago, but also in Finland, where human enhancement drugs in general or cognitive enhancement drugs in particular have not been part of the public debate or even on national research agenda in relation to general drug use, unlike for instance in the Netherlands (Schermer 2016; Hupli 2020a). Before "recreational drug use" (in Finnish, *viihdekäyttö*) became part of the national lexicon (see Salasuo & Rantala 2002), most drug use that was considered to be "extra-medical" (e.g. Sultan & Hupli 2020), often excluding alcohol and tobacco, was condemned as being either drug abuse or misuse, with criminalisation of personal use and possession coming into effect in the 1970's (Hakkarainen 1992; Salasuo & Rantala 2002).

Thus, despite increasing international literature and interest in the topic of pharmacological neuroenhancement (Jotterand & Dubljević ed. 2016), even a public debate or discussion is yet to happen in Finland. As Coveney et al. (2011, p. 389) point out "the extent to which a drug is able to move from medical treatment to pharmaceutical enhancement and leave behind cultural images of addiction, disease, side effects, health and social problems is questionable." And while the author does not advocate moving drugs from medical treatments to pharmaceutical neuroenhancements, the topic, however, is certainly worthy of wider public debate and sociological study.

As bioethicists are often concerned about how the world of medicine should be, (medical) sociologists are often trying "to study the medical world as it is" (DeVries & Subedi 1998, p. xv) and by so doing, the social world at large. Lehtonen (2015) sees that in general, sociology asks three questions, the first one being 'how are we together' and how is this togetherness socially mediated. The second question relates to this and asks how do we exclude other people out from society, and not just other people but material things, like viruses and waste? And the third question, while being slightly different, but partly dependent on the answers given to the first two questions, is who are we now? What is the "zeitgeist" of the world we live in at this moment in time, in the first years of the 2020s?

Our togetherness is often mediated by drugs, from drinking caffeine (e.g. coffee) at funerals to ethyl-alcohol (e.g. champagne) at weddings, but drugs and the laws that govern them are indeed also used to exclude people from society, especially non-white minorities, who have suffered the most severe consequences of the on-going drug war for over a century (Alexander 2010; Hart 2014; Hari 2015: IDPC 2018).

However, the global "anti-drug war movement" (Zigon 2015; 2018) is growing and new hope is emerging that eventually during the twenty-first century we will learn to be smarter with drugs.

But at least for now, the author argues that the bio- and neuroethical debate on human enhancement drugs is still very future-oriented, as it rarely includes any critical discussion about 'illegalised drugs', their users and related drug policing (Bublitz 2016). Drug policies, and their practical enforcement in the last century, has in many places caused significantly more harm to users than the drugs themselves (IDPC 2018; Global Commission on Drug Policy 2017). These effects from drug policing are referred to by the author as 'politicogenic drug effects'. As 'iatrogenic' effects refer to ill effects caused by medical activity (Illich 1976), politicogenic effects refer to ill effects caused by political activity, and in this context especially, activity in the drug policing field.

While the development of this concept is left to some extent for future publications, one 'politicogenic drug effect' identified here is that perspectives from 'drug users' are often neglected both in- and outside of the bioethical and public discussions about drugs and in the making of drug policies. And while there are a great many topics to focus our attention on, from global pandemics like COVID-19 to climate change and the rise of political authoritarianism, the author argues that identifying and following the uses and users of "smart and other drugs" can partly help answer the sociological questions above about ourselves and of our time. When the uses and users of drugs are seen as "theoretical telescopes", or as lenses to our contemporary world, it is the author's firm conviction that through closer examination something of our current 'zeitgeist' can be revealed. And the picture these lenses paint is often not pretty in relation to how we treat each other, and especially those we categorise as 'drug users' (Global Commission on Drug Policy 2017; Alexander 2010).

1.2 Smart drugs?

Inside social sciences, pharmacological neuroenhancement has been noted by few medical sociologists (Coveney et al. 2011; Vrecko 2013; Liokaftos 2021), anthropologists (Quintero & Nichter 2011; Petersen et al., 2015ab) and scholars in the fields of Science and Technology Studies (STS) (Morrison 2015) and medical humanities (Pickersgill & Hogle 2015). As prior to this doctoral thesis work, pharmacological neuroenhancement has not yet received any attention from a social

scientific perspective, at least in Finland (Hupli 2020a; 2018b), one of the aims of this thesis investigation is to partly fill this gap in our sociological knowledge by providing a 'practical' study to complement the overly 'theoretical' bioethical discussions of other authors so far published on the subject.

And while the variety and quantity of drugs that could be studied is enormous, the author's interest here is in so-called cognitive enhancement drugs which, as mentioned, are sometimes referred to as "smart drugs". Arguably, the use of 'drugs', generally speaking, has become an integral part of all fields of modern medicine, including, or maybe especially, psychiatry (Moncrieff 2009). In addition to those that could be prescribed by medical doctors, there are already numerous 'psychoactive drugs' legally available for people across the globe to use, some of which potentially enhance certain cognitive traits but not always in unproblematic ways. These types of 'soft enhancers' (Maier & Schaub 2015) include basic consumer products like coffee and tea, caffeine pills, sugar and 'energy drinks' but also more traditional herbs like ginkgo biloba and ginseng (Tully et al. 2019).

There are other types of 'smart drugs' that are sold by companies named Optimind and Vitabiotics, which offer products via their online shops and claim that their products can "contribute to normal cognitive function" and help users to "focus longer". To give a more detailed example of the contents of a 'smart drug', a Dutch company called Sapiens Biolab promises on their website that their product, Sapiens Focus, "will help you maintain your edge in the classroom, boardroom, gym or while competing in your favourite online games." Sapiens Focus, which seems to be easily available for online purchase, includes "750 mg of Acetyl-L-Carnitine to support the mitochondrion which is the powerhouse of a cell." Also "300 mg of Alpha GPC, as it is one of the most bioavailable precursors to the neurotransmitter Acetylcholine, which plays a key role in forming memories" and "added 200 mg of L-Theanine and 80 mg of Caffeine" which "have a strong synergetic effect and a long history of human use". In addition, "200 mg of Rhodiola Rosea is added as it is a powerful, natural adaptogen that reduces vulnerability to stress" and "100 mg Panax Ginseng has been added as an all-round natural cognitive enhancer" with added 4 micrograms of vitamin B12 "to finish the formula". According to the company´s webpage, Sapiens Focus is "Supported by over 35 independent, mainstream scientific studies" and 30 doses are sold for a discounted price of 39,90 (euro). The latest online review from Daniel F. in November 2019 states that "I've used a few nootropics and some of them get me anxious and hyped but this is a very calm collected energy and lasts the whole day."

Another Netherlands based company states that their product "1PD" is "the Ultimate Cognitive Enhancer" and "One tablet a day may help promote neural plasticity and may enhance cognitive function." According to the website "1PD is...Specifically designed for microdosing, 1PD may help improve productivity, mood and creativity on a daily basis."

This relation, or synergy, between different molecules, references to neuroscientific knowledge and the "remaking of the self" (Kramer 1993) will be discussed in more detail in Chapter 3. But even from these short descriptions of available "cognitive enhancers", it is possible to see how neuroscientific knowledge about drugs as well as digital technologies are greatly influencing how we market, learn about, share knowledge of and, increasingly nowadays, purchase our drugs. The above does not, however, explain why some drugs and their users are perceived as good and promoted with government support, while others are seen as bad and are prohibited with severe government sanctions, including in some countries, by extra-judicial killings of users (IDPC 2018).

Nonetheless, while still highly speculative, pharmacological and other neurotechnologies are already discussed as having the potential for "boosting brainpower" (BMA 2007; also STOA 2009; OECD 2017; Warso et al. 2019). The emphasis in the bioethical literature has been especially on prescription drugs, and especially on stimulants like methylphenidate (e.g. Ritalin™). The use of prescription stimulants among "healthy" university students seeking to enhance their attention and vigilance has been a major focus of research (Singh & Kelleher 2010; Ragan et al. 2013; Maier & Schaub 2015) and while the use of stimulants like amphetamines emerged already in the 1930's, there has been increasing empirical research for their use as cognitive enhancers in the last decade (Hupli 2013b; Ter Meulen et al. 2017; van de Ven, Mulrooney & McVeigh eds. 2019). This is despite the modest evidence of the efficacy of prescription stimulants for both therapy and neuroenhancement in and out of clinical laboratory studies (e.g. Moncrieff 2009; Smith & Farah 2011; Storebø et al. 2015; Chapter 4.3.).

In addition to empirical research, pharmacological neuroenhancement has produced numerous academic and policy commentaries concerning various ethical, social and policy implications in relation to their current and potential future use among non-clinical populations (e.g. Dees 2007; Hesse 2010; Outram 2010; 2011; Arria & DuPont 2010; Forlini et al. 2013). As argued below, this research field should have a wider perspective of which drugs are included under the term "cognitive enhancement drugs" (Hupli et al. 2016; 2019b), and maybe even more importantly, critically evaluate the politicogenic drug effects of contemporary drug policies which

maintain the activity of cognitive enhancement drug use as criminal. Some policy and research recommendations are provided in Chapter 6.

As mentioned, the working definition of pharmacological neuroenhancement used by the author is the use of drugs, legal or illegal, with the intention of improving one's cognition, mood and/or memory as well as pro-social behaviour and even 'spirituality' (see Chapter 4.2., Maier & Schaub 2015; Tully et al. 2019). And while methodologically challenging to research, there are scholars who argue that human use of drugs in efforts to improve our species has been an integral part of our co-evolution with several psychoactive plants and fungi (McKenna 1992). Thus, the use of drugs for neuroenhancement by humans might not be particularly novel phenomena (Illieva & Farah 2013; Aikins 2015) as archaeological evidence for human use of psychoactive plants and fungi dates back thousands of years and across different cultures (Evans Schultes, Hofmann & Rätsch 2001; McKenna 1992).

Closer to modern life, according to a historical analysis by Aikins (2015) in the context of the USA, drug use among contemporary youth has witnessed periodic transformations, with cognitive enhancement drug use being merely one of the latest trends. Aikins (2015) predicts that this type of "functional drug use" in higher education is likely to increase on student campuses. However, under current global and national drug policies, early adopters of certain drugs are often forced to operate in a 'grey or black market' due to the socially constructed illegal status of those drugs enforced in most nation states. This leads to another politicogenic drug effect where many contemporary 'illegal drug users', including university students, often cannot have adequate certainty and knowledge of what they are consuming, which increases the risks associated with that use (e.g. Hardon 2021). At the same time, 'legal drug users' often find that the professionally marketed effects of, for instance, several prescription drugs are ineffective and/or overshadowed by sometimes silenced adverse effects (Healy 2004; Medawar & Hardon 2004; Moncrieff 2009).

Partly to counter these politicogenic drug effects, some users (sometimes referred to as "psychonauts" or bio/neurohackers) who augment their brain and body function with various pharmacological neurotechnologies have developed their own kind of peer-review system, online and offline, as a form of "harm reduction from below" (Van Schipstal et al. 2016; Berning & Hardon 2016; Hardon & Hymans 2016; Hardon 2021). And as will become evident from the published articles that together comprise this doctoral thesis work, the focus in this research has been primarily on the perspectives of young users; more specifically on the variety of meanings around the drugs they have used, including their lived effects, both positive and negative (Hupli et al. 2016; 2019ab).

This thesis work aims to examine the use of drugs for cognitive enhancement through a set of empirically-constructed analytical frameworks to provide a way to discuss "cognitive enhancement as an observable set of practices" (Outram 2011; see Chapter 3; Hardon 2021). As outlined by Outram (2011), these frameworks can include perspectives into the phenomenon in terms of 1) risks and benefits, 2) self-medication and under-prescription, 3) prescription drug abuse and over-prescription and, finally 4) cognitive enhancement. These frameworks are not mutually exclusive and can be used to identify a variety of issues that are related to the use of psychoactive drugs, with or without a medical prescription.

Chapter 2 introduces the author's Research Questions, and the Methods and Data that was used to answer them, accompanied by a discussion of research ethics and a short summary of the key findings. The five peer-reviewed publications are re-published at the end of this summary article (Hupli et al. 2016; 2019ab; Hupli 2018a; Hupli 2020a) with more detailed descriptions of methods and empirical findings.

Chapter 3 offers one empirically-constructed theoretical framework which develops the idea of framing drugs as neurotechnologies (Hupli 2013b). While the idea of conceptualising drugs as neurotechnologies is not new (e.g. Leary 1987), the author proposes that by taking seriously the role of drugs as "non-human actors" (Latour 1994), based on Science & Technology Studies (STS), Anthropology of Pharmaceuticals and critical drugs studies literature, light can be shed into various individual and societal perceptions, reactions and restrictions that material objects like "drugs" are surrounded by. To exemplify this, the sociological concept of pharmaceuticalisation (Williams et al. 2011) is also briefly discussed in this chapter with a focus on the parallel development of Attention Deficit/Hyperactivity Disorder and use of prescription stimulants in its treatment.

Then, in Chapter 4, the author will discuss his empirical findings in relation to the academic literature on what he refers to as pharmacological neuroenhancement studies (PNS). The focus will be on definitions, bioethical discussion, prevalence in relation to stimulants, efficacy and safety issues as well as the role of previous qualitative research on user perspectives. In addition, in Chapter 5, the focus is on two groups of molecular compounds that were mentioned by our interviewees as cognitive enhancers, namely psychedelics and cannabis (e.g. Hupli et al. 2016; 2019b). As academic publications on these classes of molecules in relation to pharmacological neuroenhancement remain scarce, it has been necessary to additionally rely on media articles and expert interviews which were conducted during this doctoral thesis investigation when discussing 'betterment of the well' using cannabis and psychedelics. This chapter will also shed light on a novel user

practice known as "microdosing psychedelics" (e.g. Passie 2019) to exemplify why these compounds should be included in the pharmacological neuroenhancement literature and debate (see Hupli et al. 2019a; Liokaftos 2021). Including them in the neuroenhancement discussion does not mean that cannabis and psychedelics have definitely been proven to enhance cognition, but there are plenty of studies showcasing that they are used and researched for this purpose as well (Chapter 5).

Finally, Chapter 6 will focus on the social and policy implications of the empirical findings, again focusing on user perspectives and within the context of global mental health. Here are discussed some of the barriers and opportunities for evidence-based drug policy making that could potentially transition 'world drug problems' into 'world drug solutions'. Chapter 7 offers some concluding remarks, making recommendations for continued study in this rapidly emerging field of research.

1.3 Pragmatic positioning as a researcher

Before continuing, it is necessary to position the author pragmatically as a researcher who draws upon the tradition of Anthropology of Pharmaceuticals (Van der Geest et al. 1996; Hardon & Sanabria 2017). Whyte et al. (2002, p. 166–169) offer four kinds of positions from which medical anthropologists (and sociologists) can approach issues concerning knowledge and practices of (medicinal) drugs.

For instance, a populist approach "emphasizes the agency of consumers of medicines" concentrating on the capabilities and agency of consumers of pharmaceutical drugs. The 'enlightened version' of the populist view criticizes people's knowledge about medicines (and other drugs) and shows that knowledge to be at times irrational and inadequate. For instance, patients might have expectations about their medication that might not correlate with their actual effects: "Patients want their […] medication to be like a penicillin (or at least like an effective chemotherapy) that will eradicate their disease and not like an insulin that must be taken indefinitely to counter a permanent deficiency, promising only a future as a pharmaceutical self medicated for life" (Jenkins 2010, p. 33).

A 'critical enlightened view' on the other hand "problematizes the knowledge and practice of both specialist and lay people" in relation to their beliefs regarding the problem-solving capacities of medicinal drugs (Whyte et al., 2002). And lastly, Whyte and others offer a pragmatic position. They see that participant observation and practical handling of problems gives researchers an opportunity to create knowledge and work for change. The author identifies himself as representing the last, pragmatic

position, inspired by the European Research Council-funded ethnographic project, ChemicalYouth (Hardon 2021). The project was led by Professor Anita Hardon, one of the early developers of the anthropology of pharmaceuticals approach (Van der Geest et al. 1996; Whyte et al. 2002; Hardon & Sanabria 2017) and similar to the approach developed in ChemicalYouth (2021) the current author is interested in a very pragmatic sense what chemicals do to their users and what do young users do with chemicals (Hardon 2021). Additionally, the author is keen to grasp more fully what drug policing do to drug users, advocating for a change in current drug policy towards more evidence-based drug policy making, discussed in more detail in Chapter 6. Chapter 6 focuses further into what the author refers to as 'politicogenic drug effects' and provides some policy and research recommendations.

1.4 What are these 'things' called 'drugs'?

Before proceeding to Chapter 2, where are presented the research questions and related publications, and then on to Chapter 3 where the theoretical framework for this doctoral study is given, the author here offers a brief account of his own personal understanding of the meaning of the word "drugs". Drugs, materia medica, medicines, pharmaceuticals, psychotropics and psychoactive substances are some of the umbrella terms used in the English language to describe pharmacological molecules that have a variety of effects on the human mind and body. While these terms may all seem to be self-explanatory, sociologists often tend to be 'annoying strangers' who question 'everyday knowledge', or 'common sense', that the majority of people might consider self-evident (e.g. Bauman 1997).

Even just the word 'drug' has various meanings; for example, in his book *Forces of habit. Drugs and the making of the modern world*, David Courtwright (2002, p. 2) uses the word drug "as a convenient and neutral term of reference to a long list of psychoactive substances, licit or illicit, mild or potent, deployed for medical and nonmedical purposes." Kenneth Tupper (2012, p. 465, 467), however, does not see the word drug as neutral, as according to his analysis the English word 'drug' has witnessed a transformation from "a chemical substance other than a food that alters metabolic or other functions when absorbed into the body" into "a plant or chemical substance that alters human consciousness and has been subjected to the most rigorous forms of control - typically criminalization - under the international drug control regime". In this "drug war paradigm", according to Tupper (2012, p. 462), the word drug "refers to the broad set of ideological beliefs that underlie the

international drug control regime and justify the intimidation, surveillance, arrest, incarceration, denial of human rights, and other extreme measures of social control directed at people who produce, trade, and use certain kinds of psychoactive substances, deemed morally and criminally objectionable in the legal statutes and justice systems of countries adhering to the United Nations' international drug control conventions".

Beyond ideological beliefs, as material objects, drugs come in different shapes and sizes, in synthesised form, either from legal or illegal laboratories, or as plant material and fungi. Some drugs come from amphibians; for instance 5-MeO-DMT (5-methoxy-N,N-dimethyltryptamine) comes from the Sonoran Desert Toad, although nowadays it is also produced synthetically. In terms of effects, drugs can for example stimulate or sedate, dissociate or manifest one's mind, depending on the "class" of the drug, its dose, purity as well as the surrounding physical environment. There are several ways to consume them, from snorting, smoking and swallowing to injecting, and the motivation behind the use also contributes to the experienced effects.

To give this more of a concrete historical perspective, almost all so-called psychoactive drugs that are currently 'controlled' by international and national drug policies were once used, and are still used, as medicines (e.g. Pieters & Snelders 2009). For instance, Sigmund Freud praised the euphoric effects of cocaine on himself and some of his morphine addicted patients (Jones 1964, p. 89-107) and cocaine is still used in medicine (see Rolles, Slade & Nichols 2020). Drug use has been described by writers like Baudelaire who described the effects of hashish (see Grinspoon 1994), and William James, the "father of American psychology", was known to experiment with nitrous oxide, referred to often as 'laughing gas', which was also used as an anesthetic especially in dentistry. While pharmacologically very different, what is common to all of these drugs is that "None are inherently evil. All can be abused. All are sources of profit" (Courtwright 2002, p. 2).

Thus, it is challenging to define what the word 'drugs' really refer to as it seems to be time- and context-specific. However, there is a categorical division, even a 'double bind'[1] (Eriksen 2016) in our perception of drugs, both in drug policy and in social research, which often focuses either on 'illegalised drugs' or 'legalised pharmaceuticals'. For instance, the social effects of "deviant drugs" like cannabis were already noted by sociologists like Howard Becker (1963), but according to

[1] Eriksen (2016, p. 23-24) borrows 'double bind' from the late Gregory Bateson to describe "a self-refuting kind of communication, as when you say two incompatible things at once", for instance when advocating for unlimited economic growth together with ecological sustainability.

pharmaceuticalisation scholar Abraham (2008, p. 871) "For many years pharmaceuticals escaped sociological scrutiny, not least because of the extremely limited conception of their links with 'society'. In late 19th and early 20th century Western industrialised countries, 'society' was little more than a market receptacle for the products of an expanding industry and profession of science and medicine". I claim that this limited conception can be seen as another 'politicogenic drug effect' and it has blurred the socially constructed nature of 'drugs' to almost beyond recognition, which also obscures their relative efficacy and safety.

While pharmaceuticals have received increasing social scientific attention[2], it is common to investigate and police these categories of drugs as separate entities. Thus, in drug policy one of the biggest 'double binds' is, perhaps, the divide between preventing "bad drugs" and promoting "good medicines". In practice, it is the author's firm belief that this indicates on the "good medicines" side, costly and often bureaucratic regulatory approval processes, which are meant to protect the user, but which also incentives powerful lobby efforts and industrial marketing (Dumit 2012; Medawar & Hardon 2004; Healy 2004). On the "bad drug" side, the control of the production and distribution is mostly left to organised crime, and regulatory control to law enforcement, both of which use tactics that lead to unexpected "runaway processes" (Eriksen 2016) and cycles of violence towards users and non-users (e.g. Alexander 2010; Hari 2015).

Thus, one of the "runaway processes"[3] due to the 'War on Drugs' is that the more militarised the police become in tackling perceived social problems, like drug use, the more violent the response grows from organised crime and vice versa (Woods & Rafaeli 2018). In addition to this, another politiocgenic drug effect is that there are also hardly any forms of safety regulations for 'illegalised drugs', the main control mechanism being increasingly militarised police enforcement that prohibits individuals from even coming in close contact with the molecules, some of which are physically less harmful than 'legalised drugs', like alcohol and tobacco (Nutt et al. 2007; van Amsterdam et al. 2015).

It is the author's claim that this 'double bind' between 'good medicines' and 'bad drugs' has more to do with social factors than the pharmacological properties of the drugs in question. Thus, the categorisation between pharmaceuticals and other drugs is argued to be "fluid" (Hardon & Sanabria 2017; Hardon 2021). Thus, while

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[2] See Sismondo & Greene ed. 2015 for a contemporary volume of STS scholars working on pharmaceutical studies; Healy 2004; Medawar & Hardon 2004; Dumit 2012; Hardon & Sanabria 2017.

[3] By which Eriksen (2016, p. 21) refers to 'mutually reinforcing growth processes which eventually lead to collapse'.

contemporary societies continue to make sharp distinctions between "good medicines" and "bad drugs", between licit and illicit drug use, for instance Goodman et al. (2007, p. xiii) argue that "the categories of licit and illicit are neither static nor rigid". Instead, these categorisations have been developed, and continue to develop, in a complex interaction of various historical processes: "Evolution in legal, political and scientific thought, consumer preference, commercial activity, colonialism and globalization have impacted how societies categorize and understand drugs" (Wadley 2016, p. 139). The author will outline one way to go beyond the above mentioned 'double bind' by theoretically framing all types of drugs as pharmacological neurotechnologies, as "things with social lives" (Whyte et al. 2002, p. 3; Chapter 3).

Partly due to this 'fluidity' there is a great need to establish a critical distance not only to the academic pharmacological neuroenhancement discussion and debate (Morrison 2015; also Pickersgill & Hogle 2015) but also to the wider social and cultural context of 'psychotropic drug control' that deems certain drugs, and more importantly their users, as 'bad' and others as 'good', often depending on the social context of the specific era (e.g. Bakalar & Grinspoon 1984; Cohen 2003; Pieters & Snelders 2009; Wadley 2016). Inspired by the ChemicalYouth project (Hardon 2021, p. 4; ChemicalYouth 2021) the author approaches "the use of chemicals [and/or drugs, added by author] as situated practices that are embedded in social relations and that generate shared understandings of efficacy." The author will argue that these chemicals are "peculiar substances" that "can…be considered not so much a category in themselves but as one aspect of a potentially wide range of social activities" (Sherratt 2007, p. 7).

1.5 The social life-cycle of drugs

As mentioned, in this sociological study of cognitive enhancement drugs, the author pragmatically positions himself in line with the tradition of Anthropology of Pharmaceuticals. In this position, one of the early pioneers in this field proposed to see "[medicines] as things with social lives" (Whyte et al. 2002, p. 3). This thesis study extends this point of view and proposes to see both types of drugs, medicines and non-medicines, 'as things with social lives' as elaborated below. Following Whyte et al. the author of this present study is "more concerned with their social uses and consequences, than with their chemical structure and biological effects (ibid.)" However, here the author is also concerned with their chemical structure and biological effects, while acknowledging his limitations as a social scientist to do so

with high enough 'pharmacological (un)certainty' (see Berning & Hardon 2016; also Betsos 2019). It is left finally for the readers themselves to decide how well the author managed with that (un)certainty.

According to Whyte et al. (2002) "The medicines with the most active social lives in the world today are the commercially manufactured synthetic drugs produced by the pharmaceutical industry". The 'social life' of the pharmaceutical industry producing 'commercially manufactured synthetic drugs' happens on a global scale framed by interactions between different kinds of legal, political and social actors, from pharmaceutical research and development to marketing and distribution through different regulatory frameworks and prescription practices (e.g. Rose 2003; Petryna & Kleinman 2006; Hardon & Sanabria 2017).

However, the same can be argued to some extent about the commercially produced synthetic and non-synthetic drugs manufactured by the "illegalised drug industry" which also operates on a global scale, has its own research and development (think of 'designer drugs'), (online) marketing platforms and distribution networks (e.g. Demant, Bakken & Hall 2020), often by organised crime groups, which at least to some extent try to take into account latest regulatory developments by developing 'designer drugs' or 'new psychoactive substances' (NPS) in an effort to circumvent legal consequences (EMCDDA & EUROPOL 2019).

This also has significance when thinking about the scale of the overall 'global drug market' as in addition to pharmaceuticals and plant-derived drugs like opium, cocaine and cannabis, nowadays new synthetic substances, like 1P-LSD, MDMA, 2-CB, 3-MMC and other "alphabeticals" (often referred to as "designer drugs" or new psychoactive substances, NPS) have emerged from (usually illegal) synthetic chemistry laboratories. At the same time pharmaceutical companies have increased the amount and volume of their products worldwide (Rose 2003; Medawar & Hardon 2004; Pieters & Snelders 2009; Dumit 2012). In Europe alone, the value of the 'illicit' drug market is estimated to be worth around 30 billion euros, per year (EMCCDA & EUROPOL 2019) and the global drug market, if taken to include both "legal and illegal drugs", is of course significantly larger. The global opioid market alone is enormous, and the societal expenditure that comes with it was estimated to be $78.5 billion, per year in the USA alone (Florence et al. 2016).

Since around the 1950's both the clandestine research and development of the illegal drug market together with the ever-expanding legal drug market have become integral parts of the global economy of production, distribution and consumption of drugs. Another similarity in both cases is that the 'biography' or 'life-cycle' of the

drug (Van der Geest et al. 1996) often starts from agricultural production, for instance in countries like Afghanistan, Columbia, Mexico and India. After this initial agricultural production, for example opium, which is derived from specific poppy plants (papaver somniferum), is chemically transformed into di-a-morphine, an opioid molecule which is often referred to by its traditional brand name, heroin.

And after this initial production by agriculture, in the next phase of their 'biography' these molecules are often transferred from their production countries in the Global South to their consumption countries in the Global North, mostly to the United States and Europe (Petryna & Kleinman 2006). It is good to remember that it's not only countries like Afghanistan, Mexico and Myanmar that produce for instance opium, but also the island of Tasmania in Australia produces tons of opioids from poppy plants, mainly for the medical opioid industry (Smith 2019). Countries like the USA and the Netherlands are also one of the biggest producers of legal cocaine in the world, which is one of the many alkaloids of coca plants, and used, for example, in certain surgical procedures as a topical anesthetic (in Rolles, Slade & Nichols 2020).

The social life of drugs does not stop at their distribution via a prescription or (often illicit) sale; at the next stage of their "biography" the drug comes into the hands of the user, which is the final stage of their life-cycle (Van der Geest et al. 1996, p. 156). This is the point when drugs will be used by somebody, often "with the purpose of restoring, improving, or maintaining his or her health" (ibid.). Certain types of usage, however, are defined from an outsider perspective as being 'deviant' (Becker 1963) drug abuse or misuse, which partly reflects the "drug war paradigm" referred to by Tupper (2012).

Motivations for any type of drug use, be it medicinal, recreational, enhancing, self-medicative, self-reflective, or for pure pleasure are to a large extent empirical questions which often have a variety of answers depending on the context (e.g. Hardon 2021). But while for instance opioids are used both in- and outside of hospitals to mainly treat pain (usually physical, sometimes psychological) the social perceptions differ greatly depending on who uses a particular 'drug', and where. For instance, take a medical patient using GMP (Good Manufacturing Practices) produced prescription opioid to deal with post-surgery pain. He or she is perceived very differently than a homeless person injecting 'heroin' on a street corner in order to self-medicate his or her traumatic life situation. However, on the level of the organism's opioid system, the mechanism of drug action in relation to our innate endorphin system is basically identical in both mentioned cases, if factors like drug purity are left out of the equation. But the social effects differ greatly; in the first case

the social effects usually include receiving a medical bill, while in the latter, potentially enforced time in prison and loss of civil liberties. How factors like race, gender, religion, and national policies influence these 'politicogenic drug effects' are something that could, and should, be measured (see IDPC 2018).

Van der Geest et al. (1996, p. 156) also state that medicines have a life after their "death by consumption" which lies in their efficacy: "The fulfilment of their life purpose lies in their effect on the well-being of the person who took them. The pharmaceuticals's efficacy is its ultimate and decisive life stage." In short, medicines, materia medica, as well as arguably other drugs, have powers to transform lives (Whyte et al. 2002, p. 5-6). Usually that transformative power is used to heal or prevent diseases, or enhance, but drug effects can also be harmful and toxic (Hardon 2021). As argued below in Chapter 6, drug policies can also be harmful and cause various politicogenic drug effects.

Drugs, as Whyte et al. note (2002, p. 6, emphasis in original) "are used intentionally to achieve an effect in some body". I would add, not merely due to semantics, but when it comes to so-called 'psychoactive drugs', these intentional effects are achieved in some minds as well. But whether, and how, the use of drugs influence individual bodies and minds, and societies at large, presents often an "interpretive gap" between the "desired" and "actual" effects (Floersch 2003).

Focusing on effects that happen only on the level of biology is complex enough, as the potential interactions of neurochemicals on, and of, the brain are practically unmeasurable in their totality. This is partly because this complexity is not a new discovery, as echoed in this excerpt written over 50 years ago by a professor of biochemistry, Dr. Leo G. Abood (1970, p. 56): "The brain is simply a complex chemical system, perhaps the most complex in the universe; and in order to understand how chemicals will interact with such a complex chemical system we have to know something about what the brain is chemically and the peculiar chemical characteristics of psychochemicals which make them do what they do.". Thus, when you add to this neuronal complexity basically any 'psychoactive drug' that interacts with the brain in an individualistic way, the picture gets even more complicated, as Abood (1970, p. 56) already wrote decades ago: "Drugs…do not produce the same effects in different individuals. Some individuals are stimulated by such drugs as barbiturates and morphine, while the majority of people are sedated. It is now known that there are genetic factors that help determine drug responsiveness. Other determinants include dosage, physical health, psychological constitution, environmental setting, and past and concurrent drug usage."

In addition, when one tries to add to that discussion behavioural and societal effects that drugs are perceived to deliver, it is challenging to consider the totality of drug effects without 'cutting some corners'. Thus, to fully include this neuronal complexity is to a large extent outside the scope of this Dissertation in social sciences. Nonetheless, the focus will be on so-called cognitive enhancement drugs and on 'pharmacological neuroenhancement' which in this study refers to the use of drugs, legal or illegal, with the intention of improving one's cognition, mood and/or memory as well as pro-social behaviour and 'spirituality'.

It is appropriate to now turn to the research questions, methods and key findings of this thesis (Chapter 2). To recap, then follows in Chapter 3 a theoretical framework for the thesis investigation which is based on the idea of looking at all types of drugs as pharmacological neurotechnologies and in so doing, making it easier to navigate the vast landscape of 'psychoactive substances', which includes both 'illegalised drugs' and 'legalised medicines'. This framework partly comes from observing social practices around the phenomena (Hupli et al. 2016; 2019b) and is used in this study as a theoretical concept to discuss the 'situated practices' (Hardon 2021, p. 4) and meanings of so-called cognitive enhancement drugs.

The literature published on pharmacological neuroenhancement is presented in Chapter 4 focusing on the bioethical discussion, definitions, prevalence, efficacy and safety. In that particular chapter is also presented a more qualitative research approach to the use of cognitive enhancement drugs with a focus on how qualitative research creates its research space.

Partly because illegalised drugs like cannabis and psychedelics are often excluded from the academic discussion on neuroenhancement drug use, the author will briefly focus on cannabis and especially on microdosing psychedelics as a potential cognitive enhancer in Chapter 5. More empirical research is needed regarding both cannabis and microdosing psychedelics as cognitive enhancers in order to give a clearer picture of their potential benefits and risks.

In the final chapter the author argues that the bioethical discussion around pharmacological neuroenhancement is oriented towards a transhumanist future world where these neurotechnologies might be widely available and commonly used (Chapter 6; see also Coveney et al. 2011). This futuristic orientation is not, in the author's view, because we necessarily lack potential pharmacological neurotechnologies that in theory could augment our brain capacity to some measurably "higher than normal" level, but because in practice current international and national laws continue to frame that activity as prohibited. This prohibition is articulated in international drug treaties and national policies which use the state

apparatus to prevent such 'extra-medical' use, often even by force (Bublitz 2016; IDPC 2018; Sultan & Hupli 2020).

2 RESEARCH QUESTIONS, METHODS AND KEY FINDINGS

2.1 Research questions

The main research question in this doctoral investigation has been "What is cognitive enhancement drug use from user perspectives?" This main question has been explored through a set of sub-questions in the published articles. These have included: a) what are the reported reasons to use drugs for what is broadly referred to as pharmacological neuroenhancement; b) what are the reported drugs used for cognitive enhancement; c) what are some of the reported effects of using drugs for neuroenhancement purposes, and; d) what are some of the differences between using drugs for therapy versus using them for neuroenhancement?

Additionally, the roles of online knowledge and digital technologies are explored both as data and as a methodological tool to explore emerging drug trends. This is done in relation to microdosing psychedelics and with a focus on the video sharing platform Youtube. What are some of the social and drug policy implications of using pharmacological neuroenhancement technologies in the 21st century within the context of global mental health will also be explored more broadly.

2.2 General considerations on methods and data

Methodologically this Dissertation has made use of both researcher-provoked and naturally occurring data (Silverman 2001, p. 159) to gain knowledge about the research questions presented above. These methods are described in greater detail in the five peer-reviewed academic publications that are re-published at the end of this summary article (Chapter 9; Hupli et al. 2016; 2019ab; Hupli 2018a; 2020a).

Generally speaking, the focus has been on 'users' and their experienced effects in relation to cognitive enhancement drugs. The main method and empirical data comes from semi-structured interviews with university students, some with a self-reported neuropsychiatric diagnosis of mainly ADHD/ADD (APA 2013), and others without any reported diagnosis. All of these young adults had experiences

with 'therapeutic', 'recreational' and/or 'neuroenhancement' use of drugs (Hupli et al. 2016; 2019b).

More specifically, the data published in Hupli et al. (2016) and Hupli et al. (2019b) consisted of collaborative qualitative data analysis of interviews with a total of 35 students or students who had recently graduated. At the time of being interviewed the students lived either in Amsterdam, the Netherlands, or in Vilnius and Kaunas in Lithuania. These students had all been interviewed in 2013, as they had experimented with what is often referred to as cognitive enhancement drugs (see also Hupli 2013b). Thus, in both Hupli et al. (2016) and Hupli et al. (2019b) we combined three different qualitative data sets from two different European countries, and aimed to further develop a Crowded Theory approach (see Bröer et al. 2016) when analysing these separate reports from young adults (see Table 1 in Hupli et al. 2019b, also below).

In addition to the research-provoked data of the interviews, professional journals, scientific research articles and policy reports comprise the naturally occurring data, reviewed for instance in Hupli (2020a). Hupli (2020a), published as part of a Special Issue in Drugs & Alcohol Today (see Sultan & Hupli 2020), was a general review of available data in the Netherlands and Finland focusing especially on stimulants as cognitive enhancers among young people.

Hupli (2018a) on the other hand is a detailed case study (N=1) of a Finnish medical cannabis patient with ADHD which included several in-depth interview sessions with the patient in question. As part of the case study, clinically relevant patient records were also reviewed which the patient shared during and in-between the interviews which started in 2015.

As argued also in several of the publications (Hupli et al. 2016; Hupli 2018a; 2020a), being cognisant of the drug policy environment where drug effects take place is important when considering the context of use. Therefore, the author conducted 'ethnographic expeditions' (Martin 2007) to provide a broader and more in-depth perspective of different 'ecologies of practice' (Boothroyd & Lewis 2016) around drugs. These included "netnographic" (Kozinetz 2010) expeditions to online platforms like Youtube (Hupli et al. 2019a).

As the user interview studies had revealed the important role of online information and the variety of drugs which had been used as enhancers, including cannabis and psychedelics (Hupli et al. 2016; 2019b), in Hupli et al. (2019a) we investigated so-called "microdosing psychedelics" which has been described as a trending psychedelic drug consumption practice (e.g. Kuypers et al. 2019; Passie 2019; Liokaftos 2021). While developing digital methods for online drug trend

analysis, we explored the Youtube Data Tool to study the "descriptive assemblage" (Savage 2007) of microdosing on Youtube (Hupli et al. 2019a).

Participant observation at international high-level drug policy meetings, research conferences and events has also been part of the ethnographic data collection process, which the author has digitally documented and partially made public since 2016 (Drugventures 2020). This data will be utilised especially when talking about cannabis and psychedelics as potential cognitive enhancers (Chapter 4).

2.3 Research ethics

Interview data analysed and published in Hupli et al. (2016; 2019b) was collected during fieldwork conducted for Master and Bachelor thesis projects at the University of Amsterdam. Within these programs, all research is evaluated and reviewed in line with standard ethics operating procedures before students enter the field. In addition to institutionalised pre-evaluation of research ethics, fieldwork thesis supervisors are responsible for monitoring the implementation of ethical safeguards during the process. Ethical procedures in these publications included the use of pseudonyms and other forms of anonymization when publishing, asking for informed consent prior to interviews, and a more general ethical handling of field relations with research participants even after the research was conducted.

In the patient case study (Hupli 2018a), the case report was conducted in accordance with the ethical guidelines provided by the University of Tampere and the National Advisory Board on Research Ethics. The study was conducted with the informed consent and cooperation of the patient in question. No personal details that could be used to reveal the identity of the patient were used in the publication and sensitive patient records that the patient shared were analysed during visits to the patient's home and while in his presence.

In Hupli et al. (2019a), which focused on microdosing psychedelics on Youtube, issues were raised concerning Internet Research Ethics (IRE). Youtube has previously been used to assess healthcare information (Hasamnis & Patil 2019) and it has been shown to be a valuable tool in the field of drug research. Research has focused on Salvia divinorum and Kratom user experiences (Casselman & Heinrich 2011; Lange et al. 2010a; Prevete, Hupli, Marrinan et al. 2021), polydrug risk reports (Kataja et al. 2019) and microdosing psychedelics (Hupli et al. 2019a; Andersson & Kjellgren 2019). Several Youtube drug studies have not identified or even mentioned

IRE in their publications, until recently (Hupli et al. 2019a; Kataja et al. 2019; Andersson & Kjellgren 2019; Hupli, Berning & Alenichev unpublished manuscript).

Most Youtube video makers use pseudonyms which can give a false impression of anonymity which is not even always desired (Kozinets 2010). In our study (Hupli et al. 2019a), we notified the makers of the most viewed videos that these videos were identified and analysed more closely in our study. Issues of anonymity and informed consent in relation to Youtube drug research will be presented in more detail in a separate publication (Hupli, Berning & Alenichev, unpublished manuscript).

2.4 Brief summary of main findings

The two publications in Contemporary Drug Problems (Hupli et al. 2016; 2019b; see also Hardon & Hymans 2016) showed that the young people we had interviewed had experienced a variety of positive and negative effects from using several legal and illegal drugs in order to improve their life situations. The experiences and motivations of using different substances for both self-reportedly diagnosed students and those who did not report a psychiatric diagnosis did not differentiate to a large extent. Table 1 in Hupli et al. 2019b provides more detailed information in terms of the interviewees age, occupation, gender, location of interview, reported diagnostic status and substances used and for what purpose. Names appearing in the table are pseudonyms. These findings are limited due to unrepresentative nature of the interview and survey data, self-reported drug effects and medically unconfirmed diagnostic status of the interviewees. However, they raise bioethical and policy questions about the line between therapy and neuroenhancement, as well as between prohibited drugs versus legally promoted ones which are discussed in more detail below.

Table 1. List of Participants: Age, Gender, Occupation, Location of Interview, Diagnostic Status, Substances Used and Their Effects.

Pseudonym	Age	Gender	Occupation	Location of Interview	Diagnostic Status	Substances Used
Amelia	22	Female	Medical student	The Netherlands	ADD diagnosed	Used medication more often since the age of 15, before that didn't like the side-effects, which included loss of appetite and depression. Prescribed with Ritalin and Concerta. Experiences with other drugs.
Anna	24	Female	Political science	The Netherlands	Undiagnosed	Anna tried Ritalin once before her finals. Experienced feelings of anxiety and nervousness, no positive effects. Has tried Ritalin recreationally on three occasions. Has also used amphetamine for study purposes.
Bella	21	Female	Medical student	The Netherlands	Undiagnosed	Tried Ritalin before an exam. Experienced mild improved focus. Experiences with other drugs
Bram	21	Male	Economics and geography student	The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as a child. Has taken Concerta when he was younger, and has been using Ritalin for the past seven years. Uses it only for study purposes, during lectures, exams and other important moments. Does not experience any side effects. Experiences with other drugs.
Brian	27	Male	Economy student	The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as an adult but doesn't believe in the diagnosis. Has used caffeine pills, Modafinil and Ritalin (now with prescription), Oxazepam and methamphetamine for study purposes.
Cecilia	23	Female	Political science student	The Netherlands	ADD diagnosed	Was diagnosed with ADD as an adult. Prescribed with Ritalin. Decided to stop using because didn't find it helpful. Also had side effects.
Corinne	25	Female	Global Health student	The Netherlands	Undiagnosed	Has tried Concerta and Ritalin approximately 10 times. Did not find it useful for studying although said focus improved mildly. Also used it for creative purposes and for recreation. Felt distracted after the medicine wore off.
Dana	24	Female	Working	The Netherlands	Daytime sleepiness diagnosed	Dana was diagnosed with daytime sleepiness about two years ago. First prescribed with Ritalin, afterward Modafinil. Used it regularly while studying although had some side-effects and did not want to become dependent on it.
Diane	23	Female	Global health	The Netherlands	Undiagnosed	Has tried Ritalin twice. First time used half a pill, did not experienced any effects so tried a whole one again with motivational effects
Eglė	24	Female	Master's economics student (working)	Lithuania	Undiagnosed (self-diagnosed with daytime sleepiness)	Used Modafinil for self-treatment of daytime sleepiness she experienced in her work.
Emilia	23	Female	History student	The Netherlands	Undiagnosed	Tried Modafinil once. Used it after using other drugs the night before to stay awake at class. No strong effects.
Eric	23	Male		The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as an adult. Prescribed with Ritalin and finds it useful. Has a system of off and on periods. Also used Ritalin recreationally.
Fiona	22	Female	Education	The Netherlands	Undiagnosed	Fiona tried Ritalin once before an exam. Did not experience any effects. Also used Ginkgo biloba to improve concentration while studying.
Frank	25	Male	Social science student	The Netherlands	ADD diagnosed	Was diagnosed with ADD as an adult. Prescribed with Ritalin. Had used Ritalin before; also Adderall, amphetamine and LSD for study purposes.
Gabriel	24	Male	Psychology student	The Netherlands	Undiagnosed	Has tried Modafinil, Piracetam, Oxiracetam and Aniracetam to get better grades and improve memory. Experienced wakefulness and more focus with modafinil and better memory of at least dreams with the racetams. Experienced anxiety about possible side-effects.
Henry	26	Male	Social science student	The Netherlands	Undiagnosed	Has tried Ritalin and Concerta (about 50 times in the last nine years) and also Ephedra, amphetamine and cocaine (once) for studying, doing sports and for recreation (about 5 times). Experienced improved and longer lasting concentration, no harmful effects.
Ieva	19	Female	Publishing student	Lithuania	Undiagnosed	Used Lecitone Jeune, a food supplement for young people, during her final school year.
Iris	19	Female	Law student	The Netherlands	Undiagnosed	Has tried Ritalin because she was curious about the effects for studying. Does not want to use it often because she thinks it is not completely fair.
Jasper	21	Male	Economics student	The Netherlands	ADD diagnosed	Diagnosed with ADD, does not use his prescription but obtains Ritalin through a friend's mother who is a psychiatrist. Has many side effects and wants to use Ritalin as little as possible.
Jovita	26	Female	Art student	Lithuania	Undiagnosed	Used food supplement for the brain Neurozan to help her with some tests and exams both in school and university.
Karolis	29	Male	Working (philosophy graduate)	Lithuania	Undiagnosed	Has tried variety of drugs ranging from food supplements like Neurozan to psychedelics and cannabis to induce different states that he deemed helpful for studying.
Kipras	21	Male	International relations student	Lithuania	Undiagnosed	Used armodafinil when recommended by a friend, mainly to prepare for university exams.
Lotte	23	Female	Social sciences student	The Netherlands	ADD diagnosed	Diagnosed with ADD at the age of 19. Had so many side effects that she quit using for a while. Now uses only when she finds it absolutely necessary.
Marius	20	Male	Dentistry student	Lithuania	Undiagnosed	Used Neurozan when studying.
Marija	24	Female	Working (Directing graduate)	Lithuania	Undiagnosed	Used cannabis after a long day of studying/acting to insure a good night's sleep before another intense day.
Milda	24	Female	Doctorate student in biological sciences	Lithuania	Undiagnosed	Used Tonusan, a herb-based food supplement that is supposed to minimize tiredness and increases wakefulness. Was used during an intense period of Master's degree.
Mo	21	Male	Media student	The Netherlands	ADD self -diagnosed	Only uses Ritalin when he thinks he really needs it. Uses other recreational drugs regularly.
Neringa	23	Female	Architecture student	Lithuania	Undiagnosed	Used Neurozan food supplement for the brain during an intense period when she was both working and studying.
Petras	20	Male	Veterinary student	Lithuania	Undiagnosed	Used a range of substances. Piracetam to prepare for exams, GABA and theanine to improve work-out results as well as for improved studying. Also used Orange Triad multi-vitamins.
Robertas	20	Male	Medicine student	Lithuania	Undiagnosed	Used methamphetamine to prepare for exams and to study, but found this very unhelpful as he could not concentrate and remember.
Roderick	21	Male	Media student	The Netherlands	ADD self-diagnosed, in the process of getting diagnosed	Has been using Ritalin the past 4 months before the interview. Started because he thinks he has ADD. Obtains Ritalin from his younger brother with ADD. Thinks effect is heavy and uses only when necessary.
Simona	22	Female	Master's architecture student	Lithuania	Undiagnosed	Used methamphetamine during an intense period in order to stay awake and work longer hours.
Steponas	26	Male	Unemployed (economics graduate)	Lithuania	Undiagnosed	Used cannabis to have motivation to work.
Vaiva	25	Female	Master's economics student (working)	Lithuania	Undiagnosed	Used various kinds of vitamins and food supplements during intense periods at university.
Viktorija	23	Female	Law student	Lithuania	Undiagnosed	Used lithium and passion fruit extract to help her relax during intense periods and be able to work.

By comparing data from international, European and national sources in Hupli (2020a) this comparative review revealed some differentiating trends between Finland and the Netherlands in relation to medical and extra-medical use of stimulants. The focus was on all medical stimulant use, amphetamine use among young people (15-34 year olds) and non-medical methylphenidate use (see Table 1 in Hupli 2020a and below). However, in relation to using stimulants for cognitive enhancement in particular, the scope of these differences is challenging to evaluate as there is a chronic lack of research data and policy discussion in Finland compared to the Netherlands when it comes to stimulant or other drug use for cognitive enhancement (Hupli 2020a).

Table 1. in Hupli (2020a). Use of medical stimulants, illicit amphetamine and methylphenidate in Finland and the Netherlands according to International Narcotics Control Board (INCB), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Global Drug Survey (GDS) data between 2014 and 2018.

Study	Finland	The Netherlands
INCB 2017 (all stimulants 2014-2016)	2.26 S-DDD	9.10 S-DDD
INCB 2018 (all stimulants 2015-2017)	2.53 S-DDD	9.03 S-DDD
EMCDDA 2017 (amphetamine use in the past year)	2.4%	3.1%
EMCDDA 2018 (amphetamine use in the past year)	2.4%	3.9%
GDS 2017 (methylphenidate use in the past 12 months)	8% (N = 1,339)	6.8 % (N > 3,300)
GDS 2018 (methylphenidate use in the past 12 months)	8% (N = 2,184)	4.4 % (N > 3,400)

In our "netnographic" (see Kozinets 2010) study on videos related to microdosing, our initial data extraction, which was completed in 2016, resulted in a total of 115 Youtube videos at the time. Additional data extractions done in 2017 and 2018 showed a 290% increase in "microdosing" videos between 2016 and 2018, indicating that the phenomenon was growing empirically, at least in the "digital milieu" (Boothroyd & Lewis 2016) of Youtube. This 'digital milieu' of microdosing on Youtube included 48 videos (41.7 %) which mentioned a psychoactive substance in 2016.

The six most viewed videos were analysed in more detail and published in Performance Enhancement & Health in 2019. The six videos comprised 92% (N = 934,819) of the total view count and the "ecology of practices" (Boothroyd & Lewis 2016) described in the videos suggested that microdosing psychedelics is mainly beneficial. While these effects and dosing regimens mentioned in the videos require further critical evaluation, contrary to how typical users of illicit drugs are often portrayed in the general media and science, these videos revolved around themes like research, experiments, self-monitoring and the imperative of sharing results (Hupli et al. 2019a).

The "descriptive assemblage" (Savage 2007) of on-going psychedelic microdosing studies included in the study also demonstrated that several research projects were underway at the time of the publication (Hupli et al. 2019b; see also Hupli 2018b; 2019c). Research in this field has since then continued to proliferate, potentially influencing future user practices, knowledge and policy discussions. As part of this Summary article, the author will provide an update on the on-going research projects and a general review of results in Chapter 5, especially in relation to cognitive enhancement which is currently scarce in the PNS literature.

As the line between therapeutic and neuroenhancement is not only blurred on user level (Hupli 2013b; Hupli et al. 2016; 2019b) but in relation to drug development and policies (e.g. Schermer et al. 2009; Bublitz 2016), one of the published articles in this doctoral thesis aimed at focusing on the therapeutic potential of cannabinoids (Hupli 2018a). In addition to our findings (Hupli et al. 2016; 2019b) research done in Germany has also showcased how cannabis is also reportedly used as a cognitive enhancement by some students (Franke et al. 2016; Bagusat et al. 2018).

Hupli (2018a), published in the second volume of a new academic publication entitled Medical Cannabis and Cannabinoids (Karger publications), was a detailed medical sociological patient case report of a male ADHD patient living in Finland. In the case report is described how after experiencing adverse effects from prolonged use of methylphenidate, the patient in question discovered that

cannabinoid therapeutics (CT) had been experimented inside the EU area to treat adult patients with ADHD. The patient, who was diagnosed in adulthood (aged 33) with ADHD, and treated initially with immediate-release methylphenidate (Ritalin® 10 mg, twice daily), was subsequently evaluated by a physician in Germany (in June 2010) who prescribed cannabinoid therapeutics (Bedrocan®, Bediol®) to treat ADHD as the primary indication. Later, a Finnish neurologist confirmed the two prescribed medicines (Bedrocan®, in October 2010 and Bediol®, in May 2011) in the patient's own country of permanent residence, Finland.

During a 5-year period of legal access, Bedrocan®, which mainly contains Δ9-tetrahydrocannabinol (Δ9-THC), was found to be helpful in alleviating the patient's ADHD symptoms, in particular poor tolerance to frustration, outbursts of anger, boredom, and problems related to concentration. The second prescribed medication, Bediol®, which contains both Δ9-THC and the phytocannabinoid cannabidiol (CBD), was found to neutralize the excessive dronabinol effects of Bedrocan®, as well as to offer other therapeutic benefits (e.g., improved sleep, pain-relief and physical rehabilitation in relation to a knee injury).

In addition to being the first case report of a 'medical cannabis patient' in Finland (see also Hupli 2019b; Vihervaara & Hupli 2021), the publication also generally reviewed scientific literature surrounding the benefits of cannabinoid therapeutics for treatment-resistant adult AD(H)D, which had at the time included observational studies, clinical case reports, and one randomized clinical experiment, which showed modest benefits of the standardised medical cannabis product, Sativex, over placebo (Cooper et al. 2017). In addition, Hupli (2018a) briefly discussed the role of the endocannabinoid system in relation to ADHD.

The way drugs are understood to work in treating specific diseases has often been used to comprehend and articulate the biological processes of those diseases (Moncrieff 2009). When it comes to ADHD, the author argues that there has been overemphasis on stimulant treatments, with medicinal cannabinoids only gaining recent research interest, despite early anecdotal reports expressing potential benefits (e.g. in Grinspoon & Bakalar 1997). The role of the endocannabinoid system (ECS) in the etiology of neuropsychiatric disorders, including ADHD, has recently gained closer scrutiny and according to Navarrete et al. (2020) the "close involvement of the ECS in the etiology and neuropathology of neuropsychiatric disorders is undeniable." Although endocannabinoid system modulation with exogenous cannabinoids shows therapeutic potential for some adults with ADHD, more preclinical, clinical and real-world evidence (RWE) is needed to establish optimal cannabinoids levels as optimal dosing regimens are likely to vary greatly between

different ADHD patients (Hergenrather et al. 2020). Hopefully this area sees further research that looks at the potential of endocannabinoid system modulation with different cannabinoids, like cannabinol (CBN), and possibly other molecules found in the cannabis plant in relation to ADHD (Hergenrather et al. 2020; Navarrete et al. 2020; Hupli 2018a), as medical cannabis seems to be preferred by some ADHD patients compared to standard stimulant medications (Hergenrather et al. 2020; Hupli 2018a).

3 DEVELOPING A THEORETICAL FRAMEWORK

The five peer-reviewed publications that together comprise this doctoral thesis vary in their methodologies and data types (interviews with young users, general review of different statistical data sets, patient case study and netnographic study on Youtube), as well as their focus points (experiences and reported effects of neuroenhancing and therapeutic use of drugs, online knowledge in relation to user practices). Thus, there was a need to develop a theoretical framework to simply 'make sense of it all' and make it easier to navigate the changing landscape of (cognitive-enhancing) drug use. This chapter develops one possible approach, one that theoretically frames all drugs as pharmacological neurotechnologies. While this theoretical framework conceptualises drugs as tools or 'instruments' (Müller & Schumann 2011), it is not meant here as a theory to be empirically tested. However, the framework does have some empirical grounds as in addition to publications of this doctoral study (Hupli et al. 2016; 2019ab), several qualitative researchers have looked at the lived experiences of especially young people who have used prescription stimulants and other drugs as "technologies of the self " (Foucault 1997) in efforts to improve parts of themselves (e.g. Pienaar et al. 2020; Petersen et al. 2015ab; Vrecko 2013).

Therefore, as discussed more below, various qualitative studies have already pointed to the role of cognitive enhancement drugs and their different 'functional' significance to young people who use them (Vrecko 2013; Petersen et al. 2015ab; Vargo & Petróczi 2016). Other types of drug studies (e.g. Lende et al. 2007; Silva, Kecojevic & Lankenau et al. 2013) have arrived at similar conclusions about the "instrumental use of drugs" (Müller & Schumann 2011) in various real-life situations (Hardon 2021). As we also bring forth (Hupli et al. 2016; 2019b), both self-reportedly diagnosed and those who did not report a psychiatric diagnosis used prescription drugs, food supplements and even illegally obtained "street drugs" as functional tools or technologies to cope with the demands they faced in daily life. Our informants used terms like "tool" [hulpmiddel in Dutch; irankis in Lithuanian], "helping thing," "facilitation," "extra help," or "means" [middel in Dutch] (Hupli et al. 2019b, p. 390). These empirical findings call for a theoretical framework to situate the variety of drugs used for the practice of pharmacological neuroenhancement.

This is because "as social scientists we have to try to find the concepts which make a difference, to listen to what people are saying" (Latour in Barron 2003 ed.).

In the next sub-chapter a more detailed way of looking at drugs as neurotechnologies will be provided by focusing generally on their 'social effects' and 'modes of action' which include 'extra-pharmacological variables' (Hartogsohn 2017). In sub-chapter 3.2 the author situates this approach in the wider Science & Technology Studies (STS) discussion about 'non-human actors' (Latour 1994). In addition, to give a fuller historical context[4] of the relation between ADHD and methylphenidate, or 'Ritalin', sub-chapter 3.3 will briefly explore the increasingly prevailing use of stimulants in the Western world, inspired by Foucault's genealogy[5]. The focus is on methylphenidate as it is often used as an example of a cognitive enhancement drug. This discussion will also utilize the sociological concepts of medicalisation and especially pharmaceuticalisation (Williams et al. 2011).

3.1 Drugs as pharmacological neurotechnologies

Several things should be consider when talking about the physical effects of drugs as pharmacological neurotechnologies: firstly, what is the specific 'chemical compound' or molecule in question, its structure and whether it comes in a "natural form", like plants and fungi, or whether it is synthetically produced in crystallised or liquid form; secondly, the way the technology enters your physiology and from which part, which is often referred to as the "route of administration" (for instance, oral, intravenous,

[4] The aim here is not to discover the "true nature of ADHD", measured by some contemporary psychiatric standard of "normal attention", but instead look at what effects certain types of truth-claiming might have on social practices (Rose 1990), like treating individuals diagnosed with a neuropsychiatric diagnosis such as ADHD.

[5] According to Garland (2014, p. 372), for Foucault genealogy was a method of writing critical history: "a way of using historical materials to bring about a 'revaluing of values' in the present day." This "history of the present" (e.g. Dean 1994, p. 20-21; Foucault 1984) usually takes as a starting point something in the present that is seen as problematic and traces its history through different discoursive practices (Helen 2005). This type of genealogical approach can be seen as Mitchell Dean (1994, p. 18) states an effective history which "historicises that which is thought to be transhistorical, grasps rather than effaces the singularity of events and processes, and defines levels of analysis that are proper to its objects. An effective history both refuses to use history to assure us of our own identity and the necessity of the present, and also problematises the imposition of suprahistorical or global theory" (see also Foucault 1984, p. 86-90). Effective history is also critical although being critical does not mean denying the truth value of certain scientific knowledges. Rather the aim is in a sense to look in which conditions those knowledges emerged (e.g. Dean 1994, p. 23-24). The concern is not so much about truth as "the 'apparatus of truth' – the concepts, rules, authorities, procedures, methods and techniques through which truths are realized" (Rose 1990, p. 4).

nasal, rectal, topical or via inhalation); thirdly pharmacokinetics, which, to put it briefly, means what your physiology does to the technology; fourthly pharmacodynamics, meaning what the technology does to your physiology; and finally, but importantly, dosing.

All of these 'technical' factors surrounding physical effects, and some of the more social ones described below, are at play when your human physiology is interacting with an 'external' molecule in the form of a pharmacological neurotechnology. It is important to note that when it comes to "psychoactive" neurotechnologies, these interactions on a pharmacological scale cause mostly temporary effects that last from minutes to days, depending for example on the dose and the "half-time" of the neurotechnology in question. On a social scale, these effects can last significantly longer, for instance in the form of social stigma, imprisonment and/or individual habit formation, even dependence, towards the use of the specific neurotechnology in question. Some of these effects could be described as 'politicogenic drug effects' (see also Chapter 6).

To turn more to the 'extra-pharmacological variables' (Hartogsohn 2017) in relation to effects and efficacy, according to Whyte et al. (2002, p. 15, italics added) "efficacy relates to perceptions of the powers of medicinal substances". In other words, the effects of pharmacological neurotechnologies are not solely resulting from the pharmacological properties of the technology in question but partly also based on how they are perceived. As DeGranpre (2006) writes in his book The Cult of Pharmacology, the pharmacological properties of drugs were greatly overemphasised during the last century especially in the North American context as "drugs powers were still viewed as capable of bypassing all the social conditioning of the mind, directly transforming the drug users' thoughts and actions."

Efficacy is not only linked to perceptions, but also the immediate environment where these technologies are used contribute to the overall effect (Langlitz 2010; Hartogsohn 2017; Hardon 2021). Especially the effects of classical psychedelics seem to be linked to the specific physical and social environment where they are taken: "The effects of hallucinogens vary markedly from individual to individual and from session to session, depending on the context, expectations, and environment of the session" (Bogenschutz 2013, p. 19). This contextuality in relation to the environment, and its ability to have an impact on especially psychedelic effects in clinical settings, is further explained by James Rucker (2016), a psychiatrist who has been part of the recent psychiatric psychedelic research in the UK. Here he echoes a view that his psychedelic research colleagues expressed already decades ago: "the therapeutic effect is inextricably linked to the context it is experienced in. Provide a

safe and supportive setting for a psychedelic trip, and you are much more likely to achieve a good therapeutic outcome than otherwise."

Rucker (2016) continues that "this inextricably interactive effect is problematic for modern trial designs, which seek to isolate a drug and test it solely for its therapeutic effect. With psychedelics you cannot do this. You have to consider the drug and the context together, or you miss the point". In other words, "what is really being measured is the combined effect of the drug-psychosocial treatment combination (Bogenschutz 2013, p. 19; see also Johnson & Richards & Griffiths 2008; Langlitz 2010).

This role of so-called 'set and setting' (e.g. Hartogsohn 2017; Richards 2016; Alaeddinoglu 2020) has been mostly ignored in modern pharmaceutical drug trials which have focused on very limited outcome measures, which often only means whether the drug shows more efficacy than a placebo, a nocebo or an existing drug treatment (Healy 2004; Moncrieff 2009). Whether this 'mode of action' between 'drug effects' and the 'setting' (environment they are used in) can be generalised to all psychoactive and non-psychoactive drugs would need more research.

The current clinical trial model which often focuses on single molecules and compares whether these produce effects better than 'a placebo' is challenged not only by newly emerging psychedelic research (e.g. Sessa 2017; 2012) but to a certain extent by medical cannabis research as well. While clinical psychedelic research focuses on individual compounds (LSD, MDMA, psilocybin, ibogaine, harmaline, DMT), the Cannabis Sativa L. plant contains around 500 different chemical compounds (WHO 2018; Hill et al. 2012), many of which very little is still known about. For single molecule drug trial designs, which most contemporary clinical trials are, whole plant cannabis medicine development is maybe even more challenging than psychedelics due to the 'poly-pharmacology' of this "plant of the thousand and one molecules" (Andre, Hausman & Guerrieiro 2016).

This complexity, however, does not rule out the possibility that these groups of molecules, psychedelics and cannabinoids, cannot be effective as therapeutic and neuroenhancement "tools" but rather that future science needs to eventually verify, or contradict, current 'citizen science' (Hupli et al. 2019a; Fadiman & Korb 2019; Szigeti et al. 2021) and that extra-pharmacological factors need to be taken account (Hartogsohn 2017). Thus, it is argued that by framing both pharmaceuticals and other drugs "neutrally" and mutually as pharmacological neurotechnologies helps to approach different kinds of drug effects and use(rs) without certain pre-existing dichotomies (i.e. good vs. bad / legal vs. illegal / therapeutic vs. enhancing) and/or

negative and biased attitudes and assumptions towards certain groups of drugs, or their users.

Of course, technologies in general are not value-free; for instance, technologies surrounding atomic energy can be used to supply electrical power, or destroy cities. And as mentioned, the more general "human enhancement technology" discussion involves various neurotechnologies, from transcranial magnetic stimulation (TMS) to deep brain stimulation (DBS), with their unique ethical and other challenges (Warso et al. 2019; STOA 2009). However, even compared to invasive deep brain stimulation which requires neurosurgery, literally opening up a patient's skull and poking their brain with a surgical knife in order to implant a device that is controlled externally, there is something about "drugs", and our modern moralistic approach to them, that calls for closer inspection in the debate about human enhancement technologies.

3.2 Drugs as non-human actors

Morrison (2015, p. 10) sees that "An STS approach must adopt a critical distance from the enhancement debate, taking the concept of enhancement as a topic of investigation rather than a given 'fact' about the technologies and accounts being studied". This current thesis seeks to adopt such a critical distance to the human enhancement drug debate especially in Chapter 4. Here, drawing from STS literature (see Morrison 2015; Coveney et al. 2011; Pickersgill & Hogle 2015) and critical drug studies (e.g. Duff 2011; 2017), it is argued that this type of STS -approach, partly inspired by Anthropology of Pharmaceuticals (Van der Geest et al. 1996; Hardon & Sanabria 2017), is a useful framework to explore the role of drugs as technologies in the everyday life of users, and to give a "critical distance" (Morrison 2015) not only to the neuroenhancement debate but also to the more general drug policy debate. The author argues that framing drugs as pharmacological neurotechnologies helps to approach both legalised and illegalised drugs and their users without the normative and moral judgements often attached to them (e.g. Global Commission on Drug Policy 2017; IDPC 2018).

According to Morrison in 2015 (p. 4), "To date the topic of enhancement has been somewhat neglected by scholars in the fields of STS and the sociology of technology". Thus, to develop this scholarly field it is argued that framing drugs as neurotechnologies can also help link the pharmacological neuroenhancement debate to STS literature more generally. One way of pursuing this is by looking at drugs as

"non-human actors" (e.g. Latour 1994; Barron ed. 2003). This type of STS and Actor-Network Theory (ANT) approaches has been previously employed in social scientific research around recreational drug use, focusing especially on alcohol and harm reduction (see Duff 2011; 2012). In a very generalised way, drugs as 'non-human actors' (e.g. Latour 1994; Barron ed. 2003) means that they can be viewed as material objects that are part of co-creating different social networks, practices, effects, meanings, relations and assemblages in different times, contexts and geo-locations (e.g. Barry 2005; Wilton & Moreno 2012; Duff 2011; 2012; Pickersgill & Hogle 2015; O'Connor & Nagel 2017).

Studies in this field generally point to the interconnected agency of drugs as material things, or as Barry (2005) frames them as 'informed materials' (also Greene & Sismondo 2015; Duff 2017; Hardon 2021). According to Pienaar et al (2020, p. 2), this type of relational approach "invites us to decentre the analytic focus on the human subject and attend more carefully to the agency of non-human as well as human actors in generating drug effects." This type of emphasis on relational materiality which surrounds different social and cultural dimensions of "drugs" have been also researched in the field of the anthropology of pharmaceuticals (Van der Geest et al. 1996; Whyte et al. 2002; Hardon & Sanabria 2017). As mentioned, Whyte et al (2002, p. 3, italics added) "propose to see them [medicines] as things with social lives; we are more concerned with their social uses and consequences, than with their chemical structure and biological effects." In a similar way, Greene and Sismondo (2015, p. 2, italics in the original) also suggest that a pharmaceutical is "always a thing, a part of the material world invested with specific forms of value and stamped with highly regulated forms of knowledge." They also point out that "bare molecules do not become pharmaceuticals without ties to health concerns, scientific knowledge, appropriate regulation, effective marketing, and receptive prescribers and publics" (ibid.; see also Barry 2005; Hardon & Sanabria 2017).

Thus, by conceptualising drugs as neurotechnologies, as non-human actors, can help to see how they are surrounded by complex social networks of effects, meanings and knowledge(s) (Hardon 2021). It is important to emphasise the idea that these technologies 'signify' all kinds of specialised molecules used intentionally by individuals to modulate their life/brains through changing not only their so-called "neurochemical selves" (Rose 2003; 2007a), but their life situations in general, both legally and illegally, medically and nonmedically (e.g. Oldani et al. 2014; Hupli et al. 2019b). In this context it is also important to consider the embodied (Varela et al. 1991), extended (Clark & Chalmers 1998) and/or social (e.g. Pickersgill 2013) aspects of brain and cognition, not only for social theory but also for future clinical research.

As already noted, several scholars have indicated that the subjective effects of pharmacological neurotechnologies, such as psychedelics, are not solely dependent on their molecular structure (Langlitz, 2010) but also, importantly, on the individual meaning-making and the social setting (context of use) (e.g. Moerman 2002; Duff 2011; 2012; Hartogsohn 2017).

Both therapeutic and neuroenhancement use of pharmacological neurotechnologies, and the often blurred line between them (e.g. Schermer 2007a; Hoffman 2017; Hupli et al. 2019b), clearly requires more STS research to evaluate their potential societal and individual impacts. Whichever way pharmacological neurotechnologies are framed, as 'non-human actors' they already seem to be part of contemporary life: "Whether interpreted as medicinal, pathological, and/or addictive, psychotropics can now be obtained il/legally and have become another everyday 'set of tools' […] for human beings to modify or enhance their mood, emotional states, behavior, and social relations" (Oldani et al. 2014, p. 177; also Rose 2003; 2007a).

The complexity of this era we live in requires research on multiple levels, and social sensitivity to go beyond the static categories of 'drug use' or 'abuse', beyond 'bad drugs' and 'good medicines'. Looking 'objectively' at drugs as pharmacological neurotechnologies offers one possibility for doing this. For future studies in this field, it is therefore necessary also to include a critical distance in the pharmacological neuroenhancement debate to current drug policies and practices, which prohibit some technologies while promote others "for life" (Dumit 2012; also Moncrieff 2009). Thus, conceptualising drugs as neurotechnologies can help to reveal this socially-constructed dichotomy, or a double bind (Eriksen 2016) between 'bad drugs' and 'good medicines'.

Beyond differences, the similarities between human enhancement technologies are that they are considered not only as novel treatments for human ailments but as potential technologies for enhancing human capabilities (Wolpe 2002; Hogle 2005; Elliot 2011). For sake of simplicity, the author's approach to human enhancement technologies has focused specifically on pharmacological neurotechnologies and thus far the discussion and empirical research on the use of pharmacological neuroenhancement has focused mainly on prescription stimulants, like Adderall™ (dextroamphetamine) and Provigil™ (modafinil) (Coveney et al. 2011; Maier & Schaub 2015).

Therefore, while building and applying this theoretical Science and Technology Studies (STS) framing of drugs as neurotechnologies to some empirical examples, the author here will also focus mostly on one technology; immediate-release

methylphenidate, which is often known by its original brand name, Ritalin™, nowadays a standard stimulant drug treatment for Attention Deficit/ Hyperactivity Disorder (e.g. Moncrieff 2009; Singh et al. 2013). However, the framing provided could be explored in the future for other pharmacological neurotechnologies that have barely been discussed or researched in sociology of technology, STS or bioethics literature especially in relation to human enhancement drugs. These include the above mentioned cannabis (Franke et al., 2016) and psychedelics (HED Matters 2019; Liokaftos 2021), around which boundaries between "bad drugs" and "good medicines" have been breaking down for some time (e.g. Pieters & Snelders 2009; Langlitz 2011; Sessa 2017).

Below the author discusses the use of stimulant medications for adults with ADHD as an example of drugs as neurotechnologies and focuses on their societal effects through the sociological concept of pharmaceuticalisation (Williams et al. 2011; Coveney et al. 2011). The use of pharmacological neurotechnologies, like methylphenidate, has had a strong role in the pharmaceuticalisation thesis and it will be argued that the concept of pharmaceuticalisation seems better suited as an analytical concept to understand the proliferation of stimulant prescriptions compared to medicalisation (Williams et al. 2008; 2011). Pharmaceuticalisation takes more into account the role of pharmacological neurotechnologies, especially cognitive enhancement drugs, in societal and individual efforts to alter children's and adults hyperactive and inattentive behaviours and performance through neuropharmacology (Coveney et al. 2011).

3.3 Pharmaceuticalisation of attention?

Williams et al (2011) put forward a theoretical framework for analysing pharmaceuticalisation. They see that both medicalisation and pharmaceuticalisation "should ideally be treated as value-neutral descriptive terms and may include both gains and losses to society" (Williams et al. 2011, p. 711). They see that "the degree or extent to which they are occurring remains open to empirical investigation on a case-by-case basis" (ibid.). Thus, processes like de-medicalisation and de-pharmaceuticalisation are also plausible (Williams et al. 2011; see also Clarke et al. 2003; Abraham 2010; Bell & Figert 2012). In addition, both medicalisation and pharmaceuticalisation have their own local expressions (Williams et al. 2011; Coveney et al. 2011).

It is argued that the medicalisation thesis has not been able to capture the tension inside medical discourse and research on ADHD (Suominen 2003), focusing primarily on social controls of deviant behaviour[6] (Rafalovich 2001ab). However, the medicalisation thesis can be credited for shining light on social dimensions in the discussion around ADHD and other medical diagnosis (Conrad 1992; 2007; Conrad & Potter 2000; Suominen 2003; Filipe 2011). However, pharmaceuticalisation is preferred concept in this study, which for Coveney, Gabe, and Williams (2011, p. 387, italics in original) "is more specific in its remit [than (bio)medicalization], denoting as it does the transformation of aspects of human experience into targets for pharmaceutical intervention as opposed to biomedical interventions in general." Also, while the framework by Williams et al. (2011) address topics ranging from reconfigurations of "health problems" as having a pharmaceutical solution to drug regulation, governance and patient advocacy, one of the key sociological dimensions of modern pharmaceuticalisation they identify is the nonmedical use of cognitive enhancement drugs (Coveney et al. 2011).

In relation to a historical context for pharmaceuticalisation of attention, one of the 'origins' of pediatric drug development in relation to hyperactive children is when the 'calming' effects of amphetamines were published in 1937 on a small group of 'morally deviant' children (see Bromley 2006). This "paradoxical-effect", of stimulants being able to 'calm' hyperactivity, was for a long time difficult to explain fully, but it has worked as a testimony for the neurochemical and structural basis for attention disorders ever since (Comstock 2011, p. 46; Rafalovich 2001b, p. 404; Moncrieff 2009).

However, the history of diagnosing children with attention disorders dates back longer than their pharmacological treatment. One of the "origins" of a medical description of attention-deficit disorder can be traced back to Sir Alexander Crichton in 1798 (Palmer & Finger 2001), an era that also witnessed the beginning of policy reforms to establish compulsory education in most parts of the western world.

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[6] Compared to Peter Conrad, Rafalovich (2001a, p. 97-98) has a stronger focus of debates inside medical discourse and he sees that the "medical discourse of the past has been as integral in shaping the way childhood behavior is medicalized today as are the agents of medicalization Conrad articulates." However, Rafalovich interprets the classification of a variety of ADHD-related symptoms into sickness categories as medicalising childhood *deviance* and the "history of compiling these symptoms into formal diagnoses represents an increasing drive to medicalize unconventional childhood behavior" (Rafalovich 2001a, p. 94). This might not hold in the case for *adult* ADHD and the medicalisation of deviant behaviour arguably does not capture the contemporary hegemonial understanding of ADHD based on genetics (Suominen 2003). As Comstock (2011, p. 45) argues "it is in fact only in the movement *away* from overt moral judgment, social/expert control, and most significantly, behavioral control in general, that we can begin to understand the recent proliferation of ADHD."

According to Hinshaw and Scheffler (2014), compulsory education was the initial trigger showing that some children have difficulties sustaining attention in a school environment - an environment that requires cognitive traits most of us did not have the need for previously. They also state that "the fast-escalating rates of diagnosis and treatment we now see are linked to intense pressures for achievement and performance in the context of an increasingly competitive world economy" (p. xxviii). Increasing diagnosis and prescription rates and the use of prescription stimulants for neuroenhancement by healthy individuals is often seen as a response to that pressure (ibid., Petersen et al. 2015b; Coveney & Bjønness 2019).

Although the relation between increasing performance pressures and increasing ADHD diagnoses offered by Hinshaw and Scheffler would require more study (Hupli 2015), there are scholars who argue that in a contemporary information age individual neurocognitive capacities need to fulfill increasing demands in order to succeed in modern society (Kegan 1994; Klingberg 2009). A sign of this from a pharmaceuticalisation perspective is the global increase in the amounts of prescription stimulants for attention disorders. From 1993 to 2003 the global use of ADHD medications increased by 274 % (Scheffler et al. 2007). In the United States alone the production of methylphenidate increased by 500 % between 1990 and 1995 (Diller 1996, p. 12-13). In Finland, between 2006 and 2016, the use of ADHD medication also increased five-fold among boys and six-fold among girls (Vuori et al. 2018). Whether these increases have also led to increased prescription drug diversion for neuroenhancement purposes is not fully known, but neuroenhancement seems to occur to a less extent in Europe than in the USA (Hinshaw & Scheffler 2014; Maier & Schaub 2015; Hupli 2020a; Daubner et al. 2021).

The role of the pharmaceutical industry in advocating increased use of pharmacological treatments is well established (e.g. Healy 2004; Medawar & Hardon 2004) and this also appears to be the case with prescription stimulants (Moncrieff 2009). Also, according to Rafalovich (2001b, p. 404), the role of stimulants has played an important role in establishing a neuroscientific hegemony as these medications "validated neurology's complicated nomenclature, ratifying a biologically-oriented clinical practice, while providing a window into the true 'soul' of the ADHD child—a neurologically-challenged soul where the blame for deviant behavior was attributable to a non-human agent." In other words, following 'a disease-centred model of drug action' (Moncrieff 2009; see sub-chapter 4.3), if the drug 'works' on an individual, for instance causing a behavioural change that 'calms' a 'hyperactive child', this effect is seen as a sign of an underlying pathology.

Thus, in the case of ADHD, pharmacological neurotechnologies, like stimulant drugs, seem to be part of a dynamic relation in which they, on the other hand, validate the biological basis of attention disorders but also help the individual subject to become 'neurochemical selves'[7] (Rose 2007). The concept "neurochemical self", however, requires more empirical investigation as neither children nor adults with ADHD or, for instance depression, identify their subjectivity strictly with their diagnosis or their 'neurochemical selves' (Fullagar 2009; Fullagar & O'Brien 2013; Bolt & Schermer 2009; Bröer & Heerings 2013; Singh 2013ab).

In addition to treating ADHD, the use of prescription stimulants for neuroenhancement purposes could be, perhaps, another explanations for the proliferation of stimulant prescriptions, which as mentioned have seen significant increases in Finland (Vuori et al. 2018) and elsewhere (Scheffler et al. 2007; Hinshaw et al. 2011; Hinshaw & Scheffler 2014) especially for children and adolescents. This has raised concerns whether these neurotechnologies are used solely for therapeutic purposes (Singh et al. 2013) and Conrad and Potter (2000, p. 273-274, italics added) view that in the case of adults with ADHD, stimulants like methylphenidate (Ritalin™) are used more to tackle underperformance, instead of behavioural problems as with children (also Schermer 2007a).

The line between therapy and enhancement use can also be blurred (Hupli et al. 2019b; Schermer 2007a) as stated by this EU-funded enhancement technology assessment: "Because of the fine lines involved in the diagnosis of ADHD, which require normative judgments that are highly sensitive for diverging opinions, it is often hard to judge whether Ritalin™ is used as a therapeutic or an enhancing agent" (STOA 2009, p. 85). The bioethical discussion dealing with the use of neuroenhancers is often depicted as this dichotomy between therapy and enhancement (e.g. Wolpe 2002; Schermer 2007a; Bostrom & Sandberg 2009; Coveney et al. 2011) and as Steven Rose (2002, p. 978) points out: "there is a fine medical and ethical line between correcting deficits and improving on 'normality"'.

In addition, as Bostrom and Sandberg (2009, p. 331) speculate, looking at prescription medication only through disease categories might become outdated: "If a significant fraction of the population could obtain certain benefits from drugs that

[7] While referring to the discussion around ADHD as an example of medicalisation of problem behaviour, Nicholas Rose (2007a, p. 211) also points to the important role of the drugs: "Outside these practices of authoritative behavioural management, is this conception of the role of the drugs that is dominant. For those becoming neurochemical selves, these drugs promise to help the individual him or herself, in alliance with the doctor and the molecule, to discover the intervention that will address precisely a specific molecular anomaly at the root of something that troubles the individual concerned and disrupts his or her life, in order to restore the self to its life, and to itself again."

improve concentration, for example, it is currently necessary to categorize this segment of people as having some disease—in this case attention-deficit hyperactivity disorder (ADHD)—in order to get the drug approved and prescribed to those who could benefit from it. This disease-focused medical model will be increasingly inadequate for an era in which many people will be using medical treatments for enhancement purposes." Echoing this, Outram (2010, p. 201) also argues that the debate around the use of methylphenidate "may be the product not of its future potential as a sociologically significant form of an enhancement, but the product of a changed social context in which the barriers between enhancement and treatment are already breaking down."

Thus, part of the increase of stimulant prescriptions might be due to pharmaceuticalisation of 'underperformance' (Conrad & Potter 2000; Schermer 2007a), and/or for cognitive enhancement, not just therapy (Hupli et al. 2019b). However, whether the current 'ADHD explosion' (Hinshaw & Scheffler 2014) is due to the pharmaceuticalisation of underperformance, and whether pharmaceuticalisation in this regard is "bad" or "good" (Parens 2013), will be left for future research to fully answer as this would require more bioethical analysis and empirical research on this issue in different country-contexts (Hupli 2020a; Hupli et al. 2019b; Hinshaw & Scheffler 2014; Hinshaw et al. 2011). To put it briefly, if the expansion of the ADHD diagnosis to concern adults has been due to "over-diagnosis", and therefore amounts to "over-use" of pharmacological neurotechnologies such as prescription stimulants, this can be seen as a "bad" form of pharmaceuticalisation. If, however, adult ADHD has been under-diagnosed and under-treated, then getting more people in need of help to treatment services could be considered a "good" form of pharmaceuticalisation (e.g. Singh et al. 2013; Williams et al. 2008).

But even if stimulants would be used to treat underlying ADHD, there are potentially other non-pharmacological and pharmacological options with potentially better benefit-to-harm ratio, like medical cannabis products, although this area requires more clinical research (Hupli 2018a; Hergenrather et al. 2020). In addition, while speculative, this type of medicalisation/pharmaseuticalisation of stimulants and cannabis, for instance, could work as a form of user 'decriminalisation' (see Unlu, Tammi & Hakkarainen 2020), as medical users are sometimes, although not always, exempt from criminal prosecution. This type of pharmaceuticalisation process, of seeing drug use as a disease, or as "a treatable brain disorder" (Volkow 2021), might bring legal protection for some, but framing drug addiction as a brain disorder is far from being unproblematic (Hellman 2018).

Medicalisation/pharmaceuticalisation of drug use as a form of decriminalisation will be discussed briefly in Chapter 6. In general, the role of human enhancement drug use in various pharmaceuticalisation processes requires further attention. Part of the challenge, briefly mentioned in the introduction, is "the extent to which a drug is able to move from medical treatment to pharmaceutical enhancement and leave behind cultural images of addiction, disease, side effects, health and social problems" (Coveney et al. 2011, p. 389). In the next chapter, the focus shifts to the extent of this move by reviewing empirical literature on pharmacological neuroenhancement and the surrounding bioethical discussion.

4 PHARMACOLOGICAL NEUROENHANCEMENT STUDIES (PNS)

4.1 Definitions of pharmacological neuroenhancement

Next is offered an overview of some definitions found in the literature before a presentation of the author's own definition is again given. A rather technical definition of human enhancement by the EU-funded SIENNA project is the following: "modification aimed at improving human performance and brought about by science-based and/or technology-based interventions in or on the human body" (Warso et al. 2019; see also STOA 2009). As the project website states: "Technology can enhance our physical, cognitive, emotional and moral abilities. Implants, drugs, genetic modification or interaction with machines can have both temporary and permanent effects. This is challenging the boundaries between health and illness, treatment and enhancement, normality and abnormality." Thus, according to this definition, human enhancement technologies can already have temporary or permanent effects which challenge various socially defined dichotomies.

Farah et al. (2004) write about neurocognitive enhancement and frame it as using psychopharmacology "for improving the psychological function of individuals who are not ill" (Farah et al. 2004, p. 421). Maier & Shaub (2015, p. 156) prefer the term pharmacological neuroenhancement and define it as "the misuse of prescription drugs, other illicit drugs, or alcohol for the purpose of enhancing cognition, mood, or prosocial behavior in academic or work-related contexts". This definition created a debate between Arria (2016) and Maier et al. (2016), demonstrating clearly that issues related to definition are far from being resolved (Coveney & Bjønness 2019; Daubner et al. 2021). Other terms that have been used to research and discuss the topic of cognitive enhancement drugs have included smart drugs (Rose 2002; Singh, Bard & Jackson 2014), study drugs (Vrecko 2013), nootropics (Cakic 2009), scholastic steroids (Linton 2012), cognitive enhancement drugs (Greely et al. 2008) and the often used term especially in the literature from USA is nonmedical (ab)use/misuse of prescription drugs (Arria & Wish 2006).

The plethora of definitions in the academic literature also demonstrates a certain ambiguity around the topic (Coveney & Bjønness 2019), which is partly constructed by researchers themselves (Bullard 2018). Further ambiguity around defining particular use is due to the fact that the terms cognitive enhancement and neuroenhancement are used interchangeably in the literature, in this study as well, and there is often no clear distinction between the two concepts (Lucke et al. 2011, p. 38). According to Hildt (2013), the former stands for an improvement of cognitive functions, while the latter "is a broader term to characterise all kinds of interventions intended to improve brain functions in healthy individuals" (Hildt 2013, p. 5). However, neuroenhancement, although broader than simply cognitive enhancement, still reduces the effects of different enhancement technologies to improving only "brain functions". This does not consider the embodied (Varela et al. 1991), extended (Clark & Chalmers 1998) and/or social (e.g. Pickersgill 2013) aspects of brain and cognition. The general emphasis on enhancing "brain functions" is argued to point to the increasing role of neuroscience in scientific and public discourse which has received increasing attention in the sociology of neuroscience literature (e.g. Rose & Abu-Rached 2013).

The authors own definition of pharmacological neuroenhancement is the use of drugs, legalised or illegalised, with the intention of improving one's life situation by modulating cognition, memory, mood, pro-social behaviour and/or well-being. On a pharmacological level these modulating effects usually take place in a temporary manner. Temporary because the effects of drugs in the vast majority of non-problematic cases do not last longer than some hours depending on the molecule in question. Nonetheless, on a social level these effects can be longer-lasting; for instance, in the form of imprisonment, social stigma and related consequences, or in the form of dependence.

On a more positive side, some of these effects can also be in relation to a more open and optimistic outlook on life as seems to be the case with, for instance, some psychedelics (e.g. Elsey 2017). Discussed further in Chapter 5, the use of psychedelics and cannabis have been mostly ignored in the bio/neuroethical, sociological and policy discussion on pharmacological neuroenhancement. In spite of an on-going 'psychedelic renaissance' (Sessa 2017), supportive user reports (Hupli et al. 2019ab) and clinical studies (Elsey 2017) the use of psychedelics has not yet triggered a similar kind of academic discussion about their potential as neuroenhancers (see Langlitz 2011; Liokaftos 2021). The author argues that current definitions of pharmacological neuroenhancement are limited due to emphasis on prescription drugs, especially stimulants, and that both legalised and illegalised drugs

should be part of this bioethical discussion as both can be used with the aim of improving oneself, not just to treat an illness (Hupli et al. 2019b).

4.2 Bioethical discussion - brief overview

Despite ambiguity around definitions, the use of pharmacological neurotechnologies by healthy people has raised a heterogenous neuro- and bioethical discussion. Concerns in relation to "cosmetic psychopharmacology" (Kramer 1993) or "cosmetic neurology" (Cakic 2009) have been raised not only about 1) the safety 2) and efficacy of these technologies, as briefly discussed below, but also in relation to 3) fairness of use in competitive contexts, 4) freedom to use based on arguments for cognitive liberty, 5) coercion to use in certain work environments such as military, 6) social (in)equality around access to use various enhancement technologies, 7) their effects on personality and 8) academic integrity (e.g. Parens ed. 1998; Farah et al. 2004; Coveney et al. 2011; Jotterand & Dubljević ed. 2016; Ter Meulen et al. eds. 2017).

While the author do not present these bioethical concerns in detail, it will be argued that a similar discussion would be a welcome addition to (inter)national drug policy debates which are still in most parts focused on prevention measures, and mainly through criminalising certain drug users (Global Commission on Drug Policy 2017; Bublitz 2016). On the other hand, the bioethical PNS literature rarely considers the on-going situation of the drug war (Zigon 2015; 2018). This is discussed more fully in Chapter 6.

The bioethical discussion in relation to enhancement technologies can be crudely divided into two opposing stances, between so-called 'bioliberals' and 'bioconservatives' (see e.g. Reiner 2013; Hofmann 2017). The so-called 'bioliberal' stance argues that enhancement technologies should not only be permitted but that we even have a moral obligation to enhance ourselves (e.g. Harris 2007; 2009). To give an example of this bioliberal stance, an often referenced article about the use of cognitive enhancement drugs is a commentary made by a group of neuroscientists and bioethicists titled 'Towards responsible use of cognitive enhancing drugs by the healthy', which was published in the highly-valued scientific journal Nature (Greely et al. 2008).

According to the authors of this commentary, "cognitive enhancement has much to offer individuals and society, and a proper societal response will involve making enhancements available while managing their risks" (ibid. 702). One mechanism of

a proper societal response according to the authors is that "existing law should be brought into line with emerging social norms and information about safety" (ibid.). The authors state that this does not mean fundamentally new drug laws and that "it would be naive to expect rapid or revolutionary change in the laws governing the use of controlled substances." "Nevertheless", they continue, "these laws should be adjusted to avoid making felons out of those who seek to use safe cognitive enhancements".

Another adjustment proposed is to allow the pharmaceutical industry to develop and promote cognitive-enhancing drugs (Greely et al. 2008). Greely et al. (2008, p. 702) argue that the use of (certain) cognitive enhancement drugs, like methylphenidate, should not only be legally regulated but they "should be viewed in the same general category as education, good health habits, and information technology — ways that our uniquely innovative species tries to improve itself".

The author agrees with the idea that cognitive enhancement drugs should be viewed in the same way as other 'ways that our uniquely innovative species tries to improve itself' and this idea is developed further when framing all drugs as neurotechnologies. Through the author's empirical research with students (Hupli et al. 2016; 2019b) he has gained a wider view compared to Greely et al. of what cognitive enhancements are according to certain user groups. And while agreeing with Greely et al. that drug laws should be adjusted to avoid making users into criminals, the author of this thesis work feels that this should be the case even if their use would not be considered 'an enhancement'. The author agrees with another "bioliberal" commentary on the issue by Thaler (2009) who sees that "Cognitive enhancing drugs intended for healthy people ought to be drugs of choice. Informed free will is the ethical, and should be the practical, basis for decisions regarding their use." Hesse (2010) takes a similar stance arguing that public health interventions should focus on the regulation of use and the reduction of harmful effects of enhancement drugs but not to decide what aspects of human life should or should not be enhanced.

On the other side, 'bioconservatives', oppose enhancement technologies fearing that they will "corrupt, degrade and rob us of what is 'naturally human'"(in Schermer et al. 2009, p. 76; see also Chatterjee 2009; President's Council on Bioethics 2003). An example of this is that some authors see the use of CED´s as "cognitive cheating". Calling them "scholastic steroids", Linton (2012) argues that especially in certain academic settings, such as medical and law schools, which have unique ethical guidelines built into their profession, the use of CEDs should be explicitly forbidden.

Others see it as a form of drug abuse, and therefore more as a public health problem (see, for example, McVeigh et al. 2012).

According to Schermer (2007b), this latter 'dystopian' view on human enhancement through psychopharmacology has been dominant in the ethical debate. And as exemplified by the above commentaries, fairness, safety and freedom (also from coercion to use CEDs) are regularly mentioned ethical concerns in the existing academic literature. However, as indicated above, the on-going "war on drug users" is often left out from the bioethical discussion (Bublitz 2016). It is therefore argued that the bioethical discussion and empirical analysis presented here is preparatory work for the future (Coveney et al. 2011), not only in terms of humans having efficient pharmacological neurotechnologies that would reliably and without adverse effects enhance healthy brain function (e.g. De Jongh et al. 2008; Massie, Yamga & Boot 2017), but also in terms of nation states having drug policies that would legally allow their use (Bublitz 2016; Chatwin et al. 2017), or at least stop criminalizing their users, whether for therapeutic reasons or otherwise. As Smith and Farah (2011, p. 736) point out in relation to the cognitive enhancement drug debate: "Although ethical issues cannot be decided on the basis of facts alone, neither can they be decided without relevant facts."

4.3 Efficacy & safety

One of the golden standards of current evidence-based medicine and medical research is the double-blind randomised control design, in which both the researcher and the research participant are unaware whether they are receiving the active compound, or a so-called placebo or nocebo (active placebo). This design is supposed to eliminate the subjective preferences of the researcher, and participant, for certain empirical outcomes (Jukola 2015). There are numerous clinical trials done to investigate the safety and effectiveness of methylphenidate for attention disorders, especially for children and adolescents (Storebø et al. 2015). One would assume, that as the compound is indeed being prescribed to mainly children and adolescents, and increasingly adults at the rate as it is today (Hinshaw & Scheffler 2014), there should be well-established scientific proof for its safety and efficacy at least for therapeutic purposes.

However, the safety and efficacy of methylphenidate has been a matter of debate inside and out of medical discourse, and even the company that manufactures the drug states that there are still many uncertainties around its mechanism of action

which sometimes leads to serious adverse effects (Novartis 2020, see below). Also, stimulants (broadly speaking as there are several stimulant-type drugs), which when prescribed to children diagnosed with hyperactivity are claimed to cause therapeutic effects, but when used 'recreationally' by adults, the effects are claimed to cause unacceptable euphoria, and users are controlled as criminals. While age is an important factor when considering any type of drug use, and its effects, it is by far the only one.

For historical context, methylphenidate or Ritalin™, which is the original brand name, was synthesized in 1944 by Leandro Panizzon, who named the compound after his wife Marguerite or "Rita" (Lange et al. 2010b; Leonard et al. 2004). It was marketed by the Ciba-Geigy Pharmaceutical Company from 1954 onwards for various indications such as "chronic fatigue, lethargy, depressive states, disturbed senile behaviour, psychosis associated with depression and narcolepsy" (in Leonard et al. 2004). Ritalin™ is currently sold by the pharmaceutical company Novartis for treating ADHD and narcolepsy, with numerous generic forms now being sold as well by other companies.

According to Novartis (2020) "Ritalin is a mild central nervous system stimulant with more prominent effects on mental than motor activities." They also state that the "The mode of action in man is not completely understood, but its stimulant effects are thought to be due to cortical stimulation and possibly to stimulation of the reticular activating system." (italics added). Also, according to the company product monograph: "There is neither specific evidence, which clearly establishes the mechanism whereby methylphenidate produces its mental and behavioural effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system."

According to Novartis (2020), one of the effects of Ritalin can be 'sudden death', among other serious adverse effects. Thus, even according to the pharmaceutical company who produces methylphenidate, how it works is not completely understood, there is no specific evidence how it produces its effects in children who use it, it is 'mild', but one of those 'mild' effects could be the sudden death of the user, among others. Also, a Cochrane Database Systematic Review which assessed the beneficial and harmful effects of methylphenidate for children and adolescents with ADHD from 38 parallel-group trials and 147 cross-over trials (Storebø et al. 2015, p. 21) state that: "we judged all 185 trials to be trials with high risk of bias." The authors therefore conclude that "Despite more than 50 years of research in this field, we have no knowledge on how to identify patients that may obtain more benefits than harms" (Storebø et al. 2015, p. 35; see also Leonard et al. 2004).

The results of this systematic review were challenged by a group of scholars from Germany who claim that "The Cochrane review of the efficacy and tolerability of MPH treatment in children and adolescents with ADHD is marked by numerous inaccuracies, errors, and inconsistencies" (Banaschewski et al. 2016). However, all of the authors of the paper by Banaschewski et al. declared a conflict of interest as they have been involved with industry-sponsored research, consultancy and advocacy as paid-public speakers.

Due to these conflicts of interest it is particularly challenging to "objectively" assess the safety and efficacy of methylphenidate for therapeutic and/or neuroenhancement purposes. There seems to be a bias towards positive outcomes due to industry-sponsored research at least for the therapeutic value (Moncrieff 2009). And although Jukola (2015) uses selective serotonin reuptake inhibitors as a case study to investigate the objectivity of meta-analyses in medical research, one of results could be said to apply also for methylphenidate: "Since there is evidence of systematic disappearance of negative data, and since this seems to be connected to commercial interests, we should denounce this phenomenon as a violation of objectivity: the interests of involved parties have unduly guided research towards certain kinds of outcomes." The effectiveness of psychostimulant pharmacotherapy has also been criticised for overemphasizing the biological basis of attention disorders over social and environmental factors (e.g. Rafalovich 2001; Suominen 2003; Comstock 2011; Singh et al. 2013) leading to possible overuse of pharmaceutical treatments (Abraham 2010; Williams et al. 2011; Hinshaw & Scheffler 2014) as discussed above.

The current bioethical discussion and concern about the safety of using stimulants among healthy adults is in a way paradoxical as the drugs have, perhaps exceptionally for psychopharmaceuticals, been used mainly by children for almost 70 years. This is partly a result of what Moncrieff (2009) calls a disease-centered model of drug action[8]. This model promotes the view that drugs work completely differently for people with mental illness compared to "healthy normals" and that unwanted effects, often called side-effects or adverse effects, are separate from the

[8] According to Moncrieff, this disease-centered model of drug action has been promoted by the pharmaceutical industry and mainstream psychiatric profession, often with governmental support. The dopamine-theory of schizophrenia and the monoamine-theory of depression are prime examples of framing certain mental illnesses as having a biological basis, for which then pharmaceutical companies claim to have a patented biological solution in the form of a drug treatment, often with weak evidence for either case (Moncrieff 2009; also Healy 2004).

global effects that drugs can produce to the human organism[9]. Moncrieff advocates for a drug-centered model of drug action, and while factors like dosing, purity of the drug and indeed the context of use plays a role, including perceived expectations, the "drug-centered model of drug action suggests that we can understand effects of drugs that are used therapeutically in essentially the same way as we understand the effects of recreational drugs" (Moncrieff 2009, p. 17). Additionally, as argued in this thesis, the effects of so-called neuroenhancement drugs can also be understood in the same way.

Thus, do drugs like methylphenidate and other "smart drugs" enhance brain function in healthy people? Lanni et al. (2008) reviewed neuropharmacological literature on several "cognitive enhancers" with a focus on such cognitive functions like memory, attention and creativity. While the connection between creativity enhancement with drugs was not explicitly expressed in the literature, some of the reviewed literature suggested that different kinds of drugs, like methylphenidate, can have an enhancing impact on certain parts of memory and attention of healthy people, even though a fairly modest one (Lanni et al. 2008).

There are several reviews about the safety and efficacy of various cognitive enhancement drugs showing similar modest results (Rose 2002; Farah et al. 2004; Jones, Morris & Nutt 2007; Repantis et al. 2010; Smith & Farah 2011; Husain & Mehta 2011). However, even modest improvements in one part of cognition can be detrimental in others (De Jongh et al. 2008) and in relation to non-medical use of methylphenidate "the risk for addiction is substantial" (Massie, Yamga & Boot 2017, p. 57). Furthermore, one of the problems of measuring the effects of cognitive enhancement drugs with healthy people is the lack of agreement on a standardised test battery (Husain & Mehta 2011, p. 31) or even agreement on a standard or "normal" level of cognitive function and what constitutes an enhancement of that normal level and in what contexts (Shook & Giordano 2016).

In addition, the ways "smart drugs" like prescription stimulants are used in real-life situations vary (Smith & Farah 2011; Vrecko 2013; Petersen et al. 2015ab). According to Outram (2011, p. 9), "there is a considerable amount that we do not know concerning both motivation and self-evaluated efficacy in use; although we

[9] As Moncrieff (2009) writes in her critique of psychiatric drug treatment "the modern understanding of what drugs do in psychiatry, the basis of psychopharmacology, is fatally flawed; that most knowledge about psychiatric drugs is, at best, only a partial account." She continues that this is "because it is based on a misconception about the nature of drug action, one that has been inspired and promoted by professional, commercial and political interests. This misconception has led to the misdirection of research, the misinterpretation of available evidence and the obstruction of a fuller and more accurate understanding of what psychiatric drugs do."

cannot discount the possibility that efficacious cognitive enhancement is being experienced by some individuals." Our interviewees reported several desired and undesired effects from various CEDs and the students we interviewed were generally well aware of the risks involved and self-regulated their use (Hupli et al. 2016; 2019b see Table 1). This may not be always the case and the risks from CEDs are often downplayed in the bioethics literature when discussing pharmacological neuroenhancement with methylphenidate and other prescription stimulants (Heinz & Müller 2017).

Despite risks, the use of stimulants for neuroenhancement has been reported especially in Northern Europe and Northern America (Daubner et al. 2021; Maier, Ferris & Winstock 2018; Maier & Schaub 2015). It is to these reports that we will now turn to, first by briefly reviewing literature on the prevalence of cognitive enhancement drugs, especially stimulants, and then in the form of qualitative research.

4.4 Prevalence of stimulants as cognitive enhancement drugs

Despite ambiguity around effects and definitions, several studies have looked at the prevalence of cognitive enhancement drug use, especially among student populations and with a focus on stimulants. Thus, how prevalent is the use of cognitive enhancement drugs? In the (Anglo-Saxon) media the use of prescription drugs for neuroenhancement is often portrayed as being "as common as coffee" (Partridge et al. 2011; also Partridge 2017). Some professional academics have indeed reported that the use of "professor's little helpers" (Sahakian & Morein-Zamir 2007) is "*already happening"* (see Coveney et al. 2011, italics in the original) also among their academic peers: "In academia we know that a number of our scientific colleagues in the United States and the United Kingdom already use modafinil to counteract the effects of jetlag, to enhance productivity or mental energy, or to deal with demanding and important intellectual challenges" (Sahakian & Morein-Zamir 2007; see also Maher 2008).

However, Anglo-American (academic) culture arguably differs from other contexts and, in general, practices and "views on cognitive enhancement may differ between various social and cultural contexts (Schermer 2016, p. 181; Pustorvh & Mali 2014; Coveney & Bjønness 2019). Singh and Kelleher (2010, p. 5) wrote in 2010 that "while the evidence is at present mainly anecdotal, the use of stimulants as neuroenhancers appears to be a growing trend among university students around the

world." However, thus far epidemiological studies have focused mainly on student populations in the Global North, so it is difficult to estimate whether this is indeed a growing trend "around the world" (Daubner et al. 2021; Maier, Ferris & Winstock 2018; Coveney & Bjønness 2019).

In general, European studies have shown lower prevalence rates of enhancement stimulant use among student populations compared to North-American ones (e.g. Ragan et al. 2013; Maier & Schaub 2015; Tully et al. 2019; Hupli 2020a). However, Arria and Wish (2006) have pointed to various methodological challenges that occur when reviewing epidemiological literature especially on the non-medical use of stimulants among students. The variety of the stimulants themselves, like methylphenidate and amphetamine-dextroamphetamine combinations and their different brand names (Ritalin™, Focalin™, Adderall™) raises challenges to researchers who often focus only on a specific type of stimulant for a specific type of use (see Smith & Farah 2011; Daubner et al. 2021).

As mentioned, the concepts of nonmedical use and/or neuroenhancement use can also be defined in various ways (Arria & Wish 2006) and the distinction between therapeutic use and enhancement use can also be blurred (e.g. Schermer 2007a; Bostrom & Sandberg 2009; McKeown 2017). This implies caution when facing empirical surveys on the prevalence of cognitive enhancement drugs. In the USA among students the results on the matter vary from 4 % (Sussman et al. 2006) to 34 % (DeSantis et al. 2008) and even up to 55% among fraternity members (DeSantis et al. 2009). Prevalence often depends on the methodological framing, geo-location and population, and some scholars argue that increased research interest in the phenomenon has created 'a neuroenhancement bubble' (Lucke et al. 2011) in which the use of enhancers is often reported as widespread and their efficacy overestimated. The key research population has been university students, which might be due to the convenience of students as research participants and the higher prevalence of general drug use among that population.

As students perceive and use various drugs as "smart drugs" (e.g. Singh, Bard & Jackson 2014; Hupli et al. 2016; 2019b), for example cannabis (Franke et al. 2016), focusing only on (prescription) stimulants for neuroenhancement purposes does not give a full picture of the prevalence of 'cognitive enhancement drug use' and the various contexts, practices and 'technologies' involved (e.g. Maier & Schaub 2015; Maier, Ferris & Winstock 2018; Hupli et al. 2016; 2019b; Hupli 2020a). Prevalence differences are a fact that requires more research among the various factors (Daubner et al. 2021), and the author argues that the academic and public discussion on cognitive enhancement drugs should consider more the local context and the

drug policy of individual countries, and indeed, which drugs are included in the term 'cognitive enhancement drugs' and by who (Hupli 2020a; see also Coveney & Bjønness 2019).

4.5 Qualitative approach to cognitive enhancement drug use

As examples of prior qualitative research it is pertinent to briefly discuss Scott Vrecko´s (2013) article "Just How Cognitive is 'Cognitive Enhancement'? On the Significance of Emotions in University Students´ Experiences with Study Drugs", and an article by Vargo and Petróczi (2016) "It Was Me On a Good Day": Exploring the Smart Drug Use Phenomenon in England". Here special attention will be paid to how the papers create their own research space, and how this research space relates to the general literature on cognitive enhancement drug use. The focus will be more on structural strategies rather than on stylistic considerations.

Already from the titles one can observe that while Vrecko uses the term "Study Drugs", Vargo and Petróczi use the term "Smart Drugs". Thus, although both studies represent qualitative research of cognitive enhancement drug use among university students, as stated earlier, the PNS literature is full of differing terminology used to describe the phenomenon and the wide use of different terms can be seen to reflect specific research and ethical paradigms (e.g. Forlini & Racine 2009; Forlini et al. 2013; Daubner et al. 2021) and country contexts (Hupli 2020a) as one study was conducted in the UK (Vargo and Petróczi 2016), the other in USA (Vrecko 2013).

Early on in both articles, the author(s) point to the increasing research interest, especially in the western countries, to the use of prescription pharmaceuticals "to enhance the mental capacities of 'normal' individuals, that is, those who are not ill" (Vrecko 2013, p. 4). Vargo and Petróczi (2016, p. 2) state that "Practices involving the non-medical use of such medications on the part of healthy individuals have been coined with the term pharmacological neuroenhancement, and have received growing attention on the part of the scientific community" (italics added). Both quickly turn to one specific area of research, namely the use of stimulants by university students. Vrecko (2013, p. 4) points out how "the use of stimulant medications by individuals – particularly researchers and university students – seeking to boost their academic performance has become one of the main areas of focus within discussions of enhancement." Vargo and Petróczi (2016, p. 2) also state

that "In particular, an area of scientific interest resides in the use of these medications on the part of university students."

As Vrecko´s article was one of the early qualitative publications in this field (see Hupli 2013b), he notes that "there is at present a lack of findings from in-depth, qualitative research that examines the everyday uses and users of medications" (Vrecko 2013, p. 5), thus demonstrating a clear gap in the literature which he aims to fill. Since Vrecko´s 2013 publication, the amount of qualitative publications has increased (e.g. Vrecko 2015; Petersen et al. 2015ab; Hupli et al. 2016; 2019b; Coveney et al. 2019). Thus, to justify their research, Vargo and Petróczi (2016, p. 3) simply state that "Ethnographic research can provide qualitative information that not only contributes to a clearer understanding of new drug trends, but can also provide a term of comparison for quantitative research designs" (italics added).

Increased research interest in the scientific community is often used as a strategy to create the research space in the PNS literature. Qualitative research in particular often needs to justify itself, either comparing its value to quantitative research (Vargo and Petróczi 2016) and/or pointing to the lack of qualitative research into the phenomenon (Vrecko 2013). Thus, both papers point to the increased attention to the phenomena in the scientific community as a strategy to create the research space, with special focus on student use, which does not necessarily reflect an increase of practices outside student communities. This is a limitation of our own qualitative studies on the topics as well (Hupli et al. 2016; 2019b).

As mentioned, even from survey studies it is difficult to estimate the prevalence of CEDs and whether there is an actual increase in use practices. In the USA the results on the matter vary between 4 %- 55% (Sussman et al. 2006; DeSantis et al. 2008; 2009) and countries in Europe differ not only on prevalence but the amount and quality in monitoring the phenomena of cognitive enhancement drug use (Maier & Schaub 2015; Maier, Ferris & Winstock 2018; Hupli 2020a; Daubner et al. 2021). Nevertheless, qualitative research in this field often needs to justify itself by different means. And while there seems to be increasing empirical research on pharmacological neuroenhacement internationally (Jotterand & Dubljevic eds. 2016; Coveney & Bjønness 2019), ethnographic work, in particular, has mainly focused on university students in North-America, especially in the West and East Coast of the USA (Aikins 2011; Vrecko 2013; 2015; Petersen et al. 2015ab).

In addition, as mentioned, these studies have focused primarily on prescription stimulant use for enhancing certain cognitive and affective traits like focus and motivation (e.g. Hildt, Lieb & Franke 2014; Vargo and Petróczi 2016). However, qualitative studies have also shown that students use stimulants to affect a broad

range of functions, not purely to enhance cognition (e.g. Vrecko 2013; Petersen et al. 2015ab). We also found that both types of students, those self-reportedly diagnosed with AD(H)D and those without, used a variety of drugs, not only prescription stimulants like methylphenidate, to achieve a variety of cognitive and emotional states to improve their study, work and everyday situations while experiencing various desired and undesired effects (Hupli et al. 2016; 2019b; see also Partridge et al. 2013; Hildt, Lieb & Franke 2014; Vargo & Petròczvi 2016).

Thus, as our own empirical research showed, focusing only on prescription stimulants gives too narrow a picture of what users consider as cognitive enhancement drugs (Hupli et al. 2016; 2019b; Singh, Bard & Jackson 2014). Although we found students using the aforementioned stimulants, they also used for instance food supplements for the brain (e.g. Neurozan™), cannabis, amphetamine, methamphetamine, cocaine, and LSD as 'chemical enhancers' (Hupli et al. 2016; 2019b; see also Hardon 2021). Therefore, in the next chapters the author will briefly discuss two groups of drugs mentioned by our interviewees as potential cognitive enhancers, namely psychedelics and cannabis. As academic literature on this topic is scarce, it will additionally be necessary to rely on media articles and expert interviews conducted by the author during his PhD fieldwork period (2015-2019).

5 BETTERMENT OF THE WELL – WITH PSYCHEDELICS AND CANNABIS

5.1 Cannabis as a 'cognitive enhancer'?

Cannabis remains one of the most prevalently used illegalised plants in Europe (EMCDDA 2019). Its use both as a recreational and medicinal plant goes back thousands of years (e.g. Russo 2007; Grinspoon 1994; Clarke & Merlin 2013). The discovery of the endocannabinoid system (ECS) in the 1990s, which resulted from first isolating the active compounds of the cannabis plant, especially Δ9-THC (Δ9-tetrahydrocannabinol) (Gaoni & Mechoulam 1964), and later identifying specialized endocannabinoid receptors (cannabinoid-1 & -2, or CB1 & CB2 receptors) and neurotransmitters (anandamide, 2-AG) has been part of proliferating research around cannabinoids and their potential role in treating a variety of human ailments (Russo 2007; IACM 2020; Vihervaara & Hupli 2021), including mental and neurological disorders (e.g. Fattore ed. 2015).

It's important to note that cannabis is not just one drug; the variety of molecules, including the 120 different "phytocannabinoids", or plant-based cannabinoids, so far identified in the Cannabis Sativa L. plant, each have a unique pharmacological profile, the most well-known ones being Δ9-THC and cannabidiol (CBD; see WHO 2018; Andre, Hausman & Guerriero 2016). However, most research literature on cannabis, which often refers to it in a botanically incorrect way as 'marijuana' (see Bearman 2015) often perceive it to be a single drug. This makes evaluating evidence on its effects difficult.

Most research has also focused on the harms of cannabis, which does not give a balanced view of all possible effects. Thus, the idea that cannabis or cannabinoids could enhance human cognition might seem implausible, especially in light of an exemplary review article "of acute and long-term effects of cannabis use on executive cognitive functions" (Crean, Crane & Mason 2011). This non-systematic review summarised some of the effects of cannabis on cognition, dividing them into three groups based on the reported amount and time of exposure. Short-term effects, meaning less than 6 hours of use, presented such effects as difficulties in planning and decision-making, deterioration of information processing, reaction speed,

accuracy, and working memory. From 7 hours to 20 days of use some reported effects included difficulty paying attention and concentrating, and more than 3 weeks of use resulted in difficulties in decision making, concept formation and planning (Crean, Crane & Mason 2011).

However, the reviewers state that "Research assessing the effects of acutely administered doses of cannabis on executive functioning has yielded mixed results", as in some cases cannabis exposure improved certain aspects of attention (Crean, Crane & Mason 2011). The experience level of users, quantity, and duration of use all impacted whether cannabis use was experienced as impairing or enhancing. The quality of the cannabis matters too, and while some studies reviewed by Crean, Crane and Mason had THC percentages in relation to the cannabis used, that leaves hundreds of other molecules, their interactions (known as the "entourage effect", see Russo 2011) and the "set and setting" of the use outside of the reviewed effects.

Thus, for now it is difficult to say anything certain of the cognitive 'enhancing' effects of cannabis[10]. But while cannabis has hardly been discussed as an enhancer in the PNS literature, it´s potential enhancing properties had already been noted by the late Lester Grinspoon (1994, p. xi, 174-177), Associate Professor of Psychiatry (emeritus) at Harvard University who researched cannabis since the end of the 1960´s (e.g. Grinspoon & Bakalar 1997).

When Dr. Grinspoon was interviewed by the author in the spring of 2016 while visiting him at his house in Boston, East Coast of USA, he indicated three different usages for cannabis:

"It´s a recreational drug, it´s a medicinal drug, and it´s what I call an enhancement drug. It can enhance a variety of human experiences and people come to understand that through their own experience. Especially once medical marihuana came along in the late 1990s, people had enough opportunity to observe themselves that they were not going to turn green or fly off somewhere (laughter). They became to understand that this was not a very dangerous drug and it had utility, at least they could see the medical utility. And if they thought about it long enough, I mean what would you rather have, a bunch of people using alcohol as a recreational drug or people use cannabis? Cannabis is so much better as a recreational drug, you get a lot more out of it and no hangovers, no damage to the liver…And of course what we are learning about its capacity to enhance. A casual user can´t know about its capacity to enhance a variety of things. I mean you can know about the enhancement of taste, because that is just there. You can know about the enhancement of sexuality, that´s

[10] See Kroon, Kuhns & Cousijn (2021) Table 1 for a summary of current evidence for short-term and long-term effects of cannabis on cognition.

just there. But if you want to know how it can enhance writing, or appreciation of art or so many other things, then you got to become experienced with the drug to appreciate that."

Philosopher and cognitive neuroscientists Sebastian Marincolo (2010, italics added) also writes the following in his book dedicated to the topic: "On the way up to the most fascinating complex cognitive abilities we will see that marijuana can lead to the *enhancement* of our ability to perceive patterns, to vividly imagine situations, to introspect our own emotions and character as well as to empathically understand others. In the end we will come to understand how many of these complex cognitive abilities are *enhanced* and how their enhancement under marijuana can lead to our ability to produce insights."

In our article we also point out that our informants used various drugs, including cannabis, as an enhancer (Hupli et al. 2016; 2019b) and there are a few contemporary research articles on the topic from Germany (Franke et al. 2016; Bagusat et al. 2018). In the publication by Franke, Roser, Lieb, Vollmann & Schildmann (2016) titled "Cannabis for Cognitive Enhancement as a New Coping Strategy? Results From a Survey of Students at Four Universities in Germany", the researchers explored the use of cannabis for cognitive enhancement among German university students. As mentioned, while the literature on cognitive enhancement drugs among students has focused mainly on the use of stimulants like amphetamine and methylphenidate, the study by Franke et al. (2016) provided one of the first empirical studies of cannabis use as cognitive enhancement in relation to amphetamines.

As with their previous publications on stimulant use for cognitive enhancement among students, the authors researched the "knowledge, subjective effects, user characteristics, attitudes and factors related to academic pressure among students who reported using CAN [cannabis] for the purpose of CE [cognitive enhancement]" through survey methodology (Franke et al. 2016, p. 1857). The survey was distributed in four different German universities and received 1,538 participants. The authors state that a considerably larger amount of respondents knew about amphetamine use for cognitive enhancement compared to cannabis, although the prevalence of cannabis use was slightly higher compared to amphetamine use for the same purpose (see also Bagusat et al. 2018). Thus, cannabis use as a cognitive enhancer was more common than the use of amphetamine (3.5% vs. 2.1 %), although by far not as familiar to the overall study population (cannabis: 21.7% vs. amphetamine: 66.5%)

According to Franke et al. (2016), cannabis users reported significantly higher values for performance pressures compared to amphetamine users and non-users.

Amphetamine users, on the other hand, reported stronger effects compared to cannabis users and amphetamine was used for exam preparation more often than cannabis. In their discussion, the authors compare the prevalence of cannabis use in their study to the general prevalence of cannabis in Germany among young people and between genders. The authors also compare their findings to the only previous study that they were aware of that had reports about cognitive enhancing effects among users, although that study focused on problematic use (see Green, Kavanaugh & Young 2005). The authors state that their findings of more students knowing about amphetamines for cognitive enhancement compared to cannabis reflects the scientific and media publications on the topic, which as mentioned, have focused mainly on stimulants. In the end of the article, the authors speculate that the higher performance pressures experienced by the cannabis users while at the same time experiencing less effects on performance compared to amphetamine users is a sign of a wider concept of cognitive enhancement among cannabis users.

It is important to note that using large amounts of high-potency cannabis for a long period of time, especially in adolescence, can have detrimental effects on young users (Lorenzetti, Hoch & Hall 2020; Kroon, Kuhns & Cousijn 2021). At the same time "the exact mechanisms underlying the adverse effects of cannabis on cognition are not completely clear" (Colizzi, Tosato & Ruggeri 2020) and same can be said of any potentially 'enhancing' effects.

Thus, to conclude, the concept of cannabis as a cognitive enhancer, and as pharmacotherapy, requires further study. It is important to keep in mind that Cannabis Sativa L. has a great variety in plant species partly also due to human cultivation, and a long history of human use for medicinal and other purposes (Russo 2007; Clarke & Merlin 2013; Gloss 2015; Vihervaara & Hupli 2021). Effects of cannabinoids on neurological and mental states and disorders is complex (Fattore ed. 2015) and sometimes these effects are the opposite of enhancing (Crean, Crane & Mason 2011; Kroon, Kuhns & Cousijn 2021).

5.2 Psychedelics beyond therapy

The PNS literature has hardly researched or even discussed the topic of psychedelics (some exceptions, see Anderson 2006; Langlitz 2011; HED Matters 2019; Liokaftos 2021) even though users have reported enhancing effects from psychedelics as presented below. The current thesis will mainly focus on psilocybin when presenting

a few examples of user studies, as it is more commonly used in current clinical studies as well.

To give a little background on psilocybin, it is a psychedelic compound found in a variety of species of psilocin mushrooms, and it was first synthesised by the Swiss chemist Albert Hofmann, who also discovered the psychoactive properties of LSD (Richards 2016; Pollan 2018). Psilocybin has been increasingly researched as a pharmacological neurotechnology able to provide "mystical experiences" (Griffiths et al. 2006) and these experiences are clinically relevant as they can potentially alleviate anxiety over death among terminal cancer patients (Grob et al. 2011), work as a potential pharmacological technology for (treatment-resistant) depression (Carhart-Harris et al. 2016) and as an addiction intervention for alcoholism (Bogenschutz 2013; Bogenschutz et al. 2015) and tobacco dependence (Johnson et al. 2014).

Tobacco is one of the most widely used and legal psychoactive plants, but diseases related to its use kill over 8 million people every year around the world (WHO 2020a), and depression is currently affecting over 264 million people worldwide and it has been predicted to be the number one debilitating mental disorder in post-industrial societies (WHO 2020b). Thus, clinical psychedelic research shows great potential in alleviating some of the most debilitating illnesses that contemporary societies especially in Western countries are facing, namely depression, anxiety and addiction.

However, the potential to even research these medical implications has been stalled by stigma and extra regulatory requirements due to the alleged 'potential of abuse' of psilocybin and other psychedelics (Nutt, King & Nichols 2013). Lady Amanda Feilding (2017), the founder of the Beckley Foundation, a non-profit organisation which has been conducting and funding new research into psychedelics in the UK and elsewhere, says that although "research undertaken into psychedelic drugs so far has been fascinating and suggested many areas where they could be invaluable for therapy…further research is constantly obstructed by scheduling laws that make it extremely time-consuming, expensive, or impossible for researchers to get access to the materials we need." This is, arguably, not based on an evidence-based view of the relative harms of different psychoactive drugs (e.g. Nutt et al. 2007; Amsterdam et al. 2015).

In the USA alone, the lifetime prevalence of non-clinical usage of psychedelics, (LSD, psilocybin, mescaline, and peyote) was estimated to be around 32 million individuals (Krebs & Johansen 2013). Despite these relatively prevalent levels of use, the PNS literature has not picked up psychedelics as a major discussion point (see

Anderson 2006; Langlitz 2011; HED Matters 2019; Liokaftos 2021). In the psychedelic research community, however, "the betterment of well people" has been a topic of interest (Sessa 2008; Goldsmith 2010; Fadiman 2011; Roberts 2013). Using psychedelics for the betterment of well people is a term coined to Bob Jesse (Goldsmith 2010, p. 45), who according to Michael Pollan (2015) "will be remembered as one of two scientific outsiders who worked for years, mostly behind the scenes, to get it off the ground". The other one being Rick Doblin, the founder and the CEO of the Multidisciplinary Association for Psychedelic Studies (MAPS), who holds a PhD in public policy from the Kennedy Institute in Harvard and has several academic publications (e.g. Doblin 1998; Doblin et al. 2019) so not really a scientific "outsider", as Pollan wrote in 2015 (see also Pollan 2018).

Thus, the topic of using psychedelics beyond just treating the ill has been discussed in the field of psychedelic science and culture. For example, Feilding (2017, italics added) has written that psychedelics not only have the potential to heal but also to enhance: "If sufficient funds were available, we could expand our research, and investigate not only the potential of psychedelics to heal treatment-resistant conditions such as addiction, depression, and OCD, but also their *potential to enhance* creativity, neuroplasticity, and wellbeing". According to Feilding, if restrictions were lifted and enough funding for clinical psychedelic use would be made available "We could…conduct the full clinical trials necessary to demonstrate beyond doubt that these drugs have therapeutic value, paving the way for them to be developed into life-changing medicines."

As mentioned, the potential of psychedelics as novel antidepressants is promising (Mertens et al. 2020; see also Carhart-Harris & Nutt 2017), begging the question whether they can also work as effective "mood enhancers". The use of psychedelics on a population level has been shown to be associated with less distress and suicidality among the US adult population (Hendricks et al. 2015; see also Krebs & Johansen 2013). On an individual level, the use of psychedelics has also been associated with more inward looking and enhanced personal well-being (Griffith et al. 2006; Mòrò et al. 2011) as well as increased pro-environmental behaviour (Forstmann & Sagioglou 2017) and creativity (Sessa 2008; Prochazkova et al. 2018).

User surveys (Carhart-Harris & Nutt 2010; Winstock et al. 2021) and qualitative studies have also reported several positive effects experienced by psychedelic users (e.g. Alaeddinoglu 2020; Müller 2018) but these findings need to be confirmed by more controlled studies. In addition, in a survey in which university students from the UK and Ireland were asked to define "smart drugs", 6.2 % mentioned LSD

(Singh, Bard & Jackson 2014), showing that at least a small proportion of students also perceive psychedelics as "smart drugs" (Hupli et al. 2016; 2019ab).

Thus, the enhancing properties of psychedelics seem to have an empirical ground, as Elsey (2017 p. 5) states in his review of psychedelic studies done on healthy volunteers; "current empirical findings indicate that psychedelics have the potential to significantly improve wellbeing among otherwise healthy individuals, and may also help foster novel perspectives, supporting the resolution of professional and personal challenges." Clearly, proper empirical research on both the therapeutic and neuroenhancement uses of drugs, including "illegalised" ones like cannabis and psychedelics, is needed for a more informed ethical debate on neuroenhancement drug use and possible future implications. These future implications remain highly speculative not only because the on-going "War on Drugs" does not legally allow neuroenhancement use, but also because of the limited potential of certain psychoactive drugs to enhance the human condition, at least to the extent as is often depicted in the bioethical literature (Heinz & Müller 2017) and media (Partridge et al. 2011).

5.3 Microdosing psychedelics – a form of neuroenhancement?

Based on the above sub-chapter, the author argues that there are ample grounds for researching and discussing psychedelics as a form of pharmacological neuroenhancement. This is not because there is definite evidence for effectiveness and safety of psychedelics as neuroenhancers but because, especially a user practice now referred to as "microdosing psychedelics" has been receiving increased attention from researchers and media (Kuypers et al. 2019; Passie 2019; Hardon 2021) also as a form of cognitive enhancement (Johnstad 2018; Prochazkova et al. 2018; Hupli et al. 2019a; Rifkin, Maraver & Colzato 2020; Liokaftos 2021).

Part of our "descriptive assemblage" (Savage 2007) of microdosing psychedelics on Youtube (Hupli et al. 2019a) was to give a brief overview of published and on-going research projects in relation to microdosing psychedelics. Several publications and research projects have appeared since that publication, a few of which are presented below. The author's own initial interest in the phenomena has been described elsewhere (see Hupli 2019c; and in Finnish Hupli 2018b).

It is important to note that microdosing has several different meanings (Passie 2019). For instance, in pharmacokinetic studies, microdosing is being used as a method to investigate "new chemical entities" (NCE) (Tewari & Mukherjee 2010).

The rationale is that microdoses "would be too small to cause any major side effect after a single dose" (ibid. p. 61). This concept of microdosing, however, aims for toxicological insights: "it should be possible to undertake such studies in humans without having to complete the whole range of classical toxicology studies at therapeutically effective doses that are mandated prior to regular Phase 1 trials." (ibid). In addition to modern drug toxicology research, microdosing is also used as a novel technology in agriculture as a method of distributing plant nutrition (Passie 2019, p. 4).

What is a microdose in relation to drug toxicology research? According to Tewari and Mukherjee (2010): "Published guidelines define a microdose to be at 1/100th of the expected pharmacological dose... Studies using such a microdose are called microdosing studies." The dosages in microdosing studies are often lower than those popularised in contemporary psychedelic microdosing practices (Johnstad 2018; Kuypers et al. 2019) as well as that encountered in our research that focused on Youtube videos (Hupli et al. 2019a, see Table 1). And while the renaissance of current microdosing psychedelics research is usually credited to Dr. James Fadiman, who in his book The Psychedelic Explore's Guide published in 2011, dedicates a small chapter to describe experiences with "sub-perceptual doses" (Fadiman 2011), there was already early research done in the 1950s and 60s, especially by the US military, on low doses of LSD. These studies were reviewed by Torsten Passie and partly republished in his book The Science of Microdosing Psychedelics (2019), arguably one of the most comprehensive publications on this issue to date.

Although Fadiman noted in 2011 that the results of the self-reports he had gathered at that point were preliminary and mainly anecdotal, he concluded that: "Everyone said their experiences were positive and valuable" without experiencing significant adverse effects (see also Fadiman & Korb 2019). Fadiman also wrote that "As several reports stated, someone taking a dose this low functions […] a little better than normal", echoing similar kinds of sentiments found in the PNS literature (Elliot 2003; Farah et al. 2004; Vargo and Petróczi 2016).

Lack of research did not prevent a certain "media-hype" from developing, as prior to contemporary research publications, there were plenty of media reports around the topic of microdosing. These reports described microdosing as a "Revolutionary Way of Using Psychedelics" (High Existence 2014) and in a "brief history of microdosing" written by Vice in 2015, states that "while the idea hasn't yet catapulted itself into the mainstream, it's getting there". The following years indeed saw more mainstream media outlets writing about how LSD microdosing "became the hot new business trip" (Rolling Stone 2015) and "the new job

enhancer" (Forbes 2015). Microdosing was affiliated with work productivity as a "new brain booster" (The Times 2017) especially in the technology hub Silicon Valley located in California (Wired 2016; Huffington Post 2017; also Mishra 2018). These media reports usually included mainly positive reports from people practicing or experimenting with microdosing psychedelics despite that for a long time there was indeed a lack of published research available, as still remains the case (Kuypers et al 2019; Passie 2019; see Wired 2019).

Discoverer of the psychoactive properties of LSD, Albert Hofmann, had already mentioned in an interview in 1976 that "very small doses, perhaps 25 micrograms, could be useful as a euphoriant or antidepressant" (Horowitz 1976). According to Fadiman, Hofmann called microdosing "an under-researched area" (Fadiman 2011, p. 211; see also Passie 2019, p. 23-25) and it did take over 45 years for the topic to be picked up by modern mainstream media and research. However, the "very small dose" of 25 micrograms mentioned by Hofmann is not technically considered a microdose or "sub-perceptual dose" as described by Fadiman (2011). As the "common" recreational dose of LSD ranges from 50 to 150 micrograms (Passie et al. 2008), and in contemporary clinical settings from 20 to 200 micrograms, it is still fairly unclear what a "microdose" really is compared to a very low dose or "minidose" (Kuypers et al. 2019; Passie 2019, p. 9-10).

To elaborate on this issue, the above mentioned 20 micrograms of LSD acted as an active placebo in a study looking at LSD-assisted psychotherapy for anxiety associated with life-threatening disease (Gasser et al. 2014). The 20 micrograms was chosen "to produce short-lived, mild, and detectable LSD effects that would not substantially facilitate a therapeutic process" (Gasser et al. 2014, p. 516). As both participants and therapists in most cases correctly guessed whether the administered dose was the experimental dose of 200-µg or the active placebo dose, the authors stated that "the 20-µg dose was too low to achieve successful uncertainty about the dose" (Gasser et al. 2014, p. 518) partly limiting the validity of their findings (ibid. p. 519). However, the study was one of the first clinical LSD studies since the 1970s (Gasser et al. 2014; see Sessa 2017) and showcases here how only a miniscule dose of the neurotechnology often referred to as LSD is required to achieve a pharmacological effect. In their study, Griffiths et al. (2011) also noted effects of psilocybin on most scale measures at even the lowest dose of 5 mg of psilocybin per 70 kg.

In their comprehensive overview of the current literature Kuypers et al. (2019) state: "the term 'microdosing' appears to consist of three components: 1) The use of a low dose below the perceptual threshold that does not impair 'normal' functioning

of an individual. 2) A procedure that includes multiple dosing sessions. 3) The intention to improve well-being and enhance cognitive and/or emotional processes." Thus, the dose should be low enough so it does not at least impair "normal" functioning and in the publication the authors offer a table which includes varying doses (Microdose, Very low Dose, Low dose, Medium dose, High dose) of varying psychedelic compounds (psilocin, LSD, DMT and Ibogaine) that have been studied both in preclinical and clinical research (Kuypers et al. 2019, p. 3). The authors write that "These doses are approximate values" which were presented as "Per kilogram dose values" which had been "converted to values for a 70-kg person", thus their applicability to 'real-life settings' requires careful consideration.

The second component of microdosing according to Kuypers et al. included a procedure with multiple dosing sessions for which there is no unified protocol. This multiple dosing of psychedelic compounds, which is something that usually does not take place with higher doses, is one of the issues that has raised concerns of potential cardiovascular risks associated with nearly daily activation of serotonin receptors with potent partial serotonergic agonists like LSD and psilocin (Kuypers et al. 2019; Nichols, Roseman & Timmerman 2018, p. 83).

Kuypers et al. (2019, p. 8) conclude that "the possible effects and implications of microdosing remain largely unknown." While online forums have a vast database of reported effects, from Youtube (Hupli et al. 2019a; Andersson & Kjellgren 2019) to Reddit (Lea, Amada & Jungaberle 2019), according to Kuypers et al. (2019) "the true amount of active substance in these is unknown". Both from research and public health perspective this is problematic as even a microdose of an unknown drug can be detrimental for the user and "the criminalization of psychedelics has generated significant harms, particularly as illegal markets produce and distribute psychoactive substances that range widely in quality and potency, resulting in unpredictable toxic effects" (Haden et al. 2016 p. 245).

So far there are no wide reports of toxic effects from microdosing psychedelics as the third component of microdosing described by Kuypers et al., (2019, p. 8) "having an intention to improve well-being and enhance cognitive and/or emotional processes", is indeed something that users often seem to experience when they practice microdosing psychedelics (e.g. Lea et al. 2020; Fadiman & Korb 2019; Hutten et al. 2019). However, "while in these anecdotal reports the user deliberately ingests a substance for a reason, expecting positive effects, it is difficult to distinguish between expectation 'placebo' effects and the effect of a microdose." (Kuypers et al. 2019, p. 8; see also Szigeti et al. 2021; Passie 2019).

From a user perspective, however, there is 'an effect', whether due to pharmacology or the excitement of doing something, even something illegal, but at least some practice that might improve one's life-situation. Although some users experience also unwanted effects, microdosing psychedelics is more often claimed to bring relief for such conditions such as depression and ADHD (Fadiman & Korb 2019; Lea et al. 2020). The vast list of effects microdosing psychedelics is claimed to produce, now partly confirmed by an increasing amount of user and preclinical studies (Polito & Stevenson 2019; Hutten et al. 2019; Rifkin, Maraver & Colzato 2020) with some clinical ones completed (Family et al. 2020; Yanakieva et al. 2019; Bershad et al. 2019) and others underway (MindMed Press Release 2020; see also Hupli et al. 2019a) require further attention in the field of pharmacological neuroehancement (see HED Matters 2019; Liokaftos 2021). Thus, this trend begs for more research on the topic to distinguish "the actual from the imaginary effects of microdosing" (Passie 2019, p. 46), not only for therapy but also for neuroenhancement.

According to a recent review of microdosing psychedelic studies, focusing specifically on the potential as an enhancer, Rifkin & Maraver and Colzato (2020, p. 9, italics added) "conclude that microdosing psychedelics is a promising means for enhancing various aspects of cognition, creativity, and emotion recognition, and that they may be valuable tools to augment cognitive flexibility and neuroplasticity." However, the reviewed studies were mainly pre-clinical and the authors also acknowledge that "There…still exists almost no empirical evidence for any cognitive processes or emotion recognition enhancing effects of microdosing psychedelics" especially from controlled clinical studies (Rifkin & Maraver and Colzato 2020, p. 320).

Rifkin et al (2020, p. 323-324) also state that "These findings imply that psychedelics should not be treated as a uniform class of drugs, particularly with respect to microdosing. Various psychedelics, with their distinct receptor affinities, will almost certainly prove to be better for cognitive enhancement in small doses than others." Thus, microdosing psychedelics as a potential cognitive enhancer requires further study and some psychedelic researchers remain sceptical about microdosing (e.g. Nichols, Roseman & Timmerman 2018, p. 83; Passie 2019) while others acknowledge that "This role of psychedelics as cognitive enhancers is certainly an area in need of more research" (Sessa 2017 p. 276).

This need for more research is also due to various websites offering information about the practice (e.g. www.microdosing.nl), sometimes for monetary compensation (https://thethirdwave.co/microdosing-lsd-mushrooms/). This is

spite of the fact that published empirical research has been limited and efficacy partly explained by placebo (Szigeti et al. 2021; Family et al. 2020; Bershad et al. 2019). Moreover, the drugs in question remain illegal to use even for medicinal purposes in most parts of the world.

Nevertheless, microdosing psychedelics in the future might not be used only in attempt to enhance 'normal cognition' but indeed also to treat conditions like Alzheimer's (Vann Jones & O'Kelly 2020) or adult ADHD; for instance a Canadian based psychedelic medicine company MindMed is planning to study LSD microdosing for ADHD together with researchers at Maastricht University (MindMed Press release 2020). This type of 'novel drug use practice', such as microdosing psychedelics to enhance general performance or to (self-) medicate oneself due to a disease (see Passie 2019, p. 42-46; Lea et al. 2020) requires not only sociological investigation (Liokaftos 2021) but also drug policy discussion to ensure effective and humane harm reduction approaches.

6 DISCUSSION AND RESEARCH RECOMMENDATIONS

The final chapter of this doctoral thesis investigation aims to contribute to the public debate on drugs with the hope that we will eventually move from 'smart drugs' to 'smarter drug policies'. The focus in this chapter is on global mental health, focusing more on the therapy side than the enhancement side, although as mentioned, this line is often blurred. According to Gunter (2015, p. 733, italics added) "Cosmetic neurocognitive enhancement represents one way in which an otherwise well individual may choose to adapt to a challenging environment through the use of the services of a healthcare provider."

Gunter continues that from a bioethical perspective there is "high value on the self-maintenance of health, enhancement of self-esteem, and improved social functioning as potential goods meriting inclusion of cosmetic enhancement as a healthcare activity". However, while this might be so, the current pressure on healthcare services due to the COVID-19 pandemic makes this type of enhancement activity less of a priority compared to providing medical necessities.

The current author argues that if individuals do not have legal access to certain drugs even for legitimate and debilitating medical reasons, then granting access for neuroenhancement purposes seems implausible, and even unethical, as therapeutic access should be guaranteed first. Emphasis on therapeutic use, however, is not an argument for not researching enhancement drugs (Schermer et al. 2009) especially as it to some extent is 'already happening' (Coveney et al. 2011).

Nonetheless, drug policies that criminalise psychoactive drug users for going beyond narrowly defined medical and scientific uses are argued to be detrimental for both therapeutic and enhancement users, as well as the society at large (Bakalar & Grinspoon 1984; Bublitz 2016; IDPC 2018). Therefore, the author of this present doctoral study argues that one of the reasons why 'pharmacological neuroenhancement by the healthy' remains to be a futuristic potential is that the 'war on drug users' and its 'politicogenic drug effects' remains a too prevailing political reality and discourse for such a social practice. This is despite the fact that, generally speaking, so-called neuroenhancement drug use is something that is discussed in various governmental reports and medical association guidelines (see Outram &

Racine 2011 for a review). However, as stated in the EU-funded SIENNA project report regarding legal frameworks for enhancement technologies, the area of pharmaceuticals and other drugs "remains a heavily disputed debate" (Warso et al. 2019). While the author's aim here is not to resolve these issues, he will nonetheless map out a few potential ways forward.

6.1 The imperative to consider user perspectives

Pharmacological neurotechnologies offer promises and perils (Wolpe 2002) and their potential for "boosting brainpower" (BMA 2007) requires broader bioethical discussion over harms and benefits of novel and old neurotechnology use, and the different policy approaches regarding that use (STOA 2009; OECD 2017; Warso et al. 2019). As in preceding chapters has been highlighted, the importance of user research need to be considered when it comes to looking at the use of pharmacological neurotechnologies, such as 'drugs'.

Clearly, user-focused drug research has similarities with what Casas-Cortés et al. (2008) call 'knowledge-practices', a term coined in relation to studying social movements. According to these authors (2008, p. 21), social movements should not be seen as mere objects for analysis but "lively actors producing their own explanations and knowledges." They go on to say that "These knowledges take the form of stories, ideas, narratives, and ideologies, but also theories, expertise, as well as political analyses and critical understandings of particular contexts. Their creation, modification and diverse enactments are what we call 'knowledge-practice'" (ibid.).

Using the concept of 'knowledge-practice' allows researchers to look at knowledge and its very "concrete, embodied, lived, and situated character" (Casas-Cortés et al. 2008, p. 20). In a similar way that actors in social movements are depicted by Casas-Cortés et al. to produce their own knowledge-practices, Rose (2013) states that in relation to mental health "there are also arguments that changing the knowledge producer changes the knowledge". For example, mental health diagnostics can be seen as producing a certain kind of knowledge in relation to various populations, which does not necessarily correlate with the lived experiences of living with that diagnosis or the condition it attempts to represent. Rose (2013) also uses the example of how women were excluded from science during the Enlightenment (and remain to be excluded albeit not to the same extent): the author will, however, briefly use another example, which is, that of a drug user.

Drug users are often stigmatised, not only because the activity that they are engaged in has been deemed illegal, but also immoral (Hupli 2013a; Global Commission on Drug Policy 2017). However, as argued throughout this summary article, this illegalisation is not based on the relative harms of the drugs themselves, as alcohol and tobacco, the two widely available and legal drugs, are also among the most harmful ones, despite their legal status (Nutt et al. 2007; van Amsterdam et al. 2015). Indeed, the term 'drug user' often implies to a person who consumes "illegalised drugs" and contemporary societies tend to make sharp distinctions between "legalised medicines" and "illegalised drugs" although, as mentioned, "the categories of licit and illicit are neither static nor rigid" (Goodman et al. 2007, p. xiii).

Thus, a user-focused approach should be more utilized when it comes to (enhancement) drug research and policy making, as it has not only various ethical dimensions but also methodological ones (Hardon 2021). Rose (2013) states that "If marginalised groups produce different knowledge to conventional scientists, then the importance of user involvement in mental health research is not only ethical, it is transformative of knowledge itself." For instance, in an era when "new psychoactive substances" (NPS) are sold on dark web markets, the potential to identify emerging drug trends by utilising user knowledge has been demonstrated by using online data about drugs that have not yet been monitored (e.g. Deluca et al. 2012) such as microdosing psychedelics (Hupli et al. 2019a). Online forums produce their own specific "research culture" (Berning & Hardon 2016) which together with other open-source information and digital methods could be utilised in formal research on user, and seller, practices (Hupli et al. 2019a; Demant, Bakken & Hall 2020; Hardon 2021).

Taking user perspectives more into account, and having a critical discussion on current drug policies based on criminalising users, are important, not only from ethical and methodological perspectives, but also from a service provider perspective, as the level of liberty around drug policies might impact the willingness of users to seek medical help (Benfer et al. 2018). In addition, partly due to their illegality, drug research has focused either on the harms of illicit drugs (Hart 2014), or the benefits of legal medications (Moncrieff 2009), which skews the picture of 'drug use' and their 'effects' in profound ways. User involvement in drug research and policy-making around this "set of tools" (Oldani, Ecks & Basu 2014, p. 177), or as I have argued to frame them as pharmacological neurotechnologies, is therefore not only paramount, but as Rose (2013) exemplifies from a mental health research perspective, also possible.

6.2 Focus on country-context

Current (inter)national drug policies and current drug policy climate, which criminalise certain pharmacological neurotechnology use(rs), requires more in-depth (STS) research around the (bio)ethics and impact of pharmacological neurotechnology use, innovation, regulation and policy (e.g. Schermer et al. 2009; Forlini et al. 2013) in different country-contexts (Hupli 2020a). Nowadays regional differences in drug use prevalence can even be researched by waste-water analysis; for instance, a study by Löve et al. (2018) compared stimulant use between Nordic capitals and found that Helsinki had the highest concentrates of methamphetamine use. Even this type of 'knowledge-practice', although maybe not intended as such, can have an impact in 'evidence-based drug policy making' as argued below. However, it remains questionable how much impact scientific and "expert knowledge" has on drug policy reform, even when preventing drug deaths (Stevens 2019) as calls from researchers in favour of decriminalising personal drug use have not led to concrete governmental action, at least in Finland, at the time of this writing (Hakkarainen & Tammi 2018; see also Unlu, Tammi & Hakkarainen 2020).

Benfer et al. (2018) argue that "Effective drug policies require careful consideration of international law, national culture, public health, order and civil liberties; negotiating a balance between these concerns is a major challenge for jurisdictions across the world." Thus, country-context matters (Hupli 2020a), among other things. Researching 'the level of liberty' of nation states regarding drug policy and enhancement drug use is one potential future area of empirical inquiry. For example, is the Netherlands a more "bioliberal" country when it comes to (enhancement) drug use, while Finland could perhaps be described as a more "bioconservative" one (Hupli 2020a; see Reiner 2013)? As mentioned earlier in Chapter 4.2., so-called 'bioliberal' standpoint argues that enhancement technologies should be permitted based on, for example, informed free will, while according to the ' bioconservative' argument enhancement technologies will "corrupt, degrade and rob us of what is 'naturally human'" (in Schermer et al. 2009, p. 76). Juxtaposing a "bioliberal" country, represented here as a thought experiment by the Netherlands, with a "bioconservative" one, represented by Finland, is meant to demonstrate how the issue of cognitive enhancement drugs takes different forms depending on the country-context (Jotterand & Dubljevic eds. 2016).

This was elaborated on briefly in Hupli (2020a) in relation to drug policy context and action on cognitive enhancement drugs in the above mentioned countries, but to study the level of 'bioliberalism' of a nation state would require more conceptual

and empirical work (Benfer et al. 2018). Nevertheless, empirical research of country-context and various stakeholders in that context is argued to be an important contributor to future ethical and policy debates on the use of pharmacological neurotechnologies (Lucke 2012).

Empirically studying public discourse and attitudes of different groups is one area that could shed more light on many of the issues described above (see Coveney et al. 2019). It is important to note that studying public discourse around enhancement could also include focusing on what is not said, and what is left out from public discussions and debates in relation to drugs and other 'problematisations' (Bacchi 2009; Hupli 2013a). For instance, the topic of pharmacological neuroenhancement has hardly been discussed in either the mainstream Finnish or Dutch media (Schermer 2016, p. 190-192) unlike in some English-speaking countries (Partridge et al. 2011).

Part of this discourse is also the attitudes of medical doctors towards "smart drug" use, which will be explored briefly here in the Finnish context, where the findings of an informal survey (see Vierula 2016) will be presented to tentatively map out the attitudes of Finnish physicians towards pharmacological neuroenhancement. While having obvious methodological and conceptual limitations, the informal survey gives some indication over the attitudes of Finnish physicians towards PNS, who as the gatekeepers of medications play a pivotal role in current and future access to cognitive enhancers (Williams et al. 2011).

Finnish medical doctors have been hesitant to prescribe stimulants even for therapeutic reasons partly due to their apparent potential for abuse (see Huttunen & Raaska 2015), although prescription rates have increased significantly in the last decade (Vuori et al. 2018). However, there are hardly any empirical studies done in this specific area, at least in the Finnish context (Hupli 2020a). Nonetheless, an article that featured in a Finnish medical journal titled "Intelligence with a prescription?" (Vierula 2016) included a few expert interviews on the topic of "smart drug use". There was also an informal survey for the readers, who are mainly medical professionals (to answer the survey the respondent would need professional logins). The results of this survey are briefly presented below.

The survey had 28 respondents and gives a glimpse of the attitudes of Finnish physicians towards pharmacological neuroenhancement. The survey simply asked "Should smart drugs be made more widely available?" and 10.7 % (N=3) chose the answer "Yes, many patients could benefit from smart drugs" and the same amount (10.7%, N=3) chose "Maybe, but the use requires consideration". The majority (60.7%, N=17) chose the answer "More research is needed on smart drugs before

wider deployment" while 17.5 % (N=5) chose the answer "No, I find it unethical to try to improve cognition by chemical means."

Similar to Finnish GPs, medical doctors and university students in the Netherlands are also hesitant to freely allow enhancement drug use, at least without some forms of restrictions and regulations (see Schermer 2016). In a Dutch student survey by Schelle et al. (2015), 73.6 % of the respondents disagreed with the statement that "´Smartpills´ should be freely accessible." Thus, researching attitudes of different groups towards enhancement use inside various country contexts can bring these types of similarities and differences to the foreground (Forlini & Racine 2009; Coveney et al. 2019)

And even if one would argue, ethically or otherwise, against the use of prescription stimulants and other drugs for enhancement purposes (e.g. Arria & DuPont 2010), one of the major ethical concerns is that their possible use occurs in the safest way possible. Providing information via public discussion about possible adverse effects (Massie, Yamga & Boot 2017) experienced by young users is important in this respect but also acknowledging that some users actually experience benefits (Hupli et al. 2016; 2019b). How the situation develops in Finland, where the discussion and practice around enhancement drug use is still marginal compared to the Netherlands, would require more (longitudinal) research and engagement among users, prescribers and the public. Currently it is difficult to estimate how much, for instance, medical and non-medical stimulants might be used for cognitive enhancement purposes (Hupli 2020a). Therefore it would be imperative to move beyond the therapy/ enhancement dichotomy and focus on the real life practices of various pharmacological neurotechnologies.

6.3 Moving beyond therapy vs. enhancement

The bioethical discussion around pharmacological neuroenhancement is often framed "as a debate about where *treatment* ends and *enhancement* begins" (Maslen, Faulmüller & Savulescu 2014, p. 6, italics in the original). Thus, drugs and other technologies are seen either as a treatment for a neurocognitive impairment, like deficits in attention, or a way to enhance cognition beyond "normal species-functioning" (Daniels 2000).

On a conceptual level, "An intervention that is aimed at correcting a specific pathology or defect of a cognitive subsystem may be characterized as *therapeutic*. An *enhancement* is an intervention that improves a subsystem in some way other than

repairing something that is broken or remedying a specific dysfunction" (Bostrom & Sandberg 2009, p. 312, italics in the original). However, this distinction between therapy and enhancement "is often difficult to discern" and "lacks practical significance" (ibid.).

In research, these types of blurred boundaries have already been shown in relation to cannabis, as many "illicit" users report to grow and use cannabis for medicinal reasons, including for ADHD (Hakkarainen et al. 2015; Pedersen 2015; Hupli 2018a). While this blurring is more between "recreational" and "therapeutic" use, as mentioned, cannabis is also used as a "cognitive enhancer" by some students (Franke et al. 2016; Hupli et al. 2016; 2019b). Thus, it is possible that what has been previously categorised as recreational or illegal drug use, has in practice already been for "enhancing suboptimal performance" (Schermer 2007a, p. 33; Conrad & Potter 2000, p. 273-274) and/or self-medication against study and work-related stress (e.g. Maier, Haug & Schaub 2015), further complicating simple categorisations both in research and policy.

On a practical level, Paul Wolpe (2002, p. 390-391) sees that the distinction between treatment and enhancement requires inquiry on three different areas: 1) medicine and reimbursement 2) public policy and 3) normative behaviour. In addition, this blurred line between therapy and enhancement has implications to drug policy discussions and in relation to harm reduction and public health efforts. Thus, both in theory and practice this distinction seems to be complex (e.g. Schermer 2007a; Hoffman 2017; Hupli et al. 2019b) and even partly result of research itself into this phenomena (Bullard 2018).

As Nicholas Rose (2009, p. 80) argues "what is involved here cannot be divided according to the binary logic of treatment versus enhancement; it is a constant work of modulation of the self in relation to desired forms of life." It is argued that individuals who use various pharmacological neurotechnologies, either for therapeutic or enhancement reasons, should be simply 1) asked whether they perceive their use as treating something that is 'broken' or are they trying to enhance their capabilities to perform better, 2) whether these perceptions correlate with actual effects, 3) inquire and inform about risks and 4) design policy approaches accordingly (Hupli et al. 2019b; Coveney et al. 2019). End-user research is common place in other areas of technological consumerism and should become a standard also when it comes to pharmacological neurotechnologies, both for psychiatric and other drugs.

Psychiatric and other drugs, in a broad sense, have played an important role in how we perceive not only mental health and illness but our very selves and our

normative behaviour (Rose 2007). During the 20th century, certain psychiatric drugs were claimed to reveal the neurochemical underpinnings of severe mental disorders that were claimed to be caused by "neurochemical imbalances", and drugs were then offered as biological treatments to correct those imbalances (Moncrieff 2009). As stated earlier, at the same time as certain drugs have been promoted as "cures" for increasingly wide range of mental and somatic diseases (Dumit 2012) often with exaggerated benefits and downplayed harmful effects (Moncrieff 2009; Medawar & Hardon 2004), other drugs and their users have been prohibited, often accompanied with exaggerated harms and downplayed benefits.

How long this dichotomy between legally promoted and illegally prohibited drugs continues is difficult to predict, as are many things in our "overheating" world (Eriksen 2016). With different "runaway processes" (Eriksen 2016), this 'double bind' (ibid.) between "bad drugs" and "good medicines" is becoming increasingly blurred. Partly as a way to go beyond this 'double bind', I have proposed a theoretical framework which conceptualises both types of drugs as pharmacological neurotechnologies.

This is argued to be important for future research in this field as cognitive pressures in study and work contexts were requiring increasing capacities from our "overflowing brains" (Klingberg 2009; see Kegan 1994; OECD 2017) already before the COVID-19 pandemic. User-oriented research is already showcasing more broadly the role that these technologies have in contemporary experiences and expectations of various populations (Webster, Douglas & Lewis 2009; Coveney et al., 2019) and especially young users take decisive actions to effectively reduce potential harms from their use and to increase potential benefits (e.g. Van Schipstal et al. 2016; Hardon & Hymans 2016; Hupli et al. 2016; 2019b; Hardon 2021).

While increasing research in this area does not mean that the use of enhancement drugs should be explicitly promoted to encounter the demands of contemporary life, I do argue that the "human enhancement drug" discussion and debate requires broader sociological analysis over benefits and harms of not only "drugs" but also "drug policies" in this era between drug prohibition and promotion. This PhD has aimed to contribute to that discussion, but further research and debate is needed as there are already numerous real-life consequences of this categorical distinction between therapy and enhancement, for instance eligibility for medical services and insurance coverage (e.g. Daniels 2000). In addition, to emphasise, the use of some pharmacological neurotechnologies, like prescription pharmaceuticals without a medical diagnosis, let alone use of "illicit drugs" for enhancement use or otherwise, has various legal consequences in a form of politicogenic drug effects, as their use is

criminalized in most countries that have ratified the United Nations conventions on "psychotropic substances" (e.g. UN 1961).

There has not been serious attempts or hardly even discussion on the international drug policy debate level to change the current paradigm of access to current prescription drugs, let alone neurotechnologies that are currently illegal, for particularly enhancement purposes[11]. Thus, while there has been some theoretical speculations on how to legally regulate the enhancement use of for instance Ritalin™ and Adderall™ in the bioethical literature (e.g. Greely et al. 2008; Schermer et al. 2009; Dubljević 2013; Hall & Strang 2017) the 'enhancement drug debate' still awaits to happen on this international scale. This is despite that as Helén argued in 2004 (p. 4) "Today, the focus of advancing medical technology is less on human mortality and protection of vital processes than on life enhancement". When it comes to life enhancement with some pharmacological neurotechnologies, this advancement is facing several challenges (Rose 2007; Morrison 2015, p. 4), legality of the activity being one of them.

In another words, legally allowing certain pharmacological neurotechnologies would require significant changes in (inter)national drug policy regulations, which does not seem to reflect the realities of current drug policy debates, and often neglected in the academic literature around pharmacological neuroenhancement (Bublitz 2016; Hall & Strang 2017). Thus, most psychoactive drug use that is categorized to go beyond medical or scientific purposes, like enhancement drugs, remains not only prohibited, but in some countries severely punishable, reflecting the yet fairly 'underground' nature of certain pharmacological neurotechnology use. This also complicates public health and harm reduction practices (Csete et al. 2016; Hardon & Hymans 2016; Haden et al. 2016).

Additionally, an enormous gap remains between the ability of different populations to access even 'life-saving' pharmacological technologies (e.g. Petryna & Kleinman 2006; Eriksen 2016) let alone 'life-enhancing' ones, which has not been fully addressed in the bioethical or empirical literature (Pickersgill & Hogle 2015), or in social policy and practice. I argue that conceptualising drugs as pharmacological neurotechnologies is one way forward, as it can help to ask questions such as; why do contemporary political realities maintain the use(rs) of certain pharmacological neurotechnologies criminal with prohibitive policies that several scientists argue are not based on scientific evidence of the relative harms and benefits of these

[11] This observation is based on participation observation around UNGASS in New York City in 2016 and inside the Commission on Narcotic Drugs in Vienna between 2017-2020. See also Drugventures 2020; Rolles, Slade & Nichols 2020; IDPC 2018.

technologies (e.g. Nutt et al. 2007; Hart 2014; Stevens 2019)? What would happen if the use of pharmacological neurotechnologies for enhancement purposes was not only allowed, but promoted, in the same ways as certain medical technologies nowadays (Dumit 2012)? What would an appropriate and effective policy response be, which would reduce potential harms of professionally marketed enhancement drugs and enhance the benefits experienced by users (Van de Ven, Mulrooney & McVeigh 2019)?

A theoretical framing, which takes seriously the role of drugs as 'non-human actors' in the co-production of various self-making projects, that in our era sometimes rely on the use of pharmacological technologies, can shed light into the various individual and societal perceptions, reactions and restrictions regarding this type of technology use. Thus, researching human enhancement technologies in general and pharmacological neurotechnologies in particular from this type of STS approach can offer "the opportunity to explore different articulations of 'progress' encoded in debates around enhancement and ultimately to relate the narrow discussion of contemporary 'biotechnological' enhancement to the older, broader concepts of social enhancement" (Morrison 2015, p. 23; also Pickersgill & Hogle 2015).

6.4 Politicogenic drug effects

As mentioned throughout this study, contemporary (inter)national drug policy regulations categorise the use of certain 'drugs' as objects to be prevented, even 'a serious *evil* for the individual' (UN 1961, italics added; Tupper 2012; Sultan & Hupli 2020), while other drugs are seen as essential and medicinal (e.g. WHO Essential Medicines list). At the same time, several psychoactive plant-derivatives, like tobacco, sugar and ethyl-alcohol, are considered to be basic consumer products which need to meet certain quality regulations in order to be sold and marketed on a global scale (Goodman, Lovejoy & Sherratt 2007; Wadley 2016).

In other words, on the one hand there are certain drugs, such as pharmaceuticals, which are in some cases politically promoted directly to newly constructed consumer-patient target groups with often serious, and even lethal, physical effects (Medawar & Hardon 2004; Moncrieff 2009). And on the other hand, there are other drugs, like cannabis and psychedelics, that potentially offer physical and

psychological relief for individuals suffering from treatment-resistant conditions, but which are prohibited to access even for medical reasons, accompanied by often serious, and even lethal, political effects (e.g. Haden et al. 2016; IDPC 2018), or as the author prefers to name them, politicogenic drug effects.

I argue that for drug policy to move towards more "evidence-based policy making" (Cairney 2015) these types of politicogenic drug effects need to be taken into account. Politicogenic drug effects refer here to ill effects caused by political activity in the drug policing field. Loss of civil liberties due to criminalisation, denied access to health and social services, lack of quality control of consumed products leading to unnecessary health risks and overdose as well as militarised law enforcement could all be considered examples of politicogenic drug effects.

Part of these effects are how societies perceive 'drugs' and their users, which usually means that "different drugs are lumped together as are the individuals who use them, even though different people use different drugs for diverse reasons and under a wide range of sets and settings and to varying degrees" (Grinspoon 1994, p. 176-177; Global Commission on Drug Policy 2017). An analogy would be, for instance, to categorise depression, anxiety, and bipolar disorder all under the same umbrella term of "mental health disorders", and not design treatments and services according to the different characteristics of these disorders. And not just that, but the 'mentally ill' would be considered criminals and the 'mental health crisis' would be tackled with increasingly militarised police force.

Thus, from a public health perspective, contemporary drug policies do not reflect the 'evidence-based' view of individual and social harms associated with 'drugs' (e.g. Nutt et al. 2007), understood in this broad sense and taking into account politicogenic drug effects. This is not particularly 'new evidence', as for decades now, various individuals and groups have called for global and national drug policy reform to change the focus of drug control from criminal policy towards more health-oriented approaches (e.g. Bakalar & Grinspoon 1984; Csete et al. 2016; Global Commission on Drug Policy 2017; IDPC 2018; in the Finnish context: Hakkarainen & Tammi 2018). So far these efforts have not been able to shift the current prohibition-based focus, even in cases where there is evidence that less punitive approaches could prevent drug-related deaths (Stevens 2019).

The above demonstrates in part the political nature of evidence also in drug research, as according to Cairney (2015, p. 12) even "gathering and presentation of facts is a political exercise". The current (inter)national drug policy climate would require not only more in-depth evaluation of the politicogenic drug effects of various drug policies, especially from a public health perspective (Csete et al. 2016) but also

multi-criterion decision analysis that focuses on specific drugs, like cannabis and alcohol (Rogeberg et al. 2018) in specific country-contexts and regional policy environments (Hupli 2020a). But what would 'evidence-based drug policy making' look like, and maybe more importantly, how can it be achieved?

6.5 Evidence-based drug policymaking?

It seems vital to understand the role that evidence has, not just in drug policies, but in the processes of drug policy making. As Cairney (2015, p. 5) states: "we need to understand the policy process to explain how actors use evidence within it". In an ideal type of 'comprehensive' evidence-based (drug) policymaking, there is a scientific consensus on a given issue, which is understood by policy makers in a similar way as intended by the scientists, and policy makers rely only on scientific evidence as their main source of knowledge for their decision-making when facing a policy problem, and more practically, have ways of turning evidence of a problem into an effective solution (Cairney 2015, p. 31). However, as Cairney (2015, p. 32) describes "In the real world, the evidence is contested, the policy process contains a large number of influential actors, scientific evidence is one of many sources of information, and policymakers base their decisions on a mixture of emotions, knowledge and short cuts to gather relevant evidence."

This is clear in the world of drug policy as well; whether when advocating for drug policy reform, or maintaining the status quo, both sides of the 'world drug problem' often make references to scientific evidence in their argumentation. Use of evidence in this policy context, as in others, is not a-political; "The use of evidence is a political process; an exercise of power to characterise people and problems, and to justify beliefs and decisions" (Cairney 2015, p. 32: see also Bacchi 2009).

Health care is a particular field where reliance on medicine being 'evidence-based' is often at odds with realities of policy making (Cairney 2015, p. 33-36). Evidence-based medicine (EMB) is usually measured by its 'golden standard' of systematic reviews of randomised controlled studies (RCTs) for "the integration of the best research evidence with clinical expertise and patient values" (Cipriani et al. 2013 p. 319). Thus, EMB relies on systematic reviews of RCTs which are considered to provide the best available evidence to date of the effectiveness of health interventions in an 'objective' way: "The rationale for systematic review is the same for all questions – the avoidance of random error and systematic bias" (Cipriani et al. 2013 p. 321). However, Cipriani et al. (2013) also point to various limitations and

biases of systematic reviews and meta-analyses, including publication bias, language publication bias and over-reliance on electronic databases (see also Cairney 2015, p. 37-38; Jukola 2015).

There are, however, other biases that are not discussed by Cipriani et al. (2013; see Jukola 2015) and randomised controlled studies are methodologically challenging when designing evidence-based drug policy approaches. An example of a controlled study would be legally regulating for instance cannabis in one part of the country and keeping it illegal in other parts, which to some extent is happening with the Dutch "supply chain experiment" that allows cultivation of cannabis in 10 participating municipalities (Government of the Netherlands 2021).

However, there is long way to 'evidence-based drug policy' as illegality of using certain drugs continues to have implications for public health interventions (Haden et al. 2016; Csete et al. 2016), and for the willingness of users to seek medical help if problems arise (Benfer et al. 2018). This has major implications also for global mental health, as substance use and mental health interact in a myriad ways (WHO 2008).

In order to move drug policy towards evidence-based policy making these discrepancies would need to be taken into account and this should be done in a more realistic 'bounded rationality' way compared to the ideal-type of 'comprehensive rationality' (Cairney 2015). Policy making around tobacco demonstrates that this type of change is possible, although this requires drug policy reformers advocating for evidence-based drug policy to prepare long-term strategies, disseminate persuasive key messages and build alliances with each other and professionals working in-and outside of the larger policy making processes (Cairney 2015, p. 52). By doing so we could progress a step from 'world drug problems' towards 'world drug solutions'.

6.6 Towards smarter drug policies?

The connection between mental disorders and substance abuse disorders is clear even in the often used term MNS disorders (mental, neurological and substance abuse disorders). Alcohol and 'illicit' drug use are one of the "priority conditions" mentioned in the mental health Gap Action Programme (mhGAP) promoted by the World Health Organisation (WHO 2008). Ruggeri, Thornicroft and Goldberg (2013) point out that one of the major challenges identified in the landmark 'Grand Challenges in Global Mental Health Initiative Study' was "the fact that all care and treatment interventions – psychosocial or pharmacological, simple or complex –

should have an evidence base to provide programme planners, clinicians and policymakers with effective care packages."

The exclusion of certain compounds from this 'effective pharmacological care package', for instance medicinal cannabinoids and psychedelics, has, in the authors opinion, been detrimental for potential patients in need. Pharmacological care packages, of course, are not sufficient on their own, but for instance 'drug-assisted psychotherapy' has gained promising early research results especially in relation to psilocybin and MDMA (e.g. Nichols, Johnson & Nichols 2017; Sessa 2017; Doblin et al. 2019) requiring the attention of 'programme planners, clinicians and policymakers', among others.

This type of medicalisation and pharmaceuticalisation processes around drug use and addiction require increased attention as criminalising individuals for using certain drugs for 'extra-medical' reasons, sometimes as a form of self-medication, sometimes in a problematic way but in most cases as a way to *re-create* oneself, has burdened not only the individuals in question, but also the societies implementing such policy measures (e.g. Sultan & Hupli 2020). Medicalisation/pharmaceuticalisation of drug use is to some extent already happening with cannabis, psilocybin and MDMA as clinical trials into these technologies are moving ahead (e.g. Doblin et al. 2019) and there was a successful citizen's initiative in Oregon, USA that legalised psilocybin therapy and decriminalised use of several other drugs (Roberts 2020). The impact these events have on pharmaceuticalisation processes require further attention also in the pharmacological neuroenhancement literature.

And while medicalisation/pharmaceuticalisation of drugs like cannabis and psychedelics moves forward, prohibitive drug policies also continue to deny medical patients the right to influence their preferred treatment, slow down scientific research into severe mental health disorders (Sessa 2017) and often prevent individuals from even seeking help for drug-related problems when needed (Benfer et al. 2018). These are yet again examples of politicogenic drug effects described earlier.

Therefore, I argue that for now, the ideology described as 'War on Drug Users' is a too prevalent political reality for what Cairney (2015) calls 'bounded rationality' to take place in relation to evidence-based drug policy making. And for this reason drug policy reform that demands a more 'evidence-based drug policy' cannot rely on evidence alone. So what to do when, despite convincing evidence, drug policymaking continues to take 'moral sidesteps' (Stevens 2019), which show that current drug policies are not only ineffective but actually detrimental for public health (Csete et al. 2016) through different politicogenic drug effects? Should the public at large

demand that their cognitive right to change their neurochemistry, and in essence, their neurochemical selves, to be respected?

Criminalising people who use drugs is increasingly perceived as a human rights violation (UNDP 2019). Nonetheless, it is unlikely that even calls for human rights will be enough to persuade political actors involved in drug policy making processes to advocate for drug policy reform away from prohibition and towards legal regulation. And while calling for drug policies that would be based on evidence and respect human rights in themselves might not be enough, there are other arguments to be made, one of them being purely an economical one. In around 2016, it was estimated that in the USA alone the economic burden of prescription opioid overdose, abuse, and dependence was $78.5 billion, per year, with substance abuse treatment costs contributing to only about 4 % of the total costs (Florence et al. 2016). That economic burden has most likely increased in the following years with the current COVID-19 pandemic causing additional economic burden not only to the already fragile USA healthcare sector but to global public health efforts as well.

Reallocating funds from the ineffective and inhumane "war on drugs" in order to meet some of the challenges of global mental health care could halt the criminalisation of individuals that are already suffering not only from COVID-19 but mental, neurological and substance abuse disorders. In the authors opinion, this could even potentially narrow the gap between High income (HI) and Low and middle income countries (LAMIC) (see Ruggeri, Thornicroft & Goldberg 2013). However, this reallocation would require not only well-designed research projects to evaluate the effectiveness of such measures, but also political will.

Globally, the debate about cannabis scheduling is challenging the "Vienna Consensus" of the international drug control system (INCB 2018; IDPC 2018; Sultan & Hupli 2020). And there is some hope, as efforts to harmonise "a common position" between United Nation agencies in relation to drug policy are underway (see Jelsma 2019), and new drug strategies are being evaluated on national and European level (see Sárosi 2020). In addition, there already exists several published reports from various drug policy and research NGOs, and also state commissioned ones, that can guide us towards smarter drug policies with greater respect to human rights and public health, and by doing that, help us to at least to try and achieve the 2030 Sustainable Development Goals (Rolles, Slade & Nichols 2020; Unlu, Tammi & Hakkarainen 2020; Riboulet-Zemouli et al. 2019; Warso et al. 2019; IDPC 2018).

7 CONCLUDING REMARKS

Consideration of user perspectives, moving beyond the therapy vs. enhancement dichotomy by theoretically framing drugs as pharmacological neurotechnologies and focusing on country-contexts are some of the policy and research recommendations put forward in this PhD in order to transform world drug problems into world drug solutions through evidence-based drug policy making.

By framing both pharmaceuticals and other drugs "neutrally" as pharmacological neurotechnologies, we can try and move beyond the blurred and socially constructed boundaries between bad drugs vs. good medicines, therapy vs. enhancement, controlled vs. uncontrolled, legalised vs. illegalised, users vs. non-users, etc. We need to recognise that the effects of any pharmacological neurotechnology far exceeds their pharmacology, and that individual and social perceptions, together with the immediate and social environment where these technologies are used in, create complex networks regarding their modes of action and social effects, including politicogenic drug effects.

Technologies in general are not value-free, and the more general "human enhancement technology" discussion has various examples of neurotechnologies that have their unique ethical and other challenges, from transcranial magnetic stimulation (TMS) to deep brain stimulation (DBS). Nonetheless, even compared to invasive deep brain stimulation which requires neurosurgery, literally opening up one's skull and poking their brain with a surgical knife to implant a device which is then controlled outside of that skull, there is something about the inner workings of "drugs", and our modern moralistic approach to them, that calls for a closer investigation in relation to the debate about human enhancement technology use and practice.

In addition, there seems to be signs of an 'ADHD explosion', this time concerning adults, created partly by pharmaceuticalisation of underperformance. Increasing amounts of stimulants, both by prescription and by illicit purchase, were already used in countries like Finland and the Netherlands before the current COVID-19 pandemic which has put extra pressure on our attention as studying and work has moved increasingly online. While still relatively small amount of young adults use stimulants and other drugs in order to improve their life situations, the

fact remains that while one part of these young people are considered to be psychiatric patients, the other part are framed as criminals, both of which can seriously harm their future life trajectories.

Whether pharmaceuticalisation as a form of decriminalisation, to make criminals in to patients, could in this regard be considered "bad" or "good", will be left for future research and debate to fully answer as this research would require increasing bioethical analysis and empirical data in different country-contexts (Hupli 2020a). In general the role of human enhancement drug use, and especially users, in pharmaceuticalisation processes requires further attention. While it can be argued that drugs are not yet moving from medical treatments to pharmaceutical enhancements (Coveney et al. 2011, p. 389), some neurotechnologies, like cannabis and psychedelics, are moving from illegalised drugs to medical treatments and their potential role as neuroenhancers require further attention.

Especially the issue of cannabis as a cognitive enhancement (Franke et al. 2016) and pharmacotherapy (Hupli 2018a), requires further attention in the future as cannabis remains the most used "extra-medical" drug among young people in most European countries (EMCDDA 2019). And although medical cannabis seems to be a potential medicine for several indications (IACM 2020; Vihervaara Hupli 2021), including ADHD (Hupli 2018a), it lingers in the realm of "prohibited technologies" in Finland, and elsewhere. Even decriminalising adult use of cannabis, not to mention other psychoactive plants and fungi, continues to face political obstacles (Hupli 2019b), despite the ineffectiveness of prohibition policies to reduce drug use prevalence across the globe (Sultan & Hupli 2020; IDPC 2018).

While pharmaceuticalisation processes in the form of drug regulations are rapidly changing in countries as different as Finland and the Netherlands, this is happening at a very different scale. With cannabis for instance, the Netherlands is preparing to experiment with controlled supply chain of non-medical cannabis for adult use in 10 municipalities, which was initiated by a political party in the government. At the same time Finland is having a parliamentary debate about decriminalization of cannabis for adults, but mainly due to a citizens´ petition that managed to collect over 50 000 signatures in 2019 (Hupli 2019b). Both potential reforms require well-planned monitoring of not only prevalence of cannabis use in specific country countexts, but research into motivations, risks and benefits experienced by users, combined with sufficient harm reduction and other service provisions (e.g. Maier, Ferris & Winstock 2018; Benfer et al. 2018).

The question remains, "the extent to which a drug is able to move and leave behind cultural images of addiction, disease, side effects, health and social problems"

(Coveney et al. 2011, p. 389). More importantly the way drugs and their users are currently policed require further public debate and real life reform. To conclude, while contemporary discussion about human enhancement drugs is arguably a major change to the dominant view of perceiving (extra-medical) drug use as something else than an evil to humankind, it seems that there is a long journey to go until a "peace on drugs", and their users, will be achieved. Human enhancement drug use can, and should be, part of the "peace talks" in order for us to become collectively smarter with drugs.

However, there is also a need to recognise that there remains a long way to go before these ideas turn into drug policy action. In the meanwhile, "users" worldwide are not only being punished, they are being killed by the hundreds of thousands, whether directly by state violence and enforced prohibition laws, or by preventing effective and evidence-based harm reduction services and treatments to prevent drug-related deaths (Zigon 2018; IDPC 2018; Stevens 2019). Before we can actually start having smarter drug policies, "smart drugs" will remain an idea(l), something to aim for but never fully achievable. And as with any technology, pharmacological neurotechnologies can be used to enhance ourselves, or destroy. The choice is yours. And mine. Ours.

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9 PUBLICATIONS

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PUBLICATION I

Towards the smart use of smart drugs: Perceptions and experiences of university students in the Netherlands and Lithuania

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Toward the Smarter Use of Smart Drugs: Perceptions and Experiences of University Students in the Netherlands and Lithuania

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Abstract

The use of cognitive enhancement drugs (CEDs) among university students has raised widespread concerns about non-medical prescription drug use, safety, exam cheating, and study-related stress. While much of the empirical research to date has been conducted in the United States and Australia, this article examines perceptions and experiences of CED use among university students in the Netherlands and Lithuania. Our data come from two qualitative studies and one mixed-methods study and comprise 35 semi-structured interviews (20 in the Netherlands and 15 in Lithuania) and open-ended online survey responses from a convenience sample of 113 students in the Netherlands. Employing a crowded theory approach to interpret our qualitative data, we found most of our informants turned to CEDs to enhance their studying through better concentration and time management. Students used a broad range of pharmaceuticals (with and without a physician's prescription), recreational drugs, and nutritional supplements as cognitive enhancers, were generally well informed about the safety and efficacy of the substances they used, experienced both beneficial and adverse effects, and self-regulated their CED use to balance these effects, ensuring that their use remained moderate and thoughtful.

Keywords

neuroenhancement, smart drugs, university students, user experience, crowded theory analysis, harm reduction

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Introduction

The use of psychoactive substances by university students seeking to improve academic performance has attracted the attention of researchers, bioethicists, and government officials. While earlier research centered on North America and Australia, recent years have witnessed increased interest in many European countries, including the United Kingdom, Germany, and Switzerland (www.nerri.eu/; Forlini, Schildmann, Roser, Beranek, & Vollmann, 2015; Maier, Haug, & Schaub, 2015; Maier, Liakoni, Schildmann, Schaub, & Liechti, 2015; Maier, Liechti, Herzig, & Schaub, 2013; Singh, Bard, & Jackson, 2014; for reviews, see Maier & Schaub, 2015; Ragan, Bard, & Singh, 2013). *Pharmacological neuroenhancement* or "the misuse of prescription drugs, other illicit drugs, or alcohol for the purpose of enhancing cognition, mood, or prosocial behavior in academic or work-related contexts" (Maier & Schaub, 2015, p. 156) has been the subject of numerous government reports and policy guidelines from medical associations (for a review, see Outram & Racine, 2011). The phenomenon has also attracted media attention, which often exaggerates the popularity and efficacy of "smart drugs" (Partridge, Bell, Lucke, Yeates, & Hall, 2011; cf. Forlini & Racine, 2009; Williams, Seale, Boden, Lowe, & Steinberg, 2008). Although estimates of prevalence vary widely, studies suggest that cognitive enhancement drugs (hereafter CEDs)—including methylphenidate (e.g., Ritalin™) and dextroamphetamine (e.g., Adderall™), used mainly to treat attention deficit/hyperactive disorder (ADHD), and modafinil (Provigil™), a wakefulness-promoting drug used mainly to treat narcolepsy—are being used by many individuals without diagnosed medical conditions (Coveney, Gabe, & Williams, 2011).

Singh and Kelleher (2010, p. 5) suggest that "the use of stimulants as neuroenhancers appears to be a growing trend among university students around the world." Neuroenhancement, however, admits to different interpretations (e.g., Arria & Wish, 2006), requiring caution when interpreting figures on prevalence. Most commonly cited surveys also differ in their methods, sampling, sample size, and questions, requiring caution when examining epidemiological patterns of CED use. It is also difficult to transfer findings from the US to Europe due to different regulatory and educational contexts. In general, European studies have shown lower prevalence rates than American ones (e.g., Mache, Eickenhorst, Vitzthum, Klapp, & Groneberg, 2012; Maier et al., 2013; Ragan et al., 2013; Schelle et al., 2015). Nevertheless, students in at least some European countries seem well aware of the phenomenon, including 93.7% of respondents of a survey of 6,275 Swiss students (Maier et al., 2013; cf. Forlini et al., 2015).

While clinical trials have found the efficacy of CEDs among individuals without medical conditions to be either nonexistent or limited (e.g., Ilieva, Hook, & Farah, 2015; Repantis, Schlattmann, Laisney, & Heuser, 2010), this does not match reported user experiences in nonclinical settings (Ilieva, Boland, & Farah, 2013). This could be due to the placebo effect or the inadequacy of experimental trials to simulate real-life environments (Ragan et al., 2013). Lack of agreement on standardized tests problematizes measuring effects among healthy volunteers (Husain & Mehta, 2011). Although surveys, clinical experiments, and commentaries by bioethicists have addressed the use of CEDs by healthy individuals, "there is at present a lack of findings from in-depth, qualitative research that examines the everyday uses and users of medications" (Vrecko, 2013, p. 5). As Smith and Farah (2011) argue, we need to better understand how CEDs work in everyday practice as opposed to laboratory settings.

Despite the limited clinical evidence on efficacy for healthy individuals, the phenomenon of pharmacological neuroenhancement has produced numerous academic commentaries concerning its ethical, social, and policy implications for nonclinical populations (e.g., Bostrom & Sandberg, 2009; Farah et al., 2004; Hyman, 2011; Sahakian & Morein-Zamir, 2011). Critics have cautioned bioethicists for making unsubstantiated claims about the effects and prevalence of CED use, pointing out that the off-label use of psychoactive substances for enhancement purposes is hardly new (e.g., Bell, Lucke, & Hall, 2012; Gilbert & Baertschi, 2011; Illieva & Farah, 2013; Schermer, Bolt, de Jongh, & Olivier,

2009). Others have warned that the growing research and media interest could inflate a "neuroenhancement bubble" (Lucke, Bell, Partridge, & Hall, 2011 p. 38). Students often perceive substance use among peers as more common than it really is, and the more aware students become of others using CEDs, the more they may be inclined to see it as the norm (e.g., McCabe, 2008; Outram, 2010; Perkins, 2002). The challenge for policy makers, educators, and harm reduction practice, then, is to provide credible information on the possible harms and effects of CEDs without accelerating their use (cf. Schelle, Faulmüller, Caviola, & Hewstone, 2014; Schelle et al., 2015).

Extant studies report similar motivations for university students to use CEDs. Prescription stimulants are most often used during periods of high academic stress (DeSantis, Webb, & Noar, 2008, p. 319; cf. Hildt, Lieb, & Franke, 2014). Methylphenidate is also used for recreational purposes (DuPont, Coleman, Bucher, & Wilford, 2008). Aikins's study of licit and illicit users of prescription stimulants on an American university campus found that both types of users "overwhelmingly felt that prescription stimulants enhanced their ability to perform academic tasks" (2011, p. 566; cf. Vrecko, 2013). They also reported unpleasant side effects that were deemed to be "worth it." In addition to improving academic and cognitive performance, Mache, Eickenhorst, Vitzthum, Klapp, and Groneberg (2012) found German students using CEDs to cope with stress and pressure to succeed, out of curiosity, because others were doing it, and because they feared being at a disadvantage to CED-using peers. Because they are commonly used, legal, and seen to have fewer side effects or addiction potential than "hard drugs," young people are often not afraid to experiment with prescription medications, which they view as "soft drugs" (Quintero, 2012, pp. 513–519; cf. DeSantis & Hane, 2010; Green & Moore, 2009).

This article seeks to add to our knowledge on the practice of cognitive enhancement in real-life settings by exploring perceptions and experiences among university students in the Netherlands and Lithuania. We explore reasons why students turn to neuroenhancement, what effects—both desired and adverse—they experience, how they obtain information about CEDs, and control their use to maximize benefits and minimize harms. Based on our findings, we argue that the use of CEDs by healthy individuals is best understood as *functional drug use* (cf. Boys et al., 1999; Boys, Marsden, & Strang, 2001). Most students had clear goals behind their CED use, were well informed about the safety and efficacy of the substances they used, experienced both beneficial and adverse effects, and self-regulated their use to balance benefits and harms.

Method

Our data are drawn from three studies based on semi-structured interviews with current or recently graduated university students (20 interviews in the Netherlands and 15 interviews in Lithuania). One of the studies also included an online survey ($N = 113$) among students in the Netherlands, 24 of whom reported having used CEDs in study situations. The original data sets were gathered separately without a collaborative study design. The researchers met in early 2015 in a workshop organized by the Chemical Youth project to discuss common themes emerging from our separate data sets.

Study participants included both students with and without a neuropsychiatric diagnosis as we found their experiences to be broadly similar. Although the extant literature generally draws a sharp distinction between the use of CEDs for therapeutic reasons and for enhancement—that is, with and without a physician's diagnosis—we found this neat distinction broke down in practice. Some of our informants who had been diagnosed with ADHD used medications without prescriptions; others, without having been diagnosed by medical professionals, were convinced that they suffered from attention disorders or daytime sleepiness. Other studies have revealed that students fake symptoms to obtain prescriptions for enhancement purposes (e.g., Petersen, Nørgaard, & Traulsen, 2014), further blurring the distinction between the therapeutic use of medicines and their off-label use for enhancement.

All informants gave their oral informed consent to participate in the study and were guaranteed anonymity. All names in this article are pseudonyms.[1]

Interviews

The semi-structured interviews, which took place between March and December 2013, were recorded and transcribed verbatim in English or in their original Dutch and Lithuanian; excerpts here have been translated and edited for clarity. Informants were recruited mainly by snowball sampling from personal networks in the Netherlands and additionally by adverts in students' mailing lists, personal Facebook pages, and through a small youth community website in Lithuania. The sole inclusion criterion was that the informant had used a substance to enhance their work or studying (in Lithuania) or had experience using a CED (in the Netherlands). Some interviewees used psychostimulants with a doctor's prescription; others used them off-label. Some, mostly in Lithuania, used "recreational" drugs as well as vitamins and nutritional supplements marketed as supporting mental work as CEDs.

Twenty interviews took place in Amsterdam and 15 in Vilnius and Kaunas, Lithuania. The interviewees—15 males and 20 females—ranged in age from 19 to 29, with a mean age of 23. Eight interviewees had been diagnosed with ADHD/ADD and one with daytime sleepiness; three were in the process of getting a medical diagnosis or had diagnosed themselves as having Attention Deficit Disorder (ADD) or daytime sleepiness. Ritalin and Concerta were the most commonly used CEDs, while Modafinil, Racetam group substances, Ephedra, Gingko Biloba, food supplements for the brain (e.g., Neurozan), vitamins, cannabis, amphetamine, methamphetamine, Gamma-Aminobutyric acid (GABA), cocaine, and LSD were also mentioned by interviewees as cognitive enhancers.

Survey

An online survey was distributed through Facebook and via e-mail through academic managers (for a review of using Facebook in the social sciences, see Wilson, Gosling, & Graham, 2012). The survey consisted of 24 questions, developed by the first author after an initial round of six interviews. Data obtained from these initial interviews informed the design of the questionnaire, which included questions on basic demographics, substances used, reasons for use, and perceived effects. The survey was posted as a direct web link on social media student groups affiliated to the University of Amsterdam and the Vrije Universiteit (VU) University Amsterdam and was open from the beginning of April 2013 to the end of May 2013. These groups had in total almost 3,000 members at the time. The convenience sample consists of 113 respondents of whom 71% were female and 78% between the ages of 18 and 24. Half were social sciences and humanities majors; medical students, at 35%, were the second largest group. Fifty-nine percent of the respondents were Dutch, 25% were from another European Union country, and 15% from a non-EU country (one respondent had an unclear country of origin).

Of the 113 respondents, 24 (21%) reported having tried CEDs, defined in the survey as "prescription medication (e.g., Ritalin, Concerta, Modafinil, Adderall) used to affect study situations." Ten of these 24 students had been diagnosed with a medical condition (mostly ADD/ADHD, $n = 8$). The lifetime prevalence of off-label CED use was therefore 12% ($n = 14$). Most had discontinued use, suggesting that the point prevalence rate of off-label CED use was 1.8% ($n = 2$), which is in line with other European surveys showing relatively low prevalence rates of off-label CED use compared to the US (Mache et al., 2012; Maier et al., 2013; Ragan et al., 2013; Schelle et al., 2015). Half of the respondents ($n = 12$) who had tried CEDs reported using them less than once per semester; five reported using once per semester. Four respondents reported daily use and all were diagnosed with ADD/ADHD. This indicates that CED use was also infrequent. Several medications for ADHD were the most commonly mentioned in the survey responses: Ritalin ($n = 19$), Concerta ($n = 6$), and

Adderall ($n = 4$). Other substances used for enhancement purposes included Modafinil ($n = 1$), Racetam group substances ($n = 2$), and benzodiazepines (Oxazepam, Lorazepam, and Diazepam; $n = 2$). Almost half ($n = 11$) of the survey respondents who reported having tried CEDs named more than one substance.

The survey respondents are not a representative sample of the student population in Amsterdam, but the survey data served to triangulate our interview findings. Conversely, the interview data helped to elaborate upon findings from the survey.

Analysis

The qualitative data sets that make up this article embraced a grounded theory approach (Glaser & Strauss, 1967) that builds theory from collected data, privileging user experiences without imposing a preordained framework on their accounts. In analyzing our collective data, we made use of Bröer et al.'s (in press) crowded theory approach, in which "the idea is to use the power of online tools to enhance collaboration, validate interpretations and co-author conclusions in qualitative research" (http://aissr.uva.nl/news/content/2014/09/crowded-theory.html; retrieved July 1, 2016.). Crowded theory relies on the collective interpretation of data sets rather than line-by-line coding by individual researchers. Although designed for larger groups of analysts, it suited our purposes as we were not aiming to develop new theoretical categories but to explore emerging themes that arose from comparative interpretations of our data. As none of us were trained in using Bröer et al.'s novel software, we relied on Google Docs, video calls on Skype, and e-mail exchange when comparing interpretations of our data.

In the first phase of analysis, we shared with each other the relevant excerpts from our original interviews and the open-ended qualitative responses from the survey. This allowed us to compare initial interpretations of our own data with that of the other two researchers. In the second phase, we analyzed these thematic data sets, first individually and then as a group. Although the aim of collaborative interpretation is not to continue until consensus is reached but to give participating researchers the possibility to agree to disagree (Bröer et al., in press), there were no major disagreements over our interpretations, adding to the validity of our findings.

Why Use CEDs?

University students in the Netherlands and Lithuania reported many different reasons for using CEDs. Of the 24 Amsterdam survey respondents who had taken CEDs, 5 had doctors' prescriptions. Twelve others, without prescriptions, had tried CEDs to enhance their studying, while six reported using CEDs recreationally or out of curiosity. Interviewees mentioned getting better grades, being more creative, staying awake in class after a night out, better managing time, and improving performance while working, traveling, or doing sports as reasons to use CEDs. The breadth of reported reasons to use CEDs echoes the findings of Partridge, Bell, Lucke, and Hall (2013) who found students using prescription stimulants for all sorts of lifestyle reasons and not solely to enhance cognition in academic contexts (cf. DeSantis et al., 2008; Hildt et al., 2014).

Brian explained the range of purposes for which he and his friends used off-label Modafinil:

> We used it for working and for partying. So you go to a club until late and then you drive home sometimes. We took it to be awake in the car so you don't have car accidents. And we took it while raving to be like sharp and the next day you could still work. And we took it while studying. Enhancement actually for tests and stuff.

Echoing previous studies (DeSantis et al., 2008; Hildt et al., 2014), our informants who used CEDs to enhance academic performance were broadly seeking two goals: improved concentration and more effective time management. The latter often meant more studying in less time or extending the time of studying. Frank used CEDs off-label before he was diagnosed with ADD:

> Yeah, with most of my friends, I spoke to a couple of them because I knew I was going to be interviewed, most of them told me that they do as I do myself: when their deadline comes closer and you're running out of time, you use it mainly to stretch the limited time you have to its maximum potential so you can work in the night and still function in the day or the other way around. You can work in the daytime and then you use your nighttime to do your job or to have your social life. But you're reducing, severely reducing your amount of sleep. And then I think the second reason for most people is concentration.

Experimenting with CEDs was also occasionally linked to the knowledge students had acquired from their studies. Gabriel had tried Modafinil and Racetam-type drugs mainly to get better grades and improve memory but also because it's ''related to psychology and you do a lot of stuff about memory and a lot of stuff about neurotransmitters and stuff, so I think I was quite interested if I could sort of change it all.''

Students often expected CEDs to work as *smart drugs*, with their expectations following the drug's pharmacological profile in therapeutic settings. Ritalin was expected to improve concentration and wakefulness, Racetam group substances to improve memory, and Modafinil to help stay awake and study longer:

Aleksi Hupli (A.H.): Before you used them, what did you expect to happen?
Gabriel: I don't really know. I think I expected to be able to remember things better with the Racetam type of drugs. I think I just expected to remember better. With Modafinil I expected to be able to sit there for longer and study for longer. I don't think I had any strong expectations but you know those are the two things they say, well people have said they do so.

Experienced Effects

Did students using CEDs achieve their desired aims? With Ritalin, many of our undiagnosed informants expected improved concentration and wakefulness. But they were often disappointed with the results, either not feeling the effects at all or finding them to be mild and only slightly beneficial:

A.H.: Did it [Ritalin] work?
Fiona: Umm, well I passed the exam but didn't really have the feeling that the drug did anything.
Bella: Yeah well, a little. Like usually I just go on Facebook all the time if I'm studying, I'm really unfocused and all over the place but when I took it, Facebook wasn't interesting anymore for a while, but I didn't feel super-smart or super-focused or anything.

Taking Ritalin was no panacea; one still had to study. It could reduce distractions but did not make one, as was often expected, ''super-focused.'' Uncertainty about effectiveness—whether it was prescription medication or a food supplement—was common. Students were cautious in judging efficacy and acknowledged that the changes they experienced might be a subjective effect or a placebo:

Vaiva: I hoped that [vitamins for memory] will help, maybe because I had such hopes, I started at some unconscious level to be more attentive, but you can't dig into it now. Maybe it worked as a placebo effect as well, now I no longer know.

Henry: Yeah it's also the, what's it called ... the effect from a pill that ...
A.H.: The placebo?
Henry: Yeah, the placebo effect. That's also why I sometimes just take a quarter or a crumble of it just because I know I will think that it does work but it's not even because of the pill. It's just my head that thinks it works. But that's enough sometimes [laughter].

Despite often being disappointed with the actual effects—and sometimes acknowledging that the positive effects were due to their expectations—some students did report increased focus, motivation, and creativity, which encouraged them to continue using CEDs. Vrecko (2013) has pointed to the role played by emotions in students' use of CEDs to improve academic performance. Diane indeed confirmed that the effects of taking Ritalin were largely motivational:

> First I tried like half a pill and the second time I took a whole pill. So that's about it ... I felt like now that I took a pill I should study. It was more like a motivation for myself than it was an actual physical effect. So it was more like oh my god I'm going to take a pill so I better study [laughter]. I think I was a bit distracted and figured that, well, at the point that I'm taking this pill to study, everything seems to open to study.

Mo (self-diagnosed with ADD) emphasized that Ritalin "does not work if you don't give a shit. You can take two Ritalins, but then it won't work anyway. You have to be like: well, ok, I want to learn now." Having the motivation to study seemed to be a prerequisite for CEDs to have their desired effects. Other studies, however, have pointed to students experiencing positive effects from CEDs even when their quest to obtain better grades remained unfulfilled (Hildt et al., 2014; Partridge, Bell, Lucke, & Hall, 2013).

Greater Focus, Motivation, and Creativity

Eighteen of the 24 survey respondents who had used CEDs reported improved concentration; a further four reported increased attentiveness and improved memory. Many of our interviewees also reported that CEDs enabled them to better concentrate and remain focused. Henry (undiagnosed) had used Ritalin and Concerta about 50 times in the past 9 years:

A.H.: Could you describe the effects that you feel when you study with [Ritalin]?
Henry: Yeah, the most important thing is that my concentration goes up a lot so I can study for three hours in a row ... and doing just one thing instead of just studying for one hour and doing other things at the same time and actually not really studying. That's the main thing. And the studying days are a lot longer.

Although Roderick was undiagnosed at the time of the interview, he was convinced that he had ADD and received Ritalin from his diagnosed sibling:

Roderick: Then I did [take Ritalin for the first time] and I suddenly had an enormous focus. I found it quite heavy. Normally there are a thousand things haunting through my head, but after using Ritalin I really had only one goal, and that was studying, studying, studying.
Marte Ydema (M.Y.): How does it feel?
Roderick: What I said. Instead of getting constant stimuli from outside, or also just in your head, that is sort of cancelled out. You can think about other things than the things you have to learn, but the moment you want to think about one thing you only think about that thing and you don't get distracted by something from outside or from your own head. You are just totally concentrated.

Most of our informants had tried a variety of recreational drugs. Frank, who had used amphetamine and Ritalin to improve his focus before being diagnosed with ADD, stated that taking LSD had also improved his creative thinking:

> I got stuck in that specific paper for a week without you know anything on your screen and then in the final 36 hours I told my girlfriend, ok this is all shit. After I took the LSD I deleted I think 80% and rewrote the whole thing in I think 24 hours and then I handed it in and got an 8.5. That was good. I do consider that cognitive enhancing but in a completely different way. So the classical thing would be amphetamine.

When asked whether he had used CEDs just to get high, Brian responded:

> No, no. But it is a good feeling when you wake up, you take your pill, you drink a coffee. And you're sometimes a little bit high in the morning. It feels like ecstasy, like when ecstasy hits. It is a good feeling. I did a little methamphetamine with my Bachelor's thesis. It's great because you're so into it. But then I discovered Oxazepam too, to get all the thoughts away. I don't know. I also think that's the thing that's coming up. Because people know that you can combine it, it's even better and it's like yeah … and Oxazepam is also everywhere, it's very cheap.

The passages above suggest that the experienced effects of CEDs are comparable to those of recreational drugs, that they affect not only cognition but also mood and creativity, that illicit drugs are also used as study aids, and that prescription drugs such as Oxazepam and psychedelics which are rarely considered as cognitive enhancers are also used for this purpose. As our aim was to let users define what they perceived as CEDs, this raises issues for future studies. Our data also reveal the difficulty of clearly distinguishing between the use of CEDs for therapeutic and enhancement purposes. Some students without an official diagnosis were convinced they had ADD; others who had been diagnosed refused to accept the disease label. Some diagnosed students still obtained the drugs illegally or did not follow the treatment regimes prescribed by their doctors. Nevertheless, when describing the effects of stimulants, our informants had typically similar experiences.

Side Effects

What side effects did students experience from their use of CEDs? Both diagnosed and undiagnosed students reported adverse side effects, especially when using prescription drugs. Eighteen of the 24 survey respondents who had used CEDs reported a variety of side effects, including loss of appetite, sleeplessness, nervousness, and increased agitation. These findings from the survey were largely corroborated in the interviews.

Lotte (diagnosed with ADD) experienced numerous side effects: She lost a lot of weight and had almost black and blue hands and feet, a condition called Raynaud's disease. She only used Ritalin when she felt she really needed to: "I only take Ritalin if I am chaotic in my head for a really long period of time, and if I see no other option." Amelia (diagnosed with ADD at age 12, later with ADHD) felt that ADHD medication worked for her, even though she experienced side effects like depression and appetite loss. But she reported adverse effects when the medications wore off. Cecilia (diagnosed with ADD) decided to stop using Ritalin for "as soon as the effect wore off, my muscles were very sore and tense and it felt like my body had cramped up for a couple of hours."

Undiagnosed students also suffered adverse effects. Some, like Anna who used Ritalin once before her final exams, "got really anxious and nervous and uptight and a little paranoid and just uneasy." Eglė (self-diagnosed with daytime sleepiness) found that Modafinil "slightly erases my memory. It feels like I'm doing tasks, but the next day I might not remember what I was doing." When asked whether taking CEDs helped his studies, Gabriel answered that his grades actually went down because

he was distracted by worries that "I was going to die, you know, because there's lots of stuff about Modafinil and getting like all sorts of crazy skin diseases."

Despite experiencing benefits, Jasper (diagnosed with ADD) eventually decided to quit taking Ritalin due to its side effects (for him, aggression, difficulty sleeping, and feeling down). He struggled to balance Ritalin's benefits and harms:

M.Y.: How do you feel when you use Ritalin?
Jasper: It is just emptying your head and you can totally commit to something. Look, Ritalin has a lot of advantages, but now it is the question if it is worth the disadvantages.

Self-Regulation

Almost all of our informants experienced both beneficial and adverse effects and tried to balance between them. Before consuming CEDs, many of our study participants tried to inform themselves about the substance they intended to use. Some simply read the drug's patient information leaflet. In other cases, the drug was given to them or recommended by trusted friends or relatives:

A.H.: Did you look up information about it [Modafinil] before you used it?
Emilia: No, just from my friends who told me it was this drug that the army used and it was to stay awake and stay focused.
A.H.: So you got that information from your friend?
Emilia: Yeah, my friends because they were using it more often.

Others researched the substance online, gathering information about its effects, possible risks, and usefulness:

A.H.: Did you look at information about them before using?
Gabriel (undiagnosed): Yeah, definitely, Wikipedia was a good source but there was also a forum called LongeCity, I think it was called, and it's just a forum which is not primarily for talking about cognitive enhancements and nootropics or anything but ... that's been like one of the main focuses on people talking about it and talking about new drugs.

Others combined information from friends and the Internet. Kipras (undiagnosed) was recommended Armodafinil by his ex-girlfriend and wanted to be better informed:

Gabija Didžiokaitė (G.D.): Why did you look for info online? What did you want to find out?
Kipras: Well, just when you're doing something unfamiliar you want, well, to know more.
G.D.: Because it's a drug, or just because?
Kipras: I'm just watching out. If I would hear that there's a big risk, that something bad will happen or something, then I wouldn't have agreed [to use it].
G.D.: So in a sense you were trying to get more info about that [Armodafinil], to find out more about side effects?
Kipras: Not necessarily side effects, just effect. If it's worth it in general.

Students who had been diagnosed with a medical condition would, in addition to other sources, turn to their doctor for information. But being diagnosed by a medical professional did not necessarily translate into faith in the treatment:

A.H.: When you got the diagnosis and got prescribed did you look up, well you probably got information from your doctor but did you look up information yourself as well?

Cecilia (diagnosed with ADD): I did, I googled it of course and I got some information from my doctor, but looking back … I think I did not do enough research because I could have known that Ritalin is only helpful if you're really active, if you really have ADHD and I knew I didn't have that. So it was kind of strange why he prescribed that to me but you know then again I'm kind of experimental.

Being informed boiled down to two themes: safety and efficacy. One needs to ''watch out'' and be aware of a drug's side effects and other risks. Students sought information on usual dosages and how these can be adjusted depending on their needs, to avoid both over and under dosage and to foster safe and efficient use. Students using illegal substances also emphasized the importance of knowing where and whom the drugs came from to avoid fake or dangerous products. By searching for information on the effectiveness of a substance and other people's experiences with it, they knew what (not) to expect and whether it fit their needs.

Students who spent more time researching CEDs had specific ideas about what information was relevant as well as which sources were reliable. Our findings here echo those of Quintero and Bundy (2011) that most young people know how to navigate the wealth of information online and determine which sources are reliable. Some study participants only trusted scientific research.

G.D.: So you know [the effects and side-effects] of all of the substances you use?

Petras: Yes, I know it all.

G.D.: Side effects?

Petras: Side effects and so on. For example Creatine, they say that it ruins your kidneys, it shouldn't be used. Scientist checked: they gave it to an ill person with only one kidney. Nothing, 20 grams per day, for a month—nothing, normal.

G.D.: But if there's a risk, aren't you afraid to use it?

Petras: I'm not afraid. Until there's a scientific basis that it is [dangerous].

University students using CEDs in both the Netherlands and Lithuania emphasized the importance of being well informed. In this, they differed from their often-studied American peers (Aikins, 2011; DeSantis & Hane, 2010; DeSantis, Noar, & Webb, 2009). The widespread concern to learn as much as possible about the CED and its possible dangers—whether the drug was prescribed, used off-label, or illicit—translated into a greater sense of control over the experience.

DeSantis and Hane (2010) found that many of their American student informants regulated their CED use by limiting it to important assignments and exams, looking askance at peers who did not regulate their use. Many of our informants in the Netherlands and Lithuania expressed similar ideas:

Maria: I don't know, I have nothing against [cannabis], but on the other hand, there is this, I don't know maybe it's mom's influence, that even if it's nothing bad, but still, it shouldn't be done often. This kind of thinking. Because if it would be super good, I could use it every day. But why am I not doing that? Probably because I think it shouldn't be done every day.

Jovita: I would only use [food supplement] on certain days, not before all the tests, when it seems easy, then it doesn't matter, but if there's an exam, my hands and legs are shaking, then I would take it.

Numerous students expressed variations of the idea that there can be too much of a good thing. Using any substance too frequently undermines its purposive use; when this happened, CEDs were no

longer valued positively. Some stated that CEDs should only be used reasonably and that users needed to be clear about their motives:

Steponas: I think, that [smoking cannabis] needs ... to be done, as long as you know, why you are doing it. As long as you know, that it has an aim, as long as you can control it in some way.
Viktorija: Yes, I think it's safe and healthy, if you're doing it mindfully and with help, if you need [lithium], if it suits you, then why not.

The great majority of our informants perceived their use of CEDs to be serving a clear purpose and sought to limit their use to aiding the performance of specific tasks.

Discussion

In this article, we sought to contribute to the current academic, policy, and media discussion on neuroenhancement by focusing on the perceptions and experiences of university students in the Netherlands and Lithuania. Although the generalizability of our findings to student populations in these countries is limited, they do give a more nuanced picture of the use of CEDs in everyday life.

Our student informants used a plethora of substances for cognitive enhancement, broadly construed. Although prescription stimulants prevailed in our Dutch data sets, they were far from the only substances used by students, while in Lithuania more students turned to nutritional supplements and illicit drugs. While these differences could in part be due to the recruitment strategies of the studies that inform this article, they also reflect the availability of psychostimulants in the two countries, rooted in psychiatric practice. According to the International Narcotics Control Board (2014), the Netherlands is the 11th largest consumer of Schedule II stimulants in the world; routine prescription by psychiatrists leads to much higher diversion potential for enhancement purposes. In contrast, psychostimulants are rarely used to treat adult ADHD in Lithuania, while pharmacological treatments have only recently been introduced for children (Lithuanian Society of Child and Adolescent Psychiatry, 2015).

Future research needs to take into account the great variety of substances that students perceive and use as CEDs in real-life settings. The breadth of substances that our informants used as neuroenhancers echoes the findings of a recent survey which asked university students in the UK and Ireland to define *smart drugs*. While most students pointed to stimulants (caffeine pills, methylphenidate, energy drinks, Modafinil, Adderall, speed), others also identified vitamin supplements, cannabis, LSD, and tranquilizers as smart drugs (Singh et al., 2014).

The range of substances used by students for cognitive enhancement furthermore suggests that they are pursuing different effects: enhanced focus, motivation, memory, or creativity; better nighttime sleep or less daytime sleepiness; stimulation or relaxation. We found our informants to consider different mental and physical states as beneficial. But although the desired effects differed, how prescription stimulants, illicit drugs, supplements, and vitamins were perceived and employed as functional "tools" to attain specific goals was broadly similar.

While some of the effects experienced by our informants were clearly functional, others were adverse (cf. Van den Ende, Schoenmakers, Issa, & Van de Mheen, 2010). Both students with and without diagnosed medical conditions had to balance the beneficial and adverse effects they experienced from their use of CEDs. Some students were puzzled by the efficacy of the CEDs they consumed and attributed positive effects to a possible placebo effect (cf. Moerman, 2002). The concept, first applied in the context of medicines and treatment, can readily be applied to practices of enhancement outside of medical supervision.

For our student informants, the use of CEDs was not—as critics often assume—a reckless undertaking driven by peer pressure. They self-regulated their use of CEDs, wanting it to be moderate, controlled, and occasional. They found it important to be conscious of the reasons why they took

CEDs; when they were mindful of their use, they felt more responsible and in control of the substance, rather than being controlled by it. Losing control over one's use was associated with addiction; knowing why one uses CEDs and using them rationally were thought to inhibit addiction and dependence.

Students reported two main reasons for being well informed: to be safer in their use and to make the most of the CED. By being informed about the drug's efficacy and other people's experiences with it, they learnt what to expect and how to interpret its effects (cf. Becker, 1963). Even those who used vitamins or food supplements—generally considered as ''soft enhancement'' (Maier & Schaub, 2015)—sought to be well informed. Most students used CEDs with some knowledge of their safety and efficacy; some argued that they would never use a substance without being informed. But while simultaneous polydrug use was rare, most study participants had used CEDs without a prescription as well as more traditional recreational drugs—confirming research that off-label CED users are more likely than other drug users to report polydrug use (McCabe & Teter, 2007; cf. Hall, Irwin, Bowman, Frankenberger, & Jewett, 2005; Schelle et al., 2015).

Conclusion

Rather than seeing their practices as drug abuse or misuse, our informants perceived and experienced CEDs as functional ''tools'' to achieve specific ends. They experienced both beneficial and adverse effects and pursued strategies to maximize the benefits and minimize the harms. As students often expected substances to work as *smart drugs*, there is a need to provide evidence-based information on both their possible benefits and harms, as enhancement in one area of cognition can be detrimental to another (De Jongh et al., 2008; Husain & Mehta, 2011; Smith & Farah, 2011). The adverse effects experienced by individuals diagnosed with ADD/ADHD—some of whom reject the diagnosis—increase the likelihood of medications being diverted to their undiagnosed peers (cf. Garnier et al., 2010; Poulin, 2007; Vrecko, 2015)—an important consideration for policies that aim to reduce harm related to the (off-label) use of prescription drugs.

Finally, the perspectives of CED users deserve a more prominent place when discussing the ethics of pharmacological neuroenhancement (e.g., Maier, Liakoni, Schildmann, Schaub, & Liechti, 2015; Schelle et al., 2014). An open discussion between different stakeholders about the risks but also the perceived benefits of using pharmaceuticals and other drugs to enhance cognitive performance is vital to ensure that their use, when it occurs, happens in an informed and safe way. User participation in this discussion is therefore imperative.

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Note

1. The data presented in the article were collected during research conducted for Medical Anthropology and Sociology MSc thesis projects (in the case of Hupli and Didžiokaitė) and an Anthropology Bachelor of Arts

(BA) thesis (Ydema) at the University of Amsterdam. Within these programs, all research is evaluated and reviewed in line with standard ethics operating procedures (e.g., http://ethics.americananthro.org/category/statement/) before researchers enter the field; thesis supervisors are responsible for monitoring the implementation of ethical safeguards. These procedures include use of pseudonyms and other forms of anonymization, informed consent, and a more general ethical handling of field relations with research participants. The analysis presented was conducted with the support of the ChemicalYouth project led by Anita Hardon. The ChemicalYouth project has been approved by the ethics committee of the University of Amsterdam Faculty for Social and Behavioral Sciences.

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PUBLICATION II

Medical Cannabis for Adult Attention Deficit Hyperactivity Disorder: Sociological Patient Case Report of Cannabinoid Therapeutics in Finland

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Medical Cannabis for Adult Attention Deficit Hyperactivity Disorder: Sociological Patient Case Report of Cannabinoid Therapeutics in Finland

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Keywords
Cannabinoid therapy · Attention deficit hyperactivity disorder · Case report · Finland · Qualitative research

Abstract
This paper presents a detailed patient case report of a male patient who was diagnosed in adulthood (aged 33) with attention deficit hyperactivity disorder (ADHD) and treated initially with immediate-release methylphenidate (Ritalin® 10 mg twice daily). After experiencing adverse effects from prolonged use of this medication and afterwards other medications that were prescribed as alternatives, the patient discovered that cannabinoid therapeutics (CT) had been experimented inside the EU area to treat patients with ADHD. Subsequently, he was evaluated by a physician in Germany (June 2010) who prescribed CT (Bedrocan®, Bediol®). A Finnish neurologist later confirmed the two prescribed medicines (Bedrocan®, October 2010; Bediol®, May 2011) in the patient's own country of permanent residence (Finland). During a 5-year period of access, Bedrocan®, which mainly contains Δ9-tetrahydrocannabinol (Δ9-THC), was found to be helpful in alleviating the patient's ADHD symptoms, in particular poor tolerance to frustration, outbursts of anger, boredom, and problems related to concentration. The second CT medication, Bediol®, which contains both Δ9-THC and the phytocannabinoid cannabidiol, was found to neutralize the excessive dronabinol effects of Bedrocan® as well as zo offer other medical benefits (e.g., improved sleep). In addition to the case report, this paper also offers a brief review of the literature surrounding the medical benefits of CT for AD(H)D, which includes observational studies, clinical case reports, and one randomized clinical experiment. This paper also briefly discusses the endocannabinoid system in relation to ADHD, although more preclinical and clinical research is warranted to establish the optimal levels of cannabinoids, terpenes, and dosing regimens, which vary between different ADHD patients.

Introduction

There are numerous qualitative and quantitative studies as well as a recent online study [1] reporting an association between attention deficit hyperactivity disorder (ADHD) and cannabis use [2–4]. Many studies, however, often interpret cannabis use as nonmedical, "recreational," and/or drug abuse, not as a potential, albeit often illegal, form of (self-)medication. As with all medicines, the potential harms – and the risk of developing a substance abuse disorder – should be considered, especially for this patient group [5]. Nonetheless, it has been demonstrated that use of (non)medical cannabis can also help to keep

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adult individuals with ADHD away from other more harmful substances, like cocaine [6]. Observational studies have shown that medical cannabis patients in general use cannabinoids as a substitution for alcohol, illicit drugs, and/or commonly used prescription drugs for better symptom management, as well as to experience fewer side effects [7, 8].

This paper offers a medical sociological case study of a Finnish resident adult male diagnosed with combined-type ADHD. He was treated with standardized cannabinoids in botanical (whole-plant) form between 2010 and 2016, after experiencing adverse effects from immediate-release methylphenidate. The patient was prescribed cannabinoid therapeutics (CT) initially by a physician practicing in Germany, and the prescriptions were later confirmed by a Finnish neurologist. In December 2010 and in May 2011 the Finnish Medicines Agency (Fimea) authorized the patient's access to Bedrocan® and Bediol®, respectively, which he used on a daily basis until 2016.

A single detailed case study, although not generalizable to wider patient populations, brings important insights to further develop clinical practice and research around CT for adult ADHD patients. For a comprehensive review of cannabinoids in other neurological and mental health conditions see Fattore [9]. Before presenting the case report, this paper offers a brief review of the literature surrounding the medical benefits of CT for ADHD, which include observational research, clinical case reports, and one randomized clinical trial. This paper also briefly discusses the endocannabinoid system (ECS) in relation to ADHD. For a more comprehensive review of the ECS and impulsive behavior, see Wiskerke and Pattij [10].

Surveys and Qualitative Studies

In the author's previous study, an online survey with a convenience sample of university students in Amsterdam (n = 113), the following qualitative answer was given by a respondent who identified himself as having ADHD in an open-ended question [11]:

> Ritalin made me very slow and unable to concentrate. Cannabis on the other hand creates a state of hyperconcentration (which is more common amongst ADHDers). So it helps me sit still and read and helps me when writing essays. When in a state of hyperconcentration I write 2,000 words in an afternoon easily.

In *Marihuana, the Forbidden Medicine*, Grinspoon and Bakalar [12] offer a similar type of report from a California State University student using cannabis for his attention deficit disorder. Also, in a demographic survey of 4,117 cannabis users in California who applied to access medical cannabis between 2001 and 2007, the researchers state that "a significant percentage of male applicants under 30 had been treated or evaluated for treatment with Ritalin or other stimulants for attention deficit hyperactivity disorder (ADHD) as children and their histories of a preference for morning use of minimal amounts *(of cannabis)* strongly suggest that inhaled cannabis enhances their ability to concentrate" (italics added by the author for clarity) [13].

In a six-country survey of (illegal) cannabis cultivators, ADHD was the fifth (15.3%, n = 2,070) most commonly reported medical reason to grow and use cannabis, the most common ones being depression/anxiety and chronic pain [14]. According to the study, "Scandinavian growers seem to use cannabis for the treatment of ADHD more often than growers in other countries" [14, p. 253]. In a qualitative interview study of 100 (illegal) cannabis users in Norway, alleviating ADHD symptoms was the most common medical motive reported by the users [15].

Clinical Studies and Case Reports

In Germany, there was a detailed clinical case report in 2008 that depicted the medical benefits of cannabinoids, especially Δ9-tetrahydrocannabinol (Δ9-THC), for an adult male ADHD patient who had previously been unsuccessfully treated with methylphenidate [16]. In a larger series of clinical cases, also done in Germany with 30 treatment-resistant adults with ADHD, it was found that medical cannabis was helpful for a variety of symptoms, including improved concentration and sleep as well as reduced impulsivity [17]. Seventy-three percent (n = 22) preferred to use only cannabinoids after the study, while 27% (n = 8) continued to combine cannabinoids with other stimulant medications. The researchers also noted that "Many patients were diagnosed before with cannabis use disorders by psychiatrists in hospitals or medical practices due to misinterpretation of effective illegal self-medication. Patients reported that their therapeutic experiences were not taken seriously by most physicians and that they were not listening to them due to strong prejudices." The researchers conclude that "for adult patients with ADHD, who experience side effects or do not profit from standard medication, cannabis may be an effective and well-tolerated alternative."

So far, there is only one controlled study on cannabis-based medication in ADHD [18]. A formal clinical trial in the UK treating adult ADHD patients with the Sativex Oromucosal Spray®, a cannabinoid medication containing a 1:1 ratio of Δ9-THC to cannabidiol (CBD), found

that despite there being no statistically significant difference in the primary outcome of cognitive performance and activity level (measured by QbTest), the overall trend was that the active group (n = 15) achieved better results than the placebo group (n = 15) and reported reduced hyperactivity/impulsivity symptoms as well as improved emotional lability [18]. Further studies with other CT are warranted, as at least in Finland, the price of Sativex Oromucosal Spray® is a barrier for many patients.

The ECS and ADHD

ADHD is a multifaceted disorder involving multiple genes as well as neurobiological and environmental factors [19] in its age-related development and treatment. Recently increased attention has been given to the role of the ECS in ADHD. For instance, children with ADHD have been suggested to have impaired anandamide degradation compared to healthy control subjects [20]. In addition, genetic studies have found a correlation between the cannabinoid receptor gene and ADHD [21]. However, the link between endocannabinoids and ADHD comes often from preclinical models [22–25], which require further translation into clinical practice. This section does not seek to offer a complete picture of the ECS and the complex neurobiological and metabolic interactions involved, but rather seeks to offer some potential research directions and mechanisms of action for exogenous cannabinoids research as a potential pharmacological treatment for some of the main symptoms of ADHD.

The ECS, which includes the cannabinoid receptors (e.g., CB1, CB2) and the endocannabinoids anandamide and 2-arachidonoylglycerol, has also been found to interact with the central nervous system and the neuroimmune system [26, 27]. Traditionally, ADHD pathology has been associated with the dopaminergic system [19]. Cannabinoid 1 (CB1) receptors, which interact with the dopaminergic system [24, 28, 29], have been suggested as possible pharmacological targets to reduce hyperimpulsivity [10, 25, 30] and distractibility [16, 31, 32]. Therefore, exocannabinoids, such as Δ9-THC, hold potential as a pharmacological therapy, as they have been demonstrated to induce dopamine release in the human striatum [33]. It has been suggested that the brain regions where the modulation of endocannabinoids might lead to action restraint and to the regulation of impulsive action are the medial prefrontal cortex and the ventral tegmental area [10].

In addition to dopamine, the role of for instance glutamate, GABA, and other neurotransmitter systems need consideration, as well as *N*-methyl-D-aspartate and cannabinoid 2 (CB2) receptors, which have been suggested to modulate, for instance, impulsivity in interaction with endocannabinoids [10, 22, 23, 34, 35]. Therefore, further preclinical and clinical studies are warranted to map the complex interactions involved with the ECS in various pathophysiologies [35]. The case report presented below offers potential directions for future research and clinical practice. As the studies above and the following case study show, CT seem to provide a valuable treatment option for a treatment-resistant adult ADHD patient [31].

Case Report

The patient was contacted via the Finnish Medical Cannabis User Organization (Lääkekannabiksen käyttäjien yhdistys ry). The case report is based on a combination of interviews with the patient at his home, doctors' statements, medical records, and other documents relevant to the case provided by the patient and analyzed by the author since early 2016 with the full consent of the patient.

Results

The patient is an EU citizen, educated to Master's Degree level, and who has been permanently resident in Finland since 1995. In September 2003, at the age of 33 years, he was diagnosed with combined-type ADHD by a Finnish psychiatrist and prescribed immediate-release methylphenidate (Ritalin®, 10 mg twice daily). In particular, the patient's low frustration tolerance required pharmacological intervention to manage demanding work tasks that required sustained concentration and higher cognitive functioning, to reduce chronic distractibility, and to remain concentrated on tasks until completion.

From 2003 up until 2009, the patient consumed immediate-release methylphenidate on a regular basis, taking breaks from time to time to ease the negative impact of the medication upon his digestive system. During that 6-year period of use, methylphenidate clearly demonstrated efficacy, helping the patient to remain concentrated on work matters, particularly during work situations when he must remain seated for extended periods of time. Additionally, the patient received psychotherapy and guidance on alcohol dependency and on the management of the anger and violent outbursts that resulted from his low tolerance to frustration.

In 2009, however, under increasing work stress, the patient began noticing a lack of efficacy and an increase in the severity of the adverse effects (stomach problems, sweating, irritability, insomnia) from the immediate-release methylphenidate. These adverse effects forced him to make major changes to his diet to manage the worsening adverse effects of this stimulant medication, the most severe effects typically being stomach and lower bowel convulsions and pains. Upon further investigation, varicose veins were detected in the patient's left testicle, which became progressively more aggravated by the orally ingested methylphenidate. The patient's worsening stomach condition meant that he used methylphenidate less frequently, and he was offered a number of substitute prescriptions (e.g., Pramipexole®, Bupropion®, Buspirone®, Lorazepam®, Temazepam®, Alprazolam®) between January 2009 and August 2010. These medications, however, offered poor efficacy for the primary indication and only further exacerbated the

adverse effects suffered by the patient. The substitute prescribed to the patient that gave the worst adverse effects was the Pramipexole®/Bupropion® combination prescribed in July 2010, which rendered him unable to sleep for 4 whole days and nights, gave suicidal thoughts, pounding head pains, and excessive heart palpitations. Later, in October 2014, examination finally revealed a 2-cm hernia on the left side of the patient's lower bowel region.

Earlier in 2010, the patient became aware that there was a small European study where standardized medicinal cannabis products (manufactured by Bedrocan B.V. of the Netherlands), Bedrocan® and Bediol®, were prescribed to 2 European ADHD patients in Germany. The patient also became aware of recent amendments made to the Finnish Medicines Act, formally allowing the prescription of medicinal cannabis by Finnish doctors under special authorization by Fimea. The patient contacted the former Director of Fimea seeking clarification over the prescription of Bedrocan®. The Director informed the patient in a personal e-mail that Fimea has "no requirement regarding the prescriber which would not allow a psychiatrist to prescribe this product. Our criteria (coming from the Medicines Act) for the decision are that (1) other available treatments of the patient's condition have not given a favorable result or have been poorly tolerated and that (2) the indication applied for is medically justified."

After receiving this confirmation that the legal framework supported his right to access cannabinoids, the patient began to formally seek Bedrocan® as a substitute medication for methylphenidate. It was hoped that cannabinoids would offer equivalent or better efficacy with more tolerable adverse effects. After failing to find a Finnish psychiatrist or neurologist with sufficient medical knowledge of CT, the patient exercised his right to patient self-determination and finally, in June 2010, visited the prescribing physician behind the small European ADHD study in Germany. Afterwards, the patient returned to Finland with prescriptions for standardized Bedrocan® and Bediol® medicinal cannabis products.

Upon arrival to Finland, the next challenge for the patient was to find a suitable Finnish physician to validate the prescriptions for the cannabinoid treatment model. It took him until October 2010 – a period of almost 4 months – to find a suitably qualified neurologist who was prepared to endorse the treatment model. At that time, the patient presented the prescribing neurologist with a challenge: no Finnish neurologist or psychiatrist had previously substituted Bedrocan® for short-acting methylphenidate as a pharmacological intervention for a neuropsychiatric medical condition. Clinical guidelines for adult ADHD were only introduced in Finland in 2017, updating pediatric treatment guidelines published in 2007, which were updated for adolescents in 2013 [36]. These guidelines mention no possibility of CT for either adult, adolescent, or pediatric ADHD. However, the Bedrocan® application was submitted to Fimea in late November 2010 and approved by the end of December 2010.

As described in the statement made to Fimea by the prescribing physician, the use of Bedrocan® had a positive impact on the patient's ADHD symptoms, reducing hyperactivity, improving focus and impulse control, and giving better tolerance to frustration. However, during a period of increased stress due to the sudden and unexpected termination of the patient's full-time employment, in spring 2011, the use of Bedrocan® began to induce sleeping problems and agitation. The patient who participated in the small European study had highlighted Bediol®, the medicinal cannabis preparation rich in CBD, as being of value to reduce the potential adverse dronabinol effects of Bedrocan®, such as sleeplessness and anxiety [31]. After an urgent consultation with his neurologist, the patient's second cannabinoid medication, Bediol®, was prescribed as an evening medication to address these adverse dronabinol symptoms. The authorization to access Bediol® was processed by Fimea in May 2011. Bediol® did indeed give the desired anxiety-reducing effects, and the patient's sleeping pattern improved significantly; he was now able to fall asleep quickly and sleep through the night with only the need to get up to urinate one or two times. To our knowledge, no single patient in Finland prior to that time had ever been prescribed two separate medicinal cannabis preparations concomitantly.

It was at this time in May 2011 that the patient also noticed the beneficial effects of Bediol® for secondary medical indications. Inflammation, resulting from an anterior cruciate ligament knee injury in November 2010, was reduced, as well as the patient's chronic pain in his left ankle and lower back. In addition to the pharmacological intervention, the patient also practiced supplementary physical therapies to build up the supporting muscles around the knee, including water therapy, hyperthermia treatments, cycling, walking, and gardening. The rehabilitation of the patient's knee was accomplished without the need for surgery or the consumption of any other pain or muscle relaxant medication. Since 2010, on two occasions only, has there been any knee instability. While further studies are warranted to confirm these secondary therapeutic benefits, the synergy between the two primary cannabinoid components, THC and CBD, has been reported earlier [37, 38].

The average daily dosage for the patient ranged between 1 and 2 g, usually with a 2:1 ratio of Bedrocan® to Bediol®. For fast absorption and convenient titration, the cannabinoids were administered via a Volcano vaporizer. The patient reported that when vaporizing, this method of administration delivered the full therapeutic effects rapidly (within 10–15 min). The botanical form gave the patient the ability to control dosage more flexibly, including the possibility to produce his own cost-effective extracts and tinctures. According to the patient, Bediol® was ideal for evening use, but also during activities that required prolonged sitting. In the patient's view, this was the key therapeutic value of Bediol® in combination with the Bedrocan® stimulant. Bedrocan® aided concentration and reduced distractibility; Bediol®, on the other hand, reduced feelings of anxiety and restlessness and the need to be on the go all the time, as well as reducing the patient's chronic pain indications.

Despite these therapeutic benefits, there remain barriers to successful CT in Finland. As seen above, finding a physician willing to prescribe medical cannabis, despite being legally able to do so, is one of the barriers. The high price of the medication as well as inconsistencies with regards to reimbursement of cannabinoid medications remain other key barriers for a successful cannabinoid therapy. These topics, however, will be explored in more detail in another publication.

Discussion and Conclusions

The current study provides the first detailed investigation of CT for a male combined-type adult ADHD patient in Finland who accessed Bedrocan® and Bediol® for

more than 5 years. The patient found relief for his ADHD symptoms, the cannabinoids offering reduced hyperactivity as well as improved focus, impulse control, and better frustration tolerance. This is in line with clinical studies on medical cannabis for ADHD [16–18]. In addition, the patient experienced other medical benefits that contributed to his overall wellbeing, especially with the combination of the high-dronabinol product Bedrocan® and the moderate-dronabinol/high-CBD product Bediol® [31]. Russo and Guy [37, p. 242] have also concluded that "the data herein presented strongly support the therapeutic rationale for combining THC and CBD for therapeutic usage."

Endocannabinoid signaling modulation through the dopaminergic system offers a promising target for pharmacological interventions, not only for ADHD [31] as shown above, but also for other neuropsychiatric disorders [9, 39], such as Tourette syndrome tics [40], fears [41, 42], anxiety [43, 44], as well as improving synaptic plasticity for emotional learning [45]. Although many questions remain, this paper argues that there is a plethora of supporting evidence that, for individuals who obtain no relief for their ADHD symptoms from prescription stimulants like methylphenidate and/or experience adverse effects from other pharmacological therapies, CT can offer a safe and efficient mode of treatment, potentially in conjunction with other forms of psychotherapy [31]. This was noted already 15 years ago by Ethan Russo [46, pp. 170–171], who "in his practice of child and adult neurology, has heard dozens of unsolicited testimonials to the benefits of cannabis in attention-deficit hyperactivity disorder (ADHD)," and also stated that "although the idea of using cannabis-based medicines for this indication may seem surprising to most experts, controlled trials of cannabis medicines for children *(and adults)* with ADHD seem clearly indicated, particularly in view of the controversies and side effects of existing psychotropic medications" (italics added by the author for clarity).

However, further longitudinal studies are needed to quantify the quality of life changes of ADHD patients who use CT. Also, what are the most efficient modes of administration and dosages [47] and what kind of (phyto)cannabinoid and terpenoid combinations [38] are effective for different ADHD patient profiles [3, 10] remain open research questions. For instance, Loflin et al. [3, p. 428] hypothesized that "cannabis might compensate for low frontal alpha relative and absolute power, which potentially underlies hyperactive symptoms." Thus, therapeutic uses of cannabinoids could be more effective among hyperactive-impulsive subtypes compared to the inattentive type of ADHD [3].

Before well-designed clinical trials have established the detailed mechanisms of action and potential positive patient outcomes for using CT, especially for individuals with ADHD, but also for other patient groups, clinical practice should take seriously the experiences of patients who find relief from cannabinoids. The amount of medical conditions reported to be alleviated with CT is vast [12, 48], and while the "evidence" is not always based on the golden standard of double-blind randomized placebo-controlled clinical trials, the well-established historical use of cannabinoids across the globe to treat human ailments [49, 50] gives reason to patients and medical professional alike to consider this treatment option. More medical sociological investigation of the general attitudes and knowledge of policymakers, patients, and treating physicians is warranted to identify possible barriers for CT, as lack of training for medical professionals, the high cost of the medication, and lack of government reimbursement remain the main barriers to continued therapeutic use of cannabinoids in Finland.

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Statement of Ethics

The author has no ethical conflicts to disclose. This case report was conducted in accordance with the ethical guidelines provided by the University of Tampere and the National Advisory Board on Research Ethics [51] with the fully informed consent and cooperation of the patient.

Disclosure Statement

The author has no conflicts of interest to declare.

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PUBLICATION III

Descriptive assemblage of psychedelic microdosing: netnographic study of Youtube™ videos and on-going research projects.

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Descriptive assemblage of psychedelic microdosing: Netnographic study of Youtube™ videos and on-going research projects

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ABSTRACT

Background: Despite increasing clinical and neuroscientific research, pharmacological neuroenhancement literature rarely discusses psychedelic drugs. However, psychedelic microdosing, the ingestion of sub-perceptual doses of psychedelics like psilocybin, has gained increasing public and scientific attention. Published research on the topic is scarce and systematic studies of the digital milieus surrounding psychedelic microdosing are currently non-existent.
Methods: In this netnographic study, we explore psychedelic microdosing by focusing on Youtube™ and listing current research projects as a descriptive assemblage. We used the Youtube Data Tool (YDT) for data extraction from the YouTube™ platform. We selected videos that specifically focused on microdosing with a psychoactive substance and descriptively analysed the ecology of practices of the six most viewed videos focusing on definitions, dosages per substance and claimed effects.
Results: Our initial data extraction, completed in 2016, resulted in total of 115 Youtube™ videos. Additional data extractions done in 2017 and 2018 showed a 290% increase of "microdosing" videos between 2016 and 2018, indicating that the phenomenon is growing, at least online. The digital milieu of microdosing in 2016 included 48 videos (41,7%) which mentioned a psychoactive substance. The six most viewed videos comprised 92% (N = 934,819) of the total view count and the ecology of practices depicted psychedelic microdosing as beneficial, but the claimed effects and dosing require critical evaluation. Contrary to how typical users of illicit drugs are often portrayed in the media and science, these videos revolved around themes like research, experiments, self-monitoring and the imperative of sharing results. As our descriptive assemblage demonstrates several psychedelic microdosing research projects are under way, potentially influencing user practices and knowledge.
Conclusion: This type of online drug research can be used to gather knowledge of under-researched topics, like psychedelic microdosing. However, further digital and non-digital drug research is needed to investigate this potentially rising phenomenon.

1. Introduction

The use of drugs for human enhancement is increasingly researched and debated (e.g. Jotterand & Dubljević, 2016; Ter Meulen et al., 2017). "Pharmacological neuroenhancement" (PNE) (Maier & Schaub, 2015) literature has mainly focused on prescription pharmaceuticals, like stimulants for cognitive enhancement (e.g. methylphenidate and modafinil), antidementives for memory enhancement (e.g. piracetam and donepezil) and antidepressants for mood enhancement (e.g. selective serotonin reuptake inhibitors) (De Jongh, Bolt, Schermer, & Berend, 2008; Repantis, Schlattmann, Laisney, & Heuser, 2010). Psychedelic drugs (Rucker, Iliff, & Nutt, 2017) are rarely discussed in the literature (Anderson, 2006; Langlitz, 2011). This is despite a newly emerging "psychedelic renaissance" (Sessa, 2017) in clinical psychiatry and neuroscientific research, which has explored the potential therapeutic effects of i.e. psilocybin in treating mental disorders such as end-of-life anxiety (Grob et al., 2011), treatment-resistant depression (Carhart-Harris, Bolstridge, & Rucker, 2016) and addiction (Bogenschutz et al., 2015; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014).

While the PNE literature rarely discusses psychedelic drugs, "the betterment of well people" (Council of Spiritual Practice, 2018) has been a topic in the psychedelic (research) commu-

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nity (Langlitz, 2011). Researchers have explored the role of psychedelics in improving scientific problem-solving and creativity (Sessa, 2008; Sweat, Bates, & Hendrick, 2016), personality trait openness (MacLean, Johnson, & Griffiths, 2011), self-knowledge (Móro et al., 2011), sense of wellbeing and life satisfaction (Griffiths, Richards, McCann, & Jesse, 2006; Richards, 2015) and pro-environmental behaviour (Forstmann & Sagioglou, 2017). According to a review by Elsey (2017:5) "current empirical findings indicate that psychedelics have the potential to significantly improve wellbeing among otherwise healthy individuals, and may also help foster novel perspectives, supporting the resolution of professional and personal challenges."

A topic that has recently received attention from researchers and the public is psychedelic "microdosing" (e.g. Fadiman, 2011; Winstock & Carhart-Harris, 2017). Microdosing has become to refer to the ingestion of sub-perceptual dosages of "classical psychedelics" every few days for an extended period of time to improve cognitive and affective processes (Johnstad, 2018; Mishra, 2018). In pharmacokinetic studies, microdosing is a method to investigate new chemical entities (NCE) where one of the rationales is that microdoses "would be too small to cause any major side effect after a single dose" (Tewari & Mukherjee, 2010:61).

In this study, we explore the "descriptive assemblage" (Savage, 2007) of psychedelic microdosing. Savage argues that "the descriptive involves a process of assemblage, where processes of creativity, conceptual innovation, and observation can be used to mobilize novel insights" (Savage, 2007:170). We observe the "ecology of practices" of psychedelic microdosing in a specific "digital milieu" (Boothroyd & Lewis, 2016), namely the online video sharing website Youtube™. We see Youtube™ as "an archive awaiting curator" (Gehl, 2009) and methodologically explore the Youtube Data Tool (YDT, 2018) which is "A collection of simple tools for extracting data from the YouTube platform via the YouTube API v3" (YDT, 2018; see The Politics of Systems, 2018) developed in the Digital Methods Initiative (Digital Methods Initiative, 2018). Our empirical research questions are: 1) what is the digital milieu of microdosing on Youtube™ and 2) what is the ecology of practices of psychedelic microdosing in the six most viewed Youtube™ videos regarding definitions, dosages per substance, and claimed effects?

As psychedelic microdosing is a novel area of research, this paper offers one of the first digital investigations into the topic. However, we view the YDT as part of a broader methodological approach, namely netnography (Kozinets, 2010). Like ethnographic research, netnography combines a mixture of methods based on the topic (Kozinets, 2010). We view the collection and analysis of digital data (videos) and "offline" ethnography as complimentary. Methodologically, an approach purely based on "digital methods/data" would not "mobilize novel insights" (Savage, 2007) into current practices and scientific understandings of psychedelic microdosing. Therefore, we briefly present early history and current microdosing research projects as part of our "descriptive assemblage" which have been discovered by on-going netnography. This has included participant observation at psychedelic conferences and (online) events around psychedelic microdosing.

Savage (2007:155) states that the descriptive assemblage "is dramatically enhanced by the infrastructure of information technology and more particularly the digitalization of social relations". More generally, Savage (2007) argues that "this descriptive turn is dramatically affecting the nature of contemporary expertise, in ways which challenge academic authority." Boothroyd and Lewis (2016:295, italics in the original) also argue "that not only do peer-to-peer Internet communications around drugs and drug use produce alternative knowledges and forms of expertise, but that it is possible to discern across various *digital milieus* the emergence of forms of "practical wisdom" about drugs and drug use." Barratt, Allen, and Lenton (2014) also describe informal online drug experiments as a form of counter public health discourse, taking place outside the scientific community. This challenges the established expert-lay dichotomy (Coveney, Gabe, & Williams, 2011), which is arguably present in previous Youtube™ drug research (Hess, 2009; Manning, 2013) and in our empirical findings, where contrary to how typical users of "illicit substances" are portrayed in the media and science, the most viewed psychedelic microdosing videos revolved around themes like research, self-experiments and -monitoring. We see that the internet not only enables collective online experimentation and sharing "practical wisdom", but it can be used to monitor these experiments and to integrate their preliminary results (trip reports, videos and forum content) in "offline" field research (e.g. Krieg, Berning, & Hardon, 2017).

Whilst various websites and (digital) media articles offer information about psychedelic microdosing (e.g. thethirdwave.co; microdosing.nl), published empirical research is limited (Sessa, 2017:276; Johnstad, 2018; Prochazkova, Lippelt, Calzato et al., 2018). Also, the use of psychedelics and other "drugs" (Tupper, 2012), even in "microdoses", remain illegal in most parts of the globe. Despite theoretical speculations on how to legally regulate enhancement use of Ritalin™ and Adderall™ in the bioethical literature (e.g. Dubljević, 2013) there has not been discussions on the (inter)national drug policy level to allow access to psychedelic substances for "enhancement" purposes as even clinical research is heavily restricted (Nutt, King, & Nichols, 2013). Current drug policy situation, however, is often neglected in the bioethical literature around pharmacological neuroenhancement (President's Council of Bioethics, 2003; Jotterand & Dubljević, 2016).

1.1. Psychedelic microdosing: descriptive assemblage of research projects

Albert Hofmann, who discovered lysergic acid diethylamide (LSD-25) in 1943, mentioned "very small doses, perhaps 25 μg, could be useful as a euphoriant or antidepressant" (Horowitz, 1976). As the "common" recreational dose of LSD ranges from 50 to 150 μg (Passie, Halpern, Stichtenoth, Emrich, & Hintzen, 2008), the "very small dose" of 25 μg is considered a "microdose", as described by James Fadiman. Fadimanś book introduced the term to the public (Fadiman, 2011) and a book by Waldman (2017) also sparked public interest into the topic. Fadiman continues to gather reports from users who practice microdosing with psychedelics at even lower doses of about 10 μg of LSD (Fadiman & Korb, 2017; Fadiman, 2011). Although Fadiman noted in 2011 that the results were preliminary and mainly anecdotal, he stated that "everyone said their experiences were positive and valuable" without experiencing harmful effects. According to Fadiman "as several reports stated, someone taking a dose this low functions [. . .] a little better than normal", echoing similar kind of sentiments found in the PNE literature (Elliot, 2003).

Although psychedelic microdosing seems to be a relatively new phenomenon (Passie, 2018) there has been a similar approach to dosing psychedelics in the field of psycholytic therapy (Passie, 1997). In psycholytic therapy doses were "low" (30–200 mcg of LSD; 3–18 mg of psilocybin, Passie, 1997, p.13) compared to psychedelic therapy, in which "high" doses of psychedelic drugs (up to 1500 mcg of LSD) were used to evoke "peak experiences" (Grof, 2016). The major differences between earlier psycholytic dosing and contemporary psychedelic microdosing are the psychotherapeutic "setting" (Hartogsohn, 2017), and that in psycholytic therapy doses were "low" but aimed to be psychoactive (Passie, 1997), an attribute that is explicitly avoided in contemporary microdosing regimes (Fadiman & Korb, 2017; Fadiman, 2011).

According to Fadiman, Hofmann called microdosing "an underresearched area" (Fadiman, 2011:211), and this remains to be the case. In addition to self-reports collected by Fadiman (2011)

and Sophia Korb (Microdosing Psychedelics, 2018), only two peer-reviewed research articles on non-clinical psychedelic microdosing practices and effects exist to our knowledge. Johnstad (2018) conducted online interviews with 21 experienced male psychedelic users about their microdosing practices and discovered that the reported therapeutic and enhancing effects were mostly positive, although the users also faced challenges especially with dosing, and experienced unwanted effects like insomnia. Also, a cognitive psychology team at Leiden University are conducting a longitudinal placebo-controlled microdosing field study with healthy volunteers using legally available psilocybin containing truffles (Prochazkova, Lippelt, Colzato et al., 2018). Preliminary results show increases in creativity performance (Prochazkova, Lippelt, Calzato et al., 2018). However, some psychedelic researchers are sceptical about microdosing, also due to potential cardiovascular risks (Nichols, Roseman, & Timmermann, 2018:83), while others acknowledge that "[t]his role of psychedelics as cognitive enhancers is certainly an area in need of more research" (Sessa, 2017:276; also Carhart-Harris & Nutt, 2017). In addition to the peer-reviewed articles, there are currently several ongoing research projects that are currently examining psychedelic microdosing (e.g. Anderson, Petranker, & Dinh-Williams, 2018; Beckley / Maastricht Psychedelic Programme, 2018; Winstock & Carhart-Harris, 2017).

This descriptive assemblage of early history and contemporary research projects, while not exhaustive, reflects the increasing interest towards psychedelic microdosing among researchers in different fields. Despite the lack of published empirical research there are numerous (digital) media reports on microdosing with psychedelics that often depict the practice as increasingly common (e.g. Koebler, 2015; Glatter, 2015), especially within the tech industry (Mishra, 2018). As media reports often focus on positive effects when it comes to "smart drug" use (Partridge, Bell, Lucke, Yeates, & Hall, 2011), empirical research is needed to provide a more in-depth understanding of the potential benefits and harms of psychedelic microdosing (Johnstad, 2018). How knowledge of, and from, various research projects and media articles influence user practices, and vice versa, requires observational studies of different digital milieus (Boothroyd & Lewis, 2016) around psychedelic microdosing.

2. Digital methodology

2.1. Digital technologies around drugs and previous Youtube drug research

Digital technologies are acknowledged to play a significant role, especially for young people, in accessing (alternative) knowledge and substances (EMCDDA, 2016). Contemporary drug research primarily focuses on drug related online forums and websites (e.g. Murguía, Tackett-Gibson, & Lessem, 2007; Berning & Hardon, 2016) and on the legal (Hillebrand, Olszewski, & Sedefov, 2010) and illegal (Van Hout & Bingham, 2014; European Monitoring Agency for Drugs & Drug Addiction (EMDCCA), 2016) online drug markets. In the biomedical field, the intertwinement between (psychedelic) drugs and the web has been described both as a public health risk (Halpern & Pope, 2001) and as a potential prevention for risks associated with substance use by enabling informed use (Boyer, Shannon, & Hibberd, 2005). The potential to identify emerging drug trends has been demonstrated by using online data about substances that have not yet been monitored in any form (Deluca et al., 2012). A rapid identification of both new drugs and new patterns of use becomes increasingly important due to the increase in availability of drugs and drug knowledge via social media, apps, as well as legal and illegal online markets (Barratt et al., 2014; European Monitoring Agency for Drugs & Drug Addiction (EMDCCA), 2016; Hillebrand et al., 2010).

Previously Youtube™ has been utilized to investigate *Salvia divinorum* use (Casselman & Heinrich, 2011; Lange, Daniel, Homer, Reed, & Clapp, 2010), the sharing of polydrug risk experiences (Kataja, Hakkarainen, Koivula, & Hautala, 2018) as well as more general content analysis of "drug videos" in relation to drug discourses and education (Hess, 2009; Manning, 2013). The studies used different data extraction techniques to produce generalizable samples. However, as the ecology of Youtube™ changes by the minute, it would be difficult to replicate them (Manning, 2013). Therefore, combining various netnographic (Kozinets, 2010) methods is needed to explore contemporary knowledge around psychedelic microdosing. Previous Youtube™ drug research have only observed or "lurked" the phenomenon they researched without engaging or informing their research participants (e.g. Lange et al., 2010; Manning, 2013). This raises questions about Internet Research Ethics (Association of Internet Researchers (AoIR), 2012). These ethical aspects, however, will be explored in another article. In short, we view ethical research as a process in which "[t]rust with research participants is established and then maintained over time" (Ramcharan & Cutcliffe, 2001:363), requiring reflexivity from the researchers. That is why we notified, when possible, the makers of the videos of the present study and about their contribution to our research.

3. Material and methods

To extract data from Youtube, we used the Youtube Data Tool (YDT, 2018) developed by Bernhard Rieder (The Politics of Systems, 2018) from the Digital Methods Initiative (Digital Methods Initiative, 2018). The first step was to use the term "microdosing" in the YDT "Video list" search query ranked by the view count[1] . The search was done on June 7th 2016 providing a list of 115 videos, which can be found online (10.17632/7pkbvjtnxm.1).

The "digital milieu" (Boothroyd & Lewis, 2016) of psychedelic microdosing on Youtube™ is presented in Results 3.1. We manually inspected the 115 videos to ensure they focused on microdosing with psychoactive substances. This was done by reading the title and description of the video, and if those were unclear, we watched the video in question. Results 3.2 contains descriptive content analysis of the "ecology of practices" (Boothroyd & Lewis, 2016) of the six most viewed videos as they comprised 92% of the total view count (N = 934,819 views; see Image 2). We focused our analysis on 1) definitions of psychedelic microdosing, 2) dosages per substances used and 3) claimed effects.

4. Results

4.1. Digital milieu of microdosing on Youtube™

As shown in Image 1 below, "microdosing" videos peaked in popularity on Youtube™ in 2015, about a year prior to the initial data extraction. A second data extraction of "microdosing" done with the YDT in November 2017 provided a list of 351 videos, and a third one done in October 2018 listed 447 videos, indicating that "microdosing" has grown by almost 290% between 2016 and 2018 on Youtube™. This growing popularity is also evident in Google Trends (2018), but this increasing digital trend requires more detailed research which is outside the scope of this article.

Of the 115 videos, 41,7% (N = 48) were about microdosing with psychoactive substances. The 48 videos mentioned not only LSD

[1] The YDT (2018) has several other features which were not utilized in this study.

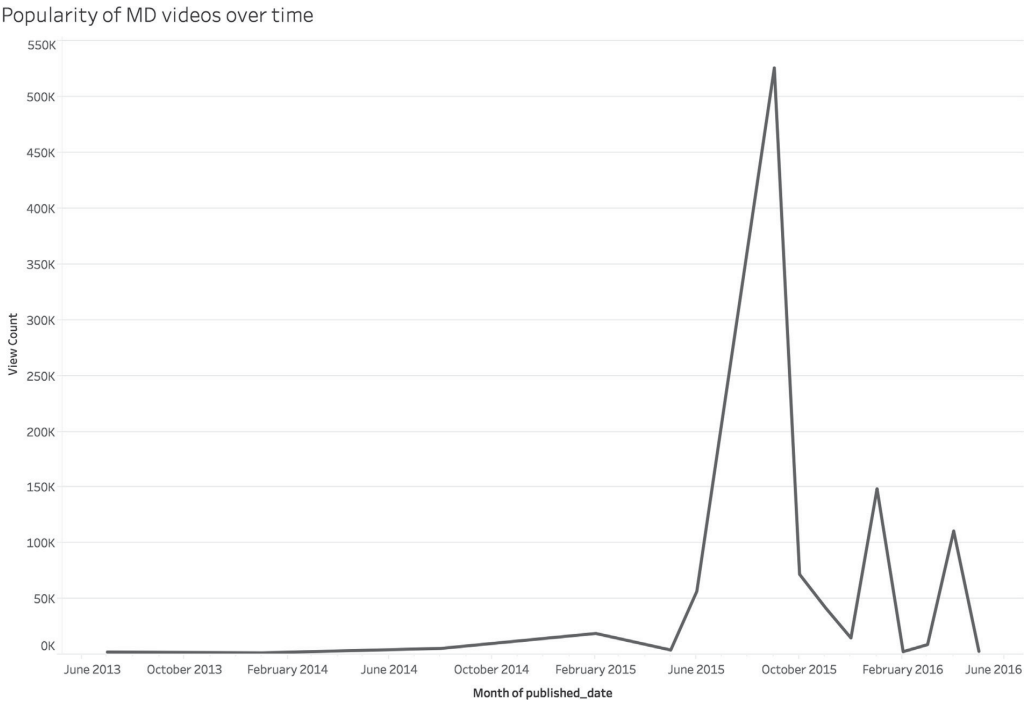

Image 1. Popularity of "microdosing" videos by view count over time.

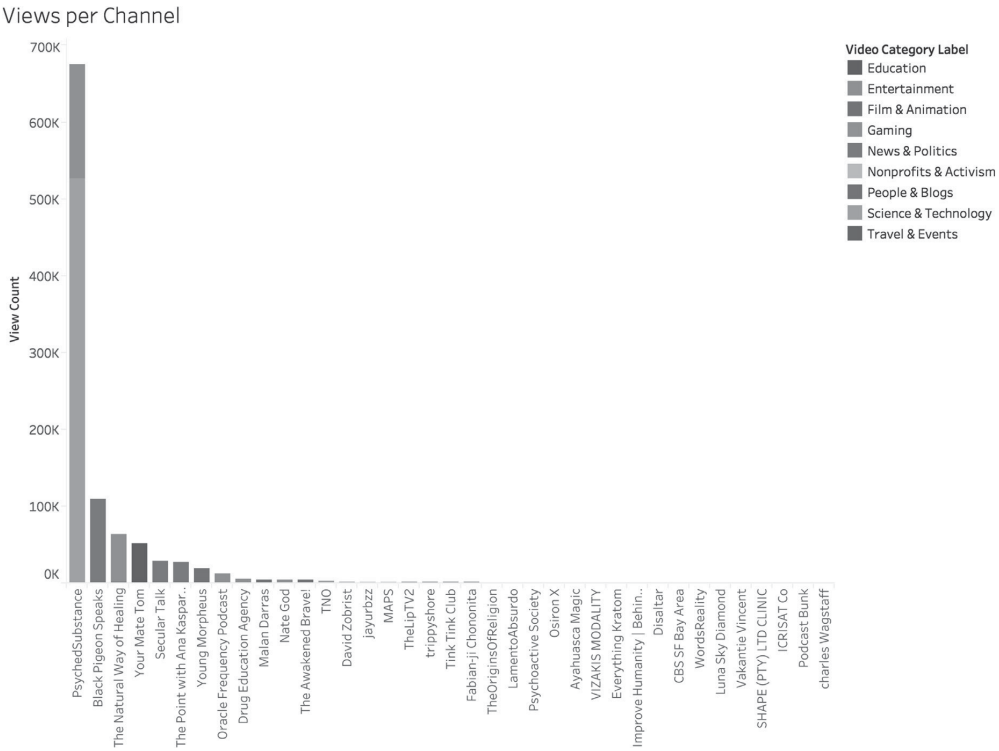

Image 2. Amount of views per channel and video category label.

and psilocybin, but also mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-bromophenethylamine (2CB) and cannabis as well as non-psychedelic substances such as kratom, anabolics/testosterones and alcohol, expanding the variety of substances usually discussed in the literature (Fadiman, 2011; Johnstad, 2018). This demonstrates that "microdosing" has multiple meanings in this digital milieu. Furthermore, at the time of the data extraction, these 48 videos had been viewed 1,017,406 times, and had 19,070 likes and 1570 dislikes. The videos had in total 8696 comments, which deserve further analysis of the participatory culture on Youtube™ (see Burgess & Green, 2009).

4.2. Ecology of microdosing practices

The six most viewed videos amounted to 92% of the total view count (N = 934,819) and they included in total 58,2 min of video material, the longest one being 13,4 min (PsychedSubstance) and shortest 7,4 min (Your Mate Tom). The two most viewed psychedelic microdosing videos were from the same channel, *PsychedSubstance*, which focuses on creating content around psychoactive substances. The two videos comprised approximately half of the 934,819 views as seen in Image 2.

The appearance of the young man in the first video, with a long white jacket, eyeglasses and prints of human anatomy on the walls represents the pop cultural idea of a scientist. This science theme is also found in several self-experimentation videos, as described below. Early in the video *PsychedSubstance* states that "This video is made for harm reduction. I do not promote the use of legal or illegal substances. Always do your own research and never do anything just because you saw it in a Youtube video." *PsychedSubstance*, and other "drug" content creators on Youtube™ have reported increased content restrictions (e.g. Codrea-Rado, 2017) and as of beginning of 2018, some of the most viewed videos are unavailable for viewing. Thus, harm reduction disclaimers are one of the strategies used to avoid such restrictions. We have marked unviewable videos with an * in Table 1 which provides details of the self-defined category, channel info and descriptive statistics including number of views, likes, dislikes and comments. While most of the videos can be categorized as "reflective discourses" (Manning, 2013), with a "harm reduction ethos" (Boothroyd & Lewis, 2016), the third and sixth most viewed Youtube™ videos were more in the "news or documentary" category (Manning, 2013).

4.2.1. Definitions

PsychedSubstance defined microdosing as "taking very small amounts of a psychedelic substance. We are talking about threshold to below threshold doses". The third most viewed video from the channel *Black Pigeon Speaks* defines microdoses as ". . .taking 10–15 micrograms [of LSD], instead of the larger doses used for drug trips". Definition of microdosing in the fifth most viewed video by *Your Mate Tom* "is taking sub perceptual doses while keeping up with once daily activities, engaging in extreme sports, appreciating nature or enhancing oneś spiritual practice".

In the sixth most viewed video, from the channel *Secular Talk*, the vlogger quotes parts of an article published on Alternet.org: "Microdosing refers to taking extremely small doses of psychedelics, so small that the effects usually associated with such drugs are not evident or are śub-perceptual; while going about one's daily activities. It's being done by anyone from harried professionals to extreme athletes to senior citizen businesswomen, and they're claiming serious benefits from it."

As clinical studies have shown that even 5 mg of psilocybin (Griffiths et al., 2011) and 20 mcg of LSD (Gasser, Holstein, & Michel, 2014) are pharmacologically active, question is what are "small" and "sub perceptual" dosages in psychedelic "microdosing" in relation to the various substances mentioned in the most viewed videos?

4.2.2. Dosages per substance

In the *Secular Talk* video, the vlogger quotes from the same Alternet.org article mentioned above:

"To trip brains (or have a transcendental experience) on LSD, a dose of 400 μg or more is called for; to explore your inner self, take 200 μg; for creative problem solving, try 100 mikes; but for microdosing, take only 10–15 micrograms [of LSD]. Similar microdoses for other psychedelics would include 0.2-0.5 g of dried mushrooms (about one-fifth the normal dose) or about 50–75 micrograms of mescaline."

In the other most viewed videos, the microdoses for LSD and dried psilocybin mushrooms are similar as mentioned in the above quote (10–30 mcg of LSD, 200–500 mg of dried psilocybin mushrooms, see Table 2). However, for mescaline, the mentioned microdose by *PsychedSubstance* is 75–80 *milli*grams, which is significantly larger than the *micro*grams depicted above. Threshold dose of mescaline on the online drug archive Erowid (erowid.org) is also depicted as milligrams (100 mg) so it is possible that there is an (unintentional) confusion between the two measures in the quote used by *Secular Talk*.

While this kind of error is potentially less harmful when stating *milli*grams while meaning *micro*grams, the potency of psychedelic drugs requires careful dosing accuracy to reduce potential harm. For instance, the video by *Your Mate* Tom starts with a tale of caution in which he described how he recently ingested more than a microdose. He took "three little mushrooms" on his way to the university to study for an exam and he "started to feel a bit funny", anxious and having mild visual distortions. He stated that "thatś what I get for not actually getting scales and measuring it. Thatś what I get for just estimating". In the video, the recommended dose of microdosing, taken from shroomery.org and other YouTube™ channels, is 0.2 to 0.5 g. He measures 0.37 g of dried mushrooms and states that at a previous time the three mushrooms he consumed most likely measured beyond the 0.5 g limit. For non-traditional psychedelics, such as 2CB, a microdose is stated as 2–6 milligrams. This is almost identical as the common threshold dose shown in Table 2 which provides info on substances and dosages in comparison to threshold doses found on the online drug archive Erowid (erowid.org)

The most viewed video from *PsychedSubstance* also provided advice on how to microdose, which has potentially influenced user practices. First step is finding a threshold dose using online sources such as Erowid.org. Then, according to the video, one should take half of the threshold amount, and if you don't feel anything, increase by 25–50% "until you hit 1.5 x of the threshold". He pointed out that the dose varies in individuals, so the key to finding a personal optimal dose is by tinkering. As mentioned, he also shared his own experience and dosages and recommended using the test kit that is linked in the video description to verify the purity of the LSD. He mentioned that there are test websites where one can send samples to know the purity, but they are expensive and work with uncertainty. He then explained how to cut a "blotter" of LSD into small pieces and how to conduct volumetric dosing using vodka or distilled water which is said to be more precise method as the amount of LSD can vary from one area to another on blotter papers. Further, due to the heighten sensitivity of LSD which can be affected by oils from finger prints and light exposure, this volumetric procedure preserves the quality of the dosage. This kind of systematic approach, borrowing from chemistry, is very similar to one found in the "research culture" around experimenting with New Psychoactive Substances (see Berning & Hardon, 2016).

Regarding the dosing regime, *PsychedSubstance* recommended that dosing every other day would be ideal, since the body builds a tolerance to classical psychedelics immediately. In addition, this

Table 1
Channel info, and number of views, likes, dislikes, comments of the six most viewed videos.

Channel	1. PsychedSubstance	2. PsychedSubstance	3. Black Pigeon Speaks	4. The Natural Way of Healing	5. Your Mate Tom	6. Secular Talk
Category	Science & Technology	Entertainment	News & Politics	Entertainment	Education	News & Politics
Subscribed	976694	976694	~290,000	~14,000	~67,000	~519000
No of Videos	90	90	230	278	142	11069
Total No of Views	~60 million	~60 million	~36 million	~880,000	~4.5 million	~406 million
Joined Youtube	20/01/2015	20/01/2015	13/11/2011	06/05/2012	24/02/2015	21/04/2008
Video title	* Microdosing LSD or any Psychedelic	* Mescaline microdose video	LSD: Microdosing & the SUPERNATURAL	* MICRODOSING MUSHROOMS: The Benefits of Microdosing Psilocybin!	Microdosing PSILOCYBIN Mushrooms Experiment | DAY 1	'Microdosing' Psychedelic Drugs Has Positive Effects
Video Published	15/09/2015	30/01/2016	23/04/2016	10/10/2015	10/11/2015	17/06/2015
Views	~500,000	~140,000	~100,000	~59,000	~36,000	~28,000
Comments	~1700	~1200	~3600	~500	~170	~330
No of likes	~7000	~3700	~4300	~870	323	868
No of dislikes	~250	~1200	~990	~35	12	26

Table 2
Substances and doses mentioned in the 6 most viewed videos.

Video	PsychedSubstance	PsychedSubstance	Black Pigeon Speaks	The Natural Way of Healing	Your Mate Tom	Secular Talk
Substance & Dosage	2CB: 2–6 mg Psilocybin: 200–500 mg LSD: 10–30 mcg Mescaline: 50–75 mg	Mescaline: 80 mg	LSD: 10–15 mcg	Psilocybin: No Mention of Dose	Psilocybin: 200–500 mg (dried) 370 mg for his own experiment	LSD: 10-15 mcg Psilocybin: 200–500 mg (dried) Mescaline: 50–75 mcg
Threshold dose for comparison (from Erowid.org)	2CB: 2 – 5 mg	Mescaline: 100 mg	LSD: 10–20 mcg	Psilocybin: 250 mg (dried)		

provides time for the user to observe his or her own thinking, emotions, behaviour etc. However, if there are any residual effects after one day remains unclear. The dosing regimen explained in the video by the *Natural way of Healing* includes two to three capsules a day, not everyday, but every other day. Time of consumption is usually in the morning or early afternoon as later it might induce sleep problems (see Johnstad, 2018). Actual dose, however, remains unclear.

As the *Secular Talk* video contained errors on dosages that required closer description, the third most viewed video had potentially harmful claims on the effects of psychedelic microdosing on insomnia and anxiety reduction. As seen below, many of the videos depict microdosing with psychedelics as having mainly positive effects. Scarce scientific knowledge is used, re-used and even created through self-experimentation throughout this digital milieu.

4.2.3. Claimed effects

According to *PsychedSubstance,* the benefits of microdosing include but are not limited to increased creativity, focus, mood and energy. He adds; "think of it in the same way as people take addictive performance enhancing drugs such as Adderall" which is referred to as "lab-grade speed" and "very addictive". Microdosing LSD, however, is portrayed as having less side effects compared to methylphenidate (Ritalin) and dextroamphetamine (Adderall) and the video refers to James Fadimanś book (2011) where Albert Hofmann is quoted to say "LSD, would have gone to be used as Ritalin if it wasn't so harshly scheduled." Reports gathered by Fadimanś are mentioned as a "success" and the area is depicted as underresearched but potentially beneficial.

In the second most viewed video, *PsychedSubstance* states in the beginning that he took 80 mg of Mescaline hydrochloride (HCL) 2 h prior to recording. He reports feeling "overall pretty damn cool", with senses heightened, skin feeling more sensitive, hearing more sensitive and smell "really" heightened. Visual functioning was the least sensitive which he found "weird". The vlogger has had former experience with microdosing LSD, psilocybin, 2CB, and mescaline, as would be evident from the first video. He found LSD and mescaline the most beneficial, and the experience between them interchangeable "I can speak from personal experience being on mescaline microdose right now that it feels extremely similar to being on LSD microdose". He reported that regarding workflow, his thoughts would run a lot smoother. However, there is no increase in physical capability when exercising (4 h after intake). He noted that there is more auditory enhancement when using mescaline versus more visual enhancement when microdosing LSD. Enhancement of smell and taste is almost indistinguishable between the compounds. There is a slight increase of touch sensitivity with mescaline although according to him it could be a memory distortion.

Similar self-experimentation is in the fourth and fifth most viewed videos. Your Mate Tom eats (psilocybin) mushrooms on camera, which were "props" according to the disclaimer in the description. 15 min after consumption he reported feeling "a bit chill, a bit calm, like I had one little tiny drag of a joint". He reported not feeling high but instead calm, despite his heart rate being slightly elevated. In his experiment he intended to stay as unbiased and objective as possible, noting it to be challenging as he also wants it to work. In his experiment *Your Mate Tom* tested microdosing across multiple categories including physical capability, creativity, focus, awareness and social interaction. He performed various activities on five separate days to test all five categories before making a summary. The results of this experiment were that "microdosing definitely does not help with physical capabilities" as mushrooms usually makes his body feel "heavy". He did feel heighten awareness, greater introspection, increased focus and social interaction. He acknowledged that it is not the most scientific study there is ("not a double-blind, peer-reviewed study") but in the absence of such studies, "as anecdotal as this might be, at least

it is something. Itś a guide map. At the end of the day, the most scientific research you can possibly do is trying it yourself", echoing the practices of the first psychedelic researchers in the West at the turn of the 19th and 20th century (see Rucker et al., 2017).

In the video from the channel *The Natural Way of Healing*, the vlogger presents pulverized, dried up psilocybin mushrooms contained in veggie caps. Similar to above, he also explained his motivation as gaining first-hand experience: "This way you get true knowledge". The vlogger mentioned that he would go running and his cardio-vascular output seems to be "off the charts". His mental focus, cognitive function and mood improved. Other benefits from microdosing psilocybin mentioned in the video included "mental clarity", "emotional balance", "positive mental attitude", "improved overall well-being", "better workouts", "better focus" and "increased mood and outlook on life." The vlogger also makes a comparison between "natureś medicine" versus synthetic pharmaceuticals, which are said to only mask symptoms and suppress emotions. Psilocybin mushrooms, on the other hand, are said to address the root cause and "works on your psyche" both in higher and microdoses so one can move forward in a more rapid pace regarding personal development.

We argue that sharing results from these self-experimentations is essential for understanding the motivations and the "ecology of practices" (Boothroyd & Lewis, 2016) around psychedelic microdosing on Youtube™. We further argue that the experiments on Youtube™ should be seen in the context of other experiments with microdosing, like written trip reports (Berning & Hardon, 2016). As seen above, the ad-hoc lay-experiments found both on Youtube™ videos and trip reports include lived experiences, as well as measurements of vital indexes such as blood pressure, and references to biological physiology and pharmacology (Hardon & Moyer, 2014). Thus, the depiction of experiments on YouTube™ can be seen in a wider context of experimental setups, generated by users themselves.

However, these claimed effects require critical evaluation. In the video from *Secular Talk*, the vlogger states that microdosing psychedelics was previously unfamiliar to him but "so far the results are very positive." In the video from *Black Pigeon Speaks*, the narrator stated how "a famed psychedelics researcher, Dr. James Fadiman, who worked with LSD until it got banned in the 1960ś, found that he gave up Facebook after he started taking tiny doses of LSD for breakfast." After this erroneous claim he continues that he [Fadiman] has said of ingesting small doses of LSD "People do it and theyŕe eating better, sleeping better, theyŕe often returning to exercise or yoga or meditation. Itś as if messages are passing through their body more easily." After this quote, that Fadiman had given in an interview with Vice a year earlier, the narrator further emphasized that "a growing movement of people are now microdosing LSD in the morning" while on the screen there is an image of the website IFLScience report on microdosing titled "Researcher Claims Small Doses Of LSD Can Alleviate Anxiety And Depression". The video also claims that microdosing LSD can cure both anxiety and insomnia, while according to user reports psychedelic microdosing can induce insomnia (Johnstad, 2018) and worsen existing severe anxiety (Fadiman & Korb, 2017).

5. Discussion

After decades of almost no research, partly due to strict scheduling of psychedelic drugs (Rucker et al., 2017), classical psychedelics are again being explored for their potential therapeutic effects. These clinical studies have investigated the safety and efficacy of psychedelic substances in clinical settings and the active doses have ranged from 5 to 30 mg (mg) of psilocybin (Bogenschutz et al., 2015; Griffiths et al., 2011; Johnson et al., 2014) and 20 to 200 μg (mcg) of LSD (e.g. Gasser et al., 2014). This "psychedelic renaissance" (Sessa, 2017) is discussed in mainstream literature and media (Waldman, 2017), and the findings point to several new avenues for research. For instance, microdosing psychedelics, like psilocybin, could be explored to maintain the therapeutic effects of a high-to-moderate dose of psilocybin for depression, initiated in the clinical setting (Carhart-Harris & Nutt, 2017; Carhart-Harris et al., 2016; Prochazkova, Lippelt, Calzato et al., 2018). However, lack of (governmental) funding and strict scheduling, serve as a major obstacle for psychedelic research (Nutt et al., 2013), although the push for "an emerging new paradigm" (Nichols, Johnson, & Nichols, 2017) remains persistent.

In this study we focused our descriptive assemblage on psychedelic microdosing and as we demonstrated, several psychedelic microdosing research projects are under way or planned, potentially influencing user practices and knowledge. A challenge with psychedelic microdosing is that it has mainly been evaluated by self-reports, using indicators such as performance and mood, and the role of the placebo effect has not yet been determined. As our descriptive assemblage demonstrates, this potential placebo effect is something current microdosing studies are aiming to explore, in a placebo-controlled open field study with legal psilocybin truffles (Prochazkova, Lippelt, Colzato et al., 2018) and in LSD microdosing studies assessing short-term acute effects (Beckley / Maastricht Psychedelic Programme, 2018; Yanakieva et al., 2018).

We also used the Youtube Data Tool to explore 1) the digital milieu of Youtube™ and 2) ecology of practices in the most viewed videos. These Youtube™ channels often focus on drug-related content and cover a wide variety of topics, and while they are not "mainstream", theyv́e attracted a wide audience on Youtube™. Already in 2016, the videos had over a million views, thousands of "likes" and comments (Table 1), which arguably indicate potential impact of the videos on spreading user knowledge and practices. Overall, the substances mentioned in the videos discuss a wider range of psychedelic and psychoactive substances than typically discussed within contemporary psychedelic microdosing research (Fadiman, 2011; Johnstad, 2018).

The six most viewed videos comprised over 92% of the total view count of microdosing videos on Youtube™ in 2016, and some depicted microdosing with psychedelics as a growing phenomenon. Similar data extractions of "microdosing" videos done with the YDT in November 2017 and October 2018 provided data lists of 351 and 447 videos, respectively (compared to the initial 115), indicating that the microdosing phenomenon has grown by almost 290% on Youtube™ in the last two years (see also Google Trends, 2018). Casselman and Heinrich (2011:663) also found that "Salvia divinorum specifically on YouTube™ and more generally on the WWW, is a growing phenomenon". However, whether user prevalence of psychedelic microdosing is increasing requires further contextualization of these findings outside the digital milieu of Youtube™, but published epidemiological studies on psychedelic microdosing are currently lacking.

The Youtube™ videos we analysed portrayed effects of psychedelic microdosing in a positive way, and the videos in general received more "likes" than "dislikes" (Table 1). Both Casselman and Heinrich (2011) and Lange et al. (2010:140) discovered that "experiences portrayed on YouTube™, are rarely negative". Although generally in line with scarce published research (Fadiman, 2011; Johnstad, 2018; Prochazkova, Lippelt, Calzato et al., 2018), some of these videos had either unsubstantiated claims on effects, or the recommended doses were larger (or exponentially smaller) than what current microdosing researchers have estimated to be optimal. While these estimations might change when more research on this topic is conducted, and while the errors might not physically endanger viewers who may act on the information, "offline" field research is demonstrating that certain

populations might experience negligible or possibly even negative effects from psychedelic microdosing (Fadiman & Korb, 2017; Johnstad, 2018). For instance, preliminary results from a recent data sample (1850 subjects from 59 countries) illustrated that while benefiting most participants, some reported no effects and a few groups (e.g. those with serious anxiety and people who were red-green color-blind) reported negative effects and stopped microdosing (Fadiman, personal communication, 12th of February, 2018; Fadiman & Korb, 2017). Therefore, Fadiman and Korb do "not recommend that people with colorblindness, who live with diagnoses of psychotic disorders or along the autism spectrum try microdosing" (Microdosing Psychedelics, 2018).

However, the reported positive effects of psychedelic microdosing warrant increased empirical research and bioethical discussion also in the pharmacological neuroenhancement literature (Pieters & Snelders, 2009). The potential breakthroughs stemming from clinical findings of recent psychedelic research also require further attention, as one of the main research areas of contemporary psychedelic research has focused on reducing anxiety among terminally ill cancer patients with psilocybin-assisted psychotherapy (e.g. Grob et al., 2011) and inducing meaningful experiences in healthy volunteers (Elsey, 2017; Griffiths et al., 2006). Ability to have reduced anxiety when facing death and meaningful experiences when alive is argued to be not only "human enhancement", but close to a human right (Krebs, 2015), especially from the standpoint of cognitive liberty (Walsh, 2016).

Microdoses mentioned in the videos have some variation and are not significantly lower than common threshold doses and even overlap with them (Table 2). Also, these "microdoses" are often larger compared to what "microdosing" means in pharmacokinetic studies (Tewari & Mukherjee, 2010). Miniscule doses of psychedelics like LSD and psilocybin required to achieve pharmacological effects demands psychedelic microdosers to experiment with various doses to achieve intended effects (Berning & Hardon, 2016). One of the difficulties for many microdosers is to identify the optimal dose that ranges between the *minimum effective dose* (MED), the minimal amount to create a desired effect, and the maximum of a microdose, a dose that remains subperceptual, all varying between individuals.

Safety measures to avoid "overdose", which is rarely harmful with psychedelic microdosing (Johnstad, 2018), are nonetheless difficult to obtain outside clinical studies as the chemical consistency and potency of the (illegal) substances are practically impossible to know for certain (Haden, Emerson, & Tupper, 2016). Despite the relative safety of psychedelics, such as psilocybin (Van Amsterdam, Opperhuizen, & van den Brink, 2011) especially in clinical and research settings (Johnson, Richards, & Griffiths, 2008), "the criminalization of psychedelics has generated significant harms, particularly as illegal markets produce and distribute psychoactive substances that range widely in quality and potency, resulting in unpredictable toxic effects" (Haden et al., 2016: 245), potentially even in "mini-doses" (see Johnstad, 2018). Therefore, various experts have called for a global drug policy reform to regulate drugs, including psychedelics, from a public health perspective (Haden et al., 2016).

The illegality of many psychoactive substances not only complicates public health policies and harm reduction approaches (Haden et al., 2016) but also serves as a major hurdle for clinical researchers (e.g. Nutt et al., 2013). This might encourage "lay people" to facilitate their own self-experimentation, and in contrast to how users of "illicit substances" are oftentimes portrayed in media and science, many videos revolved around themes like research, experiments, self-monitoring and the imperative of sharing results and relevant information. This type of "research culture" (Berning & Hardon, 2016) is not unique in microdosing communities as this trend can be found among new psychoactive substance (NPS) users (ibid.; Boothroyd & Lewis, 2016). In general, young drug users use creative means to minimize possible risks and maximize benefits (Van Schipstal, Mishra, Berning, & Murray, 2016) and experiment by "adjusting dosage[s] and mixing substances, with knowledge of the (mostly positive) 'lived effects' of drugs spreading through collective experimentation and word of mouth" (Hardon & Moyer, 2014:110), and through various digital milieus (Boothroyd & Lewis, 2016).

Several of the most viewed videos are no longer viewable, and their creators have recently reported that they are "being targeted" or "censored" by Youtube™ due to drug-related content (Codrea-Rado, 2017). This warrants further research and bioethical discussion about biomedical knowledge hegemony and knowledge production (Coveney et al., 2011) especially as the generation of online knowledge and the mechanisms of its circulation have been highlighted as a possibility to monitor drug use trends from early on (e.g. Deluca et al., 2012; Berning & Hardon, 2016; Krieg et al., 2017). The videos for instance compared psychedelic microdosing to "cognitive enhancers" like methylphenidate and dextroamphetamine, and ADHD and depression have been the most common self-reported medical indications (Fadiman & Korb, 2017). Anecdotal evidence also demonstrates that as people are microdosing psychedelics, they are weaning off from their pharmaceutical medications (Waldman, 2017, Fadiman & Korb, 2017). Thus, as researchers have also pointed out (Prochazkova, Lippelt, Calzato et al., 2018; Sessa, 2017) investigating psychedelic microdosing as a form of "cognitive enhancement" (Coveney et al., 2011) is an area requiring further research.

5.1. Benefits and limitations

Previous Youtube™ drug research has noticed the potential of this type of digital research (e.g. Casselman & Heinrich, 2011). For instance, the analysis conducted by Lange et al. (2010:138) illustrated that Youtube™ videos on Salvia users" provides a unique opportunity to observe people using salvia in settings of their choosing." Future online drug research could utilize the digital milieu found on Youtube™, and other online sharing facilities, to map the various contexts of psychedelic and other types of drug use as the effects of this "setting" (Hartogsohn, 2017) is often deemed as important as the psychological profile or mind" set" of the person and the substance consumed. According to Lange et al. (2010:138–139) another benefit of this type of research is that due to Salviaś rapid onset and short duration "many user video-posts may actually contain the entire drug experience." Their study provided measurable effects of Salvia experiences, mainly the significantly dissociative impact, and "the demonstration of the utility of YouTube videos as a resource for behavioral observation research" (Lange et al., 2010:140).

The utility of Youtube™ drug research, however, needs to be evaluated according to specific substances and use practices. Classical psychedelics, for instance, have often considerably longer duration of action than inhaled Salvia Divinorum. The visual material available also limits this type of retrospective digital research (Lange et al., 2010:140) and based on the data at hand, estimating the practical impact of the videos on "offline" microdosing practices is difficult to determine. Also, as our current data analysis provides insight into the phenomenon only within a limited time window, further longitudinal research is needed. As we focused only on "microdosing" on Youtube, other digital milieus, languages and types of dosing regimens remained outside of our empirical analysis. Digital Methods Initiative (2018) provides various digital tools that could be used to explore other digital milieus (e.g. Facebook™, Twitter™, Instagram™).

6. Conclusions

The effects of psychedelic microdosing in our Youtube™ data are depicted as positive and the practice is often portrayed as increasingly common. Using a similar approach of data extraction, we found that 16 and 26 months after the initial extraction done in July 2016 the phenomenon is growing, at least on Youtube™ and Google Trends (2018). However, both the epidemiology and efficacy of psychedelic microdosing need further "offline" studies. In addition, the role of psychedelics as pharmacological enhancers and therapeutic agents require bioethical evaluation and drug policy discussion.

We intend to utilize the novel insights we gathered through our descriptive assemblage to continue netnographic research on psychedelic microdosing in the future. We argue that the YDT is a useful method to research online drug knowledge as it allows the collection of relative videos for further analysis in a systematic and cost-effective way. The other features of the YDT require further exploration for this digital milieu and the comment section on Youtube™ deserves its own empirical analysis. Also, methodologically, only observing digital data, without "offline" interaction with the object of study, is the reason we have focused on a more "netnographic" (Kozinets, 2010) approach compared to previous Youtube™ drug research (e.g. Lange et al., 2010; Kataja et al., 2018). This type of online drug research can be used to gather knowledge of under-researched topics, like psychedelic microdosing, to monitor emerging trends and even function as an early warning system for public health services (e.g. Krieg et al., 2017), although limitations like the ones described above need consideration.

Conflict of interest

None.

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PUBLICATION IV

Beyond treatment vs. enhancement: A qualitative study of pharmacological neuro-enhancement among Dutch and Lithuanian university students.

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Beyond Treatment Versus Enhancement: A Qualitative Study of Pharmacological Neuro-Enhancement Among Dutch and Lithuanian University Students

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Abstract

This article examines the ambiguous relationship between treating illness and enhancing normalcy through the use of "cognitive enhancement" drugs. Although the literature on pharmacological neuro-enhancement generally differentiates between the "licit/therapeutic" and "illicit/enhancement" use of substances, in-depth interviews with 35 university students in the Netherlands and Lithuania—both with and without formal medical diagnoses of (mainly) Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder—reveal the fluidity of these categories. Our study of the perceptions and experiences of people who use such drugs further suggests a much broader range of substances, motives, and sought-after effects than are commonly acknowledged in the "cognitive enhancement" literature. We need a more inclusive and context-sensitive approach to study pharmacological neuro-enhancement, for instance, by approaching both licit and illicit drugs as tools or instruments.

Keywords

treatment, enhancement, bioethics, neurotechnologies, pharmacological neuro-enhancement

Introduction

While the phenomenon of "pharmacological neuro-enhancement" (Maier & Schaub, 2015) has been variously addressed as the use of "smart drugs" (S. Rose, 2002), "study drugs" (Vrecko, 2013), "scholastic steroids" (Linton, 2012), "cognitive enhancement drugs" (Greely et al., 2008), or the

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"nonmedical (ab)use of prescription stimulants" (Arria & Wish, 2006), empirical research has largely focused on healthy university students in Western countries using prescription stimulants such as methylphenidate (e.g., Ritalin) and dextroamphetamine (e.g., Adderall; Maier & Schaub, 2015; Ragan, Bard, & Singh, 2013), hitherto used mostly for children diagnosed with attention deficit [hyperactivity] disorder (AD[H]D; Conrad & Potter, 2000). But in our study of the phenomenon among university students in the Netherlands and Lithuania, we discovered students turning to a much wider range of both licit and illicit substances—from prescription stimulants to cannabis and psychedelics (Hupli et al., 2016; Table 1)—for "personalized enhancement" (Maslen, Faulmüller, & Savulescu, 2014, p. 10). And as several qualitative studies (Green & Moore, 2009; Petersen, Nørgaard, & Traulsen, 2015b; Vrecko, 2013) have suggested, we found our interlocutors turning to prescription stimulants to not only enhance "cognition" but for their emotional and pleasurable effects.

In this article, we examine the ambiguous relationship between treating illness and enhancing normalcy through the use of "cognitive enhancement" drugs. Although the literature on pharmacological neuro-enhancement generally differentiates between the "licit/therapeutic" and "illicit/enhancement" use of substances, in-depth interviews with 35 university students in the Netherlands and Lithuania—both with and without formal medical diagnoses of (mainly) attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD)—reveal the fluidity of these categories. Our study of the perceptions and experiences of people who use such drugs further suggests a much broader range of substances, motives, and sought-after effects than are commonly acknowledged in the "cognitive enhancement" literature. In this article, we therefore ask: (1) Is the practice of improving oneself through pharmacological means different when substances are used therapeutically (i.e., when prescribed by a medical doctor) and when they are used for "enhancement?" (2) What do users seek to improve in their everyday lives by using these substances? We include both licit and illicit stimulants in our study as the distinction between therapy/enhancement and licit/illicit is often far from clear-cut (e.g., Bullard, 2018). In a previous publication, we found both diagnosed and undiagnosed university students in the Netherlands and Lithuania balancing the benefits and risks of using a variety of substances mainly to enhance their time management and concentration. These results, which included data from an online survey of 113 student respondents in the Netherlands, have been reported elsewhere (Hupli et al., 2016).

The availability of licit stimulants is influenced by country-specific practices around the pharmacological treatment of attention disorders (e.g., Hinshaw & Scheffler, 2014, pp. 119–136). Although the Netherlands is famous for its liberal drug policies, neither professionals nor public opinion has embraced the use of cognitive enhancement drugs, while the growing medical use of stimulants by children is often criticized (Schermer, 2016). Nevertheless, the nonmedical lifetime use of Ritalin doubled between 2007 and 2011 among secondary school pupils in Amsterdam (Benschop, Nabben, & Korf, 2011) where we conducted most of our Dutch interviews. Compared to the Netherlands (cf. Schermer, 2016), only limited data on enhancement drug use are available from Lithuania. One survey of medical students (Lengvenytė, Strumila, & Grikiniene, 2016) found that 8.1% of respondents ($N = 47$) reported using "neuro-enhancing drugs" at least once in their lifetime, while the use of nootropics like Piracetam was more common than the use of prescription stimulants. Prescription stimulant use is less common in Lithuania than in the Netherlands (INCB, 2018) partly due to strict regulations and high prices, especially for students (Lengvenytė et al., 2016). Pharmacological treatment guidelines for ADHD have been introduced for children (Lithuanian Society of Child and Adolescent Psychiatry, 2015), but to our knowledge, not for adults.

The use of illicit stimulants, including MDMA, amphetamine, and cocaine, is also much more common among 15- to 34-year-olds in the Netherlands than in Lithuania (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2019). However, the extent to which these drugs are used for "enhancement" remains unclear. According to a survey study by Schelle et al. (2015), "substance use for cognitive enhancement" among university students in the Netherlands lags behind many Western countries, although more recent data from the Global Drug Survey suggest an upward trend

(Maier, Ferris, & Winstock, 2018). Lithuania criminalized the possession of (certain) psychoactive substances in 2017 (Kurzevic, 2017), potentially complicating public health and harm reduction efforts (e.g., Vargo & Petróczi, 2016, pp. 9–10). Sociocultural factors require further attention in the cognitive enhancement drug literature (Jotterand & Dubljević, 2016; Maier et al., 2018) as the availability and social acceptance of pharmacological neurotechnologies—licit or illicit—is heavily influenced by cultural environments, technological resources, and regulatory frameworks (Pickersgill & Hogle, 2015; Sismondo & Greene, 2015).

Between Pharmacological Therapy and Enhancement

Academic discussion in this area is often framed "as a debate about where *treatment* ends and *enhancement* begins" (Maslen et al., 2014, p. 6). In this framework, drugs are seen either as a treatment for a neurocognitive impairment, like deficits in attention, or a way to enhance oneself beyond "normal species-functioning" (Daniels, 2000). The distinction, however, is more complex in practice (e.g., Savulescu, Sandberg, & Kahane, 2011; McKeown, 2017). Coveney (2010, p. 285), among others (Bostrom & Sandberg, 2009, p. 312; Chadwick, 2008, p. 36), has argued that

> understanding and debating the use of new neurotechnologies within a therapy-enhancement dichotomy is insufficient and inadequate. Instead, one has to take into account the multiple ways in which drug use and users may be configured across different domains of social life.

The authors of the Human Enhancement study, undertaken for the European Parliament Science and Technology Options Assessment (STOA, 2009, p. 85), likewise state that "Because of the fine lines involved in the diagnosis of ADHD, which require normative judgments that are highly sensitive for diverging opinions, it is often hard to judge whether Ritalin™ is used as a therapeutic or an enhancing agent" (p. 85).

While enhancement studies often exclude the therapeutic users of prescription stimulants (e.g., Vrecko, 2013), "licit" and "illicit" users report similar experiences (cf. Bullard, 2018). Aikins (2011) interviewed North American university students using prescription stimulants, "licit" and "illicit" users as well as "'combined users': students who took stimulants nonmedically before acquiring their own prescriptions, thereby spanning both populations." According to Aikins (2011), both groups "overwhelmingly felt that prescription stimulants enhanced their ability to perform academic tasks" (p. 566). Other studies have shown that even for students who obtain prescription stimulants legally from medical professionals (Vrecko, 2015), the distinction between treatment and enhancement is embedded in moral ambivalence and that "categories of pathology and normality are negotiable; borders are increasingly blurred; and new sets of normality and pathology are emerging" (Petersen, Nørgaard, & Traulsen, 2015a, p. 6; cf. Schermer, 2007). Bullard (2018) argues that researchers are complicit in keeping the distinction afloat:

> This distinction between medicine and enhancement informs how researchers approach the investigation of cognition enhancer use among student populations. When they exclude medical users of ADHD medications as enhancemental users of ADHD medications, researchers are policing the boundary between medicine and enhancement. (p. 7)

Whether for therapy or enhancement, the use of these drugs creates relations between pharmacological "objects" and their consumers (Greene & Sismondo, 2015; Hardon & Sanabria, 2017) embedded in contemporary values around achievement and normalcy (Robitaille & Collins, 2016; N. Rose, 2007b). Some researchers of ADHD even argue that "the fast-escalating rates of diagnosis and treatment we now see are linked to intense pressures for achievement and performance in the

context of an increasingly competitive world economy" (Hinshaw & Scheffler, 2014, p. xxviii) and that the increasing use of prescription stimulants for cognitive enhancement and therapy (INCB, 2018; Maier et al., 2018) is a response to this pressure (Hinshaw & Scheffler, 2014). Hypothetically, this pharmaceuticalization (Williams, Martin, & Gabe, 2011) of cognitive performance indicates that more people without diagnosable illnesses are experiencing cognitive performance pressures, with pharmacological neurotechnologies appearing as solutions in competitive environments where even mild effects can make a difference (Cakic, 2009; Smith & Farah, 2011; STOA, 2009).

We extend this insight through our empirical analysis and argue that although the treatment-enhancement distinction has uses in academic discussions and health policy (e.g., McKeown, 2017), in everyday life the distinction is more "fluid" (Hardon & Sanabria, 2017). Therefore, it is important to explore "lay pharmacology" (Webster, Douglas, & Lewis, 2009) or the perceptions, experiences, and motives of those who use pharmacological neurotechnologies (Hupli et al., 2016).

Enhancing Cognition?

The terms *cognitive* enhancement and *neuro*-enhancement are often used interchangeably in the literature, without a clear distinction between them (Lucke, Bell, Partridge, & Hall, 2011, p. 38). The term "cognitive enhancement drugs" (CEDs) suggests that these types of substances do enhance cognitive abilities, or that they are used specifically for this purpose, and that this is indeed an improvement (e.g., Bullard, 2018; Outram, 2010). Theoretical discussions in bioethics often overestimate the "enhancing" capabilities of CEDs (e.g., Partridge, 2017) and downplay their potential adverse effects (Heinz & Müller, 2017; Hupli, Didziokaite, & Ydema, 2016). Publications and media reports are rarely critical of the term "enhancement" (Partridge, 2017), encouraging possibly unrealistic ideas about "smart drugs" (Pickersgill & Hogle, 2015) among both researchers and the public. In any case, initial enthusiasm toward the enhancement potential of CEDs for healthy people has been followed by greater scepticism, including by those who point out that the phenomenon is hardly new (e.g., Ilieva & Farah, 2013a; Lucke et al., 2011; Morrison, 2015).

In laboratory studies, the ability of CEDs to enhance healthy subjects has been found to be modest (e.g., Repantis, Schlattmann, Laisney, & Heuser, 2010; Smith & Farah, 2011). According to Outram (2011), "there is a considerable amount that we do not know concerning both motivation and self-evaluated efficacy in use, although we cannot discount the possibility that efficacious cognitive enhancement is being experienced by some individuals" (p. 9). Research outside the laboratory has broadened our understanding of why university students turn to prescription stimulants. On the basis of interviews with U.S. university students, Vrecko (2013) argued that "emotional changes brought about by stimulant use are part of what makes stimulant drugs useful in relation to academic work" (pp. 9–10; cf. Smith & Farah, 2011, pp. 723–724). Similarly, Petersen, Nørgaard, and Traulsen (2015b) found American students using prescription stimulants as a tool to prevent procrastination and to experience pleasure while studying. In Germany, Hildt, Lieb, and Franke (2014) report university students trying both licit and illicit stimulants to enhance not only academic performance but other aspects of their lives, while experiencing various positive and negative effects.

While our findings do not imply that licit and illicit stimulants do not affect cognition, they do question the literature's framing of nonmedical stimulant use as *only* enhancing cognition (cf. Vrecko, 2013). Students perceive numerous substances as potential "smart drugs" (e.g., Hupli et al., 2016; Singh, Bard, & Jackson, 2014), and research has shown them turning to prescription stimulants, "illicit drugs" and other lifestyle enhancers to deal with stress (Maier, Liechti, Herzig, & Schaub, 2013), to manage time (Krøll, 2019), and to counter the effects of other drugs (Arria et al., 2013). Nevertheless, whether and to what extent students are successful in achieving these ends through their use of pharmacological neurotechnologies remains unclear.

The Pharmaceuticalization of Everyday Life?

Whether for therapy or enhancement, reliance on drugs to cope with the demands of contemporary society has raised concerns over "the pharmaceuticalization of daily life" (Abraham, 2010; Fox & Ward, 2008; N. Rose, 2007b). For Coveney, Gabe, and Williams (2011), pharmaceuticalization "is more specific in its remit [than (bio)medicalization], denoting as it does the transformation of aspects of human experience into targets for *pharmaceutical intervention* as opposed to biomedical interventions in general" (p. 387, original italics). We follow Williams, Martin, and Gabe (2011) framework, which can "be used to establish criteria for measuring the extent of pharmaceuticalization in any given case" (p. 712). Both medicalization and pharmaceuticalization have their own local expressions, and "the degree or extent to which they are occurring remains open to empirical investigation on a case-by-case basis" (Williams et al., 2011, p. 711). While Williams et al. (2011) address topics ranging from drug regulation, governance, patient advocacy, and reconfigurations of "health" problems as having a pharmaceutical solution, one of the key sociological dimensions of modern pharmaceuticalization they identify is the nonmedical use of cognitive enhancement drugs by healthy people (cf. Coveney et al., 2011).

One limitation of the pharmaceuticalization concept is that although it has been used to emphasize different types of pharmaceutical interventions for medical and nonmedical reasons, scholars do not generally include "illicit substances" within its remit. But as we will show below, the line between "licit/therapeutic" and "illicit/enhancement" is a blurry one that changes with the context. Furthermore, the literature on pharmaceuticalization rarely considers the active role of users beyond patient advocacy (Williams et al., 2011) but instead "implies passivity on the part of the medicalised" (N. Rose, 2007a, p. 702). Exploring instrumental drug use among university students in different country contexts thus allows us to study local processes of pharmaceuticalization, user motivations, and the distinction between enhancement and therapeutic drug use in practice.

Material and Methods

Our pooled data set consists of 35 interviews with university students between March and December 2013, who at the time were enrolled at university or had very recently graduated. The overall sample includes 20 women and 15 men ranging in age from 19 to 29, with the average age being 23. Twenty interviews took place in Amsterdam; 15 in Vilnius and Kaunas, Lithuania. In both countries, our interviewees represented a variety of faculties including medicine, social and political sciences, business, and architecture. All had experience using some form of pharmacological neurotechnology, ranging from the (off-label) use of prescription pharmaceuticals to "street drugs" and "food supplements for the brain." Twenty-three of our 35 interviewees had not received a diagnosis; eight had been formally diagnosed with ADHD or ADD, and one with daytime sleepiness. Two interviewees had diagnosed themselves: one with ADD and the other with daytime sleepiness. A more detailed description of our informants—age, gender, occupation, location of interview, diagnostic status, substances used, and their primary effects—is presented in Table 1.

This study was not a planned collaboration from the outset; the three authors met for the first time in a workshop in 2015 organized by the European Research Council–funded ChemicalYouth project (http://www.chemicalyouth.org/). All three authors had interviewed enhancement drug users for their respective theses, and the workshop provided an opportunity to discuss common themes in our separate data sets. The three studies that inform this article all used a grounded theory approach (Glaser & Strauss, 1967) in their respective analyses, while the current analysis was inspired by Bröer et al.'s (2016) method of collaborative online interpretation (see http://www.crowdedtheory.com/).

The interviews were recorded and transcribed verbatim in English or their original Dutch and Lithuanian; excerpts here have been translated and edited for clarity. Participants were informed about the purpose of the studies, what their participation would entail, and gave oral informed consent.

Table 1. List of Participants: Age, Gender, Occupation, Location of Interview, Diagnostic Status, Substances Used and Their Effects.

Pseudonym	Age	Gender	Occupation	Location of Interview	Diagnostic Status	Substances Used
Amelia	22	Female	Medical student	The Netherlands	ADD diagnosed	Used medication more often since the age of 15, before that didn't like the side-effects, which included loss of appetite and depression. Prescribed with Ritalin and Concerta. Experiences with other drugs.
Anna	24	Female	Political science	The Netherlands	Undiagnosed	Anna tried Ritalin once before her finals. Experienced feelings of anxiety and nervousness, no positive effects. Has tried Ritalin recreationally on three occasions. Has also used amphetamine for study purposes.
Bella	21	Female	Medical student	The Netherlands	Undiagnosed	Tried Ritalin before an exam. Experienced mild improved focus. Experiences with other drugs
Bram	21	Male	Economics and geography student	The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as a child. Has taken Concerta when he was younger, and has been using Ritalin for the past seven years. Uses it only for study purposes, during lectures, exams and other important moments. Does not experience any side effects. Experiences with other drugs.
Brian	27	Male	Economy student	The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as an adult but doesn't believe in the diagnosis. Has used caffeine pills, Modafinil and Ritalin (now with prescription), Oxazepam and methamphetamine for study purposes.
Cecilia	23	Female	Political science student	The Netherlands	ADD diagnosed	Was diagnosed with ADD as an adult. Prescribed with Ritalin. Decided to stop using because didn't find it helpful. Also had side effects.
Corinne	25	Female	Global Health student	The Netherlands	Undiagnosed	Has tried Concerta and Ritalin approximately 10 times. Did not find it useful for studying although said focus improved mildly. Also used it for creative purposes and for recreation. Felt distracted after the medicine wore off.
Dana	24	Female	Working	The Netherlands	Daytime sleepiness diagnosed	Dana was diagnosed with daytime sleepiness about two years ago. First prescribed with Ritalin, afterward Modafinil. Used it regularly while studying although had some side-effects and did not want to become dependent on it.

(continued)

Table 1. (continued)

Pseudonym	Age	Gender	Occupation	Location of Interview	Diagnostic Status	Substances Used
Diane	23	Female	Global health	The Netherlands	Undiagnosed	Has tried Ritalin twice. First time used half a pill, did not experienced any effects so tried a whole one again with motivational effects
Eglė	24	Female	Master's economics student (working)	Lithuania	Undiagnosed (self-diagnosed with daytime sleepiness)	Used Modafinil for self-treatment of daytime sleepiness she experienced in her work.
Emilia	23	Female	History student	The Netherlands	Undiagnosed	Tried Modafinil once. Used it after using other drugs the night before to stay awake at class. No strong effects.
Eric	23	Male		The Netherlands	ADHD diagnosed	Was diagnosed with ADHD as an adult. Prescribed with Ritalin and finds it useful. Has a system of off and on periods. Also used Ritalin recreationally.
Fiona	22	Female	Education	The Netherlands	Undiagnosed	Fiona tried Ritalin once before an exam. Did not experience any effects. Also used Ginkgo biloba to improve concentration while studying.
Frank	25	Male	Social science student	The Netherlands	ADD diagnosed	Was diagnosed with ADD as an adult. Prescribed with Ritalin. Had used Ritalin before; also Adderall, amphetamine and LSD for study purposes.
Gabriel	24	Male	Psychology student	The Netherlands	Undiagnosed	Has tried Modafinil, Piracetam, Oxiracetam and Aniracetam to get better grades and improve memory. Experienced wakefulness and more focus with modafinil and better memory of at least dreams with the racetams. Experienced anxiety about possible side-effects.
Henry	26	Male	Social science student	The Netherlands	Undiagnosed	Has tried Ritalin and Concerta (about 50 times in the last nine years) and also Ephedra, amphetamine and cocaine (once) for studying, doing sports and for recreation (about 5 times). Experienced improved and longer lasting concentration, no harmful effects.
Ieva	19	Female	Publishing student	Lithuania	Undiagnosed	Used Lecitone Jeune, a food supplement for young people, during her final school year.
Iris	19	Female	Law student	The Netherlands	Undiagnosed	Has tried Ritalin because she was curious about the effects for studying. Does not want to use it often because she thinks it is not completely fair.

(continued)

Table 1. (continued)

Pseudonym	Age	Gender	Occupation	Location of Interview	Diagnostic Status	Substances Used
Jasper	21	Male	Economics student	The Netherlands	ADD diagnosed	Diagnosed with ADD, does not use his prescription but obtains Ritalin through a friend's mother who is a psychiatrist. Has many side effects and wants to use Ritalin as little as possible.
Jovita	26	Female	Art student	Lithuania	Undiagnosed	Used food supplement for the brain Neurozan to help her with some tests and exams both in school and university.
Karolis	29	Male	Working (philosophy graduate)	Lithuania	Undiagnosed	Has tried variety of drugs ranging from food supplements like Neurozan to psychedelics and cannabis to induce different states that he deemed helpful for studying.
Kipras	21	Male	International relations student	Lithuania	Undiagnosed	Used armodafinil when recommended by a friend, mainly to prepare for university exams.
Lotte	23	Female	Social sciences student	The Netherlands	ADD diagnosed	Diagnosed with ADD at the age of 19. Had so many side effects that she quit using for a while. Now uses only when she finds it absolutely necessary.
Marius	20	Male	Dentistry student	Lithuania	Undiagnosed	Used Neurozan when studying.
Marija	24	Female	Working (Directing graduate)	Lithuania	Undiagnosed	Used cannabis after a long day of studying/acting to insure a good night's sleep before another intense day.
Milda	24	Female	Doctorate student in biological sciences	Lithuania	Undiagnosed	Used Tonusan, a herb-based food supplement that is supposed to minimize tiredness and increases wakefulness. Was used during an intense period of Master's degree.
Mo	21	Male	Media student	The Netherlands	ADD self -diagnosed	Only uses Ritalin when he thinks he really needs it. Uses other recreational drugs regularly.
Neringa	23	Female	Architecture student	Lithuania	Undiagnosed	Used Neurozan food supplement for the brain during an intense period when she was both working and studying.
Petras	20	Male	Veterinary student	Lithuania	Undiagnosed	Used a range of substances. Piracetam to prepare for exams, GABA and theanine to improve work-out results as well as for improved studying. Also used Orange Triad multi-vitamins.
Robertas	20	Male	Medicine student	Lithuania	Undiagnosed	Used methamphetamine to prepare for exams and to study, but found this very unhelpful as he could not concentrate and remember.

(continued)

Table 1. (continued)

Pseudonym	Age	Gender	Occupation	Location of Interview	Diagnostic Status	Substances Used
Roderick	21	Male	Media student	The Netherlands	ADD self-diagnosed, in the process of getting diagnosed	Has been using Ritalin the past 4 months before the interview. Started because he thinks he has ADD. Obtains Ritalin from his younger brother with ADD. Thinks effect is heavy and uses only when necessary.
Simona	22	Female	Master's architecture student	Lithuania	Undiagnosed	Used methamphetamine during an intense period in order to stay awake and work longer hours.
Steponas	26	Male	Unemployed (economics graduate)	Lithuania	Undiagnosed	Used cannabis to have motivation to work.
Vaiva	25	Female	Master's economics student (working)	Lithuania	Undiagnosed	Used various kinds of vitamins and food supplements during intense periods at university.
Viktorija	23	Female	Law student	Lithuania	Undiagnosed	Used lithium and passion fruit extract to help her relax during intense periods and be able to work.

Because the use of prescription pharmaceuticals without a medical diagnosis, as well as the use of other substances our informants used as enhancers, is often illegal, providing oral consent is in the best interests of research participants (cf. Petersen et al., 2015a, p. 668; Vrecko, 2013, p. 5). To ensure anonymity, pseudonyms are used throughout the article.

Below, we group our empirical findings under two recurrent themes: (1) the distinction between enhancement and treatment in practice and (2) what is meant by the term "cognitive" in cognitive enhancement.

Analysis

Treatment Versus Enhancement in Practice

The empirical literature has focused on either therapeutic or enhancement users of prescription stimulants, a separation that our analysis suggests is problematic. Our interviews with both "therapeutic" and "enhancement" users revealed their experiences to be largely similar and the distinction between these categories to be anything but clear-cut. For instance, Dutch informants Jasper (male) and Lotte (female), although both diagnosed with ADD, still obtained Ritalin illegally. Jasper was given Ritalin by a friend's mother, a psychiatrist, with whom he had no therapeutic relationship; Lotte received Ritalin from her ADD-diagnosed sister. Both could have obtained Ritalin from their own doctors, but thought their ways were easier, illustrating how social factors often play a role in obtaining prescription stimulants (Robitaille & Collins, 2016). On the other hand, Roderick (male) and Mo (male), two Dutch students who used Ritalin illegally, had both diagnosed themselves with ADD. Roderick stated: "I know that I already have it. I don't even doubt it. I know that I have it." At the time, Roderick received Ritalin from his ADD-diagnosed brother and was in the process of getting officially diagnosed; Mo was planning to do so as well. Eglė (female) from Lithuania, self-diagnosed with excessive daytime sleepiness, used Modafinil to help her stay focused at work. She bought Modafinil online; because the drug was not licensed in Lithuania at the time of the interview, it would have been too complicated to get it through a doctor. Diagnosed students obtaining prescription stimulants "illegally," and undiagnosed students convinced that their use derives from medical necessity, exemplify the blurry distinction between licit/illicit and therapeutic/enhancement use.

Brian (Dutch, male), diagnosed with ADHD, further exemplifies this blurry line. When asked whether he had a diagnosis, Brian answered: "Yeah, I do, I do. But I don't believe it [laughter]." When asked if he was still using prescription stimulants, he answered:

> Well, I'm using daily now, methylphenidate for the ADHD. But very low doses. The psychologist told me I can kind of prescribe myself. I know about the risks. That́s the agreement we made. I can make my own dose. We talked a little about it, a chit chat, and I normally use it only when I have to do stuff, to read and stuff.

Although Brian did not fully accept an actual diagnosable deficit with his attention, he still used Ritalin when he faced demanding cognitive tasks like studying (cf. Krøll, 2019). Brian had also used methamphetamine and Modafinil bought online for enhancement purposes (Hupli et al., 2016). Even if his use of prescription stimulants could be categorized as therapeutic, which he partly rejected himself, his use of methamphetamine and Modafinil shows that even medical users sometimes rely on other substances in nonmedical ways to enhance their baseline function (Bullard, 2018; Hupli et al., 2016). As shown in Table 1, most of our informants also had prior experiences with "recreational" and broadly defined enhancement drug use.

Another similarity between the groups was that both reported periodic substance use (Hupli et al., 2016). Some diagnosed informants self-medicated, choosing their own doses and deciding when to use

Ritalin. Amelia (female, Dutch, diagnosed with ADD) and above-mentioned Lotte, Brian, and Jasper all reported that they only used medication when they "really" needed it, often during exam periods: "I think a lot of people use it [Ritalin] like David and me. Not standard, but if there is stress, if a lot needs to be learned at once. To make your work a bit quicker and a bit easier actually" (Jasper, Dutch, diagnosed with ADD). Most of the undiagnosed students also reported using substances during exam periods (cf. DeSantis, Noar, & Webb, 2009) or when they needed to absorb large amounts of study material (cf. Krøll, 2019).

Exam periods were also when drugs like Ritalin were reported to be more available. Henry (male, Dutch, undiagnosed) usually used Ritalin during exam periods because that was when his diagnosed friend usually had the pills with him: "Yeah, most often it is during exams but that's also because it's more available because a good friend of mine [diagnosed with ADD] always has it with him during this period, and he gives some to me." One of the main differences between the diagnosed and undiagnosed students was that the former had easier access through their prescriptions. But at least in the Netherlands, access was not really a problem as Amelia (female, diagnosed with ADD) stated: "Everyone knows someone who can get it." Brian also speculated that, in general, illegal nonmedical use had simply turned into legal medical use, which is partly why he got his own legal prescription:

> So, I think the illegal thing went away and now it's legal because a lot of people get diagnosed. That was the reason I got myself diagnosed with ADHD. I knew there was something wrong with me but also if you fill in the test it's so easy to get them legally. I knew I would get them like illegally but legally it's like crazy how easy it is to get them.

Vrecko (2015) also reported that some of his U.S. informants who used prescription stimulants for enhancement obtained Adderall by deceiving clinicians (cf. Petersen et al., 2015a). These findings partly explain the increasing trends of legal stimulant use (Hinshaw & Scheffler, 2014; INCB, 2018), although they problematize the notion that the increase is due to medical reasons. The similarities of the experiences between medical and nonmedical users during cognitively demanding periods shine additional light on how both kinds of users rely on substances to cope with the demands of their academic and working lives. We explore this further in the next section, which focuses on what our informants were trying to improve when they used drugs, some of which are not usually seen as "cognitive enhancers." As stimulants are rarely prescribed in Lithuania, our participants there relied more on "street drugs" and brain supplements (Hupli et al., 2016; Table 1).

The "Cognitive" in Cognitive Enhancement Drugs

Our informants did not see the drugs they used as "cognitive enhancers" which made them "better than well" (Elliot, 2003). They often pointed out that even Ritalin does not directly enhance cognition without effort from those who use it (Hupli et al., 2016). For instance, Lotte (Dutch, diagnosed with ADD) compared using Ritalin to doping in sports: "If you dope, it influences your physical performance directly, but if you take Ritalin it makes you more concentrated, and that doesn't influence whether you are smart or not. You can take Ritalin, and still procrastinate."

Similarly, when asked to compare the use of Ritalin with doping, Jasper answered: "Doping influences everything, it . . . influences the entire sport. Ritalin gives you a little push, a little push from behind." Mo (Dutch, self-diagnosed with ADD) summarized: "If you lack time it is just a useful means to use. So actually it is not cheating, it is more like a tool." Like Lotte, who pointed out that "you can take Ritalin and still procrastinate," Mo recounted a situation when he was studying with Ritalin but without the motivation to study: "But then it does not work, if you don't give a shit. You can take two Ritalins, but then it won't work anyway. You have to be, like: well, ok, I want to learn now."

This again implies that the person using the drug is no less important than the drug itself; the drug might help, but in the end, it is the user who does the work (cf. Greely, 2010). Petras (Lithuanian, male, undiagnosed) throws further light on the relationship between the pharmacological object and its user:

Gabija Didžiokaitė: Do you think that when you take GABA or Piracetam your result is such that you are less responsible for your achievements?
Petras: Yes, it has a contribution, but as I say, it might sound funny, what's more important—the sword or the hand?

In comparing our respective findings, the overlap that struck us most was that users generally saw various substances as technologies, or as Mo stated above, "more like a tool." Other informants also used terms like "tool" [*hulpmiddel* in Dutch; *įrankis* in Lithuanian], "helping thing," "facilitation," "extra help," or "means" [*middel* in Dutch] (cf. Krøll, 2019; Martin et al., 2011). Some diagnosed informants did mention that their use of prescription drugs was to "fix something in their brain." The Dutch informants Lotte (female, diagnosed with ADD), Jasper (male, diagnosed with ADD), Eric, and Bram (both male, diagnosed with ADHD) were able to explain what was "wrong" with their brains as explained to them by their psychiatrists. But when they talked about their own experiences, they still referred to prescription drugs as tools (cf. Petersen et al., 2015b; Schermer, 2007). For example, Frank (male, Dutch, diagnosed with ADD) stated:

> I consider it maybe a more expensive paint for a painter or the more expensive equipment for the artist or the muse for someone or a very good teacher that, I mean if you have a very good teacher and a life-coach of course you are going to write better stuff because you have people that really help you.

Frank implies that when drugs are used instrumentally, they can act as tools to improve performance in the same way as other technologies.

While Frank was diagnosed with ADD the day before he was interviewed, he had used prescription stimulants, amphetamine, and LSD prior to his diagnosis for enhancement purposes, further exemplifying the blurry distinction between therapeutic and enhancement use. Frank also exemplifies the range of drugs used by our informants—from prescription stimulants to LSD and (meth)amphetamine (Table 1; Hupli et al., 2016)—substances that are not usually discussed in the same terms. Although all were used to attain what is broadly understood as "enhancement," it would be inaccurate to argue that they produced the same effects. This is not to say that some practices were more effective than others, but rather to highlight that "enhancement drug use" meant different things to our respondents, depending on what they were seeking to alter or improve. They therefore had different ideas of what, for instance, "cognitive enhancement" means. Puzzled by this, one of us even questioned the Lithuanian recruitment strategy, thinking that the advertisement for research participants required a better definition of "cognitive enhancement" (the ad had stated "improvement of work or studying efficiency" in Lithuanian). After further interviewing, it became apparent that recruitment was not the problem. What we were encountering was "cognitive enhancement in the wild"—involving more substances, practices, and experiences than those usually discussed in the literature.

Our interviewees were rarely aiming to directly enhance cognition, but to enhance other areas reported to improve general performance. This was especially the case with their use of cannabis and psychedelics, drugs that are usually not discussed in the pharmacological neuro-enhancement literature (Franke, Roser, Lieb, Vollmann, & Schildmann, 2016; Hupli, Berning, Zhuparris, & Fadiman, 2019). Steponas (male, Lithuanian, undiagnosed) recalled how he used to smoke cannabis to improve both the ease and quality of his work in menial employment and customer service. The improvement did not directly concern cognition, but his motivation to work (Franke et al., 2016). On the other hand, Marija (female, Lithuanian, undiagnosed) smoked cannabis to sleep better during periods of intensive studying:

> I don't know, I just wanted to leave, disconnect, not just to sit down and listen to music, but I needed to do it in this way [by smoking cannabis]. I know the effect, I know how I would feel, and as I said, I needed to sleep because I needed to get up early, and there were occasions when I wouldn't be able to sleep. So the strong effect, I knew what it is and how it affects me, and especially weed, I know I'll get high and sleep, and I will wake up fresh in the morning. It's like a shortcut, you know.

Karolis (male, Lithuanian, undiagnosed) reported that he had used psychedelics to help him better understand the philosophical issues he was studying in class (cf. Hupli et al., 2016). The usual view of these drugs as merely "recreational" thus requires revision when viewed in the context of reported experiences and recent research (Elsey, 2017). For Steponas, Marija, and Karolis, substance use did not directly enhance their cognitive abilities; by improving motivation (Franke et al., 2016), sleep (Gabe, Coveney, & Williams, 2016), or by altering conscious perception, they aided the cognitive processes of "encoding, storing, and manipulating information" (Ilieva & Farah, 2013b, p. 1).

Even Ritalin was used not only to directly enhance cognition but for a whole range of other purposes such as feeling more awake (Hupli et al., 2016). Jasper (Dutch, diagnosed with ADD) recounted a situation when he forgot to bring Ritalin to an exam: "I once had an exam, maths, and that really sucked. Because I was quite tired then, and it works to uplift. So that is really nice if you are tired." On the other hand, Mo (Dutch, self-diagnosed with ADD) mostly used Ritalin to "get into the mood": "Well, I am really quickly distracted. And if I take Ritalin, look it is also a mental thing. It is just the idea. I am not going to take it for nothing. So I am really going to work, I am going to work for three or four hours."

Alongside seeking to improve individual emotional and cognitive states, some of our informants reported that Ritalin was used to cope with the demands of the education system. Lotte (Dutch, diagnosed with ADD) explained that schools do not cater to students with learning difficulties:

Lotte:	It would be ideal if schools would adjust to people who are not that quick with learning or who have problems focusing, instead of the other way around. Because at the moment it is like this: take a pill and then you're good enough to fit into the oiled machine of education.
Marte Ydema:	So, actually it would not have to be necessary?
Lotte:	Yes, that's my opinion, but that's just not possible in this society.

Despite experiencing adverse effects, Lotte used Ritalin when she found it absolutely necessary to do so (Hupli et al., 2016; Table 1). Similar motives to use pharmaceuticals to deal with educational pressures have been reported by Danish students; according to Krøll (2019), "experiences of urgency and time pressure makes students consider NMUP [nonmedical use of pharmaceuticals] a legitimate or necessary exception." Our informants also reported this sense of time pressure (Hupli et al., 2016), exemplified here by Neringa (Lithuanian, female, undiagnosed) who sought to preemptively improve her general well-being under stress:

Gabija Didžiokaitė:	What did you want from Neurozan [a food supplement for the brain]?
Neringa:	I felt that the semester was complicated, that I have to do a lot of things, because I was working from August to October in addition to my studies, so it's a 6-hr working day, plus studies, and then it becomes a heavy load. Then additional activities. So I would be able to do everything on time, so I wouldn't only go to work and somewhere, and then postpone everything else . . . . So that everything wouldn't pile up, because, after one exam session I only slept and ate for 3 days, and for half a year I couldn't deal with my psychological state. So, I just don't want to come to that again.
Gabija Didžiokaitė:	So, it's sort of like . . .
Neringa:	For precaution.

The technologies were often used to keep up with societal pressures and expectations. This type of "indirect" enhancement was exemplified by our participants in Lithuania such as Neringa, Marius, and Vaiva who used brain supplements and vitamin complexes to ensure performance at work or in their studies. Such "soft enhancers" (Maier & Schaub, 2015) were sometimes perceived as alternatives for healthier, wholesome lifestyles which our interviewees otherwise struggled to achieve. Some emphasized that if they led healthy lifestyles—if they slept enough hours, ate enough fruits and vegetables, exercised and meditated—they would not need the help of neurotechnologies:

> I think that if I would watch my nutrition, if I would eat all the good things, vegetables, everything perfectly, then maybe I wouldn't use [Neurozan], but now in the morning it's a sandwich, then running home [from university], make something [to eat], so I don't think it's good nutrition, that's why I use Neurozan. (Marius, Lithuanian, male, undiagnosed)

Vaiva (Lithuanian, female, undiagnosed) echoed this sentiment in her account of multivitamin use, further pointing to how substances are used to "relieve a sense of urgency and re-gain temporal agency" (Krøll, 2019):

> The need itself comes from the feeling that you are not keeping up with all the things you need to do, you're not sleeping enough, not eating enough and you don't want to lack energy. My job now is really intense, there's very little time left, sometimes I'm not going out for lunch, so I bring some sandwiches, you don't always have vegetables, so I thought that maybe some things are missing.

These examples show that "cognitive enhancement" has more dimensions to it than are generally perceived in the academic literature. Our interviewees used a broad range of drugs—not only prescription stimulants—as pharmacological neurotechnologies to alter their emotional and cognitive states, to make them more motivated to work and study, or even to aid relaxation after work so that they would be better prepared to work the next day. As other studies among students have found, "the need to enhance is a response to contextual demands linked to ecological pressures, evidencing its functional role in the daily routines of users" (Vargo & Petróczi, 2016, p. 779)—which requires further discussion and research.

Discussion

In our information age, individual cognitive capacities need to fulfill increasing demands, especially in highly technological contexts (e.g., Kegan, 1994; N. Rose, 2007b). However, it can be difficult to establish what constitutes "a normal level" of "cognitive performance," what constitutes "enhancement" of that normal level by pharmacological means, and with what kind of "cognitive trade-offs" (see De Jongh, Bolt, Schermer, & Berend, 2008; Outram, 2011). We agree with Greely et al. (2008) that the so-called enhancement drugs "should be viewed in the same general category as education, good health habits, and information technology—ways that our uniquely innovative species tries to improve itself" (p. 702), although we take a broader perspective on what those drugs are (Hupli et al., 2016; Singh et al., 2014).

While we mainly focused on stimulants in our discussion of the literature—prescription stimulants being the most prevalent in our sample (Hupli et al., 2016)—other substances like psychedelics (e.g., Elsey, 2017) would require similar attention. The so-called psychedelic microdosing is often compared to using drugs like Ritalin (Hupli et al., 2019) and is an emerging trend among young people in Amsterdam (Nabben, Luijk, & Korf, 2018). Similarly, blurry boundaries have been found for cannabis, which some of our interviewees used as an "indirect cognitive enhancer" (Franke et al., 2016; Hupli et al., 2016). Medical cannabis is reported to hold therapeutic potential for treatment-resistant ADHD

among adults (Hupli, 2018), while "recreational" cannabis remains the most widely used "illegal substance" among young people in Europe (EMCDDA, 2019).

Many of our informants did not experience Ritalin as directly enhancing cognition (Hupli et al., 2016). But as in other studies of stimulants, they reported improved mood and increased interest in performing tasks (e.g., Petersen et al., 2015b; Smith & Farah, 2011, pp. 723–724; Vrecko, 2013). Surveys among students have shown that those who engage in off-label prescription drug use do not solely aim to improve their cognitive abilities, but "for boosting drive, energy, and mood" (Ilieva & Farah, 2013b, p. 5). We thus speculate that what has been epidemiologically categorized as recreational or illegal drug use has partly been for "enhancing suboptimal performance" (Conrad & Potter, 2000, pp. 273–274) and/or self-medication for study and work-related stress (e.g., Maier, Haug, & Schaub, 2015; Schelle et al., 2015), further complicating simple categorizations (Bullard, 2018). The complexity of our era—between "cosmetic psychopharmacology" (Kramer, 1993) and "pharmageddon" (Healy, 2012)—requires research on multiple levels (Chatwin et al., 2017) and sensitivity to go beyond static categories.

Ascertaining whether "the barriers between enhancement and treatment are already breaking down" (Outram, 2010, p. 201), as our analysis partly suggests, will require further empirical research, including on local processes of pharmaceuticalization. Legal stimulants were more commonly used by our informants in the Netherlands, reflecting their greater use in Dutch society (INCB, 2018). While this finding suggests different levels of pharmaceuticalization in the two countries we studied, it could also have been influenced by our recruitment strategies: through snowball-sampling in the Netherlands and through an advertisement in Lithuania (Hupli et al., 2016). In addition, our reliance on self-reported diagnoses, and lack of robust screening for our undiagnosed informants on whether they would fit diagnostic criteria for ADHD (Arria et al., 2011), may limit the validity of our empirical findings.

Nevertheless, our analysis has broader implications for (enhancement) drug research, policy, and local processes of pharmaceuticalization. Despite attention in the bioethical literature on how to regulate the enhancement use of prescription stimulants (e.g., Bostrom & Sandberg, 2009, pp. 331–332; Greely et al., 2008), there have been no attempts on the (inter)national drug policy level to change the current paradigm of access to prescription pharmaceuticals—let alone illegal substances—for enhancement purposes (Hall & Strang, 2017). Although the distinction between therapy and enhancement is blurry in everyday practice, it does have numerous important consequences, including eligibility for medical services and insurance coverage (e.g., Daniels, 2000). Enhancement use can also have legal consequences as drug use that goes beyond medical or scientific purposes remains not only prohibited but punishable in many countries (see Bublitz, 2016).

Rather than using drugs to go beyond "normal species-functioning" (Daniels, 2000), our interviewees reported using substances to mitigate time and other societal pressures (Krøll, 2019). While research, most notably in the U.S., frames similar practices as the "illegal use of ADHD stimulants" (DeSantis & Hane, 2010), our informants used stimulants and other drugs as tools or technologies. This is in line with studies that have arrived at similar conclusions about the instrumental (Müller & Schumann, 2011) use of drugs in various real-life situations (Lende, Leonard, Sterk, & Elifson, 2007; Silva, Kecojevic, & Lankenau, 2013). Like our informants, we suggest framing "enhancement drugs"—illicit or licit—as "pharmacological neurotechnologies" (Farah et al., 2004). "*Fixers*, *facilitators*, *resources*" or "just plain *pills*" have also been suggested instead of "enhancers" (Martin et al., 2011, cited in Coveney et al., 2011, p. 391, original italics). More pressingly, terms like "emergency strategy" and "life jacket" in Danish students' descriptions of nonmedical pharmaceutical use points to their utilization in various "crises of everyday life" among young people (Krøll, 2019), which requires more attention.

Conclusion

Our analysis suggests that the typical distinction between "therapeutic/enhancement" and "licit/illicit" users is far from clear-cut and that it is problematic to speak of therapeutic and enhancement use as if these categories are fixed. In our sample of Dutch and Lithuanian university students, "therapeutic" users often turned to other drugs for enhancement purposes or received their medication outside of professional channels; "enhancement" users were sometimes convinced that their use was medically necessary due to a self-diagnosed pathology. The therapy/enhancement distinction may thus lead researchers and policy makers to overlook important factors when considering "enhancement drug" use in general, their effects in real-life situations, and the bioethical implications for prescription practices and general drug policy. The question that needs to be asked is not whether individual substance use can be categorized as treatment, enhancement, or as recreational but whether and how the drug benefits or harms the individual's quality of life.

Across user groups, the felt need to use pharmacological neurotechnologies often originated from societal pressure. The ability of substances to produce effects that would enhance cognition beyond "normal" levels appears exaggerated; our informants used them as tools to keep up with societal norms and expectations. We further found university students in the Netherlands and Lithuania using these technologies not only to improve cognition but to affect a wide array of emotional and cognitive states. Our findings, together with other studies, challenge the terms "cognitive" and "enhancement" in cognitive enhancement drug use. There is a need for a more inclusive and context-dependent approach, for instance, by framing both licit and illicit drugs as tools, instruments, or pharmacological neurotechnologies. Growing pharmaceuticalization requires local empirical research that includes a focus on "illicit" substances as well as broader bioethical debate over the benefits and harms of current prohibitive drug policies that mostly exclude pharmaceutical drugs.

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PUBLICATION V

Cognitive enhancement with licit and illicit stimulants in the Netherlands and Finland: what is the evidence?

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Cognitive enhancement with licit and illicit stimulants in the Netherlands and Finland: what is the evidence?

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Abstract

Purpose – *European studies have shown lower prevalence rates of prescription stimulant use for cognitive enhancement, especially among student populations, compared to North America. This difference requires more cross-country research of the various factors involved. To find out whether other parts of the globe are witnessing similar increases in extra-medical stimulant use, and how this might relate to cognitive enhancement, requires empirical study of local contexts. This paper aims to argue that the academic and public discussion on cognitive enhancement should consider the specific country context of drug policy and research and rethink which drugs are included under the term cognitive enhancement drugs.*

Design/methodology/approach – *This paper offers a general review and a sociological country comparison between the Netherlands and Finland, focusing not only on prescription stimulants used to treat attention deficit hyperactivity disorder but also illicit amphetamines among young adults and methylphenidate use among Dutch and Finnish participants of the Global Drug Survey. This paper emphasises sociocultural perspectives and the importance of context in cognitive enhancement in general as the line between therapeutic and enhancement use can often be blurred. Data is drawn from global, European and national sources, including the International Narcotics Control Board, European Monitoring Centre for Drugs and Drug Addiction and Global Drug Survey.*

Findings – *There are hardly any national empirical studies done on cognitive enhancement drug use in Finland. On the other hand, there have been studies in the Netherlands showcasing that the use of prescription stimulants and other drugs for enhancement purposes is something that is happening among young people, albeit yet in a relatively small scale. Illicit and licit stimulant use and drug policy action in relation to cognitive enhancement drugs in the two countries varies, emphasising the importance of country context.*

Originality/value – *Given that cross-country research is scarce, this general review provides one of the first glimpses into cognitive enhancement drug use by comparing the country context and research in Finland, where the phenomenon has not been studied, with the Netherlands, where the topic has received more research and public attention. Further research areas are suggested.*

Keywords *Pharmacological neuroenhancement, Bioethics, General review, Country context, Country comparison, Drug policy, Nonmedical use of prescription drugs, Prescription stimulants*

Paper type *General review*

1. Introduction

In the past 20 years, pharmacological cognitive enhancement (PCE), defined by Maier and Schaub (2015, p. 2) as using "prescription drugs, other illicit drugs, or alcohol for the purpose of enhancing cognition, mood, or prosocial behavior in academic or work-related contexts" has created increased research and bioethical discussion (Ter Meulen *et al.*, 2017; Chatwin *et al.*, 2017). The PCE literature has mainly focused on prescription stimulants like methylphenidate (Ritalin), dextro-amphetamine (Adderal) and modafinil (Provigil) as "cognitive enhancers", especially among healthy university students in the USA and UK (Arria and Du Pont, 2010; Ragan *et al.*, 2013; Maier and Schaub, 2015).

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Singh and Kelleher (2010, p. 5) argued already ten years ago that "the use of stimulants as neuroenhancers appears to be a growing trend among university students around the world". However, increased research and media interest into the phenomenon have inflated "a neuroenhancement bubble" (Lucke *et al.*, 2011) as the use of prescription stimulants as "cognitive enhancers" is often reported as widespread and their efficacy overestimated (Partridge, 2017). Overestimations about prevalence and efficacy might generate more use as young people might consider their use as a norm (McCabe, 2008; Outram, 2010). It is, therefore, important that the discussion and research around PCE is based on empirical knowledge about their actual prevalence and user effects to avoid giving too optimistic visions of their potential to enhance human abilities (Schleim and Quednow, 2017; Hupli *et al.*, 2016; 2019a; Partridge *et al.*, 2011).

At the same the time, psychotherapeutic use of prescription stimulants for attention deficit hyperactivity disorder (ADHD) has increased globally (Scheffler *et al.*, 2007). Singh *et al.* (2013, p. 2) argue that the globalisation of ADHD and the use of stimulant medication for cognitive enhancement have "raised fresh concerns about the validity of ADHD diagnosis and the ethics of stimulant drug treatment" (Hinshaw and Scheffler, 2014). There has also been increased diversion of prescription stimulants for extra-medical purposes, at least in North America (McCabe *et al.*, 2014); however, how much of this extra-medical use is specifically for PCE remains unclear due to methodological and conceptual differences across studies (Arria and Wish, 2006; Maier and Schaub, 2015).

Whether other parts of the globe are witnessing an "'[A]mericanization' of ADHD models of treatment, with an emphasis on medication as a primary intervention" (Hinshaw and Scheffler, 2014, p. 135), and how this emphasis on pharmacological treatments relates to PCE use, requires more cross-country research and increased attention from medical professionals, policy-makers and bioethicists (Maier *et al.*, 2018; Singh *et al.*, 2013). This general review argues that categorising prescription drug use as "therapeutic" is sometimes as problematic as calling the use that seems to go beyond therapy an (illegal) "enhancement" (Moncrieff, 2008; Healy, 2012; Bullard, 2018). Especially as, for instance, methylphenidate's efficacy in both cases seems to be limited (De Jongh *et al.*, 2008; Repantis *et al.*, 2010; Storebø *et al.*, 2015).

The review focuses on PCE use and especially on prescription stimulants used to treat conditions like ADHD, but also explores illicit stimulant use by highlighting amphetamine use among young adults in the Netherlands and Finland. It then offers a comparative analysis of existing empirical research on PCE in the two European Union (EU) countries. The focus is both on licit and illicit use of stimulants as the distinction between therapy/enhancement and licit/illicit can be blurred (Bullard, 2018). For instance, the authors of the "Human Enhancement" study by the European Parliament Science and Technology Options Assessment (STOA, 2009, p. 85) have stated that:

> [...] because of the fine lines involved in the diagnosis of ADHD, which require normative judgments that are highly sensitive for diverging opinions, it is often hard to judge whether Ritalin™ is used as a therapeutic or an enhancing agent.

This seems to be the case among young users as well; a qualitative study combining 35 user reports from the Netherlands and Lithuania found out that ADHD-diagnosed students sometimes used other drugs for enhancement purposes and undiagnosed students were occasionally convinced that their use of Ritalin was due to medical necessity (Hupli *et al.*, 2019a).

Data for this review is drawn from recent reports of the International Narcotics Control Board (INCB), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Global Drug Survey (GDS). Focus with INCB data is on all stimulants, with EMCDDA data on amphetamine use by young adults and with GDS on methylphenidate. The data is presented in Table I and discussed in more detail below. Academic literature on the topic is

Table I Use of medical stimulants, illicit amphetamine and methylphenidate in Finland and the Netherlands according to INCB, EMCDDA and GDS data between 2014 and 2018

Study	*Finland*	*The Netherlands*
INCB 2017 (all stimulants 2014-2016)	2.26 S-DDD	9.10 S-DDD
INCB 2018 (all stimulants 2015-2017)	2.53 S-DDD	9.03 S-DDD
EMCDDA 2017 (amphetamine use in the past year*)	2.4%	3.1%
EMCDDA 2018 (amphetamine use in the past year*)	2.4%	3.9%
GDS 2017 (methylphenidate use in the past 12 months)	8% (N = 1,339)	6.8 % (N > 3,300)
GDS 2018 (methylphenidate use in the past 12 months)	8% (N = 2,184)	4.4 % (N > 3,400)

Notes: * = age group 15-34 years; S-DDD = defined daily dose for statistical purposes; INCB = International Narcotics Control Board; EMCDDA = European Monitoring Centre for Drugs and Drug Addiction; GDS = Global Drug Survey (data provided by Prof Adam Winstock)

also presented when comparing research on cognitive enhancement drug use between the two countries. As PCE has not been researched in Finland, and cross-country research is scarce (Hupli *et al.*, 2019a; Maier *et al.*, 2018), this review provides one of the first empirical glimpses into the phenomena within the Finnish context while expanding the review of the Netherlands (Schermer, 2016). This comparison between the countries where the debates and practices of cognitive enhancement drug use seem to be at different stages is meant to stress the importance of context of drug use and policy (Duff, 2011). The cross-country comparison acts as a continuation of the recent emphasis in the cognitive enhancement literature on sociocultural factors (Jotterand and Dubljević, 2016; Maier *et al.*, 2018) and the importance of "context" in cognitive enhancement in general (Shook and Giordano, 2016). Thus, it is argued that country context matters when it comes to cognitive enhancement drug use. This context is elaborated below in relation to the national drug policy context and actions on cognitive enhancement drugs in both countries and followed by presentation and discussion of the available empirical data on stimulants, and especially for cognitive enhancement.

2. Drug policy context in Finland and the Netherlands

Since the 1970s, Finland and the Netherlands have followed very different trajectories in their drug policy approach. As both countries are also EU member states, drug policy harmonisation within the EU is another factor to consider in that trajectory (Boekhout van Solinge, 1999; Chatwin, 2011) but lies beyond the scope of this present review.

Finland criminalised drug use around the same time as the Netherlands reformed their Opium Act in the 1970s. Thus, Finland, together with other Nordic countries, is argued to represent a more prohibitionist drug policy culture (Hakkarainen *et al.*, 2007) compared to the Netherlands (Boekhout van Solinge, 1999; Chatwin, 2011). The Dutch drug policy system has mainly been based on a public health and harm reduction approach (Boekhout van Solinge, 1999). An example of this is that personal use and possession of "soft drugs" is *de facto* decriminalised, i.e. Public Prosecution Service does not prosecute for the possession of small amounts (5 g or less) of cannabis herb or resin (Government of the Netherlands, 2019). Cannabis has been sold in "coffee shops" and legally purchased in these outlets by adults over the age of 18 years (Chatwin, 2011). Large-scale cultivation of cannabis, however, has remained illegal.

Since the 1990s, Finland has followed a so-called dual-track drug policy (Hakkarainen *et al.*, 2007) by offering some harm reduction services while otherwise maintaining certain types of drug use as a criminal offense. These harm reduction services have included, for example, some forms of opiate-replacement therapy and needle exchange programmes. Partly due to the different legal status of drug use in the two countries, harm reduction services provided in the Netherlands include safe consumption rooms and drug checking services

(also called pill testing), both of which are currently not yet implemented in Finland. These are important factors to consider especially as more liberal drug policies can potentially impact the willingness of users to seek help (Benfer *et al.*, 2018).

2.1 Drug policy action on human enhancement drugs

The Finnish National Advisory Board on Social Welfare and Health Care Ethics has not considered human enhancement in general as an emerging discussion point (Pustovrh and Mali, 2014). On the other hand, the issue of human enhancement has been engaged with in the Netherlands on the governmental level (The Health Council of the Netherlands, 2003; Schermer, 2016). The 2003 report from the Health Council of the Netherlands on Human Enhancement discusses also pharmacological enhancement. The report (2003, p. 5) states that "[I]*n* principle, the government should adopt a neutral position towards ideas about personal well-being which are at the root of this use of enhancers". The report continues that the government does:

> [. . .] have a major responsibility to ensure that adequate information is provided, to protect minors and legally incompetent individuals, to safeguard quality, to protect public goods in so far as the use of enhancers constitutes a threat to them, to monitor access to enhancement and to encourage a public discussion (The Health Council of the Netherlands, 2003, p. 5).

However, despite the early government interest and more extensive research on the topic in the Netherlands compared to Finland the discussion on human enhancement, let alone cognitive enhancement, "has not really caught on beyond a small group of researchers, scientists, and philosophers" (Schermer, 2016, p. 190) According to Schermer (2016), the increasing medical use of stimulants among children in the Netherlands has raised more concerns and public debate than cognitive enhancement use by adults.

The issue remains marginal in the Finnish context compared to the Netherlands, as it has not reached governmental discussion or even national research level. Few medical professionals in Finland have estimated that the use of ADHD medications for cognitive enhancement might increase (Salvén, 2010; Vierula, 2016), although PCE has not been mentioned as an emerging issue. Thus, PCE has not gained attention in Finland, at least in governmental discussions and national drug research. On the other hand, despite the Dutch government report calling for increased public discussion on the topic of human enhancement already in 2003, the public debate in the Netherlands has also been limited to academics working in this field (Schermer, 2016). Arguably, the topic of PCE appearing in Dutch public debate has not led to changes in Dutch drug policy, which has now moved towards a more restrictive approach (Chatwin, 2011). Despite the relatively liberal drug policies in the Netherlands, the Dutch public and Dutch physicians remain suspicious of cognitive enhancement (Timmer and Glas, 2012; in Schermer, 2016). Thus, while some scholars have called for legal regulation of cognitive enhancers used by healthy people (Greely *et al.*, 2008; Dubljević, 2013), this does not currently seem to be on the government's agenda in either country.

3. Comparing licit and illicit stimulants for pharmacological cognitive enhancement in the Netherlands and Finland

3.1 Medical stimulant, amphetamine and methylphenidate use in Finland and the Netherlands

Since the turn of the millennium, prescription use of stimulants has increased, especially among children and adolescents both in Finland (Puustjärvi *et al.*, 2012) and the Netherlands (Van den Ban *et al.*, 2010; Hodgkins *et al.*, 2011). For example, a recent Finnish study found that between 2006 and 2016, the use of ADHD medication increased five-fold among boys and six-fold among girls (Vuori *et al.*, 2018; International Narcotics Control Board, 2018).

However, the reported medical use of stimulants is still relatively low in Finland compared to other Nordic countries (Zöega *et al.*, 2011) as well as the Netherlands (International Narcotics Control Board, 2018; Table I).

According to the INCB (2018), which measures the use of psychotropic substances in different countries, the amount of "all stimulants" per thousand inhabitants per day in the Netherlands was 9.03 between 2015 and 2017, while in Finland, the calculated amount was only 2.53 (S-DDD = defined daily dose for statistical purposes; Table I). Compared to the previous INCB (2017) report covering years 2014-2016, the amount slightly decreased in the Netherlands, from 9.1 to 9.03, while during the same period, increased in Finland from 2.26 to 2.5 (Table I). The highest calculated amount between 2015 and 2017 was in the USA (43.82), followed by Belgium (33.88) and Iceland (26.54) (International Narcotics Control Board, 2018).

In addition to pharmaceutical stimulants, illicit stimulants, like amphetamine, cocaine and methylenedioxy-methamphetamine (MDMA), are the most prevalently used illicit drugs amongst young people in Finland and the Netherlands, after cannabis (European Monitoring Centre for Drugs and Drug Addiction, 2019). The use of amphetamine has remained stable among 15-34-year olds in Finland (2.4 per cent in 2017 and 2018) but increased from 3.1 per cent in 2017 to 3.9 per cent in 2018 in the Netherlands (European Monitoring Centre for Drugs and Drug Addiction, 2018, 2019; Table I).

According to recent data from the GDS, 8 per cent of the Finnish participants reported using methylphenidate in the past 12 months in 2017 (total *N* = 1,339) and in 2018 (*N* = 2,184) (Table I; GDS Finland country reports 2018; 2019). Methylphenidate use among Dutch participants was 6.8 per cent in 2017 (*N* = 3,300) and 4.4 per cent in 2018 (*N* = 3,400) (Table I; GDS Netherlands country reports 2018, 2019).

3.2 Illegal and legal stimulant use for cognitive enhancement in Finland and the Netherlands

Whether the use of stimulants reported in INCB, EMCDDA and GDS data is for cognitive enhancement or other purposes remains unknown. The latest national drug survey in Finland found that extra-medical use of pharmaceuticals (sedatives, sleep aids and analgesics) increased from 2.8 per cent in 1992 to 6.7 per cent in 2018 (Karjalainen *et al.*, 2019). However, prescription stimulants are not monitored in the national household survey, and there is a lack of published data on extra-medical use of prescription stimulants in general. This is despite the fact that extra-medical use of prescription pharmaceuticals is now the second most commonly reported drug type after cannabis (Karjalainen *et al.*, 2019). More to that, pharmaceuticals also play an increasing role in drug-related deaths in Finland (Rönkä, 2019).

Only one study has looked at "enhancement drug use" in Finland; a nonpeer-reviewed survey commissioned by the Finnish Association for Substance Abuse Prevention (EHYT, 2017) investigated medication and drug use in working life. The survey found out that 15 per cent (total *N* = 1,000) of the Finnish respondents had used prescription pharmaceuticals, mostly opioids, to improve work performance and/or cope with the demands of their employment. Interestingly, not a single participant had previously used ADHD medications, while 2 per cent had used unspecified illegal drugs (EHYT, 2017).

As reviewed by Schermer (2016), there have been more extensive studies in the Netherlands exploring the use of stimulants, and other drugs, specifically for PCE purposes, and especially amongst students and medical professionals. The aim of this complementary review is to present few studies not mentioned by Schermer. For instance, a national survey conducted in the Netherlands on the use of illicit and licit drugs already in 2001 showed that the use of "smart drugs[1]" was highest among 20-24-year olds (12.6 per cent). The survey by Abraham *et al.* (2002) also enquired about the use of performance

enhancement drugs, which included stimulants (for instance, amphetamines, cocaine and caffeine) "taken in high doses to enhance performance" with a lifetime prevalence rate of 0.7 per cent. As reviewed by Schermer (2016), a national online survey in the Netherlands (Ganpat *et al.*, 2009) later found that 7.1 per cent of 14- to 17-year-olds had also tried prescription medications in an extra-medical way, while 2 per cent had tried stimulant medication, which they received mostly from friends. Another survey study among Dutch university students found that the use of prescription, illicit and lifestyle drugs (i.e. alcohol, nicotine, caffeine) for cognitive enhancement was 1.7, 1.3 and 45.6 per cent of the sample (N = 1,503), respectively, which is relatively low compared to prevalence rates in other European countries (Schelle *et al.*, 2015; Maier and Schaub, 2015; Schermer, 2016). Most recently, Maier *et al.* (2018) found increased PCE use among Dutch GDS participants, although the increase was moderate in comparison to several other countries in their study.

The survey by Abraham *et al.* (2002, p. 218) also found that use of "smart drugs" was especially high in the same age group in Amsterdam (21.5 per cent) compared to the same age group in Rotterdam (6.3 per cent). According to an annual mixed-method study that monitors the use of different substances among young people in Amsterdam, the extra-medical lifetime-use of methylphenidate (Ritalin) doubled from 2007 to 2011 (Benschop *et al.*, 2011), indicating the need to consider regional differences inside countries as well.

4. Discussion and conclusions

This general review highlights two findings: firstly – unlike in Finland – cognitive enhancement drugs have been researched in the Dutch context already from early 2000s onwards, and secondly, regional differences between and inside these countries show the need for more detailed research on the topic. Overall, reviewing available evidence shows differences in research and governmental action on cognitive enhancement between the two EU countries showcasing how cognitive enhancement differs depending on the context.

To this date, "getting smart by prescription" drugs (Vierula, 2016) does not seem to be common practice in Finland, although there is insufficient research data to confirm the prevalence or practices of PCE one way or another. As mentioned, national research on extra-medical use of prescription drugs has focused on the use of sleeping pills, tranquilisers and pain medications (Karjalainen and Hakkarainen, 2013; Karjalainen *et al.*, 2017, 2019), which are rarely discussed as "enhancement drugs". Thus, what is included under the term "enhancement drugs" would require rethinking (Hupli *et al.*, 2016), as prescription opioids are reportedly used in working life in Finland more than prescription stimulants (EHYT, 2017). Students in the Netherlands have also reported the use of several drugs for "cognitive enhancement", from prescription to illicit and lifestyle drugs like nicotine (Hupli *et al.*, 2016; 2019a; Schelle *et al.*, 2015; Schermer, 2016). Therefore, research in this field needs to consider other drugs used for cognitive enhancement purposes beyond prescription stimulants. For instance, cannabis as a cognitive enhancer among students (Franke *et al.*, 2016) and as a potential pharmacotherapy for ADHD (Hupli, 2018) requires further attention, as cannabis remains the most used illicit drug among young people in the two countries (European Monitoring Centre for Drugs and Drug Addiction, 2019). In addition to cannabis as a cognitive enhancer, so-called psychedelic microdosing (Hupli *et al.*, 2019b) has been identified as an emerging trend among young people in Amsterdam (Nabben *et al.*, 2018), further making the argument that cognitive enhancement takes different forms depending on the context.

Whether stimulant use reported in the INCB data is solely for medical purposes also requires a closer inspection. INCB, EMCDDA and available GDS data mainly report prevalence of use and not intention, at least beyond assumed medical (licit) and "recreational" (illicit) use. Therefore, to what extent the reported licit and illicit stimulant use

is for PCE purposes remains an open empirical question. Moreover, this review of available data demonstrates a need for more detailed data collection that goes beyond mere prevalence of use, whether for licit or illicit purposes (Nadler and Reiner, 2010; Lucke, 2012). As this review focused mainly on pharmacological means of enhancement, future cross-country research should explore other neuroenhancement technologies and evaluate their prevalence, safety and efficacy (Massie *et al.*, 2017).

Increasing prescription stimulant rates in both countries occurred approximately around the same time that global trends for prescription stimulants were on the increase (Scheffler *et al.*, 2007). This is argued to provide evidence for an ongoing process of pharmaceuticalisation (Williams, *et al.*, 2011; Coveney *et al.*, 2011; Hupli *et al.*, 2019a) or as some authors frame it, "Americanisation" of ADHD treatment (Hinshaw and Scheffler, 2014; Daniels, 2016). This seems to be increasingly prevalent in Europe (International Narcotics Control Board, 2018, p. 53), and increasing or high medical stimulant rates suggest pharmaceuticalisation of treating ADHD and other conditions in Finland and the Netherlands, requiring public debate about stimulant use in general. On the treatment side, the increased use of stimulants for ADHD has been criticised for overemphasising the biological basis of attention disorders over social and environmental factors (Hinshaw and Scheffler, 2014), leading to possible overuse of "chemical cures" (Moncrieff, 2008). While underdiagnosing and barriers to pharmacological therapies are also factors to consider (Asherson *et al.*, 2012), extra-medical stimulant use for cognitive enhancement presents a possible driver to consider behind overall stimulant use.

When it comes to overall stimulant use in both countries for cognitive enhancement and therapy, by including a focus on "illicit stimulants", this review argues that there are other processes at play besides pharmaceuticalisation (Abraham, 2010). Normalisation of drug use is one potential explanation (Hakkarainen *et al.*, 2007), and as we discovered, young users in the Netherlands and Lithuania reported several reasons for their instrumental use of cognitive enhancers, which included the use of amphetamines and other illicit drugs (Hupli *et al.*, 2016, 2019a). As shown, amphetamine use among Dutch young people has increased while staying relatively stable in Finland the past two years (European Monitoring Centre for Drugs and Drug Addiction, 2019; Table I). At the same time, while Maier *et al.* (2018) found that PCE use increased between 2015 and 2017 in the Netherlands, according to more recent GDS data, at least methylphenidate use decreased in the Netherlands, while Finland witnessed an increase in the same period. While the extent of this use for PCE purposes remains unknown, what is known is that legal restrictions have not prevented illicit use of stimulants among young people in Finland nor the Netherlands for enhancement or other purposes, demonstrating the need to evaluate the effectiveness and ethics of punitive drug policies (Bublitz, 2016; Zigon, 2015).

Even though GDS is not nationally representative (Barratt *et al.*, 2017), these recent trends indicate at minimum a need for more detailed research and public discussion in this field. And, while it is not claimed that the brief country contextualisation provided in this review was exhaustive, the insights from this kind of comparative analysis can draw out a more nuanced picture of cognitive enhancement drug use. This can guide policy-making and future research in this emerging field, especially as the line between therapeutic and enhancement use can often be blurred (McKeown, 2017; Bullard, 2018; Hupli *et al.*, 2019a).

Note

1. Defined as "a class of synthetic and natural supplements taken to enhance cognitive function".

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Further reading

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