

**The off-prescription use of modafinil and methylphenidate:**

**Perceived risks, benefits, and impact on cognitive function.**

**DOCTOR OF PHILOSOPHY (PhD)**

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# **DISSEMINATION OF FINDINGS**

**Publications**

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**Conference presentations**

Teodorini, R. D. (2019, October, 23-25). *The Off-prescription use of modafinil: an online survey of perceived risks and benefits* [Conference presentation]. Lisbon Addictions, Lisbon, Potugal.

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# **ABSTRACT**

Many psychoactive pharmaceuticals, in addition to their intended clinical benefits, can also enhance cognitive functions in healthy populations. Popularity in cognitive enhancing drug (CED) use has raised concerns about its possible risks and harms. Modafinil and methylphenidate are, perhaps, the most consumed CEDs. This thesis sought to understand more about the modafinil and methylphenidate off-prescription user and whether they are self-medicating for poor cognitive performance or enhancing. Study 1, an online survey advertised on forum sites to reach the CED-using and student populations, revealed that CED users are mostly male, North American or British, educated, employed and in their mid-20s. Use of CEDs was associated with recreational drug use and psychiatric disorders. Daily use of modafinil was reported as providing the most benefits and that benefits increased with more frequent use. Modafinil was perceived as safe, whereas methylphenidate was perceived as more dangerous. Study 1 could not assess whether CED-using respondents were self-medicating or enhancing, therefore, Study 2, an online survey, addressed this via the Cognitive Failures Questionnaire (Broadbent, Cooper, Fitzgerald & Parks, 1982), the General Procrastination Questionnaire (Lay, 1986), and the Adult ADHD Self-Report Scale, in addition to questions on CED and recreational drug use. The results revealed that the CED-user groups reported having problems with inattention and procrastination compared with controls. Study 3, an experimental study, sought to verify this objectively. The cognitive performance of 43 reported off-prescription users of modafinil and methylphenidate and 47 controls was tested using the Arrow Flanker Task (Ridderinkhof, van der Molen, Band & Bashore, 1997) and the Antisaccade task (Hallett, 1978), together with the self-report Behaviour Rating Inventory of Executive Function - Adults questionnaire (Gioia, Isquith, Guy & Kenworthy, 2000). The results indicated that the CED-user group demonstrated good cognitive performance and therefore were likely to be enhancing rather than self-medicating. The implications of these findings are discussed in relation to future research, ethical debates, and government policy.

# **CHAPTER ONE**

## **1.1 Introduction**

The Information Age makes increasing demands on individuals, with the pressure to develop new and existing skills calling upon ever-increasing cognitive abilities. Economic recessions may also result in greater competition for jobs and, perhaps, greater demands on individuals than they feel that they can meet in order to gain employment and succeed in life. In addition to this, individual differences in cognitive abilities and group differences in cognition result in variations in the speed and ability with which individuals acquire skills and information, and this may impact upon the possible opportunities and directions their lives may take. Challenges such as these have led individuals to seek, and find, a broad range of interventions allowing them to push beyond their natural cognitive abilities. Cognition involves the processes of perception, information processing, selecting information via attention, manipulating that information (if needed) through working memory and retaining it in memory to be later retrieved to guide decisions, reasoning, and behaviour (Bostrom & Sandberg, 2009). Of the many aspects of attention that have been identified in the literature, focused, sustained attention has been the aspect most implicated in learning throughout life (Fisher & Kloos, 2016). Focused, sustained attention refers to the ability to maintain undivided conscious processing of a task or stimulus for a given period of time (Unsworth & Robison, 2019). Working memory refers to the ability to maintain information in the mind whilst performing complex mental tasks (Baddeley, 2010). These processes of cognition, specifically attention and working memory, are considered to be elements of executive function (Logue & Gould, 2013). Executive functions can be seen as top-down cognitive processes required for higher order cognitive function (Diamond, 2013; Logue & Gould, 2014). Before exploring cognitive enhancement, it is first important to understand the executive functions for which enhancement is desired. The following section discusses executive functions in detail.

### **1.1.1 Executive functions**

Barkley (2001) proposed that executive functions are self-directed actions used for self-regulation. He explained that self-regulation is the ability to resist reactive behaviour, apply self-control and consider the value of modifying one’s behaviour for the purpose of altering one’s future outcomes. Although there is some agreement in the identification of three executive functions, namely, working memory, behavioural response inhibition and cognitive flexibility (Barkley, 2001; Diamond, 2013; Lehto et al., 2003; Miyake et al., 2000), Barkley (2001) proposed that working memory comprises of two executive functions, verbal, and non-verbal working memory, and he also argued for an additional executive function, which he termed self-regulation of affect/ motivation/arousal. He noted that these executive functions have evolved from being overt, publicly observable behaviours to covert, internalised behaviour to the self for the purposes of self-regulation. Barkley (2001) argued that covert self-regulation functions to achieve maximum individual benefit in longer-term over short-term goals which are largely social in nature. These five core executive functions will be discussed in turn.

#### **1.1.1.1 Working memory**

Working memory, both verbal and non-verbal, requires the ability to hold information in mind and manipulate it, whereas short-term memory simply requires holding information in mind. Non-verbal working memory may be likened to the visuo-spatial sketchpad as conceived by Baddeley (1986) which may be likened to a virtual environment allowing simulation of object and spatial information and calculation. It was referred to as “sensing to the self” by Barkley (2001, pg.7) which he proposes is the use of visual imagery and covert audition to sense a theoretical future from that which has been experienced in the past. For effective non-verbal working memory performance, Barkley (2001) suggested that interference control is required, Diamond (2013) explained this as inhibitory control of attention, fascilitating selective, focused attention and suppressing attention to irrelevant stimuli. Diamond (2013) argued that non-verbal working memory is essential for reasoning and for grasping anything that occurs over time. She explained that it is required for comprehending written and spoken language, doing mathematics, and performing mental reorganization of information such as planning. Thus, non-verbal working memory is a vital function for most cognitive tasks. Verbal working memory, as proposed by Baddeley (1992), involves two subsystems, a speech-based store capable of holding a memory trace for approximately two seconds and an articulatory control process which maintains the memory trace by a recycling process described as subvocal rehearsal. Together these subsystems form the phonological loop. Barkley (2001) proposed that verbal working memory originates in the development of internalization of speech which allows processes of reflection, problem-solving and self-directed speech such as self-questioning. A further component of working memory was proposed by Baddeley (1992) and referred to as the central executive. The central executive is argued to function in the distribution of resources between the visuo-spatial sketchad and the phonological loop. The neural substrates of the central executive have been idenfitied as the prefrontal cortex (PFC) and anterior cingulate cortex (ACC); the PFC functions in allocating attention to maintaining information, whilst the ACC supports attention management functions such as managing conflict between two tasks (Osaka et al., 2004). Regulation of working memory is dependent on dopamine (DA) neurotransmission (Chamberlain et al., 2006). Poor working memory has been found to be a common feature of underachievement in education, particularly in reading performance and mathematics (Holmes & Gathercole, 2014).

#### **1.1.1.2 Behavioural response inhibition**

As Diamond (2014) notes, inhibition allows control over habits, thoughts and actions which have become conditioned responses, thus providing the ability to choose how to act and behave. It is also essential in filtering out irrelevant external stimuli and without inhibition the conscious mind would be bombarded with a continuous flow of irrelevant information (Aron, 2007). Response inhibition is the ability to enforce inhibitory control of prepotent responses to suppress unwanted or inappropriate actions (Barkley, 2001; Chamberlain et al., 2006; Diamond, 2014). Prepotent responses are dominant responses which have been previously reinforced for automatization (Jiménez-Figueroa et al., 2017). Response inhibition is believed to consist of three processes which are the inhibition of the prepotent response, the interruption of an ongoing ineffective response, and the protection of the self-directed responses which is also referred to as interference control or resistance to distraction (Barkley, 2001). Interference control requires the inhibition of prepotent mental representations, also known as cognitive inhibition, which permits selective or focused attention to occur, preventing external stimuli from drawing attention away (Diamond, 2014). Thus, response inhibition is essential for self-control and effective cognitive performance. The PFC has been implicated in response inhibition, particularly the right inferior frontal gyrus (Chamberlain et al., 2006; Hampshire et al., 2010) and regulation of response inhibition is dependent on noradrenaline (Chamberlain et al., 2006). Poor response inhibition is noted as a symptom of a number of psychiatric disorders including attention deficit hyperactivity disorder (ADHD), schizophrenia and depression, and it is also a symptom of learning difficulties.

#### **Cognitive flexibility**

The ability to mentally shift between different cognitive tasks or concepts and adapt to changes in the environment is know as cognitive flexibility (Cools, 2015; Dajani & Uddin, 2015). Cools (2015) proposed that, in order to adapt to constant changes in the environment, a balance between cognitive flexibility and cognitive stability is required. Environmental changes which are irrelevant and may be considered noise, require cognitive stability, whereas relevant changes require cognitive flexibility. Different forms of cognitive flexibility include set-shifting, task switching and reversal learning (Cools, 2015; Dajani & Uddin, 2015). Set-shifting requires an attentional shift between modalities of the stimuli such as distinguishing between lines and shapes, within a task (Dajani & Uddin, 2015; Kehagia, Murray & Robbins, 2010). Task switching, on the other hand, requires a shift between tasks with different sets of instructions, and this is considered to be the most complex form of cognitive flexibility (Dajani & Uddin, 2015). Reversal learning is the ability to stop responding to a previously reinforced stimulus which is no longer rewarding and to respond to a stimulus which is currently rewarding but was previously not rewarding (Cools, 2015; Kehagia et al., 2010). The neural correlates of cognitive flexibility have been identified as a frontoparietal network including high-level cortical association areas (ventrolateral prefrontal cortex (VLPFC), dorsolateral prefrontal cortex (DLPFC), anterior cingulate and right anterior insula), premotor cortex, inferior and superior parietal cortices, inferior temporal cotex, occipital cortex and subcortical structures such as the caudate and thalamus (Dajani & Uddin, 2015). Cortico-striatal DA and orbito-frontal serotonin have been reported as critical for reversal learning, whereas set-shifting has been associated with noradrenaline (NE), particularly in the dorsal noradrenergic ascending bundle and task switching has been associated with DA in the dorsal cortico-striatal circuits (Kehagia et al., 2010). Diminished cognitive flexibility and working memory have been associated with academic deficits such as reading and in adults cognitive inflexibility is associated with clinical symptoms such as rumination (Dajani & Uddin, 2015).

#### **Self-regulation of affect/motivation/arousal**

The final core executive function as identified by Barkley (2001) is covert self-directed emotion or self-regulation of affect/motivation/arousal and is also referred to as emotional regulation. Barkley (2001) proposed that, although affective and motivational valences may have been expressed overtly in emotional displays, eventually these become covert and kept private. Barkley (2001) argued that this executive function “forms the wellspring of intrinsic motivation (willpower) so necessary to support future-directed behaviour (p. 8). The neural correlates of emotional regulation have been identified as the ventral anterior cingulate, ventromedial PFC, lateral PFC, and lateral parietal cortex (Etkin, Büchel & Gross, 2015) Serotonin, and genetic variations in the serotonin transporter, have been identified as playing a key role in emotional regulation (Harari & Holmes, 2006). The link between self-regulation and motivation has been highlighted by Rakes and Dunn (2010) who noted that students with greater self-regulatory skills tend to be more academically motivated and learn more than others. They investigated online students’ levels of motivation and self-regulation and found that, as levels of motivation and self-regulation decreased, levels of procrastination increased. Weaknesses in the executive functions described here have implications in relation to poor cognitive performance as previously noted and it would therefore seem possible that enhancement of these executive functions may result in an improvement in healthy cognitive performance. The concept of cognitive enhancement will be considered in the following section.

### **1.1.2 Cognitive enhancement**

Cognitive enhancement can be seen broadly as any intervention in humans which aims to improve mental functioning beyond what is necessary for good health (Juengst, 1998). It can involve improving any of these processes beyond their natural state in good health for greater mental performance. Non-pharmaceutical interventions aimed at enhancing cognition range from behavioural approaches such as computer training, mnemonics, and meditation, to physical approaches such as transcranial direct current stimulation and electroencephalogram neurofeedback, to biochemical approaches such as nutrition, natural remedies, and pharmaceuticals (Dresler et al., 2018). Whilst these many different interventions provide varying degrees of cognitive enhancement, exploring this is beyond the scope of this thesis which is focused specifically on pharmaceutical cognitive enhancement.

### **1.1.3 Thesis aims**

This thesis aims to understand the extent to which these different drivers motivate individuals to enhance their cognitive functions by pharmaceutical means. The current chapter will first look broadly at the development of cognitively enhancing drugs (CEDs), before focusing, in turn, on two of the most commonly discussed CEDs, methylphenidate and modafinil. For both drugs, their pharmacological properties and medical uses, laboratory-based studies and the risks and harms associated with their off-prescription use will be discussed. The chapter will then end by setting out the aims and scope of this thesis.

## **1.2 The rise of psychoactive pharmaceutical drugs**

A multitude of psychoactive pharmaceutical drugs have been developed since the mid-20th Century which, in addition to their intended clinical benefits, have also been found to enhance cognitive functions. Referred to commonly as ‘smart drugs’, they are prescribed for conditions ranging from dementia to ADHD and narcolepsy (Partridge, Bell, Lucke, Yeates & Hall, 2011; Sahakian et al., 2015). The off-prescription use of these drugs is illegal in the United Kingdom (UK). Combinations of various cognitive enhancing drugs and supplements, known as stacks, are designed to target enhancement of specific cognitive functions, among these are the racetam drugs such as Piracetam (Kumar & Sachdeva, 2015). However, there is the risk of potential drug interactions associated with this practice. There are also side effects or adverse effects associated with these medications, for example, possible side effects of the CED, include vomiting, tic, insomnia, irritability, and rash (Vyvanse, n.d.). The severity and number of these side effects determine whether the drug is well tolerated or not. That is to say, whether the individual taking the drug can ‘put up with’ the adverse effects to benefit from their positive effects (Aronson, 2014). There is also a novel method of consuming psychedelic drugs, known as microdosing, which has been introduced for the purposes of cognitive enhancement (Savulich et al., 2016). New drugs are also being developed and investigated for cognitive enhancement, such as ampakines (Lad & Harrison, 2012).

Of the many CEDs available on the market, the two most commonly discussed in the literature and most noted for their positive effects on cognition in healthy adults, are methylphenidate and modafinil (for reviews, see Dubljević and Ryan, 2015; Repantis, Schlattmann, Laisney & Heuser, 2010). These two CEDs will be considered in turn in the following sections.

## **1.3 Methylphenidate**

Methylphenidate is a central nervous system stimulant similar in structure and properties to amphetamine. Its mechanism of action is believed to be via the blocking of DA and NE transporters (Wood, Sage, Shuman & Anagnostaras, 2014). This action results in increased extracellular concentrations of both neurotransmitters, specifically in the prefrontal cortex (PFC) and striatum, which are areas of the brain involved in cognitive processes such as memory and motivation (Busardò, Kyriakou, Cipolloni, Zaami & Frati, 2016). Methylphenidate has a short half-life (of between two and three hours), therefore, therapeutically it must be taken in multiple daily doses. For CED users, this may be seen as an advantage giving them flexibility to adjust the length of cognitive enhancement they receive in a day. The peak plasma drug concentration after oral administration is between one and three hours (Kimko, Cross & Abernethy, 1999). Methylphenidate is absorbed quickly and completely, with a high level of the drug being available to penetrate the central nervous system, and regional uptake is seen in the striatum (Kimko et al., 1999). There is also a sustained release formulation available on the market, but with slower onset of action (Kimko et al., 1999). However, from the current literature, it is not clear whether and to what extent the sustained release formulations are used as CEDs.

The recommended daily dose for methylphenidate ranges from 10mg to 60mg and, as drug response varies depending on the individual, therapeutic doses usually start at 5mg twice daily. The most common adverse effects of methylphenidate are insomnia, decreased appetite, irritability, anxiety, headache, and weight loss (Kimko et al., 1999; Storebø et al., 2015). Methylphenidate has also been associated with the risk of priapism, causing persistent and often painful erections lasting for several hours (Busardò et al., 2016). Other adverse effects include aggression, angina, sweating, visual disturbances, hepatic dysfunction and myocardial infarction (Joint Formulary Committee, 2017; Ritalin, n.d.). Drug interactions occur with antihypertensive drugs, drugs that increase blood pressure, clonidine, and dopaminergic and serotonergic drugs (Joint Formulary Committee, 2017; Ritalin, n.d.). Although also prescribed for narcolepsy, methylphenidate has been commonly prescribed for the treatment of ADHD for the past 50 years (Ritalin; Wood et al., 2014). The frequency with which the stimulant is prescribed has increased as the diagnosis of ADHD has become more widely accepted (Busardò et al., 2016; Wood et al., 2014). Studies investigating the student use of methylphenidate in the United States (where methylphenidate is also controlled) have found widespread illegal use and misuse, primarily for gains in academic performance (McCabe, Knight, Teter & Wechsler, 2005; Teter, McCabe, LaGrange, Cranford & Boyd, 2006).

Currently methylphenidate is restricted to prescription-only use in the UK. Under the Misuse of Drugs Act (1971), specific drugs are classified by their perceived harm (with Class A being the most harmful and Class C the least harmful controlled drug), with each holding legally enforceable penalties for unauthorised possession, sale and use (Nutt, 2009). Methylphenidate is a Class B drug, therefore possession without a prescription and unauthorised sale are both illegal (Drugs penalties, n.d.).

### **1.3.1 Laboratory -based studies of methylphenidate**

Methylphenidate has been widely prescribed for ADHD since the 1960s in North America and research continues to investigate its effects in both clinical groups and healthy adults. This section will consider the more recent evidence arising from such laboratory-based studies in both clinical groups and healthy adults.

A review of 60 single dose studies of methylphenidate in healthy adults to assess its effects on cognition found that methylphenidate improves working memory and speed of processing the most, followed by verbal learning and memory, attention, reasoning, problem solving, and visual learning (Linssen, Sambeth, Vuurman & Riedel, 2014). However, the authors of the review argued that these effects were relatively weak. This may be due to individual differences in DA synthesis capacity. It is widely acknowledged that there is an inverted U-shaped relationship between DA receptor stimulation and cognitive performance (Vijayraghavan et al., 2007). It has also been found that individuals with low working memory spans have low DA synthesis capacity in the caudate nucleus compared with individuals with high working memory spans (Cools, Gibbs, Miyakawa, Jagust & D’Esposito, 2008). Therefore, individuals with low DA synthesis capacity will perform better on tests of working memory on methylphenidate and those with high DA synthesis capacity will not demonstrate any significant improvement on these tests.

Agay, Yechiam, Carmel and Levkovitz (2010) investigated the effects of methylphenidate on cognitive performance and decision making in adults with ADHD and healthy controls. Using a randomized double-blind, placebo-controlled design, ADHD-diagnosed adults and typically-developing adult controls were administered between 10mg and 20mg methylphenidate or placebo, depending on body weight. Participants underwent a battery of tests which consisted of digit span tasks to assess short-term and working memory, the Raven’s Progressive Matrices to assess non-verbal intelligence and the Test of Variables of Attention (TOVA), which was used for assessing ADHD and the beneficial medicinal effects. It was found that performance on the digit span test was significantly better in the methylphenidate group (ADHD-diagnosed and control participants), compared to those receiving placebo. No differences were found with any of the other tasks in relation to methylphenidate versus a placebo. It is surprising that methylphenidate, a medication licensed for the treatment of ADHD, did not have an effect on TOVA considering its reported common usage for assessing ADHD. The authors suggested that this may have been due to a practice effect masking the effect of medication and that the dosage may not have been high enough to elicit a group difference. Nevertheless, this study clearly demonstrates the beneficial effects of methylphenidate on working memory.

Another possible reason why methylphenidate might improve cognition is its modulation of the default mode network (DMN). The DMN is one of at least 10 identified resting state networks (RSN) which are active in the resting awake or anesthetized brain (Esposito et al., 2013; Mantini, Perrucci, Del Gratta, Romani & Corbetta, 2007). Default mode network activity is related to self-referential mental activity, and mind-wandering. The DMN becomes inactive during externally driven tasks (Liddle et al., 2011). Deactivation of the DMN appears to be related to dopaminergic activity (Liddle et al., 2011). Evidence indicates that abnormal attenuation of the DMN is associated with ADHD (Konrad & Eickhoff, 2010; Liddle et al., 2011). A failure in deactivation of the DMN can result in attentional and cognitive processing problems and, although it is not yet clear how or why this dysfunctional connectivity develops, methylphenidate has been found to modulate the DMN in individuals with ADHD, and thus facilitate cognitive processes affected by this dysfunction (Liddle et al., 2011).

In relation to the poor attention and inhibition control shown by ADHD patients, Liddle et al. (2011) investigated the relationship between hypodopaminergic reward deficit and attenuated deactivation of the DMN. Based on their findings, the authors suggested that the pathophysiological mechanism of ADHD responsible for poor attention and inhibition control is not the deactivating response of the DMN per se, but that the motivational level at which task-relevant stimuli become sufficiently salient becomes raised. The catecholamine activity of methylphenidate therefore demonstrated a normalisation of this response in children with ADHD.

Klinge et al. (2018) suggested that contradictory findings and small effects of methylphenidate may also be due to the measures used to assess performance, which lack the sensitivity needed to test healthy participants with normal motivational levels. She argued that the use of implicit measures would provide a more accurate picture as implicit tests are less easy to control. Their study investigated the effect of methylphenidate on implicit and explicit learning. Implicit learning was tested using tasks of location priming, contextual cueing, and implicit task switching, and explicit learning was measured via questionnaires assessing mood and anxiety. Their results showed that a low dose (10mg) of methylphenidate enhanced implicit learning. This effect was evident only in the male participants and the authors stated that this is consistent with a known influence of gender on the DA system. Dopamine signalling is believed to be greater in females than males due to oestradial’s enhancing effects on the DA system in women (Yoest, Cummings & Becker, 2014). However, Laakso et al. (2002) argued that lower dopaminergic activity in men may relate to greater substance abuse seen in men. This lower dopaminergic activity in men could explain the male-only enhancement reported by Klinge et al. (2018). Explicit learning, on the other hand, was not affected, supporting their theory that implicit measures of cognitive performance may be a more sensitive way of detecting the cognitive enhancing effects of methylphenidate.

In addition to its cognitive enhancing effects, methylphenidate has also been found to have mood enhancing effects. Kerr et al. (2012) conducted a randomized, double-blind, placebo-controlled trial with 30 hospice patients who had symptoms of fatigue and depression. Their findings revealed not only a significant improvement in their levels of fatigue, but also a significant reduction in their levels of depression compared with the placebo group. Further to this, stroke victims have demonstrated a significant improvement in mood with methylphenidate and levodopa compared with the placebo group (Delbari, Salman-Roghani & Lokk, 2011).

So far, the evidence reviewed demonstrates that methylphenidate does significantly improve cognitive performance in both in ADHD patients and healthy adults, and one potential explanation appears to be via modulation of the DMN, which appears to be dysfunctional, at least in these patients. However, Volkow et al. (2008) have offered another explanation for methylphenidate’s effects on cognitive performance. Their study measured brain glucose metabolism using positron emission tomography (PET) in healthy adults on three occasions, in three conditions. These were a placebo condition with a neutral non-task which involved viewing nature cards with no performance required, a methylphenidate condition administered before a cognitive task, and a placebo condition administered before the same cognitive task. A further PET scan was conducted on 16 of the participants in a methylphenidate condition, with methylphenidate administered before a neutral non-task. Volkow et al.’s findings revealed that when methylphenidate was administered before the cognitive task, a significantly lower level of increased brain metabolism (induced by the task) occurred compared with placebo and the cognitive task. This reduction (or focusing) in activation occurred in specific brain regions involved in the orienting, executive and alerting attentional networks. Executive networks are the neural networks involved with executive functions. Executive functions refer to the ability to control and coordinate other mental processes and behaviours, and include self-control, moral reasoning, planning, problem solving, attention and working memory (Friedman & Miyake, 2017; Gustavson et al., 2017). These functions are of key importance to cognitive enhancement (Enriquez-Geppert, Huster & Herrmann, 2013). This focusing of activation in these specific brain regions suggests that methylphenidate reduces the amount of attentional resources needed to perform cognitive tasks and therefore increases brain efficiency. Volkow et al. also argue that this demonstrates how methylphenidate enhances cognitive performance in those for whom neuronal resources are not most efficiently distributed. But for those who already have an efficient distribution of neuronal resources, a further reduction of activation may result in sub-optimal performance, which is in line with the inverted-U theory.

As previously mentioned in Section 1.3, methylphenidate also seems to modulate motivation (Busardò et al., 2016) which, in ADHD patients appears to have a higher “trigger level” in order for task-relevant stimuli to become salient. That is, in ADHD patients, the motivational level at which task-relevant stimuli become sufficiently salient becomes raised and methylphenidate appears to modulate a normalisation of this response. In healthy individuals, however, cognitive performance is seen to be only marginally improved and this may be due to individual differences in DA synthesis capacity. So, whether methylphenidate can be an effective cognitive enhancer in healthy individuals may depend on their cognitive baseline and level of motivation, as those with a lower baseline level are likely to experience stronger effects than those with higher baseline cognitive functions.

Overall, it would seem that methylphenidate does enhance mood, and cognitive functions, most especially working memory and processing speed and it appears to do so by focusing the activity in the brain regions involved the orienting, executive and alerting attentional networks and thus increasing brain efficiency. However, these effects of methylphenidate may be stronger in men and those with low DA synthesis, in those with dysfunctional DMN activation and individuals with low levels of motivation.

## **1.4 Modafinil**

Although structurally distinct from other stimulants such as methylphenidate, modafinil is also commonly referred to as a psychostimulant (Rugino, 2007). Its mechanism of action is thought to be primarily through NE and DA transporter inhibition, although there is still some uncertainty surrounding this (Ballon & Feifel, 2006; Wood et al., 2014). It has been found to act on many other neurotransmitters as well, including serotonin, NA, histamine, gamma-aminobutyric acid (GABA), orexin and glutamate (Wood et al., 2014). In turn, this results in increased extracellular levels of DA, serotonin, NE, histamine, orexin and glutamate, and reduced levels of GABA (Minzenberg & Carter, 2008). It is believed that modafinil’s action on orexin also results in increases in hypothalamic release of histamine (Ishizuka Murotani & Yamatodani, 2010). The histamine and orexin systems are thought to work synergistically to promote locomotion, cognition and sleep-wake regulation (Burgess, 2010). Additionally, although d-amphetamine’s and methylphenidate’s psychomotor effects are mediated by catecholaminergic actions (Ferraro et al., 1997a), modafinil’s psychomotor effects are not and may occur via the histamine and orexin systems. Modafinil is a racemate, its two isomers displaying different pharmacokinetic profiles (Darwish, Kirby, Hellriegel & Robertson, 2009). Its R-enantiomer, armodafinil, appears to maintain higher drug plasma concentrations from four to six hours after administration compared to its S-enantiomer version. This phenomenon is believed to be due to a monophasic elimination profile in armodafinil compared to the biphasic elimination profile of modafinil (Darwish et al., 2009). As a result, armodafinil maintains higher plasma concentrations late in the day (Darwish et al., 2009). Although this may prove beneficial for those with excessive sleepiness and other waking disorders, it may also make armodafinil less desirable for those who seek cognitive enhancement, if this results in insomnia.

Modafinil is well absorbed, reaching peak plasma concentration between two and four hours following oral administration, and has a long half-life of approximately 12-15 hours (Darwish et al., 2009; Wong et al., 1999). At least 40-65% of the drug is absorbed and, although food in the gastrointestinal tract may slow absorption, it does not affect the total rate (Robertson & Hellriegel, 2003). Modafinil is highly lipophilic with approximately 60% bound to plasma proteins, elimination occurs largely in the liver by mainly amide hydrolysis, and to a lesser degree via cytochrome P450 enzyme oxidation (Minzenberg & Carter 2008). Excretion is through urine, with under 10% of the drug unchanged (Robertson & Hellriegel). It has been found to be well-tolerated, with low incidence of adverse effects and low potential for abuse (Schmitt & Reith, 2011). The recommended daily dose of modafinil for narcolepsy ranges from 100mg to 400mg (Provigil, 2010).

The most common adverse effects of modafinil are headache, nausea, nervousness, rhinitis, diarrhoea, back pain, anxiety, insomnia, dizziness and dyspepsia (Provigil, 2010). Less commonly, skin rash is reported and there have been rare reports of serious rashes such as Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis and one case of multi-organ hypersensitivity (Provigil, 2010). Stevens-Johnson Syndrome affects the mucous membranes and can affect the eyes, mouth and throat but also presents as a skin rash, often with disc-shaped lesions occurring on the extremities, commonly accompanied by flu-like symptoms (Karaman & Ilhan, 2010). Toxic Epidermal Necrolysis is believed to be associated with Stevens-Johnson Syndrome, existing along a spectrum (Saurat, 2001). The hallmark of Toxic Epidermal Necrolysis is massive cell death of keratinocytes, the main epidermal cell forming the skin, and presents as a loosening of the epidermis with large sheets of skin peeling off (Pereira, Mudgil & Rosmarin, 2007). As indicated in the datasheet, the reporting rate of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis associated with modafinil use (accepted to be underestimated due to under-reporting) exceeds the background incident rate (datasheet, Provigil, 2010), which would suggest that in off-prescription users this may go undiagnosed. Drug interactions are apparent with diazepam, phenytoin, propranolol, and warfarin. In individuals who are deficient in the enzyme CYP2D6, tricyclic antidepressants and selective serotonin reuptake inhibitors may also interact (Provigil, 2010). Following the Psychoactive Substances Act (Home Office, 2016), modafinil is now illegal to buy, sell or supply in the UK. However, it is not currently listed in the Misuse of Drugs Act (Home Office, 1971) and, therefore, possession is not illegal.

### **1.4.1 Laboratory-based studies of modafinil**

Modafinil was originally developed in 1988 to treat narcolepsy. Its approved uses have since expanded to treat obstructive sleep apnea and shift-work sleep disorder, due to its waking effect (Ballon & Feifel, 2006; Keating & Raffin, 2005; Wood et al., 2014). More recently, modafinil’s uses have been extended (off-label) to treat other conditions, such as ADHD (Peñaloza, Sarkar, Claman & Omachi, 2013) and research into its other potential uses including treatment for drug addiction, is ongoing (Dackis, Kampman, Lynch, Pettinati & O’Brien, 2005; Morgan, Pace-Schott, Pittman, Stickgold, & Malison, 2010).

The most common presenting symptoms of narcolepsy are excessive daytime sleepiness and sudden sleep attacks (Mitler, Harsh, Hirshkowitz, Guilleminault & US Modafinil in Narcolepsy Multicenter Study Group, 2000). Mitler et al. conducted a nine week, double-blind, placebo-controlled, multi-centre clinical trial involving 478 patients who were enrolled in one of two 40-week, open-label extension studies, investigating the long-term safety and efficacy of modafinil for excessive daytime sleepiness. Although the two studies followed different protocols regarding dose format, the overall findings were that modafinil was effective in considerably reducing the symptoms of excessive daytime sleepiness and that this efficacy was maintained over nine weeks of daily use.

Similar results were seen for obstructive sleep apnea. Obstructive sleep apnea is a condition associated with snoring, involving obstruction of the upper airway often caused by a relaxing of the throat muscles and narrowing of the passage and resulting in excessive daytime sleepiness (Caples, Gami & Somers, 2005). A randomised, double-blind, placebo-controlled, parallel-group multi-centre trial, conducted largely in the United States and to a lesser degree in the UK, involved a 12-week treatment period. The findings were similar to the Mitler et al. (2000) study in that modafinil significantly improved objective and subjective measures of wakefulness in people with obstructive sleep apnea, and significantly improved the overall clinical condition, and this wakefulness effect persisted.

There are times when, in certain lines of work, individuals are subjected to sleep deprivation and this poses a threat both to safety and productivity. Research has therefore investigated the use of modafinil to combat the symptoms of sleep deprivation. Wesensten et al. (2002) recruited healthy adults in a double-blind placebo-controlled study with five drug conditions, placebo, modafinil at 100mg, 200mg or 400mg, or caffeine at 600mg. Participants remained awake for 54.5 hours, with tests of alertness every two hours. After 41.5 hours participants in each of the five conditions were administered the appropriate drug and this was followed by hourly tests. Modafinil was found to significantly improve performance and alertness at doses of 200mg and 400mg compared to placebo and these effects were comparable to caffeine at 600mg.

Positive results have also been found for the use of modafinil to treat shift work sleep disorder (Czeisler et al., 2005; Erman, Rosenberg & US Modafinil Shift Work Sleep Disorder Study Group, 2007). Shift work sleep disorder is a condition that develops in some shift workers for whom the disruptions in which the circadian rhythms regulating sleep and wakefulness do not resolve, impacting upon the quality of their lives, both at work and at home. In a three-month double-blind placebo-controlled study, a dose of 200mg of modafinil or placebo was given to patients with shift work sleep disorder (Czeisler et al., 2005). A Psychomotor Vigilance Test (Dorrian, Rogers & Dinges, 2004) was administered to measure alertness. The Karolinska Sleepiness Scale (Åkerstedt, Torsvall & Gillberg, 1982), completed by the patients, and an investigator-rated Clinical Global Impressions of Change scale (Guy, 1976) were used to assess the severity of sleepiness. Patients also completed electronic diaries of their experiences. Modafinil was found to reduce extreme sleepiness and that this resulted in a significant, albeit small, improvement in performance compared to placebo. Further improvement was seen in another study by Erman, Rosenberg and US Modafinil Shift Work Sleep Disorder Study Group (2007) using doses of 300mg and 200mg of modafinil and placebo in a sample of 278 patients with shift work sleep disorder. Erman et al. used Weaver et al.’s (1997) Functional Outcomes of Sleep Questionnaire (FOSQ) and Ware’s (2000) Short Form Health Survey (SFHS). Their results demonstrated that the 300mg dose of modafinil significantly improved the mean FOSQ score compared to placebo. Both doses of modafinil significantly improved the mean SFHS score compared with placebo.

Modafinil has also demonstrated positive effects for the treatment of both childhood and adult ADHD (Rugino & Samsock, 2003; Turner, Clark, Down, Robbins & Sahakian, 2004). Rugino and Samsock used a flexible dosing schedule to administer 100mg to 300mg of modafinil to children with and without ADHD over a six-week period. Results from the TOVA (Greenberg, Kindschi & Corman, 2000), the ADHD Rating Scale IV (DuPaul, Power, Anastopoulus & Reid, 1998) and the Connors Rating Scales (Connors, 2001) all demonstrated significant improvement in the ADHD group whereas the control group demonstrated no or slight improvements.

A further study involving adults diagnosed with ADHD was conducted using modafinil at a dose of 200mg (Turner et al., 2004). This was a randomized, double-blind, placebo-controlled, within-subjects crossover study, where half of the participants received a single dose of placebo one week and modafinil the following week. The other group received treatment in the reverse order. All participants underwent a comprehensive battery of tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition Ltd., n.d.). Blood pressure and pulse measures were taken and participants had to complete a subjective scale of their feelings following the intake of each week’s dose. The results indicated that modafinil significantly improved performance on measures of short-term memory, spatial planning, visual memory and motor response inhibition. The data also suggest modafinil improves accuracy through slowing response latency which the authors also suggest may demonstrate modafinil’s facilitation of cognitive performance at times where reflection is required before a response.

This off-label use of modafinil to treat ADHD may be of particular benefit to those who have experienced amphetamine abuse and cannot therefore be prescribed stimulant medication such as methylphenidate (for an example see Mann & Bitsios, 2009). While modafinil has stimulant properties, it is believed that modafinil is not amphetamine-like in its pharmacological profile and does not possess the same abuse potential that amphetamines do (Jasinski, 2000; Schmitt & Reith, 2011). This is one reason why modafinil has been the focus of much research into its potential treatment for substance abuse as its stimulant properties may also help alleviate some of the symptoms of stimulant withdrawal (McGregor, Srisurapanont, Mitchell, Wickes & White, 2008). Additionally, modafinil has been found to modulate the glutamate and GABA systems (Ferraro et al., 1997b) and the orexin/histamine systems which are both found to be dysfunctional in cocaine addiction (Anderson et al., 2009). Studies have found modafinil to be beneficial in the treatment of cocaine dependence (Anderson et al.; Dackis et al., 2005) and also in alleviating the symptoms of methamphetamine withdrawal (McGregor et al., 2008; Shearer et al., 2009).

Mood-enhancing effects have also been found with modafinil use and studies have demonstrated significant improvement in major depression (Price & Taylor, 2005) and, in bipolar depression, improvement as an adjunctive treatment (Frye et al., 2007). Modafinil was administered to patients with major depressive disorder at a dose titrated for optimal benefit, the mean dose was 184.3 + 100mg daily (Price & Taylor, 2005). This was a retrospective study of charts from a private clinical practice, so no experimentation was conducted. Significant improvement was found in all of four rating scales of depression and anxiety at two weeks and three months.

As a treatment for depression in bipolar disorder, modafinil was given as an adjunctive therapy to 85 patients over a six-week period, with significant improvements in symptoms from week two and maintained at weeks four to six compared with placebo (Frye et al., 2007). Modafinil was administered at a dose of 100mg for the first week, increasing to 200mg for the remaining five weeks. Changes were measured using the Inventory of Depressive Symptoms (Rush et al., 1986), its four-item fatigue-and-energy subset, and the Clinical Global Impression-Bipolar Version scale (Spearing, Post, Leverich, Brandt & Nolen, 1997). It should also be noted that this adjunctive treatment using modafinil did not create the added risk of mood destabilization in these patients.

Although a considerable body of work has focused on the clinical applications for modafinil (e.g. Amiri et al., 2008; Ballon & Feifel, 2006; Frye et al., 2007; Price & Taylor, 2005), research has also investigated the cognitive effects of modafinil in healthy adults. A study investigating the cognitive enhancing effects of modafinil in healthy volunteers used a selection of cognitive tests from the CANTAB battery (Turner et al., 2003). The double-blind, between-subjects study administered a 100mg or 200mg dose of modafinil, or placebo to participants two hours before testing. The results revealed significant improvements on planning, accuracy and inhibition compared to controls. As mentioned earlier in Section 1.3.1, executive functions are of key importance to cognitive enhancement and these functions include planning, accuracy and inhibition. Dose-dependent effects were on the CANTAB’s stop-signal task measuring pre-potent response inhibition, with no other dose-dependent effects reported. Pre-potent responses are the dominant and impulsive responses to stimuli and the ability to inhibit is recognised as an executive function (Hofmann, Schmeichel & Baddeley, 2012). However, as this study involved healthy individuals, the results may not be representative of individuals with impaired cognitive function or low baseline dopamine levels. The authors reported that although cardiovascular effects were noted, these were not clinically significant and modafinil was well tolerated.

Modafinil’s effects on working memory were evident in a study by Müller, Steffenhagen, Regenthal and Bublak (2004). In a double-blind, placebo-controlled, randomised and balanced cross-over study, 15 healthy participants were given 200mg of modafinil or placebo on two days, one week apart. Computerized cognitive tests measured the working memory sub-processes of maintenance and manipulation. This involved a task requiring the visuo-spatial delayed matching of target location and the short-term maintenance and the manipulation of a numeric sequence in easy and difficult conditions. Two paper-and-pencil tasks measuring attentional control were also conducted. The first was the d2-Test (Brickenkamp, 1994, as cited in Müller, von Cramon & Pollmann, 1998), a letter cancellation task which requires participants to cross out any letter ‘d’ with two marks above or below the letter. The distractors mixed in with the targets are of similar appearance, for example a ‘p’ with two marks or a ‘d’ with three marks. The second test was the Zhalen-Verbindungs-Test (Oswald & Roth, 1987; cited in Müller, von Cramon & Pollmann, 1998), a German version of the trail-making task, which must be conducted quickly and without removing pen from paper. The findings revealed a significant improvement in manipulation processes and reaction times with modafinil in the numeric sequence task. The authors reported that the slowest responses in the difficult manipulation condition of this task indicated attention lapses. They argued that these responses appeared to speed up with modafinil, suggesting modafinil’s modulation of an underlying attentional mechanism on both spatial and numerical working memory processes. However, no significant improvements in either mood or attentional control were found. The authors also reported that modafinil was well tolerated with no unpleasant side effects.

Rycroft et al. (2007) looked at response inhibition through antisaccade performance with 200mg of modafinil or 1mg of nicotine. In this double-blind, double-dummy experiment, 44 healthy male participants were administered either 200mg of modafinil and placebo spray, placebo capsule and 1mg nicotine spray, or placebo capsule and placebo spray. At peak plasma concentration of either drug, participants were required to perform the antisaccade task. Antisaccades are voluntary eye movements in the opposite direction to the stimulus. In this task, the participants focused on a centrally located small red circle and, once this had disappeared, a tone sounded at the same time as the circle reappearing at a location in the periphery. The participants were instructed to look in the exact opposite location. Increases in antisaccade errors are associated with DLPFC damage (Ploner, Gaymard, Rivaud-Péchoux & Pierrot-Deseilligny, 2005) and schizophrenia (Hutton & Ettinger, 2006). Neither drug reduced antisaccade errors, but there was a corresponding reduction in correct antisaccade latency. Thus, although in comparison with Turner et al.’s (2003) findings, inhibition did not appear to be improved, the authors argued that reduced response time for correct responses suggests improved maintenance of goals within working memory. As the process of maintaining a goal requires inhibition of other processes, including pre-potent responses, this would suggest that inhibition was improved. As none of the participants reported any negative side effects, it would seem that modafinil was also well tolerated in this study.

Modafinil’s action on alertness was further investigated by Ikeda et al. (2017) who used a randomized placebo-controlled within-subjects cross-over design combined with fMRI analysis. Twenty-three participants were analysed on two separate days, two weeks apart to allow for drug clearance. Each participant experienced 200mg of modafinil on one day and placebo on another and the fMRI scan occurred at peak plasma concentration of modafinil. The Attention Network Task (Fan, McCandliss, Fossella, Flombaum & Posner, 2005) was used. This involved identifying, in quick response, whether a central arrow pointed to the left or right, with flanker arrows either pointing in the same direction or opposite direction. The intention of fMRI use was to identify the three theorized distinct neural networks of the attention system which have been identified as alerting, orienting and executive control (Mirsky, Anthony, Duncan, Ahern & Kellam, 1991; Posner & Petersen, 1990). Ikeda et al.’s results indicated that modafinil significantly enhanced alerting in the attention neural networks and that, in the alerting neural network, activation in the left, middle and inferior occipital gyri are distinctly increased in association with enhanced alerting performance. Modafinil’s alerting effect was significant for all three attention networks and the authors attribute this specifically to its noradrenergic action. Subjective ratings were measured for mood using the Profile of Mood States (POMS, McNair, Lorr & Droppleman, 1971) and the Visual Analogue Scale (VAS, Bond & Lader, 1974). Subjective ratings of depression using the Hamilton Rating Scale for Depression (HAM-D, Hamilton, 1960) and anxiety using the Hamilton Rating Scale for Anxiety (HAM-A, Hamilton, 1959) were also taken. No significant effects were found via the responses to the Hamilton Rating Scales for depression or anxiety. Subjective mood ratings, as measured by the POMS, demonstrated a significant increase in vigour in the modafinil treatment group compared with controls and results of subjective ratings from the VAS were that these participants were significantly more alert, energetic and quick witted. The authors concluded that modafinil enhances alerting and mood in the attention networks.

As seen with methylphenidate, catecholamine modulation of the DMN was also demonstrated with modafinil (Minzenberg, Yoon, & Carter, 2011). A double-blind, placebo-controlled crossover study involving 18 healthy, right-handed adults, using a 200mg dose of modafinil or placebo took place over two days, separated by a three-day drug wash-out period. Participants performed a sensorimotor task at peak plasma level of the drug during fMRI acquisition. Participants were required to maintain focus on a central fixation cross and when a contrast-reversing checkerboard was presented they were required to press a button as quickly as possible. Neuroimaging results demonstrated that modafinil significantly augmented deactivation in all three major hubs of the DMN and enhanced processing speed.

Overall, therefore, it would appear that modafinil is well tolerated and it is an effective treatment for narcolepsy, obstructive sleep apnea and shift-worker sleep disorder due to its waking effect. In healthy individuals, the studies reviewed here indicate that modafinil significantly improves attention, alertness, executive control and working memory. It also appears that modafinil improves mood and as seen with methylphenidate, modafinil modulates the DMN and facilitates attention and processing speed. Therefore, these studies indicate that modafinil can be an effective cognitive enhancer in healthy individuals, although much stronger effects may be seen in individuals who are sleep deprived.

## **1.5 Individual differences and the effects of methylphenidate and modafinil**

Although the laboratory-based studies reviewed so far have shown the effects of both methylphenidate and modafinil in clinical samples and in healthy individuals, the effects of these drugs will vary between users due individual differences. For example, Finke et al. (2010) compared the effects of modafinil and methylphenidate on perceptual processing speed and visual short-term memory. This study used a double-blind, randomized and counterbalanced crossover design, administering a single dose of either 400mg modafinil, 40mg methylphenidate or placebo capsule. The level of dosage used for modafinil was high, at the maximum daily dose approved for narcolepsy (Provigil, n.d.), whereas the dose used for methylphenidate was just above the mid-range (10mg – 60mg) for a single dose (Ritalin, n.d.). The results demonstrated significant cognitive-enhancing effects for both drugs in relation to visual perceptual processing speed, but only in low baseline performers. No effects were seen in high baseline performers. Additionally, in relation to effects on visual short-term memory, only modafinil demonstrated cognitive enhancement, and again, this was only in low baseline performers.

The findings of the Finke et al. (2010) study may have been influenced by the chosen dosage levels of both drugs and the consequential increase of dopamine rather than a true indication of their cognitive-enhancing effects. This may be explained by the individual differences in response to methylphenidate by genotype. Mattay et al. (2000) examined the working memory performance of participants on placebo compared to performance on d-amphetamine, finding that those with low performance on placebo performed well on d-amphetamine and those who performed well on placebo were unaffected by d- amphetamine. This led to a further study by Mattay et al. (2003) where participants were divided by a specific genotype, the catechol O-methyltransferase (COMT) gene. This gene displays a polymorphism where the met allele codes for a less active version of the enzyme and results in less breakdown of dopamine and thus higher concentrations of synaptic dopamine. The val allele, on the other hand, is more active and results in greater breakdown of dopamine, resulting in lower concentrations of synaptic dopamine. Mattay et al. (2003) found that the participants with the val allele demonstrated improved performance on working memory tasks on d-amphetamine, whereas participants with the met allele showed no difference in performance on these tasks with d-amphetamine. Therefore, individual genetic differences may influence performance on stimulant drugs such as methylphenidate. This would suggest that optimal dosage levels are dependent upon the individual’s COMT allele. Thus, Finke et al.’s findings in relation to high performers demonstrating no cognitive-enhancing effects may be down to dosage level. If cognitive-enhancing effects are seen in low baseline performers rather than high baseline performers, this would also suggest that perhaps those who take these drugs without prescription may have undiagnosed reasons for doing so and may have lower DA synthesis capacity.

The latter point may also explain the findings of a systematic review of the neuro-enhancing effects of modafinil and methylphenidate in healthy participants (Repantis et al., 2010). The results of their analyses found only one significant positive effect for methylphenidate (single dose administration), which was on memory, particularly spatial working memory performance. In contrast, their findings, in relation to modafinil, revealed only a moderate positive effect for attention in a single dose administration. Another factor to note, raised by Battleday and Brem (2015), is that the cognitive tests employed by these studies were based on assessments for either clinical conditions or animal studies and therefore may not be valid or robust measurements for healthy participants. Therefore, in order to accurately assess the cognitive benefits of these and other cognitive enhancing drugs, one may need to take into account each participant’s DA synthesis capacity/ baseline level and it may also be necessary to develop a more finely tuned battery of tests.

There are a number of commonalities between modafinil and methylphenidate which may add to their appeal to prospective users and, in turn, explain the frequency with which these drugs are discussed in the literature. As discussed earlier, both drugs have been found to enhance a wide range of, largely the same, executive functions and both have been found to have mood enhancing effects. However, there are also many ways in which modafinil and methylphenidate differ. For example, modafinil has a long half-life whereas methylphenidate has a very short half-life. Of great importance is the difference in the legal status and abuse potential; modafinil is legal to possess and has not been found to have abuse potential whereas methylphenidate is not legal to possess without a prescription and has been found to have abuse potential. Table 1.1 provides further comparisons of these two drugs.

**Table 1.1 Profiles and effects of modafinil and methylphenidate**

|  |  |  |
| --- | --- | --- |
|  | **MODAFINIL** | **METHYLPHENIDATE** |
| **Prescribed for** | Narcolepsy, sleep apnoea and shift-worker sleep disorder. | ADHD. |
| **Mechanism of action** | Thought to be primarily DA and NE transporter inhibition, also acts on other neurotransmitters. | DA and NE transporter inhibition. |
| **Formulations** | Immediate release only. | Immediate and sustained release. |
| **Half-life** | Long, 12-15 hours. | Short, 2 -3 hours (immediate release). |
| **Most common side-effects** | Insomnia, nervousness, anxiety, headache, nausea, diarrhoea, rhinitis, dizziness and dyspepsia. | Insomnia, decreased appetite, irritability, anxiety, headache and weight loss. |
| **Legal status** | Prescription-only, not classified under the Misuse of Drugs Act, therefore possession is not illegal. | Prescription-only, Class B drug, possession without a prescription is illegal. |
| **Cognitive enhancing effects found in studies** | Improved working memory, processing speed, attention, alertness, executive control, planning, accuracy, inhibition, and alertness. Modulates the DMN. | Improved working memory, processing speed, attention, verbal learning, memory, reasoning, problem solving and visual learning. Modulates the DMN, increases brain efficiency, modulates motivation. |
| **Other beneficial effects** | Mood enhancing effects, increased energy. | Mood enhancing effects, decreased fatigue. |

To sum up, although some studies have documented cognitive benefits with both methylphenidate and modafinil, there are other conflicting reports and there are a number of possible reasons for this, including potentially inaccurate methods and measures for testing. It is clear that benefits are greater for those with a low baseline, suggesting individual differences in response to dosage strengths of these drugs on the inverted U-shaped performance level. Nevertheless, users are experiencing and perceiving benefits, suggesting that perhaps those who are experiencing the benefits are, in the main, low baseline performers, which also begs the question as to how many undiagnosed CED users are self-medicating, even if they are not aware that they are doing so.

## **1.6 Risks and potential addiction associated with off-prescription use**

The term misuse signifies the improper use of a drug, such as using a drug for purposes it was not designed for and/or prescribed for (Bossaer et al., 2013). Abuse, on the other hand, is defined as the continued use of a drug which results in substantial impairment, reflected in repeated use of the drug in dangerous conditions, and where this use results in social and legal issues (Kollins, MacDonald & Rush, 2001). Determining whether the off-prescription use of CEDs is misuse or abuse is difficult to accurately assess. The off-prescription use of cognitive enhancers appears to be most commonly for the purpose of enhancing higher cognitive functions, as demonstrated in the current chapter, rather than for recreational use (i.e. to get high, as seen with cocaine and hallucinogenic drugs, for example). The question then, is whether this kind of drug use results in the pattern of abuse as defined above. The pharmacological profile of methylphenidate is similar to that of stimulants such as amphetamine and cocaine, and this similarity has resulted in much debate as to its abuse potential (Kollins et al. 2001).

### **1.6.1 Risks and potential addiction: Methylphenidate**

Findings, albeit from animal rather than human studies, clearly indicate methylphenidate‘s potential for abuse, but it is also clear that this potential is less for orally administered doses.

A study on prolonged methylphenidate treatment in rats looked at how long-term treatment with methylphenidate may affect the mammalian circadian rhythm activities (Algahim et al., 2009). Circadian rhythms regulate daily physiological functions (such as secretion of hormones) and maintain homeostasis in relation to the external environmental cues, such as light and dark (Luce, 1971). These circadian rhythms operate like an internal clock (Vitaterna, Takahashi & Turek, 2001) but have been found to be modified by other psychostimulants such as cocaine and are believed to act by modifying gene expression (Wang et al., 2006). Algahim et al.’s (2009) study found that prolonged methylphenidate treatment modulated the rats’ circadian rhythms in a dose-dependent manner. The study also found indications of dose-dependent tolerance and sensitization and that withholding the drug after six consecutive days of dosing resulted in behaviour changes indicative of withdrawal effects (Algahim et al., 2009). These findings suggest a possible addictive quality/abuse potential in methylphenidate. In humans, the off-prescription use of methylphenidate may also lead to the development of insomnia via disruption to circadian rhythms.

Botly, Burton, Rizos and Fletcher (2008) investigated the self-administration of methylphenidate in rats via an intravenous catheter using schedules of reinforcement. Botly et al. (2008) found that rats willingly self-administered methylphenidate on both fixed ratio (x1) and progressive ratio (PR) reinforcement schedules in a dose-dependent manner. For the PR schedules, after each infusion of methylphenidate a greater number of responses were required for the next infusion until either a period of one hour without infusion or a maximum of five hours in length had been reached, signifying a breaking point. Their PR schedule experiments demonstrated that rats would press a lever 2500 times over 100 minutes to receive methylphenidate. The higher the dose, the higher the breaking point, indicating that rats will work hard and to high ratios to receive this drug. Botly et al. also reported that, following extinction of drug-seeking behaviour, re-exposure to methylphenidate would reinstate this behaviour. The authors argued that this behaviour is probably a significant factor in relapse and drug addiction. Their results also demonstrated lower abuse potential with orally administered doses in comparison to intravenous administration.

Wooters, Walton and Bardo (2011) conducted a conditioned place preference (CPP) study with randomly assigned orally administered (p.o.) or intraperitoneal (i.p.) injections of either 3mg/kg or 10mg/kg of methylphenidate or saline, either immediately or 30 minutes before conditioning in rats. Results showed that when methylphenidate was administered immediately before conditioning there was significant CPP at both doses of i.p. methylphenidate whereas this was only evident at the higher dose of p.o. methylphenidate. When administered 30 minutes before conditioning there was no CPP with either dose in either route of administration.

Assessment of a drug’s abuse potential involves a variety of methods, including, but not limited to, its chemical properties, pharmacodynamics effects and the resulting behaviour patterns exhibited following drug use (Keane, 2008). Kollins et al. (2001) reviewed 60 studies of methylphenidate use involving human and non-human participants, with a particular focus on the methods listed above. Their findings concluded that, even via oral administration, methylphenidate is not without abuse potential. Nevertheless, compared with other stimulants which are commonly abused, such as cocaine and amphetamine, the authors recognise that the actual rates of abuse for methylphenidate are believed to be much lower. They suggest that this may be due to differing reinforced activities or motivations for use.

As seen earlier, rats find methylphenidate very rewarding. Stoops, Lile, Fillmore, Galser and Rush (2005) investigated whether this rewarding effect was also found in humans, and whether certain behavioural demands would alter the reinforcing effects of methylphenidate. In their double-blind placebo-controlled study, seven adult participants were given either placebo or methylphenidate in doses of either 10mg, 20mg or 40mg. This was followed by either a relaxation session where they were either required to quietly sit in a darkened room for three 50-minute sessions, or a performance session where they were required to perform simple mathematical problems for three 50-minute sessions. A modified progressive-ratio procedure was also conducted where participants were offered the opportunity to earn their previously experienced dose, depending on their assigned condition (which was separated into eighths of a dose), by repeatedly pressing a keyboard key. Although the participants were unaware of the PR schedule used, the first eighth of the dose was earned on the 50th keystroke and, in order to earn each additional eighth, the number of keystrokes doubled, i.e. 100, 200, 400, 800 and so on up to 6400 keystrokes for the final eighth. The participants were also informed of the condition in which they would experience the drug, the relaxation condition or the performance condition. The results revealed that in the methylphenidate conditions, break points (that is, the last ratio of keystrokes completed) increased in the performance but not relaxation condition in a dose-dependent manner. This would suggest that methylphenidate’s performance-enhancing effects drove the reinforcing effects in the performance condition.

That said, it is apparent that some individuals choose to take these medications for recreational purposes. In support of this argument, a study by Teter et al. (2006) found that 31% of illicit prescription stimulant users took drugs such as Adderall or methylphenidate for the ‘high’, whilst 30% took it for experimentation, 10% for weight loss and 5% to counter the effects of other drugs. Of greater concern, however, were the findings in relation to routes of administration. Although 95% of users reported taking the drug orally, 38% also snorted the drug, 6% smoked the drug and 1% inhaled. When drugs are administered via routes that rapidly increase the serum concentration of the drug, such as snorting, smoking, inhaling or injecting, drug effects dramatically increase and with stimulant drugs, such as methylphenidate, this in turn increases their abuse potential and possible dependence/ addiction (Volkow & Swanson, 2003).

In sum, there is a clear risk of abuse and a potential for addiction with methylphenidate, not only due to its similar pharmacological profile to other known addictive stimulants, but also because of its available routes of administration. Laboratory studies using rats have revealed several signs indicative of potential addiction, such as tolerance, sensitization and withdrawal effects. However, it is also clear that the abuse potential is lower when methylphenidate is administered orally and that the actual cases of abuse are low in comparison with known addictive stimulants such as cocaine. This lower level of actual abuse may be due to motives for use, as it is likely that the majority of off-prescription users are doing so for its cognitive benefits rather than for recreational use. The long-term off-prescription use in individuals under 30 years of age also comes with the potential for detrimental effects in the development of their frontal lobe functions, at least in relation to methylphenidate (Urban & Gao, 2014).

### **1.6.2 Risks and potential addiction: Modafinil**

Although some may argue that modafinil’s waking effect could result in sleep deprivation and consequently impair immune functions, reports of this effect are lacking (Kim, 2012). However, as Kim emphasises, individuals who are drawn to taking modafinil are often experiencing high levels of stress, which, compounded with possible sleep deprivation may have an immunomodulating effect. That said, it may also be that those who use modafinil off-prescription may be practicing a form of edgework. Edgework is the practice of risk-taking in which the edgeworker aims to achieve maximum pleasure and excitement by pushing to the edge of risk or danger, as is often seen in those who engage in extreme sports (Quintero & Nichter, 2011).

Abuse potential may however, be of greater concern. Volkow et al. (2009) conducted a study to investigate whether modafinil increased DA levels in the nucleus accumbens, as the action of DA in this brain structure is associated with reward effects in drug abuse. Ten healthy men with the mean age of 34 (SD-7.1) participated in this PET study, in which raclopride and cocaine were used as radiotracers and modafinil was administered orally at 200mg and 400mg doses. Participants were scanned four times over two days separated by one week, revealing that modafinil does significantly increase DA in the brain and, more precisely, in the nucleus accumbens. It was also found that modafinil’s binding to DA transporters overlapped with the binding site of cocaine. These findings have two implications, one, that modafinil does have an abuse potential, and two, that it may be effective in the treatment of cocaine addiction. However, as Volkow et al. admit, modafinil’s reinforcing potential is very weak and reports of abuse are rare compared to those for stimulant drugs.

Wuo-Silva et al. (2011) argue for modafinil’s abuse potential. This study focused on the conditioned place preference paradigm and locomotor sensitization effects of modafinil as an indicator of abuse potential. Their argument was that persistent locomotor sensitization results in neuroplastic changes occurring in the circuitry involved in motivational behaviour which is believed to play a significant role in drug addiction. This animal experiment (involving mice) used modafinil at measures of 64, 128 and 300mg/kg, and cocaine-HCL at 15mg/kg in a saline solution, both injected intraperitoneally along with a saline control condition. Locomotor activity was also measured for each drug condition. The results indicated that locomotor sensitization was present after a single moderate or high dose of modafinil and a cross-sensitization effect between modafinil and cocaine was demonstrated by injection of cocaine following repeated administration of modafinil and vice versa. This behavioural sensitization effect was confirmed by the CPP paradigm - that doses that promote heightened locomotor activation produce CPP indicating addictive potential. However, it should be noted that their findings are limited to mice and at moderate to high doses. Additionally, modafinil was injected using gum Arabica. In normal situations, this mode of administration would be unlikely to occur as modafinil is practically insoluble in water, therefore it would require the motivation and knowledge of this drug delivery agent in order to successfully inject this drug (Jasinski, 2000). The addictive potential of a drug is in part measured by the routes of administration, as routes that allow the highest level of the drug to reach blood plasma most rapidly will result in higher peak plasma levels lasting for a shorter period of time. These stronger but shorter-lived effects are associated with dependence and addiction (Volkow & Swanson, 2003).

Jasinski (2000) investigated the abuse potential of modafinil in a study involving 24 males with a history of polysubstance abuse, using methylphenidate as a reference. The argument here was that, by comparing the pharmacological profile of the drug being investigated to a prototypic drug of abuse, methylphenidate, it was possible to assess its abuse potential. The participants were all inpatients at a medical centre. This was a randomized crossover study consisting of six consecutive three-day sessions with a two-day washout period between each session. The drug conditions were methylphenidate at 45mg and 90mg, modafinil at 200mg, 400mg, and 800mg and placebo. Participants provided subjective assessments of drug effects via questionnaires (including the Amphetamine Scale, which is a measure of specific, dose-related amphetamine-like effects), and those observing the participants gave their perception of the participants’ responses via similar questionnaires. Physiological measures were also taken. The findings revealed modafinil differed to methylphenidate in that there was no significant response of the Amphetamine Scale, lower orthostatic tachycardia increases or a lower reduction in caloric intake compared with methylphenidate. Jasinski reported that the overall results indicated that modafinil is not an amphetamine-like agent.

A review of preclinical, clinical and post-marketing surveillance (Myrick, Malcolm, Taylor & LaRowe, 2004) concluded that modafinil has a limited potential for abuse. Post-marketing surveillance is the practice of monitoring the safety of drugs after they have been released into the market and it employs a number of methods, including accessing data from patient health records. This is arguably the most accurate assessment of a drug’s abuse potential as the clinicians are prescribing these drugs to diverse patient groups. Myrick et al.’s (2004) review of the post-marketing surveillance, was of particular interest, they focused on the Haight-Ashbury Free Clinics Behavioural Research Group which monitored the usage patterns of modafinil over a four-year period. This was a surveillance program which gathered information from a large number of sources including multiple national and state databases, medical and popular literature, addiction focus groups and primary care patients. Over this period of time, surveillance found no misuse or abuse of modafinil and modafinil did not generate much interest on the internet. Despite this, it should be noted that this program ran from 1999 to 2003, so may not be indicative of current trends. Additionally, the program was focused on therapeutic, prescribed use and therefore may not be indicative of off-prescription use.

Overall then, although modafinil does increase DA levels in the reward areas of the brain associated with drug abuse, and modafinil’s binding to DA transporters overlaps with that of cocaine, suggesting abuse potential, this has yet to be demonstrated in actual abuse statistics. There is evidence of abuse potential through clinical studies using mice but, as before, the modafinil was injected, using moderate to high doses. It is highly unlikely that this mode of administration would be accessible to most individuals and, as modafinil cannot be smoked, this also reduces the potential for modafinil to be administered via methods that are associated with drug abuse and addiction. Indeed, very thorough post-marketing surveillance has demonstrated no misuse or abuse at least up to 2003 (Myrick et al., 2004). There is, of course, the possibility that this trend has changed but, to the author’s knowledge, there is currently no report to the contrary. The long-term effects of modafinil are largely unknown, although, evidence so far has not revealed any significant dangers in this respect.

### **1.6.3 Illicit drug use with modafinil and methylphenidate**

Another consideration in relation to potential dangers of CED use is the concomitant use of other drugs. Several studies have noted high levels of illicit drug use amongst CED users (e.g. Arria et al., 2011; McCabe et al., 2006; McDermott, Lane & Alonso, 2020; Rabiner et al., 2009). Hysek et al. (2014) investigated the pharmacodynamic effects of methylphenidate and methylenedioxymethamphetamine (MDMA) in combination or alone. Sixteen healthy participants took part in a double-blind, placebo-controlled, cross-over study with four experimental test sessions. Subjective effects were measured using a battery of psychometric tests, and emotion recognition was measured using a facial emotion recognition task where participants were required to identify the correct emotion of faces presented to them. Their findings demonstrated that the combined use of methylphenidate and MDMA did not result in additional psychoactive effects compared to single drug usage but indicated enhanced cardiovascular and adverse effects when taken together. If methylphenidate users are taking other drugs simultaneously, these findings suggest a very significant potential danger.

León and Martínez (2017) investigated motives for illicit prescription drug use in teenagers ranging from 13 years to 16 years. The authors analysed data taken from a data set maintained by the University of Michigan’s Institute for Social Research. Their findings from the 10,639 students who participated suggest that prescription stimulant drug use among their sample (4% in the past year) was strongly associated with experimental or habitual use of both legal drugs and also illegal drugs such as cannabis and alcohol. It is not altogether surprising that youths of this age report taking cannabis or alcohol, but the authors argue that their motives for using prescription stimulants at this age may be more for recreational use rather than study use. What is not clear from this study, though, is whether these students are using these drugs for both reasons or purely for recreational use alone.

The long-term effects of modafinil and methylphenidate are unknown but research suggests that the regular use of methylphenidate in adolescents and young adults up to the age of 30 years may result in detrimental effects on the plasticity of the PFC (Urban & Gao, 2014), the centre of executive functions (e.g., Rabbitt, 1997). Due to the similarity of action on DA and NE in the PFC to that of methylphenidate, regular use of modafinil may also exert detrimental effects on young adults similar to those discussed above for methylphenidate. However, it should also be noted that modafinil’s binding mechanism to DA transporters is different to that of methylphenidate, with differing affinity ratios, and it is that mechanistic difference that is believed to influence its properties and effects (Schmitt & Reith, 2011). Nevertheless, given that a large number of young adult students are using these drugs, the question is raised as to whether they are aware of the potential risks and harms involved.

## **1.7 Aims and scope of the thesis**

From the literature reviewed in the current chapter, it is evident that there are clear benefits to cognition derived from methylphenidate and modafinil use, specifically in relation to concentration, focus and alertness, and also in relation to mood and sleep deprivation. However, the evidence reviewed so far all derive from lab-based research which takes place under tightly measured and restricted conditions, controlling for variables which might influence the results. Therefore, lab-based research, although very valuable in what it can offer to the investigator, does not reflect real life conditions and experiences. Online surveys, on the other hand, do provide this real-life information and can have a global reach. The fact that they are online provides greater convenience not only for the researcher but also for respondents as it allows them to complete the survey in their own time from the convenience of their own homes and can thus attract large samples. For these reasons online surveys were favoured over the use of interviews or other qualitative methodology. To explore this issue further, the extent to which these laboratory findings translate to real life experiences will be considered in the next chapter.

Overall, this thesis aims to understand the off-prescription use of modafinil and methylphenidate by identifying the profile of the user, their experience of using these drugs and the drivers behind their use even in the face of the potential risks involved with off-prescription use. It also aims to establish whether these off-prescription CED users experience (via both self-report and lab-based test) poor cognitive performance or whether they are seeking to optimise their already good cognitive abilities.

# **2 CHAPTER TWO**

**STUDY ONE: THE OFF-PRESCRIPTION USE OF METHYLPHENIDATE AND MODAFINIL: AN ONLINE SURVEY.**

## **2.1 Introduction**

As the majority of studies to date have focused on either CEDs in general (e.g. Ott & Biller-Andorno, 2014; Vargo & Petróczi, 2016) or prescription stimulants broadly (e.g. Arria et al., 2017; Ross et al., 2018), there is a lack of research focused specifically on the off-prescription use of methylphenidate and modafinil. As noted in Section 1.7, although laboratory studies have the advantage of being in controlled environments and thus removing extraneous variables, they do not reflect real life conditions and environments. In order to obtain a greater understanding of the off-prescription use of CEDs in real life settings, research has often taken the form of paper-based surveys, typically focused on university students (e.g., DeSantis, Webb & Noar, 2008; Franke et al., 2011). But with the rise of the Internet came the emergence of online pharmacies and drug user forum sites, providing both ease of access to cognitive enhancing drugs and also an alternative platform via which to survey CED users.

The Internet is accessed by billions of people worldwide; in 2019 it was estimated that over four billion people (53.6% of the world population) use the Internet (International Telecommunications Union, 2019). Online surveys offer the kind of anonymity that face-to-face methods cannot provide, which may reduce social desirability effects (Joinson, 1999). Such effects occur when individuals provide socially acceptable answers which they believe will make them look good rather than genuine, honest answers. Cross-cultural, international, if not global, reach is also possible through online methods (Evans & Mathur, 2005; Hewson & Stewart, 2014).

The online survey has therefore become a popular choice for researching cognitive enhancing drug use. Paul, Chisolm, Johnson, Vandrey and Dredze (2016) argued that online forums are a promising source for detection of interest in emerging drugs and although modafinil and methylphenidate are not emerging drugs as such, Repantis et al. (2010) noted that the use of these drugs as CEDs appears to be increasingly popular. In an online poll of readers of the journal *Nature*, Maher (2008) reported that one in five of the 1,400 respondents reported having used CEDs off-prescription and 62% of these reported CED users stated that they had used methylphenidate and 44% stated that they had used modafinil. Online forum sites are a convenient way for people to share their experiences and information about illicit drug use. The development and popularity of online forum sites has provided the opportunity to reach hidden groups of individuals such as those using drugs illicitly, who would otherwise be difficult to reach via other methods (Miller & Sonderlund, 2010). As Wright (2005) explains, many groups and communities exist only in cyberspace. This is likely to apply to modafinil and methylphenidate off-prescription users who seek to exchange experiences, advice and information on their CED of choice.

However, there are potential weaknesses to the online survey method, which should also be considered. Self-selection bias can limit the generalizability of findings, although there are ways in which this limitation can be reduced. Reips (2002) presented a multiple site entry technique in which links to the survey are placed on several websites or platforms in order to attract different types of respondents. It has also been argued that the majority of the Internet-using population are white, middle-class, educated males (Hewson, 2003), although this trend is changing with increased accessibility of the Internet. One could also argue that many experimental studies recruit participants from a pool of undergraduate students, the majority of whom would be young, educated and part-time employed. This would suggest that online survey respondents may not be more homogenous and biased than other samples used in research. This, of course, depends on where survey links are placed, as some forum sites and other internet platforms may draw interest from less mixed groups of individuals than others.

The following section reviews the current survey literature on CEDs in general and those which include methylphenidate and modafinil.

### **2.1.1 Surveys investigating off-prescription use of cognitive enhancing drugs**

Percentages of off-prescription lifetime use of CEDs in the United States appear to be much higher than in Europe (see Table 2.1 for details). For instance, McCabe, Teter and Boyd (2006) conducted an online survey of undergraduate students in a large mid-Western USA university. The authors indicated a relatively high rate of lifetime use of CEDs and past year use of 5.4% (458 students). Of those who had indicated how they had obtained the stimulants, 92% had reported their sources as friends and peers. The authors also reported that users of illicit stimulant medications were much more likely to use other drugs such as cannabis and cocaine.

However, a much higher percentage of use was reported in a South-Eastern USA university using a mix of qualitative interview and quantitative survey methods (DeSantis et al., 2008). Of those who had reported illicit use of ADHD medications, 66% indicated their motivation for use was to help concentration on schoolwork. Interviews were conducted with 175 of these students, over two-thirds of whom admitted that the heightened pressure of finals was their motivation for stimulant use. The authors reported that none of the interviewees had sought information regarding these drugs before using them and that obtaining these stimulants was easy. The survey data indicated that 89% of illicit users reported their source as friends (87%), significant others (4%), or friends of friends (8%). In comparison to these two USA studies, a Swiss survey (Maier, Haug & Schaub, 2016), a Dutch survey (Schelle et al., 2015) and two German surveys (Franke et al., 2011; Sattler & Wiegel, 2013) found lower rates of reported lifetime off-prescription use of CEDs.

**Table 2.1. Surveys reporting the prevalence of CED use**

|  |  |  |  |
| --- | --- | --- | --- |
| **Location of survey** | **Sample size** | **% reported lifetime use** | **Study** |
| USA | 9,161 | 8.1 | McCabe, Teter and Boyd, 2006 |
| USA | 1,811 | 34 | DeSantis, Webb & Noar, 2008 |
| Switzerland | 10,171 | 4 | Maier, Haug & Schaub, 2016 |
| Holland | 1,572 | 1.7 | Schelle et al., 2015 |
| Germany | 1,547 | 1.29 | Franke et al., 2011 |
| Germany | 5,882 | 4.56 | Sattler & Wiegel, 2013 |

The studies discussed so far have focused their surveys on the off-prescription use of prescription stimulants or CEDs broadly. In all but one (Maier et al., 2016) of the studies detailed in Table 2.1 were conducted in universities and schools. Prevalence of CED use varies both geographically and according to the type of CED used. McCabe et al. (2006) conducted their survey in a Midwestern USA university whereas DeSantis et al. (2008) conducted their survey in a Southeastern USA university. Maier et al. (2016) recruited respondents for their survey from an internet panel of the LINK Institute for Market and Social Research and their sample comprised of Swiss employees and students. Schelle et al. (2015) recruited their respondents via a nationwide campaign targeting Dutch universities. Sattler and Wiegel (2013) targeted four German universities and their respondents comprised of teachers and students, whereas Frank et al. (2011) targeted a range of public grammar schools and public vocational schools in small and large cities and one university, and their respondents were therefore a mix of pupils and students. These different approaches to surveying dissimilar populations in multiple locations, whilst making it difficult to compare data, provides some insight into the varying popularity of CED use more broadly. The following section narrows this focus to surveys specifically directed at the off-prescription use of methylphenidate and modafinil.

### **2.1.2 Surveys investigating off-prescription use of methylphenidate and modafinil**

A French survey with 1718 participants found that only 1.5% had used methylphenidate off-prescription (Fond et al., 2016). Higher levels were again seen in another USA study of student use among the health-related sciences (medicine, pharmacy and respiratory therapy). Bossaer et al. (2013) found that, of the 372 participants, 11.3% reported having used prescription stimulants such as methylphenidate and modafinil. Their reasons for misuse included enhancing alertness/energy (65.9%) and to improve academic performance (56.7%).

A Canadian cross-sectional survey of adolescents from four provinces examined the relationship between ADHD and both licit and illicit use of prescription stimulants, namely methylphenidate and amphetamine (Poulin, 2007). The survey included the six-item Ontario Child Health Study Hyperactivity Scale as a screening tool for ADHD. Data from 12,990 students were analysed revealing that although the prescribed use of these medications was considered low (2.8%), a total of 2.4% of the sample who did not show symptoms consistent with a diagnosis of ADHD reported prescribed use of either medication, suggesting that there may be an element of feigning symptoms of ADHD in order to obtain the medication. This suggestion of feigning symptoms of ADHD was further supported by the fact that 26% of those who had a prescription had either given or sold some of their pills to other students. A further revelation was that only 9.2% of those who had tested positive on the ADHD screening test reported having been prescribed ADHD medication, and that 20.5% of non-medical users tested positive for ADHD. Based on these findings, Poulin argued that, not only was there a high level of under-diagnosis of ADHD in this sample, but that there was also a notable element of self-medication apparent. However, these findings may only reflect a pattern of use, misuse and issues with diagnosis in Canada. Differences in such factors as drug awareness and standards in relation to ADHD diagnosis and prescribing of such medications between countries means that the ability to extrapolate these findings internationally is questionable. That said, the possibility of self-medication should be considered as a possible reason for off-prescription use of CEDs such as modafinil and methylphenidate.

In comparison, a survey advertised in the German publication, The Handelsblatt, investigating CED use reported higher findings (Dietz, Soyka & Franke, 2016). According to Dietz et al. (2016), the Handelsblatt is the leading economics publication in German-speaking countries, read by economics professionals and students. The survey collected data from 1,021 participants with ages ranging from 17 to 71 and reported findings of lifetime illicit methylphenidate use as 5.1%.

However, a survey of CED use by university students in the UK and Ireland revealed higher rates; lifetime use of modafinil, methylphenidate or Adderall was reported as 9.4% (Singh, Bard & Jackson, 2014). Of the six CEDs included in the survey, modafinil was the most commonly used CED with lifetime use reported at 8%. This survey recruited participants from 104 universities in the UK and Ireland, 79% of which reported enrolment at a Russell Group university. Students from 23 of the 24 Russell Group universities participated in the survey, with Bristol University (N = 161) most frequently represented, followed by Manchester University (N = 96) and Cardiff University (N = 88). Of the 877 students participating (mean age of 22.7 years), 51.6% had considered taking methylphenidate but had not tried it due to a lack of availability which suggests that the numbers would be much higher should availability be as common as it is in USA universities.

The high participation of Russell Group universities, although not necessarily indicative of general patterns of CED use, may or may not have contributed to the higher reported rates of CED use, and this could suggest some engagement in CED use by students of elite universities. Survey results from the student website the Tab (Young-Powell & Page, 2014) reported that out of almost 2,000 participants recruited from 41 different universities in the UK, 26% of Oxford students reported using CEDs (modafinil) which was more than any other university. Another student website, Varsity, reported the results of their survey, completed by 1,000 students, in which 10% of Cambridge students had taken CEDs (Varsity, 2009). Such high rates of use in these prestigious universities may reflect the pressure to succeed in highly competitive environments.

It would seem, therefore, from the comparative reported popularity of use between US and European respondents, that prevalence of CED use is highest in the United States, probably due to easy access via diversion of prescription stimulants. Although the prevalence of CED use in Europe appears to be lower, most of the studies reviewed here involved university students and therefore may not be indicative of the wider CED using population. Indeed, this difference was seen between two of the German studies mentioned earlier, with the survey of university students (Franke et al., 2011) reporting a prevalence rate of just 1.29%, whereas the sample of professionals and students (Dietz et al., 2016) reported a prevalence rate of 5.1%. However, the survey of CED use by Singh et al. (2014) revealed that university students in the UK and Ireland reported an even higher rate of 9.4%, a higher prevalence rate compared to the rest of Europe. This may also reflect the pressured and competitive environments of the more prestigious universities involved in the survey, which is also suggestive of the findings of the Tab and Varsity surveys reviewed previously in this section (Varsity, 2009; Young-Powell & Page, 2014).

An online survey of 3,400 students at a USA university investigated the perceived benefits of the off-prescription use of ADHD medications (Rabiner et al., 2009). Of the 291 (9%) students who reported using ADHD medications non-medically, 89% reported that it helped them concentrate better while studying and helped them to study longer, 87% found that it helped them to concentrate better in class, 81% found that it helped them to feel less restless while studying, 75% found it helped them to keep better track of assignments and 74% found that it helped them to feel less restless in class.

In comparison, the survey previously mentioned by Singh et al. (2014) found that 77.1% of modafinil users found that the drug enhanced cognition, 61.4% found that it offset sleep deprivation, and 17.1% found that it enhanced mood. Whereas 67.3% of methylphenidate users found that methylphenidate enhanced cognition, 26.9% found that it offset sleep deprivation and 19.2% found that it enhanced mood. In the previously mentioned Varsity survey (2009), five students who had recently tried modafinil reported increased alertness, four had found their ability to concentrate on work improved, and two of the students felt more motivated. Thus, it would seem that the off-prescription use of modafinil and methylphenidate may be motivated by a desire for cognitive enhancement rather than for recreational use.

A further, and individual, report of perceived benefits of modafinil comes from Dr Anders Sandberg, a research fellow at Oxford University’s Future of Humanity Institute who has been using modafinil non-medically since 2007 (Schmitt, 2014). Dr Sandberg explained that he can achieve more, and he feels more able to tackle difficult problems. He argued that modafinil does not improve his ability to tackle ordinary problems, although it does provide a boost of energy.

### **2.1.3 Ethical concerns and risks and harms associated with off-prescription use**

This trend in the growth of CEDs raises a number of ethical issues. As highlighted by Sahakian and Morein-Zamir (2011), people may feel coerced into taking CEDs in order to keep up with their peers in situations such as competitive work environments, where top performers are rewarded, or night shift work where alert performance is required. This can, in turn, promote an even more demanding 24/7 society with greater demands on workers’ performance and time. Fairness is also a concern. Fitz, Nadler, Manogara, Chong and Reiner (2014) presented a vignette to 4,011 participants relating to fairness and found that participants judged cognitive enhancement as unfair if the individual did not work hard either in acquiring the money to afford the CED or in attaining the achievement facilitated by the CED. Greely et al. (2008) made the point that, if costly to obtain, cognitive enhancement may become a privilege enjoyed solely by the rich and this could lead to a further social divide, leaving the less fortunate even more disadvantaged. There is also a wider debate around safety in relation to the risks versus the benefits to healthy individuals taking these drugs, which Brűhl, d’Angelo and Sahakian (2019) suggest has implications for regulatory and policy making decisions.

In addition to this, popularity in the off-prescription use of these CEDs has risen in recent years due, in part, to their easy access via online sources, as mentioned earlier, (Ragan, Bard & Singh, 2013; Sahakian & Morein-Zamir, 2011). As a result of this increased popularity, concerns have been raised in relation to the potential risks and harms associated with off-prescription use. Ethical issues in relation to the safety of using CEDs have also centred on the potential for users to develop addictions, sleep disorders and mental health problems, as well as the adverse effects they may experience (Schelle, Faulmuller, Caviola & Hewstone, 2014). Schermer, Bolt, de Jongh and Olivier (2009) argue that the conditions for which these CEDs are prescribed provide benefits which outweigh the associated risks but, perhaps, in relation to cognitive enhancement for non-clinical groups, the benefits may not outweigh the risks and harms. That said, Schermer et al. did not support their argument with evidence related to CEDs and did not specify what these risks and benefits were. Conversely, a qualitative study by Aikins (2011) reported that all 12 USA students interviewed stated that they considered the negative trade-offs worth the benefits. This question of risk/benefit trade-off in relation to the off-prescription use of CEDs has, therefore, become one of the topics investigated by this study.

Although several studies have sought to evaluate prevalence of use and awareness of risk, most of these are based on data solely from the United States (e.g. Barrett, Darredeau, Bordy & Pihl, 2005; Maher, 2008). It is, therefore, still unclear how widespread the off-prescription use of these drugs is in the UK and also internationally. There is also a dearth of research investigating the self-prescribed use of CEDs for poor cognitive performance. In order to assess the potential risks and harms associated with CEDs, it is important to understand what motivations are driving this increasing popularity in pharmaceutical cognitive enhancement. Studies investigating motivation for use have focused specifically on one class of CEDs, namely stimulants and, again, most of these studies are based on data from the United States (Drazdowski, 2016). The documented potential risks and harms associated with the use of CEDs, in general, include not only prison sentences for illegal use and possession but also the possible development of obsessive-compulsive behaviours and general behavioural inflexibility issues (Urban & Gao, 2014).

In addition to understanding the motivations behind the desire to seek CEDs, as mentioned earlier, the possibility of self-medication for poor cognitive functioning should also be considered. For example, previous studies have found prospective memory impairments in children with ADHD (Kerns & Price, 2001; Kliegel, Ropeter & Mackinlay, 2006).

Prospective memory involves the ability to remember previously planned actions at the appropriate time in the future (Kliegel & Jager, 2006). Prospective memory is an important function in the performance of everyday life, as is retrospective memory. Retrospective memory is the ability to remember past episodic experiences and semantic information (Smith, Del Sala, Logie & Maylor, 2000). Fuermaier et al. (2013) investigated complex prospective memory in adults with ADHD and found significant impairment specifically, in task planning abilities, compared with controls. The Prospective and Retrospective Memory Questionnaire (PRMQ, Smith, et al., 2000) is a well-established self-report measure which has demonstrated good reliability in each of the Total, Prospective and Retrospective scales with Cronbach alphas of 0.89, 0.84 and 0.80 respectively (Crawford, Smith, Maylor, Della Sala & Logie, 2003). Crawford et al. (2003) also provided normative data for each of the scales as *t* scores, thus providing the ability to determine whether an individual’s scores demonstrate normal or abnormal levels of prospective and retrospective memory. Studies have reported that cognitive enhancing drugs improve memory. Repantis et al. (2010) reported that a single dose of modafinil improved memory and Linssen, Vuurman, Sambeth and Riedel (2012) reported a significant improvement in declarative memory consolidation following administration of methylphenidate compared with controls. Husain and Mehta (2011) also reported episodic memory improvement with modafinil. If modafinil and methylphenidate improve memory functions, it is quite possible that these drugs are being used off-prescription to enhance these cognitive processes. The PRMQ would therefore be an appropriate tool to assess memory functions.

## **2.2 Online forum survey, Study 1a**

### **2.2.1 Aims and objectives**

The literature discussed in this chapter has looked more broadly at survey studies of CED use and more specifically, at modafinil and methylphenidate use. The literature reviewed previously in this chapter has highlighted a number of issues and the current study sought, therefore, to address the issues raised by conducting a survey focused on the off-prescription use of modafinil and methylphenidate, targeting the population of CED users via online drug forum sites. Additionally, as the therapeutic effects of modafinil and methylphenidate, which were discussed in Chapter 1, may also contribute to its popularity, the current study also aimed to address this issue.

There were five aims. The first was to describe in more detail the modafinil and/or methylphenidate using population by collecting data on demographics, mental health and illicit drug use. The second aim was to understand the pattern of use and the motivations for off-prescription use of these drugs. The third aim was to investigate the positive and negative effects of modafinil and methylphenidate off-prescription use and, considering these potential risks and harms, how this might translate into a risk/benefit trade off. The fourth aim was to understand how these risks and benefits relate to patterns of use, mental health and illicit drug use. The fifth aim was to investigate whether reported modafinil and methylphenidate off-prescription users perceive that they have poor cognitive performance for which they may be self-medicating.

The findings reported by Rabiner et al. (2009) and Singh et al. (2014), discussed in Section 2.1.2, indicate that off-prescription users of CEDs perceive many benefits from CED use, particularly in fascilitating study. Therefore, it was hypothesized that 1) more frequent use of modafinil/methylphenidate would yield greater perceived benefits and 2) the perceived benefits would outweigh the perceived negative effects (or risks). Furthermore, as it appears that modafinil and methylphenidate have the effect of ameliorating poor performance (e.g. Rabiner et al., 2009; Varsity, 2009), it seemed very plausible to assume that the benefits provided by these drugs cease to be present once the drug has worn off. Therefore, it was also hypothesized that 3) these reported benefits would not persist beyond the immediate use of modafinil/methylphenidate. Bearing in mind the mood-enhancing effects of modafinil (Price & Taylor, 2005) and methylphenidate (Delbari et al., 2011; Kerr et al., 2012), it was also hypothesised that 4) individuals with a self-declared psychiatric diagnosis would perceive greater benefits of modafinil/methylphenidate use compared with those not reporting a psychiatric diagnosis. Finally, as the literature suggests that there may be an element of self-prescribing with off-prescription ADHD medications (Poulin, 2007) it was hypothesised that 5) modafinil and methylphenidate reported off-prescription users would demonstrate poor cognitive performance as measured via the PRMQ.

### **2.2.2 Methods**

#### **2.2.2.1 Respondents**

A convenience sample of 404 respondents were recruited through online forums: Bluelight (http://www.bluelight.org) and Drugs-Forum (http://www.drugs-forum.com) were selected as they are platforms for a wide range of drug users. Reddit (http://www.reddit.com) was selected as it offers specific platforms (sub-Reddits) for discussions of illicit drug and CED use. Members of many of these forums are recreational drug users (and, in some cases, specifically CED users). They, therefore, tend to be well informed about the drugs in question. These forum members, thus, reflect specific populations of drug users. Although seven of the selected sub-Reddits were drug-related, a further four of the selected sub-Reddits were student forums. As there have been many reports of student use of CEDs during assessment periods (Lanni et al., 2008; Sattler & Weigel, 2013), the Student Room (http://www.thestudentroom.co.uk) and the student forum sub-Reddits were selected in order to obtain a broader picture of modafinil use than could be obtained through drug user forums alone. Due to the anonymous nature of data collection, however, it was not possible to separate the data collected from these two population samples. The respondents were recruited by posting an advertisement with a link to the survey on all of the forum sites (see Appendix A(ii) for details). No reward was offered for their participation. The survey was conducted over a two-month period from August 12th to October 12th, 2016. Respondents included in the study had either taken modafinil or methylphenidate or they reported that they had been aware of CEDs in general and/or the specific CEDs in question. Two exclusion criteria were used; firstly, respondents had to be aged over 18 years and, secondly, they must not be under the influence of a psychoactive drug whilst completing the survey.

#### **2.2.2.2 Materials**

The survey was constructed following an analysis of other recent drug and CED-user surveys (Schelle et al., 2015; Singh et al., 2014; Winstock et al., 2011) and the identification of the outstanding questions from the current literature regarding motivations for use and access to CEDs (Ragan et al., 2013), see Appendix A(i) for full details. QualtricsXM survey software was used to create the online survey and the survey was piloted by 10 respondents, resulting in no changes being made.

The presentation of an information sheet was followed by the consent form which, once clicked on, indicated informed consent. The questionnaire, which was divided into individual sections (which are detailed below), was then presented and ended with a debriefing page which contained the option to submit the questionnaire or exit without submitting. In total, 97 questions were presented (although, depending on their responses, respondents were not necessarily required to answer every question). The estimated response time varied from five to 25 minutes, depending respondents’ extent of knowledge and experience of use of the drugs.

#### **2.2.2.3 Demographics**

In order to gain a greater insight into the profile of the modafinil and methylphenidate users frequenting these forum sites, demographic information was collected. This section consisted of nine questions covering age, gender, nationality, country of residence, educational and employment details.

#### **2.2.2.4 Drug awareness**

The two questions in this section focused on the awareness of CEDs and the respondent’s willingness to take them. Respondents who reported awareness of either drug but indicated that they did not use either drug themselves, were then directed to the statements of opinions detailed in Section 2.3.2.

#### **2.2.2.5 Drug use**

This section comprised of 18 questions relating to drug use history (marijuana, cocaine, amphetamines such as speed, and MDMA/ecstasy). Drug use questions required respondents to indicate, with a ‘yes’ or ‘no’ response, lifetime use, use in the last year and attendance at drug and alcohol treatment programmes (e.g. “Have you ever been treated for a drug or alcohol-related problem?”). Data from drug use history were also analysed to investigate the impact of recreational drug use on the perceived effects of taking modafinil and methylphenidate.

#### **2.2.2.6 Psychiatric health**

There were four questions in this section relating to psychiatric diagnosis and psychiatric treatment. Example questions were “Have you ever been diagnosed with a psychiatric condition?”, “What was the diagnosis?”, and “Are you still receiving treatment?”. The term ‘psychiatric diagnosis’ was used in order to highlight that a formal diagnosis of mental health issues was required and to avoid any cultural or international differences in how the term ‘mental health’ might have been perceived by respondents. Given that the questions were framed in this way, the term ‘psychiatric diagnosis’ has continued to be used when reporting the responses to these questions in the Results section.

#### **2.2.2.7 Modafinil and methylphenidate use**

These two sections were devoted to the CEDs, modafinil and to methylphenidate, each consisting of 16 questions. These included questions on frequency of use, dosage taken, how the drugs were obtained, concurrent use of other drugs, motivations for use and perceived positive and negative effects (referred to in this thesis as benefits and risks) experienced after taking either drug. Positive effects were drawn from previous surveys and reviews of both modafinil and methylphenidate (Dietz et al., 2016; Kinman, Armstrong & Hood, 2016; Rabiner et al, 2009; Repantis et al., 2010), and from online forum posts on the Reddit site ([www.reddit.com](http://www.reddit.com)). Negative effects were drawn from the pharmaceutical data sheets for both drugs (Provigil, n.d.; Ritalin, n.d.). A list of 14 known positive effects (including ‘none’) was presented, for example, “increased concentration”, “motivation”, “clarity of mind”, “ability to focus” and “alertness”. The list format for this question was chosen in preference to providing a free text response in order to avoid respondents misinterpreting the nature of what was required by the question and to facilitate data entry and analysis. A total of 24 negative effects (including ‘none’) were presented in the same way, examples include anxiety, insomnia and chest pains. Both lists were presented twice, respondents were asked to self-report their experiences with modafinil/methylphenidate during two timeframes, namely ‘immediate – whilst on the drug’ and ‘longer-lasting – once the drug has worn off’. All four lists had the option for respondents to select as many items as they felt applied to them, as well as the option to tick ‘other’ which, if selected, brought the participant to a text box where further effects could be added via keystrokes. Further questions were included to assess knowledge of recommended dosages, perceptions of harmful use and dependency on modafinil/methylphenidate. See Appendix B(i) for full details.

#### **2.2.2.8 Prospective and Retrospective Memory Questionnaire (PRMQ)**

The PRMQ (Smith et al., 2000) consists of 16 items presented as questions, for example, “Do you forget something that you were told a few minutes before?”. Response selection is presented with a five-point Likert scale with each response scored as ‘very often’ = 5, ‘quite often’ = 4, ‘sometimes’ = 3, ‘rarely’ = 2 and ‘never’ = 1. Total scores range from 16 to 80 indicating performance ranging from normal to extremely poor respectively. The questions cover eight aspects of memory, namely, prospective short-term self-cued, prospective short-term environmentally-cued, prospective long-term self-cued, prospective long-term environmentally cued, retrospective self-cued, retrospective short-term environmentally-cued, retrospective long-term self-cued, and retrospective long-term environmentally-cued. Scores for each section range from two to 10. Environmentally-cued refers to external stimuli which evoke bottom-up responses, whereas self-cued refers to internally driven, self-directed, top-down responses (Smith et al., 2000).

#### **2.2.2.9 Design**

A three-way mixed-design ANOVA was used to investigate the perceived effects of modafinil and methylphenidate and their frequency of use. There was one between-group factor, frequency of use of modafinil/ methylphenidate (with five levels: every day, three or more times a week, once or twice a week, two or three times a month and six times or less a year). The two within-group factors were the timeframe over which the effects of modafinil/ and methylphenidate were reported (with two levels: immediate and longer-lasting) and the perceived effects of modafinil/ methylphenidate (with two levels: benefits and risks).

Further to this, a between-group design was used to investigate whether reported psychiatric diagnosis status had an effect on the perceived effects of either modafinil or methylphenidate.

#### **2.2.2.9 Procedure**

Ethical approval was granted for the study by the School of Applied Sciences Research Ethics Committee at London South Bank University, UREC 1626. A link to the survey, along with an advertisement, was posted, with appropriate permission, to the selected forum sites. The advertisement explained the nature of the survey and that individuals would be invited to participate if they had either heard of modafinil or methylphenidate or any other CEDs but had not tried them, or if they had tried them. The link to the survey first presented an information sheet, followed by a consent form which had to be clicked on for the survey to commence. At regular intervals, on the recommendation of the Research Ethics Committee, an option to exit the form was provided. Those who had not taken either modafinil or methylphenidate were directed straight to the section relating to opinions about CEDs. The survey ended with a debriefing text and a submit button which had to be clicked in order for the data to be logged and included in the analyses.

### **2.2.3 Results**

This study focused on individuals who reported using modafinil or methylphenidate without a prescription and reported choosing to do so specifically for the purposes of cognitive enhancement. Therefore, the data from individuals who were prescribed these drugs for medical reasons rather than for enhancement were not relevant to this research. Survey questions relating to prescribed medication use and psychiatric diagnosis made it possible to identify and exclude respondents who had prescriptions for either drug. The final sample size was 336, following the removal of the data from 70 respondents who were prescribed either modafinil or methylphenidate.

Of the final sample size, 253 (75.30%) respondents reported taking either modafinil or methylphenidate, 149 (45.35%) indicated that they took modafinil only, 34 (10.12%) had reported taking methylphenidate only, 70 (20.83%) had reported taking both and 83 (24.70%) had reported taking neither drug, 10 of which reported that they were not aware of CEDs.

In the following results sections, the term “reported off-prescription modafinil users” refers to all respondents who reported using modafinil and the term “reported off-prescription methylphenidate users” refers to all respondents who reported using methylphenidate. Therefore, there was some overlap of reported modafinil use between these groups.

#### **2.2.3.1 Demographic information**

Most of the respondents (including those who had never taken or heard of CEDs) were male (77%), the mean age was 26 years (SD = 9.12), with a range of 50 years (18-68). The majority of the respondents reported being USA citizens (37%), followed by British (24%), Europeans (excluding British) made up 15% of respondents, followed by Australians (8%), Canadians (6%) and the remaining 8% reported being from a mix of other countries.

The majority of respondents stated that they were university educated (59%), with 19% indicating that they had been awarded post-graduate degrees and 40% stating that they had obtained undergraduate degrees. The remaining 40% indicated that they were educated to age 18 and less than 1% were educated to age 16. A total of 56% of respondents reported that they were currently studying for a qualification and 79% of those respondents said they were university students.

Of the respondents, 41.4% were in full-time employment, 28.4% were in part-time employment (paid and unpaid) and 30.1% were unemployed. The questions asked here did not allow confirmation of whether the unemployed were students or not.

#### **2.2.3.2 Mental Health**

The proportion of respondents who reported having been diagnosed with a psychiatric condition totalled 25.7%, and of those, 41.7% were diagnosed with depression, 9.5% were diagnosed with anxiety and 31% were diagnosed with both. See Appendix A(vi) for details.

#### **2.2.3.3 Illicit Drug Use**

Levels of reported illicit drug use among the respondents in this study were high. A total of 81% of respondents reported lifetime use of cannabis, 36% reported lifetime use of cocaine, 40% reported lifetime use of stimulants and 42% reported lifetime use of MDMA. See Appendix A(vii) for full details.

#### **2.2.3.4 Modafinil and Methylphenidate**

##### **2.2.3.4.1 Sources of access**

The main source of access to modafinil was reported to be via online sources (e.g. online pharmacies), and this was reportedly the sole source of access for the majority of modafinil users. For methylphenidate, the reported main source was through a friend and, again, this was reportedly the sole source of access for the majority of the methylphenidate users (see Table 2.2 for full details).

**Table 2.2. Sources of access to modafinil and methylphenidate\***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Sources of access to CED** | **Modafinil N (%)** | | **Methylphenidate N (%)** | |
|  | **Total** | **Sole access\*\*** | **Total** | **Sole access\*\*** |
| **GP script** | 14 (6.39) | 9 (4.11) | 18 (17.31) | 14 (13.46) |
| **Someone else’s prescription** | 4 (1.83) | 1 (0.46) | 34 (32.69) | 17 (16.35) |
| **Friend** | 18 (8.22) | 11 (5.02) | 46 (44.23) | 22 (21.15) |
| **Dealer** | 16 (7.31) | 8 (3.65) | 18 (17.31) | 9 (8.65) |
| **Online** | 170 (77.63) | 151 (68.95) | 12 (11.54) | 9 (8.65) |
| **Other** | 22 (10.05) | 18 (8.22) | 11 (10.58) | 7 (6.73) |

**\* Numbers quoted (N) are frequency data**

**\*\* Most participants reported using one, sole, source to obtain these drugs**

**Modafinil N = 219, Methylphenidate, N = 104**

##### **2.2.3.4.2 Motivations for use**

The most commonly reported motivation for use of both modafinil and methylphenidate was for attention and focus. This was the most common sole motive for using modafinil and methylphenidate (for modafinil this was alongside ‘Exams’). This was followed, both for modafinil and methylphenidate, by ‘to get more done’ (see Table 2.3 for details).

**Table 2.3. Motivations for use of modafinil and methylphenidate\***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Motivations for use** | **Modafinil N (%)** | | **Methylphenidate N (%)** | |
|  | **Total** | **Sole motive** | **Total** | **Sole motive** |
| **Long hours** | 119 (54.34) | 4 (1.83) | 31 (29.81) | 3 (2.89) |
| **For attention and focus** | 183 (83.56) | 8 (3.65) | 77 (74.04) | 11 (10.58) |
| **To get more done** | 169 (77.17) | 5 (2.28) | 65 (62.50) | 3 (2.89) |
| **Exams** | 71 (32.42) | 8 (3.65) | 43 (41.35) | 2 (1.92) |
| **Night work** | 42 (19.18) | 1 (0.46) | 17 (16.35) | 1 (0.96) |
| **To think more clearly** | 120 (54.80) | 3 (1.37) | 38 (36.54) | 1 (0.96) |
| **Other\*\*** | 28 (12.79) | 6 (2.74) | 17 (16.35) | 10 (9.61) |

**\* Numbers quoted (N) are frequency data**

**\*\* See Appendix A(vii) for full details**

**Modafinil N = 219, Methylphenidate N = 104**

Although the majority of modafinil users reported between one and five reasons for use (most commonly three reasons), some reported up to seven. The majority of the methylphenidate users reported between one and four reasons for use (most commonly four reasons).

##### **2.2.3.4.3 Modafinil**

The following section reports findings relating solely to reported modafinil use.

###### **2.2.3.4.3.1 Dosage**

The most common reported doses of modafinil were 200mg (28.7%) and 100mg (22.8%). See Appendix A(viii) for full details.

###### **2.2.3.4.3.2 Perceived effects and frequency of use of modafinil**

The overall number of reported effects was calculated by summing the total number of boxes ticked in the perceived benefits and risks section of the questionnaire. Respondents taking modafinil on a daily basis reported the greatest number of both benefits and risks. The means and SDs are displayed in Table 2.4.

**Table 2.4. Means for perceived effects of modafinil.**

*Percentages relate to the number of respondents within each category of usage frequency***.**

|  |  |  |
| --- | --- | --- |
| **Frequency of**  **Modafinil use** | **% of respondents**  **reporting frequency of modafinil use** | **Mean (SD) overall number of effects** |
| **Every day** | 10.48% | 4.39 (0.27) |
| **Three or more days per week** | 30.48% | 3.68 (0.17) |
| **Once or twice per week** | 24.76% | 3.70 (0.19) |
| **Two or three times per month** | 17.14% | 3.17 (0.22) |
| **Six times or less per year** | 17.14% | 2.27 (0.22) |

There was a significant main effect of frequency of modafinil use on the number of effects reported, F(4, 214) = 6.91, MSE = 7.42, *p*< .001, ηp2 = 0.114. Compared with the respondents who’s reported modafinil usage was six or fewer times per year, Bonferroni post hoc tests confirmed significant differences in the number of effects identified between those who reported taking modafinil once or twice per week, *p* = .010, three times or more per week, *p* = .007, and every day, *p* < .001. A significant difference was also found in the number of benefits reported between those respondents who reported taking modafinil two or three times per month and those who reported taking it every day, *p* = .006. A higher number of effects was reported by more frequent users of modafinil.

The respondents reported experiencing more immediate effects (mean = 4.99, SE = 0.14) than longer-lasting effects (mean = 2.07, SE = 0.10) and there was a significant main effect of timeframe of modafinil use, F(1, 214) = 465.21, MSE = 3.648, *p* < .001, ηp2 = 0.685.

The respondents reported more benefits (mean = 5.26, SE = 0.17) than risks (mean = 1.80, SE = 0.07). There was a significant main effect of perceived benefits and risks on modafinil use, (*F*(4, 214) = 379.3, *MSE* = 6.264, *p* < .001, ηp2 =.639).

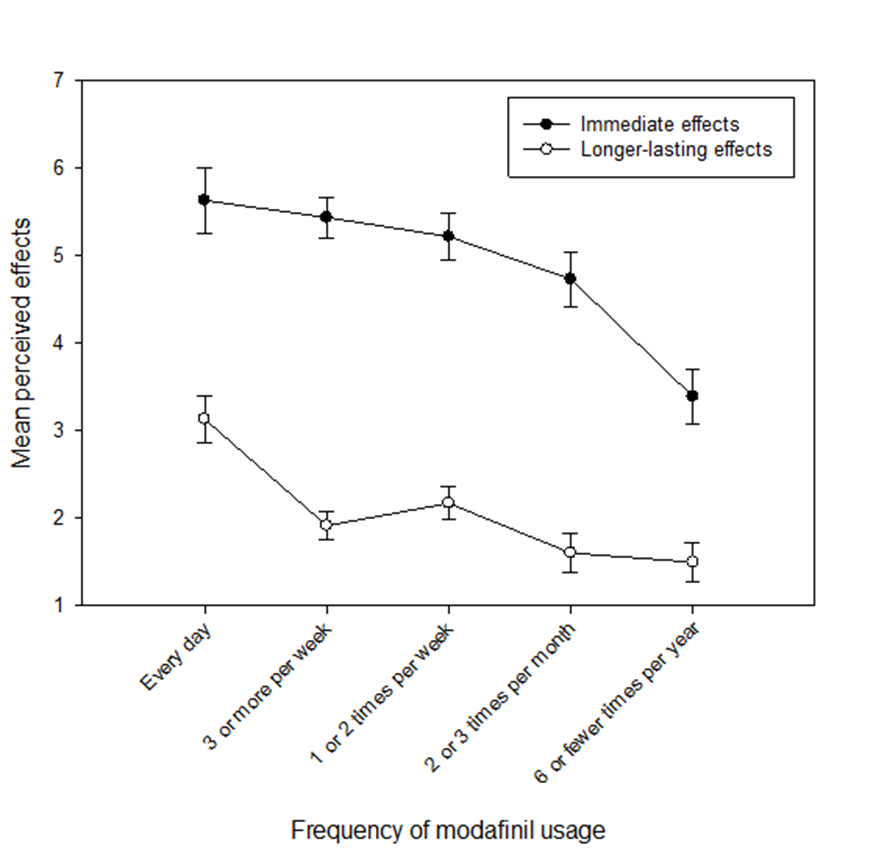
###### **2.2.3.4.3.3 Timeframe and frequency of use of modafinil**

There was a significant interaction between timeframe and frequency of use of modafinil, F(4, 214) = 2.53, MSE = 3.648, *p* = .041, ηp2 = 0.045. Figure 2.1 shows that the number of immediate effects was reported as being greater with more frequent use of modafinil. Post-hoc within-subjects *t*-tests confirmed that the difference between immediate and longer-lasting effects was significant for all five frequency of use groups (all *p*’s < .04). The data presented in the 2 x 2 x 5 ANOVAs were not normally distributed. However, the overall pattern of the results remained the same after log transformation of the ANOVAs (see Appendix A(ix) for the analysis).

In order to determine the relative magnitude of the differences between the perceived immediate and longer-lasting effects, Cohen’s *d* was calculated to establish the effect size for the difference for each frequency of use group (see Table 2.5 for details). The results indicated that the effect size was smaller for both once or twice per week and six or fewer times a year than for all other frequency of use groups. The two-way interaction appears, therefore, to be due to a smaller difference between the reported immediate and longer-lasting effects in the most and least frequent use groups. Figure 2.1 suggests that every day users reported a higher number of long-term effects (risks and benefits combined) and those that reported a frequency of use of six times or fewer reported fewer immediate effects (both risks and benefits combined).

**Table 2.5. Cohen’s *d*’s for difference between immediate and longer-lasting effects by frequency of modafinil use**

|  |  |
| --- | --- |
| **Frequency of use** | **Cohen’s *d*** |
| **Every day/almost every day** | 1.29 |
| **Three or more times per week** | 1.40 |
| **Once or twice per week** | 1.23 |
| **Two or three times per month** | 1.32 |
| **Six times or less per year** | 1.00 |



**Figure 2.1. The interaction between the reported immediate and longer-lasting effects and the reported frequency of use of modafinil.**

###### **2.2.3.4.3.4 Perceived benefits and risks and frequency of modafinil use**

There was a significant interaction between perceived benefits and risks and the reported frequency of use of modafinil, F(4, 214) = 4.597, MSE = 6.264, *p* < .001, ηp2 = 0.079, and this is plotted in Figure 2.2. Post-hoc within-subjects *t*-tests confirmed that significantly more benefits than risks were reported for all five frequencies of use groups (all *p*’s < .001). Cohen’s *d* was calculated to establish the effect size for the difference between risks and benefits for each frequency of use group. The effect size was smallest for six or fewer times a year (see Table 2.6).

**Table 2.6. Cohen’s *d*’s for frequency of use of modafinil**

|  |  |
| --- | --- |
| **Frequency of use** | **Cohen’s *d*** |
| **Every day/almost every day** | 1.40 |
| **Three or more times per week** | 1.48 |
| **Once or twice per week** | 1.37 |
| **Two or three times per month** | 1.46 |
| **Six times or less per year** | 1.14 |

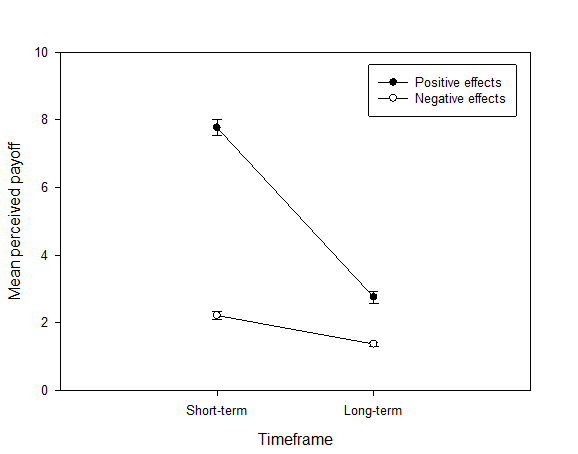
Figure 2.2. demonstrates that the reported frequency of use of modafinil of less than once a month yielded a smaller difference between its perceived risks and benefits.

C:\Users\Rachel T\Dropbox\PhD\THESIS\Fig 2.TIF

**Figure 2.2. The interaction between the numbers of benefits and risks identified by respondents and the frequency of reported use of modafinil.**

**2.2.3.4.3.5 Timeframe and perceived benefits and risks of modafinil**

The interaction between timeframe and perceived benefits and risks was also significant, F(1, 214) = 313.32, MSE = 2.739, *p* < .001, ηp2 = 0.594, as shown in Figure 2.3. The reported immediate benefits were higher than the immediate risks (mean(benefit) = 7.77, SE = 0.24, mean(risk) = 2.22, SE = 0.11, *t* = 22.758, df = 218, *p* < .001, *d* = 1.54). Longer-lasting benefits were also higher than longer-lasting risks (mean(benefit) = 2.76, SE = 0.17, mean(risk) = 1.38, SE = 0.06, *t* = 8.111, df = 218, *p* < .001). The effect size for the difference between the immediate risks and benefits was higher (*d* = 1.54) than the effect size for the longer-lasting risks and benefits (*d* = 0.54). A table of the means and SEs for immediate and longer-lasting risks and benefits for both modafinil and methylphenidate can be found in Appendix A(x).



**Figure 2.3. The interaction between the numbers of perceived benefits and risks and the immediate and longer-lasting effects for modafinil.**

The three-way interaction between perceived benefits and risks, timeframe and frequency of use of modafinil was not statistically significant, F(4, 214) = 1.53, MSE = 2.739, *p* = .195.

##### **2.2.3.4.4 Methylphenidate**

This section reports findings relating solely to reported methylphenidate use.

###### **2.2.3.4.4.1 Dosage**

The most commonly reported dosage of methylphenidate taken at any one time was 20mg (7.8%) and 10mg or less (4.9%). See Appendix A(xi) for full details.

###### **2.2.3.4.4.2 Perceived effects and frequency of use of methylphenidate**

Respondents reported more benefits (mean = 4.68, SD = 0.28) than risks (mean = 2.71, SD = 0.27). There was a significant main effect of perceived benefits and risks on methylphenidate use, F(12, 99) = 33.989, MSE = 5.908, *p* < .001, ηp2 = .256.

The main effect of frequency of use of methylphenidate was not significant, F(4, 99) = 1.943, MSE = 9.873, *p* = .109. The means and SDs are displayed in Table 2.7.

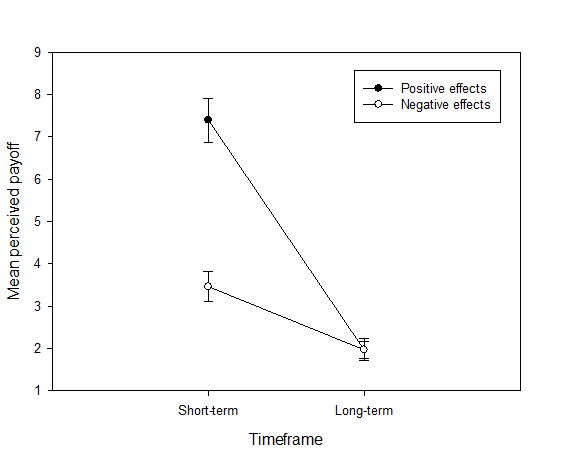
**Table 2.7. Frequency of Methylphenidate Use Means (SD)**

|  |  |  |
| --- | --- | --- |
| **Frequency of methylphenidate use** | **% of respondents reporting frequency of methylphenidate use** | **Mean (SD)**  **Overall number of effects** |
| **Every day** | 10.2% | 4.00 (0.45) |
| **Three or more days per week** | 4.08% | 2.80 (0.70) |
| **Once or twice per week** | 9.18% | 3.89 (0.52) |
| **Two or three times per month** | 15.31% | 4.43 (0.42) |
| **Six times or less per year** | 61.23% | 3.36 (0.20) |

###### **2.2.3.4.4.3 Timeframe and frequency of use of methylphenidate**

Respondents reported more immediate effects (mean = 5.43, SD = 0.35) than longer-lasting effects (mean = 1.97, SD = 0.17). There was a significant main effect of timeframe on methylphenidate use, with more immediate effects reported than longer-lasting effects, F(1, 99) = 103.361, MSE = 6.016, *p* < .001, ηp2 = 0.511.

The interaction between timeframe and frequency of use of methylphenidate was not significant, F(4, 99) = 1.013, MSE = 6.016, *p* = .404. The interaction between perceived effects and frequency of use of methylphenidate was also not significant, F(4, 99) = 0.785, MSE = 5.908, *p* = .538. However, the interaction between timeframe and perceived effects was significant, F(1, 99) = 46.936, MSE = 4.287, *p* < .001, ηp2 = 0.32, indicating a pattern similar to modafinil of greater immediate benefits (*d* = 0.97) with no difference between longer-lasting benefits and risks (*d* = -0.10). The interaction is plotted in Figure 2.4.



**Figure 2.4. The interaction between the immediate and longer-lasting effects and the reported numbers of benefits and risks for methylphenidate.**

###### **2.2.3.4.4.4 Timeframe and perceived effects of methylphenidate**

The interaction between timeframe, perceived effects and frequency of use of methylphenidate was not significant, F(4, 99) = 0.087, MSE = 4.287, *p* = .986.

##### **2.2.3.5 Perceived dependency, safe dosage and use of other drugs**

###### **2.2.3.5.1 Perceived dependency and safe dosage for modafinil and methylphenidate**

Only 5.5% of respondents reported feeling dependent on modafinil and only 6.7% of respondents reported feeling dependent on methylphenidate. In response to the question “How much modafinil/methylphenidate do you think it is safe to take at any one time”, the majority of respondents (50.7%) reported believing that a dose of 200mg of modafinil was safe to take at any one time (all frequency categories for modafinil are shown in Table 2.8).

**Table 2.8. Perceived safe dosage for modafinil**

|  |  |  |
| --- | --- | --- |
| **Dosage** | **Frequency** | **Percentage** |
| **50mg** | 4 | 1.8% |
| **100mg** | 12 | 5.5% |
| **200mg** | 111 | 50.7% |
| **Up to 400mg** | 69 | 31.5% |
| **More than 400mg** | 23 | 10.5% |

There was no distinct majority for any dosage of methylphenidate and roughly similar numbers of respondents selected doses from 20mg to more than 60mg as shown in Table 2.9.

**Table 2.9. Perceived safe dosage for methylphenidate**

|  |  |  |
| --- | --- | --- |
| **Dosage** | **Frequency** | **Percentage** |
| **None** | 6 | 5.8% |
| **5mg** | 2 | 1.9% |
| **10mg** | 7 | 6.7% |
| **20mg** | 19 | 18.3% |
| **30mg** | 13 | 12.5% |
| **40mg** | 15 | 14.4% |
| **50mg** | 12 | 11.5% |
| **60mg** | 13 | 12.5% |
| **More than 60mg** | 17 | 16.3% |

In response to the question “Would you be putting yourself in danger if you took modafinil?” a high majority (98.2%) of respondents answered ‘No’ to the options ‘Six times or less per year’ and ‘twice per month’, as well as ‘once per week’ (97.3%) and ‘Three or more times per week’ (85.4%). A slight majority of 53.9% felt that taking modafinil every day would not put them in danger (see Table 2.10).

Taking methylphenidate every day was perceived as being dangerous (68%). A slight minority of respondents felt that it was safe to take methylphenidate three or more times per week and taking methylphenidate once per week to six times or less per year was perceived as being safe (see Table 2.10).

**Table 2.10. Responses to the question asking whether respondents felt they would be putting themselves in danger by taking modafinil/ methylphenidate at different levels of frequency**

|  |  |  |
| --- | --- | --- |
| **Frequency of dose** | **Yes modafinil** | **Yes methylphenidate** |
| **Every day** | 101 (46.1%) | 70 (68%) |
| **3 or more times per week** | 32 (14.6%) | 47 (45.2%) |
| **Once per week** | 6 (2.7%) | 17 (16.3%) |
| **Twice per month** | 4 (1.8%) | 8 (7.7%) |
| **6 times or less per year** | 4 (1.8%) | 5 (4.8%) |

##### **2.2.3.4.6 Drug use and perceived effects of modafinil and methylphenidate**

Mann-Whiney U tests were performed to establish whether mental health diagnostic status and drug use had any impact on perceived effects of modafinil and methylphenidate. For this analysis, the total number of perceived risks was subtracted from the total number of perceived benefits. This created an index of benefits versus risks, with positive scores indicating that benefits outweighed risks. Mann-Whitney U tests were performed for both immediate and longer-lasting risks/benefits of modafinil and methylphenidate on the following questions: ‘Have you ever been diagnosed with a mental health condition?’, ‘Have you ever taken cannabis, ecstasy, speed or amphetamines?’ (referred to here as ‘lifetime use’) and ‘Have you taken cannabis, ecstasy, speed or amphetamines in the last year?’.

Using cannabis was not related to perceived effects of modafinil and methylphenidate (p’s >0.1) for all comparisons. Using cocaine was related to greater immediate benefits from taking methylphenidate. Individuals who reported lifetime use of cocaine (mean = 1.40, SD = 3.03) experienced greater immediate benefits of methylphenidate than those with no lifetime use of cocaine (mean = 0.95, SD = 2.45). This difference was significant, U = 11205.5, N*user* = 119, N*nonuser* = 211, *p* = 0.038. Using cocaine in the last year was not related to perceived effects of modafinil and methylphenidate (p’s > 0.15 for all comparisons).

Using amphetamines was related to greater perceived immediate benefits of both modafinil and methylphenidate. Individuals who reported lifetime use of amphetamines (mean = 4.14, SD = 4.02) experienced greater immediate benefits of modafinil than those with no lifetime use of amphetamines (mean = 3.22, SD = 3.83). This difference was significant, U = 11337.0, N*user* = 133, N*nonuser* = 198, *p* = .027. Individuals who reported lifetime use of amphetamines (mean = 2.05, SD = 3.40) reported experiencing greater immediate benefits of methylphenidate than those with no stated lifetime use of amphetamines (mean = 0.52, SD = 1.89). This difference was statistically significant, U = 9430.0, N*user* = 133, N*nonuser* = 198, *p* < .001. Lifetime reported use of amphetamines was not related to perceived longer-lasting effects of modafinil (*p* = .95) and methylphenidate (*p* = .33). Using amphetamines in the last year was related to greater perceived immediate benefits of methylphenidate only. Individuals who reported using amphetamines in the last year (mean = 2.57, SD = 3.75) reported experiencing greater immediate benefits of methylphenidate than those with no recent use of amphetamines (mean = 0.77, SD = 2.36). This difference was significant, U = 4543.5, N*user* = 67, N*nonuser* = 195, p < .001. All other comparisons for using amphetamines in the last year were not significant (all p’s > 0.44).

Using MDMA was related to greater perceived immediate benefits and greater longer-lasting risks of methylphenidate. Individuals who reported lifetime use of MDMA (mean = 1.36, SD = 2.86) reported experiencing greater immediate benefits of methylphenidate than those with no lifetime use of MDMA (mean = 0.95, SD = 2.56). This difference was significant, U = 12473.5, N*user* = 141, N*nonuser* = 193, *p* = .030. Individuals who reported lifetime use of MDMA (mean = -0.21, SD = 1.73) stated that they experienced greater longer-lasting risks of methylphenidate than those with no lifetime use of MDMA (mean = 0.02, SD = 0.82). This difference was significant, U = 11996.0, N*user* = 141, N*nonuser* = 193, *p* = .018. Lifetime use of MDMA was not related to perceived immediate (*p* = .114) or longer-lasting (*p* = .77) effects of modafinil. Use of MDMA in the last year was not related to perceived effects of modafinil or methylphenidate (p > 0.1 for all comparisons).

#### **2.2.3.5 Mental health**

Reported mental health diagnostic status was related to longer-lasting effects of modafinil only. Individuals who reported a psychiatric diagnosis reported experiencing greater longer-lasting benefits of modafinil than those without a diagnosis (see Table 2.11). All other comparisons (i.e. longer-term risks/benefits of modafinil and methylphenidate, immediate risks/benefits of methylphenidate) were not significant (p’s > 0.17).

**Table 2.11. Effects of mental health diagnosis on perceived effects of modafinil.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Yes/No\*\*\* (N)** | **Immediate effects\*** | | | **Longer-lasting effects\*** | | |
|  |  | **Mean (SD)** | **M-W\*\*** | ***p*** | **Mean (SD)** | **M-W\*\*** | ***p*** |
| **Psychiatric diagnosis** | Yes (48) | 5.10 (4.01) | 3737.5 | 0.343 | 1.98 (2.88) | 3259.0 | 0.021 |
| No (171) | 5.65 (3.48) | 1.16 (2.28) |

**Respondents (N = 219)**

**\* Scores reported are a ‘risk-benefit’ trade off calculated by subtracting the number of negative effects from the number of positive effects.**

**\*\* M-W = Mann-Whitney U**

**\*\*\* Yes/No indicates those who had not reported having had a psychiatric diagnosis.**

#### **2.2.3.6 PRMQ**

In order to compare scores on the PRMQ for reported off-prescription modafinil and methylphenidate users, scores from respondents who reported only using modafinil (modafinil-only group, N = 148) were compared with those from respondents who reported using methylphenidate (methylphenidate group, N = 106) and may or may not also use modafinil. These groupings were used to allow comparison of these data to the groups used in Study 2. Means and SDs for scores on the Prospective, Retrospective, and total PRMQ scores for these two groups are detailed in Table 2.12, along with the normative data provided by Crawford et al. (2003).

**Table 2.12. PRMQ Means and SDs for modafinil and methylphenidate and normative data.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Total PRMQ score** | | **Prospective score** | | **Retrospective score** | |
|  | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** |
| **Modafinil-only** | 38.59 (9.99) | 21-72 | 21.08 (5.64) | 11-38 | 17.51 (4.90) | 9-35 |
| **Methylphenidate** | 40.26 (13.51) | 16-80 | 21.76 (7.26) | 8-40 | 18.50 (6.77) | 8-40 |
| **Normative data[[1]](#footnote-2)** | 38.88 (9.15) | 17-67 | 20.18 (4.91) | 8-35 | 18.69 (4.98) | 8-33 |

Normative data provided by Crawford et al. (2003) in the form of *t*-scores was used, where scores below the mean (*t* = 50, SD = 10) reflect poorer self-rated memory. The reported off-prescription modafinil users’ total PRMQ mean score is within the estimated population mean, their prospective mean score was 0.02 SDs below the population mean and their retrospective mean score was 0.01 SDs above the population mean. The reported off-prescription methylphenidate users’ total PRMQ mean score is 0.01 SDs below the population mean, their prospective mean score is 0.04 SDs below the population mean and their retrospective mean score is 0.01 SDs below the population mean. Using Crawford et al.’s critical values, it was found that there were no apparent differences between CED users and population scores.

### **2.2.4 Discussion**

To the author’s knowledge, this is the first study to report multiple aspects of the off-prescription use of modafinil and methylphenidate from an international sample of respondents who frequent online forum communities. Many previous surveys have reported the off-prescription use of ADHD medications or prescription stimulants only (e.g. Rabiner et al., 2009; Ross et al., 2018), in some cases, without separating out differences between the prescription stimulants (McCabe et al., 2006), or only separating out the difference by class of drug (Holloway & Bennett, 2012). Other surveys focused solely on pupils and students (Franke et al., 2011; Singh et al., 2014). Whilst these limitations may have suited the focus of each of the studies mentioned, the present study provides information on a much broader population of reported off-prescription modafinil and methylphenidate users. The current study used an online survey to investigate the patterns of off-prescription use of modafinil and methylphenidate among an international sample of individuals who were either visitors of drug user and CED forums or student forums. The survey covered various aspects of off-prescription CED use including demographics, illicit drug use and mental health. The overall aim of the survey was to investigate the modafinil and methylphenidate users’ perceived experiences of these drugs and how this related to their frequency of use. The results indicate that both modafinil and methylphenidate were perceived as having greater benefits than risks and a greater reported frequency of use of modafinil was found to result in greater reported benefits. However, the frequency of use of methylphenidate did not show any relationship with perceived effects of this drug.

By targeting specific drug user and CED forum sites, 75% of respondents reported the use of either modafinil or methylphenidate. Many more respondents reported taking only modafinil than only methylphenidate which may reflect either easier access to modafinil than methylphenidate or a preference for modafinil over methylphenidate. The majority of respondents reported themselves to be male, employed and university-educated. The perceived dependency on modafinil and methylphenidate was low, despite 10.48% of the sample using modafinil and 10.2% using methylphenidate reportedly every day. Overall, modafinil was perceived to being a safe drug, even when taken three times or more per week. In comparison, regular use of methylphenidate was perceived as carrying a higher level of risk. This suggests that respondents were aware of the addictive potential of methylphenidate and this may also be reflected in the lower number of respondents who reported taking this drug. However, those who reported taking methylphenidate seemed unaware of what dose to take. Relatively equal numbers of individuals stated the perceived safe dosage of methylphenidate was 20mg to 60mg. Cognitive enhancing drug users may be unaware of the recommended dose of methylphenidate, or, higher doses may be perceived as safe by those who have developed tolerance to lower doses. Alternatively, it may be down to individual differences in how methylphenidate is experienced. Volkow and Swanson (2003) noted individual differences in the clinical use of methylphenidate in children with the effective dose ranging from 5mg to 20mg regardless of the size of the child. They also noted individual differences in methylphenidate’s effects on dopamine. Conversely, most respondents appear to be aware of the recommended dose range for modafinil of 200mg. Although perceived dependency on modafinil was low, the link between frequency of use and perceived benefits suggest that there is a possibility that dependency may develop over time.

The data show that more frequent reported use of modafinil led to greater perceived benefits. It appears that the reported use of modafinil on at least a monthly basis resulted in a higher number of reported benefits whilst reported risks remain low. A plausible explanation could be that more frequent reported use occurs as a consequence of greater perceived benefits since it seems unlikely that continued use would occur without experiencing the benefits of the drug. Chronic drug use is, however, known to lead to tolerance. This is caused, in part, by a reduction in receptor numbers (O’Brien, 2011) but this may not always be the case with modafinil. Nasr, Wendt and Steiner (2006) reported that long-term use of modafinil in patients with affective disorders did not induce tolerance. Therefore, it is plausible that continued, long-term use of modafinil could still provide these perceived benefits.

The data also showed that the perceived benefits of taking modafinil outweighed the perceived risks. The respondents reported significantly more benefits than risks. It is known that modafinil is well-tolerated and lacks the undesirable adverse effects of other stimulants (Schmitt & Reith, 2011). It was, therefore, expected that the benefits would outweigh the risks based on the range of potential benefits that it offers, which include enhanced attention, comprehension and working memory (Gilleen et al., 2014), as well as alertness, vigilance and enhanced executive functions (Walsh, Randazzo, Stone & Schweitzer, 2004).

The perceived benefits also persisted beyond immediate use of modafinil. Reported everyday use of modafinil resulted in higher reported longer-lasting effects. While relatively high effect sizes might be expected when exploring differences between immediate and longer-lasting effects of modafinil, it was not expected that there would be a higher reported level of longer-lasting effects in the ‘every day’ user group. To the author’s knowledge, modafinil has not been found to exhibit any significant positive neuroplastic changes in humans. It was, therefore, expected that modafinil’s positive effects would no longer be reported to be experienced when the drug has ceased to be active. This finding may, however, be explained by the pharmacokinetic profile of modafinil. As the half-life of modafinil is approximately 12-15 hours (Darwish et al., 2009; Robertson & Hellriegel, 2003), daily use of modafinil would result in a constant, and possibly increasing, plasma concentration of modafinil, which also suggests constant, higher levels of synaptic DA and NE (in addition to other neurotransmitters that are modulated by modafinil). Increased synaptic DA and NE have been associated with improved cognitive function (Logue & Gould, 2014; Wood et al., 2014). It would seem reasonable, therefore, to argue that everyday use would lead to greater reported long-term benefits as levels of modafinil would decline to approximately 25% (i.e. two half-lives) by the time the next dose was taken, resulting in increased concentrations of modafinil in the blood. Modafinil has also been found to have an effect on the glutamate receptors of the hippocampus at ascending doses (Ferraro et al., 1997) and may well have a supportive effect on long-term potentiation and positive neuroplastic changes which could also explain the increase in longer-lasting effects in the ‘everyday’ user group.

The benefits of taking methylphenidate were also found to outweigh the risks and greater immediate (as compared with longer-lasting) effects were reported. The reported immediate benefits were much greater than the reported immediate risks, whilst there was no difference between longer-lasting benefits and risks. Again, this may be an expression of the pharmacokinetic profile of methylphenidate. As methylphenidate has a very short half-life of two to three hours (Kimko et al., 1999), it would seem reasonable that the effects of immediate-release methylphenidate would be seen over a shorter time period, following which the drug is eliminated from the body and therefore no longer-lasting effects would be present. However, to the author’s knowledge, there are only two studies that have carried out repeated dose trials of methylphenidate on healthy subjects. Gilbert, Donnelly, Zimmer and Kubis (1973) found only a reduction of fatigue following six weeks of daily methylphenidate use. Gobbi, Slater, Boucher, Debonnel and Blier (2003) reported one subjective effect of increased energy following one week of methylphenidate use. However, methylphenidate was used as a control by Gobbi et al., (2003) as the focus of their paper was on another drug. The lack of reported longer-lasting effects of methylphenidate in the current study is consistent with the profile of the immediate-release formula. Nevertheless, a limitation of this study is that the survey did not include questions relating to methylphenidate formulations, whether extended- or immediate-release tablets were used. This would have an effect on the dosage used and the experience of the drug, for example, whether one 20mg extended-release dose was used or a single 20mg immediate-release dose, which would have a much stronger effect for a shorter period of time. Therefore, the findings in relation to methylphenidate must be treated with caution.

From the current results, it would seem that the reported daily use of modafinil was found to provide the greatest perceived cognitive benefits, both immediate and longer-lasting, with a minor risk of adverse effects, whereas methylphenidate was perceived to be more of a ‘quick fix’ with no significant reported longer-lasting benefits. However, it should also be noted that the findings of online surveys can only provide a certain level of insight. The weakness of the survey method of investigation has already been discussed in the introduction of this chapter. Whilst this weakness must be acknowledged, the current study has offered useful insights into the perceived effects of both drugs and is comparable with the approach taken in other studies (Morgan, Noronha, Muetzelfeldt, Fielding & Curran, 2013; Singh et al., 2014).

One-quarter of respondents reported having been diagnosed with a psychiatric condition and a large number of those stated that they were diagnosed with depression, anxiety or both. Prevalence of mental health problems varies from country to country, by gender and by age group making direct comparisons from this study to the general population difficult. Rates of diagnosis among CED users do, however, seem to be higher than the 17.9% (of all adults in the USA) stated in the 2015 National (USA) Survey on Drug Use and Mental Health (Bose et al., 2016). One possible reason for this finding could be self-medication for fatigue and confusion. It is believed that deficiencies in DA, NE and serotonin underpin major depressive disorder (Montgomery, 2008). As both modafinil and methylphenidate intake results in higher levels of both DA and NE, and modafinil intake also results in higher levels of serotonin, it seems quite possible that the benefits of these drugs experienced by individuals with a psychiatric disorder may be due to the poorer functioning of these neurotransmitter systems. As reported by Cools et al. (2008) and Finke et al. (2010), low baseline performers (who are believed to have lower rates of DA synthesis) demonstrate much greater cognitive-enhancing effects of modafinil and methylphenidate. It seems plausible that people with potentially dysfunctional DA and NE systems may also perceive these drugs as beneficial.

The finding that people with a psychiatric diagnosis reported reduced immediate benefits of modafinil was, therefore, surprising. Modafinil has shown some efficacy for treating depression (Price & Taylor, 2005), although such studies usually involve daily administration of 200mg modafinil for six to eight weeks. The data reported in the current study are on the perceived effects of acute or one-off, non-prescribed use. One potential explanation for the reported reduced immediate benefits could be that the dysfunction in serotonergic, noradrenergic and dopaminergic systems associated with depression, anxiety and other psychiatric diagnoses (Dunlop & Nemeroff, 2007; Ressler & Nemeroff, 2000) attenuates, rather than enhances, the acute effects of modafinil. It is difficult to explore this explanation further without more detailed information on the psychiatric history of these respondents. There may also be interactions between some medications taken for anxiety or depression and modafinil, similar to the reduced subjective effects of MDMA reported by people taking selective serotonin reuptake inhibitors (Liechti & Vollenweider, 2001). Again, detailed information on the current use of prescribed medication was not collected in the current study. However, it does seem plausible that the subjective effects of modafinil, a drug with a seemingly unique, complex and not fully understood pharmacological mechanism of action, may be influenced by pre-existing differences in the functioning of neurotransmitter systems and/or concurrent use of other drugs or medication.

As would be expected from the recruitment of respondents via online drug user forums, the levels of reported illicit drug use in the sample were high. The reported lifetime use of cannabis was much higher than among the general population of Europe and America as represented by data from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2013) and the National Institute of Drug Abuse (NIDA, 2015) from America. Compared with data from the EMCDDA and NIDA, the data from the survey reported in the current chapter reveal markedly higher illicit drug use in all four categories of illicit drugs. These findings are consistent with those of Ott and Biller-Andorno (2014) who reported very similar percentages of lifetime illicit drug use among CED users. A Swiss study of CED use also reported high levels of illicit drug use, although not as high as the data in the current study (Maier et al., 2016). The findings of the current study may indicate, as suggested earlier, that illicit drug users are more likely to take CEDs since they report being more open to taking drugs in general. Conversely, although this may reflect the specific drug population targeted, it does suggest that those who are taking CEDs tend to use recreational drugs as well.

Cannabis use was not found to be related to perceived effects of modafinil and methylphenidate. There is, therefore, no evidence from this study that people are using CEDs to ameliorate the sedative or impairing effects of smoking cannabis. Users of cocaine, MDMA and amphetamine reported more immediate benefits from methylphenidate. Amphetamine users also reported more immediate benefits of modafinil. The majority of these findings relate to lifetime use of the drug, not use in the last year, suggesting that this may be related to individual differences in the perceived effects of stimulant drugs. Users of recreational drugs do tend to show higher scores on some personality measures, such as impulsivity, sensation seeking and reward sensitivity (e.g. Daumann, Pelz, Becker, Tuchtenhagen & Gouzoulis-Mayfrank, 2001; Patton, Stanford & Barratt, 1995; Wills, Vaccaro & McNamara, 1994) and people who display these personality traits may also show enhanced responses to stimulant drugs. For example, Kirkpatrick, Johanson & de Wit, (2013) found that the personality traits of impulsivity, reward sensitivity and physical fearlessness (harm non-avoidance) predict subjective responses to amphetamines. Kelly et al. (2009) reported that people who score highly on sensation seeking also report greater subjective effects of amphetamine. The data from the current study appear to support these experimental studies. Enhanced subjective effects of CEDs were seen amongst recreational users of stimulant drugs outside of laboratory conditions.

The finding that reported modafinil and methylphenidate off-prescription users did not rate themselves as poorer on prospective and retrospective memory compared to population norms suggests that this aspect of their cognitive performance is not causing these respondents problems. Perhaps the PRMQ was not the most appropriate questionnaire to use. The most commonly selected motivations for use were for attention and focus. It may be then that these are the cognitive processes which are experienced as poor. Ilieva and Farah (2015) reported low attention functioning and lower motivation in off-prescription users of ADHD mediations compared with controls using the Murphy and Barkley Diagnostic and Statistical Manual of Mental Disorders 4 (DSM-IV) ADHD Checklist (1995) self-report measure and the TOVA (Greenberg, 1990) objective measure. However, another very common motivation was ‘to get more done’, suggesting that without modafinil or methylphenidate, it was perceived that not enough was being accomplished. This may suggest a lack of motivation or an element of procrastination. This was also reported by Ilieva and Farah, following the TOVA, participants provided their self-reports on their motivation during the test and results showed that CED users reported lower motivation compared with controls. Additionally, Petersen, Norgaard and Taulsen (2015) reported that the 20 students they interviewed had reported using stimulants to prevent procrastination. Therefore, it seems likely that inattention and procrastination may be motivations for the off-prescription use of modafinil and methylphenidate.

As previously discussed in Section 2.1, the use of a survey method has its limitations. This study recruited respondents specifically from drug and CED forum sites and student forums, the sample was therefore, self-selecting and may only represent the profile and patterns of CED use of visitors of these sites. However, the intention of the current study was to learn more about CED users and the findings of this study, therefore, contribute to the knowledge and understanding of this section of the population. A further limitation is that the current study did not include questions testing for attentional problems as it is possible that there may be an element of self-medication by individuals with low baseline levels of DA and NE. Additionally, the survey did not include questions on alcohol use or routes of administration of modafinil and methylphenidate. However, to include more questions would have extended the length of the survey thus possibly deterring respondents.

To the author’s knowledge, this is the first piece of research to report a detailed understanding of the CED users’ profile and perceived experience of modafinil and methylphenidate. In sum, this study has provided insight into the profile of CED users who are, in this study, mostly male, North American or British, educated, employed and in their mid-20s. There is a pattern of recreational drug use associated with CED use and an association with psychiatric disorders, largely depression and anxiety. It was also revealing that daily use of modafinil was reported as providing the highest level of benefits and it may be possible that cognitive benefits of modafinil increase exponentially through daily use. It is interesting that this was not seen with reported methylphenidate use, suggesting that modafinil is being experienced differently. Overall, modafinil was perceived, by those who reported taking it, as safe, whereas methylphenidate was perceived as more dangerous and its benefits more of a ‘quick fix’.

The findings of this research raise a further question, namely, whether individuals are using CEDs as a supportive treatment for psychiatric disorders. Further, the question as to whether CED users are self-medicating for attentional and motivational problems remains unanswered. The suggestion that modafinil may be experienced differently to methylphenidate warrants further investigation to understand whether modafinil and methylphenidate users are two distinct groups or if they are just part of one homogenous CED user group. The following chapter addresses the weaknesses of the current study and seeks to answer the questions raised in light of the findings of Study 1.

## **2.3 Study 1b: Survey of London South Bank University students and staff.**

### **2.3.1 Introduction**

Although online surveys can provide very detailed and useful information, this information reflects that of a population of individuals who spend their time online. As such, this population may differ from the general population in relation to their views about CED use and their behaviours. Therefore, the findings of Study 1a may not reflect the broader population. They do, however, provide a greater understanding of this specific population and, with the technical advances in our information age, as discussed in Section 1.1, resulting in more affordable and accessible technology for online use, this population is likely to continue to grow in size and significance. Another significant population from which a greater understanding of CED use can be generated is the student population. A number of CED studies have surveyed university students (e.g. Bossaer et al. 2013; McCabe et al. 2006; Singh et al., 2014). As mentioned earlier, Singh et al. surveyed 104 universities, the majority of which were Russell Group universities and they reported a 17.1% lifetime use of Adderall, methylphenidate or modafinil. Modafinil use comprised of 8% (N = 70) and methylphenidate use comprised of 5.9% (N = 52). A survey of Cambridge students reported 10% lifetime use of CEDs (Varsity, 2009) and another survey reported 26% lifetime use of modafinil by Oxford students. The high reported use of CEDs in these prestigious universities may be related to the pressure to succeed in such highly competitive environments. It would, therefore, be useful to collect data from a sample of London South Bank University students and compare it with the findings of these studies in order to investigate differences in prevalence rates. It was therefore decided that this survey would be repeated within London South Bank University (LSBU) and that the data collected could then be compared with the that of Study 1a, as well as with other surveys.

### **2.3.2 Method**

The same survey as detailed in section 2.2.2 was advertised within LSBU, using posters, email notices, and via the Division of Psychology’s Research Participation Scheme (RPS) where points are accrued through study participation allowing students to use this system for their own studies. The survey was conducted between February 2017 and December 2019. A section of the survey focused on opinions about the off-prescription use of modafinil and methylphenidate. These data collected from this section of the survey were not reported in the first study as the responses would be coming from reported users of these drugs and therefore would be biased. Eight statements were presented separately for modafinil and methylphenidate with the options “strongly agree, agree, neither disagree nor agree, agree, and strongly agree”. The statements focused on whether it was safe to take modafinil/methylphenidate and whether it was fair. For example, “If my peers were taking modafinil/methylphenidate to help them achieve more I would feel pressured to do the same”. These statements were generated from the ethical concerns raised in the literature (e.g. Bostrom & Sandberg, 2009; Farah et al., 2004; Schelle et al., 2014; Singh et al., 2014).

### **2.3.3 Results**

A total of 285 respondents completed the survey of whom 55 (19.3%) were male and 230 (80.7%) were female, and the mean age was 24 years (SD = 8.45) with a range of 44 years (18-62). Of those who took part in the survey, 224 respondents signed up via the Division of Psychology’s RPS. There was a total of 19 (6.66%) reported modafinil off-prescription users and a total of 12 (4.21%) reported methylphenidate off-prescription users, which together totalled 28 (9.83%) reported users of either drug (3 respondents, 1.05%, reported using both drugs). Of these reported users of either drug, 9 (32.1%) were male and 19 (67.9%) were female, the mean age was 26 years (SD = 7.07). It was not, therefore, possible to repeat the analysis presented above from such a small sample of reported users of these drugs. Of those who had not reported taking modafinil or methylphenidate, 211 (74%) reported awareness of CEDs and when asked “If you could take a drug to increase your attention/concentration/memory, would you?” 16 (5.6%) responded “yes”, 27 (9.5%) responded “no” and 31 (10.9%) responded “maybe”.

In response to the statement of opinions relating to modafinil, a total of 45 respondents completed this section following the removal of the data from the 21 respondents who had reported having taken modafinil (see Table 2.13). These data are compared with those of Study 1a (N = 284) in Table 2.13. In response to the statements about safety, more university respondents (Study 1b) did not feel that it was safe to take modafinil (37.8%) than those who did (20%), whereas the forum users (Study 1a) took the opposite view with a high majority stating that they felt that it was safe (70.7%). Most university respondents (73.3%) did not feel pressured to take modafinil, nor did they feel that it would it affect their choices if their peers were taking it (62.2%). This was also the case, for the forum users, the majority of forum users did not feel pressured to take modafinil (54.9%), nor would it affect their choices if their peers were taking it (54.6%). However, the majority of the university respondents felt that taking modafinil was cheating (46.6%) and 40% did not agree that there was nothing wrong with taking modafinil. Conversely, a high majority of forum users did not feel that taking modafinil was cheating (84.1%) and did agree that there was nothing wrong with taking modafinil (80.3%).

**Table 2.13. Comparisons of statements of opinions of the off-prescription use of modafinil between Study 1a and Study 1b**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Study 1b (N = 45)** | | **Study 1a (N = 284)** | |
|  | **Disagree or strongly disagree**  **N (%)** | **Agree or strongly agree**  **N (%)** | **Disagree or strongly disagree**  **N (%)** | **Agree or strongly agree**  **N (%)** |
| I feel it is entirely safe for people to take modafinil for cognitive enhancement | 17 (37.8) | 9 (20.0) | 31 (10.9) | 201 (70.7) |
| I feel that taking modafinil for cognitive enhancement is dangerous | 16 (35.6) | 13 (28.9) | 221 (77.8) | 14 (5.0) |
| If my peers were taking modafinil to help them achieve more I would feel pressured to do the same | 33 (73.3) | 7 (15.6) | 156 (54.9) | 72 (25.4) |
| If my peers were taking modafinil to help them achieve it would not affect my choices | 10 (22.2) | 28 (62.2) | 82 (28.8) | 155 (54.6) |
| People should be able to take modafinil to help them succeed if they want to | 16 (35.5) | 16 (35.5) | 15 (5.3) | 248 (87.3) |
| Taking modafinil to get ahead gives those individuals an unfair advantage | 14 (31.1) | 15 (33.3) | 210 (73.9) | 33 (11.6) |
| People who take modafinil for cognitive enhancement are cheating | 10 (22.2) | 21 (46.6) | 239 (84.1) | 16 (5.6) |
| There is nothing wrong with people taking modafinil to get ahead | 18 (40.0) | 11 (24.5) | 21 (7.4) | 228 (80.3) |

In response to the statements of opinions relating to methylphenidate, a total of 115 respondents completed this section following the removal of the data from the 18 respondents who had reported having taken methylphenidate (see Table 2.14). As before, these data are compared with that of Study 1a (N = 311) in Table 2.14. In response to the statements relating to safety, 43.9% of university respondents did not feel that it was safe to take methylphenidate and 48.7% felt that it was dangerous. The majority of forum users also did not feel that it was safe to take methylphenidate (42.1%), and 35.1% felt that it was dangerous. The majority of the university respondents did not feel pressurised to take methylphenidate (74.8%) and 65.2% reported that it would not affect their choices if their peers were taking it. This was also the case for the forum users, the majority of whom did not feel pressurised to take methylphenidate (64.9%) and 59.5% felt that it would not affect their choices. The majority of university respondents (49.6%) did not agree that there was nothing wrong with taking methylphenidate, whereas the majority of forum users (52.1%) did agree that there was nothing wrong with taking methylphenidate.

**Table 2.14. Comparisons of statements of opinions of the off-prescription use of methylphenidate between Study 1a and Study 1b**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Study 1b (N = 115)** | | **Study 1a (N = 311)** | |
|  | **Disagree or strongly disagree**  **N (%)** | **Agree or strongly agree**  **N (%)** | **Disagree or strongly disagree**  **N (%)** | **Agree or strongly agree**  **N (%)** |
| I feel it is entirely safe for people to take methylphenidate for cognitive enhancement | 62 (43.9) | 11 (9.6) | 131 (42.1) | 76 (24.5) |
| I feel that taking methylphenidate for cognitive enhancement is dangerous | 14 (12.2) | 56 (48.7) | 74 (23.8) | 109 (35.1) |
| If my peers were taking methylphenidate to help them achieve more I would feel pressured to do the same | 86 (74.8) | 21 (18.2) | 202 (64.9) | 48 (15.4) |
| If my peers were taking methylphenidate to help them achieve it would not affect my choices | 23 (20.0) | 75 (65.2) | 61 (19.6) | 185 (59.5) |
| People should be able to take methylphenidate to help them succeed if they want to | 48 (41.8) | 29 (25.2) | 51 (16.4) | 185 (59.5) |
| Taking methylphenidate to get ahead gives those individuals an unfair advantage | 25 (21.8) | 60 (52.2) | 175 (56.3) | 56 (18.1) |
| People who take methylphenidate for cognitive enhancement are cheating | 36 (31.1) | 45 (39.1) | 204 (65.6) | 38 (12.2) |
| There is nothing wrong with people taking methylphenidate to get ahead | 57 (49.6) | 22 (19.1) | 60 (19.3) | 162 (52.1) |

### **2.3.4 Discussion**

In comparison with Study 1a, the majority of respondents were female, which may reflect the large number of respondents recruited via the LSBU Psychology Division’s RPS site, as the majority of psychology students at LSBU are female. The percentage of reported modafinil and methylphenidate off-prescription users in the university sample is in line with that reported by Singh et al. (2014). Off-prescription reported use of modafinil in the current study is somewhat lower than the reported use of modafinil for cognitive enhancement in their study. The reported off-prescription use of methylphenidate in the current study was slightly lower than that reported by Singh et al. Whilst the reported use of modafinil and methylphenidate in the current study is in line with the 10% of Cambridge students reported by Varsity in 2009, it is still much lower than the reported modafinil use by 26% of Oxford students (Young-Powell & Page, 2014). Although the study by Singh et al. involved mainly Russell Group universities, the Oxbridge universities are internationally recognised as being the most revered and, as the Cambridge study is 11 years old, it is likely that CED use may have increased since then.

Comparisons of the responses to the statements of opinions questions relating to modafinil use between the university respondents (Study 1b) and the forum user respondents (Study 1a) revealed that both groups of respondents did not feel pressured to take modafinil, nor would it affect their choices if their peers were taking it. However, whilst a large majority of forum users felt that it was safe to use modafinil for cognitive enhancement, a slight majority of university respondents did not agree. Similarly, a large majority of forum user respondents felt that there is nothing wrong with people taking modafinil to get ahead and that taking modafinil for cognitive enhancement is not cheating whereas a slight majority of university respondents did not agree and did feel that it was cheating. The forum users would be likely to be biased in their opinions of the off-prescription use of modafinil and the much higher percentages of these respondents who indicated positive opinions of modafinil use for each of the statements may reflect this. Overall, it would seem then that although there is a clear majority of university respondents who do not agree with the use of modafinil for cognitive enhancement, this is not felt by all university respondents.

Responses in relation to the statements of opinions relating to methylphenidate use show a different trend. The majority of both university and forum user respondents agreed that it is not safe to take methylphenidate for cognitive enhancement and that it is dangerous. As with the responses to modafinil, both groups of respondents did not feel pressured to take methylphenidate, nor would it affect their choices if their peers were taking it. However, the majority of university respondents did not feel that people should take methylphenidate to help them succeed, that it gives users an advantage and that it is wrong to take methylphenidate to get ahead. The majority of forum users had opposite opinions to the university respondents for all three of these points. Although the majority university respondents felt that taking methylphenidate for cognitive enhancement was cheating, this was a slight majority, whereas a larger majority of forum users disagreed with this statement. Overall, then, the majority of university respondents did not agree with the use of methylphenidate for cognitive enhancement, that it was dangerous and unfair. The majority of forum users also felt that taking methylphenidate for cognitive enhancement was dangerous but they did not agree that it is unfair. This supports the finding from Study 1a, that methylphenidate is perceived as dangerous.

In support of the finding that reported modafinil and methylphenidate users do not feel that it is unfair to use these drugs for cognitive enhancement, Frank, Bonertz, Christmann, Engeser and Lieb (2012) in their German study, also found that reported users of CEDs felt that it was fair, compared with non-users who disagreed. Frank et al. also reported that success was more important to the reported users of CEDs than non-users. A Swiss study also supported this finding, Maier, Liakoni, Schildmann, Schaub and Liechti (2015) found that 24% of CED users compared with 11% of non-users were more likely to consider CED use as fair. Unlike the university respondents of the current study who did not feel pressured to take modafinil or methylphenidate if their peers were taking them, Maier et al. (2015) reported that only the non-users in their study felt that CED use might increase pressure to use CEDs. The opinion that taking methylphenidate for cognitive enhancement is unfair was also shared with the majority of 19 Australian university students who were interviewed by Bell, Partridge, Lucke and Hall (2013) in a qualitative study. The opinions of the university respondents in the current study demonstrate that there is a commonly held view that CED use, at least in the university setting, is unfair and that it is cheating and this opinion was also reported by Frank et al. (2012), Maier et al. (2015), and Bell et al. (2013), demonstrating a common, internationally felt view.

The opinions of the reported modafinil and methylphenidate users in the current study are likely to be biased and may be based on a number of underlying beliefs. DeSantis and Hane (2010) interviewed 175 undergraduate students who reported the illegal use of ADHD stimulants to investigate their justifications for using CEDs. Their study revealed four common perceptions or beliefs which they felt justified their illicit use of CEDs. By favourably comparing CEDs as ‘good’ pharmaceutical drugs to ‘bad’ recreational drugs and by considering their use of CEDs to be only at specific times and therefore only taken in moderation. By perceiving ADHD stimulants as benign and harmless, these students considered their use as justifiable. However, the fourth reason given was self-medication as they felt that they probably had ADHD. Whilst DeSantis and Hane argued that their participants have trivialised ADHD as a periodic inability to concentrate, it is possible that these students in their sample are struggling with poor concentration and other cognitive problems. Similarly, it may be that the reported modafinil and methylphenidate users in the current study also hold such beliefs and may also feel that they have problems with cognitive functioning. This, again, raises the question presented at the end of Study 1a, whether reported off-prescription modafinil and methylphenidate users are self-medicating for learning and attentional problems. Additionally, considering the views expressed by university students in relation to fairness in the current study, Study 2 will seek to explore whether off-prescription users of modafinil and methylphenidate are seeking to improve their good cognitive abilities or if they are self-medicating for poor cognitive performance.

# **3 CHAPTER THREE**

**STUDY TWO: EVERYDAY ATTENTION AND DRUG USE IN REPORTED OFF-PRESCRIPTION USERS OF MODAFINIL AND METHYLPHENIDATE, AN ONLINE SURVEY**

## **3.1 Introduction**

Following the results of Study 1, the aim of Study 2 was to use a range of self-report questionnaires to explore whether self-medication may play a role in off-prescription use of modafinil and methylphenidate. Undiagnosed ADHD symptoms among college students have been noted previously by Garnier-Dykstra, Pinchevsky, Caldeira, Vincent and Arria (2010). Their study found over 10% of students who had no current ADHD diagnosis (N = 972) had high levels of ADHD symptoms. Poulin (2007) used a six-item Ontario Child Health Study Hyperactivity Scale, including questions relating to inattention, which was completed by 12,990 adolescent students. Participants, all of whom were students also reported prescription and off-prescription use of methylphenidate. She reported that the estimated prevalence of exclusively non-medical use of methylphenidate was 6.2% and that 20.5% of this group tested positively for ADHD symptomatology on the ADHD screening test. She also stated that these respondents had a 2.3-fold independent increased likelihood of non-medical use of methylphenidate, compared with those in the group who tested negative on the ADHD screening test. This suggests that students may be self-medicating for ADHD symptoms.

Ilieva and Farah (2015) used the Barkley and Murphy Current Symptom Scale (1998) to measure symptoms of inattention and impulsivity and an objective measure known as the TOVA. As discussed in Section 1.3.1, the TOVA is a continuous performance test requiring participants to make a ‘go’ or ‘no go’ response to the presentation of a sequence of geometric figures. Their 128 participants, including 61 reported off-prescription stimulant users, completed this questionnaire and the TOVA test. The results of the questionnaire indicated that the off-prescription use of ADHD medication, including methylphenidate, related positively with subjectively perceived attention problems. The results of the TOVA indicated a higher number of omission errors among off-prescription users than controls but no other correlations or effects were significant, suggesting that off-prescription users were not more likely to perform in the clinical range but do display increased attentional problems on this objective test of attention.

In the workplace, ADHD symptomology was noted in a broad range of employees from a number of private and public organisations by Rosario-Hernández et al. (2020). They found that increased levels of ADHD symptoms had a detrimental effect on job performance and counterproductive work behaviour increased. Workplace CED use has also been documented several times in the literature (e.g. Bloomfield & Dale, 2015; d’Angelo, Savulich & Sahakian, 2017; Leon, Harms & Gilmer, 2019). That said, to the author’s knowledge, there is no documented association between problems with inattention, hyperactivity and impulsivity and the off-prescription use of CEDs, such as modafinil and methylphenidate, in the workplace. However, the off-prescription use of modafinil and methylphenidate in the workplace is not well documented as many studies take place in a university setting. Recruiting respondents via online drug user forums allows access to a broader base of respondents. Indeed, this was seen in Study 1 where over 40% of modafinil and methylphenidate respondents were in full-time employment. A number of studies have also found associations between students’ off-prescription use of stimulants, such as methylphenidate, and either symptoms of inattention (Arria et al., 2011; Ilieva & Farah, 2015; Rabiner et al., 2009) or positive scores on an ADHD test (Peterkin, Crone, Sheridan & Wise, 2011; Poulin, 2007).

Both Arria et al. (2011) and Peterkin et al. (2011) used the World Health Organisation (WHO) Adult ADHD Self-Report Scale (ASRS; Kessler et al., 2005) to assess ADHD symptoms. The ASRS is a standardized and well-validated tool for assessing adult ADHD symptoms (Gray, Woltering, Mawjee & Tannock, 2014). It was developed by two board-certified psychiatrists and the WHO advisory group of clinical experts in adult ADHD to assess ADHD symptoms in adults (Kessler et al., 2005). One question was developed for each of the 18 DSM-IV Criterion A symptoms and a further 11 questions were developed to reflect symptoms not in the DSM-IV but were believed by experts to be common expressions of adult ADHD. The questions cover problems with inattention, and hyperactivity and impulsivity equally. The ASRS is comprised of 18 items, the first six items of the scale, Part A, were designed to screen adults for ADHD and consist of three questions addressing inattention and three questions addressing hyperactivity and impulsivity. Frequency scores for items seven onwards, Part B, are intended to provide additional information rather than serving as a diagnostic tool. Arria et al. argued that problems with inattention rather than hyperactivity and impulsivity are more likely to be associated with the non-prescription use of stimulants as they found a relationship between inattention and academic performance difficulties, but no relationship between hyperactivity and impulsivity and academic performance.

Arria et al. (2011) asked 470 university students to provide information regarding off-prescription use of stimulants such as methylphenidate and their self-reported ratings on the ASRS. They found strong associations between the off-prescription use of stimulants and ADHD symptoms and these symptoms were related to inattention and not hyperactivity and impulsivity. Similar results were previously reported by Rabiner et al. (2009). In this sample of 291 university students, 5.4% reported non-medical use of prescription stimulants and this was also associated with symptoms of inattention rather than hyperactivity-impulsivity.

Peterkin et al. (2011) used the ASRS Part A in their survey to investigate the possible link between the off-prescription use of ADHD medications such as methylphenidate and positive screening for ADHD symptoms. They analysed 184 North Virginia university student survey responses, comparing non-prescribed use of ADHD medications for academic purposes amongst those who did or did not screen positive for ADHD. Peterkin et al. (2011) noted that these misusers were found to be seven times more likely to be symptomatic for ADHD than those who were not misusers of ADHD medications. They found that, of the 39 respondents who reported misuse of ADHD medications for academic purposes, 77% tested positive for ADHD symptoms compared with just 10% of those who reported no misuse of ADHD medications.

Besides the possibility that modafinil and methylphenidate off-prescription users may be experiencing ADHD symptoms, it is also possible that they are experiencing an increased number of everyday cognitive lapses. The frequency with which an individual makes absentminded errors including perceptual, action and memory failures, referred to as cognitive failures (Broadbent et al., 1982), has been found to vary. It is recognised that cognitive slips occur in everyday life but these slips have been found to have been greater in individuals with cognitive conditions such as dyslexia (Smith-Spark Fawcett, Nicolson and Fisk, 2004), ADHD (Kim Liu, Glizer, Tannock and Woltering, 2014) and Parkinson’s disease (Poliakoff & Smith-Spark, 2008).In the studies by Smith-Spark, et al. (2004), Kim, et al. (2014), and Poliakoff and Smith-Spark (2008), the Cognitive Failures Questionnaire (CFQ) was used to identify the level of cognitive slips in these groups of individuals. The CFQ was developed by Broadbent et al. (1982) to evaluate the frequency with which cognitive failures occur in everyday life. The 25-item CFQ (Broadbent et al., 1982) measures lapses in a broad range of cognitive functions within the past six months and has good external validity (e.g. de Paula, Costa, Miranda & Romano-Silva, 2018; Ekici, Uysal & Altuntas, 2016; Kim et al., 2014; Poliakoff & Smith-Spark, 2008; Smith-Spark et al., 2004; Wallace & Vodanovich, 2003).

Broadbent et al. (1982) argued that the CFQ provides a measure of general cognitive failure which is important for external validity, as the individual’s view of themselves is also shared by those who know them. Broadbent et al. did consider whether a total score or individual item score would be more appropriate by performing a factor analysis. However, the factors found could not be replicated and it was concluded that the CFQ’s structure is unidimensional, thus using a total score as representative. Subsequent to this, a number of other studies have attempted to identify factors within the CFQ (e.g. Larson, Alderton, Neideffer & Underhill, 1997; Pollina, Greene, Tunick & Puckett, 1992; Wallace, Kass & Stanny, 2002) but there was no commonality between the studies on the factors themselves. That said, the only study which was retested and confirmed by confirmatory factor analysis (Wallace, 2004) was the analysis by Wallace et al. (2002) which found four factors, memory, distractibility, blunders and names. If off-prescription users of modafinil and methylphenidate are self-medicating for poor cognitive performance, it is likely that this is being experienced more broadly in their everyday lives.

One of the most common motivations for using modafinil and methylphenidate in Study 1 was ‘to get more done’. Similar findings have been reported in other online studies, Fond et al. (2016) reported ‘increased academic performance’ as one of the main motivations for use of modafinil and methylphenidate amongst medical students. Novak, Kroutil, Williams and Van Brunt (2007) reported productivity as one of the main motives for the non-medical use of ADHD medications. A common barrier to accomplishing tasks is procrastinatory behaviour, which Steel (2007) defined as a conscious delay of a planned course of action even though this delay is likely to have negative outcomes. Procrastination is noted as a problem particularly for both students (Rabin, Fogel & Nutter-Upham, 2011) and workers (Nguyen, Steel & Ferrari, 2013).

The 20-item General Procrastination Scale (GPS, Lay, 1986) was developed to assess trait procrastinatory behaviour. Both Rabin et al. (2011) and Ferrari and Saunders (2006) used the GPS to assess levels of procrastination in their studies. Ferrari and Saunders looked at the levels of procrastination in patients with ADHD compared with healthy controls and found significantly higher rates of procrastination in the ADHD group compared with controls. Ferrari and Saunders’ study investigated the frequency of reported rates of procrastinatory behaviour in adults with and without ADHD. A total of 131 participants, 29 of whom were clinically diagnosed with ADHD, completed three standardized procrastination scales, the GPS, Mann’s (1982) Decisional Procrastination Scale (as cited in Ferrari, Johnson & McCown, 1995) and McCown and Johnson’s (1989) Adult Inventory of Procrastination (as cited in Ferrari, Johnson & McCown, 1995). Their findings indicated significantly higher levels of procrastination across all three scales, demonstrating both cognitive (i.e. indecision) and behavioural procrastination were associated with ADHD, and the authors suggested that such procrastinatory behaviour may be symptomatic of ADHD.

Niermann and Scheres (2014) had similar findings. They recruited 54 university students who had tested positive on a self-report scale for ADHD in a pre-screening test for the study. Procrastination was measured using three procrastination scales, the Procrastination Assessment Scale for Students (Solomon & Rothblum, 1984), an academic procrastination measure (untitled) used previously by Ackerman and Gross (2005) and the Pure Procrastination Scale (Steel, 2010). Their findings demonstrated that ADHD-related symptoms were associated with procrastination and that symptoms of inattention, but not hyperactivity or impulsivity, were positively correlated with procrastination.

The ASRS, CFQ and GPS all appear to be widely used, robust instruments which together measure a broad range of cognitive and behavioural problems. These questionnaires have therefore been selected for the current study to investigate whether reported modafinil and methylphenidate users may perceive themselves to be experiencing cognitive and behavioural problems and may therefore be using modafinil and methylphenidate to self-medicate.

The findings reported in Study 1 of the current thesis also revealed that more frequent reported use of modafinil resulted in increased perceived benefits although the reported risks remained relatively unchanged regardless of frequency of use of modafinil. This finding was not reported by methylphenidate users, suggesting that modafinil may be experienced differently. This also indicates that reported modafinil and methylphenidate users may be two distinct groups and not a single homogenous CED-user group as previously thought. As this finding has not been reported in the literature before, one further aim of Study 2 was to investigate whether a relationship would emerge between the reported effects of modafinil and methylphenidate and the behaviours and abilities that these questionnaires assess.

Study 1 also found a high percentage of respondents who reported having been diagnosed with a psychiatric condition and that this may suggest self-medication for the symptoms of anxiety and depression. The findings of Study 1 suggested that some individuals may be using modafinil and methylphenidate as a supportive treatment for depression and anxiety. This study therefore aimed to investigate in more detail what psychiatric diagnoses respondents report having received and what medications they may have been prescribed.

The current study also aimed to address some of the weaknesses of Study 1, namely, identifying routes of administration of modafinil and methylphenidate, the extent to which immediate- and prolonged-release methylphenidate formulations are used, the inclusion of questions on alcohol and nicotine use, concurrent use of psychiatric medications, and greater detail on psychiatric diagnoses. The current study also sought to attain greater understanding in relation to the type of qualifications respondents report that they are currently studying for. More detail in relation to a wider range of recreational drug use was also sought.

The current study had hypothesized that self-identified modafinil and methylphenidate users will score significantly higher on the CFQ, GPS and the inattention component of the ASRS compared with controls.

## **3.2 Methods**

### **3.2.1 Respondents**

A convenience sample of respondents was recruited through the online forums Bluelight (<https://www.bluelight.org>) and Reddit (<https://www.reddit.com>). The sub-Reddits which were selected for Study 1 were selected again for consistency (see Appendix A(xii) for details). In addition to these, three further sub-Reddits were selected for the recruitment of control participants, these were r/SampleSize, r/GetSmarter and r/motivation. The first, r/SampleSize is a platform for researchers to post online surveys regardless of the topic. The remaining two, r/GetSmarter and r/motivation are devoted to the topics of improving memory and brain health and inspiration and motivation respectively. These sub-Reddits were chosen as they attract individuals who are interested in learning and the drive to accomplish but may not do this through the use of CEDs. They thus reflect a similar kind of respondent to the other sub-Reddits but represent individuals who are less likely to take CEDs. As with Study 1, these respondents were recruited by posting an advertisement with a link to the survey on all of the forum sites. No reward was offered for their participation. The survey was conducted between February 11th 2018 and June 2nd 2018 and, following preliminary analysis, further control participants were recruited between October 4th 2018 and November 17th 2018. Respondents included in the study had reported taking either modafinil and/or methylphenidate or, in the case of the control group, reported never having taken either modafinil or methylphenidate. Anyone stating that they were under the age of 18 and/or under the influence of a psychoactive drug at the time of commencing the survey was excluded from the study.

### **3.2.2 Materials**

The survey was constructed to answer questions raised by Study 1 and focus on the self-reported cognitive performance of people who report taking CEDs. QualtricsXM survey software was used to create the online survey and feedback was provided by 107 respondents. This resulted in the inclusion of a wider range recreational drugs for the recreational drugs questions. The presentation of an information sheet was followed by a consent form which required each statement to be clicked on to indicate informed consent. The questionnaire, which was divided into a number of sections (detailed below), then commenced and concluded with a debriefing page and the option to exit and submit the questionnaire or exit without submitting. In total, 99 questions were presented (although, depending on their responses, respondents were not necessarily required to answer every question). The estimated response time therefore varied from eight minutes to 30 minutes, depending on the respondents’ extent of knowledge and experience of use of the drugs.

### **3.2.3 Demographics**

In order to ensure consistency with Study 1, demographic information was collected. In addition to the questions asked in Study 1 which covered age, gender, nationality, education and employment details, a question asking whether respondents were currently engaged in study was presented, offering a broader range of responses to include vocational, continuing professional development and ‘high school/ A Level’ in addition to university degrees.

### **3.2.4 Psychiatric health**

This section consisted of six questions, such as “Have you ever been diagnosed with a psychiatric condition?” and “What was the diagnosis?”. A list of 24 psychiatric conditions taken from the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013) was provided and ‘other’, allowing respondents to add any diagnosis not provided in the list. Further questions relating to prescribed medications were also provided along with the question “Have you ever been treated for a drug or alcohol problem?”.

### **3.2.5 Cannabis, Nicotine and Alcohol use**

This section comprised three sub-sections relating to cannabis, nicotine and alcohol use respectively. Seven questions relating to cannabis use were included, covering lifetime use of cannabis, whether respondents had a prescription for medicinal cannabis, their age of first use, frequency of use, type of cannabis used and method of administration. In the nicotine section, two questions were provided, covering frequency of use by type of product and length of time since last use. In the alcohol section, the Alcohol Use Disorders Identification Test (AUDIT; Babor, de la Fuente, Saunders & Grant, 1992) was used. The AUDIT is a 10-item questionnaire created by the World Health Organisation (WHO) as a brief screening tool to identify individuals with hazardous and harmful alcohol use behaviour (Babor, Higgins-Biddle, Saunder & Monteiro, 2001). Questions are presented with a five-point Likert scale response and total scores range from zero to 40. Scores of between eight and 15 represent a medium level of self-reported alcohol problems and scores above 16 represent a high level of alcohol problems (Babor et al., 2001).

### **3.2.6 Usage of other Recreational Drugs**

Two questions comprised this section. The first question asked “How frequently in the past six months have you taken this drug”. This question was designed to identify what other drugs respondents are taking recreationally or without a prescription. The second question asked “How long has it been since you last used this drug?” and was designed to provide finer details about the use of these drugs in respondents who do not use these drugs frequently. A list of 28 recreational drugs was provided (see Appendix B(i) for the questionnaire). This list was first created with known drugs included but, following feedback from the initial 107 respondents (not included in the study), additional drugs were included in the list.

### **3.2.7 Modafinil and Methylphenidate use**

These two sections were devoted to modafinil and methylphenidate use. The modafinil section consisted of eight questions and the methylphenidate section consisted of 10 questions. These questions covered lifetime use, age of first use and usual dosage[[2]](#footnote-3). Maximum and minimum doses were asked for both drugs as well as the usual route of administration of the drug and for methylphenidate a question was also asked about whether immediate-release or extended release formulas were most commonly used.

### **3.2.8 Adult ADHD Self Report Scale (ASRS-V1.1)**

The ASRS (Kessler et al., 2005) uses a five-point Likert scale response to indicate the frequency of occurrence of symptoms within the past six months with scores from 0 to four (never = 0, rarely = 1, sometimes = 2, often = 3 and very often = 4). A total score is not intended for screening purposes of this scale, rather, each number represents a position, shaded or unshaded, on a grid (see Appendix B(vii) for details). The paper questionnaire is designed with some of the response boxes shaded and if four or more marks appear in the shaded boxes of items one to six, this indicate symptoms highly consistent with ADHD. Whilst the shaded boxes were not visible to participants in the online survey, analysis was performed on the number of these responses marked. Items one to four and seven to 11, nine items in total, address inattention and all other items address hyperactivity and impulsivity (Kessler et al., 2005). It is important to state that the purpose of using this scale was not to attempt to diagnose ADHD in respondents and that this may only be done by qualified professionals. Instead, the ASRS was employed in the current study simply to identify whether, and to what degree, respondents perceived that they had problems with inattention, hyperactivity and impulsivity. The items were presented without any indication of what the questionnaire was measuring, so respondents were unaware that they were completing an ADHD questionnaire. The ASRS has been reported to have good test-retest reliability, with Chronbach’s alpha of 0.885, followed by a two-week test-retest reliability Chronbach’s alpha of 0.878, *p* < .001 (Kim, Lee & Joung, 2013). The Chronbach’s alpha for the current study was 0.85.

### **3.2.9 Cognitive Failures Questionnaire (CFQ)**

The 25-item CFQ (Broadbent et al., 1982) is presented with a five-point Likert scale response with each response scored as ‘very often’ = 4, ‘quite often’ = 3, ‘occasionally’ = 2, ‘very rarely’ = 1 and ‘never’ = 0. Total scores range from 25 to 100, with higher scores indicating higher levels of susceptibility to cognitive slips. The questionnaire has good test-retest reliability. Broadbent et al.’s study reported two groups, one retesting after 21 weeks gave a correlation of *r* = 0.824 (n = 57) and the other one retesting after 65 weeks gave a correlation of *r* = 0.803 (n = 32). Additionally, Broadbent et al. reported the results of a sample of 98 women between the ages of 20 and 40 years, with the Coefficient alpha in this case being 0.89, demonstrating good internal consistency. The Chronbach’s alpha for the current study was 0.85.

### **3.2.10 General Procrastination Scale (GPS)**

The 20-item GPS (Lay, 1986) is presented, again, with a five-point Likert scale response with each response scored as ‘extremely untrue’ = 1, ‘moderately untrue’ = 2, ‘neutral’ = 3, ‘moderately true’ = 4 and ‘extremely true’ = 5, although 10 of the items are reverse scored. Higher scores indicate higher levels of reported procrastination. Total scores range from 20 to 100 with higher scores indicating higher levels of procrastination. The GPS is a unidimensional questionnaire and this was confirmed by Sirois, Yang and Eerde (2019), with a coefficient alpha of 0.82 (Lay) and Ferrari (1989) reported good test-retest reliability of 0.80. The Chronbach’s alpha for the current study was 0.88.

### **3.2.11 Questionnaire responses on modafinil and methylphenidate**

In order to assess the perceived effects of modafinil and methylphenidate on cognitive functions, additional questions were asked about the perceived effects of these two drugs on cognitive functions. For each question in each of the three questionnaires (i.e. the ASRS-V1.1, CFQ and GPS), an additional question was presented relating to the experience of modafinil and methylphenidate. This question asked whether the respondent felt that functioning in response to each item on the questionnaires was improved or worsened after taking modafinil and methylphenidate with additional options of ‘not affected and ‘don’t know’ to select. For example, the question “How often do you have problems remembering appointments or obligations?” and under the sub-heading “without drugs” response options were never, rarely, sometimes, often and very often. Under the sub-headings “on modafinil” and “on methylphenidate” the response options were ‘more often’, ‘less often’, ‘not affected’ and ‘don’t know’. See Appendix B(i) for further details.

### **3.2.12 Design**

An independent-samples design with three groups was used. The first group was a control group of respondents who reported never taking modafinil or methylphenidate. The second group was a “modafinil-only” group who reported taking modafinil but not methylphenidate. The third group was a methylphenidate group who reported taking methylphenidate and may or may not have taken other CEDs (including modafinil). These groups are referred to by their names (modafinil-only, methylphenidate and control) in the remainder of this chapter. In order to investigate whether there was a difference in the kind of illicit drugs used and whether there was a pattern of illicit drug usage between reported modafinil and methylphenidate off-prescription users and controls, a three (group type) by five (drug type) by three (frequency of use) design was used. The three levels of group were modafinil-only, methylphenidate and controls and the five levels of drug type were stimulants, depressants, opium-related pain killers, hallucinogens and cognitive enhancers (see Appendix B(xii) for details). The three levels of frequency of use were once or more per week, less than once a week and never.

### **3.2.13 Procedure**

Ethical approval was granted for the study by the School of Applied Science Research Ethics Committee at London South Bank University (reference number SAS1733). With permission from the forum moderators, an advertisement and link to the survey was posted on the selected forum sites. The advertisement detailed the nature of the survey and invited individuals to participate if they had taken either modafinil or methylphenidate and also if they had not taken either drug. When clicked on, the link brought up an information sheet. This was followed by a consent form which had to be clicked on to indicate informed consent had been given and only then could the survey commence. Demographics, psychiatric health status and drug use questions were presented first, followed by questions relating to modafinil and methylphenidate use. Respondents who had not taken either modafinil or methylphenidate were not required to answer questions on CED usage and instead were directed straight to the questionnaires on cognitive performance, commencing with the ASRS questionnaire. The survey ended with an option to exit without submitting the individual’s responses or to exit with submitting responses. Following this, a debriefing text was presented.

## **3.3 Results**

### **3.3.1 Participant characteristics**

The final sample size was 249 following the removal of the data from 76 respondents who reported having been prescribed either modafinil or methylphenidate. Questions relating to psychiatric diagnosis and prescribed medications as well as the question in both the modafinil and methylphenidate section asking if the respondent had a prescription for either drug, made it possible to identify and exclude such respondents.

Of the final sample size, 57% (N = 143) of respondents reported taking either modafinil or methylphenidate. A total of 35% (N = 86) of respondents reported that they took modafinil only and 23% (N = 57) indicated that they took methylphenidate and may or may not have taken other CEDs (8%, N = 19 reported taking methylphenidate only). The remaining 43% (N = 106) of respondents reported that they had not taken either modafinil or methylphenidate.

#### **3.3.1.1 Demographic information**

##### **3.3.1.1.1 Gender, age and nationality**

The majority of both the modafinil-only group and the methylphenidate group reported to be male whereas the control group reported roughly equal numbers of males compared with females (see Table 3.1 for details).

**Table 3.1. Gender by group**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Modafinil-only N (%)\*** | **Methylphenidate N (%)\*** | **Control N (%)\*** |
| Female | 16 (19.00) | 12 (21.00) | 46 (43.00) |
| Male | 68 (79.00) | 44 (77.00) | 58 (55.00) |
| Other gender | 2 (2.00) | 1 (2.00) | 2 (2.00) |

**\* Percentages relate to group and not to the whole sample**

The mean age for the modafinil-only group was 29 years (*SD* = 9.91), with a range of 50 years (18 – 68), compared with the methylphenidate group, which was 25 years (*SD* = 6.79), with a range of 25 years (18 – 43) and the control group which was 27 years (*SD* = 8.61), with a range of 37 years (18 – 55).

There was a roughly equal number of modafinil-only respondents who reported being North American or British whereas a greater number of the methylphenidate group reported being North Americans compared with those who reported being British. There was also a greater number of the control group who reported being North American compared with those who reported being British. See Table 3.2 for details of all nationalities.

**Table 3.2. Nationalities by group**

|  |  |  |  |
| --- | --- | --- | --- |
| **Nationality** | **Modafinil-only N (%)\*** | **Methylphenidate N (%)\*** | **Control N (%)\*** |
| **North American** | 24 (27.91) | 20 (35.09) | 38 (35.85) |
| **British** | 23 (26.75) | 9 (15.79) | 14 (13.21) |
| **Australian** | 12 (13.95) | 3 (5.26) | 9 (8.49) |
| **Canadian** | 2 (2.33) | 4 (7.02) | 7 (6.60) |
| **German** | - | 8 (14.04) | 7 (6.60) |
| **Rest of Europe** | 11 (12.79) | 8 (14.04) | 18 (16.98) |
| **Rest of world** | 11 (12.79) | 4 (7.02) | 9 (8.49) |

**\* Percentages relate to group and not to the whole sample**

##### **3.3.1.1.2 Level of education**

Within the modafinil-only group, the majority of respondents stated that they were university educated (72%, N = 62), and this was also the case for the control group, 55% (N = 58) of whom were university educated. In contrast, the majority of the methylphenidate group (56%, N = 32) reported that they were educated to the age of 18 years, and just 40% (N = 23) of respondents in the methylphenidate group reported having received university degrees (see Figure 3.1 for full details).

**Figure 3.1. Education level by group**

##### **3.3.1.1.3 Current educational status**

In the modafinil-only group, 48% (N = 41) of respondents stated that they were currently studying for a qualification, of which 16% (N = 14) reported having been educated to either 16 years or 18 years. The majority (42%, N = 36) reported that they were studying for a university degree. This was also the case with the methylphenidate group, 58% (N = 33) of respondents reported that they were currently studying for a qualification, of which 40% (N = 23) reported having been educated to 16 years or 18 years. A total of 39% (N = 22) reported that they were studying for a university degree. The control group also demonstrated this trend, 25% (N = 27) reported that they were currently studying for a qualification, of which 18% (N = 19) comprised those who reported having been educated to 16 years or 18 years. A total of 20% (N = 21) reported that they were studying for a degree (see Table 3.3 for full details of respondents reporting their current studies).

**Table 3.3. Currently studying for a qualification**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Modafinil-only**  **N (%)\*** | **Methylphenidate**  **N (%)\*** | **Control**  **N (%)\*** |
| **Currently studying for a qualification** |  |  |  |
| Yes | 41 (47.67) | 33 (57.90) | 27 (25.47) |
| No | 45 (52.33) | 24 (42.11) | 79 (74.53) |
| **Course type** |  |  |  |
| Vocational | 2 (2.33) | 2 (3.51) | - |
| CPD | 3 (3.49) | 3 (5.26) | - |
| A Levels | - | 6 (10.53) | 6 (5.66) |
| University Bachelor's Programme | 18 (20.93) | 14 (24.56) | 18 (16.98) |
| University Master's Programme | 11 (12.79) | 5 (8.77) | 3 (2.83) |
| Doctoral Studies | 7 (8.14) | 3 (5.26) | - |

**\* Percentages relate to group and not to the whole sample**

##### **3.3.1.1.4 Employment**

The majority of modafinil-only respondents reported being in employment (70%, N = 60), with 50% (N = 43) of respondents stating they were in full-time employment and 20% (N = 17) stating they were in part-time employment and just 29% (N =25) reported that they were unemployed. The majority of the self-identified unemployed respondents stated that they were studying currently (21%, N = 18). Further details on the study status of the unemployed respondents can be found in Figure 3.2. The majority of the methylphenidate respondents also reported being in employment (54%, N = 31), 35% (N = 20) reported being in full-time employment and 19% (N = 11) reported being in part-time employment and 44% (N = 25) reported being unemployed. The majority of reported unemployed methylphenidate users stated that they were studying (16%, N = 17). The majority of the control group reported being employed (65%, N = 69), 45% (N = 48) of whom stated that they were in full-time employment and 20% (N = 21) of respondents stated that they were in part-time employment, and 31% (N = 33) reported being unemployed. The majority of reported unemployed control group respondents stated that they were not studying (19%, N = 20).

**\* Percentages relate to group**

**Figure 3.2. Study status of unemployed respondents**

#### **3.3.1.2 Mental Health**

Of the modafinil-only respondents, 33% (N = 28) reported having been diagnosed with a psychiatric disorder. The most commonly reported mental health conditions were depression (22%, N = 19) and anxiety (16%, N = 14), and 13% (N = 11) reported having been diagnosed with both depression and anxiety. This was also the case with the methylphenidate group, with 28% (N = 16) respondents reporting that they had been diagnosed with a psychiatric disorder. The most commonly reported conditions were, again, depression (33%, N = 19) and anxiety (25%, N = 14), and 18% (N = 10) reported having been diagnosed with both depression and anxiety. Similarly, 38% (N = 40) of the control respondents who reported having been diagnosed with a psychiatric condition, most commonly reported a diagnosis of anxiety (29%, N = 31) and depression (25%, N = 27), and 21% (N = 22) reported having been diagnosed with both depression and anxiety. Full details can be found in Appendix B(viii).

In the modafinil-only group, 15% (N = 13) reported currently taking medication for a psychiatric disorder, similarly 14% (N = 8) of the methylphenidate group reported that they were currently taking psychiatric medications and a slightly higher percentage, 21% (N = 22) of the control group report currently taking psychiatric medications.

In response to the question “Have you ever been treated for a drug or alcohol problem?” 2% (N = 2) of the modafinil-only group, 12% (N = 7) of the methylphenidate group and 4% (N = 4) of the control group stated that they had, and 4% (N = 4) of methylphenidate respondents and 1% (N = 1) of control respondents stated that they were still receiving treatment.

#### **3.3.1.3 Cannabis, Nicotine and Alcohol**

##### **3.3.1.3.1 Cannabis**

The highest level of lifetime use of cannabis was reported in the methylphenidate group, with 98% (N = 56) reporting having taken cannabis. This was followed by 81% (N = 70) of modafinil-only group, compared with 60% (N = 64) of the control group.

The reported age of first use of cannabis was roughly the same between the modafinil-only group (18 years, *SD* = 3.28), the methylphenidate group (17 years, *SD* = 1.85) and the control group (17 years, *SD* = 3.73).

Only 2% (N = 2) of the control group, 2% (N = 2) of the modafinil-only group and 1% (N = 1) of the methylphenidate group reported having a prescription for medicinal cannabis.

The majority of modafinil-only respondents (36%, N = 31) reported having not taken cannabis in the past six months, and this was also the case with the control group (20%, N = 21), whereas the methylphenidate group percentages for frequency of use were roughly equal between usage ‘every day/almost every day’ (21%, N = 12), ‘3 to 4 times per week’ (19%, N = 11), ‘up to 3 times in total’ (21%, N = 12) and none (18%, N = 10). Full details are presented in Table 3.4.

**Table 3.4. Frequency of use of cannabis within the last six months**

|  |  |  |  |
| --- | --- | --- | --- |
| **In the past six months, how regularly have you taken cannabis?** | **Modafinil-only**  **N (%)\*** | **Methylphenidate**  **N (%)\*** | **Control N (%)\*** |
| **Every day/ almost every day** | 8 (9.30) | 12 (21.05) | 9 (8.49) |
| **3-4 times per week** | 5 (5.81) | 11 (19.30) | 7 (6.60) |
| **Once per week** | 8 (9.30) | 4 (7.02) | 7 (6.60) |
| **1-2 times per month** | 6 (6.98) | 7 (12.28) | 7 (6.60) |
| **Up to 3 times in total** | 12 (13.95) | 12 (21.05) | 13 (12.26) |
| **None** | 31 (36.05) | 10 (17.54) | 21 (19.81) |

**\* Percentage refers to group only**

The most common type of cannabis used was reported to be ‘normal weed’ by the modafinil-only group (65%, N = 56), the methylphenidate group (74%, N = 42), and the control group (44%, N = 47). Please see Appendix B(ix) for full details.

The most common route of administration of cannabis was reported as a ‘joint’ by the modafinil-only group (55%, N = 47), the methylphenidate group (65%, N = 37), and the control group (48%, N = 51). Full details can be found in Appendix B(x).

##### **3.3.1.3.2 Nicotine**

Due to a technical error in Qualtrics, responses were only collected in the ‘every day/almost every day’ option for the frequency of use question and the ‘today’ options for the question relating to the length of time since nicotine was last used. The modafinil-only group reported the highest level of everyday use of nicotine (53%, N = 46), followed closely by the methylphenidate group (42%, N = 24) compared with controls (21%, N = 22). The most common form of nicotine used was vaping in the modafinil-only group (36%, N = 31) and in the methylphenidate group (30%, N = 17) compared with the control group who reported cigarettes as the most common form of nicotine used (11%, N = 11).

For the modafinil-only group, reported frequency of use of nicotine in the past six months was most commonly for ‘vaping’ (36%, N = 31), whereas there was a roughly equal number of controls reporting daily cigarette use (10%, N =11) and daily use of ‘vaping’ (8%, N = 8). Due to the technical error in Qualtrics, the methylphenidate group did not answer this question. For the second question, the modafinil-only group most commonly reported using cigarettes ‘today’ compared to all other products (29%, N = 25). This was also true of the methylphenidate group (23%, N = 13) and the control group (12%, N = 13). Full details can be found in Appendix B(xi).

##### **3.3.1.3.3 Alcohol**

Total scores on the AUDIT were highest in the control group, with a mean of 13.96 (*SD* = 4.71), this was followed by the methylphenidate group, the mean total score was 7.30 (*SD* = 5.08) and the modafinil group had the lowest total score, the mean was 6.40 (*SD* = 4.44).

#### **3.3.1.4 Other Recreational Drugs**

##### **3.3.1.4.1 Frequency of recreational drug use within the past six months**

Due to issues with small Ns in each of the frequencies of use variables, it was decided to collapse the drug categories (see Appendix B(xii) for full details). This resulted in five categories, namely, stimulants, depressants, opium-related pain killers, hallucinogens and cognitive enhancers for each of the two questions. Frequency of use categories were also condensed, “every day/almost every day”, “3-4 times per week” and “once per week” were condensed to form the category “once or more per week”. The categories “1-2 times per month” and “up to 3 times in total” were condensed to form the category “less than once a week” and, for the “never” category, the mean N for each drug category was used.

As this was a three by five by three design, a log-linear test was conducted as the log-linear test allows for more levels than a Chi-Square test. The analysis produced a final model with a likelihood ratio of χ2= 0.00, *p* = n.s., indicating that the model fits the data well. This model indicated that the three-way interaction was significant (group type\*drug type\*frequency of use, χ2 = 27.76, *p* = .034). To break this down further, separate Chi-square tests were performed on the modafinil-only, methylphenidate and control groups, the drug types and frequency of use.

The Chi-square analysis found that there was no significant association for group type (modafinil-only, methylphenidate and control) and drug type (stimulants, depressants, opium-related pain killers, hallucinogens and cognitive enhancers), χ2 (8, 249) = 12.93, *p* = .114. Reported modafinil-only users, methylphenidate users and controls were not more likely to use any particular drug type.

The Chi-square analysis found that there was a significant association for group type and frequency of use, χ2(4, 249)= 98.74, *p* < .001. Reported use of recreational drugs once or more times per week was more likely in the modafinil-only group and less likely in the methylphenidate and control groups. Whereas reported use of recreational drugs less than once per week was more likely in the methylphenidate and modafinil-only groups and less likely in the control group. The control group were more likely to have never used recreational drugs and the modafinil-only and methylphenidate groups were more likely to have used recreational drugs. However, Cramer’s V was .17 indicating that this was a weak association.

A further Chi-square analysis that there was a significant association between frequency of use and drug type χ2(8, 249)= 181.62, *p* < .001. Stimulants were more likely to be used once or more time per week and all other drug types were less likely to be used once or more times per week. Stimulants were also more likely to be used less than once per week and all other drug types were less likely to be used less than once per week. It was more likely that opium-related pain killers and depressants were never used compared with all other drug types. Cramer’s V was .23 indicating that this was a weak association.

##### **3.3.1.4.2 Length of time since last use of recreational drugs**

This question provided a finer level of detail about reported recreational drug use, but only in those who reported less frequent use of recreational drugs. Therefore, these data are of less relevance to the central focus of this thesis and so have not been reported here and can instead be found in Appendix B(xii).

#### **3.3.1.5 Modafinil and Methylphenidate**

##### **3.3.1.5.1 Modafinil only**

The mean age of first use of modafinil reported by the modafinil-only group was 27 years (*SD* = 9.47) with a range of 47 years (16 – 63). The only route of administration reported by this group was by swallowing a pill.

The most common dosage taken in any day was reported by 34% (N = 29) to be 200mg (see Table 3.5 for full details).

**Table 3.5. Dosage levels of reported modafinil use**

|  |  |
| --- | --- |
| **Dosage** | **N (%)\*** |
| **Less than 50mg** | 1 (1.16) |
| **50mg** | 13 (15.12) |
| **100mg** | 28 (32.56) |
| **150mg** | 7 (8.14) |
| **200mg** | 29 (33.72) |
| **300mg** | 3 (3.49) |
| **400mg** | 4 (4.65) |
| **More than 500mg** | 1 (1.16) |

\* Percentage refers to group only

There was almost an equal split between those who reported always taking the same dose (52%, N = 45) and those who reported not always taking the same dose (48%, N = 41).

The most commonly reported maximum dose taken was 200mg (42%, N = 36). This was followed by 400mg (19%, N = 16) and 100mg (16%, N = 14). The most commonly reported minimum dose was 50mg (36%, N = 31), followed by 100mg (29%, N = 25) and less than 50mg (17%, N = 15), see Appendix B(xiii) for full details.

##### **3.3.1.5.2 Methylphenidate**

The mean age of first use of methylphenidate was 21 years (*SD* = 6.15) with a range of 29 years (13 – 42). The most common dosage, reported by 25% (N = 14) of this group, was 20mg (see Table 3.6 for full details).

**Table 3.6. Dosage levels of reported methylphenidate use**

|  |  |
| --- | --- |
| **Dosage** | **N (%)\*** |
| **Less than 10mg** | 3 (5.26) |
| **10mg** | 12 (21.05) |
| **20mg** | 14 (24.56) |
| **30mg** | 9 (15.79) |
| **40mg** | 6 (10.53) |
| **50mg** | 8 (14.04) |
| **60mg** | 2 (3.51) |
| **70mg** | 1 (1.75) |
| **80mg** | 2 (3.51) |

\* Percentage refers to group only

The most commonly reported maximum dose of 30mg was reported by 23% (N = 13), followed by 50mg (18%, N = 10) and 40mg (16%, N = 9). The most commonly reported minimum dose was 10mg (42%, N = 24), followed by less than 10mg (28%, N = 16) and 20mg (18%, N = 10. The majority of respondents reported that they did not always take the same dose (70%, N = 40). There were slightly more respondents who reported most commonly taking extended-release formulas (42%, N = 24) compared with those who reported most commonly taking immediate-release formulas (33%, N = 19) and 25% (N = 14) reported that they were unaware of the type of formula they most commonly took. The most frequently used brand was Ritalin and the most common route of administration was reported to be swallowing a pill, although 14% reported snorting methylphenidate. Full details can be found in Appendix B(xiv).

### **3.3.2 Self-reports of cognition**

#### **3.3.2.1 Adult ADHD Self Report Scale**

Due to an error on Qualtrics, twenty-two control respondents and one methylphenidate respondent did not answer the first question and their data were therefore removed from the analysis for this section. Scoring for Part A revealed that 34% (N = 29) of the modafinil-only respondents, 49% (N = 28) of the methylphenidate respondents and 11% (N = 12) of the control respondents scored at the level indicating symptoms highly consistent with ADHD.

A Kruskal-Wallis test was performed on the complete ASRS under three conditions of group type. To avoid Type 1 errors, a Bonferroni correction was applied to the α-level, resulting in a corrected critical value of .025. The differences between the mean ranks of 126.32 (methylphenidate), 119.84 (modafinil-only) and 95.28 (control) were significant, with *H(2)* = 9.58, *p* = .008.

*Post hoc* Mann-Whitney U tests revealed that both the modafinil-only scores and the methylphenidate scores were significantly higher compared with the control group scores (see Tables 3.7 and 3.8 for full details). There was no significant difference in scores between the modafinil-only group and the methylphenidate group (see Table 3.9 for full details).

**Table 3.7. Effects of group type (methylphenidate and controls) on ASRS scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **N** | **ASRS** |  |  |
| **Group** |  | **Mean (*SD*)** | **M-W** | ***p*** |
|  |  |  |  |  |
| Methylphenidate | N = 57 | 6.84 (3.56) |  |  |
|  |  |  | 1702.50 | .006 |
| Controls | N = 82 | 5.29 (2.41) |  |  |

**Table 3.8. Effects of group type (modafinil-only and controls) on ASRS scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **N** | **ASRS** |  |  |
| **Group** |  | **Mean (*SD*)** | **M-W** | ***p*** |
|  |  |  |  |  |
| **Modafinil-only** | N = 85 | 6.48 (3.37) |  |  |
|  |  |  | 2707.50 | .012 |
| **Controls** | N = 82 | 5.29 (2.41) |  |  |

**Table 3.9. Effects of group type (modafinil-only and methylphenidate) on ASRS scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **N** | **ASRS** |  |  |
| **Group** |  | **Mean (*SD*)** | **M-W** | ***p*** |
|  |  |  |  |  |
| **Modafinil-only** | N = 85 | 6.48 (3.37) |  |  |
|  |  |  | 2269.00 | .521 |
| **Methylphenidate** | N = 82 | 6.84 (3.56) |  |  |

A Kruskal-Wallis test was performed on the complete ASRS inattentive scores under three conditions of group type. To avoid Type 1 errors the Bonferroni correction was again used, resulting in a critical value of .025. The differences between the mean ranks of 130.32 (methylphenidate), 127.39 (modafinil-only) and 86.37 (control) were significant, with *H(2)* = 22.49, *p* < .001.

*Post hoc* Mann-Whitney U tests revealed that both the modafinil-only scores and the methylphenidate scores were significantly higher compared with the control group scores (see Tables 3.10 and 3.11 for full details).

**Table 3.10. Effects of the methylphenidate and control groups on ASRS inattentive scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **N** | **ASRS** |  |  |
| **Group** |  | **Mean (*SD*)** | **M-W** | ***p*** |
| **Methylphenidate** | N = 57 | 4.53 (2.39) |  |  |
|  |  |  | 1472.0 | <.001 |
| **Controls** | N = 83 | 2.99 (1.55) |  |  |

**Table 3.11. Effects of the modafinil-only and control groups on ASRS inattentive scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **N** | **ASRS** |  |  |
| **Group** |  | **Mean (*SD*)** | **M-W** | ***p*** |
|  |  |  |  |  |
| **Modafinil-only** | N = 85 | 4.31 (2.19) |  |  |
|  |  |  | 2211.0 | < .001 |
| **Controls** | N = 83 | 2.99 (1.55) |  |  |

A Kruskal-Wallis test was performed on the ASRS hyperactive/impulsive scores under three conditions of group type. The differences between the mean ranks of 116.82 (methylphenidate), 107.05 (modafinil-only) and 117.90 (control) were not significant, with *H(2)* = 1.41, *p* = .494.

#### **3.3.2.2 Cognitive Failures Questionnaire**

Due to a Qualtrics error, no control participants answered the first question. To resolve this issue, the four-factor model proposed by Wallace et al. (2002) was used and the mean score for all other items of the Distractibility factor was used to replace the missing score. A factor analysis was then performed to assess the robustness of this approach. The principal component analysis using a varimax rotation revealed six factors with all items loading on a factor and only two items loading two factors. Additionally, Wallace et al.’s (2002) Distractibility factor consisted of nine items and the current factor analysis identified one factor comprising of seven of the same items, including item one, the unanswered question. As this factor consists of most of the same items, it would seem likely that the mean score for all other items would provide an accurate estimate of the missing response. The factor analysis and scree plot can be found in Appendix B(xv).

A Kruskal-Wallis test was performed on the CFQ scores under three conditions of group type. To avoid Type 1 errors the Bonferroni correction was used, resulting in a critical value of .025. The differences between the mean ranks of 72.41 (methylphenidate), 82.76 (modafinil-only) and 187.55 (control) were significant, with *H(2)* = 139.95, *p* < .001.

*Post hoc* Mann-Whitney U tests revealed that both the modafinil-only scores and the methylphenidate scores were significantly lower compared with the control group scores (see Tables 3.12 and 3.13 for full details).

**Table 3.12. Post hoc Mann-Whitney U test on methylphenidate and control group CFQ scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **N** | **CFQ** |  |  |
|  |  | **Mean (*SD*)** | **M-W** | ***p*** |
| **Methylphenidate** | N = 57 | 54.35 (13.49) |  |  |
|  |  |  | 316.50 | < .001 |
| **Controls** | N = 106 | 85.28 (13.06) |  |  |

**Table 3.13. Post hoc Mann-Whitney U test on modafinil and control group CFQ scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **N** | **CFQ** |  |  |
|  |  | **Mean (*SD*)** | **M-W** | ***p*** |
| **Modafinil-only** | N = 86 | 56.77 (14.25) |  |  | |
|  |  |  | 632.50 | < .001 | |
| **Controls** | N = 106 | 85.28 (13.06) |  |  |

#### **3.3.2.3 General Procrastination Scale**

Due to a Qualtrics error, all respondents who reported using either modafinil or methylphenidate did not answer the first question, therefore Question 1 was removed from the analysis.

A Kruskal-Wallis test was performed on the GPS scores under three conditions of group type. To avoid Type 1 errors the Bonferroni correction was used, resulting in a critical value of .025.The differences between the mean ranks of 150.51 (methylphenidate), 131.73 (modafinil-only) and 105.83 (control) were significant, with *H(2)* = 15.42, *p* < .001.

*Post hoc* Mann-Whitney U tests revealed that both the modafinil-only scores and the methylphenidate scores were significantly higher compared with the control group scores (see Tables 3.14 and 3.15 for full details).

**Table 3.14. Post hoc Mann-Whitney U test on methylphenidate and control group GPS scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **N** | **GPS** |  |  |
|  |  | **Mean (*SD*)** | **M-W** | ***p*** |
| **Methylphenidate** | N = 57 | 64.65 (13.37) |  |  |
|  |  |  | 1947.0 | < .001 |
| **Controls** | N = 106 | 56.11 (13.47) |  |  |

**Table 3.15. Post hoc Mann-Whitney U test on modafinil-only and control group GPS scores**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **N** | **GPS** |  |  |
|  |  | **Mean (*SD*)** | **M-W** | ***p*** |
| **Modafinil-only** | N = 86 | 61.06 (13.14) |  |  |
|  |  |  | 3599.5 | 0.012 |
| **Controls** | N = 106 | 56.11 (13.47) |  |  |

#### **3.3.2.4 Questionnaire responses when using modafinil and methylphenidate**

The responses of ‘better’ or ‘worse’ in relation to the ASRS, CFQ and GPS when respondents are using modafinil and methylphenidate were analysed. A three-way log-linear test was conducted, the analysis produced a final model with a likelihood ratio of χ2= 8.32, *p* = .216, with the three-way interaction removed, indicating that the model fits the data well. Three groups, group type, questionnaire type and valence of outcome, were analysed. Group type had two levels, modafinil-only and methylphenidate. Questionnaire type had three levels, ASRS, CFQ and GPS. Valence of outcome had three levels, improved, worsened, and not affected. The model indicated that the two-way interactions were significant (group type\*questionnaire type, χ2 = 29.97, *p* < .001, questionnaire type\*experience type, χ2 = 334.37, *p* < .001). To break this down further, separate Chi-square tests were performed on the modafinil-only and methylphenidate groups and the questionnaire type and reported valence of outcome.

The means and SDs for the modafinil-only and methylphenidate groups are reported in Table 3.16.

**Table 3.16. Questionnaire type on modafinil and methylphenidate**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Modafinil-only**  **Mean (SD)** | **Methylphenidate**  **Mean (SD)** |
| **CFQ** | **Better** | 7.52 (5.11) | 7.19 (6.36) |
|  | **Worse** | 1.47 (1.80) | 1.75 (2.25) |
|  | **Not affected** | 11.09 (7.34) | 9.54 (7.94) |
| **GPS** | **Better** | 5.79 (3.49) | 6.05 (3.74) |
|  | **Worse** | 3.43 (2.04) | 3.04 (2.15) |
|  | **Not affected** | 6.92 (5.84) | 5.79 (5.85) |
| **ASRS** | **Better** | 6.21 (2.94) | 6.05 (4.32) |
|  | **Worse** | 3.04 (2.15) | 3.54 (2.87) |
|  | **Not affected** | 6.85 (4.05) | 5.21 (5.28) |

The Chi-square analysis found that there was a significant association between group type and questionnaire type, χ2(2, 249) = 29.40, *p* < .001. The modafinil-only group were more likely to report a valence of outcome on modafinil with the CFQ compared with the ASRS and GPS and compared with the methylphenidate group. The most commonly reported valence of outcome on modafinil was ‘not affected’. However, Cramer’s V was .057 indicating that this was a weak association.

The Chi-square analysis found that there was a significant association between questionnaire type and reported valence of outcome, χ2(4, 249) = 314.87, *p* < .001. The modafinil-only and methylphenidate groups were more likely to report no effects via the CFQ whilst on modafinil and methylphenidate compared to the ASRS and GPS. The most commonly reported valence of outcome on modafinil for the GPS was ‘not affected’ although this was only slightly higher than ‘better’, whereas on methylphenidate the most common valence of outcome for the GPS was better, but this was only slightly higher than ‘not affected’. For the ASRS, the most commonly reported valence of outcome on modafinil was ‘not affected’, but again, this was only slightly higher than ‘better’, whereas on methylphenidate the most common valence of outcome was ‘better’, but again, this was only slightly higher than ‘not affected’. However, Cramer’s V was .117, indicating that this was a weak association.

## **3.4 Discussion**

This study used an online survey to further investigate the self-reported cognitive performance of reported off-prescription users of modafinil and methylphenidate among an international sample of individuals who were either visitors of CED forums, student forums and other non-CED forums. In line with Study 1, this survey covered various aspects of off-prescription use, including demographics, psychiatric health and illicit drug use, but this study also included cannabis use, nicotine and alcohol use. The overall aim of this study was to investigate whether reported off-prescription users of modafinil and methylphenidate perceive that they have poorer cognitive performance for which they may be self-medicating. This was achieved through the use of the ASRS, CFQ and GPS. The results indicate that both the modafinil-only and methylphenidate groups reported significantly greater symptoms of inattention and procrastination compared with the control group, and significantly lower cognitive failures relating to everyday memory, distractibility, blunders and names compared with the control group.

Consistent with Study 1, many more respondents reported taking only modafinil than only methylphenidate and again, this may be due to easier access to modafinil than methylphenidate, with a greater number of websites offering access to modafinil than to methylphenidate (Hockenhull, Wood & Dargan, 2020). The heavier penalty for possession of methylphenidate in Britain (Drugs penalties, n.d.) and in America (Yeh, 2011) may also be a factor. The majority of both the modafinil-only and methylphenidate groups were male, which again is consistent with Study 1, compared with the roughly equal split between males and females in the control group. It was unclear from the results of Study 1 whether the high majority of males was an artefact of recruiting via online forums. As the control group in the current study were also recruited via online forums, this suggests that males are, in fact, more likely to use CEDs. In support of this finding, a higher majority of CED-using males was also reported in earlier studies (Frank et al., 2011; McCabe et al., 2006; Rabiner et al., 2009). The majority of respondents were North American and British which was also seen in Study 1. However, greater numbers of British than North Americans were reported in the modafinil-only group and this may be due to the easier access to modafinil in Britain (Hockenhull et al., 2020). The majority of modafinil-only and control respondents reported having been awarded with a university degree whilst the majority of the methylphenidate group reported having been educated to 18 years. However, the majority of reported methylphenidate users also stated that they are currently studying for a qualification. Roughly half of the modafinil-only group reported that they were currently studying whereas the majority of controls reported that they were not studying. This suggests that modafinil-only and methylphenidate respondents may be using modafinil and methylphenidate specifically for study purposes rather than for work, or that students are more likely to use modafinil and methylpenidate. However, the literature so far has focused mostly on student use. One study advertised in the Handelslblatt, a leading German economics publication collected data from office workers, students and unemployed respondents in relation to a wide range of legal and illicit cognitive enhancers (Dietz et al., 2016). Although the majority of respondents were office workers rather than students, Deitz et al.’s (2016) study did not identify the percentage of each group who were using off-prescription cognitive enhancers such as modafinil and methylphenidate. To the author’s knowledge, only Study 1 and the current study have looked at the off-prescription use of modafinil and methylphenidate more broadly across students, the employed and unemployed. The data from the current study suggests that off-prescription use of modafinil and methylphenidate is more common amongst students than other online forum users. Whilst this suggests that modafinil and methylphenidate are being used as study drugs, there is a lack of research on the use of CEDs in the workplace or amongst the unemployed and this should be a focus of future research.

The percentages of respondents who reported a psychiatric diagnosis were roughly equal between groups, although highest amongst the controls. Study 1 interpreted the rates of psychiatric diagnosis as being higher amongst CED users. However, the findings of the current study suggest that this may instead reflect a feature of those who use online forums, or at least the forum sites targeted in Study 1 and in the current study. The use of social media platforms has been associated with depression and anxiety (e.g. Kross et al., 2013; Lin et al., 2016; Primack et al., 2017). As Shelton, Lo and Nardi (2015) found, the anonymity offered by forum sites such as Reddit allow users the disinhibition and open disclosure without the accountability and for those with psychiatric disorders who may experience the stigmatisms associated, this may provide an attractive platform through which to engage with others. Some reported modafinil and methylphenidate users state that they are still taking psychiatric medications and these may impair their cognitive abilities and may also interact with modafinil and methylphenidate. A higher percentage of reported methylphenidate users stated that they had been diagnosed with a drug or alcohol problem. This may suggest that people who are more likely to experience problematic drug use are more drawn to using methylphenidate than modafinil or that methylphenidate users are more likely to engage in recreational drug than modafinil users and controls.

Lifetime use of cannabis was higher for both the modafinil-only and methylphenidate groups compared with controls, and this was highest in the methylphenidate group. Additionally, a higher percentage of reported methylphenidate users indicated regular cannabis use compared with the modafinil-only and control groups, which also suggests greater recreational drug use in the methylphenidate group. McCabe et al. (2006) also found that, compared with non-users, students who reported illicit use of prescription stimulants were much more likely to use other drugs such as marijuana and cocaine. However, this may only be true of methylphenidate users. The findings of the current study revealed that the reported use of stimulants, cocaine and the use of cannabis within the past six months between off-prescription modafinil users and controls were very similar.

Although little data were gleaned from respondents in relation to nicotine, it was apparent that the modafinil-only group had the highest level of everyday use of nicotine and tended towards vaping, but also reported smoking ‘today’ which may suggest that this group alternates between smoking and vaping. The methylphenidate group also reported similarly high levels of everyday use of nicotine and also reported smoking ‘today’. The control group, on the other hand, reported much lower levels of ‘everyday’ and ‘today’ nicotine use. Based on these findings, it would seem that reported off-prescription modafinil and methylphenidate users tend to use nicotine on a daily basis, possibly for the cognitive enhancing effects it provides. Heishman, Kleykamp and Singleton (2010) demonstrated that the effects of nicotine are likely to provide true cognitive enhancement rather than an artefact of withdrawal or classical conditioning in smokers, as previously suspected.

Scores on the AUDIT for the modafinil-only and methylphenidate groups were low compared with controls suggesting that reported modafinil and methylphenidate users are not inclined to consume much alcohol. This finding also suggests that methylphenidate users are not more likely to engage in alcohol use than modafinil users, as proposed earlier. The modafinil-only group were more likely to use recreational drugs on a regular weekly basis, but this was not evident for the methylphenidate group, again suggesting that methylphenidate users are not more likely to engage in recreational drug use than modafinil users, as previously suggested. However, whilst the frequency of reported recreational drug use in the methylphenidate group was low, the findings still present an element of risk in relation to potential drug interactions among those who use methylphenidate for cognitive enhancement. Not surprisingly, stimulants were reported as the more frequently used class of drug amongst the modafinil and methylphenidate groups, although this was also reported amongst controls. The fact that methylphenidate and modafinil are both psychostimulants suggests that those who consume these drugs perceive benefits from stimulant drugs. Additionally, as mentioned in Chapter 2, users of recreational drugs tend to score higher on personality traits of impulsivity, reward sensitivity and physical fearlessness. Specifically, these traits were found to predict subjective responses to amphetamines (Kelly et al., 2009). The loglinear findings of the current study were significant and, although the association was weak, it can only explain a small amount of the variance, other unknown factors will have also contributed to this.

The data in relation to modafinil use is consistent with, and supports, the findings of Study 1 which stated that reported users of modafinil appear to be aware of the safe dosage of modafinil. However, the data in relation to methylphenidate use demonstrates a different trend compared with study one, particularly in relation to dosage level. The findings of Study 1 revealed no distinct majority in relation to perceived safe dosage for methylphenidate and that roughly similar percentages of respondents selected dosages from 20mg to 60mg. The current study found that the most common dosage was 20mg and the most common maximum dosage was 30mg, demonstrating a safer pattern of reported use than Study 1. The age of first use of methylphenidate appears to be several years younger than that reported for modafinil. This may suggest that methylphenidate is being accessed during university study and probably most commonly accessed through a friend, as found in Study 1, especially in America. In a North American qualitative study by Aikins (2011), university residence halls and friends with prescriptions were reported as two common ways to access drugs such as methylphenidate. McCabe et al. (2006) also found that North American undergraduate students most commonly access prescription stimulants such as methylphenidate via their friends and peers. The findings from Study 1 also found that methylphenidate was most commonly accessed via someone else’s prescription or a friend. A fair proportion of respondents in the current study did not know whether they were taking extended or immediate release methylphenidate formulas. This may suggest a lack of knowledge about the drug that they are taking off-prescription. Although most respondents reported swallowing a pill, there were some who reported snorting methylphenidate, which is suggestive of problematic drug use amongst methylphenidate users as it increases the risk of abuse liability and dependence due to the rapid increase in serum concentration of the drug (Teter et al., 2006; Volkow & Swanson, 2003). Previous studies have also noted an element of reported snorting of prescription stimulants (Garnier-Dykstra et al., 2010; Teter et al., 2006).

Scoring on Part A of the ASRS revealed that both the modafinil-only group and the methylphenidate group reported symptoms highly consistent with ADHD and this was not found for the control group. These are self-reported perceptions of respondents and as such may over-reflect or under-reflect prevalence rates of ADHD and, therefore, it is important to note that the use of this scale was not intended for diagnostic purposes. However, this finding does suggest that reported modafinil and methylphenidate respondents perceive that they have difficulties with attention that may be similar to those experienced by people with a diagnosis of ADHD. This finding is consistent with Peterkin et al. (2011) who used the ASRS Part A in their study. They found that a high majority of students who reported off-prescription use of ADHD medications tested positive for ADHD symptoms. Additionally, the off-prescription users of ADHD medications were seven times more likely to be symptomatic for ADHD than those who did not use these mediations off-prescription.

The analysis of the full ASRS questionnaire scoring revealed that both the methylphenidate and modafinil-only group scores were significantly higher compared with the control group scores. In addition, when comparing the inattentive item scores for each group, both the modafinil-only and methylphenidate groups scored significantly higher compared with controls. Analysis of the hyperactive/impulsive items demonstrated no significant difference between these groups. Findings from the scoring of Part A, the complete 18-item questionnaire and the inattentive items in this study support the first hypothesis, that reported modafinil and methylphenidate users will score significantly higher on the ASRS compared with controls, particularly for the inattentive component. This is consistent with the findings reported by Arria et al. (2011). Their findings demonstrated a strong link between non-medical prescription stimulant use and symptoms consistent with ADHD, specifically symptoms of inattention rather than hyperactivity and impulsivity. Similarly, Rabiner et al. (2009) also reported an association between off-prescription use of stimulants and symptoms of ADHD. They reported that students scoring high on attention difficulties were almost twice as likely to be non-medical users of ADHD medications as students scoring lower on attention difficulties. Additionally, hyperactive/impulsive symptoms were not found to predict non-medical ADHD use. Poulin’s (2007) study also found an association between non-medical use of prescription stimulants and a positive ADHD screening test. However, Poulin did not report distinguishing between scores of inattention and scores of hyperactivity and impulsivity. Ilieva and Farah (2015) also reported a relationship between non-prescribed stimulant use and attentional problems. As discussed in Section 3.1, they used the TOVA (Greenberg, 1990) as their objective measure and the Barkley and Murphy Current Symptom Scale (1998) as their subjective measure. The results of their objective test revealed that the subjectively-rated attentional problems were disproportionally greater than the objective dysfunction. Perhaps then, the self-reports in the current study and those of the studies reviewed here reflect a level of attentional problems but they may not be as severe as they are perceived to be. This will be explored further as a focus of Study 3, when both self-reports and objective measures will be used to assess whether poor cognitive function is perceived and measured in off-prescription users of modafinil and methylphenidate.

The findings of the current study in relation to the CFQ are surprising. Both the modafinil-only and methylphenidate groups scored significantly lower on the CFQ compared with the control group. The second hypothesis was therefore not supported. If the CFQ is perceived in relation to the factors identified by Wallace et al. (2002), this would suggest that reported off-prescription users of modafinil and methylphenidate do not have problems with memory, distractibility, blunders and names. In fact, it would suggest that these off-prescription CED users have improved memory, they are less distracted, they make less blunders and remember names better than other online forum users. One possible explanation might be that, as found in Study 1, more regular use, at least of modafinil, is related to greater perceived benefits and this may account for some of the reported results on the CFQ. However this explanation would only explain lower CFQ scores in the modafinil group and possibly only amonst those who use modafinil every day. Another possible explanation is that those who may be self-medicating might be doing so for problems with attention but not the problems which the CFQ tests for. Previously, the CFQ has been used to measure the cognitive performance of groups such as those with traumatic brain injury (Dockree et al., 2006), Parkinson’s disease patients (Poliakoff & Smith-Spark, 2008) and Dyslexic students (Smith-Spark et al., 2004) amongst others. Self-report questionnaires focusing on attention may be better attuned to probing these issues.

Additionally, those who report taking modafinil and methylphenidate off-prescription and do not report doing so to ameliorate any attention or poor cognitive performance problems, may be using these drugs to “get ahead”. The high percentages of reported modafinil users in particular who were awarded degrees or currently studying would suggest that this may be likely. Although the majority of controls were university educated, they were not studying and the majority of unemployed controls were not studying. Whereas the majority of unemployed reported modafinil and methylphenidate users were studying. Studying and being tested on a regular basis, have been found to improve long-term retention (Roediger & Nestojko, 2015). Perhaps then, the lower scores on the CFQ for both the modafinil-only and methylphenidate groups compared with the control group reflects the cognitive benefits of studying and being tested whilst working towards a qualification.

Analysis of the scores on the GPS revealed, as predicted, that both the modafinil-only and methylphenidate groups scored significantly higher than the control group. The third hypothesis was therefore supported. This supports the findings of Ferrari and Saunders (2006) and Niermann and Scheres (2014). Ferrari and Saunders tested clinically diagnosed ADHD participants, demonstrating empirically that adults with a clinical diagnosis of ADHD also demonstrate procrastination. Niermann and Scheres, on the other hand, used a self-report screening tool for ADHD as did the current study. Nevertheless, this does suggest an association between symptoms of ADHD and procrastination. Additionally, Niermann and Scheres (2014) reported that procrastination was only associated with ADHD symptoms of inattention and not hyperactivity and impulsivity. This is consistent with the earlier finding that the ASRS subscale of inattention was significantly higher in the modafinil-only and methylphenidate groups but not the subscale of hyperactivity and impulsivity.

The analysis of the relationship between the reported effects of modafinil and methylphenidate and the behaviours and abilities assessed via the ASRS, CFQ and GPS demonstrated the whilst on modafinil and methylphenidate, respondents were not likely to report any effect via the CFQ, but they were likely to report effects via the ASRS and GPS. This is consistent with the analyses of the performance on these questionnaires as discussed earlier. Modafinil and methylphenidate do not appear to improve behaviours and problems highlighted in the CFQ but the modafinil-only and methylphenidate groups scored lower on this questionnaire anyway, demonstrating fewer problems relating to everyday cognitive failures. This would suggest ceiling effects as, if the performance on the CFQ was already good, improvement via the use of modafinil or methylphenidate would not expect to be seen. Modafinil and methylphenidate do appear to improve problems highlighted in the ASRS and GPS, and analyses of performance on these questionnaires demonstrated significant reported problems with inattention and procrastination. However, it is important to note that the difference between reports of ‘better’ and ‘not affected’ was very small and, in the case of modafinil for all three questionnaires, reports of ‘not affected’ were greater than reports of ‘better’. This adaptation to these questionnaires was novel and relied on participants’ retrospective self-reporting of drug-induced changes. Lab-based drug administration studies are a better way of measuring precisely, what aspects of cognition are improved.

While giving important insights into the self-rated cognitive performance of off-prescription users of modafinil and methylphenidate, the current study does, however, have a number of weaknesses. In addition to the usual weaknesses of online surveys which were discussed in Section 2.1, the current study did not collect responses in relation to full details of nicotine use for the methylphenidate group, due to a Qualtrics error. However, the data that were collected provided an insight into the daily use of nicotine possibly for further cognitive enhancement. Additionally, the data in relation to detailed nicotine use were not the main focus of this study and therefore do not have a bearing on the main findings reported here. Of greater significance is the fact that self-reports of cognitive and behavioural performance are subjective perceptions and this must be taken into consideration when interpreting the results. Objective measures are required to provide robust support to the key findings of the current study. Moreover, the subtle differences in reported methylphenidate use between Studies 1 and 2 reflect the variable nature of online data collection and this must also be taken into consideration.

To conclude, this study reports the findings of an online survey advertised on drug-user and other forum sites on the reported off-prescription use of modafinil and methylphenidate and the possible association between symptoms of ADHD and reported modafinil and methylphenidate use. Consistent with Study 1, the profile of the reported off-prescription modafinil and methylphenidate user, at least those who frequent English language online forums, is likely to be male, in their mid to late twenties, university educated, North American or British, currently studying and employed. Equal frequencies of reported psychiatric diagnoses were seen in all three groups and this may reflect a commonality amongst online forum users rather than reported use of modafinil and methylphenidate as previously thought. More frequent recreational drug use was seen in the modafinil-only group and stimulants were more likely to be more frequently used than any other class of drug. Performance on the ASRS revealed that a much higher percentage of reported modafinil and methylphenidate users compared with controls scored at the level indicating symptoms highly consistent with ADHD. The reported modafinil and methylphenidate users also rated themselves has having significantly greater ADHD symptoms of inattention and procrastination compared with the control group, but these self-reports may not be as severe as they are perceived to be. Performance on the GPS revealed that a much higher percentage of modafinil and methylphenidate users rated themselves as having high levels of procrastination compared with the control group. Performance on the CFQ however, indicated that modafinil and methylphenidate users rated themselves as having lower cognitive failures compared with controls. This may be a reflection of more frequent use of modafinil or an indication that those who may be self-medicating are doing so for problems with attention and not for problems which the CFQ tests for. Additionally, the reported effects of modafinil and methylphenidate appeared, subjectively, to improve the behaviours and problems assessed via the ASRS and GPS, namely inattention and procrastination but not in relation to the behaviours and problems assessed via the CFQ, everyday cognitive failures.

The symptoms of inattention perceived in reported modafinil and methylphenidate users required further investigation through the use of objective measures and self-reports, and this will be the focus of Study 3. A self-report questionnaire probing inattention will be included in the next study, and the question as to whether self-reported levels of inattention may not be as severe as they are perceived to be will also be addressed.

# **4 CHAPTER 4**

**STUDY THREE: THE COGNITIVE PERFORMANCE OF THE OFF-PRESCRIPTION USERS OF MODAFINIL AND METHYLPHENIDATE, WITHOUT CURRENT ENHANCEMENT**

## **4.1 Introduction**

The findings of Study 1 suggested that modafinil is experienced differently to methylphenidate as more frequent reported use of modafinil led to greater perceived benefits, but this pattern was not seen with reported methylphenidate use. The results of Study 2 revealed that reported off-prescription users of both modafinil and methylphenidate indicated higher frequencies of problems with inattention, consistent with a diagnosis of ADHD, and procrastination. These symptoms appear, subjectively, to have been alleviated via the use of modafinil and methylphenidate. It appears from these two studies, therefore, that the greater perceived benefits of modafinil may not be due to poorer self-reported cognitive performance amongst modafinil, as compared with methylphenidate, users. To follow up on this, it is necessary to determine whether these subjectively-perceived self-reports reflect poorer cognitive performance when measured objectively. Although, to the author’s knowledge, there are no established objective experimental tests measuring levels of procrastination, there are a number of well-established tasks measuring the cognitive performance of executive functions such as focused, sustained attention. Poorer perceived ability to stay focused on task goals could, perhaps, underly the lower scores on both the ASRS and GPS in Study 2. The questionnaires in Study 2 were used to identify respondents’ perceptions of their cognitive functions, revealing that these respondents perceived themselves as having problems with inattention and procrastination as measured by the ASRS and GPS respectively. The ASRS measures attention, impulsivity and hyperactivity whereas the BRIEF-A measures a broad range of executive functions, including those covered in Section 1.1.1, and provides nine individual measures in addition to three broader measures.

In a study investigating executive function performance in children with high and low attentional skills, Scope, Empson and McHale (2010) found that, although all scores were within the typical range on the standardized tasks, the low attentional skills group performed significantly poorer on most of the tasks of executive function. More specifically, Scope et al. (2010) reported that the differences between the two groups related to working memory and inhibitory control and that this supported the concept of a continuum of attentional skills (Connor, 1997), with varying levels of severity across the population. It would seem then that tasks measuring focused, sustained attention, working memory and inhibition would be most appropriate in the follow-up objective assessment of the subjectively-reported symptoms of ADHD in reported off-prescription users of modafinil and methylphenidate. It has been argued that working memory is, in part an attentional construct as working memory assists in the maintenance and execution of tasks in spite of interference from automatic, habitual responses (Kane, Bleckley, Conway & Engle, 2001; Meier, Smeekens, Silvia, Kwapil & Kane, 2018; Unsworth, Schrock & Engle, 2004). Therefore, tasks measuring attention may also measure working memory. Additionally, by using tasks involving goal maintenance, procrastination may also be tested (to a certain extent) as it is believed that procrastination is apparent not only in delaying the initiation of goals, but also in goal maintenance failure (Svartdal, Klingsieck, Steel & Gamst-Klaussen, 2020). Three tests involving goal maintenance, measuring focused, sustained attention, working memory and inhibition of inappropriate responses were used in Study 3 and are discussed in the following paragraphs.

The antisaccade task is a well-established test measuring pre-potent response inhibition, the ability to suppress automatic, externally-driven responses in favour of conscious, internally-driven responses (Hallett, 1978; Massen, 2004; Munoz & Everling, 2004). The term saccade is used to describe quick, simultaneous movements of both eyes rather than the smooth pursuit eye movements. Prosaccades are saccades towards a target whereas antisaccades are saccades in the opposite direction of a target. Prosaccades are executed constantly in everyday life in order to focus on stimuli whereas antisaccades are argued not to be a function of daily life as the desire to look away from a stimulus into blank space is not a natural action. Thus, executing the antisaccade task requires a strong top-down, goal-oriented executive load (Munoz & Everling, 2004). The task consists of two phases, the prosaccade phase and antisaccade phase. In the prosaccade phase the participant is required to look at a target which appears either to the left or right of the central fixation point, once the fixation has disappeared. In the antisaccade phase, the participant is required to resist looking at the target and look towards an empty region of space in the opposite, mirror image position instead. In both phases, the participant is required to work as quickly and accurately as possible. In the antisaccade phase, the pre-potent automatic response to produce a prosaccade is met with a deliberate suppressing response, these responses have been argued to function as parallel neural processes (Massen, 2004; Noorani & Carpenter, 2012). Whether antisaccade errors or correct antisaccades will be produced will depend on which of these processes is faster. Noorani and Carpenter also argue for an additional process in suppressing this response which they refer to as a stop unit. Although the frontal eye fields (FEF) and superior colliculus are believed to be involved in executing the saccade (Munoz & Everling, 2004), the supplementary motor area and DLPFC are believed to be responsible for saccade inhibition (Munoz & Everling, 2004; Noorani & Carpenter, 2012). The DLPFC is associated with executive functions, including working memory and focused attention (Curtis & D’Esposito, 2003). The cognitive processes underlying the antisaccade task include inhibition, working memory and attention (Hutton, 2008). Therefore the antisaccade task is a powerful and very specific tool with which to measure executive functions, specifically the ability to inhibit automatic responses. Futher, the antisaccade task is sensitive to group differences and effects of drugs. Schwerdtfeger et al. (2013) found that adults with ADHD demonstrated greater activation in the DLPFC during antisaccade responses and demonstrated longer reactions times compared with controls. Rycroft et al. (2007) found that both nicotine and modafinil reduced the response latency for correct saccades.

The Eriksen flanker task, first devised by Eriksen and Eriksen (1974) is a well-established test of inhibition and focused attention. The task involves the presentation of seven horizontally presented letters, the participant is instructed to focus on the central letter only (the target) and to press one key if the target is either the letter H or K and another key if the target is S or C. In different conditions, the target is flanked by congruent or incongruent letters. An adaptation of this task uses arrows instead of letters in three different conditions (Ridderinkhof & van der Molen, 1995). In the congruent condition, the target is flanked by arrows pointing in the same direction as the target. In the incongruent condition, the target is flanked by arrows pointing in different directions to the target. In the neutral condition, the target is flanked by diamond shapes. The participant must work as quickly and accurately as possible by pressing one key when the target is pointing left and another key when the target is pointing right. The task becomes more challenging in the incongruent condition when the goal action is met with interference from conflicting response impulses, resulting in longer latencies and a greater number of errors compared with the congruent condition (Gratton, Coles & Donchin, 1992; Sanders & Lamers, 2002). One theory explaining cognitive control when faced with conflict such as this, is the conflict monitor control system, proposed by Botvinick, Braver, Barch, Carter and Cohen (2001). This theory proposes that the ACC functions as a monitor, detecting the level of task conflict and the DLPFC acts as the controller by modulating attentional control to the target. The conflict monitor control system provides a good explanation of how inhibition and focused attention operate during the flanker task. The Eriksen flanker task is also sensitive to the effect of nicotine, for example, Franken, van Strien and Kuijpers (2019) finding that smokers demonstrated increased error rates on incongruent trials and suggested that cognitive deficits may contribute to persistant smoking behaviour.

Both the antisaccade task and the arrow flanker task measure the ability to maintain task goals and inhibit distractors, although in slightly different ways. In addition to task goal maintenance, the flanker requires some low-level perceptual processes and is affected by key pressing speed. The antisaccade task only requires eye movements therefore the load on perceptual processes is very low and motor control, the ability to press keys quickly, is not relevant. The antisaccade task measures the ability to inhibit a prepotent response instead of a learned response such as striking a key in response to the appearance of a number. Other commonly used tests such as the CANTAB (Cambridge Cognition Ltd., n.d.), although more limited in its range of measures of inhibition, may otherwise have also been suitable, however they were not available. For these reasons, the antisaccade and the flanker task were chosen as they measure goal maintenance, measuring focused, sustained attention, working memory and inhibition of inappropriate responses as indicated earlier.

A well-known and widely used task measuring sustained attention is the Sustained Attention to Response Task (SART, Robertson, Manley, Andrade, Baddeley & Yiend, 1997, see Smilek, Carriere & Cheyne, 2010 for a review). The task uses a continuous performance paradigm which involves pressing a keyboard key every time a number (between one and nine) appears in the centre of the computer screen except for the number three (the target). Participants must work quickly and accurately, in equal measure, but they must also withhold responding on the appearance of the target. An important element of the SART is that it encourages attentional drift due to the repetitive, habitual nature of responding to non-target stimuli (Manly et al., 2003). The SART requires continuous, sustained attention as well as withholding of the endogenous habitual, motor response on appearance of the infrequent target. The SART is recognised to be a test sensitive to sustained attention deficits (Manley et al.; Robertson et al.; Smallwood, Riby, Heim & Davies, 2006; Smallwood et al., 2004) and therefore appears to be an appropriate tool with which to measure focused, sustained attention.

In addition to these objective tests, the Behaviour Rating Inventory of Executive Function – Adult Version (BRIEF-A) was chosen as it is a standardized self-report measure of an adult’s (aged 18 to 90) views of their own executive functions as experienced in their everyday life (Roth, Isquith & Gioia, 2005). The objective measures in the current study assess attention, working memory and inhibition and the BRIEF-A provides self-report measures these functions in addition to other executive functions. Therefore, in order to understand whether self-reports of levels of cognitive functions map on to performance on objective measures of cognition, it seemed reasonable to include a robust self-report measure of executive functioning. Additionally, Weyandt et al. (2013) noted that a number of studies investigating the performance of university students with ADHD using neuropsychological tasks have produced mixed findings (e.g. Boonstra et al., 2005; Grant & Berg, 1948, Greenberg, 1990; Weyandt et al, 1998). They suggested that this may be due to the type of task used and the dependent variables employed and they argued that both lab-based (experimental) and non-lab based (self-report) measures should be used.

The BRIEF-A consists of 75 items belonging to one of nine, non-overlapping scales which measure different aspects of executive functioning, these are: Inhibit, Shift, Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organise, Task Monitor and Organisation of Materials. The first four of these scales comprise the Behavioural Regulation Index (BRI) which reflect affective behavioural responses. The remaining five scales comprise the Metacognition Index (MI) which reflects cognitive control. Together the scores on the MI and BRI form the Global Executive Composite (GEC) which is a summary score reflecting the individual’s level of executive function or dysfunction.

The Inhibit scale measures the ability to resist impulses and stop behaviours which may not be appropriate in certain situations, or which do not serve specific goals, but are more aligned with immediate gratification and relates to the executive function of behavioural response inhibition which was detailed in Section 1.1.1.2. The Shift scale measures the ability to move cognitively from one concept or problem to another and may be reflected in flexible problem solving, shifting attention or adapting to changes in routine and relates to the executive function of cognitive flexibility as detailed in Section 1.1.1.3. The Emotional Control scale measures the ability to modulate emotional responses whilst remaining effective and relates to the executive function of emotional regulation as detailed in Section 1.1.1.4. The Self-Monitor scale assesses the ability to observe one’s own behaviour and its effect on others, using this feedback to alter behaviours accordingly. This Self-Monitor scale relates to self-regulation as discussed in Section 1.1.1. The Initiate scale relates to the ability to start tasks and produce ideas or problem-solve independently. Individuals who are disorganised, for example, may feel overwhelmed with large tasks. The Working Memory scale measures the ability to hold information in the mind whilst manipulating it or completing a task and relates to the executive function of working memory as discussed in Section 1.1.1.1. The Plan/Organise scale assesses the ability to manage both existing and future tasks within a situation. The Task Monitor scale relates to the ability to maintain awareness of previous successes and failures and relate them to a relevant situation, to learn from experience. Finally, the Organisation of Materials scale assesses the ability to be organised in everyday life, including the work environment and home life.

The BRIEF-A has three validity scales designed to detect potential bias in the self-report. The Negativity scale measures whether the participant is responding in an unusually negative way. The Infrequency scale measures whether the participant is responding in an atypical manner, which may suggest that the participant is displaying either haphazard or extreme responding. The Inconsistency scale measures whether the participant is responding inconsistently to similar statements. The BRIEF-A is reported to have good test-retest reliability with alpha coefficients ranging between .82 and .93 across all scales over a four-week period (Weyandt et al., 2013).

Weyandt et al. (2013) investigated the performance of university students with and without an ADHD diagnosis using the BRIEF-A as one of their measures. Their findings indicated that the students with ADHD reported significantly more difficulties on all sub-scales of the BRIEF-A compared with the students without ADHD. However, only three scales reached the clinically significant range as indicated by the BRIEF-A standardization sample (Roth et al. 2005).

The self-report data from Studies 1 and 2 have indicated that reported off-prescription users of modafinil and methylphenidate may be self-medicating for attention and learning problems. The antisaccade task, the Erikson flanker task and the BRIEF-A are all noted to be robust tools, as reviewed above, and together measure various aspects of executive functioning via objective and subjective measures. Therefore, these measures were administered in Study 3 to investigate whether the cognitive functions of reported off-prescription users of modafinil and methylphenidate are poorer compared with controls over both laboratory and everyday settings.

The current study had three hypotheses, 1) off-prescription users of modafinil and methylphenidate will have higher rates of antisaccade errors on the antisaccade task compared with controls, 2) off-prescription users of modafinil and methylphenidate will have higher errors on incongruent trials of the flanker task, and 3) reported off-prescription users of modafinil and methylphenidate would score significantly higher scores on each of the BRIEF-A scales, particularly the Inhibit and Working Memory scales, compared with controls.

Both Studies 1 and 2 found relatively high levels of reported recreational drug use in CED users and reports of having received a psychiatric diagnosis. Therefore, the current study also aimed to investigate whether these trends continue to be seen in the current sample compared with controls. Likewise, the current study aimed to collect modafinil and methylphenidate use and demographic data for the same purposes.

## **4.2 Methods**

### **4.2.1 Participants**

A convenience sample of respondents was recruited through online forums Bluelight (<https://www.bluelight.org>) and Reddit (<https://www.reddit.com>). The sub-Reddits which were selected for Study 1 were selected again for consistency (see Appendix A(xii) for details). As with Studies 1 and 2, the respondents were recruited by posting an advertisement on all of the forum sites. The advertisement asked them to provide an email address to contact for participation details. A reward of £15 in Amazon vouchers was offered for their participation. Recruitment and testing were conducted between February 2019 and December 2019. The inclusion criterion for the experimental group were that they had to be users of either modafinil or methylphenidate. The exclusion criteria for all participants were being under the age of 18, being under the influence of a psychoactive drug at the time of commencing the study and a diagnosis of ADHD and/or a legitimate prescription for modafinil or methylphenidate. Experimental group participants were also instructed to avoid taking modafinil and/or methylphenidate for 24 hours before testing. A list of pseudonyms and email addresses which would not identify potential participants was collected during the recruitment phase of Study 2 via the same Bluelight and Reddit platforms (see Appendix C(i) for details of the advertisement). Ethical approval for the collection of the contact details of potential participants was granted by the School of Applied Science Research Ethics Committee at London South Bank University, (reference number SAS 1733). Potential participants who submitted their contact details during the recruitment phase of Study 2 were contacted and provided with information relating to the study. Potential participants would then make contact via the email address provided.

The control group were recruited from within London South Bank University either via advertisements on posters placed around the University campus or through the Research Participation Scheme (RPS) within the Division of Psychology.

The majority of CED users were male (76.6%) whereas the majority of the control group were female (76.74%). The mean age for the CED-user group was 29.72 years (SD = 8.75) with a range of 50 years (18 – 68). This was also roughly the same as the control group where the mean age was 28.74 (SD = 11.71) with a range of 39 years (18 – 57). The reported nationality of the majority of participants in the CED-user group (61.7%) and in the control group (53.5%) were British. See Appendix C(ii) for details. The number of university-educated CED-users was much higher than that of the control group (see section 4.3.4.1).

### **4.2.2 Materials[[3]](#footnote-4)**

### **4.2.3 Demographics, psychiatric health and drug use questionnaire**

In order to maintain consistency with Studies 1 and 2, demographic information was collected via a short paper-based questionnaire which covered age, gender, nationality, education, current study status, and employment details. Questions relating to psychiatric diagnosis were also included and a free text box was provided for participants to detail what diagnoses they have had. A question asking whether the participant had ever been treated for a drug or alcohol problem preceded the drug use questions relating to cannabis, modafinil and methylphenidate use. The questions covered frequency of use and length of time since last use (see Appendix C(iii) for details of the questionnaire). A free text box was presented for participants to provide details of what drugs (including alcohol) they have consumed, again, asking the frequency of use within the past six months and length of time since last use.

### **4.2.4 Antisaccade task**

Participants sat approximately 70 cm in front of a 24.5” monitor and a chin rest was used to prevent head movements. Their eye movements were recorded with an Eyelink 1000 Desktop eyetracker (SR-Research, Ontario, Canada). Participants were instructed to focus on a small red circle (subtending approximately 0.5°), the central fixation stimulus, in the middle of the screen. They were advised that this circle would move to the left and right of the screen and to follow it with their eyes for the first half of the task. The central fixation target would appear at random intervals between 1,000 and 1,500 milliseconds (ms), following which it would disappear for 200ms and be replaced by a peripheral target (a red circle of the same size). The peripheral target appeared in one of four positions, 4° and 8° to the left and right of the fixation. This process was repeated for 48 prosaccade trials. Following this, participants were instructed that for the second half of the task they must resist looking at the peripheral target, but instead position their gaze in the mirror image location for each trial. There were 48 antisaccade trials in the second half of the task. The performance measures for this task were the number of prosaccade and antisaccade errors, latency for correct prosaccades and antisaccades, latency for prosaccade and antisaccade errors and the time taken to correct antisaccade errors.

### **4.2.5 Arrow Flanker task**

The Arrow Flanker task using E-Prime 3.0 software was accessed via Psychology Software Tools. (<https://pstnet.com/>). Participants sat in front of a monitor, approximately 40 cm away. Stimuli were presented in the centre of the screen in a black font, font size 18, with a white background. The stimuli consisted of five horizontally presented arrows which, in a congruent trial, pointed in the same direction (i.e. “> > > > >”) and in the incongruent trial pointed in different directions (i.e. “> > < > <”) and in the neutral trial, a single central arrow was presented with two diamond shapes on either side (i.e. “XX>XX”). Participants were instructed to focus on the central arrow only and to press the numeric keyboard numbers one or two when the arrow pointed left or right respectively. A practice block of 14 trials was followed by 120 randomly presented congruent, incongruent and neutral experimental trials presented in a fixed order. For each trial, the stimulus was presented for a maximum of 1,500 ms with a 1000 ms blank interval. There were seven performance measures, namely, the numbers of correct congruent, incongruent and neutral trials, response latency for correct congruent, incongruent and neutral trials and the difference in response latency between the incongruent and congruent trials.

### **4.2.6 Sustained Attention to Respond Test (SART)**

The SART using E-Prime 3.0 software was accessed via Inquisit (<https://www.millisecond.com/>). Participants sat in front of a monitor, approximately 40 cm away. The stimuli consisted of digits one to nine, each randomly presented 25 times (totalling 225 single digits) in the centre of the screen in a black font with a white background. Each digit was presented in font sizes 48, 72, 94, 100 and 120. Each stimulus was presented for 250 ms which was then replaced by a mask in the form of an X inside a circle, for 900 ms. Participants were instructed to focus on the central of the screen and to press the F key every time a number appeared on the screen except for the number three, which they should not respond to. Participants were asked to work as quickly and as accurately as possible. A practice block of 18 stimuli, including two targets, was followed by the task which lasted for 4.3 minutes. There were 5 performance measures, namely, the numbers of correct and error trials, response latency for correct trials, the response latency for the four presses prior to correctly withheld responses and the four presses prior to error responses. Robertson et al (1997) demonstrated that subjects had significantly shorter response latencies prior to error responses, indicating a waning of attention to response. Subjects also had longer response latencies following error responses, demonstrating a return to sustained attention to response.

### **4.2.7 Behaviour Rating Inventory of Executive Function – Adult Version**

The BRIEF-A (Roth et al., 2005) is a paper-based questionnaire and the items are presented as statements reflecting problem behaviours, for example “I forget instructions easily”. The response options of “never”, “sometimes” and “often” are provided for each statement to indicate whether these behaviours have been a problem for the participant within the past month. Scores are produced for each of the sub-scales as well as the BRI, MI and GEC. Normative data indicates each of these scales has a mean of 50 and a standard deviation of 10 (Roth et al., 2005). Scores at or greater than 65 are considered clinically significant.

### **4.2.8 Design**

An independent samples design with two groups was used. The first group was a control group of respondents who reported never having taken modafinil or methylphenidate; the second group was a CED-user group who reported use of modafinil or methylphenidate at least 10 times within the past year. These groups will be referred to by their names (CED-user and control) in the remainder of this chapter. Outliers exceeding 2.11 standard deviations for variables within the antisaccade and Arrow Flanker tasks and the BRIEF-A were removed (see Appendix C(vii) for details). The number of university-educated CED-users was much higher than that of the control group. As a result, level of education was included in the antisaccade, Arrow Flanker and BRIEF-A analyses as a covariate.

A series of one-way related ANCOVAs were used to investigate the effect of group type (CED-user and control) on each of the seven, previously mentioned, measures of the antisaccade task. Bonferroni corrections were applied, resulting in a *p*-value of .007.

For the Arrow Flanker, two-way mixed design, 2 (group type: CED user vs. control) x 3 (trial type: congruent, incongruent and neutral) ANCOVAS were used to investigate the effect of group type on latency for correct congruent, incongruent and neutral trials and the number of correct congruent, incongruent and neutral trials. A one-way ANCOVA was also used to investigate the effect of group type on the difference in response latency between the incongruent and congruent trials.

For the BRIEF-A, three MANCOVAs were performed to investigate the effect of group type on the scores for the four BRI subsets and the five MI subsets. Independent samples *t*-tests were also performed on the BRI, MI and GEC.

### **4.2.9 Procedure**

Ethical approval was granted for the study by the School of Applied Science Research Ethics Committee at London South Bank University (reference number SAS1834). With permission from the forum moderators, an advertisement for the study was posted on the selected forum sites. The advertisement provided information about who would and would not be eligible to participate. It explained that this was a lab-based study about the use of CEDs, where the study would take place, the reward for participation, and contact details to use for further information. The advertisement also advised that those interested should use a pseudonym and an email address that would not identify them in any way. Individuals who were interested were emailed the information sheet which explained what the experiment would involve and asked participants to refrain from taking recreational and off-prescription CEDs for 24 hours before testing (see Appendix C(viii) for full details). On the day of testing the participant was presented with a consent form (see Appendix C(ix) for details) which they were required to sign. Following this the demographics and drug use questionnaire was presented and once completed the participant was given instructions for the antisaccade task as explained earlier. Following the antisaccade task, participants were presented with the SART test and were given a practice run before taking the SART test. There was then a short break while the arrow flanker test was set up. Once this task was completed the participant was positioned in front of another computer monitor and provided instructions for the arrow flanker task. A practice round of 14 trials preceded the experimental part of the task as explained earlier. On completion of this task the participant was given the BRIEF-A form to complete and given instructions on how to complete the form. The debriefing sheet (see Appendix C(x) for details) and Amazon vouchers were provided once the BRIEF-A was completed.

## **4.3 Results**

A total of 90 participants completed the study, of which 43 were controls and 47 identified themselves as modafinil and/or methylphenidate (CED) users. Of the 47 CED users, 28 were reported modafinil-only users, six were reported methylphenidate-only users and 13 were reported users of both modafinil and methylphenidate.

### **4.3.1 Level of education**

The majority of the CED-user group reported that they were university educated (68%, N = 32). The majority of the control group, on the other hand, reported that they were educated to 18 years of age (65%, N = 28). See Appendix C(iv) for full details.

### **4.3.2 Current studies**

In the CED-user group, 51% (N = 24) of participants stated that they were currently studying for a qualification, the majority of whom stated that they were studying for a degree. In the control group, 88% (N = 38) of participants stated that they were currently studying for a qualification, the majority of whom, again, stated that they were studying for a degree. Full details can be found in Appendix C(v).

### **4.3.4 Employment**

The majority of the CED-user group reported being in employment (77%, N = 36). The majority of the control group also reported being employed (67.4%, N = 29). See Appendix C(vi) for full details.

### **4.3.5 Mental Health**

Within the CED-user group, 21% (N = 10) reported having been diagnosed with a psychiatric disorder and the most commonly reported condition was depression (13%, N = 6). Within the control group, 9% (N = 4) reported having been diagnosed with a psychiatric disorder of depression or anxiety. See Appendix C(xi) for full details.

### **4.3.6 Cannabis, modafinil and methylphenidate**

#### **4.3.6.1 Cannabis**

The highest level of reported lifetime use of cannabis was in the CED-user group, of whom 87% (N = 41) reported having taken cannabis compared with 40% (N = 17) of the control group. Full details of reported cannabis use can be found in Appendix C(xii).

#### **4.3.6.2 Modafinil**

A total of 87% (N = 41) of CED-users stated that they had taken modafinil. The mean age of first use of modafinil was 25 years (SD = 5.64). The reported frequencies of use of modafinil are detailed in Table 4.1. Full details of reported modafinil use are found in Appendix C(xiii).

**Table 4.1. Frequency of modafinil use**

|  |  |
| --- | --- |
| **Frequency of use within the past six months** | **CED user group N (%)\*** |
| **Every day** | 7 (17.1) |
| **Three or more days per week** | 4 (9.8) |
| **Once or twice per week** | 13 (31.7) |
| **Two or three times per month** | 8 (19.5) |
| **Six times or less per year** | 5 (12.2) |

\* Percentages relate to group and not to the whole sample

#### **4.3.6.3 Methylphenidate**

Within the CED-user group, 40% (N = 19) of CED-users stated that they had taken methylphenidate. The mean age of reported first use of methylphenidate was 22 years (SD = 6.05). See Appendix C(xiii) for full details.

### **4.3.7 Alcohol and nicotine**

#### **4.3.7.1 Alcohol use was higher in the CED-user group**

A greater number of the CED-user group (47%, N = 22) compared with controls (28%, N = 12) reported that they had consumed alcohol at least once a week within the past six months and a greater number of the CED-user group (62%, N = 29) compared with controls (35%, N = 15) reported having consumed alcohol within the last week. See Appendix C(xv) for full details.

#### **4.3.7.2 Nicotine**

The majority of both the CED-user group (57%, N = 27) and the control group (53%, N = 23) reported that they had not taken nicotine within the past six months. See Appendix C(xvi) for full details.

### **4.3.8 Other recreational drugs**

Due to the range of drugs provided by participants and issues with small Ns in each of the variables, it was decided to collapse the drug categories. This resulted in five categories, namely, stimulants, depressants, opium-related pain killers, hallucinogens and cognitive enhancers for both frequency of use and length of time since last use. There was much greater reported use of drugs by the CED-user group in all categories compared with controls. There was greater reported use of stimulants by both groups compared to all other drug categories. Full details of the reported recreational drug use can be found in Appendix C(xvii).

### **4.3.9 Antisaccade task**

Prosaccade measures are presented first, followed by antisaccade measures, in order to identify group differences on automatic, prepotent responses and responses that require top-down or executive control.

#### **4.3.9.1 Prosaccade measures**

The means and SDs for response latencies for the prosaccade measures are displayed in Table 4.2.

**Table 4.2. Means and SEs for prosaccade measures**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Prosaccade correct response latency\***  **mean (SE)** | **Prosaccade error response latency\***  **mean (SE)** | **Number of Prosaccade errors**  **mean (SE)** |
| **CED-user group** | 137.77 (5.23) | 85.20 (11.37) | 4.52 (0.59) |
| **Control group** | 143.50 (5.49) | 79.69 (11.52) | 4.46 (0.62) |

\* Latency is reported in milliseconds

The following are the results of one-way related ANCOVAs. Group type did not have a significant effect on the response latency for correct prosaccades, *F*(1,85) = 0.54, *p* = .464, ηp2 = .006. Group type also did not have a significant effect on the response latency for prosaccade errors, *F*(1,78) = 0.112, *p* = .739, ηp2 = .001.

Group type did not have an effect on the number of prosaccade errors, *F*(1,85) = 0.04, *p* = .948, ηp2 < .001.

#### **4.3.9.2. Antisaccade measures**

The means and SDs for response latencies and numbers of errors for the antisaccade measures are displayed in Table 4.3.

**Table 4.3. Means and SEs for antisaccade measures**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Antisaccade correct response latency\* mean (SE)** | **Antisaccade error response latency\* mean (SE)** | **Number of Antisaccade errors**  **mean (SE)** | **Response latency to correct errors mean (SE)** |
| **CED-user group** | 227.69 (11.53) | 150.55 (6.60) | 18.76 (1.36) | 173.23 (7.94) |
| **Control group** | 260.58 (12.10) | 175.55 (7.10) | 19.36 (1.43) | 224.93 (8.54) |

\* Latency is reported in milliseconds

Group type did not have a significant effect on the latency for correct antisaccades *F*(1,85) = 3.67, *p* = .059, ηp2 = .041. However, there was a significant effect of group type on the latency for antisaccade errors, *F*(1,83) = 6.31, *p* = .014, ηp2 = .071, with the CED-user group having faster response latencies for antisaccade errors compared with controls. The CED-user group took significantly less time to make antisaccade errors compared with controls (see Table 4.3). There was a significant effect of group type on the time taken to correct antisaccade errors, *F*(1,83) = 18.68, *p* < .001, ηp2 = .184, again with the CED-user group having faster error correction latencies compared with controls.

Group type did not have a significant effect on the number of antisaccade errors, *F*(1,85) = 0.09, *p* = .770, ηp2 = .001. .

### **4.3.10 Arrow Flanker task**

The means and SEs for correct response latencies and mean difference in response latency between congruent and incongruent trials for the arrow flanker measures are displayed in Table 4.3.

**Table 4.3. Means and SEs for arrow flanker measures**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Congruent correct response latency\* mean (SE)** | **Incongruent correct response latency\* mean (SE)** | **Neutral correct response latency\* mean (SE)** | **Difference in response latency between congruent and incongruent trials\* mean (SE)** |
| **CED-user group** | 392.21 (7.81) | 461.59 (8.36) | 395.26 (7.43) | 69.38 (4.37) |
| **Control group** | 434.84 (8.10) | 500.90 (8.66) | 437.38 (7.70) | 66.06 (4.52) |

\* Latency is reported in milliseconds

The data were analysed using 2 x 3 ANCOVAs. The CED-user group (mean = 416.35, SE = 7.57) had significantly faster response latencies on correct trials compared with the control group (mean = 457.71, SE = 7.84). There was a significant main effect of group type on the latency for correct trials, *F*(1,86) = 13.64, *p* < .001, ηp2 = .137. There was also a significant main effect of trial type on response latency, F(2,172) = 29.69, *p* < .001, ηp2 = .257. Planned contrasts were used to explore this main effect. The latency for incongruent trials (mean = 481.24, SD = 5.85) was significantly longer than for congruent (mean = 413.53, SD = 5.47, *p* < .001) and neutral (mean = 416.32, SD = 5.20, *p* < .001) trials. However, the difference in latency between congruent (mean = 413.53, SE = 5.47) and neutral (mean = 416.32, SE = 5.20) trials was not significant, *p* = .224. Both these main effects are displayed in Figure 4.1. The interaction between group type and trial type was not found to be significant, *F*(2,172) = 0.205, *p* = .754, ηp2 = .002.

**Figure 4.1. Interaction between the CED-user and control group latencies for correct trials**

The number of correct trials was similar between the CED-user group (94.9%) and controls (94.95%). Group type did not have a significant effect on the number of correct trials, *F*(186) = 0.001, *p* = .971, ηp2 < .001. There was a significant main effect of trial type on the number of correct trials, *F*(2,172) = 4.69, *p* = .028, ηp2 = .052. Planned contrasts revealed that the number of correct congruent (98.13%) versus correct neutral (97.05%) trials was not significant, *p* = .365. There was a significant difference for the number of correct incongruent (89.58%) versus neutral trials (97.05), *p* = .038. There was also a significant difference for the number of correct incongruent (89.58%) versus correct congruent trials (98.13%), *p* = .038. The interaction between group type and trial type was not significant, *F*(2,172) = 2.71, *p* = .098, ηp2 = .030 (see Figure 4.2).

**Figure 4.2. The interaction between Group type (CED-users and controls) and trial type (congruent, incongruent and neutral) for the numbers of correct trials**

The effect of group type on the mean difference in latency between incongruent and congruent trials was not significant, *F*(1,86) = 0.264, *p* = 609, ηp2 = .003. The mean difference in latency between incongruent and congruent trials for the CED-user group (mean = 69.38, SE = 4.37) was not significantly different to that of the control group (mean = 66.06, SE = 4.52).

### **4.3.11 BRIEF-A**

Means and SEs for scores on the BRI, MI, GEC and all subtypes can be found in Table 4.4.

**Table 4.4. Means and SEs for BRIEF-A scores**

|  |  |  |
| --- | --- | --- |
| **Scale/Index** | **CED-user group mean (SE)** | **Control group mean (SE)** |
| **Inhibit** | 56.55 (1.69) | 54.41 (1.75) |
| **Shift** | 58.02 (1.57) | 55.43 (1.63) |
| **Emotional Control** | 50.68 (1.97) | 56.67 (2.04) |
| **Self-Monitor** | 48.67 (1.51) | 51.52 (1.57) |
| **Initiate** | 59.47 (1.80) | 56.13 (1.89) |
| **Working Memory** | 60.55 (1.75) | 61.75 (1.83) |
| **Plan/Organise** | 56.61 (1.63) | 54.22 (1.71) |
| **Task Monitor** | 58.15 (1.80) | 57.56 (1.89) |
| **Organization of Materials** | 52.06 (1.70) | 50.50 (1.78) |
| **BRI** | 53.11 (1.51) | 55.30 (1.53) |
| **MI** | 56.58 (1.57) | 56.43 (1.59) |
| **GEC** | 55.61 (1.47) | 56.49 (1.47) |

#### **4.3.11.1 BRI, MI and GEC**

On average, the CED-user group scored lower on the BRI compared with controls. However, the difference was not statistically significant, *t*(86) = -.42, *p* = .667. There was no significant difference between the CED-user group and controls on MI scores, *t*(86) = .11, *p* = .913. On average, the CED-user group scored lower on the GEC compared with controls. However, the difference was not significant, *t*(87) = .163, *p* = .871.

#### **4.3.11.2 BRI and MI scales**

The multivariate test indicated that group type had a significant effect on the BRI sub-scales, *F*(4,83) = 3.79, *p* = .010, Wilk’s Lambda = .85, partial ηp2 = .149. Follow-up univariate *F*-tests indicated that group type significantly affected the score on Emotional Control, *F*(1,87) = 4.63, *p* = .034, partial ηp2 = .051, with the CED-user group scoring significantly lower on the Emotional Control scale than the control group. Group type had no significant effect on the scores for the remaining three scales, namely, the Inhibit score, *F*(1,87) = 1.35, *p* = .249, partial ηp2 = .015, the Shift score, *F*(1,87) = 1.09, *p* = .299, partial ηp2 = .012, and the Self-Monitor score, *F*(1,86) = 1.61, *p* = .208, partial ηp2 = .018.

The multivariate test indicated that group type did not have a significant effect on the MI sub-scales, *F*(5,83) = 0.83, *p* = .535, partial ηp2 = .051. The univariate analyses are not reported here as the multivariate effect was non-significant (Brace, Snelgar & Kemp, 2012).

## **4.4 Discussion**

This lab-based study used both objective tests and self-reports to investigate the un-medicated cognitive performance of reported off-prescription users of modafinil and methylphenidate compared with controls. In accordance with Studies 1 and 2, the current study collected data related with various aspects of off-prescription use such as demographics, psychiatric diagnosis and drug use. The overall aim of this study was to determine whether reported off-prescription users of modafinil and methylphenidate exhibit attention and learning difficulties for which they may be self-medicating. This was achieved through the use of the antisaccade and flanker tasks and the BRIEF-A.

The results indicated that, compared with controls, the CED-user group demonstrated shorter response latencies on antisaccade errors and corrected these errors more quickly, therefore the hypothesis, CED users would perform significantly poorer on the antisaccade task compared to controls, was not supported. The CED-user group also demonstrated shorter response latencies (with no corresponding increase in errors) on all three correct flanker trial types compared with controls. This indicates that the hypothesis proposing that CED users would perform significantly poorer than controls on the flanker task, was not supported. Additionally, the BRIEF-A findings revealed that scores on only one scale differed significantly between the groups. The CED-user group rated themselves as having significantly less difficulties with Emotional Control compared with the control group. Therefore, the hypothesis that CED users would score significantly higher on each of the BRIEF-A scales, particularly the Inhibit and Working Memory scales, was also not supported.

The possibility that the CED-user group may have better emotional control compared with controls may be due to the effects of modafinil and, possibly, methylphenidate, although this was not verified in the current study as no objective measures such as blood tests, were included. In a blood oxygenation level dependent (BOLD) fMRI study using modafinil, healthy participants performed an emotion information-processing task, a working memory task and a variable attention control task (Rasetti et al., 2010). During these tasks modafinil reduced BOLD signal in the PFC and anterior cingulate. Their findings indicated that modafinil enhanced the effectiveness of the PFC processing of cognitive information, while reducing reactivity to threatening stimuli in the amygdala, which is involved in anxiety (Davis, 1992). The very fact of being present in a laboratory and participating in experiments would be likely to cause elevated levels of stress and anxiety (Hopko, Hunt & Armento, 2005). The CED users in this study may, therefore, have been more able than the controls to regulate the impact that stress and anxiety could have on cognitive performance. Another study investigating levels of emotional dysregulation in children with ADHD following a year of treatment with methylphenidate found a significant improvement in emotional dysregulation symptoms (Kutlu, Ardic & Ercan, 2017). However, it is not clear whether methylphenidate also improves emotional regulation in adults. If continued use of modafinil and methylphenidate in ADHD results in improved emotional control, as suggested by Rasseti et al. and Kutlu et al., perhaps healthy off-prescription users may also experience the benefits of improved emotional control.

The fact that the BRIEF-A did not reveal poorer performance in any of the scales as rated by the CED-user group is surprising, especially when compared with the self-reported cognitive performance of CED-users in Study 2. Alternatively, it is also very likely that the CED-user group in the current study are taking modafinil and/or methylphenidate to enhance their already good cognitive functions and that they are not taking these drugs to self-medicate.

A further consideration is that there may be a difference in the kind of person who would complete an online survey compared with someone willing to come into a university laboratory to perform experimental tasks. It should also be noted that Studies 1 and 2 involved an international sample whereas the current study was London-based. This may also explain the much lower number of reported methylphenidate users in the current study. Access to methylphenidate is much more common in the United States compared with Britain. This was noted in Study 1 and reported access to methylphenidate was typically via a friend or someone else’s prescription. Therefore, the difference in findings in relation to attentional problems in the current study may reflect a different sample from a different population of CED users. Also, as suggested at the end of the previous chapter, it may be that the symptoms of inattention are not as severe as they are perceived to be. The theory of a continuum of attentional skills, as discussed by Scope et al. (2010), suggests that the level of attentional lapses across populations can vary and that individuals can experience difficulties with attention whilst remaining within the clinically healthy range and intellectual ability.

What is also interesting is that the findings from the BRIEF-A and the experimental measures were not consistent with each another as one would expect if these measures were all assessing executive functions. Differences between performance on laboratory tasks of executive functions and scores on the BRIEF-A was also found by Weyandt et al. (2013). Toplak, West and Stanovich (2013) argue that this is because performance-based measures and rating measures assess different aspects of cognitive and behavioural functions. Performance-based measures typically assess reaction time and accuracy and requires fast responses, thus demonstrating optimal performance. Whereas rating measures assess typical behaviours and performance is dependent upon the participant interpreting the task and relating their assessment of their own processes and behaviours to the statements or questions presented. Stanovich (2009) argues that optimal performance tests assess, what he refers to as, the algorithmic mind whereas typical performance, in this instance relating to rating measures, assess, what he refers to as, the reflective mind. The algorithmic mind can be seen as being involved with efficiency in information processing and being able to manipulate a concept whilst also keeping that original concept cognitively separate, for example, working memory. The reflective mind, on the other hand, is involved with rational thinking and decision-making in relation to an individual’s goals. Performance-based and rating measures therefore appear to measure different aspects of executive functions and so provide complementary approaches to the assessment process. Perhaps, however, neither approach is able to tap the typical performance in which attention often lapses, such as when engaged in a boring task where reading or listening to someone is involved, or in situations where cognitive demands are overloaded, such as when learning complex concepts with unfamiliar jargon.

The finding that the CED-user group had shorter response latencies on antisaccade errors and shorter response latencies on correcting antisaccade errors may be related to levels of performance anxiety. As mentioned earlier, participating in experiments in a laboratory is likely to increase levels of stress and anxiety (Hopko et al., 2005). The CED-user group scored lower on the Emotional Control scale of the BRIEF-A indicating greater emotional control compared with the control group. Highly anxious individuals have been found to have reduced processing efficiency in their performance of the antisaccade task, but not effectiveness (Derakshan, Ansari, Hansard, Shoker & Eysneck, 2009). Derakshan and Eysneck (2009) used the terms processing efficiency and processing effectiveness to explain latency and accuracy respectively. They argued that anxiety disrupts the balance between the bottom-up, stimulus-driven attentional system and the top-down, goal-driven attentional system which were discussed in the introduction. Heightened anxiety has also been found to be related to increased amygdala activation and reduced recruitment of DLPFC and VLPFC (Bishop, 2007). Both the DLPFC and the VLPFC are involved in inhibition. Derakshan and Eysneck (2009) also argued that that anxiety impairs the efficiency of inhibition and shifting functions which, they argue, results in reduced processing efficiency and increased antisaccade response latency in high-anxious compared with low-anxious participants. This, however, does not have an effect on processing effectiveness, the number of correct trials. If the CED-user group had greater emotional control, they may have had lower levels of anxiety compared with the control group, which could explain the CED-user group’s shorter latencies for errors and for correcting errors. Additionally, when errors are made they are followed immediately by large amplitude negative waveform known as error-related negativity (ERN) which fMRI studies confirm, are generated by the dorsal anterior ACC (Carter & van Veen, 2007). Error correction time is believed to be one of the fastest known cognitive processes (Cooke & Diggles, 1984; Rodrı́gues-Fornells, Kurzbuch & Munte, 2002). The dorsal anterior ACC also has strong connections with the amygdala, and the ventral pregenual ACC has widespread connections with the lateral PFC and some connections with the amygdala (Stevens, Hurley & Taber, 2011). Therefore, in relation to the control group, anxiety might again increase amygdala activation and, via its connections with the ACC, reduce the recruitment of the ACC in its ability to generate ERN, thus resulting in longer response latencies for correcting errors compared with the CED-user group (Carter & van Veen, 2007).

This difference in emotional control and therefore difference in the strength of amygdala activation, would also explain the CED-user group’s shorter response latencies on all three correct flanker trial types compared with controls. As mentioned in the introduction, in accordance with the conflict monitor control system, ACC and DLPFC are believed to work together to monitor conflict and modulate attentional control to the target (Botvinick et al., 2001). As this system is reliant on the input of both the ACC and DLPFC, reduced amygdala activation from increased emotional control would allow greater recruitment of the ACC in its role of detecting conflict. The ACC and bilateral insula together form the saliency network (Sidlauskaite, Sonuga-Barke, Roeyers & Wiersema, 2016). The saliency network (SN) is believed to function as a between-network switching hub, operating between the dorsal attention network (DAN), which is involved in goal-driven attention, and the ventral attention network (VAN), which is involved in stimulus-driven attention. Sidlauskaite et al. reported an imbalance between SN-VAN and SN-DAN connectivity in ADHD, resulting in greater distractibility. However, if greater emotional control allows greater recruitment of the ACC, thus providing stronger SN activity, this may reduce the imbalance enough to improve attentional control, particularly if Barkley’s (2015) theory is correct and ADD is only weakly associated with executive dysfunction.

The majority of the CED-user group were university-educated. In contrast, the majority of the control group were educated to 18 years of age which was expected due to the control group being recruited via the University’s RPS system which draw mostly first year undergraduate students. The latter also explains the majority of the control group reporting to be currently studying for a qualification, which was most commonly a bachelor’s degree. The roughly equal split in the CED-user group currently studying or not studying suggests that modafinil and methylphenidate are used both for study and work purposes. The majority of CED-users who reported to be studying, reported to be doing so for a degree. As would be expected, the majority of the control group reported to be in part-time employment, whereas the majority of the CED-users were in full-time employment, again suggesting that modafinil and methylphenidate are used for work purposes in addition to studying.

In keeping with the findings of Study 1, a relatively large percentage of the CED-user group stated that they had received a psychiatric diagnosis and this is compared with a much smaller percentage for the control group. Again, mental health problems were almost entirely reported as depression, anxiety or both. The CED-user group reported much higher recreational drug use compared with controls. Reported nicotine use was also higher in the CED-user group. The recognised cognitive enhancing effects of nicotine (Heishman et al., 2010) may explain this reported higher use in the CED-user group.

The data relating to modafinil usage supports the findings of Studies 1 and 2. The age of first use of modafinil in the current study was similar to that of Study 2 and the most common dose of modafinil reported in the current study was consistent with both Studies 1 and 2. The most common frequency of use of modafinil in the current study was similar to that reported in Study 1, although this was slightly less frequent in the current study. The maximum and minimum doses of reported modafinil use were also in keeping with Study 2. Unsurprisingly, the most common mode of administration of modafinil was by swallowing a pill.

There were far fewer reported methylphenidate users than reported modafinil users in the current study probably due to accessibility of methylphenidate as well as the fact that illegal use of methylphenidate carries a five-year prison sentence in Britain which presents not only a deterrent to use methylphenidate without a prescription but also in admitting to doing so (Drugs penalties, n.d.). Age of first use of methylphenidate in the current study was similar to that of Study 2 and the most common dosage reported in the current study was also consistent with the findings of Studies 1 and 2. The most common maximum and minimum dose reported in the current study reflect an awareness of the safer level of dosage, which was also found in Study 2, compared with that seen in Study 1. It would appear then that Study 1 is the outlier, with those participants reporting the widest range of dosage of methylphenidate. The most common route of administration of methylphenidate in the current study was by swallowing a pill with only a few reporting that they snorted methylphenidate. These findings suggest that both modafinil and methylphenidate are being used sensibly and cautiously.

Although the findings in relation to demographics, mental health and drug use support the findings from the previous studies, there are some weaknesses and limitations to the current study which must be considered. The participants were not screened for drugs currently in the bloodstream, and therefore it is not clear whether the presence of any drug would have influenced their performance on the tests. However, to have included a screening procedure such as this would not only have required considerable amounts of money, medical supervision and administration, it would have presented a deterrent to potential participants. Although participants were instructed to avoid using any psychoactive drugs for 24 hours prior to participation, nicotine and caffeine may not have been perceived as psychoactive drug and consumption of either could have had an effect on performance. A further limitation to the findings of the current study is that the majority of the control group were studying for a degree at the time of testing due to the method of recruiting via the RPS.

To conclude, this study reports the findings of a lab-based study of the off-prescription use of modafinil and methylphenidate and the un-medicated cognitive performance of the reported off-prescription users of modafinil and methylphenidate. The findings revealed that the CED-user group rated themselves as having greater emotional control and faster response latencies in both the antisaccade and flanker tasks, compared with controls. Although it is not possible to make assumptions as to why these CED users rated themselves as having greater emotional control without further investigation, the results may suggest that modafinil and methylphenidate improve emotional self-regulation. Alternatively, the CED-user group may have already had improved emotional self-regulation before they started using modafinil and methylphenidate. The CED-user group’s faster response latencies on antisaccade errors may be a result of their greater emotional control compared with the control group. It is also conceivable that the faster latencies with no reduction in errors seen in the CED-user group are due to faster information processing. This would suggest that the cognitive functioning of this group is good and that they are not self-medicating but instead using modafinil and/or methylphenidate to enhance their already good cognitive performance. Future research is, therefore, warranted in order to distinguish whether greater emotional control or naturally faster information processing is causing these effects.

# **5 CHAPTER FIVE**

**DISCUSSION**

## **5.1 Summary of the research aims of the thesis**

This thesis aimed to understand the off-prescription use of modafinil and methylphenidate by identifying the profile of these users and their experiences of using these drugs as well as their motivations for use, despite the risks and dangers involved. Additionally, it also aimed to determine whether off-prescription users of modafinil and methylphenidate chose to take these CEDs to enhance their already good cognitive functions or if they were self-medicating for poor cognitive functions. The following section summarises the key findings of all three studies.

## **5.2 Summary of the key findings**

### **5.2.1 Study 1**

Study 1 had two target populations and sought to investigate how these drugs were experienced in the real world. A survey was constructed based on a review of the literature on CED use, modafinil and methylphenidate in particular. Study 1a, targeted visitors of online forums relating to illicit drug and nootropic use and student forums. The results identified the typical profile of the modafinil and methylphenidate off-prescription user (at least those who visit these online forums), as being male, North American or British, educated, employed and in their mid-20s. Illicit drug use was found to be associated with reported off-prescription modafinil and methylphenidate use. There also appeared to be an association with psychiatric disorders, specifically depression and anxiety which required further investigation. Greater reported frequency of modafinil use was associated with greater benefits whilst the number of risks remained relatively unchanged regardless of the frequency of use. This pattern was not evident for methylphenidate. Furthermore, modafinil was perceived as a safe drug whereas methylphenidate was seen as dangerous and more of a ‘quick fix’. These findings suggest that modafinil may be experienced differently to methylphenidate and that CED users may not be one homogenous group. The reported motivations for use were mostly for attention and focus and to “get more done” which suggested that, if these drugs were being used as self-medication for poor cognitive function, the users may be taking them to counter problems with inattention and procrastination. These findings directed further empirical investigation, specifically, to determine whether modafinil and methylphenidate off-prescription users are self-medicating for inattention and procrastination and if modafinil and methylphenidate off-prescriptions users are two distinct groups rather than one homogenous CED user group.

Study 1b used the same survey and targeted students and staff at London South Bank University to compare levels of reported modafinil and methylphenidate off-prescription use with those in the previously reviewed literature. Further to this, responses to the statements of opinions about the off-prescription use of modafinil and methylphenidate from Study 1a and 1b were compared. The findings indicated that the percentage of reported off-prescription use of modafinil and methylphenidate was slightly lower than the percentages reported by Singh et al. (2014) and much lower than the percentage of modafinil use reported by Oxford students (Young-Powell & Page, 2014). This may suggest that the pressure to succeed in these elite universities is related to this greater reported use compared with the percentage of reported off-prescription use at London South Bank University, an inner city ex-polytechnic university. Comparisons of the responses to the statements of opinions between CED users and university respondents indicated that methylphenidate is perceived as dangerous by the majority of both samples which supported the findings of Study 1a. Unsurprisingly, most of the reported CED users in Study 1a stated that they did not feel that taking modafinil or methylphenidate was unfair, and cheating whereas the majority of university respondents did. That said, these opinions were not held by all university respondents.

### **5.2.2 Study 2**

Study 2 used another online survey, targeting the same online forums as Study 1a with additional forums targeted for the purpose of attracting individuals who are interested in learning and achievement but who may not do this through the use of CEDs. This study aimed to investigate whether off-prescription users of modafinil and methylphenidate are self-medicating for inattention and procrastination, and whether users of these two drugs represent two distinct groups or if they are part of one homogenous group of CED users. In order to address the first aim, the survey included three questionnaires, namely, the ASRS (Kessler et al., 2005), CFQ (Broadbent et al., 1982) and GPS (Lay, 1986). Comparisons were made between the responses made by reported modafinil and methylphenidate users and controls. To address the second aim, a further question was presented relating to the behaviours and abilities assessed by the ASRS, CFQ and GPS whilst on modafinil and methylphenidate. A further aim was to identify whether modafinil and methylphenidate were being used as a supportive treatment for depression and anxiety.

The results supported the CED user profile which had been identified in Study 1a. A psychiatric diagnosis, specifically of depression and anxiety was associated equally with all three groups, namely the modafinil-only, methylphenidate and control groups, suggesting that this may reflect the online forum user more broadly rather than specifically those who use CEDs. Illicit drug use was found to be more frequent in the modafinil-only group and stimulants were more likely to be used. Responses to the ASRS revealed that, compared with controls, a much higher percentage of reported modafinil and methylphenidate off-prescription users scored at the level consistent with ADHD and that they rated themselves as having greater symptoms of inattention rather than hyperactivity or impulsivity. Similarly, performance on the GPS demonstrated a greater level of self-reported procrastination in the modafinil-only and methylphenidate groups compared with controls. Conversely, the modafinil-only and methylphenidate groups rated themselves as having fewer cognitive failures compared with controls, suggesting either that more frequent use of (at least) modafinil may reduce cognitive failures or that those who may be self-medicating for poor cognitive performance may be doing so for inattention and not for problems which the CFQ assesses. However, this does not explain why the modafinil-only and methylphenidate groups rated themselves as having fewer cognitive failures than controls. Unsurprisingly therefore, whilst on modafinil and methylphenidate, respondents were not likely to report any changes in the abilities which the CFQ assesses, as they reported fewer cognitive failures anyway. However, respondents were more likely to report effects via the ASRS and GPS whilst on modafinil and methylphenidate suggesting that these drugs do improve problems with inattention and procrastination. Overall, the findings from Study 2 suggested that modafinil users are more likely to take illicit drugs frequently, modafinil and methylphenidate users rate themselves as having problems with inattention and procrastination, and these problems appear to be improved with modafinil and methylphenidate use. These findings warranted further investigation using both self-report and performance-based measures to assess the extent to which self-perceived cognitive problems are demonstrated objectively.

### **5.2.3 Study 3**

Study 3 was a lab-based study using two performance-based measures, the antisaccade task (Hallett, 1978) and the arrow flanker task (Eriksen & Eriksen, 1974; Ridderinkhof & van der Molen, 1995), and a self-report measure, the BRIEF-A (Roth et al., 2005) as well as a demographics and drug use questionnaire. Modafinil and methylphenidate users, who were asked to refrain from taking modafinil and/or methylphenidate 24 hours before participation, were recruited via the same online forum sites used in Studies 1 and 2. The control group were recruited via advertisements on campus walls or via the RPS at London South Bank University. The tasks measured sustained attention, working memory and inhibition and the BRIEF-A measured elements of executive function. The results indicated that the CED users did not perform significantly more poorly than controls on the antisaccade task or the flanker task and the only group difference on the BRIEF-A was that the CED users rating themselves as having significantly fewer difficulties with emotional control.

The results of the BRIEF-A may help to explain the CED-user group’s performance on the antisaccade and flanker tasks. Compared with the control group, the CED-user group had shorter response latencies both for antisaccade errors and correcting these errors and they demonstrated shorter response latencies on all three correct flanker trial types. It was argued that the heightened anxiety from participating in experimental tasks in a laboratory (Hopko et al, 2005) increases amygdala activation which also taxes the ACC and reduces the recruitment of the DLPFC and VLPFC (Bishop, 2007; Stevens et al., 2011). This, in turn, has the effect of reducing PFC processing of cognitive information and processing efficiency (but not effectiveness, Derakshan et al., 2009), and reducing the ACC’s ability to generate ERN (Carter & van Veen, 2007), detect conflict (Botvinick et al., 2001) and balance the DAN and VAN networks (Sidlauskaite et al., 2016). The self-reported, greater emotional control would suggest lower state anxiety, and therefore less activation of the amygdala, resulting in greater processing speed and efficiency and thus shorter response latencies. It was noted that the findings from the BRIEF-A and the experimental tasks are not consistent with each other, which may suggest that neither the BRIEF-A self-report measure nor the performance-based measures are effective in assessing the typical performance in which attention often lapses. That said, it is likely that the self-report and performance-based measures assess different aspects of cognitive and behavioural functions and so, together form a complementary approach to assessment. Toplak and colleagues (2013) argued that the two different approaches measured different aspects of cognitive function which Stanovich (2009) referred to as algorithmic and reflective. The algorithmic mind represents intelligence and cognitive aptitude reflective of information processing, whereas the reflective mind represents rational thinking which incorporates in individual’s understandings and beliefs in relation to the current environment and desired goals. Toplak and colleagues (2013) argued that laboratory tasks which involve optimal performance assess the algorithmic mind whereas self-reports relate to typical performance and assess the reflective mind and therefore present complementary measures which can offer a greater understanding when used together rather than one approach alone. Thus, the results from the BRIEF-A and experimental tasks have provided complementary rather than contradictory findings.

In the following sections, these findings of all three studies will be considered in relation to the main aims of the thesis and in relation to one another.

## **5.3 The profile of the off-prescription modafinil and methylphenidate user**

Similarities in all three studies of this thesis are evident in relation to gender, rates of reported modafinil versus methylphenidate off-prescription users and the level of education. Greater numbers of males reported using CEDs in all three studies and this pattern has also been found in previous surveys (Arria et al., 2011; McCabe et al., 2006; Peterkin et al., 2010; Rabiner et al, 2009; Singh et al., 2014). This gender bias may be due to the fact that males are more likely to use and abuse drugs than females (Cotto et al., 2010; McCabe et al., 2007) and greater substance abuse may result in lower DA activity (Laakso et al., 2002). Therefore they may be more open to taking CEDs. Alternatively, as discussed in Section 1.3, the greater numbers of males reporting the use of CEDs may be due to the influence of gender on the DA system as it is believed that DA signalling is greater in females due to the enhancing effect of oestradial on the DA system (Yoest et al., 2014). If males experience lower DA signalling, they may be more inclined to seek enhancement via CEDs and, based on the inverted-U theory discussed in Section 1.3.1, they are also more likely to experience benefits from its use (Vijayraghavan et al., 2007).

Greater numbers of reported modafinil users than reported methylphenidate users has also been seen in all three studies. Based on the findings of Study 1, this could be due to the fact that methylphenidate is perceived as dangerous either because it is internationally recognised as a Schedule II controlled substance and therefore illegal to use without a prescription (Green List, 2003) or because of its addictive potential, as discussed in Section 1.5. Methylphenidate may also be more difficult to access, at least in the UK; Hockenhull et al. (2019) found 55 websites from which modafinil may be obtained but only 14 websites from which methylphenidate can be obtained without a prescription. Alternative access via someone else’s prescription is reported commonly in America (e.g. Arria et al., 2011; McCabe et al., 2006). Vargo and Petróczi (2016) investigated CED use among students in England in a qualitative study and they noted greater reported use of modafinil and as suggested earlier, they also explained that this was due to the easy access via online sources and the fact that it posed no legality issues. They also noted that methylphenidate and Adderall seemed more difficult to access off-prescription within the UK and stated that the participants who had obtained them had done so via individuals who had prescriptions which were usually from the United States.

In all three studies the majority of CED users reported that they were university-educated. In Study 2, although a large percentage of methylphenidate users stated that they were educated to 18 years of age, most of them were currently studying for a degree. This may suggest that they were using the CEDs for study purposes. However, in Study 2 a greater number of modafinil users were employed compared with methylphenidate users, which suggesting that modafinil is also being used in the workplace. Vargo and Petróczi (2016) reported that 11 of the 13 reported CED users in their study stated that they contemplated using CEDs again either during post-graduate studies or for work with tight deadlines or specific projects. It may be that CED users begin using these drugs for study purposes but then continue CED use in employment when work demands and pressure to perform exceed their self-perceived ability to deliver.

The association between CED use and the diagnosis of a psychiatric disorder, primarily depression and anxiety was identified in Study 1 and the findings of Study 2 indicated that depression and anxiety were not specifically related to CED use but to the online forums instead. So, the association between CED use and depression and anxiety may only relate to CED users who visit online forums and social media. A systematic review by Keles, McCrae and Grealish (2020) found a relationship between social media use and depression and anxiety in adolescents, providing support to Lin et al.’s (2016) findings of a linear association between social media use (including Reddit) and depression in young adults. However, the direction of this association is unclear. Although, as briefly discussed in Section 3.4, people with depression and anxiety are drawn to social media as it offers anonymity and a lack of accountability. Lin et al. argued that depressed individuals may seek validation through social media and that they may prefer online rather than face-to-face interactions. Conversely, visiting social media sites may result in the development of depression. Kross et al. (2013) found that Facebook use predicted a decline in subjective well-being and life satisfaction. Experiences of cyberbullying and trolling may also have an impact and contribute to feelings of depression and anxiety (Zezulka & Seigfried-Spellar, 2016).

The pattern of illicit drug use among reported CED users was relatively high in all three studies and in Studies 2 and 3 illicit drug use among reported CED users was high compared with controls. Similar findings have been found in other studies of CED use (e.g. McCabe et al., 2006; Rabiner et al., 2009; Schelle et al., 2015; Vargo & Petróczi, 2016). One possible explanation for this is provided by Vargo and Petróczi who reported that the CED users they interviewed had often practiced polysubstance use where several CEDs and legal or natural cognitive enhancers are combined for heightened effect, and recreational drugs are used to relieve the side-effects of CEDs. This suggests a lifestyle use of drugs, where drugs are seen as instruments, facilitating the pursuit of the individual’s desires and goals (d’Angelo et al., 2017; Műller & Schumann, 2011).

The greater emotional control reported by the CED using participants in Study 3 might also be suggestive of blunted affect. As Glannon (2006) argued, emotional and cortical processes are interconnected and regulated by cortical limbic pathways and enhancing cognitive functions may result in reducing emotional affect. These CED users may not be aware of this potential trade-off. That said, both modafinil and methylphenidate have been noted to have mood-enhancing effects (Kerr et al., 2012; Price & Taylor, 2005) which may attenuate this effect. As discussed in Section 1.5, polymorphism of the COMT gene can result in a val/val or met/met genotype (Mattay et al., 2003). Those with the val allele have a more active version of the COMT enzyme, resulting in a more rapid breakdown of catecholamines such as dopamine, whereas those with the met allele have a less active version and thus slower breakdown of catecholamines. Catecholamines are recognised to be involved in mood regulation (Nutt et al., 2007) and individuals with the val allele may have lower levels of available catecholamines. Modafinil acts on the dopaminergic, noradrenergic and serotonergic systems (Minzenberg & Carter, 2008) whilst methylphenidate acts on the dopaminergic and noradrenergic systems (Wood et al., 2014), all of which are implicated in mood.

In addition to this, psychostimulants can demonstrate dose-dependent concurrent linear and quadratic (i.e. U-shaped) effects, (Tannock, Schachar, & Logan, 1995). Tannock et al. reported that, at different doses (0, 0.3, 0.6 and 0.9 mg/kg), children with ADHD demonstrated a linear effect on behavioural motor activity whereas response inhibition was better at the lower doses and worse at the higher dose, demonstrating a U-shaped effect. Konrad, Gűnther, Hanisch and Herpertz-Dahlmann (2004) also reported that at different doses (0, 0.25 and 0.5 mg/kg) children with ADHD demonstrated different effects on attentional functions. Alertness, focused and sustained attention improved in a linear effect, whereas performance on the two executive tasks of inhibition and set-shifting was only enhanced at the low dose and worsened on the higher dose. Konrad and colleagues explained that alertness and focused, sustained attention seem to be localized within the frontosubcortical network in the right hemisphere whereas executive functions are more localized within the PFC. Konrad and colleagues (2004) argued that these different brain regions and networks have different dose-response curves. This suggests that a dose which enhances one cognitive function may also have the opposite effect on another. This also may explain the different doses of methylphenidate reported by respondents in Studies 1 and 2.

Furthermore, it was discussed in Section 1.5 that the benefits of modafinil and methylphenidate are greater for low baseline performers and that this suggests that users are predominantly low baseline performers. However, CED-using participants in Study 3 did not demonstrate low baseline performance and yet they must experience benefits from CED use otherwise they would not take them. The linear effects reported for behaviour motor activity, alertness, and focused, sustained attention may explain why high performing individuals, such as the CED-using participants in Study 3, might still experience benefits from taking modafinl and methylphenidate.

### **5.3.1 Laboratory studies versus real world reports**

It should also be noted that some laboratory studies reported weak effects or no effects of modafinil and methylphenidate (e.g. Finke et al., 2010; Linssen et al., 2004; Műller et al., 2004) and this may be related to individual differences in relation to optimal dosage, whereas the survey data from Studies 1 and 2 and the questionnaire data from Study 3 reflect real world experiences where users tailor their dose to meet their own requirements. Further to this, and as previously noted in Section 1.5, the cognitive tests used in laboratory studies are often designed to assess clinical conditions and may not accurately measure the performance of healthy individuals, whereas surveys and self-reports reflect real world experiences. However, both approaches have great value in their own right. As previously discussed in Section 4.4, self-reports reflect typical performance or behaviours and real world experiences as perceived by respondents and participants (Stanovich, 2009; Toplak et al., 2013). Conversely, laboratory tasks are less likely to be influenced by the individual’s interpretations of their own behaviour and performance, occur in standardized conditions and commonly assess optimal performance or behaviour, as tasks often require the participant to perform at speed whilst also ensuring accuracy of response. However, this is not always relevant; Studies 1 and 2 focused only on self-reports for the specific intention of understanding real world experiences and the findings from these studies directed the approach of the final study which used these complementary measures.

## **5.4 Modafinil and methylphenidate off-prescription users are not one homogenous group**

The sample of CED users in Study 3 may reflect a sub-type of CED-users (who frequent the forum sites targeted in the study) who are not self-medicating but instead are using modafinil and methylphenidate to improve their already good cognitive functions, thus suggesting that CED users are not one homogenous group. The findings of Study 1 also suggested that off-prescription users of modafinil and methylphenidate may also not represent one homogenous group but, instead, represents two separate groups whereas the findings of Study 2 only found a difference between the modafinil and methylphenidate groups in the likelihood of more frequent use of illicit drugs by the modafinil group. It may be that the main difference between the two groups is that users of modafinil perceive that it is easier to access, safer and that more frequent use provides greater benefits without greater risks and that modafinil users also take illicit drugs frequently. Conversely, methylphenidate is perceived as having more risk attached to its use and being more difficult and dangerous to obtain, particularly in the UK (Vargo & Petróczi, 2016). A further difference was noted from the findings of Study 3. As the CED-using participants did not appear to have poor cognitive functions, they also represented a sub-type of CED users who are prepared to contribute their time to participate in a lab-based study. It would seem that sub-groups may exist within the CED-using population and that these sub-groups may be defined by their perceived experiences, behaviours and motivations for use. Therefore, identifying these different sub-groups and their drivers for obtaining and using CEDs in the face of the potential dangers and risks is essential for informing future research and government bodies in relation to ethical considerations and legislation. The following section considers the off-prescription use of modafinil and methylphenidate for self-medication and for enhancement in relation to the studies’ findings.

## **5.5 Are modafinil and methylphenidate used for self-medication or enhancement?**

The findings of Study 3 indicated that the CED users demonstrated good cognitive function and greater emotional control compared with the control group, therefore they are unlikely to be self-medicating for poor cognitive performance. It may be that the influence of providing socially acceptable answers is greater when face-to-face with the researcher rather than in the ‘virtual’ setting of an online survey. However, Weigold, Weigold and Russell (2013) investigated whether online or lab-based questionnaire completion would yield different results and they found that pen-and-paper and online questionnaire results were generally equivalent so the possibility that the participants were providing socially acceptable answers is unlikely. Additionally, the objective measures used in Study 3 did not reveal poor performance, in fact the CED-user group demonstrated better performance on response latencies for correcting errors in the antisaccade task and faster response latencies on the correct flanker tasks, with no corresponding increase in errors. As previously discussed in Sections 4.4 and 5.2.3, self-reports and performance-based measures tap different aspects of cognition, and this was demonstrated by the finding from the BRIEF-A, that the CED user group rated themselves as having fewer problems with emotional control. This helped to explain the differences in response latencies, as performance anxiety would be less likely to be experienced by the CED user group and therefore the amygdala activation would be lower, resulting in greater recruitment of the ACC, DLPFC and the VLPFC, resulting in shorter response latencies. However, the findings of Study 2 revealed that the off-prescription reported modafinil and methylphenidate users rated themselves as having problems with inattention and procrastination. As mentioned earlier, in Section 5.4, this could represent two distinct groups of off-prescription CED users, those who self-medicate for poor cognitive performance and those who chose to enhance their already good cognitive functions. These two motivations for use will be discussed in the following sections.

### **5.5.1 Modafinil and methylphenidate use as self-medication**

The findings of Study 2 in relation to self-reports of inattention and procrastination are, as yet, unconfirmed via lab-based methods. However, these findings do suggest that a sub-group of modafinil and methylphenidate off-prescription users may be self-medicating for perceived inattention and procrastination. As suggested by Ilieva and Farah (2015), the perceptions of inattention and procrastination, or indeed poor cognitive function more broadly, may not be as severe as they are perceived to be, however, there is little evidence, as yet, to support this. Understanding the possible causes of inattention and procrastination may help in the assessment and identification of these problems in individuals who use modafinil and methylphenidate off-prescription.

There are several possible causes for inattention, the most obvious being related to ADHD. In a longitudinal study assessing the symptoms of ADHD in 128 boys over five years, Biederman, Mick and Faraone (2000) found that symptoms of hyperactivity and impulsivity tend to decline at a higher rate than inattention. This supports the finding of Millstein, Wilens, Biederman and Spencer (1997) who assessed 149 clinically referred adults with ADHD and found that the majority of adults with ADHD are of the inattentive type. However, there is a growing argument that inattention and ADHD are two distinct and separate disorders (e.g. Barkley, 2001; Carlson & Mann, 2000; Diamond, 2005; Milich, Balentine & Lynam, 2001). The theory that attention exists along a continuum (Connor, 1997), supported by Scope et al. (2010), suggests that symptoms of inattention can occur at a subclinical level, which may require the development of tests which are more sensitive to subclinical levels of inattention. As Battleday and Brem (2015) indicated, the tests that are currently utilised in studies assessing whether CEDs are used for self-medication are based on assessments of clinical conditions and therefore may not be robust or sensitive enough for assessing healthy participants.

As previously noted in Section 3.1, inattention has been found to be correlated with procrastination (Niermann & Scheres, 2014). Bolden and Fillauer (2019) found that the executive functions of self-management of time, organisation/problem-solving, self-restrain, self-motivation and self-regulation of emotions mediated the association between procrastination and symptoms of ADHD. However, Elisa, Balaguer-Ballester and Parris (2016) found that poor complex verbal working memory is associated with inattention. Scope et al. (2010) also found that working memory, as well as inhibitory control, was associated with low attentional skills. It would seem then that there may be a complex interaction between inattention, procrastination and executive functions.

Another possible contribution to the cause of inattention can be found in the polymorphism of specific genes. Although polymorphisms of the dopamine transporter gene DAT1 has been linked specifically to the hyperactive/impulsive type of ADHD and not to the inattentive type (Gizer et al., 2008), the polymorphism of the DRD4.7 gene coding for the D4 dopamine receptor has been linked more to the inattentive type than the hyperactive/impulsive type of ADHD (McCracken et al., 2000; Rowe et al., 1998). According to McCracken et al. the DRD4.7 gene is highly expressed in the PFC. Diamond (2005) argues that the primary structural dysfunction in inattentive types is located in the PFC and Herrmann et al. (2007) found that the DRD4.7 modulates activation of the PFC during working memory tasks demonstrating ineffective brain activation. Together, these findings suggest a genetic component to inattention causing ineffective brain activation, specifically in the PFC, which relates to working memory and as working memory and attention are so closely related (as discussed in Section 4.1). This conclusion is likely to relate equally to attention. Additionally, Diamond argues that inattentive types are responsive to amphetamines such as Adderall and to low doses of methylphenidate, and that both inhibit the reuptake of dopamine and noradrenaline but that Adderall also promotes the release of dopamine and noradrenaline and that methylphenidate has been found, at low doses, to preferentially release noradrenaline in the rat brain (Ishimatsu, Kidani, Tsuda, & Akasu, 2002). As modafinil also inhibits the reuptake of noradrenaline, this may contribute to its popular use.

Causes for procrastination are generally recognised to involve poor self-regulation and poor self-efficacy (Klassen, Krawchuk & Rajani, 2008; Steel, 2007; Yerdelen, McCaffrey & Klassen, 2016). Steel (2007) presented his Temporal Motivation Theory (TMT) to explain procrastination. The TMT is presented as an equation where Utility (how desirable a task is to complete) is dependent upon Expectancy (the probability that an outcome will be achieved) multiplied by Value (how much the expected outcome is valued). The formula denominator relates to time, Delay (the length of time before the reward) and sensitivity to delay, which can be perceived as the level of impulsivity. Expectancy is related to self-efficacy, Value is related to task aversiveness, and Delay is related to low organisation and an inability to meet one’s own expectations. Therefore, procrastination depends on poor self-efficacy and high task aversiveness, high impulsivity and poor organisational skills resulting in a greater length of time before the reward is achieved. Attempts have been made to identify the neural substrates underlying procrastination and Zang, Wang and Feng (2016) identified abnormalities in the VMPFC and the lateral PFC (LPFC) in high procrastinators. Zang, Liu and Feng (2019) argued that damage to the VMPFC is related to impulsivity and poor emotional regulation. They also made the point that the LPFC in involved in different aspects of executive behavioural control via its function in voluntary reallocation of attention. If the VMPFC and LPFC are displaying abnormal activity in high procrastinators, this suggests that the relationship between procrastination and inattention might be due to dysfunction in the LPFC.

Overall, considering these many possible causes for poor cognitive function and the fact that it is very possible that a sub-group of CED users are self-medicating, this does suggest that these individuals are not being helped and supported via the appropriate channels and may have therefore resorted to self-medication in spite of the risks and dangers involved.

### **5.5.2 Modafinil and methylphenidate use as cognitive enhancers**

The CED user’s motivation for enhancing already good cognitive skills may, perhaps, be inspired by the need to meet the demands and pressures of the current competitive “24/7” society. Indeed, d’Angelo, Savulich and Sahakian (2017) argued that the demand for increased workplace productivity may be one of the drivers behind CED use. Brűhl and Sahakian (2016) explained that in our modern society the need for physically skilled labour has been replaced by the need for cognitively skilled work whilst the threat of job losses in competitive work environments and a need to work beyond their natural capacities has motivated the use of CEDs. Pustovrh, Mali and Arnaldi (2018) supported this view, arguing that the pressure to constantly improve performance and work at greater intensity for longer periods, leads to exhaustion and cognitive fatigue, and CEDs offer workers the ability to cope with these demands. They also made the point that the development of modern technology has facilitated and further promoted greater efficiency, and productivity and that the presence and availability of CEDs have played a significant role in reinforcing this ever-increasing demand on work performance. Műller and Schumann (2011) argued for the use of non-addictive psychoactive drugs as instruments, facilitating individuals in pursuing their goals. Whilst they point out that some psychoactive drugs such as caffeine, nicotine and alcohol are commonly used as instruments, the act of using a psychoactive drugs for this purpose may result in a sort of psychopharmaceutical ‘crutch’ where users become dependent on a psychoactive drug such as a CED, overextending their physical bodies and increasing their exhaustion and sleep deficit further, rather than addressing the situation for which the psychoactive drug is used. The authors do, however, recognise that long-term regular use of CEDs to counter cognitive exhaustion and fatigue can lead to dependency. Although there are commercially-driven, unhealthy reasons behind some individuals’ motivations for cognitive enhancement and obvious potentially detrimental consequences to enhancing already good cognitive performance, CEDs can serve as a necessary means with which to overcome obstacles and challenges to an individual’s goals and autonomy. As highlighted by d’Angelo et al. some of the main reasons for CED use include maintaining attention and performance when jet-lagged, coping with the pressure to succeed and maintaining a desired work-life balance. It is clear that the heavy demands of the “24/7” society are not likely to diminish and that off-prescription CED use is a reality and a necessity for some. What has been demonstrated through all three studies of this thesis is that the majority of reported off-prescription users of modafinil and methylphenidate appear to be responsible users who recognise the appropriate dosage and who are aware of the dangers of methylphenidate use. That said, the respondents and participants in the studies reported in this thesis are online forum users who may be more educated in the off-prescription use of these drugs compared with the broader CED-using population. Additionally, and as previously noted in Section 2.2.4 the link between frequency of use of modafinil and the perceived benefits from its use suggest that dependency may develop over time.

Whether the off-prescription use of modafinil and methylphenidate is intended for self-medication or enhancement, without being monitored by a physician, the responsibility lies with the user, not only to become cognisant of the potential dangers in relation to serious adverse effects, but also to be self-aware, in relation to the potential development of dependency and addiction. The latter will be considered in relation to both modafinil and methylphenidate in the following section.

### **5.5.3 Dependency and addiction**

Modafinil has been noted in the literature as having low addictive potential, partly due to the fact that, as explained in Section 1.6.2, it is extremely difficult to inject and impossible to snort modafinil effectively and therefore it cannot reach the bloodstream rapidly (e.g., Jasinski, 2000; Myrick et al., 2004). However, the risk of dependency is less well documented. In addressing this gap in the literature, Study 1 revealed the perceived dependency on modafinil was reported by only 5.5% of respondents. Nevertheless, as previously stated, the relationship between more frequent use and greater perceived benefits suggests the possibility of dependency developing. A case report by Krisnan and Chary (2015) detailed one case of a 44-year-old man who had been prescribed modafinil at a dose of 200mg for excessive daytime sleepiness and antipsychotics for symptoms of auditory hallucinations, delusions and fear following the death of his father. Over a six-month period, the patient increased his dose of modafinil to 1200mg and reported suffering symptoms of lethargy, anxiety and disruption to his sleeping patterns without the daily dose of 1200mg of modafinil, only achieving a sense of well-being at this daily dose. However, this is noted by Krisnan and Chary (2015) as a rare case and the patient was also suffering from poor mental health, following the patient’s report, this was managed by a medical professional. That said, it is important to note that a significant percentage of respondents and participants stated that they had been diagnosed with a psychiatric disorder. This may suggest that vulnerability to dependency may increase with the diagnosis of a psychiatric disorder and this presents an area for future investigation.

Methylphenidate is known to have addictive potential, but less so if the only route of administration is orally (e.g., Botly et al., 2008; Wooters et al., 2011). Study 2 and Study 3 revealed that 14% of respondents, and 10.5% of participants, respectively, stated that they snorted methylphenidate. However, one report by Teter et al. (2006) revealed that 38% snorted, 6% smoked and 1% inhaled methylphenidate (or Adderall) by other means. The fact that methylphenidate is not just used off-prescription as a cognitive enhancer, but also as a recreational drug may, in part, explain the users’ other chosen routes of administration. Barrett, Darredeau, Bordy and Pihl (2005) interviewed 50 university students who reported methylphenidate misuse and 50 controls. They reported that the college students who used methylphenidate off-prescription for recreational purposes were more likely to report intranasal use compared with the students who reported off-prescription use of methylphenidate for the sole purpose of studying.

## **5.6 Relevance to informing policy makers and society**

The studies in this thesis present important information on the profile of the off-prescription users of modafinil and methylphenidate (who frequent online forums) and their perceptions and experiences of using these drugs for cognitive enhancement. This thesis has suggested that there are sub-groups of CED users and as such, off-prescription users of CEDs should be considered in relation to their individual group membership. This thesis has proposed the (possible) self-medicating group, the enhancing group and different groups represented by off-prescription modafinil use and off-prescription methylphenidate use as well as the possible drivers behind their use. There may also be other, possibly problematic, sub-groups of CED users such as methylphenidate users who take methylphenidate by non-oral means, such as snorting. There may also be a sub-group who have previously experienced mental health problems and are also using a range of recreational drugs, perhaps concurrent to the use of CEDs. The culmination of these findings is relevant to policy makers and medical practitioners.

Additionally, as previously noted in Section 2.1.2, it is possible that some individuals are feigning symptoms of ADHD for the purpose of acquiring CEDs such as methylphenidate. Poulin (2007) found that some students who screened negative for ADHD reported having a prescription for ADHD medications whilst only a small percentage of students who screened positive for ADHD reported having a prescription for ADHD medications. Whilst the issue of inappropriate prescribing, under- and over-diagnosing ADHD has been the focus of debate largely in the United States and Canada (Poulin; Singh, Filipe, Bard, Bergey & Baker, 2013) there is evidence that the rate of prescribing ADHD medications in Britain has increased dramatically over the past two decades (Renoux, Shin, Dell’Aniello, Fergusson & Suissa, 2016). The use of CEDs such as methylphenidate and, possibly, modafinil by children and adults under the age of 30 may also have detrimental effects on the development and maturation of the PFC and plasticity, possibly resulting in behavioural inflexibility and the development of addictive behaviours (Urban & Gao, 2014). For individuals who do experience the symptoms of ADHD, there is a clear trade-off but this may not be the case for individuals who use CEDs purely for enhancement.

Considerations should be made in relation to whether adults with poor cognitive functions are not being given the help and support they need. Ginsberg, Beusterien, Amos, Jousselin and Asherson (2014) reported poor uptake of the the UK National Institute for Health and Care Excellence (NICE) ADHD guidelines and reports of adults who experienced long and difficult struggles in attaining a diagnosis of ADHD due to the negative attitudes towards ADHD by healthcare professionals (Matheson et al., 2013). For adults with poor cognitive function unrelated to ADHD the situation is less clear and, therefore, this should be considered for future investigations. The drivers in relation to these two groups, those who enhance and those who (may) self-medicate, should also be considered in relation to the ongoing ethical debate around the use of CEDs, for as long as there are such strong societal/environmental pressures and un-met needs, there will always be those who are driven to seek solutions, whatever the cost.

## **5.7 Limitations**

Whilst the studies reported in this thesis have highlighted a number of important issues and provided a greater understanding of the off-prescription use of modafinil and methylphenidate in contribution to the growing knowledge in this field, there are some limitations to these findings which should be taken in to consideration.

One of the main aims of this thesis was to assess whether off-prescription users of modafinil and methylphenidate are self-prescribing for poor cognitive function. Whilst the findings of Study 2 have suggested that there may be a sub-group of modafinil and methylphenidate off-prescription users who are self-medicating for perceived inattention and procrastination, this remains an open question and will be further discussed in the following section. It is not possible, therefore, to discuss with certainty, the use of these drugs for self-medication. Further, the question as to whether respondents/ participants were using modafinil and methylphenidate for cognitive enhancement or self-medication was not asked directly. However, to do so may have resulting in priming responses to questions relating to the use of these drugs and their cognitive performance. This could, however, be addressed in a qualitative study where reported CED-users have the opportunity to discuss their use of CEDs such as modafinil and methylphenidate without the restriction of just answering questions.

The fact that all respondents and participants, with the exception of the control group in Study 3, were recruited through online forums and therefore, may only represent the population of online forum visitors who use modafinil and methylphenidate off-prescription. This signifies a weakness as the findings cannot be interpreted in relation to the wider population of off-prescription users of modafinil and methylphenidate. However, reaching this wider population would require a considerable financial investment in order to advertise on the kind of platforms that are visible to the wider population.

Furthermore, there was no way of confirming whether the respondents and participants in all three studies complied with the requirement to not be under the influence of psychoactive drugs during their participation. Although there is evidence that drug users who know that their hair, blood or urine samples will be tested as part of a drug-related research project, provide accurate self-reports of use which correspond well to the objective data (e.g., Johnson et al., 2000), the accuracy of self-reports in the absence of a test to verify them is not known. However, it is unlikely that the online forum using respondents are providing inaccurate information about their CED use as the online surveys were anonymous and the forum sites are platforms which where individuals discuss their drug use openly and anonymously. That said, it is not known for certain whether the respondents and the participants in Study 3 complied with the requirements to abstain from psychoactive drug use during participation and this is a weakness, particularly in relation to the findings of Study 3.

Additionally, the use of university undergraduates as a control group in Study 3 is also a weakness as university undergraduate psychology students do not represent a broad enough range of healthy adults (Coolican, 2017). However, the use of university students as participants or respondents is common practice in academic research and serves as a good comparison with CED-using students. A further weakness of Study 3 is that the participants were not screened for drugs and the influence of any drugs could have had an effect on task performance.

Finally, as discussed in Section 2.1, the use of online surveys comes with recognised weaknesses including self-selection bias and recruiting from only the Internet-using population. However, online surveys have become increasingly popular in academic research and provide benefits such as reaching a wide population.

## **5.8 Future Directions**

It has been previously argued in Section 1.5 that if some CED users are self-medicating for poor cognitive performance, this may be related to the baseline performance level of the individual taking CEDs. As Finke et al.’s (2010) study indicated, low baseline performers may experience greater cognitive enhancing effects of drugs such as modafinil and methylphenidate. Related to this is the polymorphism of the COMT gene, with poor cognitive performers possessing the val allele, as suggested by Mattay et al. (2003). Therefore, it may be beneficial for future research to investigate the baseline level and specific allele of the COMT gene of CED users in relation to poor cognitive performance. Similarly, the polymorphism of the DRD4.7 gene has been linked to inattention, as previously discussed, and this also presents an area of future research investigating the presence of the DRD4.7 gene in CED users in relation to poor cognitive performance.

As the findings from the studies of this thesis relate only to the online forum off-prescription user of modafinil and methylphenidate, these findings now needs to be expanded upon to reach the wider population of off-prescription users of modafinil and methylphenidate, perhaps via a multi-centre study so that the international element of Studies 1 and 2 may be replicated via a lab-based approach. As procrastination was only measured in Study 2 via the GPS (Lay, 1986), this could also be tested in a naturalistic situation. Zuber et al. (2020) conducted a lab-based study where the participants completed the Pure Procrastination Scale (Rebetez, Rochat, Gay, & Van der Linden, 2014) and at the end of the session they were presented with an attendance sheet which they were told they were required to sign, scan and email by a specific date and failure to do so by this specific date would result in invalidate of their course credits. Their results indicated that participants’ self-reports significantly predicted procrastinatory behaviour. Therefore, the inclusion of a naturalistic test of procrastination should also be considered in future investigations.

The online forum sites targeted in all three studies of this thesis draw a wider range of people than just students, therefore the samples in each study consisted of a mix of students and workers. Students are typically working towards an end goal and require attention, concentration, focus and avoidance of procrastination in order to achieve for good grades. In comparison, in many areas of employment, the work is ongoing rather than working towards an end goal, and the worker brings to the job their skills and expertise, often in very competitive work environments where greater demands are placed upon the worker’s time and performance (Brűhl & Sahakian, 2016). With this in mind, it may be that a greater majority of CED-using students are self-medicating rather than enhancing and a greater majority of CED-using workers are enhancing their already good cognitive functions. However, as the studies conducted for this thesis were not designed in such a way to allow students and workers to be separated, this has not yet been explored and presents an area for future investigation.

As discussed in Section 5.4.3, there is a risk of dependency with the regular off-prescription use of modafinil and methylphenidate and this risk may increase with the diagnosis of a psychiatric disorder. Kandel, Huang and Davies (2001) investigated the pattern of concurrent dependence on licit and illicit drugs in adults with psychiatric syndromes from data collected from the National Household Survey on Drug Abuse. They found that individuals with probable drug dependency had higher rates of psychiatric syndromes and that rates of psychiatric syndromes doubled for those dependent on both licit and illicit drugs. The possibility that the development of dependency from the regular off-prescription use of modafinil and methylphenidate increases with the diagnosis of a psychiatric disorder should therefore be investigated.

Given the many possible motivations and drivers behind off-prescription use of CEDs, this issue should be further explored in relation to the ethical debate and could be addressed via a qualitative study investigating the beliefs and opinions about the use of CEDs in relation to self-medication, enhancement and the struggle to meet the pressure and demands of the modern Western society. A qualitative study could also investigate whether adults with poor cognitive functions unrelated to ADHD have the support and help they need. Investigating the drivers, motivations and pressures behind the use of CEDs could also be addressed more directly in a qualitative study, which could also explore whether poor cognitive performance or the pressures and demands of the Information Age are driving individuals to improve their cognitive abilities through the off-prescription use of CEDs.

## **5.9 Conclusions**

In sum, this thesis set out to identify the profile of the off-prescription CED user and to understand their experience of using these drugs as well as the drivers behind off-prescription use, even in the face of the potential risks involved. This aim was achieved via the findings of the profile and experiences identified in Study 1 and supported via the findings of Studies 2 and 3. The profile of the online forum-using CED user has been identified as mostly male, in their mid-20s, educated, employed and either North American or British. The CED user who frequents online forums is also likely to use illicit drugs. The reported dosage and patterns of use of modafinil and methylphenidate by these respondents and participants, overall, appears to be responsible and informed. However, there is the potential for dependency to develop through more frequent use and this needs to be investigated.

This thesis also aimed to establish whether users are self-medicating for poor cognitive performance or if they are enhancing their already good cognitive functions. The findings of Study 2 suggested that some users may be self-medicating but this was not evident from the findings of Study 3, which found that the CED-using participants were likely to be enhancing their already good cognitive functions. However, this finding may only represent a sub-group of users and whether modafinil and methylphenidate off-prescription users are self-medicating has yet to be clarified. The findings of Study 2 represent the perceptions of CED users in the context of real world experiences and therefore the suggestion that some CED users are self-medicating for, what they experience as, inattention and procrastination is an important contribution to the body of work in this field.

The culmination of the results from these studies have also indicated that CED users should not be considered as one, homogenous group as different groups of individuals are drawn to different drugs. Whether they obtain them from their friends and colleagues, which has been seen commonly with methylphenidate, or if they have learned about certain CEDs through online forum sites, if they are occasional users or frequent users who find greater benefits from more frequent use, these differences in the approach to and the patterns of CED use alters the profile of the user. Motivations and drivers behind their use are also varied. The possibility that there may be these different sub-groups of CED users needs to be acknowledged and considered in relation to future research conducted in this field and in relation to the wider debate around CED usage and in relation to policy decisions. Considering these varied reasons behind the off-prescription use of CEDs is essential if this developing trend is to be managed effectively as dealing with the cause is as important as dealing with the resulting situation.

This thesis has provided important evidence about the real-life use of the CEDs, modafinil and methylphenidate, and also laboratory evidence, which is intended to contribute to the growing body of knowledge in the field of CED use. It is also hoped that the findings herein may help to provide a greater understanding of reasons behind the off-prescription use of modafinil and methylphenidate, even in the face of the potential risks and harms, and how CED users perceive themselves and are perceived in society.

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**APPENDICES**

# **Appendix A: Study One**

## **A(i) Questionnaire**

**MODAFINIL AND METHYLPHENIDATE QUESTIONNAIRE**

**Demographics (*please note, these headings were not visible to respondents)***

1. How old are you? (en*ter number*)
2. Are you male female (*tick boxes*)
3. What is your nationality *(free text box)*
4. What country do you live in? *(free text box)*
5. What is your highest level of education

*dropdown menu: No formal qualifications,*

*Educated to age 16 (e.g. G.C.S.E.),*

*Educated to age 18 (e.g. A-level, High School, I.B.),*

*University Degree (BSc, BA),*

*Post-Graduate Degree (MSc, MA, PhD)*

1. Are you currently studying for a qualification? (click yes or no)

If yes, are you a university student? (click yes or no)

1. Are you working at the moment? (select from options)

Yes, full-time paid

Yes, part-time paid

Yes, full-time voluntary

Yes, part-time voluntary

No

If in employment, please state your job title or role (*enter text)*

**Drug awareness**

1. Are you aware of cognitive enhancing drugs? Yes/No options

(*yes leads to Medical health and drug use)*  No (*no leads to next question)*

1. If you could take a drug to increase your attention/concentration/memory, would you?

Options of Yes, No or Maybe

**Medical health and drug use**

1. Have you ever been diagnosed with a psychiatric condition?

Yes(*leads to next question*) No (*leads to Q.14*)

1. What was the diagnosis? *enter text (leads to next question)*
2. When was the diagnosis made? *Type year*
3. Are you still receiving treatment? Options of Yes or No

**Drug use**

For each of the following drugs, questions ‘Ever used’ and ‘Used in the last year’ were presented with options of Yes or No and ‘age when first used’ was presented with a free text box.

Cannabis

Cocaine

Amphetamines (speed)

MDMA

1. How often have you taken the drugs listed below in the last month?

*Select one answer for each drug taken.*

Cannabis

Cocaine

Amphetamines (speed)

MDMA (ecstasy)

**Options are: Every day/ Most days; once/twice per week; once/twice per month; less than once** **per month**

1. Have you ever been treated for a drug or alcohol-related problem? Options of Yes or No

If yes, are you still receiving treatment? Options of Yes or No

**Modafinil use**

1. Are you aware of the cognitive enhancing drug, Modafinil (Provigil, Modalert)?

Options of Yes or No (*no leads to methylphenidate use)*

1. Have you ever taken it?

Options of Yes or No (*no leads to methylphenidate use)*

1. How many times have you taken modafinil?

*Dropdown scale: 1, 2 etc. to 10, then 10-20, more than 20*

1. How often do you take modafinil?

*Options of: every day; 3 or more times per week; once or twice per week; two or three times per month; 6 times or less per year*

1. How much do you take at any one time?

Options of: L*ess than 100mg; 100m; 200mg; more than 200mg; 400mg; more than 400mg and don’t know*

1. Do you usually use any other drugs at the same time? Options of Yes or No

If so name them and specify level of dose (*free text box)*

1. How did you hear about modafinil?

*Options of: News article; Chat room; Friend; online pharmacy; dealer; academic paper/lecture; medical professional; other (please specify)- (free text box)*

1. How do you get modafinil (tick all applicable)

*Options of: GP prescription; someone else’s prescription; friend; dealer; online pharmacy; other (please specify) (free text box)*

1. Why do you take it?

*Options of: To work longer hours; for attention and focus; to get more done; for exams; night work; to think more clearly; other (please specify) (free text box)*

**Risk awareness**

1. What immediate positive effects do you experience from modafinil? (tick all applicable)

*Options of: Increased energy; ability to focus; clarity of mind; motivation; confidence; alertness; increased productivity; increased concentration; improved reasoning; increased creativity; enhanced mood; more outgoing/extraverted; improved ability; to enter a ‘flow-like’ state; appetite suppression; none; other (please specify) (free text box)*

1. What longer-lasting (i.e. once the drug has worn off) positive effects do you experience from modafinil? (tick all applicable)

Same options as no. 26

1. What immediate negative effects do you experience from modafinil? (tick all applicable)

*Options of: Anxiety; insomnia; diarrhoea; dizziness; nausea; headache; indigestion/acid reflux; inflammation of the nose; abnormal heart rhythm; low blood pressure; cannot empty bladder; chest pain; chills; confusion; depression; fast heart beat; mood changes; problems with vision; throat irritation; dry mouth; tremor; vomiting; loss of appetite; none; other (please specify) (free text box)*

1. What longer-lasting negative (i.e. once the drug has worn off) effects do you experience from modafinil? (tick all applicable)

Same options as no. 28

1. Do you feel dependent on modafinil? Options of Yes or No
2. How much modafinil do you think it is safe to take at any one time?

Options of: None; *50mg; 100mg; 200mg; 400mg; more than 400mg*

1. Do you think you would you be putting yourself in danger if you took modafinil

*Options of: every day; 3 or more times per week; once per week; twice per month; 6 times or less per year;* no danger

**Methylphenidate use**

1. Are you aware of Methylphenidate (Ritalin, Rubifen, Concerta)?

Options of Yes or No (*no leads to PRMQ Questions*)

1. Have you ever taken it?

Options of Yes or No *(No leads to PRMQ Questions. Yes for either leads next question*)

1. How many times have you taken methylphenidate?

*Dropdown scale: 1, 2 etc. to 10, then 10-20, more than 20*

1. How often do you take methylphenidate?

Options of: *every day; 3 or more times per week; once or twice per week’; two or three times per month; 6 times or less per year*

1. How much do you take at any one time?

*Options of: 10mg or less; 20mg; 30mg; 40mg; 50mg; 60mg; more than 60mg; don’t know*

1. How much do you take in any full day?

Options of: 1*0mg or less; 20mg; 30mg; 40mg; 50mg; 60mg; more than 60mg; don’t know*

1. Do you usually use any other drugs at the same time?

Options of: Yes or No if Yes, name them and specify level of dose (*free text box)*

1. How did you hear about methylphenidate?

*Options of: News article; chat room; friend; online pharmacy; dealer; academic paper/lecture; medical professional; other (please specify) (free text box)*

1. How do you get methylphenidate (tick all applicable)

*Options of: GP prescription; someone else’s prescription; friend; dealer; online pharmacy; other (please specify) (free text box)*

1. Why do you take it?

Options of: *To work longer hours; for attention and focus; to get more done; for exams; night work; to think more clearly; other (please specify) (free text box)*

**Risk awareness**

1. What immediate positive effects do you experience from methylphenidate?

*Increased energy; ability to focus; clarity of mind; motivation; confidence; alertness; increased productivity; increased concentration; improved reasoning; increased creativity; enhanced mood; more outgoing/extraverted; improved ability to enter a ‘flow-like’ state; appetite suppression; none; other (please specify (free text box)*

1. What longer-lasting (i.e. once the drug has worn off) positive effects do you experience from methylphenidate?

Same options as no. 43

1. What immediate negative effects do you experience from methylphenidate?

*Anxiety; insomnia; diarrhoea; dizziness; nausea; headache; indigestion/acid reflux; inflammation of the nose; abnormal heart rhythm; low blood pressure; cannot empty bladder; chest pains; sweating; confusion; depression; fast heart beat; mood changes; aggressive behaviour; throat irritation; dry mouth; tremor; vomiting; loss of appetite; none; other (please specify) (free text box)*

1. What longer-lasting (i.e. once the drug has worn off) negative effects do you experience from methylphenidate?

Same options as no. 45

1. Do you feel dependent on methylphenidate?  *Options of Yes or No*
2. How much methylphenidate do you think it is safe to take at any one time?

Options of: none; *5mg; 10mg; 20mg; 30mg; 40mg; 50mg; 60mg; more than 60mg*

1. Do you think you would you be putting yourself in danger if you took methylphenidate

*Options of: every day; 3 or more times per week; once per week; twice per month; 6 times or less per year; no danger*

**A(ii) Advertisement to online forum sites**

**SMART DRUG SURVEY**

**Recruiting – The off prescription use of modafinil and methylphenidate – all welcome (over 18)!**

[Smart Drug Survey](https://lsbupsychology.qualtrics.com/SE/?SID=SV\_5yFEq1OIKZMaov3)I am a PhD student at London South Bank University and I am researching the off prescription use of modafinil and methylphenidate, and also opinions on the use of cognitive enhancers. If you can spare 15-20 minutes, please complete this online survey (link found below) – you would be contributing to this investigation into use of these drugs, awareness of risks and harms and also opinions on the use of cognitive enhancers. You don’t need to have taken these drugs to participate, although anyone who has would also contribute greatly! This survey is completely confidential and anonymous so no details that could identify you will be recorded. As long as you are over 18 years of age and have an opinion about this topic you are most welcome to participate. This study is not restricted to any country and welcomes people from all countries to participate. Our findings will contribute to informing research on the extent of use of these drugs within the UK and internationally and will form the basis of a journal article that may be published in a peer reviewed journal.   
The study has been approved by the Research Ethics Committee of London South Bank University (ref. 1626).   
To participate, just follow this link: [Smart Drug Survey](https://lsbupsychology.qualtrics.com/SE/?SID=SV\_5yFEq1OIKZMaov3)

## **A(iii) Participant information sheet**

**Participant Information Sheet**

**Title of study: The off—prescription use of Modafinil and Methylphenidate for cognitive enhancement, a web-based survey**

You are invited to take part in a survey investigating the use of modafinil (also known as Modalert or Provigil) and methylphenidate (also known as Ritalin) for cognitive enhancement. This is a completely anonymous survey and no information that could identify you will be collected. Participation is entirely voluntary and you are free to opt out at any time during completion of the questionnaire by clicking on the ‘exit’ button. This study is being conducted as part of Rachel Teodorini’s PhD programme at London South Bank University.

This survey aims to increase our understanding of current awareness of the effects of off-prescription use of methylphenidate and modafinil and why people are using them. It seeks to identify the extent of users’ of awareness of the risk and harms associated with taking them and to investigate public opinion of cognitive enhancement.

As we are also interested in opinions of the use of cognitive enhancing drugs, anyone who has an opinion on this is invited to participate, even if they have never taken these drugs themselves. However, anyone under the age of 18 is excluded from participating in this study.

Please take time to decide if you would like to take part and please be aware that you are under no obligation to do so and have the right to withdraw at any point. The survey will take approximately 15 to 20 minutes to complete and will involve a minimal amount of typing as the questions have mostly tick box options. The questions being asked relate to:

* awareness of cognitive enhancing drugs
* the use of methylphenidate and modafinil
* understanding of potential risks and harms associated with taking these drugs
* opinions of the use of cognitive enhancing drugs
* self ratings of your memory abilities.

The information that participants provide through this survey will contribute to informing research on the extent of use of these drugs within the UK and Europe and will form the basis of a journal article that may be published in a peer reviewed journal. All information collected from this survey will be securely stored on a password protected computer that will only be accessed by the researcher (Rachel Teodorini) and supervisors (Dr Nicola Rycroft and Dr James Smith-Spark) both of whom are Senior Lecturers at London South Bank University and have expertise in substance abuse and memory. This information will be stored for a period of time (approximately 5 years from publication) to comply with journal regulations.

Other than contributing to a knowledge base that will help to inform research on the prevalence of use of these drugs, it is unlikely that you will gain any personal benefit from participating in this research. It is not anticipated that you will be disadvantaged by participating in this research.

This study has been organized by the PhD student and aforementioned supervisors and funded by the London South Bank University. It has also been ethically approved by the London South Bank University Research Ethics Committee.

If you would like to take part in this study, please click on the ‘Continue’ button below. This will lead you to a consent form consisting of a number of statements which you are required to answer by clicking on the tick boxes. Only by ticking on the boxes will you be indicating consent to each of these statements and only by ticking all consent boxes will you be able to continue to the survey. Should you change your mind and wish to cancel at this stage or at any stage during the survey there is an exit button at the bottom each page you may click on to exit the survey. Each question in the survey requires an answer, even if the answer is ‘no’.

On completion of the survey you will be shown a debriefing page, providing you with further information regarding this study. At this point you may still withdraw your participation by clicking on a ‘cancel’ button and your data will be deleted. If you click on the ‘submit’ button you will no longer be able to withdraw. This is because each submission is entirely anonymous and there is no way of identifying your submission.

The survey will be live until 30th September 2016 when it will be reviewed and may remain open for a further 3 months, until the 31st December 2016. Therefore, if you would like to participate please ensure that you do so within this time period. Also, if you would like to take part, you are free to discuss this with your GP, friends or family.

For additional information and further clarifications about the study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Contact details for supervisors are: Dr Nicola Rycroft, email: [rycroftn@lsbu.ac.uk](mailto:rycroftn@lsbu.ac.uk); Dr James Smith-Spark, email: [smithspj@lsbu.ac.uk](mailto:smithspj@lsbu.ac.uk). If you have any concerns or complaints you may contact the Chair of the University Research Ethics Committee at ethics@lsbu.ac.uk.

## **A(iv) Participant consent form**

**Title of study: The off—prescription use of Modafinil and Methylphenidate for cognitive enhancement, a web-based survey**

**Please tick all boxes to indicate your agreement with the following statements.**

***All boxes must be ticked to enter the survey. If you do not agree with any of the statements you should press the ‘exit’ button at the end of the page to leave the survey.***

I have read the attached information sheet about this. I have had the opportunity

to discuss the details and ask questions about this study. 🞎

The nature and purpose of this study has been explained and I believe that I

understand what is being proposed. 🞎

I understand that my personal involvement and my particular data from this study

will remain strictly confidential and entirely anonymous and therefore the data

will not be identifiable in any way, even by the researchers involved in the study. 🞎

I have been informed about what the data collected will be used for, to whom

it may be disclosed, and how long it will be retained. 🞎

My questions have been answered through the information in the information

Sheet. 🞎

I hereby fully and freely consent to participate in the study which has been

fully explained to me. 🞎

I understand that I am free to withdraw from the study without giving a

reason for withdrawing at any time up to and including the debrief sheet

end until I click on the ‘submit’ button when it is no longer possible to withdraw. 🞎

I am over 18 years of age. 🞎

I am not currently under the influence of any psychoactive drug. 🞎

NOTE TO ETHICS COMMITTEE: As this is an online survey, participants will be asked to click on each of the points to indicate their informed consent before starting the questionnaire. Hard copies of a signed consent form will not be asked for in this instance.

IF YOU ARE AT ALL CONCERNED ABOUT THE EFFECT OF ANY DRUG YOU ARE RECEIVING PLEASE CONTACT YOUR GP.

If you have any concerns about this research study, please contact:

Rachel Teodorini

[teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk)

## **A(v) Participant debriefing information**

**Debriefing Information**

**Title of study: The use of Modafinil and Methylphenidate for cognitive enhancement, a web-based survey**

Thank you for participating in our survey. This survey aims to increase our understanding of current awareness of the effects of off-prescription use of methylphenidate and modafinil and why people are using them. It seeks to identify users’ level awareness of the risk and harms associated with taking them and to investigate public opinion of cognitive enhancement.

Although studies have sought to evaluate prevalence of use and awareness of risk, most of these are based on data from the United States. A survey conducted at a US college of higher education (Babcock & Byrne, 2000) found that over 16% of participants reported that they had used methylphenidate non-medically. Another study of 3,407 North American undergraduates found that 8.9% reported using ADHD medication (such as methyphenidate and modafinil) non-medically of which, 54% reported using exclusively for academic reason due to attention problems (Rabiner et al, 2009). The studies mentioned here demonstrate the widespread use of these drugs in the United States. Considering these trends, it is important to understand whether users are aware of the risks and harms associated with taking these medications, and, to what extent. Regular use of modafinil and methylphenidate in young adults up to the age of 30 may interfere in the development of prefrontal cortex, the centre of executive cognitive functions (Urban & Gao, 2014). The term executive cognitive functions refers to the ability to control and coordinate other mental processes and behaviours, such as self-control, moral reasoning, planning, problem solving, attention and working memory. In addition to potential harms such as this, one of the risks involved, at any age, is the illegal use of methylphenidate which is punishable by a prison sentence of up to 5 years and/or unlimited fine (Drugs penalties, n.d.). Both Modafinil and Methylphenidate are relatively new drugs and therefore the potential harms of long-term use are still unclear (Urban & Gao, 2014).

The information collected from this survey will contribute to informing research on the extent of use of these drugs within the UK and Europe and will form the basis of a paper that may be published in a peer-reviewed journal.

You are reminded that you are under no obligation to participate in this study and you have the right to withdraw by simply clicking the cancel button below following which your answers will not be submitted and will instead be deleted. This will also happen if you close your browser. All information in this survey is collected anonymously and therefore no-one can be identified from any publication of the results.

Only by clicking on the ‘submit’ button below will your participation be submitted and at this point you will no longer be able to withdraw from the study.

**Cancel** Submit

If you have concerns about any aspect of this study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Following which, if you still have concerns, you may contact the Chair of the University Research Ethics Committee at ethics@lsbu.ac.uk.

If you would like more information about these drugs please visit the following site: <https://www.erowid.org/psychoactives/psychoactives.shtml>

Modafinil and methylphenidate are illegal without prescription and liable to up to a prison sentence of up to 5 years.

Finally, if you have any concerns about your use of these drugs please consult your GP.

**References**

Babcock, Q., & Byrne, T. (2000). Student Perceptions of Methylphenidate Abuse at a Public Liberal Arts College. *Journal of American College Health,* *49*(3), 143-145.

Drugs penalties. (n.d.). Retrieved March 27, 2016, from https://www.gov.uk/penalties-drug-possession-dealing

Rabiner, D. L., Anastopoulos, A. D., Costello, E. J., Hoyle, R. H., McCabe, S. E., & Swartzwelder, H. S. (2008). Motives and Perceived Consequences of Nonmedical ADHD Medication Use by College Students: Are Students Treating Themselves for Attention Problems? *Journal of Attention Disorders,* *13*(3), 259-270.

Urban, K. R., & Gao, W. (2014). Performance enhancement at the cost of potential brain plasticity: Neural ramifications of nootropic drugs in the healthy developing brain. *Frontiers in Systems Neuroscience,* *8*(38), 10-3389.

## **A(vi) Mental Health**

**Table A.1. Psychiatric diagnosis**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Modafinil**  **N (%)\*** | **Methylphenidate N (%)\*\*** | **Modafinil and Methylphenidate N (%)\*\*\*** |
| **Have you received a psychiatric diagnosis?** | | | |
| **Yes** | 48 (21.9) | 28 (26.9) | 62 (24.5) |
| **No** | 171 (78.1) | 76 (73.1) | 191 (75.5) |
| **Psychiatric Diagnosis** | | | |
| **Depression** | 21 (44.7) | 11 (39.3) | 28 (45.9) |
| **Anxiety** | 3 (6.4) | 2 (7.1) | 5 (8.2) |
| **Depression and Anxiety** | 13 (27.7) | 7 (25.0) | 16 (26.2) |
| **Other** | 10 (21.3) | 8 (28.6) | 12 (19.7) |

Percentages relate to group only

\* The modafinil group represents all respondents who reported modafinil usage

\*\* The methylphenidate group represents all respondents who reported methylphenidate usage

\*\*\* The modafinil and methylphenidate group represent all respondents who reported either modafinil or methylphenidate usage.

## **A(vii) Illicit drug use**

**Table A.1. Modafinil, methylphenidate and control respondents’ reported illicit drug use**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Modafinil N (%)\*** | **Methylphenidate N (%)\*\*** | **Modafinil and Methylphenidate N (%)\*\*\*** |
| **LIFETIME USE** | | | |
| **Cannabis** | 180 (53.57) | 96 (28.57) | 265 (78.87) |
| **Cocaine** | 89 (26.49) | 58 (17.28) | 116 (34.52) |
| **Speed** | 98 (29.17) | 76 (22.61) | 127 (37.80) |
| **MDMA** | 103 (30.66) | 66 (19.64) | 137 (40.77) |
| **PAST YEAR USE** | | | |
| **Cannabis** | 112 (33.33) | 58 (17.28) | 158 (47.02) |
| **Cocaine** | 35 (10.42) | 23 (6.85) | 42 (12.50) |
| **Speed** | 45 (13.39) | 42 (12.50) | 66 (19.64) |
| **MDMA** | 49 (14.58) | 32 (9.52) | 64 (19.05) |

\* The modafinil group represents all respondents who reported modafinil usage

\*\* The methylphenidate group represents all respondents who reported methylphenidate usage

\*\*\* The modafinil and methylphenidate group represent all respondents who reported either modafinil or methylphenidate usage.

## **A(vii) Other motivations for using modafinil and methylphenidate**

**Table A.2. Additional motivations for using modafinil and methylphenidate**

|  |  |
| --- | --- |
| **Modafinil** | **Methylphenidate** |
| Depression | Depression |
| Wakefulness after late nights | wakefulness |
| Fatigue | Energy booster |
| Self-development and productivity | Partying and studying |
| Experimentation | Euphoria and sex |
| To write articulately | Recreation/ fun |
| Alertness | To reduce the undesirable effects of oxycontin |
| Multitasking – for clarity |  |
| Weight loss |  |
| Mood elevation |  |

## **A(viii) Reported modafinil dosage**

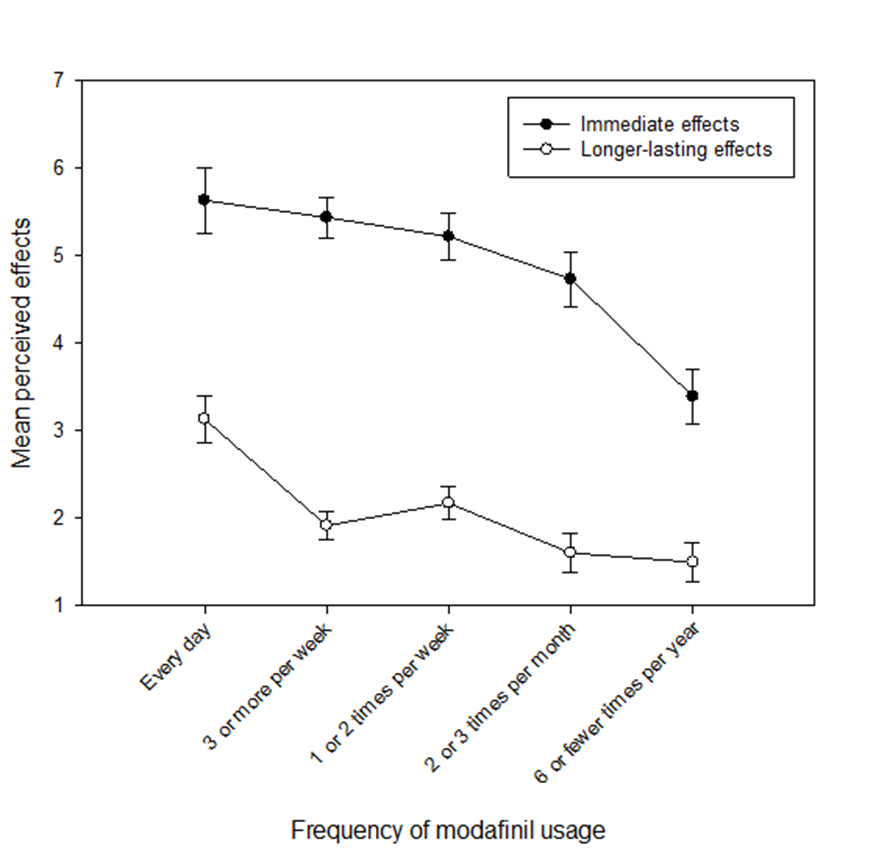
**Table A.3. Reported modafinil dosage**

|  |  |
| --- | --- |
| **Modafinil Dosage** | **N (%)\*** |
| **Less than 100mg** | 16 (4.78) |
| **100mg** | 75 (22.39) |
| **200mg** | 96 (28.66) |
| **More than 200mg** | 11 (3.28) |
| **400mg** | 8 (2.39) |
| **More than 400mg** | 1 (0.30) |
| **Don’t know** | 3 (0.90) |

**\* Percentage relates to total sample N = 335**

## **A(ix) Log-transformed analysis of Timeframe and frequency of use of modafinil**

Log-transformed significant interaction between timeframe and frequency of use of modafinil, F(4, 214) = 3.92, MSE = 0.281, *p* = .004, ηp2 = 0.068. Figure A.1 shows that the number of immediate effects was reported as being greater with more frequent use of modafinil. Post-hoc within-subjects *t*-tests confirmed that the difference between immediate and longer-lasting effects was significant for all five frequency of use groups (see Table 2).



**Figure A.1. The interaction between the reported immediate and longer-lasting effects and the reported frequency of use of modafinil.**

**Table A.4. Post-hoc within –subjects *t*-tests**

|  |  |  |  |
| --- | --- | --- | --- |
| **Frequency of use** | **df** | ***t*** | ***p*** |
| **Every day/ almost every day** | 25 | 6.91 | < .001 |
| **3-4 times per week** | 65 | 14.00 | < .001 |
| **Once per week** | 51 | 11.76 | < .001 |
| **1-2 times per month** | 37 | 10.15 | < .001 |
| **Up to 3 times in total** | 36 | 8.39 | < .001 |

## **A(x) Immediate and longer-lasting risks and benefits of modafinil and methylphenidate**

**Table A.5. Immediate and longer-lasting risks and benefits of methylphenidate and modafinil**

|  |  |  |
| --- | --- | --- |
|  | **Modafinil**  **Mean (SE)** | **Methylphenidate**  **Mean (SE)** |
| **Immediate risks** | 2.22 (0.11) | 3.46 (0.36) |
| **Immediate benefits** | 7.77 (0.24) | 7.39 (0.52) |
| **Longer-lasting risks** | 1.38 (0.06) | 1.97 (0.26) |
| **Longer-lasting benefits** | 2.76 (0.17) | 1.96 (2.00) |

## **A(xi) Reported methylphenidate dosage**

**Table A.6. Reported methylphenidate dosage**

|  |  |
| --- | --- |
| **Methylphenidate Dosage** | **N (%)\*** |
| **10mg or less** | 24 (7.16) |
| **20mg** | 21 (6.27) |
| **30mg** | 6 (1.79) |
| **40mg** | 3 (0.90) |
| **50mg** | 7 (2.09) |
| **60mg** | 5 (1.49) |
| **More than 60mg** | 12 (3.58) |

**\* Percentage relates to total sample N = 335**

## **A(xii) List of sub-Reddits selected for Study 1 and 2**

**Reddit forum sites where the surveys were advertised**

r/Nootropics

r/afinil

r/Stims

r/AskDrugNerds

r/StackAdvice

r/darknet

r/Drugs

r/UKUniversityStudents

r/UniUK

r/lifelonglearning

r/Scholar

# **Appendix B: Study Two**

## **B(i) Questionnaire**

**Demographics**

1. How old are you? (slide bar to indicate age)
2. Are you male or female (*tick boxes*) Prefer to self-describe free text box
3. What is your nationality *dropdown menu to select from*
4. What is your highest level of education *dropdown menu: options are: No formal qualifications, Educated to age 16 (e.g. G.C.S.E.), Educated to age 18 (e.g. A-level, High School, I.B.), University Degree (BSc, BA), Post-Graduate Degree (MSc, MA, PhD)*
5. Are you currently studying for a qualification? Options are: Yes (yes leads to next question) or No (no skips next question)
6. Which of the following most accurately describes your course: Options are: *Vocational (learning in a practical way about a job); Continuing Professional Development; High school/ college/ A levels; University bachelor’s program; University master’s program; Doctoral studies*
7. Are you working at the moment? Options are: Yes, full-time paid; Yes, part-time paid; Yes, full-time voluntary; Yes, part-time voluntary; No

If in employment, please state your job title or role *free text box*

**Mental health and drug use**

1. Have you ever been diagnosed with a psychiatric condition? Options are: Yes (*leads to Q.9*) or No (*leads to Q.12*)
2. What was the diagnosis?
3. What medications have you been prescribed (if any)? Type medication names or ‘N/A’(free text box)
4. If you were prescribed medication, are you currently taking it? Options are: Yes or No *(If you were not prescribed any, please select 'No')*
5. Have you ever been treated for a drug or alcohol-related problem? Options are: Yes or No *(leads to next section)*

If yes, are you still receiving treatment? Options are: Yes or No

**Cannabis**

1. Have you ever taken cannabis? Options are: Yes or No (*No leads to next section)*
2. Do you have a prescription for medicinal cannabis? Options are: Yes or No
3. What age were you when you first took cannabis? (type age)
4. In the past six months, how regularly have you taken cannabis? Options are: every day/almost every day, 3-4 times per week, once per week, 1-2 times per month, up to 3 times in total, none
5. What type of cannabis do you use most commonly? Options are: Resin/hash, normal weed, kief, edible, oils/concentrates, butane hash oil, high potency herbal/skunk
6. How do you take it? Options are: Medical spray, tea, joint, pipe, bucket bong, bong/water pipe, eaten in food, vaporiser, blunt
7. How much do you take in any single day of use (please state amount in relation to type, e.g. grams, ml etc.) Free text box

**Modafinil**

1. Are you aware of the cognitive enhancing drug, Modafinil (Provigil, Modalert Options are: Yes or No (no leads to methylphenidate)
2. Have you ever taken it? Options are: Yes or No *(*no leads to methylphenidate*)*
3. Have you been prescribed Modafinil? Options are: Yes or No
4. What age were you when you first took Modafinil? (slide bar to indicate age)
5. In the past six months, how regularly have you taken Modafinil? Options are: every day/almost every day, 3-4 times per week, once per week, 1-2 times per month, up to 3 times in total, none
6. How do you take it? Options are: Swallow pill, snort, smoke, inject, vaporise, other
7. How much do you take in any single day of use Dropdown box ranging from less than 50mg to more than 500mg
8. Do you always take the same dose? Yes (Yes leads to next question) No (No skips the next question)
9. What is the typical maximum and minimum dose you would take at any one time? Dropdown box ranging from less than 50mg to more than 500mg

**Methylphenidate**

1. Are you aware of Methylphenidate (Ritalin, Rubifen, Concerta)? Options are: Yes or No (no leads to )
2. Have you ever taken it? Options are: Yes or No *(*No leads to debrief)
3. Have you been prescribed Methylphenidate? Options are: Yes or No
4. What age were you when you first took Methylphenidate? (slide bar to indicate age)
5. In the past six months, how regularly have you taken Methylphenidate? Options are: every day/almost every day, 3-4 times per week, once per week, 1-2 times per month, up to 3 times in total, none
6. How do you take it? Options are: Swallow pill, snort, smoke, inject, vaporise, rectal, other
7. How much do you take in any single day of use (dropdown box ranging from less than less than 10mg to more than 80mg)
8. Do you always take the same dose? Options are: Yes (Yes leads to next question) or No (No skips the next question)
9. What is the typical maximum and minimum dose you would take at any one time? (dropdown box ranging from less than 10mg to more than 80mg)

**Smoking and nicotine replacement**

1. How frequently in the past SIX MONTHS have you taken nicotine**.** Nicotine options for Q.58 and Q.59 are tobacco/cigarettes; vaping/ electronic cigarettes and Replacement products (e.g. gum, spray etc.) Please click on the option(s) which are the most accurate**.** Options are: Every day/ almost every day, 3-4 times per week, once per week, 1-2 times per month, up to 3 times in total, never
2. How long has it been since you last used this drugOptions are: Within the last week; Within the last month; Within the last year; Within the last 5 years; Within the last ten years; Over 10 years ago; Only ever took it once; Can’t remember

**Other recreational drugs**

1. *The following are a list of recreational drugs.  Please click to indicate the frequency of any/all drugs that you have used and also use the drop-down button to the right to indicate how long it has been since you have taken the drug.*

(*If you have not taken any of the drugs here, simply choose 'never' for one drug and select 'can't remember' on the drop down menu beside.)*

1. For each drug the question: How frequently in the past SIX MONTHS have you taken this drug.  Please click one option per drug that is the most accurate**.** was presented with options of: Every day/ almost every day, 3-4 times per week, once per week, 1-2 times per month, up to 3 times in total, never
2. For each drug the question: How long has it been since you last used this drug was presented with options of: Within the last week; Within the last month; Within the last year; Within the last 5 years; Within the last ten years; Over 10 years ago; Only ever took it once; Can’t remember

The list of drugs presented were: Benzodiazepines; Zolpidem (Ambien); Oxycodone (Dihydrohydroxycodeinone, Percocet, OxyContin); Pethidine (Meperidine, Demerol); Tramadol (Ultram, Ralivia, Tramal); Tapentadol (Nucynta, Palexia); Barbiturates; Morphine; Opium; GHB (Gamma-Hydroxybutyric Acid, Xyrem, Alcover); Fentanyl (China White); Heroin; Methadone; MDMA; LSD; Cocaine; Psilocybin; Ketamine; Benzedrine; Dextroamphetamine (Dexedrine); Mixed Amphetamine Stereoisomer Salts (Adderall); Lisdexamfetamine (Vyvanse, Elvanse); Ephedrine (Ephedra); Solvents (glue etc.); Anabolic steroids; Pregabalin (Lyrica); Racetams; Adrafinil; Adderall.

**QUESTIONNAIRE ONE**

***Please answer the following questions below, rating yourself on each of the criteria shown using the options provided.***

***PLEASE NOTE, you will be asked each question in relation to how you are when you are taking modafinil/ methylphenidate AND when you are not taking modafinil/methylphenidate. Please answer the second time reflecting back on how you are without modafinil or methylphenidate or any other cognitively enhancing drug or stimulant.***

***As you answer each question, click on the option that best describes how you have felt and conducted yourself.***

Q.1 How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 2 How often do you have difficulty getting things in order when you have to do a task that requires organization?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q.3 How often do you have problems remembering appointments or obligations?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q.4 when you have a task that requires a lot of thought, how often do you avoid or delay getting started?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q.5 How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q.6 How often do you feel overly active and compelled to do things, like you were driven by a motor?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 7 How often do you make careless mistakes when you have to work on a boring or difficult project?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q.8 How often do you have difficulty keeping your attention when you are doing boring or repetitive work?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 9 How often do you have difficulty concentrating on what people say to you even when they are speaking directly to you?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 10 How often do you misplace or have difficulty finding things at home or at work?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 11 How often are you distracted by activity or noise around you?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 12 How often do you leave your seat in meetings or other situations in which you were expected to remain seated?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 13 How often do you feel restless or fidgety?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 14 How often do you have difficulty unwinding and relaxin when you have time to yourself?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 15 How often do you find yourself talking too much when you are in social situtations?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 16 When you’re in a conversation, how often do you find yourself finishing sentences of the people you are talking to,m before they can finish them themselves?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 17 How often do you jhave difficulty waiting your turn in situations when turn taking is required?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

Q. 18 How often do you interrupt others when they are busy?

*(on Modafinil/ Methylphenidate) options are: Never, Rarely, Sometimes, Often, Very Often*

*(off Modafinil/Methylphenidate/ and all other cognitively enhancing drugs) options are: Never, Rarely, Sometimes, Often, Very Often*

**The CFQ and GPQ were presented as the ASRS above.**

## **B(ii) Advertisement to online forum sites**

**Recruiting – even if you have taken the pilot of this survey, please participate, this is the full survey**

Click here to take survey: [Everyday attention and drug use survey]( <https://lsbupsychology.qualtrics.com/jfe/form/SV_4JcyBYKV5VaCf9H>)

I am a PhD student at London South Bank University and I am researching the use of psychoactive drugs and everyday attention. Based on the results of my first study (“Smart Drug Study”), a further study is required to understand in greater detail the off-prescription use of modafinil and methylphenidate, recreational drug use and also how people who take these drugs feel that their attention is like both on and off these drugs. If you are over 18 years of age and can spare 15-20 minutes, please complete this online survey (link found below).\*\*This survey is completely confidential and anonymous so no details that could identify you will be recorded. This study is not restricted to any country and welcomes people from all countries to participate. Even if you have no experience of taking these drugs you are still invited to participate. This survey will be open for a three month period between 6 February 2018 and 6 May 2018, after which time the survey will close. Our findings from this study will contribute to informing research on the extent of use of these drugs within the UK and internationally and will form the basis of a journal article that may be published in a peer reviewed journal.

The study has been approved by the School of Applied Science Ethics Committee of London South Bank University (ref. SAS 1733).

To participate, just follow this link:

[Everyday attention and drug use survey]( <https://lsbupsychology.qualtrics.com/jfe/form/SV_4JcyBYKV5VaCf9H>)

## **B(iii) Advertisement for controls to online forum sites**

**Recruiting – looking for people who have NEVER taken modafinil, armodafinil, adrafinil, methylphenidate and adderall**

Click here to take survey: [Cognitive function and drug use survey]( <https://lsbupsychology.qualtrics.com/jfe/form/SV_29bHZ8aCJm0IwkZ>)

I am a PhD student at London South Bank University and I am researching the use of psychoactive drugs and everyday attention. Based on the results of my first study (“Smart Drug Study”), a further study was required to understand in greater detail the off-prescription use of modafinil and methylphenidate, recreational drug use and also how people who take these drugs feel that their attention is like both on and off these drugs. We have collected this data but we still require data from participants who have never taken these drugs. If you are over 18 years of age and can spare 15-20 minutes, please complete this online survey (link found below). This survey is completely confidential and anonymous so no details that could identify you will be recorded. This study is not restricted to any country and welcomes people from all countries to participate.

**If you have NO experience of taking modafinil, armodafinil, adrafinil, methylphenidate and adderall you are invited to participate. Please do not participate if you have already taken this survey.**

This survey will be open for a one month period between 4th October 2018 and 4 November 2018, after which time the survey will close. Our findings from this study will contribute to informing research on the extent of use of these drugs within the UK and internationally and will form the basis of a journal article that may be published in a peer reviewed journal.

The study has been approved by the School of Applied Science Ethics Committee of London South Bank University (ref. SAS 1833c).

To participate, just follow this link:

[Cognitive function and drug use survey]( <https://lsbupsychology.qualtrics.com/jfe/form/SV_29bHZ8aCJm0IwkZ>)

## **B(iv) Participant information sheet**

**Participant Information Sheet**

**Title of study: Everyday attention and drug use: for better or worse, a web-based survey**

You are invited to take part in a survey on the relationship between drug-use and everyday attention.

This is a completely anonymous survey and no information that could identify you will be collected. Participation is entirely voluntary and you are free to opt out at any time during completion of the questionnaire by closing your browser window. Only participants who click the ‘submit’ button at the end of the survey will have their responses recorded. This study is being conducted as part of Rachel Teodorini’s PhD programme at London South Bank University.

You can only take part in this study if you are over 18.

Please take time to decide if you would like to take part and please be aware that you are under no obligation to do so and have the right to withdraw at any point up until you press submit. The survey will take approximately 20 minutes to complete and will involve a minimal amount of typing as the questions have mostly tick box options. The questions will ask about use of drugs, including alcohol, nicotine, modafinil, methylphenidate, cannabis and recreational stimulant drugs. You will also be asked to provide self-ratings of your cognitive performance.

This study will form part of my PhD thesis and may also be published in a peer reviewed journal. All information collected from this survey will be securely stored on a password protected computer that will only be accessed by me (Rachel Teodorini) and my doctoral supervisors (Dr Nicola Rycroft and Dr James Smith-Spark) both of whom are Senior Lecturers at London South Bank University and have expertise in substance use and cognitive performance. This information will be stored for a period of time (approximately 5 years from publication) to comply with journal regulations.

Other than contributing to a knowledge base that will help to inform research on the prevalence of use of these drugs, it is unlikely that you will gain any personal benefit from participating in this research. It is not anticipated that you will be disadvantaged by participating in this research.

This study has been organized by the PhD student and aforementioned supervisors and funded by London South Bank University. It has also been ethically approved by the School of Applied Sciences Research Ethics Committee.

If you would like to take part in this study, please click on the ‘Continue’ button below. This will lead you to a consent form consisting of a number of statements which you are required to answer by clicking on the tick boxes. Only by ticking on the boxes will you be indicating consent to each of these statements and only by ticking all consent boxes will you be able to continue to the survey. Should you change your mind and wish to cancel at this stage or at any stage during the survey simply exit the survey and your responses will not be included in this study. Each question in the survey requires an answer, even if the answer is ‘no’.

On completion of the survey you will be shown a ‘submit’ button. At this point you may still withdraw your participation by closing your browser page. If you click on the ‘submit’ button you will no longer be able to withdraw. This is because each submission is entirely anonymous and there is no way of identifying your submission. Once you have clicked on the ‘submit’ button you will be shown a debriefing page, providing you with further information regarding this study.

If you would like to take part, you are free to discuss this with your GP, friends or family.

For additional information and further clarifications about the study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Contact details for supervisors are: Dr Nicola Rycroft, email: [rycroftn@lsbu.ac.uk](mailto:rycroftn@lsbu.ac.uk); Dr James Smith-Spark, email: [smithspj@lsbu.ac.uk](mailto:smithspj@lsbu.ac.uk). If you have any concerns or complaints you may contact the Chair of the School of Applied Sciences Research Ethics Committee at [sasethics@lsbu.ac.uk](mailto:sasethics@lsbu.ac.uk).

## **B(v) Participant consent form**

**Title of study: Everyday attention and drug use: for better or worse?**

**Please tick all boxes to indicate your agreement with the following statements.**

***All boxes must be ticked to enter the survey. If you do not agree with any of the statements you should press the ‘exit’ button at the end of the page to leave the survey.***

I have read the information sheet about this. I have had the opportunity to discuss the details and ask questions about this study. 🞎

The nature and purpose of this study has been explained and I believe that I

understand what is being proposed. 🞎

I understand that my personal involvement and my particular data from this

study will remain strictly confidential and entirely anonymous and therefore

the data will not be identifiable in any way, even by the researchers involved

in the study. 🞎

I have been informed about what the data collected will be used for, to whom

it may be disclosed, and how long it will be retained. 🞎

I hereby fully and freely consent to participate in this study. 🞎

I understand that I am free to withdraw from the study without giving a

reason for withdrawing at any time up to and including the debrief sheet

and until I click on the ‘submit’ button when it is no longer possible to

withdraw. 🞎

I am over 18 years of age. 🞎

I am not currently under the influence of any psychoactive drug. 🞎

NOTE TO ETHICS COMMITTEE: As this is an online survey, participants will be asked to click on each of the points to indicate their informed consent before starting the questionnaire. Hard copies of a signed consent form will not be asked for in this instance.

IF YOU ARE AT ALL CONCERNED ABOUT THE EFFECT OF ANY DRUG YOU ARE RECEIVING PLEASE CONTACT YOUR GP.

If you have any concerns about this research study, please contact:

Rachel Teodorini

[teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk)

## **B(vi) Participant debriefing information**

**Debriefing Information**

**Title of study: Everyday attention and drug use: for better or worse?**

Thank you for participating in our survey. The present survey was developed based on the results of a previous study which found that people who use modafinil and methylphenidate off-prescription show higher than expected rates of recreational drug use. It also showed that those who use amphetamines, cocaine and MDMA reported greater immediate subjective effects of methylphenidate and those who use amphetamines also reported greater immediate subjective effects of modafinil. One further finding was that no differences were found between users and non-users of modafinil and methylphenidate in prospective memory ability.

The three questionnaires at the end of this survey have been developed to measure everyday cognitive abilities such as attention, short-term memory and procrastination. The information collected from this survey will contribute to informing research on the use of these drugs internationally and will form the basis of a paper that may be published in a peer-reviewed journal.

Data from the questionnaires will be analysed to compare users of modafinil and methylphenidate to non-users. We will also compare frequency of drug use and scores on the questionnaires. This study may also provide an indication of which abilities are affected by modafinil and methylphenidate intake outside of laboratory conditions.

You are reminded that, if you have provided an email on which you may be contacted at a future date to participate in a lab-based study, you are under no obligation to participate and you have the right to withdraw during the lab-based study at any time. If you provide an email address, this will be kept entirely confidential and only the researcher will have access to the email address. All other information in this survey is collected anonymously and therefore no-one can or will be identified from any publication of the results.

If you have concerns about any aspect of this study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Following which, if you still have concerns, you may contact the Chair of the School of Applied Science Ethics Panel at sasethics@lsbu.ac.uk.

If you would like more information about these drugs please visit the following site: <https://www.erowid.org/psychoactives/psychoactives.shtml>

Modafinil and methylphenidate are illegal to take without prescription and illegal use is liable to a prison sentence of up to 5 years.

Finally, if you have any concerns about your use of these drugs please consult your GP.

Please be reminded that as this study is fully anonymous, you cannot withdraw your responses at a later date.

## **B(vii) ASRS**

**Table B.1. Shaded grid for the ASRS**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Question no.** | **Never** | **Rarely** | **Sometimes** | **Often** | **Very Often** |
| **PART A** | | | | | |
| **1** |  |  |  |  |  |
| **2** |  |  |  |  |  |
| **3** |  |  |  |  |  |
| **4** |  |  |  |  |  |
| **5** |  |  |  |  |  |
| **6** |  |  |  |  |  |
| **PART B** | | | | | |
| **7** |  |  |  |  |  |
| **8** |  |  |  |  |  |
| **9** |  |  |  |  |  |
| **10** |  |  |  |  |  |
| **11** |  |  |  |  |  |
| **12** |  |  |  |  |  |
| **13** |  |  |  |  |  |
| **14** |  |  |  |  |  |
| **15** |  |  |  |  |  |
| **16** |  |  |  |  |  |
| **17** |  |  |  |  |  |
| **18** |  |  |  |  |  |

## **B(viii) Mental Health**

**Table B.2. Psychiatric diagnosis and medication**

|  |  |  |  |
| --- | --- | --- | --- |
| **Have you received a psychiatric diagnosis?** | **Modafinil-only N = 86** | **Methylphenidate N = 57** | **Controls N = 106** |
| **N (%)** | **N (%)** | **N (%)** |
| Yes | 28 (32.56) | 16 (28.07) | 40 (37.74) |
| No | 58 (67.44) | 41 (71.93) | 66 (62.26) |
| **Psychiatric diagnosis** |  |  |  |
| Anxiety disorder | 14 (16.28) | 14 (24.56) | 31 (29.25) |
| Panic disorder | 1 (1.16) | - | 7 (6.60) |
| Social phobia disorder | 1 (1.16) | 9 (15.79) | 6 (5.66) |
| Agoraphobia | - |  | 3 (2.83) |
| Autism spectrum disorder | 2 (2.33) | 2 (3.51) | 6 (5.66) |
| Acute stress disorder | 1 (1.16) |  | 1 (0.94) |
| PTSD | 1 (1.16) | 3 (5.26) | 5 (4.72) |
| Dissociative disorder | 1 (1.16) |  | 2 (1.89) |
| Eating disorder | 3 (3.49) | 2 (3.51) | 2 (1.89) |
| Depressive disorder | 19 (22.09) | 19 (33.33) | 27 (25.47) |
| Bipolar disorder | 4 (4.65) | 3 (3.51) | 2 (1.89) |
| Antisocial disorder | 1 (1.16) | - | - |
| Avoidant personality disorder | - | - | 1 (0.94) |
| Dependant personality disorder | - | - | - |
| Borderline personality disorder | 2 (2.33) | 2 (3.51) | - |
| Narcissistic disorder | 1 (1.16) | - | - |
| OCD | - | 2 (3.51) | 2 (1.89) |
| Paranoid personality disorder | - | - | - |
| Delusional disorder | - | - | - |
| Schizophrenia | 2 (2.33) | 1 (1.75) | - |
| Paraphilic disorder | - | - | - |
| Gender dysphoria disorder | - | - | 2 (1.89) |
| Suicidal disorder | 2 (2.33) | 5 (8.77) | 5 (4.72) |
| Substance-induced disorder | - | 1 (1.75) | 2 (1.89) |
| Other | - | - | 4 (3.77) |
| **If you were prescribed medication, are you currently taking it?** | | | |
| Yes | 13 (15.12) | 8 (14.04) | 22 (20.75) |
| No | 15 (17.44) | 9 (15.79) | 18 (16.98) |

## **B(ix) Type of cannabis used**

**Table B.3. Type of cannabis used by group**

|  |  |  |  |
| --- | --- | --- | --- |
| **What type of cannabis do you use most commonly?** | **Modafinil-only**  **%\* (N)** | **Methylphenidate**  **%\* (N)** | **Control**  **%\* (N)** |
| Resin/ hash | 6.98 (6) | 5.26 (3) | 3.77 (4) |
| Normal weed | 65.12 (56) | 73.68 (42) | 44.34 (47) |
| Kief | 1.16 (1) | - | - |
| Edible | 2.33 (2) | 7.02 (4) | 4.72 (5) |
| Oils/ concentrates | 1.16 (1) | 3.51 (2) | 4.72 (5) |
| Butane hash oil | - | - | - |
| High potency herbal/ skunk | 4.65 (4) | 8.77 (5) | 2.83 (3) |

**\* Percentages relate to group only**

## **B(x) Route of administration of cannabis**

**Table B.4. Method of administration of cannabis by group**

|  |  |  |  |
| --- | --- | --- | --- |
| **How do you take it** | **Modafinil-only**  **%\* (N)** | **Methylphenidate**  **%\* (N)** | **Control %\* (N)** |
| Medical spray | 1.16 (1) | 1.75 (1) | 0.94 (1) |
| Tea | 2.33 (2) | 3.51 (2) | 0.94 (1) |
| Joint | 54.65 (47) | 64.91 (37) | 48.11 (51) |
| Pipe | 29.07 (25) | 42.11 (24) | 24.53 (26) |
| Bucket bong | 10.47 (9) | 10.53 (6) | 10.38 (11) |
| Bong/water pipe | 33.72 (29) | 40.35 (23) | 21.70 (23) |
| Eaten in food | 24.42 (21) | 38.60 (22) | 17.93 (19) |
| Vaporiser | 20.93 (18) | 28.07 (16) | 15.09 (16) |
| Blunt | 24.42 (21) | 22.81 (13) | 15.09 (16) |

**\* Percentages relate to group only**

## **B(xi) Frequency of nicotine use by product**

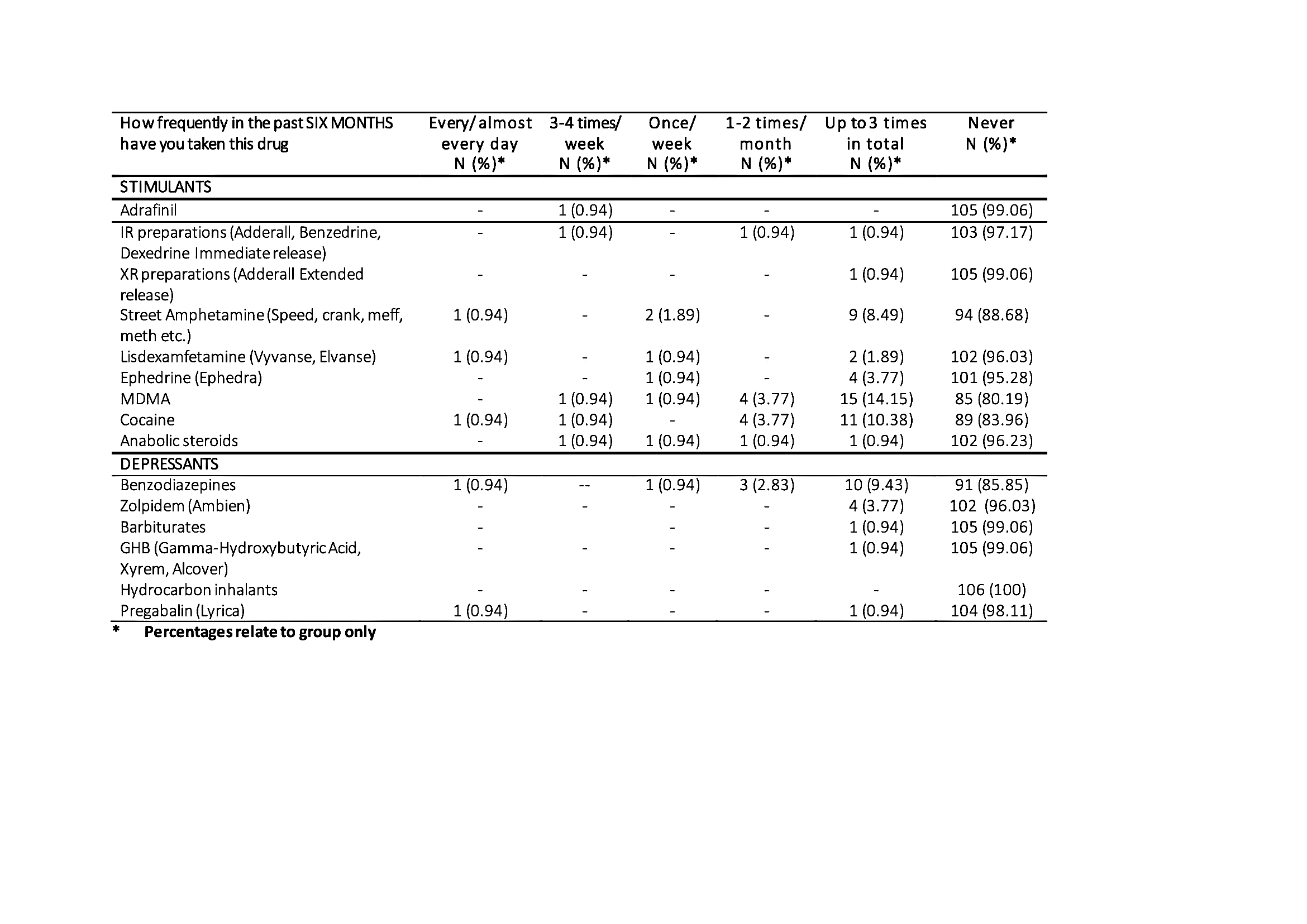
**Table B.5. Frequency of nicotine use by type of product**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Modafinil-only %\* (N)** | **Methylphenidate %\* (N)** | **Controls %\* (N)** |
| **CIGARETTES** |  |  |  |
| Every day/almost every day | 1.16 (1) | --- | 10.38 (11) |
| **VAPING** |  |  |  |
| Every day/almost every day | 36.05 (31) | --- | 7.55 (8) |
| **GUM/SPRAY ETC.** |  |  |  |
| Every day/almost every day | 16.28 (14) | --- | 2.83 (3) |

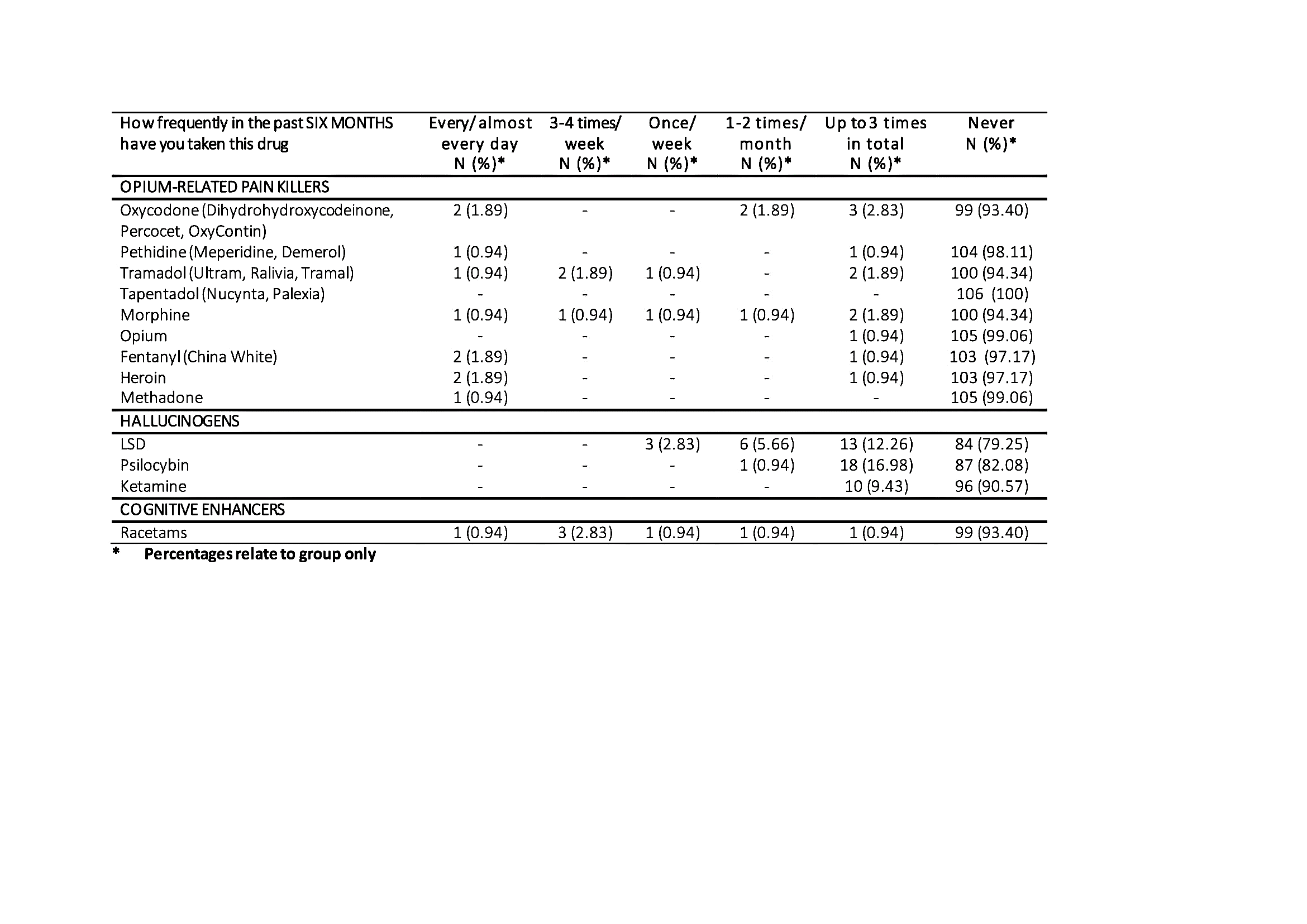
\* Percentages relate to group only

## **B(xii) Recreational drug use**

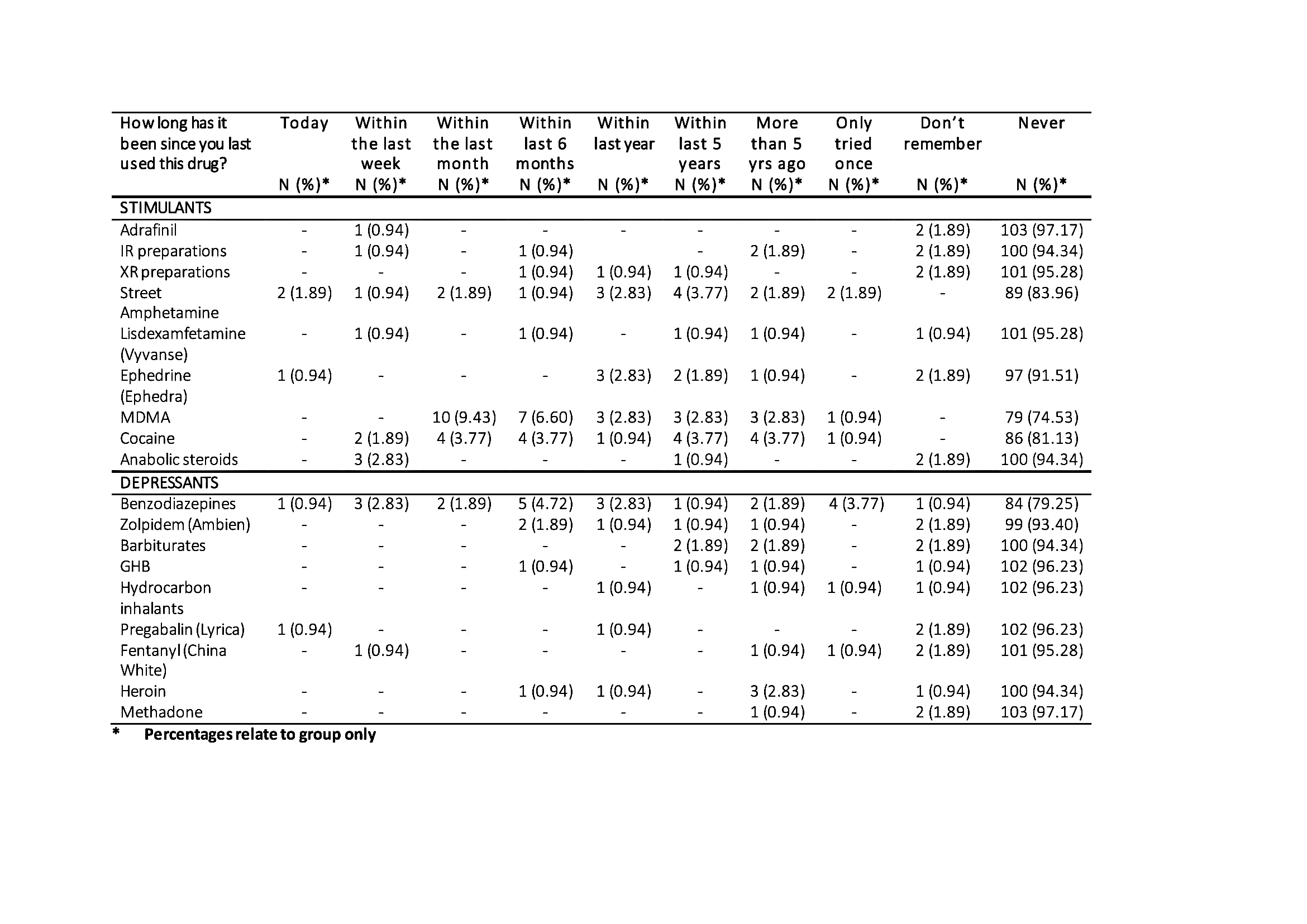
**Table B.6. Frequency of recreational Drug use for control group**



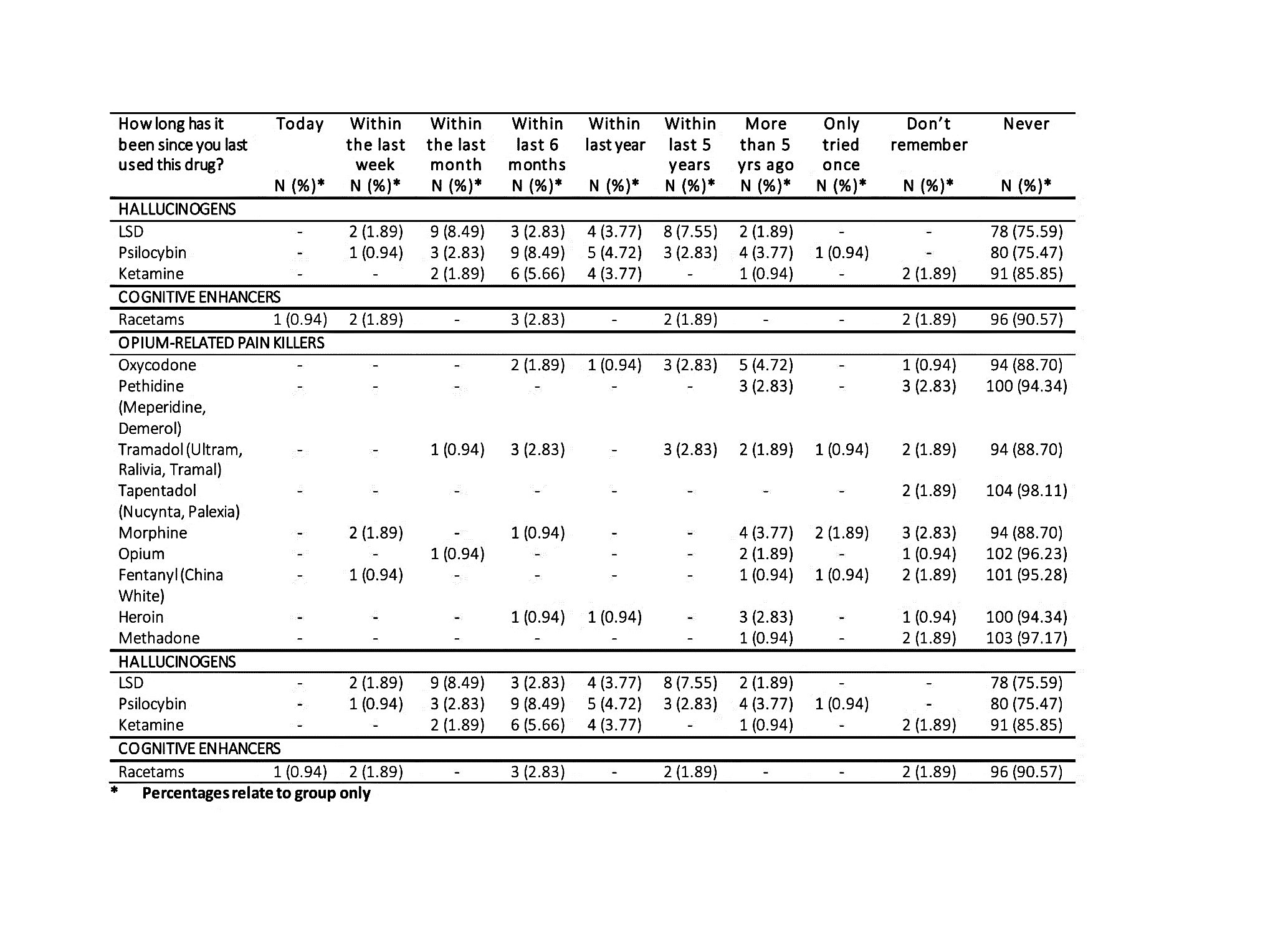
**Cont./**



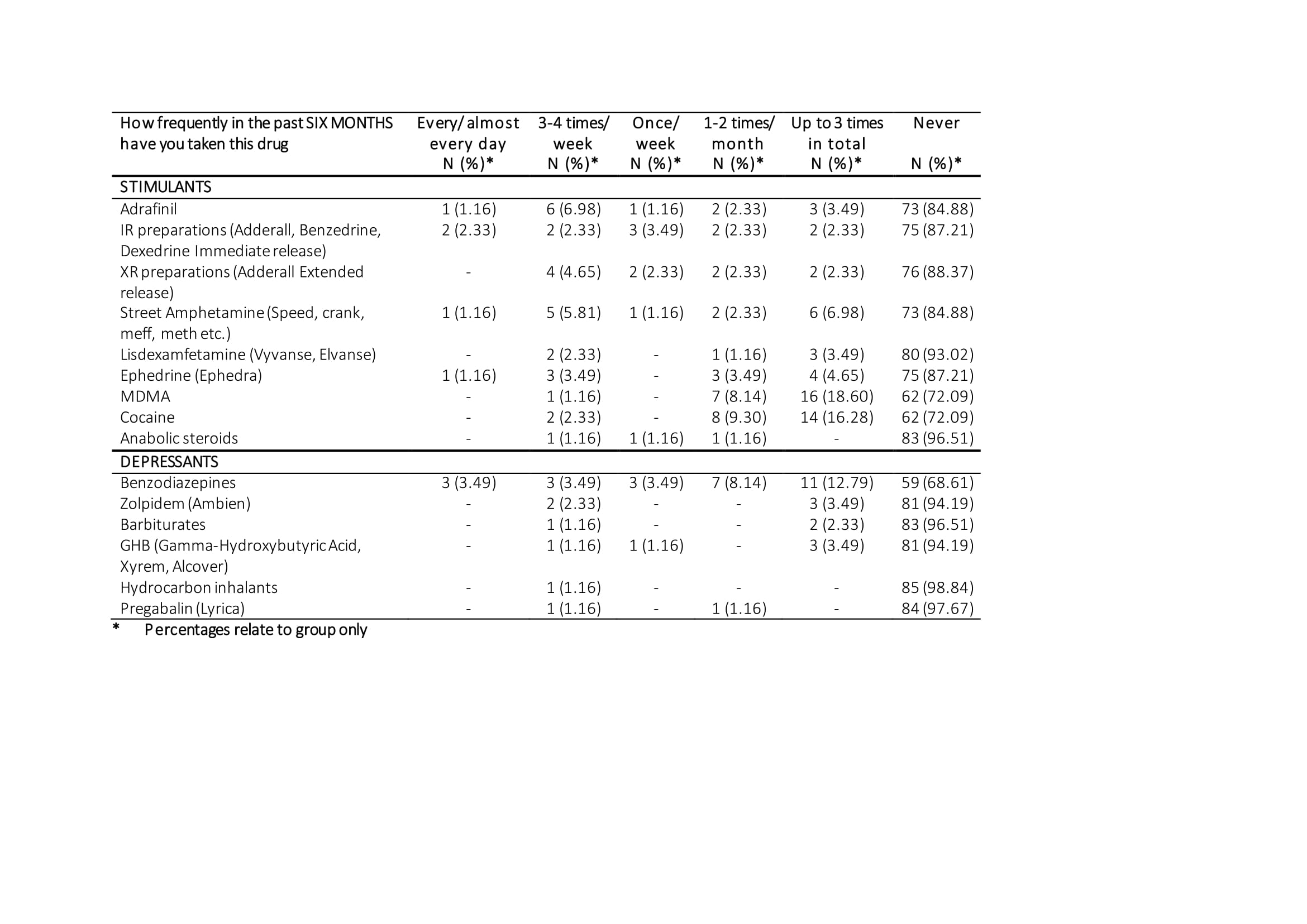
**Table B.7. Length of time since last use of recreational drugs by control group**

****

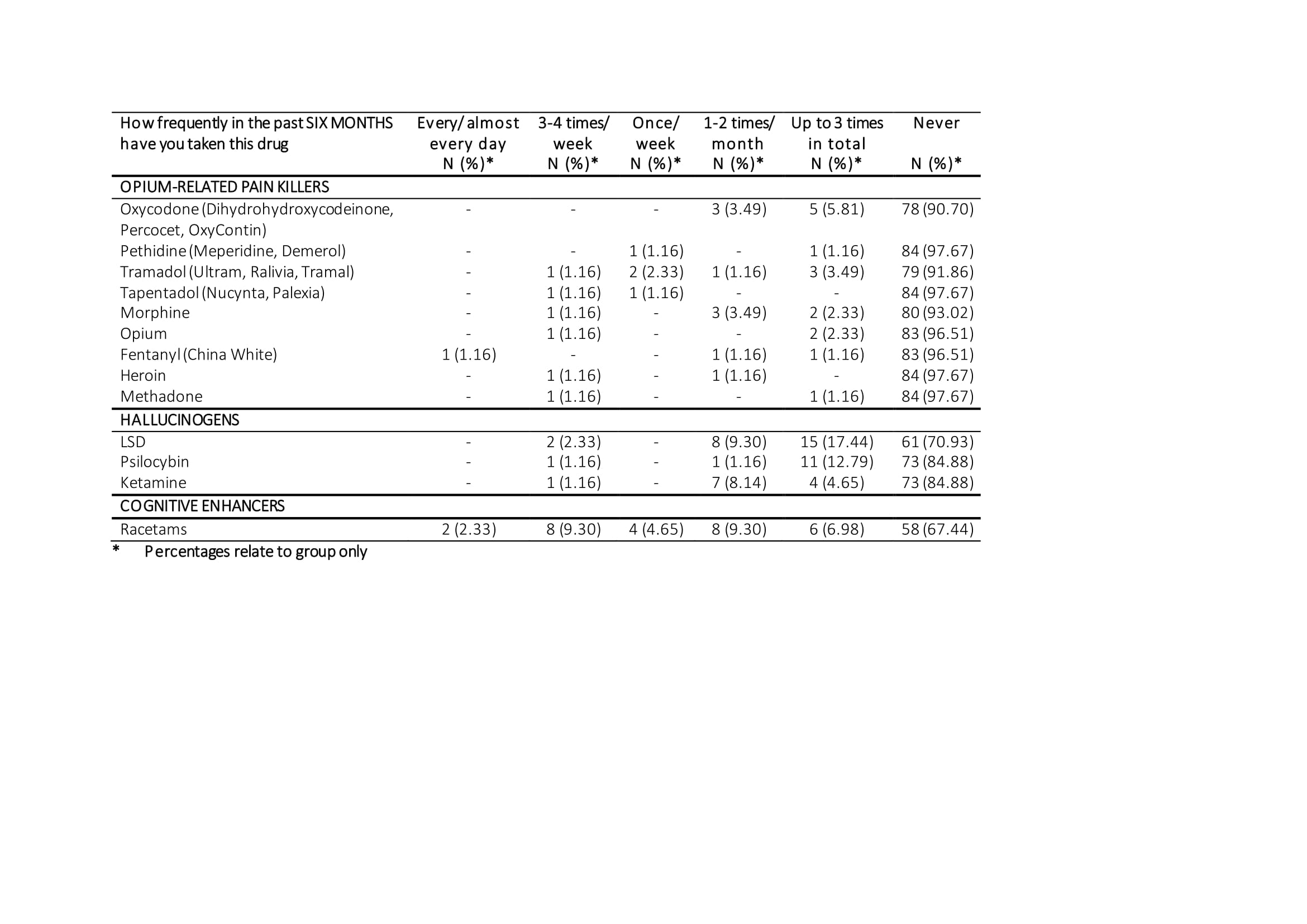
**Cont./**

****

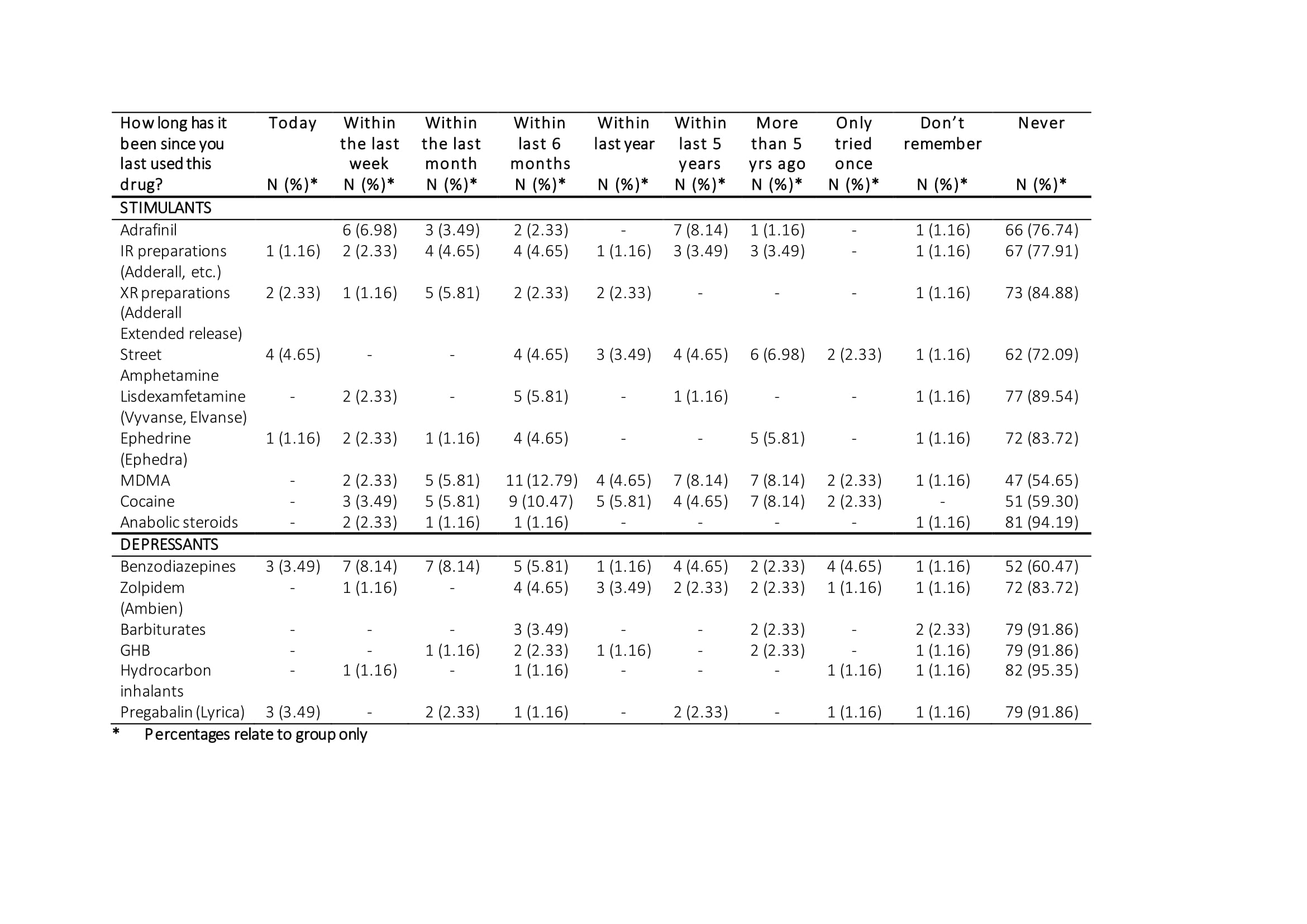
**Table B.8. Frequency of use of recreational drugs by modafinil group**

****

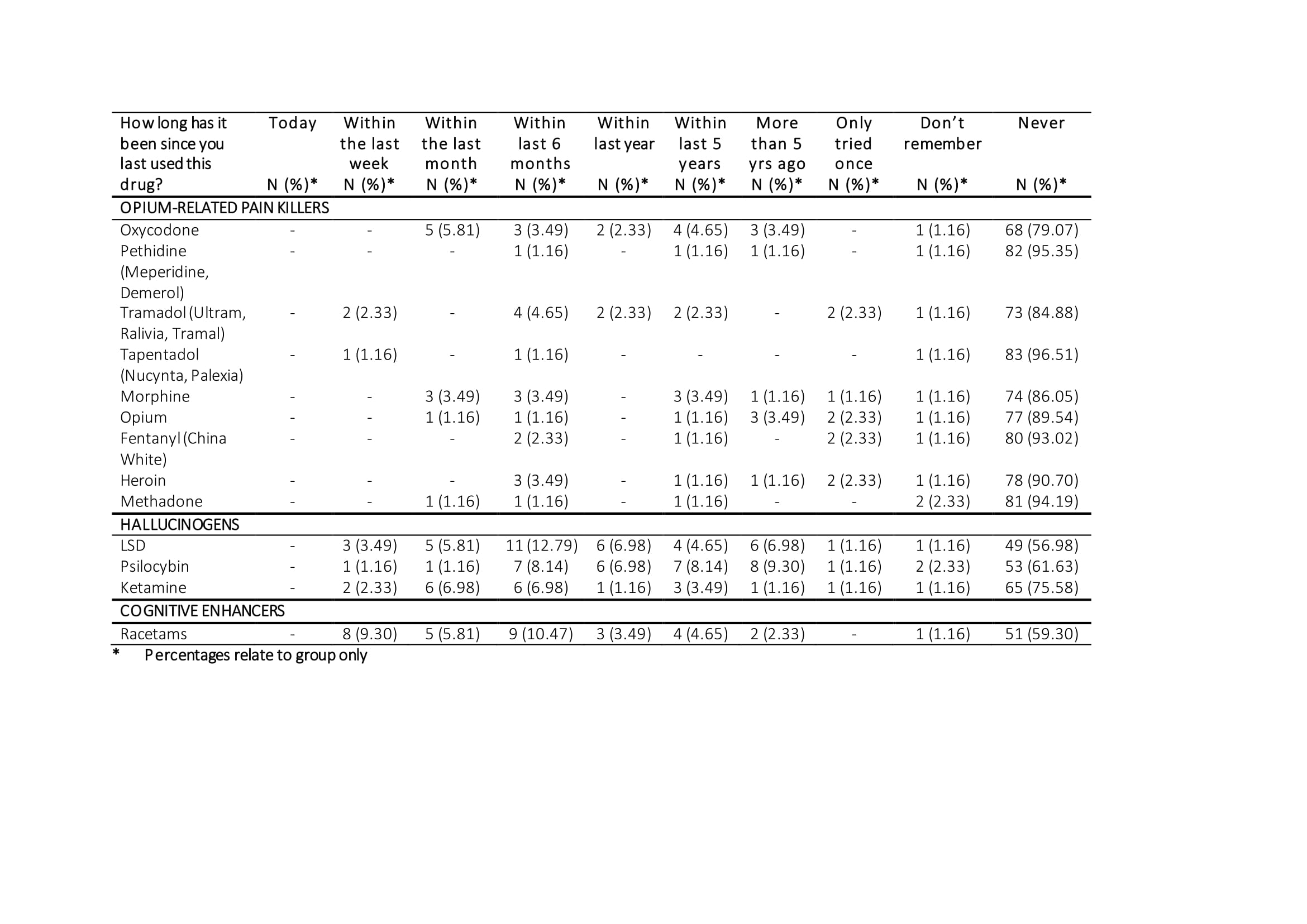
**Cont./**

****

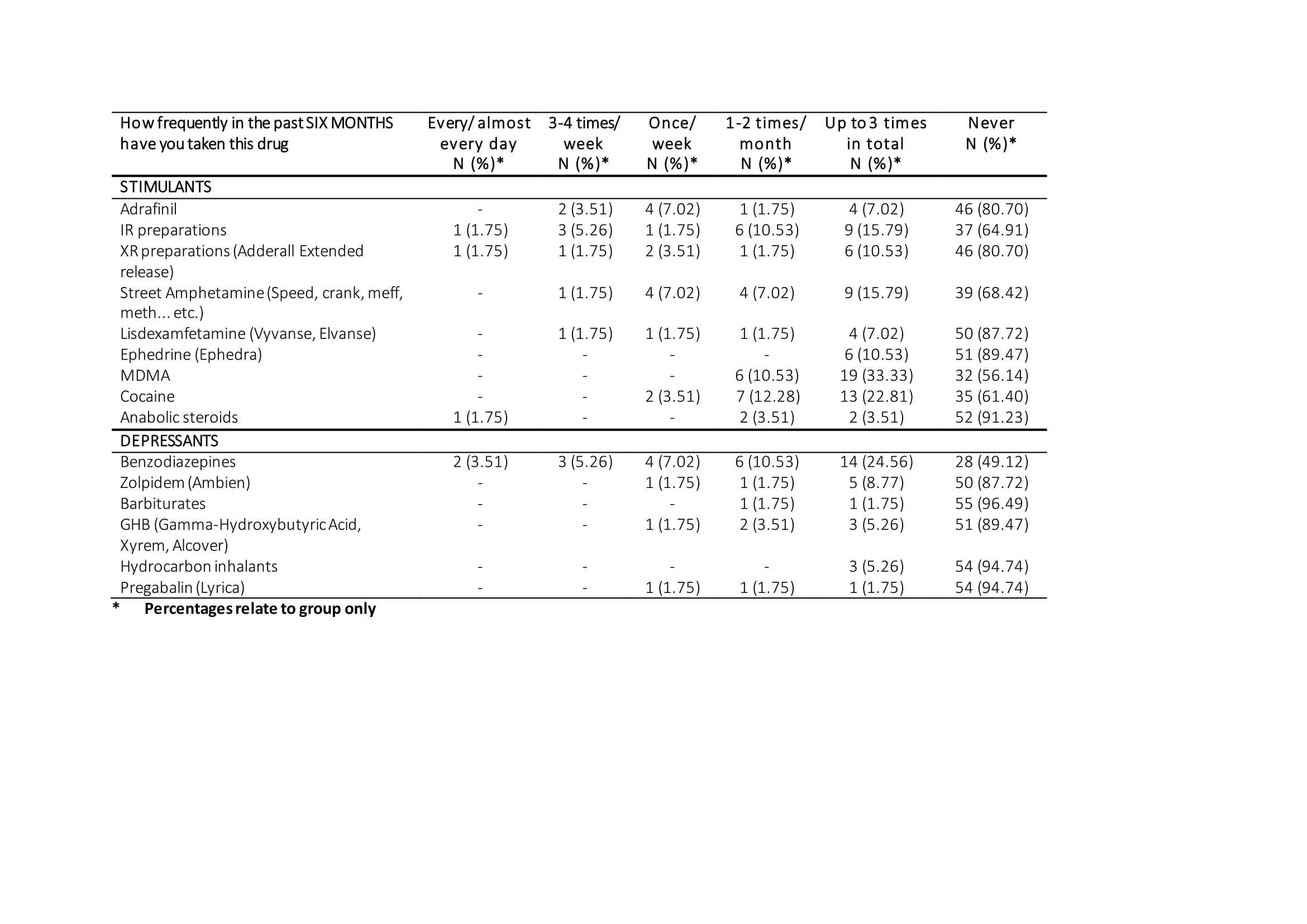
**Table B.9. Length of time since last use of recreational drugs by modafinil group**

****

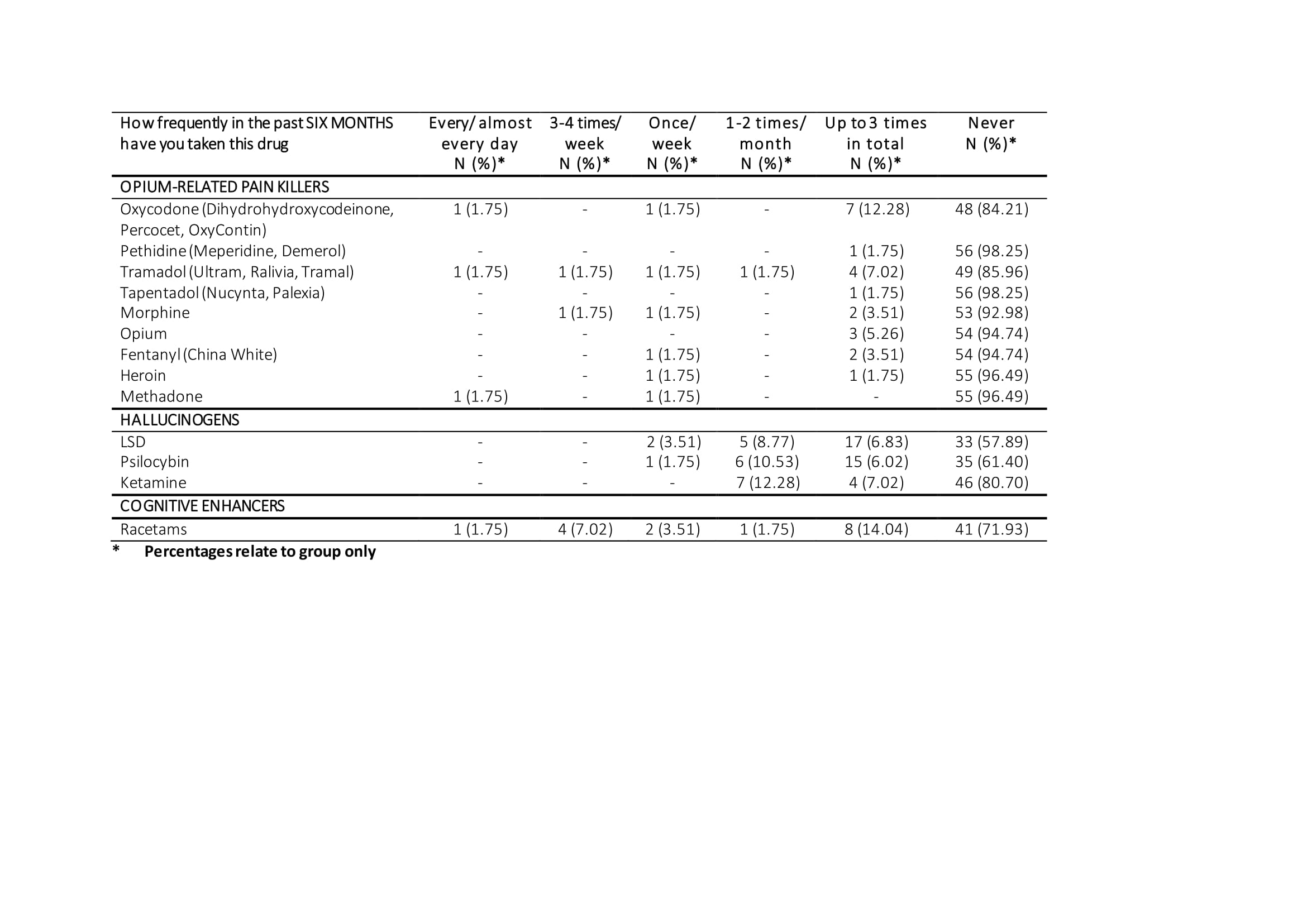
**Cont./**

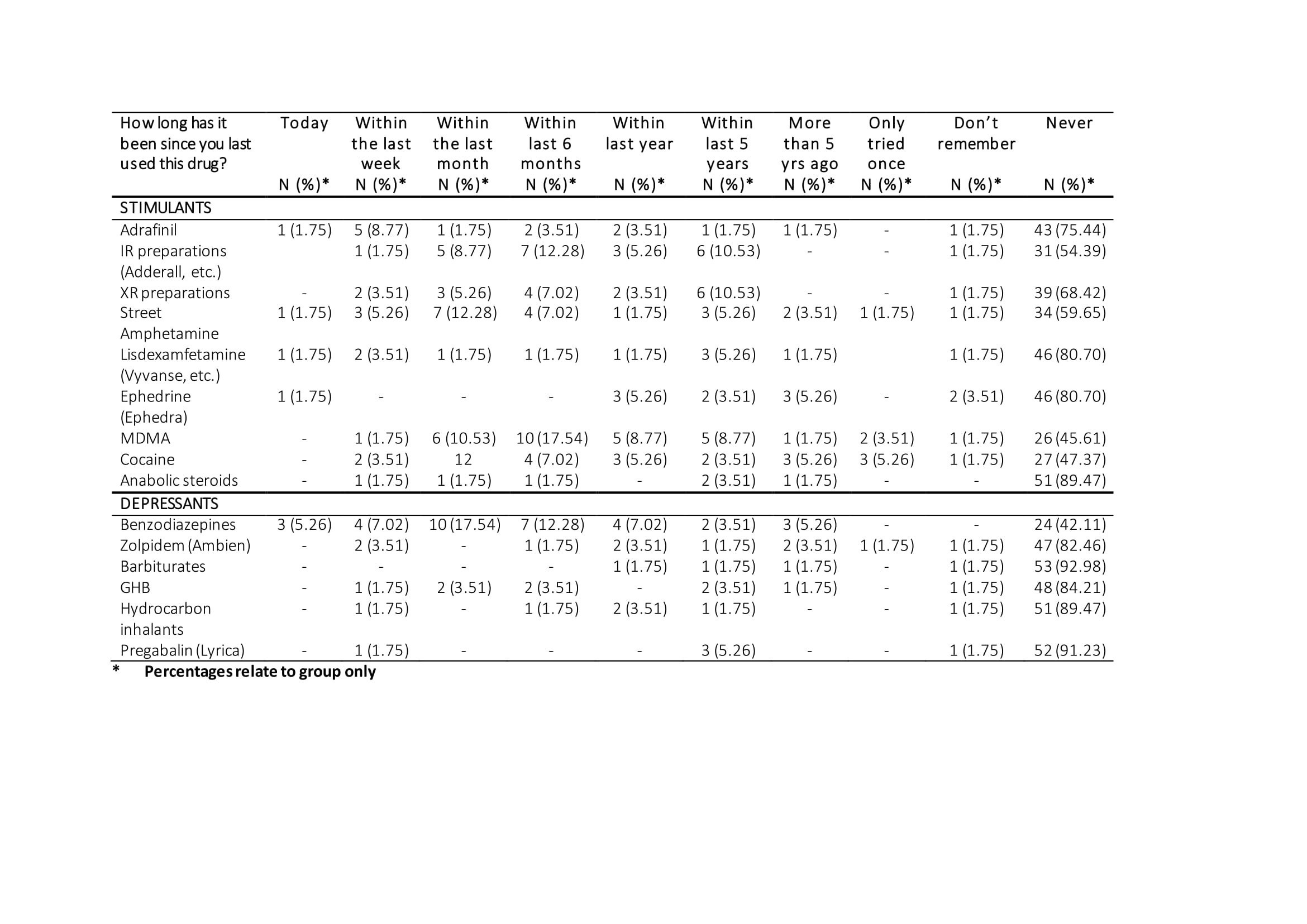
****

**Table B.10. Frequency of recreational drug use by methylphenidate group**

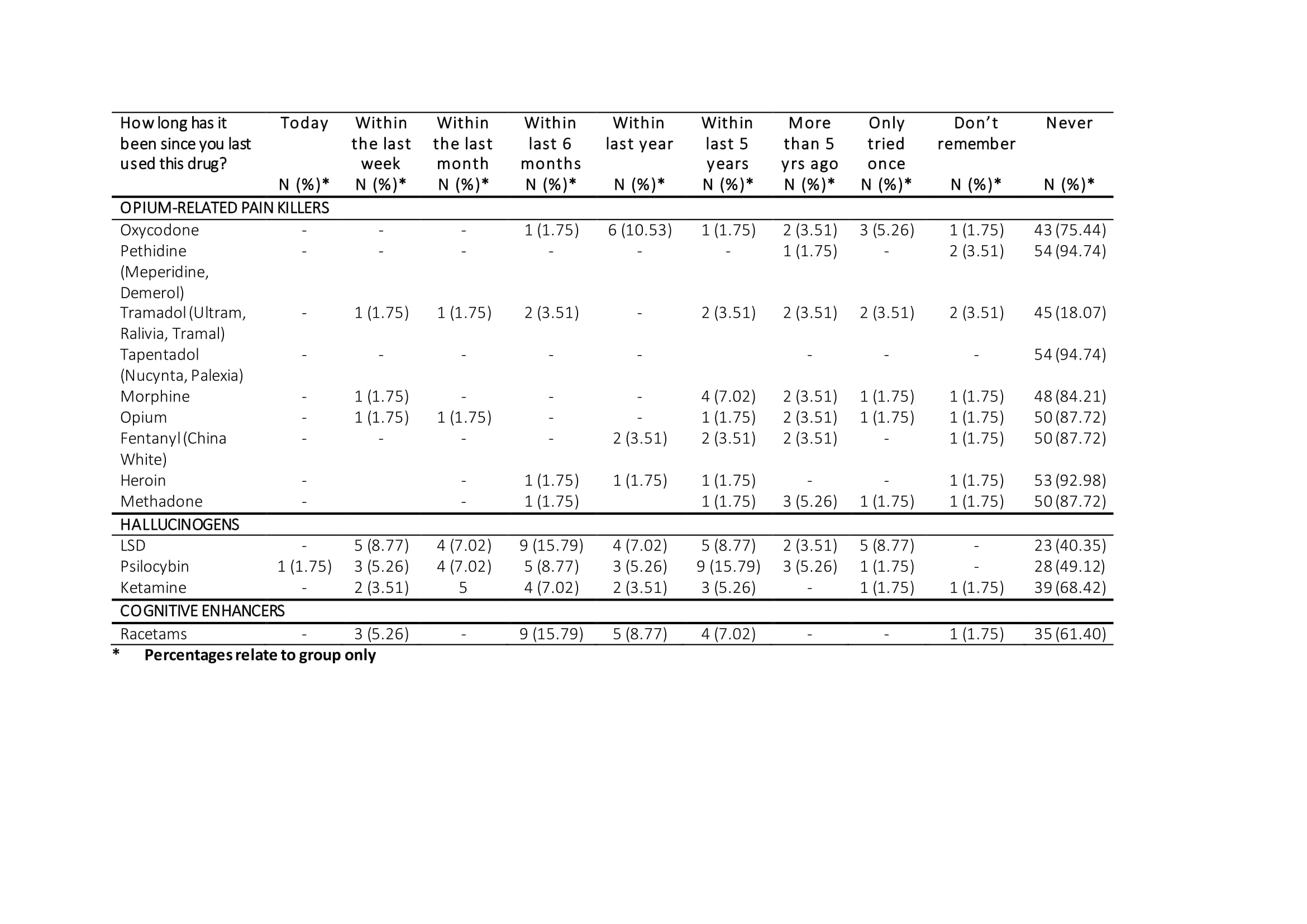
****

**Cont./**

****

**Table B.11. Length of time since last use of recreational drugs by methylphenidate group **

**Cont./**

****

## **B(xiii) Modafinil dosage**

**Table B.12. Maximum and minimum reported dose of modafinil taken**

|  |  |  |
| --- | --- | --- |
| **Dosage** | Maximum  N (%)\* | Minimum  N (%)\* |
| **Less than 50mg** | - | 15 (6.02) |
| **50mg** | 1 (0.40) | 31 (12.45) |
| **100mg** | 14 (5.62) | 25 (10.04) |
| **150mg** | 7 (2.81) | 3 (1.21) |
| **200mg** | 36 (14.46) | 11 (4.42) |
| **250mg** | - | - |
| **300mg** | 8 (3.21) | 1 (0.40) |
| **350mg** | - | - |
| **400mg** | 16 (6.43) | - |
| **450mg** | 2 (0.80) | - |
| **500mg** | 2 (0.80) | - |
| **More than 500mg** | - | - |

**\* Percentages relate to group only**

## **B(xiv) Methylphenidate dosage, formula and brand**

**Table B.13. Maximum and minimum reported dose of methylphenidate use**

|  |  |  |
| --- | --- | --- |
| **Dosage** | Maximum  N (%)\* | Minimum  N (%)\* |
| Less than 10mg | - | 28.07 (16) |
| 10mg | 1.75 (1) | 42.11 (24) |
| 20mg | 5.26 (3) | 17.54 (10) |
| 30mg | 22.81 (13) | 8.77 (5) |
| 40mg | 15.79 (9) | - |
| 50mg | 17.54 (10) | 3.51 (2) |
| 60mg | 7.02 (4) | - |
| 70mg | - | - |
| 80mg | 5.26 (3) | - |
| More than 80mg | 8.77 (5) | - |

**\* Percentages relate to group only**

**Table B.14. Methylphenidate formulations**

|  |  |
| --- | --- |
| **Do you most often take immediate-release or extended release formula?** | **N (%)\*** |
| Immediate-release | 19 (33.33) |
| Extended-release | 24 (42.11) |
| Don’t know | 14 (24.56) |

**\* Percentages relate to group only**

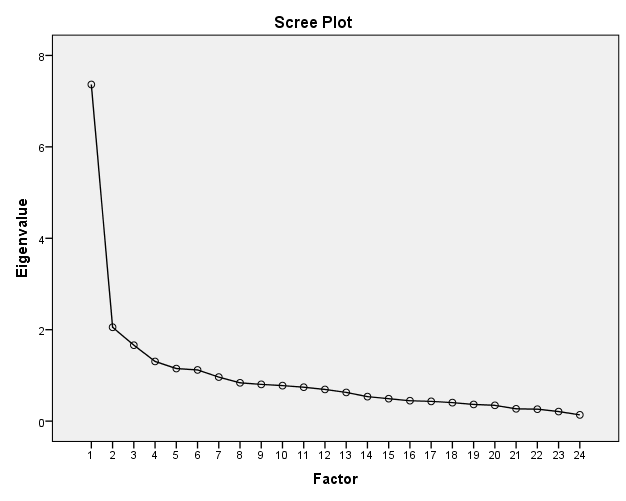
**Table B.15. Methylphenidate brands**

|  |  |
| --- | --- |
| **What brand do you usually take?** | **N (%)\*** |
| **Atensio** | 1 (1.75) |
| **Biphentin** | 1 (1.75) |
| **Concerta** | 10 (17.54) |
| **Equasym** | 1 (1.75) |
| **Mediikinet** | 5 (8.77) |
| **Ritalin** | 20 (35.09) |
| **Ritalina** | 1 (1.75) |
| **Rilatine** | 1 (1.75) |
| **Tranquilyn** | 2 (3.51) |
| **Other (generic)** | 2 (3.51) |

## **B(xv) Factor analysis and scree plot of CFQ control group responses**

**Table B.16. Factor loading of control group CFQ responses**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Item number** | **Factor 1** | **Factor 2** | **Factor 3** | **Factor 4** | **Factor 5** | **Factor 6** |
| CFQ.16 | .696 |  |  |  |  |  |
| CFQ.17 | .668 |  |  |  |  |  |
| CFQ.6 | .544 |  |  |  |  |  |
| CFQ.2 | .509 | .475 |  |  |  |  |
| CFQ.3 | .498 |  |  |  |  |  |
| CFQ.11 | .469 |  |  |  |  |  |
| CFQ.23 |  |  |  |  |  |  |
| CFQ.9 |  |  |  |  |  |  |
| CFQ.1 |  | .869 |  |  |  |  |
| CFQ.21 |  | .615 |  |  |  |  |
| CFQ.19 |  | .558 |  |  |  |  |
| CFQ.22 |  | .515 |  |  |  |  |
| CFQ.25 |  | .490 |  |  |  |  |
| CFQ.15 |  | .416 |  |  |  |  |
| CFQ.14 |  |  | .575 |  |  |  |
| CFQ.13 | .512 |  | .543 |  |  |  |
| CFQ.10 |  |  | .528 |  |  |  |
| CFQ.8 |  |  | .411 |  |  |  |
| CFQ.18 |  |  |  | .613 |  |  |
| CFQ.4 |  |  |  | .561 |  |  |
| CFQ.24 |  |  |  | .447 |  |  |
| CFQ.12 |  |  |  |  |  |  |
| CFQ.7 |  |  |  |  | .871 |  |
| CFQ.20 |  |  |  |  | .588 |  |
| CFQ.5 |  |  |  |  |  | .606 |



**Figure B.2. Scree plot of eigenvalues for CFQ factors**

# **Appendix C: Study Three**

## **C(i) Online forum advertisement**

**Recruiting for a confidential experimental study**

If you take modafinil and/or methylphenidate without prescription (i.e. you have not been diagnosed with ADD/ADHD) and would/may be interested in participating in a lab-based study later this year about the use of cognitive enhancing drugs please provide an email address, in the space below, on which you may be contacted or you can email me, Rachel Teodorini at [teodorir@lsbu.ac.uk](mailto:teodorir@lsbu.ac.uk). You may only participate if you are over 18 years of age, you have not been diagnosed with Attention Deficit/Hyperactivity Disorder, and you are not currently taking any prescribed medications for any mental health problem. Participants will be awarded for their participation with £15 in vouchers. If you would like to participate in the study you will be provided with an information sheet explaining what the study will involve.

The study will take place at London South Bank University, located in Elephant and Castle, London, UK in January 2019 and participation will take 75 minutes. Please provide a false name/ pseudonym and ensure that the email address you provide will not identify you. The email address you provide will be stored on password protected computers only accessible by the researcher, Rachel Teodorini.  It will only be used to contact you for possible participation in a lab-based study. Your email address will be deleted in May 2019, at the end of the funding period for my PhD. Please also note that if you do provide an email address you are under no obligation to participate in this lab-based experiment and may also opt out at any time during the experiment.

## **C(ii) Nationalities**

**Table C.1. Nationalities by group**

|  |  |  |
| --- | --- | --- |
| **Nationality** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| British | 29 (61.7) | 23 (53.5) |
| Rest of Europe | 11 (23.4) | 9 (20.93) |
| Rest of world | 7 (14.89) | 11 (25.58) |

\* Percentages relate to group and not to the whole sample

## **C(iii) Demographics and Drug Use Questionnaire**

**Demographics and Drug Use Questionnaire SAS1834**

**Study title: The cognitive performance of off-prescription users of modafinil & methylphenidate**

*Please print your answers clearly*

**Participant no**.\_\_\_\_\_\_\_\_\_\_

**Age** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Gender** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Nationality** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Please indicate your level of education by ticking the appropriate box**

|  |  |
| --- | --- |
| **No formal qualifications** |  |
| **Educated to age 16 (e.g. G.C.S.E.)** |  |
| **Educated to age 18 (e.g. A-level, High School, I.B.)** |  |
| **University Degree (BSc, BA)** |  |
| **Post-Graduate Degree (MSc, MA, PhD)** |  |

**Are you currently studying for a qualification?** **Yes □ No □**

**If yes, which of the following most accurately describes your course**

*(please tick the appropriate box):*

|  |  |
| --- | --- |
| **Vocational (learning in a practical way about a job)** |  |
| **Continuing Professional Development** |  |
| **High school/ college/ A levels** |  |
| **University bachelor’s program** |  |
| **University master’s program** |  |
| **Doctoral studies** |  |

**Are you working at the moment?** (*please tick the appropriate box*)

|  |  |
| --- | --- |
| **Yes, full-time paid** |  |
| **Yes, part-time paid** |  |
| **Yes, full-time voluntary** |  |
| **Yes, part-time voluntary** |  |
| **No** |  |

**If in employment, please state your job title or role** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Have you ever been diagnosed with a psychiatric condition?** **Yes □ No □**

**What was the diagnosis?** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Have you ever been treated for a drug or alcohol-related problem?** **Yes □ No □**

**Have you ever taken cannabis? Yes □ No □**

**Do you have a prescription for medicinal cannabis?**  **Yes □ No □**

**What age were you when you first took cannabis?** \_\_\_\_\_\_\_\_\_\_\_

**In the past six months, how regularly have you taken cannabis?**

(*please tick the appropriate box*)

|  |  |
| --- | --- |
| **Every day/almost every day** |  |
| **3-4 times per week** |  |
| **Once per week** |  |
| **1-2 times per month** |  |
| **Up to 3 times in total** |  |
| **None** |  |

**MODAFINIL**

**Are you aware of the cognitive enhancing drug, Modafinil (Provigil, Modalert)? Yes** □  **No** □

**Have you ever taken it? Yes □ No □**

**Have you been prescribed Modafinil? Yes □ No □**

**What age were you when you first took Modafinil? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**In the past six months, how regularly have you taken Modafinil?**

(*please tick the appropriate box*)

|  |  |
| --- | --- |
| **Every day/almost every day** |  |
| **3-4 times per week** |  |
| **Once per week** |  |
| **1-2 times per month** |  |
| **Up to 3 times in total** |  |
| **None** |  |

**How do you take it?** (*please tick the appropriate box*)

**Swallow pill □ Snort □ Smoke □ Inject □ Vaporise □ Other □**

**How much do you take (in milligrams) in any single day of use** \_\_\_\_\_\_\_\_\_\_\_\_\_

**What is the typical maximum dose (in milligrams) you would take at any one time?** \_\_\_\_\_\_\_\_\_

**What is the typical minimum dose (in milligrams) you would take at any one time?** \_\_\_\_\_\_\_\_\_

**METHYLPHENIDATE**

**Are you aware of Methylphenidate (Ritalin, Rubifen, Concerta)? Yes □ No □**

**Have you ever taken it? Yes □ No □**

**Have you been prescribed Methylphenidate? Yes □ No □**

**What age were you when you first took Methylphenidate? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**In the past six months, how regularly have you taken Methylphenidate?**

(*please tick the appropriate box*)

|  |  |
| --- | --- |
| **Every day/almost every day** |  |
| **3-4 times per week** |  |
| **Once per week** |  |
| **1-2 times per month** |  |
| **Up to 3 times in total** |  |
| **None** |  |

**How do you take it?** (*please tick the appropriate box*)

**Swallow pill □ Snort □ Smoke □ Inject □ Vaporise □ Other □**

**How much do you take (in milligrams) in any single day of use \_\_\_\_\_\_\_\_\_\_\_\_\_**

**What is the typical maximum dose (in milligrams) you would take at any one time? \_\_\_\_\_\_\_\_\_**

**What is the typical minimum dose (in milligrams) you would take at any one time? \_\_\_\_\_\_\_\_\_**

**OTHER RECREATIONAL DRUGS**

*If you have taken any other non-prescribed and/or recreational drugs (including nicotine and alcohol) in the last six months, please write the drug name in the left-hand column and provide details on frequency of use*

|  |  |  |
| --- | --- | --- |
| **DRUG NAME**  (*please print name of drug and usual dose, specifying if extended/prolonged release)* | **How frequently in the past 6 MONTHS have you taken this drug.** | **How long has it been since you last used this drug** |
| **Please write one of the following:**  Every day/ almost every day  3-4 times/ week  Once/ week  1-2 time/ month  Up to 3 times in total  Never | **Please write one of the following:**   * Within the last week * Within the last month * Within the last year * Within the last 5 years * Within the last ten years * Over 10 years ago * Only ever took it once * Can’t remember |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

## **(iv) Education**

**Figure C.3. Education level by group**

## **C(v) Current studies**

**Table C.2. Currently studying for a qualification**

|  |  |  |
| --- | --- | --- |
|  | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Currently studying for a qualification** |  |  |
| Yes | 24 (51.1) | 38 (88.4) |
| No | 23 (48.9) | 5 (11.6) |
| **Course type** |  |  |
| Vocational | 1 (4.2) | - |
| CPD | 1 (4.2) | 2 (4.7) |
| A levels | 2 (8.3) | 1 (2.3) |
| University Bachelor's Program | 10 (41.7) | 32 (74.4) |
| University Master's Program | 5 (20.8) | 2 (4.7) |
| Doctoral Studies | 5 (20.8) | 1 (2.3) |

\* Percentages relate to group and not to the whole sample

## **C(vi) Employment**

**Table C.3. Employment status**

|  |  |  |
| --- | --- | --- |
| **Employment status** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| Full-time paid | 26 (55.3) | 8 (18.6) |
| Part-time paid | 10 (21.3) | 21 (48.8) |
| Part-time voluntary | 3 (6.4) | 1 (2.3) |
| Unemployed | 8 (17.0) | 13 (30.2) |

\* Percentages relate to group and not to the whole sample

## **C(vii) Outliers for the antisaccade, arrow flanker and BRIEF-A**

**Table C.4. Outliers**

|  |  |  |  |
| --- | --- | --- | --- |
| **TASK** | **Participant number** | **Data** | **No. OF SDs** |
| **Antisaccade task** | | | |
| Antisaccade latency to correct errors | 4 | 505.10 | 3.7 |
| 39 | 643.57 | 5.4 |
| Latency for antisaccade errors | 7 | 363.76 | 2.9 |
| 44 | 589.69 | 6.3 |
| **Flanker task** | | | |
| Latency for congruent correct trials | 9 | 564.15 | 2.74 |
| 28 | 542.21 | 2.34 |
| Latency for incongruent correct trials | 9 | 629.55 | 2.55 |
| 50 | 643.45 | 2.78 |
| Latency for neutral correct trials | 9 | 567.69 | 2.87 |
| 22 | 560.09 | 2.72 |
| 56 | 301.15 | 2.16 |
| Difference in latency between incongruent and congruent correct trials | 31 | 128.44 | 2.11 |
| 32 | 157.0 | 3.13 |
| 86 | 5.34 | 2.17 |
| Number of correct congruent trials | 20 | 31 | 6.45 |
| 22 | 35 | 3.33 |
| Number of correct incongruent trials | 20 | 16 | 4.51 |
| 27 | 22 | 3.15 |
| 48 | 20 | 3.60 |
| **BRIEF-A** | | | |
| Self-Monitor | 4 | 80 | 2.75 |
| 27 | 93 | 3.96 |
| 68 | 89 | 3.59 |
| Initiate | 27 | 93 | 2.93 |
| Plan/Organise | 24 | 86 | 2.83 |
| 79 | 91 | 3.29 |
| Task Monitor | 24 | 86 | 2.37 |
| 32 | 90 | 2.7 |
| 58 | 86 | 2.37 |
| 80 | 86 | 2.37 |

**C(ix) Participant information sheets**

**EXPERIMENTAL PARTICIPANTS**

**Participant Information Sheet SAS1834**

**Title of study: The cognitive performance of off-prescription users of modafinil and methylphenidate**

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

The present study was developed based on the results of a previous study which found that people who use modafinil and methylphenidate off-prescription report differences in their mental abilities with and without the use of these drugs. As the previous study was a survey where respondents gave self-reports of their mental abilities, the next step is to measure mental abilities in a laboratory-controlled environment. Therefore, the aim of the current study is to ascertain whether the results of the laboratory tests of cognitive performance reflect those of the self-reports.

The testing session will run for approximately 30 minutes. You will be given a questionnaire to complete which asks questions about age, gender and education, as well as drug use questions. You will then be given another questionnaire to complete which asks questions about your mental abilities such as attention, planning and memory. You will then be asked to perform some computer tasks which will either require you to press a button or to look in a certain direction. Your eye movements will be recorded during one task. This means you will be asked to sit with your chin on a chin rest while a camera on the desk records your eye movements. Following these tests you will be given a debriefing sheet which will explain this study in more detail.

You have been asked to participate in this study as you have reported that you take modafinil and/or methylphenidate off-prescription. In total, we are inviting 100 people to participate in this study. In return for your participation you will be rewarded £15 for your time and contribution to our study. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This can be done before the experiment by contacting me on the email address or telephone number at the end of this sheet, or during the experiment by informing me that you would like to withdraw, stating your participant number. You are still free to withdraw anytime up to the submission of the manuscript and without giving a reason. Again, this can be done by contacting me on the email address or telephone number below.

**You may only participate if you are over 18 years of age, you have not been diagnosed with Attention Deficit/Hyperactivity Disorder, you are not currently taking any prescribed medications for any mental disorder and have not taken any recreational or off-prescription psychoactive drugs in the past 24 hours.**

This is a completely anonymous study and no information that could identify you will be collected. This study is being conducted as part of Rachel Teodorini’s PhD programme at London South Bank University. This study will form part of my PhD thesis and may also be published in a peer-reviewed journal. All information collected from this survey will be securely stored on a password protected computer that will only be accessed by me (Rachel Teodorini) and my doctoral supervisors (Dr Nicola Rycroft, Senior Lecturer and Dr James Smith-Spark, Associate Professor) both of whom belong to the Division of Psychology at London South Bank University and have expertise in substance use and mental abilities. This information will be stored for a period of time (approximately 5 years from publication) to comply with journal regulations.

Other than the £15 (in Amazon vouchers) reward, and contributing to a knowledge base that will help to inform research on the prevalence of use of these drugs, it is unlikely that you will gain any other personal benefit from participating in this research. You will not be disadvantaged by participating in this research. This study has been organized by the PhD student and aforementioned supervisors and funded by the Centre for Addictive Behaviour Research and London South Bank University. It has also been ethically approved by the School of Applied Sciences Research Ethics Committee.

If you would like to take part in this study, please contact me via email, using an email address that will not identify you. If you choose to participate, you will need to attend one session in the laboratory at London South Bank University in Elephant and Castle in Central London.

All the information collected about you and other participants will be kept strictly confidential (subject to legal limitations). Data generated by the study must be retained in accordance with the University's Code of Practice. All data generated in the course of the research must be kept securely in paper or electronic form for a period of 10 years after the completion of a research project. Your privacy and anonymity will be ensured in the collection, storage and publication of research material as no personally identifiable information about you will be collected. If the results of this research are published in a peer-reviewed journal and you would like to obtain a copy of the published research, please contact me via email and I will advise you as to how to obtain a copy of the published research.

For additional information and further clarifications about the study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Contact details for supervisors are: Dr Nicola Rycroft, email: [rycroftn@lsbu.ac.uk](mailto:rycroftn@lsbu.ac.uk); Dr James Smith-Spark, email: [smithspj@lsbu.ac.uk](mailto:smithspj@lsbu.ac.uk). If you have any concerns or complaints about the way in which the study has been conducted, you may contact the Chair of the School of Applied Sciences Research Ethics Committee at [sasethics@lsbu.ac.uk](mailto:sasethics@lsbu.ac.uk).

If you would like to take part, you are free to discuss this with your GP, friends or family. Thank you for taking the time to read this information sheet.

**rachel teodorini**

**15/02/2019**

**Please note**: The following contact details are provided for you to use if you have any concerns about your drug use.

**SupportLine**

**Telephone Helpline: 01708 765200**email: [info@supportline.org.uk](mailto:info@supportline.org.uk)

[www.supportline.org.uk/](http://www.supportline.org.uk/)   
Provides emotional support and keeps details of local agencies providing help and support for all issues relating to Drugs.

**Release**

Telephone Helpline: 020 7324 2989

email: [ask@release.org.uk](mailto:ask@release.org.uk)

[www.release.org.uk](http://www.release.org.uk)

Release is the national centre of expertise on drugs and drugs law. The organisation provides free non-judgmental, specialist advice and information to the public and professionals on issues related to drug use and to drug laws.

**CONTROL PARTICIPANTS**

**Participant Information Sheet SAS1834**

**Title of study: The cognitive performance of off-prescription users of modafinil and methylphenidate**

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

The present study was developed based on the results of a previous study which found that people who use modafinil and methylphenidate off-prescription report differences in their cognitive performance with and without the use of these drugs. As the previous study was a survey where respondents gave self-reports of their cognitive performance, the next step is to measure cognitive performance in a laboratory-controlled environment. Therefore, the aim of the current study is to ascertain whether the results of the laboratory tests of cognitive performance reflect those of the self-reports.

The testing session will run for approximately 75 minutes. You will be given a questionnaire to complete which asks questions about age, gender and education, as well as drug use questions. You will then be given another questionnaire to complete which asks questions about your mental abilities such as attention, planning and memory. You will then be asked to perform some computer tasks which will either require you to press a button or to look in a certain direction. Your eye movements will be recorded during one task. This means you will be asked to sit with your chin on a chin rest while a camera on the desk records your eye movements. Following these tests you will be given a debriefing sheet which will explain this study in more detail.

You have been asked to participate in this study as you have reported that you have never taken modafinil or methylphenidate. In total, we are inviting 100 people to participate in this study. In return for your participation you will be rewarded £15 or 10 RPS Credits for your time and contribution to our study. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This can be done before the experiment by contacting me on the email address or telephone number at the end of this sheet, or during the experiment by informing me that you would like to withdraw. You are still free to withdraw anytime up to the submission of the manuscript and without giving a reason. Again, this can be done by contacting me on the email address or telephone number below, stating your participant number. By choosing to either take part or not take part in the study will have no impact on your marks, assessment or future studies.

**You may only participate if you are over 18 years of age, you have not been diagnosed with Attention Deficit/Hyperactivity Disorder, you are not currently taking any prescribed medications for any mental disorder and have not taken any recreational or off-prescription psychoactive drugs in the past 24 hours.**

This is a completely anonymous study and no information that could identify you will be collected. This study is being conducted as part of Rachel Teodorini’s PhD programme at London South Bank University. This study will form part of my PhD thesis and may also be published in a peer-reviewed journal. All information collected from this survey will be securely stored on a password protected computer that will only be accessed by me (Rachel Teodorini) and my doctoral supervisors (Dr Nicola Rycroft, Senior Lecturer and Dr James Smith-Spark, Associate Professor) both of whom belong to the Division of Psychology at London South Bank University and have expertise in substance use and cognitive performance. This information will be stored for a period of time (approximately 5 years from publication) to comply with journal regulations.

Other than the £15 (in Amazon vouchers) reward or 10 RPS credits, and contributing to a knowledge base that will help to inform research on the prevalence of use of these drugs, it is unlikely that you will gain any other personal benefit from participating in this research. You will not be disadvantaged by participating in this research. This study has been organized by the PhD student and aforementioned supervisors and funded by the Centre for Addictive Behaviour Research and London South Bank University. It has also been ethically approved by the School of Applied Sciences Research Ethics Committee.

If you would like to take part in this study, please follow the instructions on the RPS site or contact me via email. If you choose to participate, you will need to attend one session in the laboratory at London South Bank University.

All the information collected about you and other participants will be kept strictly confidential (subject to legal limitations). Data generated by the study must be retained in accordance with the University's Code of Practice. All data generated in the course of the research must be kept securely in paper or electronic form for a period of 10 years after the completion of a research project and if the results of this research are published, all data will be kept securely for five years. Your privacy and anonymity will be ensured in the collection, storage and publication of research material as no personally identifiable information about you will be collected as part of the data. If the results of this research are published in a peer-reviewed journal and you would like to obtain a copy of the published research, please contact me via email and I will advise you as to how to obtain a copy of the published research.

For additional information and further clarifications about the study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Contact details for supervisors are: Dr Nicola Rycroft, email: [rycroftn@lsbu.ac.uk](mailto:rycroftn@lsbu.ac.uk); Dr James Smith-Spark, email: [smithspj@lsbu.ac.uk](mailto:smithspj@lsbu.ac.uk). If you have any concerns or complaints about the way in which the study has been conducted, you may contact the Chair of the School of Applied Sciences Research Ethics Committee at [sasethics@lsbu.ac.uk](mailto:sasethics@lsbu.ac.uk).

If you would like to take part, you are free to discuss this with your GP, friends or family. Thank you for taking the time to read this information sheet.

**rachel teodorini**

**15/02/2019**

**Please note**: The following contact details are provided for you to use if you have any concerns about your drug use.

**SupportLine**

**Telephone Helpline: 01708 765200**email: [info@supportline.org.uk](mailto:info@supportline.org.uk)

[www.supportline.org.uk/](http://www.supportline.org.uk/)   
Provides emotional support and keeps details of local agencies providing help and support for all issues relating to Drugs.

**Release**

Telephone Helpline: 020 7324 2989

email: [ask@release.org.uk](mailto:ask@release.org.uk)

[www.release.org.uk](http://www.release.org.uk)

Release is the national centre of expertise on drugs and drugs law. The organisation provides free non-judgmental, specialist advice and information to the public and professionals on issues related to drug use and to drug laws.

## **C(viii) Advertisement**

**Recruiting for a confidential experimental study**

If you take modafinil and/or methylphenidate without prescription (i.e. you have not been diagnosed with ADD/ADHD) and would/may be interested in participating in a lab-based study later this year about the use of cognitive enhancing drugs please provide an email address, in the space below, on which you may be contacted or you can email me, Rachel Teodorini at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk).   
  
You may only participate if you are over 18 years of age, you have not been diagnosed with Attention Deficit/Hyperactivity Disorder, and you are not currently taking any prescribed medications for any mental health problem. Participants will be awarded for their participation with £15 in Amazon vouchers. If you would like to participate in the study you will be provided with an information sheet explaining what the study will involve.

The study will take place at London South Bank University, located in Elephant and Castle, London, UK in January 2019 and participation will take 75 minutes.   
  
Please provide a false name/ pseudonym and ensure that the email address you provide will not identify you.  
  
The email address you provide will be stored on password protected computers only accessible by the researcher, Rachel Teodorini.  It will only be used to contact you for possible participation in a lab-based study. Your email address will be deleted in May 2019, at the end of the funding period for my PhD.   
  
Please also note that if you do provide an email address you are under no obligation to participate in this lab-based experiment and may also opt out at any time during the experiment.

## **C(ix) Participant consent form**

**Research Project Consent Form SAS1834**

**Full title of Project:** The cognitive performance of off-prescription users of modafinil and methylphenidate

**Ethics approval registration Number: SAS1834**

**Name: (Please only provide initials) Participant No. \_\_\_\_\_\_\_\_\_\_**

**Researcher Position:** Principal Investigator

**Contact details of Researcher:** Rachel Teodorini email: [teodorir@lsbu.ac.uk](mailto:teodorir@lsbu.ac.uk) Tel: 020 7815 5431

|  |  |  |
| --- | --- | --- |
| **Taking part (please tick the box that applies)** | **Yes** | **No** |
| I confirm that I have read and understood the information sheet/project brief and/or the student has explained the above study. I have had the opportunity to ask questions. |  |  |
| I understand that my participation is voluntary and that I am free to withdraw at any time, without providing a reason. |  |  |
| I agree to take part in the above study. |  |  |
| I confirm that I have not taken any cognitive enhancing drug for the past 24 hours |  |  |
| I confirm that I am over 18 years of age, I have not been diagnosed with ADHD and that I am not currently taking any prescribed medications for any mental disorder |  |  |
|  |  |  |
| **Use of my information (please tick the box that applies)** | **Yes** | **No** |
| I understand that my data may be quoted in publications, reports, posters, web pages, and other research outputs. |  | ☐ |
| I agree for the data I provide to be stored in a specialist data centre and I understand it may be used for future research. |  |  |

|  |  |  |
| --- | --- | --- |
| UNDISCLOSED  Participant | \_\_\_\_\_\_\_\_  Date | \_\_\_\_\_\_\_\_  Pease sign your initials only |
| Name of Researcher | \_\_\_\_\_\_\_\_  Date | \_\_\_\_\_\_\_\_  Signature |

**Project contact details for further information:**

Project Supervisor/ Head of Division name: Dr Nicky Rycroft

Phone: +44 (0)20 7815 8047

Email address: [rycroftn@lsbu.ac.uk](mailto:rycroftn@lsbu.ac.uk)

## **C(x) Participant debriefing information**

**Debriefing Information SAS1834**

**Title of study: The cognitive performance of off-prescription users of modafinil**

**and methylphenidate**

Thank you for participating in our study. This study was developed based on the results of a previous study which found that people who report using methylphenidate (trade name Ritalin) off-prescription also reported experiencing poor cognitive performance without the use of methylphenidate. However, people who reported using modafinil without a prescription did not report experiencing poor cognitive performance without the use of modafinil. The difference in these self-reports of cognitive performance without the use of these cognitive enhancers may reflect different motivations for using these drugs (to improve poor cognitive performance or to facilitate increased cognitive performance for longer periods of time).

However, these reports of cognitive performance are purely subjective and therefore need to be verified objectively. The questionnaire that you completed at the beginning of the session is the Behaviour Rating Inventory of Executive Function questionnaire (Gioia, Isquith, Guy & Kenworthy, 2000) for adults (BRIEF-A) which assesses cognitive functions such as emotional control, the ability to observe and regulate one's own behaviour in a social context, working memory, planning and organisation. The computer tasks you completed were the Sustained Attention to Response (SART) task (Robertson, Manley, Andrade, Baddeley & Yiend, 1997) which measures working memory performance, sustained attention, and impulse/inhibitory control. The Arrow Flanker Task (Ridderinkhof, van der Molen, Band & Bashore, 1997) measures the ability to control impulsive behaviour and the ability to focus on a particular object in the environment for a certain period of time. The task measuring eye movement is called the Antisaccade task (Hallett, 1978). This task measures distraction and processing control of impulsive behaviour.

Together, these tasks tap the same mental processes as those measured in the previous study. Data from this study will be analysed and compared to the self-report data from the previous study, allowing for more accurate assessments of whether and to what extent poor cognitive performance is being experienced by individuals who take modafinil and/or methylphenidate off-prescription. In addition, it is hoped that the data collected will confirm whether there is a split in the cognitive performance of modafinil and methylphenidate users and in turn this will help to understand motivations for the off-prescription use of these drugs.

If you have concerns about any aspect of this study please contact the researcher, Rachel Teodorini, at [teodorr2@lsbu.ac.uk](mailto:teodorr2@lsbu.ac.uk), tel: 020 7815 5431. Following which, if you still have concerns, you may contact the Chair of the School of Applied Science Ethics Panel at sasethics@lsbu.ac.uk.

If you would like more information about these drugs please visit the following sites: https://www.release.org.uk

https://www.drugwise.org.uk

Modafinil and methylphenidate are illegal to take without prescription and illegal use is liable to a prison sentence of up to 5 years. Finally, if you have any concerns about your use of these drugs please refer to your information sheet for further support or consult your GP.

## **C(xi) Mental Health**

**Table C.5. Psychiatric diagnosis**

|  |  |  |
| --- | --- | --- |
|  | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Have you been diagnosed with a psychiatric disorder?** |  |  |
| Yes | 10 (21.3) | 4 (9.3) |
| No | 37 (78.7) | 39 (90.7) |
| **What was the diagnosis?** |  |  |
| Depression | 6 (54.5) | 1 (2.3) |
| Anxiety | 1 (9.1) | 1 (2.3) |
| Depression and Anxiety | 2 (18.2) | 2 (4.7) |
| Complex PTSD | 1 (9.1) |  |

\* Percentages relate to group and not to the whole sample

## **C(xii) Cannabis**

**Table C.6. Reported Cannabis use**

|  |  |  |
| --- | --- | --- |
|  | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Have you ever taken cannabis?** |  |  |
| Yes | 41 (87.2) | 17 (39.5) |
| No | 6 (12.8) | 26 (60.5) |
| **Do you have a prescription for medicinal cannabis?** |  |  |
| No | 6 (54.5) | 1 (2.3) |
| **Age of first use of cannabis** | Mean = 16.66 (SD = 3.13) | Mean = 18.29 (SD = 3.85) |
| **Frequency of Cannabis use in past 6 months** |  |  |
| Every day/almost every day | 2 (4.9) | 0 |
| 3-4 times per week | 5 (12.2) | 0 |
| Once per week | 2 (4.3) | 0 |
| 1-2 times per month | 7 (17.1) | 3 (6.98) |
| Up to 3 times in total | 7 (17.1) | 4 (9.3) |
| None | 18 (43.9) | 11 (25.58) |

\* Percentages relate to group and not to the whole sample

## **C(xiv) Modafinil\***

\* All participants stated that they did not have a prescription for modafinil.

**Table C.7. Lifetime use of modafinil**

|  |  |
| --- | --- |
| **Have you ever used modafinil?** | **CED user group N (%)\*** |
| **Yes** | 41 (87.2) |
| **No** | 6 (12.8) |
| **Age of first use of modafinil** | Mean = 24.56 (SD = 5.64) |

\* Percentages relate to group and not to the whole sample

**Table C.8. Dosage levels of reported modafinil use**

|  |  |
| --- | --- |
| **Dosage** | **N (%)\*** |
| 50mg | 2 (4.3) |
| 75mg | 3 (6.4) |
| 100mg | 16 (34.0) |
| 150mg | 3 (6.4) |
| 200mg | 10 (21.3) |
| 300mg | 3 (6.4) |
| 400mg | 1 (2.1) |

\* Percentages relate to group and not to the whole sample

**Table C.9. Maximum and minimum dose of modafinil**

|  |  |  |
| --- | --- | --- |
| **Dosage (mg)** | **Maximum N (%)\*** | **Minimum N (%)\*** |
| 25 | - | 4 (8.51) |
| 50 | - | 13 (19.1) |
| 75 | - | 2 (4.3) |
| 100 | 9 (19.1) | 16 (34.0) |
| 150 | 4 (8.51) | - |
| 200 | 16 (34.0) | 3 (6.4) |
| 250 | 2 (4.3) | - |
| 300 | 2 (4.3) | - |
| 400 | 4 (8.5) | - |
| 600 | 1 (2.1) | - |

**Table C.11. Routes of administration of modafinil**

|  |  |
| --- | --- |
| **Route of administration** | **N (%)\*** |
| Swallow pill | 39 (95.1) |
| Swallow pill and snort | 1 (2.4) |
| subcutaneous | 1 (2.4) |

## **C(xv) Methylphenidate\***

\* All participants stated that they did not have a prescription for methylphenidate.

**Table C.12. Lifetime use of methylphenidate**

|  |  |
| --- | --- |
| **Have you ever used methylphenidate?** | **CED user group N (%)\*** |
| **Yes** | 19 (40..4) |
| **No** | 28 (59.6) |
| **Age of first use of methylphenidate** | Mean = 22.39 (SD = 6.05) |

\* Percentages relate to group and not to the whole sample

**Table C.13. Dosage levels of reported methylphenidate use**

|  |  |
| --- | --- |
| **Dosage** | **N (%)\*** |
| 10mg | 4 (33.3) |
| 20mg | 5 (41.7) |
| 30mg | 1 (8.3) |
| 60mg | 2 (16.7) |

\* Percentages relate to group and not to the whole sample

**Table C.14. Maximum and minimum dose of methylphenidate**

|  |  |  |
| --- | --- | --- |
| **Dosage (mg)** | **Maximum N (%)\*** | **Minimum N (%)\*** |
| 5mg | - | 1 (8.3) |
| 10mg | 1 (8.3) | 4 (33.3) |
| 20mg | 5 (41.7) | 5 (41.7) |
| 30mg | - | 2 (16.7) |
| 40mg | 1 (8.3) | - |
| 60mg | 3 (25.0) | - |
| 80mg | 1 (8.3) | - |
| 120mg | 1 (8.3) | - |

\* Percentages relate to group and not to the whole sample

**Table C.15. Frequency of methylphenidate use**

|  |  |
| --- | --- |
| **Frequency of use within the past six months** | **CED user group N (%)\*** |
| **Every day** | - |
| **Three or more days per week** | 2 (10.5) |
| **Once or twice per week** | - |
| **Two or three times per month** | 4 (21.1) |
| **Six times or less per year** | 4 (21.1) |

\* Percentages relate to group and not to the whole sample

**Table C.16. Routes of administration of methylphenidate**

|  |  |
| --- | --- |
| **Route of administration** | **N (%)\*** |
| Swallow pill | 14 (73.7) |
| Swallow pill and snort | 3 (15.8) |
| subcutaneous | 2 (10.5) |

\* Percentages relate to group and not to the whole sample

## **C(xv) Alcohol**

**Table C.17. Frequency of alcohol use and length of time since last use**

|  |  |  |
| --- | --- | --- |
| **ALCOHOL** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | 1 (2.10) | 1 (2.3) |
| 3-4 times per week | 6 (12.80) | 3 (7.0) |
| Once per week | 15 (31.90) | 8 (18.6) |
| 1 – 2 times per month | 10 (21.30) | 2 (4.7) |
| Up to 3 times in total | 1 (2.10) | 6 (14.00) |
| None | 14 (29.80) | 23 (53.50) |
| **Length of time since last use** | | |
| Within the last week | 29 (61.7) | 15 (34.88) |
| Within the last month | 5 (10.64) | 1 (2.3) |
| Within the last 6 months | - | - |
| Within the last year | - | 4 (9.3) |

\* Percentages relate to group and not to the whole sample

## **C(xvi) Nicotine**

**Table C.18. Frequency use and length of time since last use of nicotine**

|  |  |  |
| --- | --- | --- |
| **NICOTINE** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | 12 (25.53) | 7 (16.28) |
| 3-4 times per week | 1 (2.13) | 1 (2.3) |
| Once per week | 1 (2.13) | - |
| 1 – 2 times per month | 6 (12.77) | 1 (2.3) |
| Up to 3 times in total | - | 1 (2.3) |
| None | 27 (57.45) | 23 (53.49) |
| **Length of time since last use** | | |
| Within the last week | 16 (34.04) | 8 (18.6) |
| Within the last month | 4 (8.51) | - |
| Within the last 6 months | - | - |
| Within the last year | - | 3 (6.98) |

\* Percentages relate to group and not to the whole sample

## **C(xvii) Recreational drug use**

**Table. C.19. Previous diagnosis of a drug/alcohol problem**

|  |  |  |
| --- | --- | --- |
| **Have you ever been treated for a drug/alcohol problem?** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| Yes | 2 (4.3) | 0 |
| No | 45 (95.7) | 43 (100) |

\* Percentages relate to group and not to the whole sample

**Table C.20. Stimulants**

|  |  |  |
| --- | --- | --- |
| **STIMULANTS** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | - | - |
| 3-4 times per week | 1 (2.13) | - |
| Once per week | - | - |
| 1 – 2 times per month | 13 (27.66) | 1 (2.3) |
| Up to 3 times in total | 17 (36.17) | 4 (9.3) |
| None | - | - |
| **Length of time since last use** | | |
| Within the last week | 4 (8.51) | - |
| Within the last month | 9 (19.15) | 4 (9.30) |
| Within the last 6 months | - | - |
| Within the last year | 17 (36.17) | 1 (2.3) |

\* Percentages relate to group and not to the whole sample

**Table C.21. Depressants/anxiolytics/sedatives**

|  |  |  |
| --- | --- | --- |
| **DEPRESSANTS/ANXIOLYTICS/SEDATIVES** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | - | - |
| 3-4 times per week | 1 (2.13) | - |
| Once per week | 2 (4.26) | - |
| 1 – 2 times per month | 5 (10.64) | - |
| Up to 3 times in total | 1 (2.13) | - |
| None | - | - |
| **Length of time since last use** | | |
| Within the last week | 6 (12.77) | - |
| Within the last month | 2 (4.26) | - |
| Within the last 6 months | - | - |
| Within the last year | 1 (2.31) | - |

\* Percentages relate to group and not to the whole sample

**Table C.22. Hallucinogens**

|  |  |  |
| --- | --- | --- |
| **HALLUCINOGENS** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | - | - |
| 3-4 times per week | 1 (2.31) | - |
| Once per week | 4 (8.51) | 1 (2.3) |
| 1 – 2 times per month | 5 (10.64) | - |
| Up to 3 times in total | 20 (42.55) | - |
| None | - | - |
| **Length of time since last use** | | |
| Within the last week | 2 (4.26) | 1 (2.3) |
| Within the last month | 13 (27.66) | - |
| Within the last 6 months | - | - |
| Within the last year | 16 (34.04) | - |

\* Percentages relate to group and not to the whole sample

**Table C.23. Opioid pain killers**

|  |  |  |
| --- | --- | --- |
| **OPIOID PAIN KILLERS** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | - | - |
| 3-4 times per week | - | - |
| Once per week | 1 (2.31) | - |
| 1 – 2 times per month | 2 (4.26) | - |
| Up to 3 times in total | 3 (6.38) | - |
| None | - | - |
| **Length of time since last use** | | |
| Within the last week | - | - |
| Within the last month | 2 (4.26) | - |
| Within the last 6 months | - | - |
| Within the last year | 3 (6.38) | - |

\* Percentages relate to group and not to the whole sample

**Table C.24. Nootropics/ Cognitive enhancers**

|  |  |  |
| --- | --- | --- |
| **NOOTROPICS/ COGNITIVE ENHANCERS** | **CED-user group N (%)\*** | **Control group N (%)\*** |
| **Frequency of use with the past 6 months** | | |
| Every day/almost every day | - | - |
| 3-4 times per week | - | - |
| Once per week | - | - |
| 1 – 2 times per month | 2 (4.26) | - |
| Up to 3 times in total | - | - |
| None | - | - |
| **Length of time since last use** | | |
| Within the last week | 2 (4.26) | - |
| Within the last month | - | - |
| Within the last 6 months | - | - |
| Within the last year | - | - |

\* Percentages relate to group and not to the whole sample

# **Appendix D: Abbreviations and Accronyms**

**ACC** anterior cingulate cortex

**ADD** Attention Deficit Disorder

**ADHD** Attention Deficit Hyperactivity Disorder

**ASRS** Adult ADHD Self-Report Scale

**AUDIT** Alcohol Use Disorders Identification Test

**BOLD** blood oxygenation level dependent

**BRIEF-A** Behaviour Rating Inventory of Executive Function – Adult Version

**CANTAB** Cambridge Neuropsychological Test Automated Battery

**CED** cognitive enhancing drug

**CFQ** Cognitive Failures Questionnaire

**COMT** catechol O-methyltransferase

**CPP** conditioned place preference

**DA** dopamine

**DAN** dorsal attention network

**DLPFC** dorsolateral prefrontal cortex

**DMN** default mode network

**DSM-IV** Diagnostic and Statistical Manual of Mental Disorders 4

**EMCDDA** European Monitoring Centre for Drugs and Drug Addiction

**ERN** error-related negativity

**FEF** frontal eye fields

**FOSQ** Functional Outcomes of Sleep Questionnaire

**GABA** gamma-aminobutyric acid

**GEC** Global Executive Composite

**GPS** General Procrastination Scale

**HAM-A** Hamilton Rating Scale for Anxiety

**HAM-D** Hamilton Rating Scale for Depression

**i.p.** intraperitoneal

**LPFC** Lateral prefrontal cortex

**MI** Metacognition Index

**Ms** milliseconds

**NE** noradrenaline

**NICE** The National Institute for Health and Care Excellence

**NIDA** National Institute of Drug Abuse

**PET** positron emission tomography

**PFC** prefrontal cortex

**p.o.** orally administered

**POMS** Profile of Mood States

**PR** progressive ratio

**PRMQ** Prospective and Retrospective Memory Questionnaire

**RPS** Research Participation Scheme

**SART** Sustained Attention to Response Task

**SFHS** Short Form Health Survey

**SN** saliency network

**TMT** Temporal Motivation Theory

**TOVA** Test of Variables of Attention

**UK** United Kingdom

**VAN** ventral attention network

**VLPFC** ventrolateral prefrontal control

**VMPFC** ventromedial prefrontal cortex

**WHO** World Health Organisation

1. **Normative data was drawn from Crawford et al.’s (2003) study which specifically focused on providing normative data for the PRMQ.** [↑](#footnote-ref-2)
2. A question relating to frequency of use of modafinil and methylphenidate was intended to be included but due to a technical error in QualtricsXM, these data were only collected for the modafinil user group and therefore are not reported here. [↑](#footnote-ref-3)
3. The Sustained Attention to Response task (SART) was also included in the study but due to a technical error the relevant data were not collected. Therefore, details of this task have been removed from the write-up of this study. Please see Appendix C(iv) for details of the SART as it had been originally intended to be run. [↑](#footnote-ref-4)