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Sleep- and Wake-Promoting Drugs: Where Are They Being Sourced, and What Is Their Impact?

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ABSTRACT

Background: Recent decades have seen both an increased number of shift workers in order to deliver services 24/7, and increased potential for social interactions at all hours of the day. People have sought to engage in strategies, which either promote vigilance or facilitate sleep, with the use of sleep- and wake-promoting drugs representing one strategy. *Methods:* We investigated use of sleep- and wake-promoting drugs in participants ($n = 377$) who completed a survey investigating the type and source of sleep- and wake-promoting drugs, and their impact on sleep and performance outcomes. *Results:* The most commonly reported wake-promoting drugs were amphetamine and dextroamphetamin salts, modafinil, and illicit substances including methamphetamine and cocaine, while the most commonly reported sleep-promoting drugs were benzodiazepines and antihistamines. Use of a sleep-promoting drug in the past month was associated with higher odds of having poorer sleep quality (OR = 3.15) and moderate-high insomnia (OR = 3.30), while use of a wake-promoting drug was associated with poor sleep quality (OR = 3.76), or making a fatigue-related error (OR = 2.65). *Conclusions:* These findings represent novel data on the use and source of sleep- and wake-promoting- drugs, and suggest that despite their use, poor sleep and performance outcomes persist, likely representing individuals struggling to keep up with the 24/7 world.

KEYWORDS

Sleep-promoting drug; wake-promoting drug; sleep quality; performance; insomnia; daytime dysfunction

Introduction

The 24/7 society

We live in a society where services across industries are increasingly available across all hours of the day, with an increasing proportion of the population engaged in employment during non-traditional hours (Rajaratnam & Arendt, 2001). In addition to employment, social interactions including online services and social media have resulted in more people being awake at times opposing their natural biological drive for sleep (Levenson et al., 2016; Garett, Liu, & Young, 2018). Regardless of the impetus underlying this drive to be awake, the 24/7 world presents an environmental challenge to underlying human physiology (Monk, 1988), which has biologically adapted to the light-dark cycle (Reppert & Weaver, 2002). Homeostatic circadian rhythmicity is pervasive across both physiological and biochemical outputs (Czeisler et al., 1999; Pevet & Challet, 2011). In addition, circadian rhythmicity underlies performance and behavioral outputs including sleep-wake states, alertness, and mental performance (Carrier & Monk, 2000; Rajaratnam & Arendt, 2001; Schmidt, Collette, Cajochen, & Peigneux, 2007).

There is increasing recognition of poorer health and safety outcomes in groups that act in opposition to this circadian drive (Harrington, 2001; Lockley et al., 2004; Rajaratnam et al., 2011; Barger et al., 2015). For example, shift workers have increased prevalence of cardiovascular disease (Bøggild & Knutsson, 1999; Kivimäki, Kuisma, Virtanen, & Elovaino, 2001; Vyas et al., 2012), type II diabetes (Kivimäki, Batty, & Hublin, 2011; Vetter et al., 2015), poorer mental health (Bara & Arber, 2009; Thun et al., 2014; Lee et al., 2017) and increased levels of sleep disturbance (Axelsson, Åkerstedt, Kecklund, & Lowden, 2004; Rajaratnam et al., 2011). Beyond discrete health outcomes, there is also evidence of poorer work performance, alertness, and an increased propensity to make errors in those who work nights, rotating or extended shifts (Rogers, Hwang, Scott, Aiken, & Dinges, 2004; Barger et al., 2006). These decrements in performance associated with increased sleepiness are not trivial, with performance impacted to a similar magnitude as having a blood alcohol concentration, which approaches or exceeds the legal limit for

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driving (Dawson & Reid, 1997; Arnedt, Wilde, Munt, & MacLean, 2001).

To combat the environmental challenges associated with being awake during the circadian nadir, people have sought to engage in strategies which either facilitate sleep (e.g., after a night shift) or promote vigilance (e.g., to remain 'on task' while at work, or to stay up to engage with social contacts) (Keith, Gunderson, Haney, Foltin, & Hart, 2017). One strategy involves the use of sleep- and/or wake-promoting drugs, however to date there has been limited investigation of where such drugs are sourced, and whether or not their use is associated with better or poorer outcomes, particularly in the general population.

Who is using sleep and wake-promoting drugs?

Approximately one-in-ten adults have used alcohol as a sleeping aid (Roehrs & Roth, 2001a), with increased use reported by shift workers where one-in-six have consumed alcohol to help initiate sleep between shifts (Dorrian, Heath, Sargent, Banks, & Coates, 2017). In addition to alcohol, benzodiazepine use is common, with 5% of adults in the United States having used a benzodiazepine across a 12-month period, with higher rates in the elderly (Olfson, King, & Schoenbaum, 2015). Benzodiazepine use is also common among shift workers (Dorrian et al., 2006) and astronauts (Barger et al., 2014) in order to help initiate sleep. Despite this, both high alcohol or long-term benzodiazepines use is of concern (Brett et al., 2017), given that tolerance to their effects develops, with a subsequent risk of dependence (Urru, Pasina, Minghetti, & Giua, 2015), which can then impact on performance (Schuckit, 2009). Roche, Pidd, Berry, and Harrison (2008) for example, reported that high-risk drinkers were more than 20 times more likely than low-risk drinkers to be absent from work due to their alcohol use, placing a large burden on the economy due to lost productivity.

While sleep-promoting drugs are used to help initiate sleep, wake-promoting drugs are used to promote vigilance, or to increase concentration. Wake-promoting drugs comprise a heterogeneous group that includes widely available drugs such as caffeine and nicotine, in addition to prescription and over-the-counter medications or supplements. Caffeine use is ubiquitous and its use is associated with the promotion of alertness, mood, and mental performance (Sahakian & Morein-Zamir, 2007; Smith, 2002, 2009). However, reliance on caffeine has been associated with poorer sleep quality, increased levels of daytime dysfunction, and increased levels of night time disturbance (Ogeil & Phillips, 2015). Other drugs with wake-promoting properties have been proposed as countermeasures to excessive sleepiness especially within shift work settings including modafinil, amphetamine, and pemoline (Åkerstedt & Ficca, 1997), however there is limited data on their effectiveness. For example, a Cochrane review reported limited efficacy of wake-promoting agents including modafinil and caffeine in shift workers (Liira et al., 2014). Both illicit use of prescription stimulants such as methylphenidate and dextroamphetamin salts and other putative cognitive enhancers have been used by college students to aid concentration (Hall, Irwin, Bowman, Frankenberger, & Jewett, 2005; Teter, McCabe, LaGrange, Cranford, & Boyd, 2006; Ram, Hussainy, Henning, Jensen, & Russell, 2016; Papazisis et al., 2018). As with sleep-promoting medication, there may be negative consequences that accompany their use (Smith, Martel, & DeSantis, 2017). For example, nicotine dependence has been associated with poorer sleep quality, and increased use of sleep medication and sleep disturbances (Ogeil & Phillips, 2015). A recent study reported that wake-promoting medication use, high caffeine use, and smoking to stay awake were associated with increased odds of fatigue-related errors, and increased stress and burnout in police officers (Ogeil et al., 2018) suggesting a relationship with psychological distress.

Despite recent interest in this area, few studies have investigated important facets of the use of sleep- and wake-promoting drugs including: (i) an assessment of the type of drug(s) being used beyond binary categories; (ii) their source (e.g., whether they were prescribed, diverted or sourced online) and their (iii) impact on sleep and performance outcomes. The present study examined which drugs were reportedly used to promote sleep/wake states, their source, and whether use of these drugs impacted upon specific sleep (e.g., sleep quality, insomnia symptoms and excessive sleepiness) and psychological distress outcomes. Importantly, we then investigated whether use of sleep- and/or wake-promoting drugs was associated with an increased risk of having clinically relevant sleep problems, high psychological distress, and/or a greater propensity to make errors.

Method

Participants

Participants from the general community ($n = 377$, 55% female) were recruited via online message boards and social media advertising (e.g., Twitter, Facebook, Reddit) between August 2015 and May 2017, where they were invited to take part in a survey which aimed

to investigate the use of sleep and wake promoting drugs among the general population. Prior to beginning the survey participants were provided with an explanatory statement, which included details on the purpose of the research, provided contact details of the researchers, as well as links to online clinical services that provide support for people that are concerned about their drug use or sleep.

The mean age of participants was 26.31 (SD ± 8.49), with many participants having attained a university degree ($n = 205$, 54.4%). Overall many participants were employed either full time ($n = 139$, 36.9%) or on a casual or part-time ($n = 96$, 25.5%) basis. Participants ($n = 55$) nominated they were current shift workers, 179 were not shift workers, and 234 declined to answer. While participants were not provided with payment to complete the study, they were eligible to enter a prize draw to win a $50 gift card for completing the study. The study received approval from the Monash University Human Research Ethics Committee.

Materials

A battery of online materials investigating use of sleep and wake promoting drugs was presented and completed online by participants. This included demographic data, validated sleep tools, and questions on their use of sleep and wake promoting drugs elicited via self-report. Specifically, we asked participants "In the past month have you used a medication or other drug to help you stay awake?", and then asked them to specify relevant medications and drugs, and their source (where they had obtained the medication/drug) in subsequent online fields. Given previous associations with poorer health and performance outcomes in smokers (Ogeil et al., 2018), we also asked participants whether or not they current smoked cigarettes.

Validated sleep tools assessing sleep quality, excessive daytime sleepiness and insomnia used in this study were:

- The Pittsburgh Sleep Quality Index (PSQI), a 19-item scale assessing sleep quality during the past month. This scale has seven subscales, contributing to a total score, with scores of >5 used to identify clinically relevant sleep quality disturbance (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).
- The Epworth Sleepiness Scale (ESS), an 8-item scale (each item scored 0–3) assessing daytime sleepiness (Johns, 1991). Scores of 10+ are used to identify clinically relevant levels of sleep-related daytime dysfunction (Johns, 1992).
- The Insomnia Severity Scale (ISI), a 7- item scale assessing insomnia (Bastien, Vallieres, & Morin, 2001; Morin, Belleville, Belanger, & Ivers, 2011). Total scores of 0–7 indicates no clinically significant insomnia, 8–14 represent sub-threshold insomnia, 15–21 indicate moderate insomnia, and 22–28 represent severe insomnia.
- The Shift work disorder (SWD) scale, a 4-item scale assessing risk of SWD. Risk is assessed as a binary outcome, being either "high" or "low" (Barger et al., 2012).

In addition the K-10 was used to assess psychological distress (Kessler et al., 2002), given that sleep and mood states impact upon each other (Wirz-Justice, 2006). The scale contains ten items that are combined to give a global score out of 50, with higher scores indicating greater distress. The K-10 is widely used in both research and clinical settings and has excellent internal consistency and reliability metrics (Kessler et al., 2002).

Participants were asked as to whether in the past month they believed that sleep deprivation or fatigue had caused them to make a mistake, error or behave unnecessarily unsafe in some way. We also asked participants a similar question as to whether they believed they had made a mistake, error, or behaved unnecessarily unsafe in some way that was not caused by sleep deprivation or fatigue in the past month.

Data analysis

Frequency data were used to describe use of sleep and wake promoting drugs in the past month, with chi-square analyses then used to compare outcomes on the sleep and psychological distress scale using validated cutoff scores. Hierarchical binary logistic regression models were used to examine whether use of sleep- or wake-promoting medications and medications that listed sleep as a side-effect were predictive of poor sleep outcomes, controlling for: gender, age, K-10 score, and shift work status.

Results

Use and source of sleep and wake promoting drugs

In the past month, 114 participants (30.2%) reported using a medication or other drug to help them stay awake with 47 (12.5%) reportedly using >1 wake promoting agent in the past month (see Table 1). The most common drugs used were those prescribed for

the treatment of attention deficit disorder (ADD) including amphetamine and dextroamphetamin salts, modafinil, and illicit substances including methamphetamine and cocaine. In addition, 96 participants (25.9%) identified as current smokers, and 350 (94.1%) had consumed a beverage containing caffeine.

In the past month, 210 participants (55.7%) reported using a medication or drug to help them sleep, with 53 (14.06%) using >1 sleep-promoting agent in the past month. The most commonly reported drugs were benzodiazepines, antihistamines and melatonin (see Table 2).

Association between drug use and sleep outcomes

Figure 1 shows mean differences in the use of wake promoting agents and sleep outcomes.

Participants using a medication for "wake" scored significantly higher on the PSQI subscales: Sleep Quality ($p = .002$), Duration ($p = .001$), Sleep Efficiency ($p = .005$), Use of sleep medication, ($p < .001$), and Daytime Dysfunction ($p = .002$). Smokers scored significantly higher on the PSQI subscales: Sleep Quality ($p = .001$), Sleep Latency ($p = .033$), Duration ($p < .001$), Sleep Disturbances ($p < .001$), Use of Sleep Medication ($p = .03$), and Daytime Dysfunction ($p = .009$).

Participants using a medication for "sleep" scored significantly higher on the PSQI subscales: Sleep Quality ($p = .005$), Sleep Latency ($p < .001$), Sleep Disturbances ($p = .003$), and Use of Sleep Medication ($p < .001$). Participants using a medication with "sleepiness as a side-effect" scored significantly higher on the subscales: Sleep Disturbances ($p = .004$), Use of Sleep Medication ($p < .001$), and Daytime Dysfunction ($p = .038$).

Clinical relevance

Use of a wake-promoting drug was associated with: a greater risk of poor sleep quality as indicated by a PSQI score of >5 (92.9% vs 70.7%, $\chi^2(1df) = 21.94$, $p > .001$), a greater risk of daytime sleepiness as indicated by an ESS Score >10 (25.4% vs 12.9%, $\chi^2(1df) = 8.71$, $p = .003$), a greater risk of moderate-severe insomnia $\chi^2(1df) = 5.03$, $p = .025$, and no greater risk of SWD: $\chi^2(1df) = .018$, $p > .05$. In addition, those who had used a wake promoting drug were more likely to have a K-10 score of 16 + χ^2 (1df) = 9.72, $p = .002$.

Current smoking status was associated with: greater risk of poor sleep quality as indicated by a PSQI score of 5+ (88.2% vs 73.8%, $\chi^2(1df) = 8.20$, $p = .004$), no difference in proportion of ESS Scores >10 (18.8% vs 17.5%, $\chi^2(1df) = .82$, $p > .05$), a greater risk of moderate-severe insomnia (36.5% vs 18.9%, $\chi^2(1df) = 12.21$, $p < .001$, and no greater risk of SWD: $\chi^2(1df) = .287$, $p > .05$. In addition, those who had used a wake promoting drug were more likely to have a K-10 score of 16+ (94.0% vs 80.3% χ^2 (1df) = 8.52, $p = .004$).

Use of a sleep-promoting drug was associated with: a greater risk of poor sleep quality as indicated by a PSQI score of 5+ (87.5% vs 65.4%, $\chi^2(1df) = 23.76$, $p < .001$), tended to have a greater risk of an ESS Score >10 (21.0% vs 12.7%, $\chi^2(1df) = 3.83$, $p = .05$), a greater risk of moderate-severe insomnia $\chi^2(1df) = 21.83$, $p < .001$, and no greater risk of SWD: $\chi^2(1df) = .562$, $p > .05$. In addition, those who had used a sleep promoting drug were more likely to have a K-10 score of 16+ χ^2 (1df) = 5.45, $p = .020$.

Females had higher mean: K-10 scores (26.22 ± 9.54) and ISI scores (11.033 ± 9.57) compared with males (K-10: 24.13 ± 8.93, ISI: 9.57 ± 5.29), $p < .05$, however did not significantly differ on AUDIT C, SWD risk, total ESS total scores, or use vs nonuse of a sleep- or wake-promoting drug in the past month. Given these relationships, we controlled for gender in our hierarchical logistic regression.

Association between drug use and fatigue and non-fatigue related errors

A higher proportion of those using a wake-promoting medication (46.2%) in the past month reported making a mistake, error or behaving in an unnecessarily safe way due to sleep deprivation or fatigue compared to those who had not used such a medication (30.7%) $\chi^2(1df) = 7.60$, $p = .006$. The same relationship was not evident in smokers χ^2 (1df) = 2.59, $p > .05$, or when asked whether a mistake or error had been made which was not attributable to fatigue.

Logistic regression

Hierarchical binary logistic regression models examined whether use of sleep- or wake-promoting medications and medications that listed sleep as a side-effect were predictive of poor sleep outcomes (see Table 3).

Table 1. Type and Source of wake-promoting drug used in the past month.

		Source						
Drug type	*n*	Prescription (for myself)	OTC	Family/friend gave it to me	Internet	Dealer	Prescription (for another person)	Other/ not specified
Stimulants primarily for ADD	**86**							
Amphetamine and dextroamphetamin salts	47	26		5	1	3	10	2
Dexamphetamine/ dextroamphetamin	12	7		3	1		1	
Methylphenidate	19	10		2	1	1	2	3
Lisdexamfetamine	8	7		1				
Stimulants primarily for narcolepsy	**14**							
Modafinil/armodafinil	13	5		3	3		1	1
Adrafinil (prodrug of modafinil, discontinued)	1				1			
Nasal/Sinus decongestants and asthma	**4**							
Pseudoephedrine	2		2					
Propylhexedrine	1		1					
Ephedrine Sulfate-Guaifenesin	1		1					
Stimulants for weight loss	**4**							
Phentermine	2	1	1					
Ephedrine	2		1					1
Primarily Illicit stimulants	**22**							
Methamphetamine[a]	10	1		3		3		3
Cocaine	7			3		2		2
Amphetamine 'Speed'	2					2		
MDMA	2							2
LSD	1							1
Putative cognitive enhancers/ nootropic supplements	**5**							
Bromantane	1				1			
N-Phenylacetyl-L-prolylglycine ethyl ester	1				1			
N.A.L.T	1				1			
Piracetam	1	1						
Alpha gpc	1				1			
Designer Drugs	**6**							
Methiopropamine (analogue of methamphetamine)	2				1			1
3-FPM	2				2			
a-PHP	1				1			
3'-Fluorophenmetrazine	1							1
Others	**16**							
Nicotine	2		2					
Ethylphenidate/ Isopropylphenidate (analogues of methylphenidate)	4				2			2
Kratom	1				1			
Vitamin B supplements	6		6					
Combination pain relief (contains caffeine)	1							1
Levothyroxine	1		1					
Bupropion	1	1						

[a]Available by prescription under the trade name Desoxyn in the United States.
[b]Twenty-nine participants listed a drug normally associated with sleepiness.

Predicting poor sleep outcomes

Use of a sleep-promoting drug in the past month was associated with higher odds of having poorer sleep quality (OR = 3.15) and moderate-high insomnia (OR = 3.30), while use of a wake-promoting drug was associated with poor sleep quality (OR = 3.76), or making a fatigue-related error (OR = 2.65). Psychological distress remained a significant predictor of poor sleep quality, moderate-high insomnia, and making a fatigue-related error in the past month. The overall models for daytime sleepiness and making a non-fatigue error were not significant.

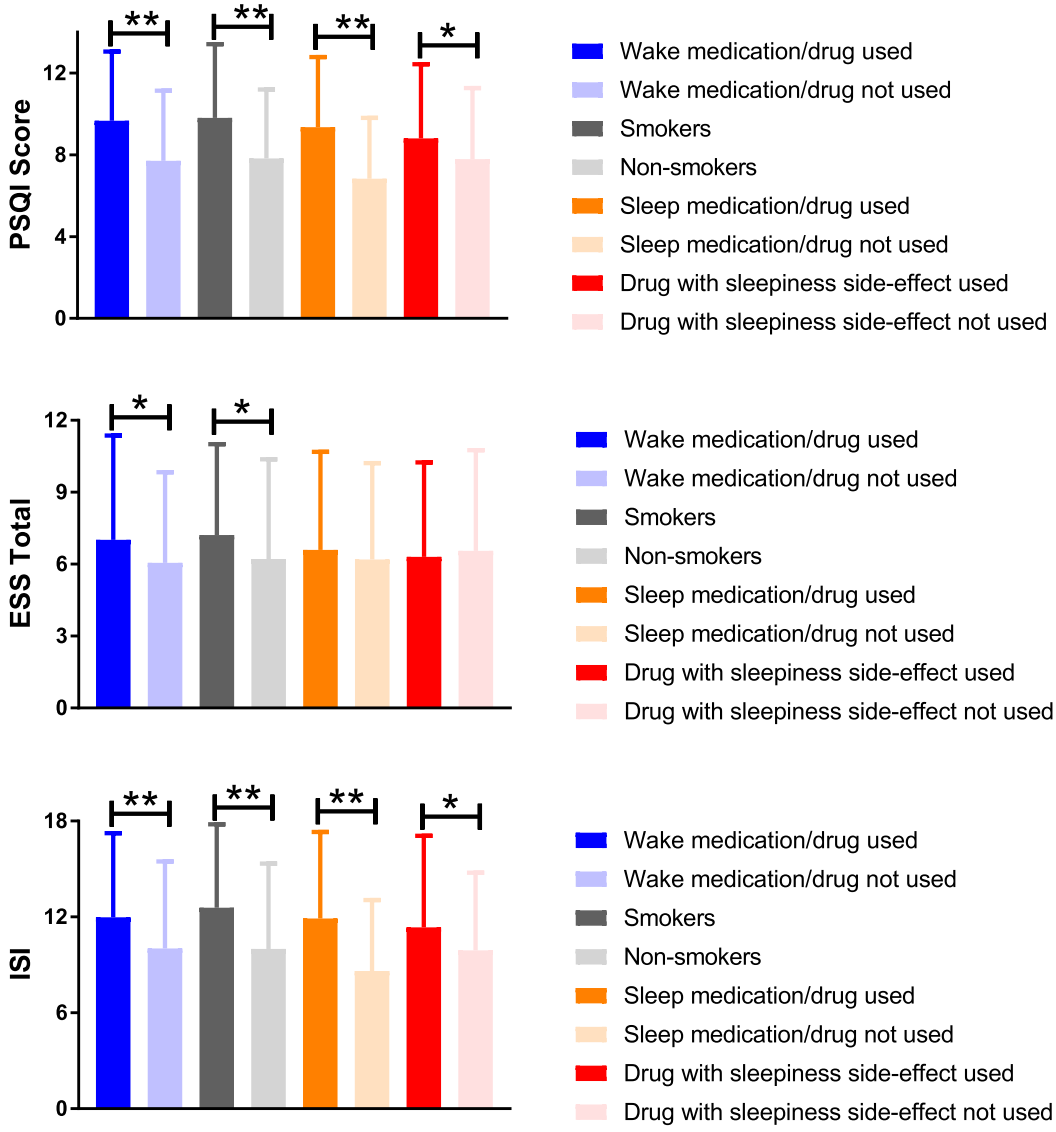
Discussion

The present study indicated that use of sleep- and wake-promoting drugs was associated with poorer sleep outcomes, higher psychological distress, and a

Table 2. Type and Source of sleep-promoting drug used in the past month.

		Source						
Drug type	*n*	Prescription (for myself)	OTC	Family/friend gave it to me	Internet	Dealer	Prescription (for another person)	Other/ not specified
Benzodiazepines and benzodiazepine-like substances for anxiety/insomnia	**81**							
Diazepam	14	9		1	1			3
Alprazolam	23	17		2	1		1	2
Clonazepam	18	16		2				
Lorazepam	6	3		1			2	
Temazepam	5	4					1	
Benzodiazepine (unspecified)	2	1			1			
Zolpidem	9	7					2	
Zopiclone	5	4		1				
Antihistamines	**62**							
Diphenhydramine	33		31	1				1
Doxylamine	9		8					1
Hydroxyzine	4	4						
Antihistamines (unspecified)	2		1					1
Combination antihistamine/ pain reliever	14		14					
Antipsychotics	**15**							
Quetiapine	13	11					1	1
Chlorpromazine	1	1						
Olanzapine	1	1						
Antidepressants	**9**							
Trazodone	6	6						
Mirtazapine	2	1						1
nortriptyline	1	1						
Drugs for Circadian disturbance	**40**							
Melatonin	39	1	36	1				1
Agomelatine	1	1						
Drugs for seizures and muscle relaxants	**10**							
Cyclobenzaprine	1	1						
Pregabalin	1							1
Phenobarbitone	1	1						
Carisoprodol	2		1	1				
Tizanadine	1	1						
Gabapentin	3	3						
Muscle relaxant (unspecified)	1	1						
Drugs for pain	**8**							
Oxycodone	3	1		1		1		
Codeine preparations (w/paracetamol)	1	1						
Tramadol	1						1	
Opioids (unspecified)	2				1			1
Hydrocodone/paracetamol	1	1						
Other	**38**							
Alcohol	17		10					7
Promethazine (motion sickness, antiemetic)	2	2						
Heroin	3			1		1	1	
Valerian or other herbal formulations	3		3					
Phenibut (CNS depressant)	2	2						
Nixofipam (designer drug / benzo derivative)	1							1
Prazosin (blood pressure, anxiety)	1	1						
Gbl (desingner drug)	1							1
Kava	1		1					
Dimenhydrinate	3		3					
Xyrem (GHB)	1	1						
Guanfacine (ADHD)	1		1					
Cough sirup (unspecified)	1		1					
Clonidine (blood pressure, ADHD)	1							1

higher propensity to make errors that were attributed to fatigue, supporting recent work in a police cohort (Ogeil et al., 2018). Importantly, the present study demonstrates that these associations exist in the general population, rather than a group of shift workers likely prone to circadian disturbance. Stimulants



PSQI = Pittsburgh Sleep Quality Index, ESS=Epworth Sleepiness Scale, ISI=Insomnia Severity Index; ** = *p*<.01, *= *p*<.05

Figure 1. Use of sleep- or wake-promoting drug use and sleep outcomes amongst drug using groups.

Table 3. Binary logistic models predicting poor sleep and errors.

Dependent variable	Model Chi-square (7*df*), sig value	Variance explained[a]	Significant predictors[b]	*B* (S.E)	OR (95% CI)
Poor Sleep Quality (PSQI > 5)	38.73, $p < .001$	.18–.27	K-10 Score	1.328 (.437)	3.77 (1.60–8.89)
			Sleep-promoting drug	1.146 (.389)	3.15 (1.47–6.75)
			Wake promoting drug	1.325 (.582)	3.76 (1.20–11.77)
Moderate–high insomnia (ISI 16+)	25.04, $p = .001$	.121–.198	K-10 Score	2.36 (1.08)	10.63 (1.28–88.12)
			Sleep-promoting drug	1.20 (.50)	3.30 (1.23–8.86)
Daytime sleepiness (ESS >10)	10.05, $p > .05$	.050–.083	n/a	n/a	n/a
Fatigue Error	24.06, $p = .001$	.117–.161	K-10 Score	1.01 (.50)	2.74 (1.03–7.31)
			Wake-promoting drug	.974 (.35)	2.65 (1.32–5.29)
Non-fatigue error	7.95, $p > .05$	.041–.065	n/a	n/a	n/a

[a]Estimates here represent Cox & Snell R Square and Nagelkerke R-square values.
[b]Predictors and levels entered into the model: Level 1 (gender, age, K-10 score (High vs Low), Shift work (Y vs N)); Level 2 (wake medications: used in the past month vs not used), (sleep medications: used in the past month vs not used), (medication with sleepiness as a side effect: used in the past month vs not used).

primarily used to treat ADD and/or narcolepsy were the most commonly used wake-promoting agents, with amphetamine and dextroamphetamin salts the most commonly reported substance within this category. While in many cases wake-promoting medications were prescribed to the individual, in a number of cases, these drugs were diverted. Similar to a recent review, which reported that pharmaceutical drugs are most often sourced via close social networks (Hulme, Bright, & Nielsen, 2018), we found that diversion of drugs considered in this article was most common through a family member or friend, followed by purchase(s) over the internet (McCabe & Boyd, 2005; Novak et al., 2016). Diversion of medication may contribute to an increased risk of harm given that use is occurring outside of any professional oversight, or medical supervision (Islam & McRae, 2014; Ogeil, Heilbronn, Lloyd, & Lubman, 2016).

Illicit substances were also reportedly used by participants to stay awake including methamphetamine, cocaine, and MDMA. While these substances have wake-promoting effects, use of these drugs is associated with significant side-effects including an impaired ability to drive and operate machinery safely and/or legally (Davey, Richards, & Freeman, 2007; Matthews, Bruno, Dietze, Butler, & Burns, 2014), and the risk of adulteration (Busardò, Pichini, Pacifici, & Karch, 2016). Similarly, obtaining pharmaceutical drugs via the internet also carries risks if these drugs are tainted, contain inaccurate dose and/or instructions for use (Blackstone, Fuhr, & Pociask, 2014; Monteith, Glenn, Bauer, Conell, & Bauer, 2016), or are contraindicated for use by an individual (Rajagopal, 2016). Also within the wake-promoting category, participants reported using cognitive enhancers, cognitive enhancers, and/or designer drugs. Use of these adds to the growing concern of use of such drugs by students (Teter et al., 2006; Weaver, Hopper, & Gunderson, 2015; Smith et al., 2017) given that the evidence base underlying use of these drugs for this purpose is not clear. For example, piracetam has been used as a cognitive enhancer in patients with an underlying neurological disorder, however any beneficial effect in boosting memory, attention and/or concentration in other populations is unclear (Malykh & Sadaie, 2010). Additionally, while there has been an increasing use of the internet by individuals to obtain drug information (Rajagopal, 2016), many claims made via non-expert sources do not adequately address the evidence-base regarding medications, or tend to focus on benefits without addressing the risks and/or side-effect profiles of drugs (Tyrawski & DeAndrea, 2015).

Benzodiazepines, alcohol, and antihistamines were the most commonly used sleep-promoting drugs. Benzodiazepines are indicated for the treatment of short term insomnia (Holbrook, Crowther, Lotter, Cheng, & King, 2000; Riemann et al., 2015), and were most commonly prescribed to the participant. However, there were also indications that some benzodiazepines were diverted from prescriptions provided to others, carrying similar risks as per the wake-promoting drugs discussed above. While alcohol has been commonly used to promote sleep (Roehrs & Roth, 2001a), its effects in the long-term are detrimental. While initially reducing sleep latency and promoting sleep (Roehrs & Roth, 2001a), tolerance to this effect rapidly develops, resulting in increased doses needed to achieve the same effect which can result in dependence (Roehrs & Roth, 2001b; Chakravorty, Chaudhary, & Brower, 2016).

Despite use of these drugs to overcome sleepiness or promote wakefulness, their use was associated with two important negative outcomes: poorer sleep, and an increased propensity to make fatigue attributable errors. To further investigate this, we examined the components of sleep that were most disturbed. Use of wake-promoting drugs was associated with higher levels of insomnia symptomology and poorer sleep quality, particularly on the following domains: sleep duration, sleep efficiency, use of sleep medication and daytime dysfunction. While the insomnia symptoms may be a side-effect associated with use of a stimulant drug (Ogeil & Phillips, 2015), the poorer sleep quality which is measured over the past month, suggests longer term disruption of sleep and/or non-restorative sleep in individuals. Given potential longer term disruption, this suggests a role for the medical and allied health communities to promote alternative approaches that are not solely reliant on the use of sleep- and or wake-promoting drugs including enhanced lighting in work environments where shift work is common (Chinoy, Harris, Kim, Wang, & Duffy, 2016). Indeed, previous studies have noted that all shift workers would benefit about education around vulnerable times of performance impairment, the use of naps to promote wakefulness, and tips on improve sleep and health practice in general (Wright, Bogan, & Wyatt, 2013).

The finding of increased daytime dysfunction is important; particularly given our regression models also associated this with an increased likelihood of making a fatigue-attributable error. This supports the

findings of previous work describing increased use of psychostimulants associated with higher rates of crashes by truck drivers (Williamson, 2007), with both wake-promoting (Drummer et al., 2004) and sleep-promoting (Drummer et al., 2003) drugs implicated.

If use of sleep-promoting drugs are associated with poorer sleep then why are they being used? While recommended and effective for short-term insomnia (Ashton, 2005), drugs including benzodiazepines are associated with the development of tolerance, and are associated with withdrawal symptoms upon discontinuation (Petursson & Lader, 1981; Brett & Murnion, 2015). It could be that longer-term use of these drugs, which contradicts their prescribed use is associated with such negative effects, given that we asked participants about their sleep in the past month, and found associations with heightened sleep latency. Alternatively, it may reflect the underlying nature of the sleep problems being experienced. For example, while we found that insomnia symptoms were heightened in those using sleep-promoting drugs for which these medications are indicated, there were also increases in sleep disturbances and poorer sleep quality reported, which may not be alleviated by use of these drugs.

Given that we found that a proportion of benzodiazepines were diverted and/or sourced online, people may be choosing to self-medicate a sleep issue by "popping a pill" rather than seeking expert advice. Such a notion fits with a broader emphasis in society on self-management and greater personal responsibility for one's health and health care (Lupton, 1997; Petersen, 1997). Indeed, there is converging evidence from both popular media and academia of people relying on their own internet searches (Rajagopal, 2016), and the experiences of friends and/or family in making decisions to self-medicate for conditions including fatigue and/or a lack of vigilance, rather than seeking out medical expertise (Harmon, 2005; Monteith & Glenn, 2018). To some degree, public health policies and professionals also encourage patients to be digitally engaged and seek out information and be informed about risks, health issues, healthy lifestyles, and how to self-manage issues (Lupton, 1997), and corresponding reports that pharmaceutical companies are spending more on marketing direct to consumers (Applbaum, 2006).

An important finding in the present study is that use of sleep and/or wake-promoting drugs was associated with fatigue-related errors, rather than non-fatigue errors suggesting that there may be a subgroup of people who are reliant on use of these drugs in order to cope with the 24/7 world. Previous studies have suggested that further research is needed to understand the inter-individual variability in sleep-wake responses in populations where this is disturbed (e.g., shift work), in order to identify those vulnerable or resilient to assist them in managing shifts (Van Dongen, 2006; Ogeil et al., 2018), and a strength of the present article is the consideration of a general community of users of these medications rather than shift workers per se. Future work is needed to characterize the types of errors that are being made to determine whether these errors may be associated with a heightened risk of the health and safety of individuals and/or the community.

Limitations and future directions

The present study utilized subjective self-report measures in order to elicit drug use, sleep, and error information from participants. These data may be limited from either a non-disclosure or social desirability bias, and we do not have access to objective data (e.g., Actigraphy) or comprehensive medical records of prescription medication data, past physical and mental health history, or other drug use. However, the present study represents a novel and comprehensive analysis examining both the use and source of sleep- and wake-promoting medications used within a non-clinical or shift work group. The specificity of medications provided by participants, often down to the level of individual drugs and/or preparations demonstrates that they felt comfortable to disclose this information via an online survey.

The present analysis represents a cross-sectional snapshot of how people in the general community, rather than a targeted group from an alcohol or other drug or sleep laboratory per se were using sleep and wake-promoting drugs; hence, their use of these may not be generalizable to the whole population. While we report associations between the use of sleep-and wake-promoting drugs and sleep and performance decrements, we cannot infer causal relationships between these variables nor quantify objectively the drugs used. Any performance or sleep decrements may predate the use of sleep- and wake-promoting drugs, and therefore use of these drugs may represent one marker of sleep problems. However, the present methodology provided participants with a degree of anonymity, which is advantageous when assessing information about illicit drug use (Ogeil, Rajaratnam, Phillips, Redman, & Broadbear, 2011). Previous research has also reported high concordance between

subjective-data (surveys) and objective data (hair sample analysis) (Scholey et al., 2011), suggesting that subjective recall of drug use provides a good proxy when investigating these behaviors.

Additionally, we did not assess participants' chronotype in the present analysis. Previous studies have demonstrated relationships between some sleep and wake-promoting drugs (cigarettes, alcohol) and an evening chronotype. Future prospective studies are needed to investigate how use of these drugs changes over time, and whether this relationship is impacted by circadian factors including chronotype (Whittier et al., 2014), or socio-demographic factors including whether having children or the menstrual cycle (Baker & Lee, 2018) affect these relationships. It may be that the components of sleep affected by use of these drugs changes as a function of when use is considered at different intervals (e.g., weekly, monthly). Future qualitative studies on the reasons why, and circumstances and situations in which people use sleep and wake promoting drugs would also be useful.

Conclusion

Increasingly people are using sleep and/or wake medications in order to help regulate behavior, including when to be vigilant for work, and when to assist sleep. Sources of these drugs are varied, with some representing diverted and or online sourcing that is harder from a public policy perspective to track. Use of such drugs was associated with poorer sleep, and an increased propensity to make fatigue-attributable errors. Taken together, these findings suggest that poor outcomes persist, in spite of use of these drugs, and there are likely individuals struggling to cope with the 24/7 world.

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