The diffusion of Performance and Image-Enhancing Drugs (PIEDs) on the Internet: The Abuse of the Cognitive Enhancer Piracetam

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Introduction: Performance and image-enhancing drugs (PIEDs), also known as “lifestyle drugs,” are increasingly sold on the Internet to enhance cognitive as well as sexual, muscular, attentive, and other natural capacities. Our analysis focuses on the misuse of the cognitive enhancer piracetam.

Methods: A literature review was carried out in PsychInfo and Pubmed database. Considering the absence of peer-reviewed data, review of additional sources of unstructured information from the Internet was carried out between February 2012 and July 2013. Additional searches were conducted using the Global Public Health Intelligence Network (GPHIN), a secure Internet-based early warning system developed by Health Canada and the World Health Organization (WHO), which monitors media reports in six languages, Arabic, Chinese, English, French, Russian, and Spanish.

Results: Piracetam is sold via illicit online pharmacies with no need of prescription at low prices. Buyers, mainly healthy individuals, purchase the product to enhance study- and work-related performances as well as for recreational purposes. Its nonmedical use is often associated with the occurrence of side effects such as hallucinations, psychomotor agitation, dysphoria, tiredness, dizziness, memory loss, headache, and severe diarrhoea; moreover, several users declared to have neither felt any cognitive improvement nor psychedelic effects.

Conclusions: This is a new and fast-growing trend of abuse that needs to be extensively monitored and studied also by using near real-time and unstructured sources of information such as Internet news and online reports in order to acquire rapid knowledge and understanding. Products sold online might be counterfeits and this enhances related health risks.

Keywords piracetam, performance and image-enhancing drugs, addiction, drug abuse, cognitive enhancer, online pharmacies

INTRODUCTION

In recent years, a rapidly spreading of substances known as ‘Performance and image-enhancing drugs’ (PIED), also known as ‘lifestyle drugs’, has been recorded (Evans-Brown, McVeigh, Perkins, & Bellis, 2012). PIEDs are mainly sold online, via illicit online pharmacies, as the most immediate way to enhance cognitive, sexual, muscular, attentive, and other natural capacities, even if their level of safety, composition, and legal status are mostly unknown (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2010; EMCDDA, 2011; Advisory Council on the Misuse of Drugs [ACMD], 2011; Corazza et al., 2011; Schifano et al., 2006; Larance, Degenhardt, Copeland, & Dillon, 2008). These also include a wide range of pharmaceutical products, which can be bought without a prescription and at discounted prices, such as Pregabalin and Adderall (Orizio et al., 2009; Littlejohn, Baldacchino, Schifano, & Deluca, 2005).

In particular, this article will focus on piracetam, a cognition enhancer, which has been abused by healthy individuals to enhance their functions in study- and work-related performances (Corazza et al., 2013; Schifano et al., 2003).

Piracetam is a cyclic derivative of the neurotransmitter γ-aminobutyric acid (GABA), originally marketed in 1971 by UCB Pharma. It was the first ‘nootropic’ drug (Giurgea, 1972), an agent that acts on cognitive function...
without causing sedation or stimulation (Winblad, 2005). It was found originally to be effective as a protective agent in hypoxia-induced amnesia.

Although piracetam is a derivative of GABA, its mechanism of action appears to be unrelated to the properties of this neurotransmitter. Piracetam affects a number of neuronal proteins; some evidence suggests that piracetam can act at the α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor as an allosteric modulator binding in six different positions (Ahmed & Oswald, 2010) and that it may have an effect on N-methyl-D-aspartate receptor (NMDA) glutamate receptors (Cohen & Müller, 1993). However, although the exact mode of action of piracetam is a matter of debate, there is increasing evidence that its underlying effect is to restore cell membrane fluidity (Fassoulaki, Kostopanagiotou, Kaniaris, & Varonos, 1985; Peuvot, Schank, Deleers, & Brasseur, 1995). Restored membrane fluidity induced by piracetam may have a number of physiologic consequences including restored neurotransmission (Winblad, 2005), increased oxygen consumption in the brain (Jordaan, Oliver, Dormehl, & Hugo, 1996), enhanced neuroplasticity (Brandao et al., 1996), neuroprotection (Brandao, Paula-Barbosa, & Cadete-Leite, 1995), and anticonvulsant action (Benesova, 1980).

Consistent with its varied pharmacologic effects, piracetam has documented benefit in a diverse range of indications. The largest amount of data is about the therapeutic use of piracetam to treat early Alzheimer’s disease and age-associated memory impairment (Waegemanns et al., 2002); a large meta-analysis of all available clinical studies provided compelling evidence for the global efficacy of piracetam in a diverse group of older subjects with cognitive impairment (Waegemanns et al., 2002). This proposal was later supported by observations that piracetam specifically enhances membrane fluidity in aged brain material, showing no effect in membranes from young brains (Müller et al., 1997).

In addition to Alzheimer’s disease and age-associated memory impairment, piracetam showed good clinical outcomes in the treatment of a range of neuropsychiatric disorders including vertigo, cortical myoclonus, dyslexia, neuropathic pain, and tardive dyskinesia (Winblad, 2005; Danilova Grafova, & Reshetniak, 1996; Libov et al., 2007).

Piracetam doses usually range between 2.4 g/die and 8 g/die, and even if used in the treatment of cortical myoclonus, it can be administered at higher dosages (up to 24 g/die) (Winblad, 2005).

In this context, the present study aims to identify and investigate the nonmedical use of piracetam, while collecting unprecedented information on its psychoactive effects.

**MATERIALS AND METHODS**

The literature on piracetam misuse was searched in PsychInfo and Pubmed databases. Considering the absence of peer-reviewed data on its misuse, results were integrated with a multilingual qualitative assessment of a range of websites, drug fora and other online resources (i.e.: news- groups, chat-rooms, mailing lists, e-newsletters, bulletin boards and videos). Between February 2012 and July 2013, exploratory qualitative searches of 227 websites have been carried out in English using generic and specific keywords, such as “legal highs”, “research chemicals”, “online pharmacy”, “piracetam”, and “nootropil” in the Google search engine. These websites were monitored on a regular basis, daily (n = 32), weekly (n = 168), or monthly (n = 27) depending on relevance. Links from forums, websites, and other related material, including newspapers and magazines, were followed as well. Additional searches were carried out in the database provided by the Global Public Health Intelligence Network (GPHIN). This is a secure Internet-based early warning system that gathers preliminary reports of public health significance by monitoring global media sources in near ‘real-time’, 24 hours a day, on 7 days a week basis. GPHIN is operated by the Public Health Agency of Canada, and monitors news sources and websites across the globe in nine languages (e.g. English, French, Farsi, Portuguese, Arabic, Russian, Spanish, and Chinese simplified/traditional) (Keller et al., 2009). Although a series of algorithms are used and adjusted to capture relevant information, analysis of relevant data since 2003 was also carried out manually by a multidisciplinary and multilingual team of analysts. Permission for the study was granted by the School of Pharmacy Ethics Committee, Hatfield, UK (15 December, 2010; PHAEC/10–42).

**RESULTS**

Piracetam is sold online via illicit websites with no need for prescription (see Table 1). Some retailers require an initial ‘online consultation’ with an unknown ‘cyber-doctor’ before shipping their products in return for online credit-card payment. Products are then sent directly to the buyers, but these are often counterfeits as recently alerted by the US Food and Drug Administration (FDA) (2010).

Prices of piracetam vary according to the retailers from approximately 0.70 to 1.10 € for 1 gram; it is mainly sold in form of tablets and bulk powder (Nootropic reviews, 2013; Nootrabiolabs, 2013) (Table 1). Videos on the YouTube featuring how to use piracetam, where to get it, its effects and its dosages also emerged from our searches (Piracetam Smart Drug Secret, 2010; Smart drugs make learning easier, 2010; Piracetam Review, 2011).

A summary of the characteristics of the nonmedical use of piracetam is showed in Table 2.

**Piracetam as a Cognitive Enhancer for Nonmedical Purposes**

Piracetam appears to be widely used by healthy individuals to enhance cognitive functions in study- and work-related performances. The majority of the users report satisfactory improvements in different cognitive
functions including learning, memory, concentration, and ‘verbal intelligence’. It is taken orally with dosages up to 9.6 g/die. It is often assumed in comcomitance with other psychoactive supplements including choline, caffeine, Adderall, and acetylcarnitine (Drugs-forum, 2006a; Longecity, 2007; Brainmeta, 2011). A selected number of personal accounts has been reported in Table 3.

**Piracetam as a Recreational Drug**

In addition to its cognition-enhancing features, piracetam is widely used from polydrug abusers for its psychedelic properties. According to online anecdotal reports, it has hallucinogenic and mood-improving effects and appears to enhance dream experiences. It is taken orally at dosages up to 80 g/die or through nasal insufflations at dosages up to 7 g/die. Piracetam is often ingested in combination with other recreational drugs to enhance its desired effects as well as to reduce the emergence of unwanted negative effects and improve sensory feelings. In particular, accounts about its concomitant use with ketamine, methamphetamine, LSD, cocaine, alcohol, and kratom have been recorded (Drugs-forum, 2005; Drugs-forum, 2006b; Drugs-forum, 2009a; Drugs-forum, 2009b; Drugs-forum, 2011; Erowid Experience Vault, 2007; Erowid Experience Vault, 2008). Some relevant user experiences are mentioned in Table 3.

**Unwanted Effects**

Several misusers reported unwanted side effects related to piracetam. The severity of the effects seems to be dose-dependent; however, as the online sources can be imprecise, it is not possible to postulate a clear relation between dosages and effects. The unwanted side effects reported from piracetam misusers include psychomotor agitation, dysphoria, ‘feeling weird’, tiredness, dizziness, memory loss, headache, and severe diarrhoea; moreover, several users declared to have neither felt any cognitive improvement nor psychedelic effects (Drugs-forum, 2005; Drugs-forum, 2006b; Drugs-forum, 2011).

**DISCUSSION**

To the best of our knowledge, this is the first study on the nonmedical use of piracetam, which uncovers previously unknown psychoactive effects.

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**TABLE 1. Examples of piracetam prices reported in pharmacies online**

| Nootropil 800 mg 90 pills | $29.00 |
|--------------------------|-------|
| Nootropil 800 mg 180 pills | $49.00 |
| Nootropil 800 mg 270 pills | $69.00 |
| Nootropil 800 mg 360 pills | $85.00 |
| Nootropil 1200 mg 60 pills | $40.00 |
| Nootropil 1200 mg 120 pills | $75.00 |
| Nootropil 1200 mg 180 pills | $99.00 |
| Nootropil 1200 mg 240 pills | $125.00 |
| Generic Piracetam 400 mg 60 pills | $40.00 |
| Generic Piracetam 400 mg 120 pills | $75.00 |
| Generic Piracetam 400 mg 180 pills | $99.00 |
| Generic Piracetam 400 mg 240 pills | $125.00 |
| Generic Piracetam 400 mg 300 pills | $145.00 |
| Generic Piracetam 400 mg 400 pills | $165.00 |
| Piracetam 100 g bulk powder | $9.99 |
| Piracetam 200 g bulk powder | $19.99 |
| Piracetam 500 g bulk powder | $47.99 |

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**TABLE 2. Summary of the characteristics of the nonmedical use of piracetam**

| Reasons                              | Descriptions                                                                                                                                                                                                 |
|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Online availability                  | Piracetam is easy to purchase over the Internet, where it is sold at a discounted rate and may be adulterated                                                                                               |
| Price                                | Prices of piracetam sold online vary from about 0.70 to 1.10 € for 1 gram;                                                                                                                                     |
| Effects                              | Improvement in learning, memory, concentration, and “verbal intelligence”; mood improvement; enhancement of dream experiences                                                                                             |
| Dosages and way of assumption        | As a cognitive enhancer it is taken orally with dosages up to 9.6 g/die. As a psychedelic drug it is taken orally at dosages up to 80 g/die or through nasal insufflations at dosages up to 7 g/die       |
| Use in combination with other substances | It is often consumed in concomitance with other cognitive enhancers such as choline, caffeine, Adderall, and acetylcarnitine or other psychoactive drugs such as ketamine, methamphetamine, LSD, cocaine, alcohol, and ‘kratom'/Mytragina speciosa |
| Side effects                         | Psychomotor agitation, dysphoria, “feeling weird”, tiredness, dizziness, memory loss, headache, and severe diarrhoea                                                                                      |
| Misusers                             | Misusers are generally students who use piracetam to improve their cognitive performances and/or polydrug abusers who use it to experience a range of psychedelic states |
I am studying Spanish right now pretty intensely, and piracetam is one of many among my supplement arsenal. I can tell you that it is much easier for me to memorize vocab and verbs. Also, I am becoming more and more fluent by the day. I believe that piracetam is enabling me comprehend and converse in Spanish very well. Granted, I took 3 years in high school and 3 quarters in college, but now that I am self-learning “the rest”, it is all coming together quite nicely. Piracetam provides me with extreme focus and an unreal ability to memorize though (Longevity, 2007).

I take 1.2–1.6 g of piracetam 3 times a day 4–5 hours spaced out between dosages. I take around 1.5–2.1 g of choline bitartrate with my breakfast. I would also add some acetyl-l-carnitine to the mix, around 1–3 g a day. The dosage, I believe, have a whole lot to do with the end-product you will experience. Superhuman memory? Well, just as a little marker of results, I’ve been periodically tested my digit span on the brain site. I’m up to 14 now (Treato, 2013).

I’ve used 1000mg of piracetam with 500mg choline source. It works, whatever that means. You feel more articulate and you can literally feel your head throb. I found improved verbal intelligence more than anything. Everything seemed to require less effort, there were less mental blocks etc. I noticed my typing speed improved, although I made more spelling errors (Brainmeta, 2011).

SWIM often used caffeine (500–600 mg) with an attack dose of piracetam (8000 mg) for staying awake at night for learning. The combo works well, it really helps SWIM focus (Drugs-forum, 2006b).

**Effects of piracetam as an hallucinogenic/recreational drug**

Back in the store, the colors and the entire scene stood out to me. In particular, I had a slightly empathic experience where I felt the negative/fear/frustration energies of all the people in the room (Erowid Experience Vault, 2007).

I noticed that the right side of my body is more closed up than the left side and it seemed that I was able to direct an inner energy-flow so that the right side could open up and I became more balanced (Erowid Experience Vault, 2008).

YES YES YES! It has been so relaxing! The music sounded more clear and detailed than usual and my attention was completely in it. I feel unusually fresh and fit, no more tiredness! Suddenly I started to dance spontaneously in my room (on music), just because it felt good, very satisfying! I was much more aware of/incontact-with my body (Erowid Experience Vault, 2008).

The most worthwile use SWIM has found for this substance was for enhancing dreams. 1–2 g taken before going to bed was found to enhance dream recall and vividness, helping SWIM wake more often with the feeling that the night had been at least as long and eventful than the day before in waking reality (Drugs-forum, 2008).

**Effects of piracetam in combination with other recreational drugs**

Yet all of Piracetam + LSD trips had one thing in common — they were profoundly powerful, although LSD dosage was 1/4 to 1/2 of what I usually take without Piracetam (Erowid Experience Vault, 2001).

It increases many folds effects of stimulants and hallucinogens, while decreases or eliminates negative symptoms (Erowid Experience Vault, 2001).

SWIM has found it to inhibit the action of Ketamine, though SWIM wished it had done so more the last time he sat on the edge of a bed trying to persuade his hands to cramp Piracetam pills in his mouth after a 250 mg K nightmare. SWIM has really tried to like that substance but it seems like K and SWIM just aren’t meant for each other (Drugs-forum, 2006b).

Meth is more intense, more happy. I need a lot less of meth, if combining it with 2400 mg of Piracetam. The most important part however is that even though I usually have a very hard crash from meth, accompanied by painful cravings, Piracetam seem to eliminate it totally. I just gradually come down and go to sleep (Erowid Experience Vault, 2001).
of piracetam usually prescribed by physicians (expressed in grams and not in milligrams) and from the general idea that something that is legal (and openly available for sale on the Internet) must necessary be safe (Corazza et al., 2013). Conversely, the misuse of piracetam as a recreational drug seems to be limited to individuals, often marginalized, with a history of recreational polydrug misuse.

From a clinical point of view, although cases of piracetam dependence have not been described, physicians should be aware of piracetam misuse issues, so that signs and symptoms of possible piracetam side effects may be recognized. Moreover, as piracetam is often sold through unreliable online sources, misusers may present with an increased risk of ingesting a range of adulterated products with potential toxic effects (Evans-Brown, McVeigh, Perkins, & Bellis, 2012).

When considering the question of who might use online pharmacies to buy piracetam or other drugs, it is possible to identify at least three prerequisites. These are (1) literacy: using the Internet to order drugs requires basic literacy and numeracy skills; (2) Internet access: the largest increase in Internet access has been seen in those with the highest incomes; and (3) credit card ownership. In summary, these misusers are most likely to come from the socioeconomically privileged sections of society, where high levels of education and employment are likely to be the rule rather than the exception. For these reasons, the stereotypical image of the ‘drug-abusing patient’ may need to change, in favor of a new class of ‘expert’ patients who use a website to obtain a self-diagnosis and a treatment, often without medical prescription.

One could wonder about the limitations of carrying out a risk of misuse assessment of a drug while taking into account the online comments only; in fact, it may be inappropriate to trust information obtained from the Internet without independent verification. However, in the absence of relevant peer-reviewed data, this seems to be the only valid method to obtain preliminary information about new and emerging phenomena (Schifano et al., 2003; Corazza et al., 2013); moreover, the Web monitoring has proved that Internet is an important source of information for understanding users’ point of view about the effects of drugs: writing in a Web forum allows the user to hide his/her identity and to comment without any hesitation.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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THE AUTHORS

Dr Ornella Corazza leads the academic research at the Department of Postgraduate Medicine at the University of Hertfordshire in the UK. Her research interest is in the field of addictive behaviors, mainly substance abuse. She has managed and was awarded the prestigious 2013 Health Award for RedNet, a project funded by the European Commission, which developed innovative methodologies for the prompt identification and dissemination of evidence-based information on new drug trends and cultural/lifestyle issues behind risky behaviors. She has contributed to the generation of original data on over 700 new drugs (or “designer drugs”) presented in 60 peer-reviewed publications, 13 monographs, and numerous invited lectures, seminars, and media appearances. As a consequence of working internationally in different academic environments, especially at the University of Tokyo in Japan, she has developed a unique specialization in the combined fields of health, culture, and legislation. The basic theme of her research is to find out new strategies to enhance our lifestyles by bridging science and Oriental traditions.

Francesco Saverio Bersani is a resident physician at the Department of Neurology and Psychiatry of Sapienza University of Rome and visiting research fellow at University of Hertfordshire. Major areas of interest: biological psychiatry, psychopharmacology, brain modulation techniques, substance misuse, and psychoneuroendocrinology.

Roberto Brunoro is a PhD student at University of Padua. Currently, he is studying the THC misuse in adolescence as a risk factor in schizophrenia, in COMT Val transgenic mice. He gained his Pharm.D. in 2013 at the University of Padua and has collaborated with RedNet project in 2012 as a visiting researcher at the University of Hertfordshire where he studied the abuse of Performance and Image Enhancing Drugs (PIED) among college students under the supervision of Dr. Ornella Corazza and Professor Fabrizio Schifano.
Giuseppe Valeriani is a resident physician at the Department of Neurology and Psychiatry of Sapienza University of Rome and visiting research fellow at University of Hertfordshire. Major areas of interest: biological psychiatry, psychopharmacology, substance misuse, novel psychoactive substances, and behavioral addictions.

Giovanni Martinotti is currently Senior Researcher in Psychiatry and Academic Lead of the Research Unit on Addiction at the Department of Neuroscience and Imaging, University “G.d’Annunzio” of Chieti-Pescara. In his career, he has developed a strong clinic and academic expertise in the field of substance abuse, as well as other forms of addiction including pathologic gambling and behavioral addictions. He is author/coauthor of more than 180 papers on peer-reviewed journals with impact factor and he has published 11 books as editor and one monograph. He is also associate editor of different scientific journals. He has recently been elected president of the Young Section of the Italian Society of Psychiatry.

Professor Fabrizio Schifano is one of the very few physicians with training and specialist qualifications in both psychiatry and clinical pharmacology and has contributed to the biomedical science as well as the clinical science of addiction. He has also made a significant contribution to several areas in addiction psychiatry and general psychiatry, including: stimulant addiction psychiatry and general psychiatry of substances, and behavioral addictions. He is author/coauthor of more than 185 papers on peer-reviewed journals with impact factor and he is a range of substances used to enhance cognitive as well as sexual, muscular, attentive, and other natural capacities.

Cognitive enhancers are drugs to treat cognition deficits mainly used in patients suffering from Alzheimer’s disease, schizophrenia, stroke, attention-deficit hyperactivity disorder, or aging.

Nootropics: The term nootropics was coined by the father of piracetam Corneliu Giurgea in 1972; it derives from the Greek words “nous”, meaning “mind”, and tropein, meaning “to bend/turn”.

Novel psychoactive substances: Novel (or new) psychoactive substances (NPS) are an ever-increasing group of synthetic, semi-synthetic, or natural compounds, often advertised and sold as ‘legal’ and ‘safer’ alternatives to illicit drugs.

Online pharmacies: Online pharmacies are often illicit online shops selling medications of possible counterfeit nature without any medical prescription or control.

PIEDs: Performance and image-enhancing drugs (PIEDs) are a range of substances used to enhance cognitive as well as sexual, muscular, attentive, and other natural capacities.

Piracetam: Piracetam is a cyclic derivative of the neurotransmitter γ-aminobutyric acid (GABA). It was the first “nootropic” drug, originally marketed in 1971 by UCB Pharma.

Recreational Drugs Use: Recreational drug use is the use of a drug (legal, controlled, or illegal) with the intention of enhancing life (increasing euphoria, blocking unhappy memories, or creating pleasure).

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GLOSSARY

Cognitive enhancers: Cognitive enhancers are drugs to treat cognition deficits mainly used in patients suffering from Alzheimer’s disease, schizophrenia, stroke, attention-deficit hyperactivity disorder, or aging.
and excellence to face the rapid diffusion of Novel Psychoactive Substances (NPS) in the EU: The outcomes of the ReDNet project. Human Psychopharmacology, 28(4), 317–323.

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