

Lifestyle drugs, mood, behaviour and cognition

Simon N. Young, PhD

Co-editor-in-chief, *Journal of Psychiatry & Neuroscience*, and Department of Psychiatry, McGill University, Montréal, Que.

According to a recent article in *Nature Medicine*,¹ the market for lifestyle drugs is forecast to rise from its current \$20 billion to over \$29 billion by 2007. As a result of this booming market, companies have invested over \$20 billion in research on such drugs since the 1990s. Obviously, lifestyle drugs have important financial implications, but what exactly is a “lifestyle drug”? The above-mentioned article defines lifestyle drugs as medicines that treat conditions associated with lifestyle; examples include drugs to treat weight loss, smoking, impotence, baldness and the effects of aging, as well as medications that improve mental agility. This definition is not satisfactory, however. An antipsychotic medication will certainly improve the lifestyle of a patient with schizophrenia and therefore fits the definition, but the term lifestyle drug obviously has a somewhat different meaning.

The controversy about lifestyle drugs was stimulated mainly by the use of fluoxetine (Prozac) and sildenafil (Viagra). In the case of fluoxetine, the issue was its use in people who did not fulfill the criteria for a psychiatric disorder. However, although paroxetine (Paxil), another selective serotonin reuptake inhibitor (SSRI), is not usually considered a lifestyle drug when it is used to treat depression, the popular press has certainly written about it as a lifestyle drug when it is used to treat social anxiety disorder. Obviously, social anxiety disorder is not considered to be on par with disorders such as depression or schizophrenia. This is despite the fact that social anxiety disorder is clearly defined, is closely related to other anxiety disorders and can cause considerable disability.

Lexchin² addressed some of the controversies sur-

rounding lifestyle drugs and discussed 2 definitions of lifestyle drugs offered in a recent report.³ The first is any drug intended or used for a condition that falls into the border zone between medical and social definitions of health. The second is any drug intended to treat a disease that results from a person’s lifestyle choices. The second definition certainly does not fit with the way the term is typically used — baldness and social anxiety disorder are not the result of lifestyle choices. The first definition is better, but not entirely satisfactory. Attempts to treat baldness and enhance mental agility are not matters of health, but preference.

Two factors seem to be important when the term “lifestyle drug” is used. The person taking the drug perceives that it will increase her or his happiness, and the person using the term, or a significant portion of society, does not consider the target symptom or symptoms to be a “real” disease or disorder. This raises the issue of what is and is not considered a disease. In a survey reported in the *British Medical Journal* in 1979,⁴ various groups were asked whether they considered certain conditions to be diseases. The percentages of medical academics who did not consider schizophrenia, alcoholism and depression to be diseases were about 20%, 40% and 50%, respectively. However, attitudes have probably changed over the past 2 decades, particularly in relation to depression. More recently, the *British Medical Journal* ran a vote on *bmj.com* to identify the “top 10 non-diseases.”⁵ The top 6 were aging, work, boredom, bags under the eyes, ignorance and baldness. Unhappiness came in at number 14 and loneliness at 20. Although most would agree that unhappiness and loneliness are

Correspondence to: Dr. Simon N. Young, Department of Psychiatry, McGill University, 1033 Pine Ave. W, Montréal QC H3A 1A1; fax 514 398-4370; simon.young@mcgill.ca

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not diseases, they are feelings that most people would prefer not to have and can predispose to diseases. But to what extent should unhappiness, as opposed to clinical depression, be something that is treated with a drug?

Attempts to increase happiness through pharmacology go back to our earliest history with the use of alcohol, the cannabinoids and other naturally occurring compounds. The extensive use of drugs of abuse is, in part, a short-sighted attempt to increase happiness. The future will see increasing demand for drugs that increase happiness and do not have the adverse effects of the older drugs. The debate about the use of fluoxetine in people without a DSM disorder will pale in comparison with the debates that will ensue with the discovery of drugs that raise mood in mentally healthy people, with limited or no side effects. Will such drugs really be discovered? The idea that a single compound could raise mood; decrease blood pressure, cortisol and subjective responses to acute psychological stress; and increase the frequency of sexual intercourse in healthy young adults (particularly in women) without any important side effects is one that invites skepticism. However, if results in recent issues of *Psychopharmacology*⁶ and *Biological Psychiatry*⁷ are to be believed, such a compound already exists. It is high-dose (3 g/d) ascorbic acid. There is also accumulating evidence that the omega-3 fatty acids in fish oils have beneficial effects on mood and behaviour that may not be limited to the treatment of psychopathology. If ascorbic acid and fish oils can have these effects, surely other more effective but still nontoxic compounds will be discovered.

The debate about lifestyle drugs that influence the brain is caused in part by the continuum in some areas between normal and abnormal functioning. This is an issue that psychiatry has grappled with for a long time — for example, in debates about the boundaries of an adjustment disorder and the extent to which bereavement precludes the diagnosis of depression. Many people now accept that those suffering the extremes of depressed mood have a disorder for which treatment might be appropriate. However, the characterization of paroxetine as a lifestyle drug when it is used to treat social anxiety disorder suggests that there is less acceptance of the idea that extreme shyness is a disorder. Once there is acceptance of the need for treatment of conditions at the extremes of the distribution curve, there is often debate about those that deviate less from the norm. As society accepts increasingly that depression is a disorder for which pharmacological treatment

is often appropriate, the debate moves on to the degree of unhappiness for which a pharmacological intervention is appropriate. The next step is to consider if or when it is appropriate to use chemicals to change a neutral mood to happiness or increase the degree of happiness. A similar debate has already started in the area of memory and cognition. A recent review in *Nature Reviews Neuroscience*⁸ entitled “Smart Drugs: Do they work? Are they ethical? Will they be legal?” lists 9 classes of drugs that are currently under investigation as cognitive enhancers and discusses some of the issues related to the use of such drugs by people whose cognitive abilities are in the normal range.

The development of drugs that healthy people may take to enhance their mental state creates considerable problems for regulatory agencies. Even for one of the original lifestyle drugs, alcohol, there is little agreement on how it should be regulated. Some countries use total prohibition, and others place limits on where it can be sold, the age of those who can buy it and when and where it can be drunk or increase taxation to decrease the amount sold. In some situations, regulations owe more to tradition than to rational consideration of risk and benefit. Current governmental regulations permit a 9-year-old who is about to take an exam to buy and ingest a mixture of 2 compounds, both of which may enhance exam performance. The mixture comes in the form of a cola, and the 2 compounds are caffeine and glucose. Caffeine can enhance arousal and attention, but can also enhance anxiety and, in excess, can cause insomnia and a variety of other symptoms. Caffeine dependence can occur, although withdrawal symptoms are relatively mild. If caffeine was not used traditionally and it was proposed as a cognitive enhancer today, the chances of it being approved for use in children would be small. The memory-enhancing effect of glucose in humans is now well established.⁹ Glucose intake can decrease the intake of micronutrients and is associated with obesity and diabetes. It also would not likely be approved as a cognitive enhancer in children. Caffeine, like alcohol, certainly seems to fit some of the definitions of a lifestyle drug, even if it is not usually considered one. People have a strong attachment to these drugs; attempts are often made to overcome the regulations concerning alcohol, and any attempt to regulate the use of caffeine would be unthinkable. When drugs are developed that provide the benefits of these compounds and none of their adverse effects, people will acquire them by legal or illegal means. There needs to be a

debate on an appropriate regulatory framework for the use of mood and cognitive enhancers by healthy people.

As far as regulatory policy is concerned, there are likely to be 4 different types of lifestyle drugs.

- **Drugs approved for specific indications** (e.g., baldness or social anxiety disorder). They are classified as lifestyle drugs because of a feeling in society, that may or may not be justified, that pharmacotherapy for these types of problems is in some way frivolous.
- **Drugs, approved for specific indications, that are used for other purposes.** At the moment, the main examples of this are the SSRIs, which are sometimes used in people who do not have a DSM disorder. However, in the future, this class will probably include other drugs approved for the treatment of mood or cognitive disorders but used by those anywhere in the normal range to enhance their mood or cognitive ability. They will be used in this way because some physicians will be willing to write prescriptions for these drugs, even for people who do not have a disorder. They will also be taken by people who obtain them through illegal means.
- **Drugs that have been used traditionally** and are therefore not usually thought of as lifestyle drugs but are taken for the purpose of altering mood or social behaviour in people who may or may not be mentally healthy. This includes illegal drugs of abuse, as well as those that are legally sanctioned, such as alcohol and caffeine.
- **Natural products.** Potential examples of this category include ascorbic acid and fish oils, but also include a wide range of other products, such as herbal extracts. These are minimally regulated by governments unless they are clearly toxic or specific claims are made by the manufacturer about their actions. Use of this type of product depends on information, sometimes correct, about their actions that is distributed by anyone other than the manufacturer. Overall, the regulations are based more on factors such as traditional patterns of use and whether the product is synthesized by living organisms or by drug companies than on consideration of the implications of the use of lifestyle drugs for the individual and society.

Before a rational and consistent policy for the regulation of lifestyle drugs is developed, there has to be much more consideration of the desirability of enhancing mental states to please the individual. Currently, the main focus is on the adverse effects of drugs of abuse, because those are the main drugs taken to alter mental state in

those without psychopathology. However, with the development of compounds that enhance normal mood or cognition, but have limited or no adverse effects, the potential positive aspects have to be considered. One issue that has been raised is whether the increasing use of lifestyle drugs is an attempt to homogenize society.² Should those who are less smart or less happy accept the mental state allocated to them by their genes and environment, or should they be allowed to take compounds that will move them toward the upper half of the distribution curve? Is popping a pill for mild dysphoria an abrogation of personal responsibility? Is taking a pill to move mood from mildly happy to euphoric acceptable in any circumstances, if the pill has no direct adverse effects? Should parents be allowed to help their children gain a university education in part through pharmacology if the only adverse effect to the parents and child is financial? Or should society be paying for all children to take cognitive enhancers if ones without side effects or adverse effects are ever developed?

Society has not to any great extent attempted to come to grips with issues such as these. Meanwhile, there are increasing signs that more effective and less toxic lifestyle drugs will be developed long before there is any broad agreement that will enable rational and consistent regulation of them. This is a sharp contrast with some other areas of research, such as genetics and reproductive technologies, where the ethical and societal implications of research developments, as well as proposals for keeping regulations responsive to new discoveries, have been widely discussed.

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