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# **Review** article

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#### ABSTRACT

*Objective:* To review the effects of methylphenidate on cognitive enhancement, memory, and performance in medical students.

*Methods*: A review of four databases (LILACS, PubMed, ScienceDirect, and SciELO), analyzing the title and abstract of all articles published between 1990 and 2012 in English, Portuguese, and Spanish. Selected articles were read in entirety, including in the review those that met the established criteria.

Results: The prevalence of use among medical students reached 16%, with no gender difference. Most students began using the drug after entering the university, and the reasons cited to justify it are related to enhancing academic performance.

*Conclusion*: There is no evidence in the literature that the use of methylphenidate is beneficial in terms of memory or learning. The drug simply increases wakefulness and alertness, reducing the time of sleep.

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# Uso de metilfenidato entre estudantes de medicina: revisão sistemática

# RESUMO

*Objetivo*: Revisar o uso de metilfenidato em estudantes de medicina hígidos, abordando a prevalência, variáveis demográficas, motivos e possível melhora do desempenho acadêmico desta população.

Métodos: Realizou-se uma revisão nas bases de dados LILACS, PubMed, ScienceDirect e Sci-ELO, analisando-se o título e resumo de todos os artigos publicados entre 1990 e 2012 nos idiomas inglês, português e espanhol. Os artigos selecionados foram lidos de forma integral, incluindo-se na revisão aqueles que atenderam aos critérios determinados.

Resultados: A prevalência do uso em estudantes de medicina chega a 16%, não havendo diferença entre os gêneros. A maioria dos alunos iniciou o uso após ingresso no nível superior e os motivos citados para justificá-lo estão relacionados à melhora do desempenho acadêmico.

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Conclusão: Não existe evidência na literatura contemporânea que o uso de metilfenidato é benéfico em relação à memória ou aprendizagem. A droga apenas torna o usuário mais desperto e alerta, reduzindo o tempo de sono.

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# Introduction

The university is an environment that encourages learning and research to develop science. Higher education thus requires a high level of work and dedication by students, especially in medical school. After six years at university, graduating medical students have to undergo an exam to qualify for a residency. This makes medical school highly competitive.<sup>1</sup>

Under these circumstances, healthy college students have been using psychoactive substances to allow them to study for longer hours and to optimize their academic efficiency.<sup>2</sup>

Stimulant drugs are used to increase energy level and concentration, diminishing the need for rest. The most often used medicine is methylphenidate hydrochloride, which stimulates the central nervous system (CNS) and acts by blocking dopamine reuptake and by releasing dopamine and norepinephrin into the synaptic space. In Brazil, this drug is commercialized as Ritalin<sup>®</sup> (Novartis) and Concerta<sup>®</sup> (Janssen-Cilag).<sup>3,4</sup>

Legal indications for the use of methylphenidate are restricted to children diagnosed with attention deficit and hyperactivity disorder (ADHD) in whom the drug improves attention. The United Nation's 1971 Psychotropic Substances Convention classified methylphenidate as a psychotropic drug with a risk of abuse and dependence, hence its prescription is controlled.<sup>3,5</sup>

Due its probable benefit to cognition, methylphenidate is frequently used for non-medical reasons, mainly among university students, since university requires a high standard of work and the students must stay awake for longer periods.<sup>1,6</sup>

#### Objectives

The main objective of this article is to review the usage of methylphenidate in healthy medical students, addressing the prevalence, demographic variables, reasons for use, and possible beneficial effect on academic performance.

### Methods

A systematic research was performed in four databases (LILACS, PubMed, ScienceDirect, and SciELO), including all articles published between 1990 and 2011 written in English, Portuguese, or Spanish. The key words used for the research were "Methylphenidate", "Ritalin", "Methylphenidate" AND/OR "Students", "Methylphenidate" AND/OR "College students", "Methylphenidate", "Ritalin" AND/OR "Students", "Ritalin" AND/OR "College students", "Ritalin" AND/OR "Students", "Ritalin" AND/OR "College students", "Ritalin" AND/OR "Students", "Ritalin" AND/OR "College students", "Ritalin" AND/OR "Medical students".

The following exclusion criteria were applied: publication before 1990, case reports, series case reports, articles that ana-

lyzed populations other than college students, and articles that did not analyze methylphenidate.

Articles included in the study were analyzed concerning the prevalence of psycho-stimulating drug abuse, demographic variables among users (gender, age, undergraduates or graduates), reasons for use, possible benefits, period in which methylphenidate use began, route of administration, and knowledge about the drug.

#### Results

The total number of articles retrieved using the keyword results of four databases was 875. Five of the articles were found in LILACS, 38 in SciELO, 93 in PubMed, and 739 in ScienceDirect (Table 1).

The title and abstract of these articles were analyzed, and those that did not discuss the proposed topic were excluded. A total of 21 articles were selected and thoroughly analyzed according to the exclusion criteria. 12 articles did not meet the criteria and were excluded (Fig. 1), resulting in the inclusion of nine articles in this review: one from LILACS, three from SciELO, four from PubMed, and one from ScienceDirect (Table 2).

#### Prevalence

Studies that evaluated use of methylphenidate at least once in lifetime identified a prevalence between 8.3% and 9%, while for those studies that asked questions about use in the last year, the prevalence ranged from 3% to 16%.<sup>1,2,5–7</sup> In one of the articles, 14.5% of medical students answered positively to the question "Have you ever used methylphenidate to improve academic performance?".<sup>7</sup>



Fig. 1 - Research results.

| Table 1 – Number of articles found in each database. |        |        |        |               |  |  |  |
|--|--------|--------|--------|---------------|--|--|--|
|  | LILACS | SciELO | PubMed | ScienceDirect |  |  |  |
| Methylphenidate                                      | 5      | 38     | 6,200  | 13,785        |  |  |  |
| Methylphenidate + college students                   | 2      | 0      | 30     | 1,091         |  |  |  |
| Methylphenidate + students                           | 2      | 1      | 93     | 2,889         |  |  |  |
| Methylphenidate + medical students                   | 0      | 0      | 7      | 739           |  |  |  |
| Ritalin  | 3      | 3      | 6,250  | 2,244         |  |  |  |
| Ritalin + college students                           | 1      | 1      | 30     | 315           |  |  |  |
| Ritalin + students                                   | 0      | 0      | 94     | 669           |  |  |  |
| Ritalin + medical students                           | 0      | 0      | 7      | 251           |  |  |  |

#### Demographic variables

Regarding gender, results vary according to the study. Teter et al.<sup>1</sup> did not identify a difference between males and females. Bogle et al.,<sup>8</sup> however, noticed a higher prevalence among male college students, while dos Santos et al.<sup>9</sup> identified a higher prevalence in females.

As to ethnicity, a higher prevalence was found among whites (7%), followed by Asians and blacks.<sup>1,8</sup>

The correlation between the use of methylphenidate and average academic grades showed a greater prevalence of use in the group of students with a lower grade average.<sup>6</sup>

#### Reasons

College students use CNS stimulating agents for recreational reasons in order to increase time awake and disposition for leisure, to lose weight, and finally to enhance cognitive performance and, consequently, to improve professional and academic achievement.<sup>3</sup>

According to Teter et al., the main motives for the illicit use of methylphenidate are to improve concentration (65.2%), help studying (59.8%), and increase wakefulness (47.5%). Other reasons described were recreational as narcotics (31%), experimentation (29.9%), and to stay awake.<sup>1</sup>

According to Habibzadeh,<sup>6</sup> who evaluated medical students in Iran, 41.7% of those who used methylphenidate did so in order to help concentration. Other reasons for using were, in decreasing order of importance: to stay alert, for curiosity, to have more energy, to have higher self-confidence, due to environmental pressure, and to lose weight.

Results of an American review performed in Maryland show that the reasons for using methylphenidate included better intellectual performance (23%) and for greater efficiency while performing academic tasks (22%).<sup>5</sup>

According to a study by Uregon,<sup>7</sup> at Manizales University the most frequent reasons to consume methylphenidate are, in decreasing order: personal pleasure, social pressure, curiosity, friends' influence, to avoid fatigue, and finally for recreational reasons. Other reasons cited in the article include use in order to lose weight, and the association of methylphenidate use with alcoholic beverages.<sup>1,4</sup>

#### Benefits

A single dose use of methylphenidate showed benefits for memory; however, this result is not maintained after prolonged abuse of the drug. Other outcomes often analyzed, such as attention, mood, and executive functions, did not show any difference when comparing students who used the drug with others who denied use.<sup>4</sup>

#### Initial use

When students were asked at what time they began to use the medication, most of them (65.2%) reported that the first time was during college. Only 34.8% had already used methylphenidate before attending university. It is noteworthy that these groups have different reasons for using the drug. Those who began to use methylphenidate during college describe an academic purpose, such as increased concentration and to help studying. On the other hand, the group that began to use methylphenidate before college did that as a narcotic, to lose weight, or even to discover its effect.<sup>1</sup>

Among the students who used methylphenidate for the first time during college, its use varied during the school year. Periods close to exams or the end of semester, due to final exams, are associated with a higher demand for prescription stimulants, especially methylphenidate.<sup>6</sup> In the article by Mazzoglio et al., when only the group that reported the use of stimulating substances was analyzed, 65% reported that they start studying the subject in the last three days before the exam.<sup>2</sup>

#### Administration routes

Methylphenidate has different forms of commercialization, of which pills or liquid solution, which can be administered intravenously or nasally, are highlighted. Among these different types and routes of administration, pills are the most

| Table 2 – Article analysis for inclusion. |        |        |        |               |       |  |  |
|---|--------|--------|--------|---------------|-------|--|--|
|   | LILACS | SciELO | PubMed | ScienceDirect | Total |  |  |
| Total articles                            | 5      | 38     | 93     | 739           | 875   |  |  |
| Selected articles                         | 2      | 3      | 8      | 8             | 21    |  |  |
| Included articles                         | 1      | 3      | 4      | 1             | 9     |  |  |

common for non-medical conditions, corresponding to 95.3% of use. Next, in terms of prevalence, is the nasal route; the least common route is intravenously.<sup>1,6</sup>

# Discussion

Neural enhancement is a term used to describe improvement of cognitive, emotional, and motivational functions in healthy subjects, acquired by different types of intervention. If this enhancement is achieved by psychopharmaceutical substances, it is called pharmacologic neuroenhancement.<sup>4</sup>

Pharmacological neuroenhancement has increased in the academic environment, mainly among college students, to such an extent that the use of psychostimulating drugs to improve academic performance is considered a public health problem in various countries.<sup>1,7</sup> American data from 2003 estimated that 4.1 million people above the age of 12 had already used methylphenidate at least once in their lifetime without a medical prescription.<sup>5</sup> Moreover, drug production and consumption has steeply increased in the last decades. According to the United Nations report on the production of agents,<sup>10</sup> the worldwide production of methylphenidate increased from 2.8 tonnes in 1990 to, almost, 38 tonnes in 2006, and the United States was the main producer and consumer.

In Brazil, consumption has also increased over the years. In 2000, the Brazilian national consumption was around 23 kg, and the Brazilian production increased from 40 kg in 2002 to 226 kg in 2006.<sup>11</sup> Unofficial information conveyed in nonscientific media shows that this major rise turned Brazil into the second leading in the world for methylphenidate prescription.

Nevertheless, there is little Brazilian medical literature on this subject, with few articles published in specialized magazines. In Brazil, this subject is more widely discussed in the lay media than in scientific literature. The media publishes texts based on a single specialized opinion, or on the ideas of non-specialized people, without any scientific foundation to allow for consistent conclusions about the Brazilian national standard of use.<sup>3</sup>

Stimulants vary according to their pharmacokinetic and pharmacodynamic properties, and their benefits for patients diagnosed with ADHD are incorrectly extrapolated to healthy individuals who aim for a better academic performance. Methylphenidate is a CNS-stimulating agent whose use without a medical prescription has increased steeply.

A non-medical use of a neurostimulating drug is defined as the use of a drug prescribed by a doctor, but at a different dosage than recommended, or drug use by a different person who does not have a medical prescription.<sup>5</sup> The second definition includes most college students who admitted to methylphenidate abuse in order to enhance academic performance, and increase concentration and alertness.<sup>6</sup>

Current literature does not allow for a definite conclusion on the potential benefits of this medicine in non-ADHD subjects. Existing studies does not show consistent evidence of the optimizing effects on the CNS; however, one article suggests a positive effect of methylphenidate on the working memory.<sup>4</sup> Contrary to popular and college students' beliefs, there is no evidence that methylphenidate increases attention. Attention is defined as a proper allocation of mental procedural resources in response to relevant stimuli.<sup>4</sup> It is believed that the effect of methylphenidate to better target and focus on stimuli occurs due to the greater release of dopamine in the CNS.

One of the possible reasons for the low efficiency of methylphenidate as a neuroenhancement drug for healthy individuals is that most studies used 12m to 20 mg doses. This is probably a sub-dose for the expected effects of the drug. However, there is no scientific study comparing the effects of different doses on academic performance.<sup>4</sup> In pathologies in which methylphenidate is proven beneficial, the indicated dosage is 20 mg to 30 mg a day in patients who suffer from narcolepsy, and the dose can be increased until a limit of 40 mg to 60 mg a day. In children with a diagnosis of ADHD, the initial dose is approximately 5 mg to 10 mg daily, and in cases that require higher doses, it should be gradually raised to a maximum of 60 mg a day.

Another probable cause of failing in academic enhancement is the fact that the drug is mostly used three days before the tests. This method of studying impairs academic performance, since the amount of information to which the student is exposed during the period just before exams is higher than the amount that they are able to acquire in such a short time.<sup>2</sup> Besides, stimulating agents, in these cases, make it even more difficult to learn because the individual becomes euphoric and wakeful, preventing the adequate amount of rest that is required for memory consolidation.

Besides little scientific support to advocate methylphenidate use by healthy individuals with no medical indication, even fewer studies analyze its possible side effects. Those that evaluate this issue describe the side effects as benign, such as tachycardia not followed by hypertension.<sup>4</sup> Only one study cited possible severe side effects, including visual hallucinations, dyskinesias, triggering of mania syndromes, and also Tourette's syndrome.<sup>8</sup> Furthermore, other less severe drug-related side effects include vertigo, sleepiness, headache, lack of appetite, nausea, anxiety, stomach pain, and sleep disorders. No scientific article described the possibility of pharmacological addiction, emotional distress, and long-term intellectual deficit.<sup>2</sup>

The opinion of college students about stimulating medicine, its possible benefits, and forms of use is based on information obtained in the lay media and from the opinion of friends.<sup>3</sup> Therefore, the level of knowledge about the physiological and psychological side effects and legal consequences of its illicit use is below the expected, suggesting that this topic has not been sufficiently discussed in the curriculum of modern medical schools.<sup>6,9</sup>

## Conclusion

Current literature does not present sufficient evidence to support methylphenidate use among healthy college students in order to improve cognition. There is no evidence that it enhances the capacity for memorization or associative learning. The drug appears to increase waking hours. Thus, expectations about its efficiency exceed its real benefits. In addition, users often fail to mention the side effects of methylphenidate abuse. Finally, the development of clinical, educational, and preventive strategies to reduce the illicit prescription of psychostimulating agents should be included in the curriculum of Brazilian universities and colleges as an initiative of the faculty and the institution.

# **Conflicts of interest**

The authors declare no conflicts of interest.

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