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Prevalence of antidepressants and biosimilars in elite sport – a follow-up study

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Abstract

Antidepressants are not prohibited by the World Anti-Doping Agency for the use in elite sports since the deregulation of amineptine in 2003. A study by Machnik et al. indicated a rise in antidepressant usage by athletes. Based on this survey a follow-up research was initiated to investigate the onward usage of these substances in relation to the general population.
From 1999 to 2011 approximately 116,000 doping control samples from 236 sporting different disciplines were analysed for the presence of antidepressants with an analytical-chemistry-based screening procedure routinely used by WADA-accredited laboratories by means of gas chromatography-mass spectrometry. Assessing the results for elite sport, prescription data for the general population were consulted provided by the German statutory health insurance.
The prevalence of antidepressants in elite sports (0.35%) was well below the medication in the general population (2.25%). The results revealed a steady rise from 1999 to 2006, an abrupt increase in 2007 and 2008 followed by a decrease in 2009 to 2011 to the level of 2007. Most of the detected substances belonged to the class of selective serotonin reuptake inhibitors. The dimension of depressive disorders in elite sports remains vague according to the study design. There is no indication for an application of antidepressants as neuroenhancement by athletes to a greater extent.

Introduction

Being the most prevalent psychiatric diseases, depressive disorders arise from a complex and multi-factorial disharmony in social and chemical structures. More recent theories allocate permanent stress a major role in the genesis of mental disorders [1]. Proven in severe depressive disorders, however, the effectiveness of antidepressants (AD) in mild versions or healthy subjects is controversial. Indeed healthy humans and athletes use those substances to sustain daily routine and as neuroenhancement [2,3]. Nevertheless, the administration of ADs is not prohibited by the World Anti-Doping Agency (WADA) since 2003 [4].
A study by Machnik et al. prescribed an increasing AD usage by elite athletes from 1999 to 2008 [5]. Based on that survey, the aim of this study was to evaluate the progress of AD use in elite sport in relation to the general population.

Experimental

Doping control samples of the Doping Control Laboratory of Cologne from the years 1999 to 2011 were re-evaluated for the presence of ADs. 115,903 samples out of 236 different sporting disciplines were obtained from male (69.3%) and female (23.0%) athletes and unspecified gender specimen (7.7%). Double testing of the same athlete cannot be excluded. The disciplines were categorized by their main character to seven categories: (1) athletics, (2) disability sports, (3) endurance, (4) fighting, (5) miscellaneous, (6) power&strength, (7) teamsports.
The sample preparation followed a validated routine screening procedure for the detection of unconjugated neutral and basic compounds. This method is described elsewhere [6]. Briefly, 1-(N,N-diisopropylamino)-n-dodecane as internal standard and approximately 3 g sodium sulphate were added to 5 mL urine under alkaline conditions (pH = 14) and the analytes were extracted with 2 mL tert-butylmethylether. The analysis was performed on a combined system of gas chromatography-mass spectrometry and gas chromatography-nitrogen-phosphorus detector (GC-MS/NPD).

 ISBN 978-3-86884-038-4

The finding of an AD user was proved by the detection of either parent compound or a metabolite. All relevant AD were detected, except for opipramol and duloxetine due to the molecular structure.
Data for the general population (GP) were obtained from annuals of the statutory health insurance in Germany [7].

Results and Discussion

In 0.35% of the samples, in total 405, at least one AD was detected. The results revealed a slight increase from 1999 to 2006, an obvious increase in 2007 and 2008 followed by a decrease in 2009 to the level of 2007 (Figure 1, right scale). Male and female specimens were equally effected (data not shown).
According to the statutory health insurance approximately 1.5% male and 3% female insurants obtained a prescription for an AD [8]. Contrary to the athletes, the prescriptions of the GP aged 15-35 years showed an even development with a steady increase thenceforward 2006 (Figure 1, left scale). Substantial differences between the methods used to obtain the data have to be considered.

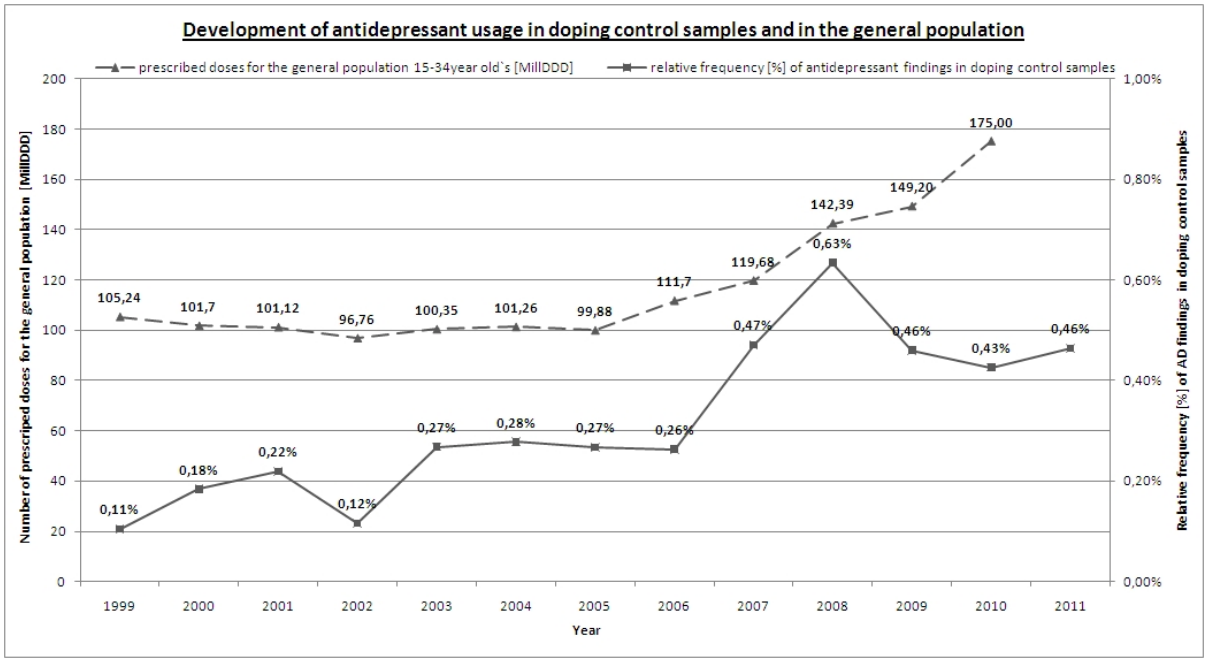

Figure 1. Development of the prescription data for AD for the reference population aged 15 to 34 years [7] and of the relative frequencies [%] of AD findings for doping control samples in the years 1999 to 2011

The categories endurance and power&strength revealed a higher prevalence according to the average (Figure 2). The high amount in disability sports was likely due to the low number of analysed samples. The categories fighting and teamsports were below the average relative frequency.
In total 58 distinct disciplines (24.6%) were affected. They enfolded 88.9% of the samples. The prevalence was highest in cycling (1.07%), powerlifting (0.80%) and handball (0.72%). Affecting other sports to a minor extent, in basketball (0.51%), athletics (0.40%), weightlifting (0.28%) and football (0.17%) ADs were detected as well (data not shown).
25 distinct substances were detected in elite sport. The annuals provided 26 different AD. Being different for the minor utilised substances, the frequently used ADs were reported in athletes and in the GP (Figure 3). Noticeable was the high proportion of selective serotonin reuptake inhibitors (SSRI) in comparison to the tricyclic antidepressants (TCA) in the athletes group (58.21% vs. 13.43%). For the GP those substance classes were almost equally prescribed, with a slight advance for the SSRI (37.35% vs. 29.47%). Regarding the different age distribution of the GP, the taking of distinct ADs cannot reflect the consumption of athletes. In contrast to the TCA, SSRI have a better side-effect profile. They do not cause weight gain and fatigue and are better tolerated.

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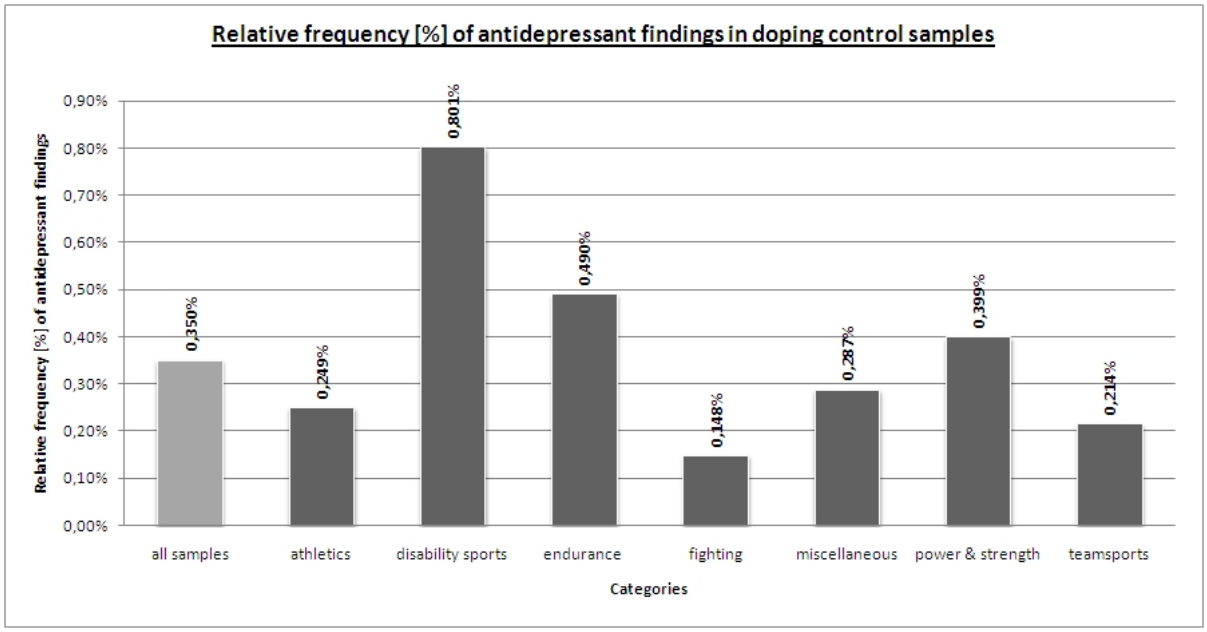

Figure 2. Relative frequencies [%] of AD findings in doping control samples in distinct sporting disciplines from 1999 to 2011

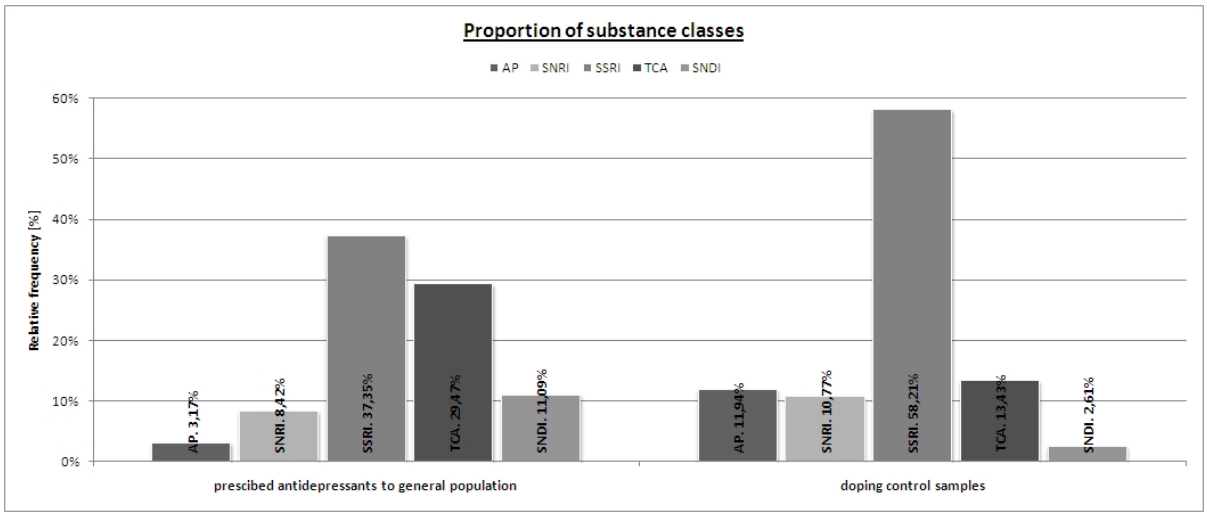

Figure 3. Proportion of distinct substance classes for frequently prescribed respectively detected AD for the general population [7] and in elite sports; (AP) antipsychotic, (SNDI) serotonin noradrenalin disinhibitor, (SNRI) serotonin noradrenalin reuptake-inhibitor, (SSRI) selective serotonin reuptake-inhibitor, (TCA) tricyclic antidepressant

Exceeding the prescription data fivefold, the most frequently detected AD in elite sport was fluoxetine (23.1% vs. 4.5%) (data not shown).

Conclusions

Compared to the prescription data of the general population, the prevalence of AD, detected in doping control samples of elite athletes, was considerably lower. Restricting the comparison, the methods used to obtain the data were substatial different. However, the extent of mental disorders in elite sport remains vague according to the study design and the method used. Mild depressions do not necessarily require a medication with AD. Contrary, there is currently no indication for an application of AD as neuroenhancement in elite sports to a greater extent.

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