

The evolution of European legislation on doping: new challenges in the age of NPS

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Abstract. – The fight against doping in sport, formally started in 1960 with the constitution of the International Olympic Committee (IOC) and culminated in 1999 with the birth of the World Anti-Doping Agency (WADA), commissioned to chair various activities, including the publication of the annual list of prohibited substances and methods for doping.

In Europe, as early as 1967, the Committee of Ministers of the Council of Europe adopted a resolution to stigmatise the intake of substances foreign to the body for the sole purpose of artificially and unfairly influencing sports performance. In 2002, the Council of Europe adopted an Additional Protocol to the 1989 Strasbourg Convention against Doping to ensure mutual recognition of doping controls and to strengthen the enforcement of the Convention.

In Italy, the Law of 14 December 2000 n. 376 "Discipline of the health protection of sports activities and the fight against doping", defines doping as "the administration or intake of drugs or biologically or pharmacologically active substances and the adoption or submission to medical practices not justified by pathological conditions and suitable to modify the psychophysical or biological conditions of the organism in order to alter the athletic performance of athletes". The same law regulates the use of drugs or biologically or pharmacologically active substances and update an annual list in agreement with WADA. The article aims to analyse the legislation from a national perspective, offering as complete a view as possible of the current situation.

Key Words:

Sport, Doping, European legislation, Italian legislation, New psychoactive substances (NPS).

Introduction

Doping is not a discovery of modern society, on the contrary, it is a very ancient practice

that has been known since the time of the first Olympics. In classical culture, sporting success also had a political and cultural significance, and athletes who brought glory to their country were deified. In fact, it seems that as early as the Olympic Games of 668 BC, or among the athletes of ancient Rome, it was common to take natural stimulants to increase physical performance.

In the 19th century, Dutch sailors were given substances (known as 'doop' in Dutch language) to make them braver when facing bad weather at sea¹.

From the term 'doop', in the 20th century the verb 'to doop' and the noun 'doping' were coined, referring to the practice of using performance-altering substances in sport.

With the advent of the pharmaceutical industry in the 19th century, new substances appeared on the market which, taken in certain doses, showed doping effects: alcohol, strychnine, caffeine, opium and nitroglycerine, the latter of which was probably linked to the first doping-related death, that of cyclist Arthur Linton in 1896².

From the 1960s onwards, with the advent of amphetamine-based stimulant drugs, a progressive 'state' legitimisation of the use of doping substances was observed, defined as the phenomenon of 'state doping'³. In few words, the systematic and studied use of doping substances, especially by athletes from Warsaw Pact countries⁴. This phenomenon involved the technical and pharmacological evolution of the chemical doping substances, starting from the use of the now obsolete amphetamine type substances to the current use of innovative compounds such as anabolic steroids, capable of significantly increase muscle performance.

At the seventeenth Olympic Games in Rome (1960), there was the first fatal event in the history of the Olympic Games, when a Danish cyclist died for a strong dose of amphetamines and a nicotine acid derivative. Other cases, such as the death of Tony Simpson at Mont Ventoux in 1967 at Tour de France, after having taken amphetamines, strongly affected the public opinion. The phenomenon continued to grow and began to threaten all sports, undermining the very foundations of the Olympic thinking and ideal. The sports world, concerned by the rapid expansion of doping, tried to circumscribe its effects and set limits.

The fight against doping in sport began formally in the 1960s, when the International Olympic Committee (IOC) established a Medical Commission responsible for developing a list of prohibited substances and methods, culminating in 1999, with the creation of the World Anti-Doping Agency (WADA). WADA was established as a single independent international agency composed and funded equally by sport movements and governments of the world, with the aim of promoting a universal Anti-Doping Code (or Code) that synchronized anti-doping policies among all stakeholders. Its key activities were established as scientific research, education (promoting preventive and educational actions), development of anti-doping capacities (harmonizing scientific and technical standards and procedures for analyses and equipment), and monitoring of the Code. The Code entered into force in 2004.

De facto, WADA delegates the anti-doping territorial activity to the Nations and to the ADOs (Anti-Doping Organizations), controlling that their action complies with the Code.

Specifically, as reported by the same WADA, “the Code is the core document that harmonizes anti-doping policies, rules and regulations within sport organizations and among public authorities around the world. It includes, among others, the list of prohibited substances and methods.

Even though the Code has to be approved by the National sport authorities of member states joining Olympic Games and international sport meetings, the code “*per se*” is not a law. In order to join international sport events, National sport authorities of member states have to agree to the principles of the Code, to implement and comply with the Code and finally to enforce rules and policies in accordance with the Code.

In this review, we report the evolution of European and Italian legislative scenario concerning legislation of doping including critical issues in

the Italian anti-doping regulatory framework and national criminal code and concluding with some remarks on new challenges for the sport medicine physicians such as neuromodulation, brain stimulation with the new health risks for athletes in the light of the recent SARS-CoV-2 pandemic.

The European Legislative Scenario: from the Strasbourg Convention to Italian Law 376/2000

The birth and development of the doping phenomenon has certainly had a difficult path, not only due to the evident opposition and obstacles raised by those sports federations that considered competitive exaltation as a decisive element for the lustre of their country, but also because behind the doping phenomenon, an ‘illegal’ market had in fact been created on which to profit⁵. In addition, the continuous and constant evolution of substances that affect the psychophysical capacities of sportsmen and women made the work of the legislator on duty difficult. It was therefore crucial to establish a clear and unambiguous definition of doping. The first official definitions of the term date back to the early 1960s and are clearly expressed first by the Dutch Federation of Sports Testing Centres in 1961 while, in the following year, the German League of Sports Physicians defined doping as: “*any drug, whether effective or not, intended to increase performance in competition*”⁶. In the same year, Italy, by analogy with the German declaration, considered doping to be “*the taking of substances designed to artificially increase a competitor’s performance in a competition, to the detriment of his sporting ethics and his physical and mental integrity*”⁷. Between 1964 and 1989, the subject in question was addressed by many medical commissions, sports federations, scientific committees and the Committee of Ministers of the Council of Europe, which set out the definition in the 1967 Resolution 12⁸. The issuing of such a Resolution thus highlighted the desire to make the Governments of the European Union Member States aware of the need to adopt measures and behaviour based on the indications and guidelines codified therein⁹.

The year 1989 resulted fundamental in the fight against doping in sport with the creation of a European Convention against doping which, in addition to establishing the standards to define doping in sport, also established which pharmacological classes and methods are prohibited. On 16 November 1989, in Strasbourg, in the presence

of the member states of the Council of Europe, the “Strasbourg Convention”, also known as the “Anti-Doping Convention”, was drawn up with the aim of reducing and even eliminating doping in the world of sport. However, it should be noted that, if some European countries – including Italy – have shown greater attention to the phenomenon, it is still difficult to foresee a prospect of harmonisation of the legislation, especially in the criminal field.

Countries, such as France, Sweden and Italy pursued a more ‘interventionist’ policy in the fight against doping, while northern European countries such as Great Britain and the Netherlands have adopted a more tolerant approach. By going into detail on the various European regulations, it is possible to better understand the fracture points between the two schools of thought. France’s approach to doping has always been considered important and innovative: as early as 1965, France tried to combat the phenomenon with Law 65-412¹⁰, which was considered to be a forerunner of all current European legislation. However, in spite of this law and its decree of 10 June 1966 and the further law 89-432 of 28 June 1989¹¹, the continuously renewed legislation did not succeed in being incisive in controlling and repressing the doping phenomenon. Therefore, the French Parliament issued law No 99-223 of 1999 on the ‘protection of the health of sportsmen and sportswomen and the fight against doping’, which is still one of the strictest and most intransigent laws in the European regulatory panorama. Sweden has also always been very sensitive to this issue, partly because of the strong sense of sporting loyalty that has always characterised Swedish sporting tradition. Thus, in 1991, Sweden passed Law No. 1969, which provided for a list of prohibited substances to be formally drawn up and for which the attempted sale, production and/or purchase of prohibited substances was made punishable¹².

On the other hand, the more permissive and tolerant northern European view, is undoubtedly that of the British and Dutch governments.

The Netherlands has always had a permissive attitude towards drugs, especially the so called “soft” drugs, which has also been reflected in the possibility of use of substances intended for sports athletes. In the Netherlands, therefore, there is up to now no anti-doping legislation and the use of doping substances by sportsmen and women is not punishable under criminal law. The only criminally relevant aspect concerns the sale

of drugs or substances prohibited by law, which is therefore prosecuted by the Dutch judiciary and investigative bodies¹³. The British approach is different, but also permissive, and is followed by independent bodies such as the *United Kingdom Sports Council Doping Control Unit* and the official anti-doping body *UKAD United Kingdom Anti Doping*¹⁴. The main weakness in the UK legislation lies in the nature of the institutions involved which are devoid of ‘governmental’ authority, but are rather based on a private type of relationship, hence unable to be effective enough in the role they were designed for, with an obvious level of inefficiency in combating the phenomenon in question¹⁵.

Nevertheless, it is worth bearing in mind that the European Parliament approved another resolution (PE 205.677) calling on the Member States to adopt supplementary legal provisions prohibiting doping in sport. Finally, with the International Convention against Doping in Sport, adopted in Paris at the XXXIII Unesco General Conference, held on October 19, 2005¹⁶, all the signatory countries of the aforementioned UNESCO Convention were obliged to comply with the principles enshrined in the World Anti-Doping Code adopted by WADA¹⁷.

The Evolution of Italian Legislation on Doping, from the Strasbourg Convention to Law 376/2000

Italy began to deal with the subject of doping and the relative prohibited substances through the promulgation of Law No. 1099 of 26 October 1971¹⁸ and the subsequent decree of the Ministry of Health of 5 July 1975¹⁹. This law, however, presented a real “Achilles’ heel” in the regulatory system, in consideration of the fact that although it recognised doping as a crime, it never resulted in criminal prosecution. In addition, in 1981 the offence of doping was decriminalised by Law No 689/1981²⁰, creating a regulatory chaos in the attempt to interpret other laws r to prosecute the offence of doping. This is the case of the challenge relating to Article 1 of Law No. 401/1989, which dealt with the issue of fraud in sporting competition²¹. The interpretation and challenge of this law was the subject of analysis and study by the Court of Cassation, which in fact declared that it did not apply to the offence of doping²². However, even if the Court of Cassation with its judgments did not succeed in undermining a criminal system integrated into the connective tissue of Italian

sport, it must be acknowledged that these two regulatory provisions, Law No. 1099/1971 and Law No. 409/1981, played the role of repression towards doping conduct prior to the legislative intervention of Law 376/2000. In the meantime, the awareness of the consequences in terms of health of the immoderate and inconsiderate use of these substances led the Italian Parliament to ratify the 1989 Convention with Law 522/1995²³. In this regulatory chaos, the subject of doping became the prerogative of the sporting system and in particular of the Italian National Olympic Committee. It is clear, therefore, that in the event of a violation and/or transgression, the consequences from a legislative point of view might have been different depending on the state system, focusing primarily on the protection of the citizens health, or the sporting legal system, which based its principles and values on the fairness and correctness of sporting competitions. The transgression of the 'state' hypothesis would be punished with the implication of criminal aspects, whereas the sporting legal system would only have the power to impose suspensions, fines, etc.

At the end of the 1980s, Italy for the first-time defined doping as: "*the use by the professional or amateur athlete of exogenous interventions implemented with the intention of improving performance outside of the adaptation induced by training*"²⁴. The phenomenon of doping was taken up by the Italian Parliament through a bill presented to the Senate in 1998 (legislative initiative no. 3412/1998), which, while leaving the bill 1797/1998 unchanged, went to intervene where there seemed to be a "regulatory hole" in the criminal code. Specifically, there was a need to place the rules that would result from the new draft law within the Criminal Code, in particular with an addition to Article 445 concerning "administering medicines in a manner dangerous to public health". These aspects would therefore have implemented Article 446 with an area relating to 'offences against public safety'²⁵ and 'offences of common danger by fraud'. However, the Bill 3412 of 1998, compared to the previous legislative initiatives, proved to be new in its contents and substance: the new regulatory intervention clearly identified the type of offence and established the relative penalties, leaving, however, to the sports system the tasks which are proper to it, among which the prevention, the control of the illicit activities and the subsequent, if provided for by the respective regulations, imposition of

the disciplinary sanctions provided for.

Italy, along with other states, including France, which had already addressed the issue of doping in 1965, began to take on board the messages of the 1989 European Anti-Doping Convention, issuing its own legislation to combat the phenomenon²⁶.

In the last two decades, in Italy, anti-doping rules are laid down in Law 376 of 14 December 2000 '*Disciplining the health protection of sporting activities and the fight against doping*', which is considered to be a regulatory cornerstone, especially with the issuing of its implementing regulations, established thanks to a ministerial decree in 2002, which, when it came into force, immediately had to interface and comply with the 'WADA Code'.

From its very first article, Law 376 of 2000 clearly establishes what is meant by doping, but above all, introduces those criminal aspects of the phenomenon that were previously underestimated, while at the same time creating a control commission capable of understanding which substances can create a doping effect. The criminal issue, which is extensively regulated by this law, focuses not only on public health, but also on the person or persons who procure drugs or biologically active substances not justified by pathological conditions²⁷.

Critical Issues in the Italian Anti-Doping Regulatory Framework

The analysis of the entire Italian legislation on the subject of combating the phenomenon of doping, the administration of prohibited substances and the receipt of such substances, shows how it was originally a vice of the legislator to 'armour' with rigid and slow regulatory instruments a phenomenon which instead evolves with an often-unpredictable speed. This is demonstrated by the need to coordinate national and transnational, legislative and technical-specialist sources, which could somehow bridge the pharmacological and scientific gaps inherent in the doping phenomenon. This necessity translates into a 'six-monthly' updating of the ministerial tables that establish which substances and practices are fully covered by the practice of doping. This is not always easy, given the complexity of identifying substances that are always new, sophisticated and difficult to identify^{28,29}. Moreover, the heart of the legislative apparatus 376/2000 is referred to constantly evolving ministerial tables drawn up by the Ministry of Health, which only serves to create an area of regulatory uncertainty that fuels doubts and uncertainties as to what constitutes lawful

and unlawful conduct. Moreover, the tables are continuously updated not only on new pharmacological substances, but also on scientifically questionable physiotherapy practices and on new chemical elements, all of which creates a very wide margin of interpretation that could inhibit a real action of contrast to those behaviours which are criminally relevant³⁰.

Doping, Sporting Offence and Crime

There are a number of contradictions between Italian sporting legislation and existing national legislation on doping, such as Law 376/2000 and the articles of the Criminal Code relating to the offences of fraud, receiving stolen goods, etc.

The sporting offence of doping is a case of violation of the anti-doping rules laid down in the WADA code. However, this code, which was created to standardise the world anti-doping regulatory system, has been transposed differently by each State. It can therefore happen that one country decides on its own to interpret the WADA Code differently from another country. This 'interpretative autonomy' of the WADA Code is probably due to the scarcity of anti-doping controls in most of the member states, but also to the adoption in many cases of the minimum sanctions of the legislation in question. In addition, the ownership of the punitive claim with penal repercussions is the exclusive competence of the State; this makes the system of control and repression "sport-criminal" asynchronous. The crucial point that distinguishes the sports offence from the related criminal offence is based on the principle of imputation. The criminal system only penalises presumed or actual autodoping and heterodoping conduct and the attempt to commit it. It follows that, from a purely criminal point of view, the possession of doping substances is not a criminal offence, except to the extent that the qualifying elements of a legally relevant attempt are present. But the element which represents the real point of fracture in the criminal system is ascribable to the absence of a real form of sanctioning towards that athlete and the structure connected to him (staff, athletic trainers, reference doctors) who refuses to submit to anti-doping controls, an element supported by the Constitutional Court ruling No. 238 of 1996³¹. According to this judgment, together with the absence of penalties provided for by Law 376/2000 for athletes who refuse to undergo anti-doping controls, no sentence can be imposed on 'doped' athletes. Moreover, the legislation in force does not provide for any penalty for the purchase and

possession of prohibited substances with a view to their transfer. Another aspect which renders the current legislation ineffective in combating the phenomenon in question is that of 'collaborators with justice'. In fact, there is no reduction in punishment for those who cooperate in investigations. This not only makes law enforcement even more difficult, but also hampers investigative activities 'before and after' the crime. This lack of cooperation with the investigating authorities does not allow to understand and therefore to adequately fight the *modus operandi* of the organisational system that manages the traffic of doping substances and the commercial phenomena that revolve around the figure of the athlete³².

It is therefore clear that the legislation in force and the criminal law system would be inadequate without the real contribution of sports law, which provides for the application of disciplinary sanctions in the event of an athlete's refusal to submit to biological samples.

In the two regulations, the concept of the subjective element comes to the fore. This element becomes the key to understanding how the same issue is dealt with differently. In the offence of doping, it is essential to have the concept of general intent, i.e., the full awareness and at the same time the will to engage in conduct that is punishable under criminal law: this translates both into the will to alter competitive sporting performance (through the use of illegal substances and/or methods), and through a change in the results of doping controls. This, however, does not apply to sporting offences, since the subjective element and the relevant investigation are not sufficient for the imposition of penalties.

New Challenges for the Sport Medicine Physicians

In modern sport, measures are taken to improve an athlete's physical performance that are not always respectful of sporting ethics. Recent discoveries in the field of neuroscience suggest that the abilities underlying sporting performance can be improved using technologies that modify brain activity. These may include motor learning, increased muscle strength or increased fatigue tolerance.

In fact, devices are already available on the market that can produce changes in short or long-term performance by modulating brain activity during training, leading to benefits comparable to those induced by the use of drugs/doping substances. In the light of this, one wonders what role

the doctor should play in a context where there is no clear and uniformly recognised legislative line in a society where the consumption of new psychoactive substances such as Smart Drugs^{28-30,34-36} is increasing, or the methods of administration are changing³⁷⁻⁴⁰. Such an evolution has forced law enforcement agencies to adapt their detection^{41,42} and screening methods in order to meet such new challenges^{43,44}, particularly during the COVID-19 pandemic⁴⁵.

In order to answer this question, the concept of neuro-enhancement should be better framed, and above all it should be clarified to what extent it is to be understood as a cure or as the result of a desire aimed at achieving a sporting/professional result. Particularly when the subjects being treated are considered 'healthy' and therefore the potential side effects of drugs and/or physical practices should not be overlooked, with potential permanent long-term damage.

According to some authors, the sports doctor must not subject the athlete to medical treatments which, although not prohibited by legal or regulatory provisions, produce an artificial alteration in athletic performance or induce in the athlete an unnatural condition; the sports doctor should also be reserved any decision on the athlete's participation in a competition, without any interference from third parties⁴⁶ and, given the central role played by the doctor, as the person responsible for the athlete's health, the potential risks and effects on the central nervous system caused by substance abuse in subjects considered healthy cannot be overlooked.

Neuromodulation and the Role of the Sport Medicine Physician

The field of neuromodulation (pNE) is the subject of numerous studies of great scientific interest, but at the same time it is not fully understood, and its possible negative consequences should be faced with particular caution, and therefore, regulated. Neuropotentiation or 'brain doping' can be pharmacological or non-pharmacological. In the first case, it involves an attempt by healthy individuals to increase their state of attention and alertness, learning and memory, and to improve mood and behaviour by taking prescription drugs. In the second case, however, PNE is achieved through surgical, neurotechnological (low frequency transcranial magnetic stimulation – LF-rTMS, transcranial direct current stimulation – tDCS, deep brain stimulation with depth electrodes, and CNS

interfaces) or behavioural approaches⁴⁷. As the post-war generation ages, there is an increased demand for and development of drugs for the treatment of neurocognitive disorders such as Alzheimer's disease, and these drugs are used off-label or abused not to restore a pathological state but to further improve or optimise a physiological state, as advocated by pNE. In light of this, the last definition of Health formulated by the World Health Organisation (WHO) in 1946 as 'a state of physical, mental and social well-being and not merely the absence of disease or infirmity'⁴⁸ no longer fits the current aims of health policies. Therefore, a change in emphasis of the definition towards the ability to adapt and self-manage in the face of physical, social and emotional challenges has been suggested^{48,49}. In conclusion, it is generally accepted that pNE is used by healthy individuals, with the subjectivities that the term 'health' provides, on the other hand, the drugs used for pNE are the same as those used to treat defined disease states and that the motivating factors for pNE do not meet these criteria. It is therefore necessary to clarify whether pharmacological/therapeutic strategies aimed at treating severe pathological conditions should be made available in the context of 'psycho-aesthetics' or 'cosmetic neurology' for the sole purpose of enhancing performance at work/sport, or whether we should be more restrictive and therefore only allow curative interventions, i.e., those that presuppose an underlying psychophysical pathology. The legal and, above all, deontological role of sports and non-sporting doctors should be aimed at monitoring the type of substances taken or practices carried out, the doses, the timing of application, the abuse and its prolongation, without neglecting any prodromal signs of a possible cerebral modulation. For example, in the United States, data on the one-off prevalence for non-medically indicated use of prescription stimulants varies from 5 to 35 %⁵⁰, without indicating what personal goals and specific desirable expectations of the application are. Therefore, the use of these technologies, especially with regard to possible sporting and/or professional applications, should be regulated, i.e., it should be made clear when neurostimulation should be considered lawful and when it should be considered neurodoping.

Areas of Application of Brain Stimulation

In the absence of an ethical framework in which to consider the phenomenon of doping,

the issue has been discussed for decades in view of competitive sport. One of the most frequently invoked arguments against the use of doping substances in sport concerns the competitive advantage they create in those who use them⁵¹⁻⁵³. Therefore, if on the playing field, an athlete's victory or defeat is decided in the laboratory, then the competitive arena would be uneven because the athletes would not be playing on equal terms. It is therefore often concluded that doping in sport is a form of cheating as it gives the doped athlete an unfair advantage over those who do not use doping substances or methods⁵⁴.

As far as neuromodulation is concerned, there are essentially two levels of application in sport and these are divided into immediate gains resulting from increased cortical excitability, and long-term gains resulting from stimulation during training.

In the 'acute' phase of stimulation, studies show that the athlete develops greater motor capacities including improvement in fatigue time⁵⁵, response time⁵⁶ and suppression of muscle tremor⁵⁷. These effects are best documented in those subjects who undergo neuromodulation by transcranial direct current stimulation (tDCS), the effects of which reach a peak after the end of stimulation and gradually diminish in approximately 20-60 minutes. Therefore, it is possible to imagine a time when an athlete could undergo a 'hit' of stimulation before starting a possible competition and have a competitive advantage in terms of performance and response to fatigue greater than an athlete who does not use it. A second use concerns the acquisition of new skills⁵⁸⁻⁶⁰. Sporting performance, especially at the highest level, requires good technique and timing and involves skills learned during training. Therefore, improving learning efficiency during training will be of greater benefit during competition. These effects are particularly noticeable among students who use inotropic substances to improve academic performance. Studies have shown that in the United States, the non-medical use of methylphenidate and amphetamines on university campuses affected 25% of the student body in 2004⁶¹. The most commonly cited reasons for routine use of these substances included 1) improving concentration (58%) and 2) increasing alertness (43%). Among men and women, the patterns of pNE application do not appear to differ significantly. In addition to classic oral intake, other, non-oral routes of application such as injections and intranasal administration have also been described⁶².

However, these para-oral routes of administration often appear to be associated with the use of other illicit drugs, e.g., ecstasy, cocaine, cannabis and amphetamines⁶³⁻⁶⁵.

New Health Risks for Athletes in the Light of the Recent SARS-CoV-2 Pandemic

In the light of the recent pandemic and the socio-economic difficulties experienced by the world's populations, one wonders about the reasons that may have altered the well-being of many athletes and whether demanding or seeking drugs to act on these aspects was always a legitimate act of care. The 2020 Tokyo Olympics, postponed because of the SARS-CoV-2 emergency, have affected the lives and training of many athletes who have had to prolong and adapt their training to the postponement of the world event. This requirement has undoubtedly burdened many sportsmen and women and has required not only physical but also mental efforts to the point of resorting to pharmacological and psychological support⁶⁶⁻⁶⁹.

Today we are increasingly witnessing one of the sequelae of COVID-19, with which many health care professionals are or will inevitably be confronted, namely Long Term Covid. This pathological condition, unlike neurological damage related to SARS-CoV-2 infection, is characterised by symptomatic persistence 4-12 weeks after illness. Among the post-disease symptoms, an increase in depression, anxiety and suicide has also been observed, conditions which the sports physician himself will be able to interface with and which he will have to differentiate from other psychological conditions that may not have a pathological substratum at their base⁷⁰.

In view of the above and in light of the latest research findings on the subject, it seems necessary for WADA to make itself heard and take a stand on the issue of neurostrengthening, in order to safeguard the three fundamental principles of the World Agency, but above all for the protection of the health of all those athletes who currently use neurostrengthening practices without shared safety standards and may even fall ill as a result of a wait-and-see attitude⁷¹.

Neuropowering: When can it be Considered Neurodoping?

Today, neurostimulation and neurostrengthening practices are being used more and more frequently, both in the working environment and in amateur and competitive sport, in order to im-

prove one's neural performance. This raises the question of when neurostimulation can be defined as doping and when it cannot. According to the World Anti-Doping Agency (WADA), one criterion for banning a drug in sport is whether or not it poses an actual or potential risk to an athlete's health. For example, chronic use of anabolic steroids can lead to liver disease⁷² and cardiovascular complications often with adverse outcomes⁷³.

Neuroenhancement, a term referring to the improvement of cognitive⁷⁴, affective and motor skills, refers to the use of legal or non-prescription psychoactive substances by healthy individuals with the intention of enhancing neuronal activity. It can be mental and cerebral, pharmacological and non-pharmacological⁷⁵.

In the sporting sphere, it consists of improving the psychophysical/professional performance of athletes through the use of substances or instruments aimed at improving some kind of cerebral or mental function with significant benefits during sporting activity⁷⁶⁻⁷⁸.

According to some authors⁷⁹, it is necessary for each sports club to decide whether the use of neuro-enhancement techniques is to be considered doping or a legitimate aid to training and thus to the athlete's performance. For others, however, the legalisation of neural enhancement is not considered to be a fair choice, as it creates inequalities in the chances of victory between athletes who do and do not use neurostrengthening techniques⁸⁰, for others still, it would not represent a threat to the integrity of sport and sportsmen and women in general⁸¹.

In line with the latter theory, it can be argued that neurodoping adds little to the performance of elite athletes who are already performing as they are close to the physical limits allowed by the human body and therefore may not be taking real advantage of the potential benefits of brain stimulation.

Not all sports, however, require commitment and muscular effort. This is the case for chess competitions, in fact, some authors argue that improving mental endurance could eliminate chess from being a sport, although they consider the criminalisation of practices that are not considered harmful in any case to be disproportionate⁸². Overall, transcranial direct current stimulation (tDCS) is considered to be a technique that promises to improve performance without posing significant health risks to athletes⁸³. However, the effects of tDCS are considerable and growing. However, there is no simple and easily accessi-

ble way to reliably detect whether a person has recently experienced brain stimulation. Reported damage to the central nervous system would be diagnosed and confirmed, at currently very high costs, through the use of magnetic resonance spectroscopy (MRS), which is a technique capable of detecting alterations in the concentrations of metabolites and related neurotransmitters, and thus may have the ability to detect the possible use of neurodoping⁷⁹. Anodal and cathodal tDCS modulate GABAergic and glutamatergic processing differently⁸⁴, whereas deep transcranial magnetic stimulation (TMS Theta-burst) appears to affect inhibitory feedback from gamma-aminobutyric acid (GABA) but does not affect excitatory glutamatergic stimulation⁸⁵. When the region of the brain targeted by TMS or tDCS is specifically observed, detectable changes in chemical composition, i.e., in brain metabolite concentration, are in the order of 10% at MRS. Therefore, the diagnosis of neurodoping requires not only ultra-specific instrumentation, but also a high level of diagnostic accuracy capable of detecting the slightest movement of brain metabolites. These reasons, as well as the high costs of production and use, are some of the reasons why the MRS is of little practical use in the diagnosis of neurodoping. Secondly, MRS is not able to perform a thorough and detailed analysis of the entire brain, as it is necessary to identify a candidate brain region for comparative and simultaneous comparison. Finally, brain changes resulting from stimulation may not be distinguishable from normal performance-related changes per se, so the risk of false positives is high. Especially when one considers the cognitive and motor acts of sports performance, which are extreme versions of the activities of an individual's daily life. There is obviously a large gap between those who wish to rehabilitate motor functions after brain injury or physical trauma, and those who aim to improve sporting skills for competitive purposes.

Ethical Issues

Currently, despite the widespread use of pNE, there are numerous, predominantly illicit, ways of acquiring pNE drugs or accessing pNE methods. It is important to emphasise the questionability of pNE drugs obtained on the black market, as it is difficult to establish whether they meet the quality criteria of the drugs originally prescribed, and therefore whether they pose a huge risk to the health of the individual and to public health in general⁸⁶. It might be tempting to speculate

that legalising the pNE market could reduce or eliminate a black market and be beneficial to the safety aspects of pNE use. However, this potential positive effect of legalisation seems to be short-sighted for several reasons. In practice, it is illusory that there will be worldwide agreement on legalising the pNE market. There is fundamental country- and region-specific differences in tradition, attitude and philosophy regarding the aspect of neuroenhancement and its pharmacological modulation. Regulatory/legal differences persist as well, although attempts have been made towards harmonisation in general⁸⁷. In addition, there would be no systematic monitoring of the potentially harmful long-term effects of pNE drug use and a lack of proper consumer information. Another concern would be the interaction with other drugs, which could have devastating consequences for patients, especially if, as is the case on the black market, consumption occurs without medical supervision or advice. In the worst case, with users suffering from pre-existing conditions, the short- and long-term adverse effects of pNE use could lead to life-threatening acute conditions or exert chronic somatic and/or mental damage. A special, non-self-related ethical issue of pNE is related to its altruistic use by, for example, doctors, surgeons, nurses, caregivers, soldiers, pilots, air traffic controllers, police officers and firefighters in national or global emergencies/catastrophes. This has become urgent these days as the COVID-19 pandemic wears on. Even in such circumstances, however, it must be clear to the managers, supervisors and professionals involved that pNE can use pose serious health risks.

Conclusions

The different views on ethics and the related medical, legal and social issues have been controversially discussed in the past, and the ethical aspects and dilemmas associated with doping in healthy individuals are the subject of a debate that is still ongoing and will probably not come to an end if the aim is to manage the phenomenon through a regulatory system that is slow to evolve and always outdated in relation to the pharmacological and scientific progress that revolves around the doping phenomenon.

With regard to pNE, its regulated and managed use in a hospital environment can bring significant benefits in the rehabilitation of physical,

mental and social health related to circumstances that depend solely on a pathological substratum. In contrast, its use in healthy subjects does not meet these criteria. The fact that our current socio-cultural environment forces people to use pNE to cope with the physical, mental, and social implications in a rapidly changing digital world suggests that our current working and living environment is unhealthy and pathogenic. A necessary consequence would be to redefine and adapt our work-life philosophy and to systematically provide and implement powerful and effective resilience tools. Clearly, with the exception of emergency situations, pNE is not an option in healthy individuals, considering the potential side effects of taking drugs, socio-cultural consequences and ethical implications. Again, from the perspective of drug regulation, the benefit/risk is always negative as the risks, i.e., the potential side effects always outweigh the benefits.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

All authors contributed, read, and approved the final version of the manuscript.

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