Comment on the article by Zaami et al "Increasing abuse of anabolic steroids and chemsex drugs as performance and image-enhancing agents". Eur Rev Med Pharmacol Sci 2021; 25: 455-458

F. UMANI RONCHI, M.C. VARONE, G. RALLO

Department of Anatomical, Histological, Forensic Medicine and Orthopedic Science, "Sapienza" University of Rome, Rome, Italy

Dear Editor,

We have read with great interest the commentary titled "Increasing abuse of anabolic steroids and chemsex drugs as performance and image-enhancing agents"1, and we believe that the insightful remarks and warnings laid out therein take on even greater relevance against the backdrop of the ongoing SARS-CoV-2 pandemic. There is no denying that the unprecedented and broad-ranging magnitude of the pandemic has laid bare or exacerbated substance abuse disorders mental distress both in those already afflicted by such maladies and in "new" sufferers, whose mental health has become vulnerable and unsteady, making such individuals susceptible to substance abuse tendencies. Social and economic hardships, in addition to restrictions and containment measures, have been found to severely affect mental health, particularly in vulnerable population segments, such as the unemployed² or those whose livelihoods were jeopardized by the crisis and ensuing closures and restrictions. Such negative trends^{3,4} have been recorded in previous economic crisis as well. difference in nature, and scale notwithstanding. Higher levels of stress stemming from uncertainty and worry, in addition to anxiety and isolation, can make substance abuse, addiction and relapse more likely. Recent findings⁵ have shown high increases in alcohol abuse (23%) and drug abuse (16%) related to the pandemic for people who already used substances prior to the pandemic. Alarmingly, the dynamics which have been unfolding since the pandemic started disrupting our daily lives have made users of image-enhancing drugs more likely

to spiral into mental illness, addiction and potentially harmful habits⁶. That is hardly surprising, since social interactions have largely shifted to video and social networks, and physical appearance is scrutinized like never before7. Not only are people concerned, or even anxious, about how others may judge their appearance, but are themselves becoming unreasonably critical about how they look. Such overblown concerns and anxiety haunt them in ways that are totally different from the feelings linked to face-to-face interactions8. Again, lockdowns, stay-at-home mandates and the inability to engage in physical activity other than home workouts, make dissatisfaction with one's body more likely to get out of control, much to the detriment of mental health⁹. It has been reported that such misperceptions contribute to the development of eating disorders¹⁰ and Body Dysmorphic Disorder (BDD), which may be the underlying factors causing people to consider taking image-enhancing drugs in an attempt to ease their anxiety and distress. BDD is a notoriously hard to treat mental health condition characterized by an obsessive focus on one's physical flaws, whether real or imaginary, causing people to perceive themselves in a distorted way, and technology may be exacerbating their condition. BDD and can grow to be intense to the point of impairing daily functioning. "Zoom dysmorphia", misperceptions of oneself triggered by abnormally long exposure to social media and online interactions, is thought to be a potential contributor to BDD¹¹. Unsurprisingly, an increase has been reported in those seeking cosmetic procedures, due to the urge to improve their distorted appearance and perceived flaws on social networks and in virtual interactions¹². The prospect that increasing numbers of people may turn to image-enhancing drugs in order to cope with such malaise and negativity is particularly alarming, in light of the noxious impact that such substances can have on individuals and society at large. Research has found that male BDD sufferers are often concerned with muscularity, according to a stereotyped and often unrealistic masculine ideal, whereas women exhibit a substantial drive for thinness, making them more vulnerable to eating disorders^{13,14}. It appears reasonable to assume that many people could resort to maladaptive coping mechanisms when faced with distress and anguish arising from body dissatisfaction, among which substance use. Drug trafficking and all related dynamics¹⁵ have profoundly changed as a result of the pandemic¹⁶⁻¹⁸, with far reaching implications for abuse prevention and treatment, as well as toxicological screening strategies¹⁹⁻²³. Still, to date, there are relatively few research studies centered around image and performance enhancing drugs (IPED) in times of COVID-19. Some studies^{24,25} looked into the relationship between crime and steroid use, highlighting how steroid users might be more likely to engage in criminal activity involving weapons and fraud²⁴, although a causal relationship remains uncertain, especially in light of the frequent element of co-occurring polysubstance abuse²⁵. Psychiatric and neurological implications can be substantially adverse as well²⁶: hypomania or manic episodes have also been observed, in addition to depression or suicidal tendencies and ideation, psychotic incidents and higher level of aggressiveness²⁷, sometimes associated with violent behaviors²⁸. Anabolic steroids (AS) compounds can either flow through the bloodstream without being conjugated or via plasma proteins (e.g., albumin and sexual hormone-binding globulin, SHBG). Free flowing AS thus reaches target tissues and exert their physiological effects. The apolar traits and the ability to cross hydrophobic layers composed by lipids are due to the molecular structure of AS, rich in hydrocarbons. From a systemic standpoint, such characteristics enable AS to overcome the blood-brain-barrier and other physiological barriers between capillaries and target tissues. Moreover, from the cellular standpoint, the high hydrophobicity enables AS to cross plasma membranes without necessarily binding to membrane-associated proteins²⁹. AS affect locations of the brain closely associated with mood regulation, sexual urges and aggression, which often cause users to develop psychiatric

conditions of potentially major severity, including cognitive deterioration, depression, anxiety, and psychotic reactions. AS in fact impact the serotonin and dopamine neurotransmitter networks within the brain. Dopamine, i.e., a multi-function neurotransmitter participating in the regulation of mobility, learning, emotions, appetite and positive reinforcing effects, operates the reward system, which makes it highly relevant for addiction development. Serotonin, on the other hand, plays a major role in sleep pattern regulation, appetite, sexuality and movement. Research has also linked it to memory and ability to concentrate. A recent study³⁰ focused on the magnetic resonance imaging (MRI) of the brains of athletes with a history of prolonged AS use as opposed to others who had never used such substances. Machine learning was used to establish the predicted brain age of each participant and the brain age gap, i.e., the difference between the chronological age and their predicted brain age of each participant. AS users exhibited a larger brain age gap in comparison with non-users. Brain aging, linked to substantial degrees of cognitive performance impairment and higher risk for neurodegenerative illnesses, was also observed to be more severe in those with AS addiction issues, or those who had used AS longer. The difference between the two groups could not be accounted for by polydrug use.

In conclusion, we feel that in light of the highly complex dynamics triggered by the pandemic, new and unprecedented challenges have risen in the ongoing struggle against drug abuse. Health care systems and professionals must work alongside all stakeholders to make sure that future strategies take into account clinical, demographic and socioeconomic factors, with full awareness of the peculiarities and unique impact that extraordinary circumstances can entail for mental health and substance abuse disorders, particularly when substance abuse becomes a widespread means of coping with highly traumatic stress symptoms.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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