Can Doping be a Good Thing? Using Psychoactive Drugs to Facilitate Physical Activity Behaviour

Samuele Marcora¹

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1 A Psychobiological Approach to Facilitate Physical Activity Behaviour

A physically active lifestyle has so many health benefits that the Academy of Royal Medical Colleges in the UK has recently defined exercise as the “miracle cure” [1]. Unfortunately, however, most people do not meet current guidelines for physical activity. Therefore, effective interventions to facilitate physical activity behaviour can have a great impact on public health worldwide [2].

At present, recommended interventions to reduce physical inactivity are based on (1) campaigns and informational approaches, (2) behavioural and social approaches, and (3) environmental and policy approaches [3]. Examples of such interventions include mass media campaigns, social support, and creation of places for physical activity. These interventions are necessary to promote physical activity, and should be widely implemented. However, despite all the efforts, maintenance of physical activity behaviour change is still a major issue [4], and we urgently need to develop and implement new interventions. As suggested by Bauman et al. [5], innovative interventions may come from a better understanding of how the brain regulates physical activity behaviour, i.e. a psychobiological approach. Physical activity is a very complex behaviour, and only a combination of different interventions that target behaviour at all levels is likely to succeed [6].

2 Humans are Inherently “Lazy”

In my opinion, we have not paid enough attention to the core psychobiological reason for why most people do not regularly engage in physical activity: humans do not like to exert effort [7]. This is not surprising because, when humans evolved, energy was not readily available and wasting it via unnecessary physical activity could have reduced survival. In other words, famine, infectious disease, the energy needs of a large brain, or other evolutionary pressures may have led to the selection of a “sloth gene” in early humans [8]. Our inherent “laziness” was not a problem then because the need to hunt, farm, go to places, and fight against other humans provided strong motivation for physical activity. However, aversion to effort motivated us to progressively build the current hypokinetic environment. I also argue that perception of effort is the main reason why most people choose sedentary activities for their leisure time. Compared to watching television (zero effort), even moderate-intensity physical activities like walking require considerable effort. These considerations are supported by early surveys showing that “physical exertion/effort” is one of the main barriers to regular physical activity [9, 10]. More recently, laboratory and prospective studies of affect during and after exercise [11, 12] have provided further evidence that sensations experienced during exercise are important correlates of physical activity behaviour in adults [5].

From an exercise adherence point of view, the main recommendation based on these findings is that moderate-intensity exercise is preferable to vigorous exercise as the latter is more effortful and unpleasant [13, 14]. This is a sensible recommendation because, at present, the only way to substantially reduce perception of effort and discomfort

✉ Samuele Marcora
s.m.marcora@kent.ac.uk

¹ School of Sport and Exercise Sciences, University of Kent, Chatham, UK

during exercise is to reduce exercise intensity. However, we should consider the following issues. Firstly, current physical activity guidelines recommend that individuals should aim to accumulate over a week at least 150 min of moderate-intensity physical activity in bouts of at least 10 min or more. This is double the time required to meet the vigorous physical activity guidelines (75 min per week). Given that time is perceived to be one of the main barriers to regular physical activity [9, 10], vigorous exercise has a clear advantage over moderate-intensity exercise as a way to meet the current physical activity guidelines. There is also growing physiological and epidemiological evidence that vigorous exercise may be essential to maximise the benefits of physical activity [15–18]. Therefore, I believe it is worthwhile to find ways to facilitate vigorous exercise in the general population so that it is not limited to relatively few athletes and fitness enthusiasts. Moreover, prolonged moderate-intensity exercise may be needed to prevent and treat obesity [19, 20], and exercise duration also increases perception of effort [21]. Clearly, we need to find ways to significantly reduce perception of effort and discomfort during exercise without reducing exercise intensity and/or exercise duration, i.e. without reducing the most effective exercise dose.

3 Caffeine and Other Psychoactive Drugs

In this editorial, I propose what may at first seem a drastic or even unethical intervention: the use of psychoactive drugs to facilitate physical activity behaviour (Fig. 1). Psychoactive drugs are bioactive substances that target the brain and induce significant changes in mood and cognition. In the context of physical activity behaviour, the primary target of these drugs should be a reduction in perception of effort and discomfort during exercise in order to facilitate exercise adherence. According to motivational intensity theory [22] and the hedonic theory of motivation

[12], a psychoactive drug that reduces perception of effort and discomfort during vigorous exercise should directly facilitate adherence to this kind of exercise. In addition, motivational intensity theory predicts that reducing perception of effort during moderate-intensity exercise may help people with very low potential motivation. These are the people for whom even the moderate effort required by physical activities like walking is too much. Importantly, there are common conditions like obesity [23] and mental fatigue [24] that exacerbate perception of effort during exercise. Therefore, a psychoactive drug that reduces perception of effort during exercise may be particularly useful for the many people who are overweight and/or exercise after work in a state of mental fatigue. Such a drug may also reduce health inequalities by facilitating physical activity behaviour in people with physical disabilities or chronic health conditions for which the strongest barrier responses are “exercise tires me”, “exercise is hard work for me”, and “I am fatigued by exercise” [25].

In addition to its direct effects, a psychoactive drug that reduces perception of effort during exercise may have a significant effect on self-efficacy, the main correlate of physical activity behaviour in adults [5]. This hypothesis is based on evidence that a reciprocal relationship exists between perception of effort during exercise and self-efficacy [26]. This means that an inactive person beginning exercise with low self-efficacy would perceive exercise to be more effortful. In turn, higher perception of effort during exercise would reduce his/her post-exercise self-efficacy. A drug that breaks this vicious circle by reducing perception of effort may therefore be very helpful, especially if we consider that beliefs about capabilities are among the strongest predictors of physical activity maintenance [27].

The good news is that a safe, cheap, and widely available psychoactive drug that reduces perception of effort during exercise already exists, and it is caffeine. The results of several studies demonstrate that caffeine reduces

Fig. 1 Theory-based psychological mediators of the hypothesised positive effect of psychoactive drugs on physical activity behaviour

perception of effort and improves exercise performance [28], and this is one of the main reasons why three out of four elite athletes consume caffeine before or during competitions [29]. The positive effect of caffeine on perception of effort is associated with changes in motor-related cortical activity during exercise [30], most likely in areas upstream of the primary motor cortex [31–33]. Caffeine can also reduce exercise-induced muscle pain [34, 35], increase pleasure during exercise [36], and increase exercise enjoyment [37]. Importantly, caffeine can reduce perception of effort and exercise-induced muscle pain even at relatively low doses [38] and in habitual high caffeine consumers [39]. We should also consider that, in real-life applications, the efficacy of caffeine would be enhanced by its placebo effect [40] and associated changes in motor-related cortical activity [41]. In addition to these positive psychobiological effects, caffeine can also create a greater energy deficit after exercise [37] thus helping with the prevention and treatment of obesity.

Although very promising, most studies demonstrating the positive effects of caffeine on perception of effort and discomfort during exercise are acute studies conducted in physically active participants. Therefore, we need to investigate further the acute and chronic effects of caffeine on perception of effort and other psychological responses to exercise in sedentary people [42]. After this developmental research, we need to establish whether caffeine can actually change physical activity behaviour. Examples of this research include a randomized placebo-controlled trial to establish the effect of pre-exercise caffeine supplementation on adherence to vigorous exercise, followed by a larger pragmatic trial to evaluate the effectiveness of caffeine in increasing physical activity in the long term.

More research is also needed to evaluate stimulants other than caffeine as potential candidates for the psychopharmacological treatment of physical inactivity. The most promising ones include methylphenidate [43], already used for the treatment of attention deficit hyperactivity disorder [44], and modafinil. The latter is used off-label by many healthy people to reduce mental fatigue and sleepiness [45], and enhance cognition [46]. In one study, modafinil was shown to reduce perception of effort and improve performance during vigorous exercise [47], and it seems to have a good safety profile [46]. However, further studies on the side effects of prolonged modafinil use in healthy humans are necessary.

In parallel to the evaluation of currently available stimulants, we should try to develop psychoactive drugs that can reduce perception of effort by more than 1 point on the 6–20 ratings of perceived exertion scale [28]. Psychoactive drugs that could reduce perception of effort from 15 (“hard”) to 11 (“easy”) would be very effective indeed. The prerequisite for the development of such drugs is a

more advanced understanding of the neurobiology of the sensations experienced during exercise. We have a reasonable understanding of the neurobiology of exercise-induced muscle pain [48]. However, we are still debating whether the sensory signals processed by the brain to generate perception of effort originate from the brain itself (corollary discharge model) or interoceptors (afferent feedback model) [32]. Animal studies suggest that the positive effect of caffeine on perception of effort observed in humans may be mediated by the interaction between adenosine and dopamine in the nucleus accumbens, and other brain structures like the anterior cingulate cortex, the amygdala, and the ventral pallidum [49–51]. Further basic research on effort-based decision making, exercise performance, and voluntary physical activity in animals may lead to discovery of more powerful psychoactive drugs to facilitate physical activity behaviour. On the contrary, there is no robust evidence in favour of the once famous serotonin hypothesis of “central fatigue” [52]. Therefore, it is unlikely that manipulations of central serotonin would be effective as pharmacological treatment for physical inactivity in non-depressed adults.

In addition to the use of stimulants to reduce perception of effort, another psychopharmacological strategy to consider is the use of drugs acting on the opioid system to enhance the positive feelings experienced after exercise, the so-called “runner’s high” [53]. In this way, the decisional balance between pros and cons of exercise would favour its adoption and maintenance as predicted by the transtheoretical model [54]. Enhancing the immediate psychological reward of exercise may also be very effective at increasing potential motivation because many of the rewards associated with regular exercise are probabilistic and/or delayed (e.g. a reduction in cardiovascular risk and increased longevity) [22].

4 Conclusion

As discussed above and shown in Fig. 1, the use of psychoactive drugs to facilitate physical activity behaviour has strong theoretical bases. It is therefore psychobiologically plausible that this novel strategy may be effective in reducing physical inactivity and improving public health. However, I am afraid that the negative ethical connotations of drug use in sport (doping) may be a barrier to further investigation and, eventually, implementation of psychopharmacological interventions in the field of physical activity and health. I still remember the first horrified reaction of an exercise psychologist when I told him about this idea. Interestingly, however, I have never come across ethical opposition to the use of psychoactive drugs to facilitate another healthy behaviour: reduce energy intake

to lose weight. This strategy is already a reality, as six out of seven drugs with an FDA-approved indication for obesity are appetite suppressants [55]. Given that physical inactivity is responsible for twice as many deaths as obesity [56], I hope that psychopharmacological treatment for physical inactivity will be considered fairly and seriously rather than immediately rejected using ethical arguments related to doping. After all, a drug used as doping (e.g. erythropoietin) can be a good thing when used for appropriate medical reasons (e.g. to combat anaemia and fatigue in dialysis patients) [57]. The current pandemic of physical inactivity [58] and the associated burden of disease [2] seem to me valid medical reasons for more psychobiological, clinical and ethical research on the use of psychoactive drugs to facilitate physical activity behaviour.

Compliance with Ethical Standards

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