Title: Placebo and nocebo effects in sport

Sub-heading: How physiologists can harness knowledge of placebo and nocebo effects to maximise an athlete's performance

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Dr Philip Hurst is a Senior Lecturer in the School of Psychology and Life Sciences at Canterbury Christ Church University. His research examines the role of the mind in the effectiveness of performance enhancing substances and the psychological antecedents of substance use behaviour. With a background in psychology and sport science, alongside strong interests in both physiology and neurobiology, he examines his research from an interdisciplinary perspective.

Overview

Placebo and nocebo effects can significantly influence sport performance (Hurst et al., 2020b). In the past two decades, research has identified various neurobiological mechanisms of its response and how an athlete's expectation and previous experiences, can alter the effectiveness of various treatments, such as medications, nutritional ergogenic aids, and altitude training. Importantly, this research has highlighted how physiologists can harness knowledge of placebo and nocebo effects to maximise an athlete's performance during competition and training. In this paper, I briefly review evidence for the magnitude of placebo and nocebo effects on sport performance, before providing a description of the mechanisms in which they can be induced. To help athletes perform at their highest level, I also highlight the ways in which physiologists can maximise placebo effects and minimise nocebo effects and propose future research directions to provide greater understanding of these putative phenomena on sport performance.

What are placebo and nocebo effects?

In its broadest sense, placebo effects are an improvement in a person's symptoms following the administration of a placebo, which cannot be attributed to the properties of the placebo itself. However, the placebo effect is a misnomer because in some cases there is no need to use a placebo to induce a placebo effect. Placebo effects can be induced after administration of a treatment (e.g., physiotherapy, altitude chamber, caffeine) and by factors that include the treatment context, expectations, and previous experiences. In short, placebo effects are the response to the psychosocial treatment context surrounding the athlete and the effect that this context has on their brain, mind, and body. On the other hand, nocebo effects are a negative response and are essentially the opposite of placebo effects, which relate to the negative aspects of the psychosocial context (e.g., negative experiences and expectations).

What is the evidence for placebo and nocebo effects on sport performance?

In the last two decades, a body of literature has examined placebo effects on several outcomes related to sport performance (Hurst et al., 2020b). This research has shown that when an athlete receives a placebo, but believes it is beneficial, this belief can significantly improve sport performance. Maganaris et al. (2000) showed that when national level weightlifters received a placebo, but told that it was an anabolic steroid, they improved to an international standard and increased the amount of weightlifted in bench press, deadlift, and squat by on average 3.8%. Beedie et al. (2006) reported that cyclists improved their time to complete 10-km time-trials by 1.3% and 3.1% after they believed they had received a moderate and large dose of caffeine, respectively, whereas they performed -1.4% worse when they believed they received a placebo. More recently, Hurst et al. (2020a) found that when middle-distance runners received a placebo and told it was caffeine, time to run 1,000-m was similar than when they received caffeine and told it was caffeine. In fact, when runners received caffeine, but informed it was a placebo, their performance did not improve compared to baseline (Figure 1). In short, evidence indicates that when an athlete believes they received a beneficial treatment, their performance can significantly improve.

While a body of evidence has shown the influence placebo effects can have on sport performance, the evidence for nocebo effects is less developed. This is likely to be related to ethical constraints in deceptively administrating placebos to athletes and the harmful effects they can cause (e.g., increase in anxiety). Nevertheless, a handful of studies have shown that nocebo effects are powerful and can affect a treatment's effectiveness (Hurst et al., 2020b). Beedie et al. (2007) administered placebos to two groups of athletes and told the first group (i.e., positive belief) that it was a supplement that would improve performance and the second group (i.e., negative belief) that it was a supplement that would worsen performance. After running 3 x 30-m sprints, athletes in the positive belief group ran 2.8% faster than the negative belief group. These results were replicated in a follow-up study (Hurst et al., 2017) and highlight that athletes expectations about a treatment can negatively affect their performance.

What causes placebo and nocebo effects?

Several researchers in sport have examined the existence and magnitude of placebo and nocebo effects in the last two decades (see Hurst et al., 2020b for review). However, there are few that have sought to understand the mechanisms of its response. Most of our understanding of what causes placebo and nocebo effects comes from psychology and neuroscience. This research has identified not one, but many placebo and nocebo effects operating across different neurobiological pathways and receptors of the brains that are driven by various psychological processes. While it is outside the scope of this article to provide an explanation of each one in detail (see Petrie and Rief (2019) for review), the main psychological and neurobiological mechanisms will be briefly discussed below.

Research over the past 30 years has centred upon two psychological mechanisms: expectancy and classical conditioning. Expectancy is underpinned by a person's belief that an effect will occur, which can be generated by, for example, verbal suggestions (e.g., this drug will improve your performance), environmental cues (e.g., having a degree certificate on the wall of a physiologist's office) and interactions with others (e.g., observing a competitor improve after altitude training). To put this into context, when an athlete is administered a placebo and told it is an anabolic steroid, that athlete is likely to develop the expectation that it will increase strength and power. These expectations, in turn, can influence psychological and physiological processes, which improve performance. Alternatively, classical conditioning indicates that a conditioned stimulus (e.g., placebo) elicits a conditioned response (e.g., placebo or nocebo effect) by virtue of its previous coupling with an unconditioned stimulus (e.g., the drug purported to be inside the pill). For example, an athlete with previous experience of caffeine can lead to a conditioned response (e.g., increase in heart rate), whereby a placebo on its own can create a similar response to caffeine. The placebo is thus the conditioned stimulus, and the placebo effect is the conditioned response.

In neuroscience, a plethora of evidence has identified that placebo effects act on the dopaminergic (i.e., reward) and endogenous opioid (i.e., pain) system. Using state-of-the-art technology, such as functional magnetic resonance imagining (fMRI) and positron emission

tomography (PET), researchers have shown that when a person is administered a placebo and told it is a potent drug, this can have profound effects on the brain. For example, after participants were exposed to the opioid drug, buprenorphine, Amanzio et al. (2001) reported significant reductions in pain via activation of the endogenous opioid pathway when the drug was replaced with a placebo. Similarly, de la Fuente-Fernández et al. (2001) demonstrated that administration of a placebo, described as an active drug, increased dopamine and offset the effects of Parkinson disease. In fact, the increase in dopamine concentration correspond to a change of 200%, which is comparable to the response related with amphetamine use.

Understanding of the psychological and neurobiological mechanisms of placebo and nocebo effects has rapidly increased in the last two decades. This has been reported across several conditions, such as pain, immune function, anxiety, and motor control, which have relevance for physiologists aiming to facilitate sport performance. In short, this research highlights that placebo and nocebo effects share similar mechanisms to those activated by actual treatments and can mimic the effects of those treatments. This has important implications for how physiologists support athletes and how they can capitalise on placebo effects and minimise nocebo effects.

How can I capitalise on placebo effects and minimise nocebo effects?

A large body of evidence has highlighted that placebo and nocebo effects are genuine psychobiological responses to the context surrounding the administration of a treatment. This highlights that those administrating a treatment can shape how well, or not so well, it will influence performance. That is, when an athlete believes they received a beneficial treatment, they are likely to report greater improvement in performance than when they do not believe in it, and when they believe it is harmful, they are less likely to obtain the full benefits of that treatment and/or underperform than when they believe it is beneficial. Given this, it is important that physiologists consider the context in the administration of their treatments.

Evidence from placebo and nocebo effect research indicates that benefits of treatments are often due to the interaction between the verum (e.g., the physiological or pharmacological effects)

and psychological (e.g., placebo effects) components of that treatment. On this basis, it is important that physiologists endeavour to maximise the placebo effect component of a treatment by engendering a positive belief in its effectiveness. The words used, the context it is delivered in, and previous experiences should be considered when administering a treatment to an athlete. Imagine for example, a physiologist aiming to implement heat-acclimatisation into an athletes training programme. If that athlete had a negative experience of using it (e.g., underperformance) and did not believe that it is important for their competition preparation, the athlete is less likely to fully maximise from the purported benefits. To ensure that benefits are maximised, the physiologist can capitalise on knowledge of placebo and nocebo effects to provide that athlete with evidence of its effectiveness, what benefits it is likely to have and how it can be specifically tailored to that athletes training programme. In short, a physiologist can apply an understanding of heat-acclimatisation and placebo effects to potentiate a beneficial response.

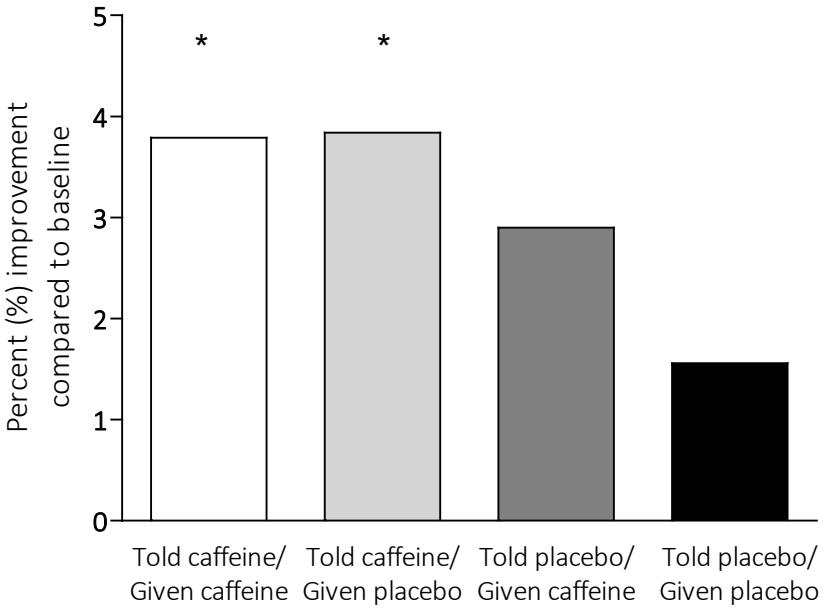
It must be stressed however, that using a treatment, without evidence of effectiveness, should be avoided. For a physiologist to knowingly promote the benefits of a placebo, for example, through deception and false information, is unethical and counter to professional guidelines. Although evidence for the use of open-label placebos (i.e., administrating a placebo and informing the athlete it is a placebo) suggests a means in which to achieve this ethically (Saito et al., 2020), evidence is limited and this could induce effects that are counter-productive, unstable and unpredictable (see Beedie et al., 2017 for commentary). In short, the need for evidence-based treatments that are administered openly and honestly is fundamental to physiological support.

What is next for placebo and nocebo effect research?

In the past two decades, placebo and nocebo effect research in sport has grown substantially. At the turn of the millennium, little was known about its existence and magnitude on sport performance and what factors may influence its response. Today, physiologists and the larger sport science community can harness placebo and nocebo effect research to ensure an athlete maximises their potential when competing and training. Placebo and nocebo effects are induced by expectations

and prior experiences, which have a direct impact on neurobiological pathways, such as dopaminergic and endogenous opioid system. However, while such advancement has been achieved, a need exists in understanding the mechanisms that can directly influence sport performance, and under which contexts they are more likely to be induced. For instance, placebo and nocebo research is often conducted in tightly controlled conditions, which have little validity to the actual demands an athlete would experience during competition and training. Similarly, with the advancement of technology that can directly examine neurobiological responses during exercise (e.g., functional-near-infrared-spectrometry) and more rigorous research designs that delineate the physiological and psychological effects of treatments (e.g., balanced placebo design), physiologists are in a position to further enhance insight and understanding of placebo and nocebo effects and the significant influence treatments can have on an athlete's brain and mind during performance.

Figure 1. Data from Hurst et al., (2020) reporting the percent improvement in 1000-m running time compared to baseline. * = p<0.01 compared to baseline



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