

## EDITORIAL COMMENT

# Psychiatric Medications and Cardiovascular Performance

## Uncommon Depressing Side Effects\*

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Perceived exercise intolerance and decreased performance are perhaps the most common complaints encountered by sports cardiologists. In this issue of *JACC: Case Reports*, Tanayan et al<sup>1</sup> present the case of an endurance athlete with impaired cardiovascular performance due to chronotropic incompetence, eventually attributed to tricyclic antidepressant (TCA) use. This case illustrates several important points for cardiologists and other clinicians who care for athletic populations.

Mental health is a critical concern for athletes and a progressing area of medical investigation. Alarmingly, depression may be even more prevalent in athletes than in the general population, with 34% of active athletes and 26% of former athletes reporting symptoms of depression or anxiety.<sup>2</sup> Inasmuch as mental health conditions are clearly a relevant issue for all clinicians, cardiologists who care for athletes should have at least some degree of familiarity with commonly prescribed psychiatric medications. Unfortunately, whether due to lack of familiarity or assumed irrelevance, noncardiac medications are frequently overlooked as a potential cause of reduced physical performance.

Pharmacologic therapy is a mainstay of major depression treatment. Multiple classes of antidepressant medications are currently available and

novel treatment strategies continue to emerge. Treatment regimens are selected on the basis of multiple factors including clinician practice pattern, individual patient response, and even geographic region.<sup>3</sup> TCAs are among the earliest antidepressants, developed and having been in use since the 1950s. Over the past several decades, TCA use has declined significantly in the United States and much of Europe, replaced with selective serotonin reuptake inhibitors as the preferred initial drugs for depression.<sup>3,4</sup> The selective serotonin reuptake inhibitor fluoxetine, in particular, is an antidepressant of choice in athletes as it is generally well tolerated and without negative impacts on performance.<sup>5</sup>

Because of concerns that exercise may induce fluctuating toxic TCA levels, TCAs are generally avoided as first-line therapy in athletes.<sup>5</sup> Nevertheless, TCAs are still relatively common despite their well-recognized toxicities, including anticholinergic effects and cardiac conduction alterations that can degenerate into lethal arrhythmias.<sup>6</sup> Chronotropic incompetence is not a common TCA side effect, and most of the cardiac-depressing effects of TCAs are associated with toxicity rather than with long-term therapeutic use. Tanayan et al,<sup>1</sup> however, make a compelling case for a depressing effect of TCAs on exercise heart rate by citing experimental evidence suggesting decreased  $\beta_1$  adrenergic receptor activity with TCA use.<sup>7</sup> Furthermore, repeated cardiopulmonary exercise testing confirmed restoration of appropriate chronotropic response and restored aerobic performance upon cessation of the offending medication.

The medication regimen of bupropion, an atypical antidepressant, and desipramine, a TCA, used in this case suggests a complicated depression history, and it is likely that multiple other medications were trialed

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before arriving at this combination. Interestingly, bupropion may have ergogenic properties, particularly in warm climates.<sup>8</sup> Although bupropion is not outright banned in sport, the World Anti-Doping Agency (WADA) has included bupropion in the WADA monitoring program. Psychiatrists should be consulted when considering altering antidepressant medications, especially more complicated regimens or in severe cases. For recreational athletes, the benefit of a stable and effective treatment for major depressive disorder may outweigh the risk of relapse for the sake of athletic performance. This calculus becomes more complicated for professional athletes, whose livelihoods are dependent on their continued ability to perform. In cases such as these, shared decision making is vital and should include detailed discussion with our psychiatric colleagues to arrive on an optimal medication regimen.

Many other medications can have unintended effects on athletic performance. Stimulants such as amphetamine salts and methylphenidate, commonly used to treat attention deficit hyperactivity disorder, increase exercise heart rate and have established performance-enhancing effects.<sup>9</sup> Given the potential for misuse, these drugs are banned in professional sport. Even more ubiquitous medications such as some forms of oral contraceptive pills have been linked to decreased aerobic performance.<sup>10</sup> Athletes are focused on their performance and may not consider other medical treatment (for depression, as in this case, or for other common conditions such as hypertension or metabolic disorder) as possible determinants of cardiovascular fitness. Aside from prescription medications, many athletes take legal ergogenic supplements. Some of these are understudied and may actually harm performance, be contaminated with unknown or prohibited substances, and/or increase cardiovascular risk.<sup>11</sup> It is therefore the duty of the clinician to thoroughly interrogate the patient-athlete regarding all ingested substances. Although it is impossible for cardiologists to be intimately familiar with all possible side effects of all substances, practitioners should maintain an

awareness of the potential cardiovascular effects associated with common supplements and noncardiac medications. When in doubt, there should be a low threshold to involve experts from other specialties.

Athletes are meticulous individuals and frequently arrive at clinic with copious personal training data that can aid with early diagnosis. It should be noted that in this case, as is often the case in medicine, the cause of the patient's symptoms could have been deduced primarily from the clinical history and presenting information. His symptoms first appeared as he started his new antidepressant regimen, strongly suggesting that these medications may have been responsible. Furthermore, his wearable heart rate device revealed a decreased exercise heart rate that corresponded with his subjective complaints. Drug-induced chronotropic incompetence as the cause of decreased performance could therefore have been identified even before any cardiac testing was performed. Although wearables have current clinical limitations, it is clear that this is another important evolving area that sports cardiologists must familiarize themselves with.<sup>12</sup>

The world of sports cardiology is an exciting and growing one. While athlete patients tend to be physically "healthier" than patients seen in the typical general cardiology clinic, quality of life can revolve around the ability to participate in sport. To allow athletes to live long and satisfactory active lives, it is our job as clinicians to consider the athlete's entire medical history and to be cognizant of rare but adverse side effects of certain drugs.

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