# Caffeine for Sports Performance

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For Anne, Andrew, Stephanie, and Sarah—you keep me high on life, and then some!

—Lawrence

For Jane, Jemima, and Ella—my three strongest addictions.

—Ben

For John and Jack, the boys who give me wings, and in honor of the Coke habit of the older one and the caffeine-free energy of the younger. Things go better with you two around me.

—Louise

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# Contents

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# Preface

Professor Ron Maughan, a world-renowned sport nutrition expert, often talks about his three laws of dietary supplements and sports performance:

1. If a supplement works, it's probably illegal (for use in sport).
2. If a supplement is legal, it probably doesn't work.
3. There may be exceptions.

This book is about one of the exceptions.

Caffeine is a fascinating substance that has become entrenched in our everyday lives. Around the world, most adults consume it on a daily basis in a variety of forms. Many people consider their caffeine habits to be an important social activity or linked to their quality of life or dietary enjoyment. In fact, the underlying reason for caffeine intake is usually performance. Whether we realize it or not, most of us consume caffeine to help us get through the day feeling better, having more energy, or being able to achieve our daily tasks more effectively. Most people seem to work out a way to get the best out of the ability of caffeine to assist with these goals. At times, however, some of us get it wrong and suffer from side effects or poor use outcomes. We have had centuries of experience with caffeine intake to get to this point. Nevertheless, scientists and health experts have developed some general guidelines for the safe use of caffeine, and there is always new information coming from research on caffeine.

In this book, we look at caffeine from the perspective of sports performance. We will find that although there is a history of caffeine use in sport, the science behind it is just decades old. Consequently, it is still on a reasonably steep learning curve that has been sidetracked at times. It is only recently that some new insights into caffeine and sports performance have allowed us to realize that it has more similarities to the general population's use of caffeine than we previously thought. There is a lot to learn from our knowledge and experiences of everyday caffeine use that could be applied to this specialized area.

Our journey through the caffeine story takes the following path. Chapter 1 presents a brief history lesson on the discovery of caffeine and the evolution of the drinks that provide the main sources of caffeine in our everyday eating patterns and social rituals. You'll also find some background information on how caffeine was used in sport and attracted the attention of exercise scientists over the decades preceding the 1980s, from where this book will pick up the tale in more detail.

Chapter 2 summarizes the way caffeine acts on our bodies at various levels of intake, trying to explain how it could enhance sports performance. This is a chapter with technical details that will not appeal to every reader. Feel free to skip it, but know that we have included this information because many athletes and coaches have developed a sophisticated interest in the chemistry and biochemistry behind supplements. At the very least, it may help you to make sense of the claims made by manufacturers of sport supplements, who often try to market their products by blinding with science (or quasi-science).

Chapter 3 will hopefully bring all readers back to the fold, providing information on where caffeine is found in both the general food supply and in specialized products and how much you can count on consuming from these sources. Explanations of the regulation of caffeine in foods and supplements around the world will help to explain why certain products are found in some countries but not others. In chapter 4, you'll learn how we've come to make use of these caffeine sources, by habit, accident, or design. We will summarize typical patterns of caffeine use in everyday diets as well as specific intakes by various populations, including athletes.

The next chapters of the book work through the questions that every athlete should ask when considering the use of a supplement: Does it work? Is it safe? Am I allowed to use it? In chapter 5, we delve into the modern research literature to isolate the studies on caffeine and exercise that have relevance to the real world of sports performance. We examine the evidence that caffeine enhances the performance of various types of sporting events, and we find which protocols of caffeine use (sources, doses, and timing of intake) provide consistent results. We'll even try to leave you with the tools to extract the bottom line from future studies of caffeine and sports performance.

Once you know whether caffeine is likely to offer benefits for your type of sport, you'll want to consider the information in chapter 6 on health risks, side effects, and general cautions associated with such caffeine use. Chapter 7 follows up with the position of caffeine in antidoping programs and the historical changes to this position. Caffeine in sport remains an area that is emotive and often misunderstood.

If, after reading the previous chapters, you have decided that you want to use caffeine to assist in the achievement of your training and competition goals, the final section of the book will help you to develop a personalized plan. Chapter 8 considers the effect that caffeine might have on other important elements of your preparation and recovery from exercise sessions—for example, hydration, sleep, and refueling. After all, your caffeine use needs to fit into the big picture of your goals. In chapter 9, you'll learn that your plan needs to account for potential factors that might alter the wanted and unwanted effects of caffeine. Some

of these are fixed (e.g., sex, genetically determined response to caffeine), while others can be changed (e.g., background caffeine use, withdrawing from caffeine use for a couple of days, using it repeatedly, using it with other supplements).

Having all of this new knowledge is helpful, but it can be tricky to organize it into new practices. Therefore, chapter 10 provides the goods to help you put your personalized program together, using checklists to work through the issues for training and competition scenarios and offering tools to assemble and monitor the outcomes. We also describe a framework that might help the world of sport to develop a sensible and unified view of caffeine use by athletes.

Along the way, we will drop in quotes and anecdotes about the use and abuse of caffeine in sport. Some of this information is in the public domain, so we can name names. On other occasions, we provide some candid and personal insights about caffeine use from athletes we know, some of whom would rather not be identified due to the funny emotions that caffeine use seems to elicit in the general population. Finally, we will provide you with a reading list of the references we have consulted to write this book.

In summary, this book will provide you with the definitive *how*, *what*, and *why* or *why not* guide to the role of caffeine in your sport. We hope you enjoy our insights.

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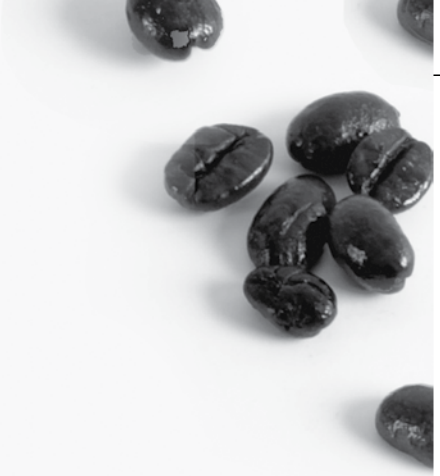

Chapter

# 1

# A Brief History of Caffeine in Sport

Nearly 200 years ago, Friedlieb Ferdinand Runge, a 25-year-old German analytical chemist, isolated a special chemical in coffee beans. Shortly afterward, some French scientists working independently on a similar project produced the same results. Their work was inspired by scientific curiosity into the popularity of coffee drinking in Europe, a habit ingrained for several centuries; in fact, it often took place in special coffeehouses that could be seen as the Starbucks of their time. The unmistakable flavor and aroma of coffee were an obvious attraction, but it seemed that something more was involved. The effects seemed both euphoric and addictive. The newly identified compound was translated from German and French terms meaning "something from coffee" into the English word *caffeine*.

The discovery of caffeine suddenly began to make sense of many observations of human behavior dating back to the Stone Age. Across countries, cultures, and eras, there are consistent stories of people consuming parts of plants to provide an energy boost. Legends involve animals or people accidentally consuming a plant and subsequently experiencing wakefulness, elation, and vitality. With this discovery, consumption of the plant would become a ritual in the community. Tea leaves, cocoa beans, kola nuts, yerba maté, and guarana are all examples of this model. We now know that the common denominator of these and more than 60 other plant species is the presence of caffeine. And as far back as records exist, it seems that people have sought this natural stimulant to include in cultural and social activities, to enhance their performance of various pursuits, and to treat headaches, lethargy, and pain.

## History of Caffeine Use

Around the world, coffee and tea have become the major sources of caffeine intake. The preparation of coffee from roasted coffee beans apparently started in the Middle East in the 1400s before spreading to Europe around 1600 and then the Americas in the 1700s. The brewing of tea from tea leaves can be traced back to various Chinese dynasties from several centuries BC. However, globalization required the efforts of Marco Polo (1200s) and the Dutch East India Company (1600s), with tea drinking gaining popularity in Europe in the late 1600s and coffeehouses becoming fashionable from the 1600s onward. Although these establishments were primarily centers of social interaction, coffee and particularly tea were noted as tonics and used to treat a variety of ailments.

The evolution of the world's third most popular caffeine source, cola drinks, is an interesting tale involving both health and sport. Mineral waters from natural springs had been popular as both baths and beverages for centuries because of beliefs about their health-promoting properties. The late 1700s was the era of campaigns to produce a human-made version of these tonics. The first such glass of carbonated water was created by an English scientist, Dr. Joseph Priestley, who was also credited with the discovery of oxygen and carbon monoxide. Other scientists also found ways to achieve this feat, but their outcomes were always on a small scale.

It took the combination of a jeweler named Johann Jacob Schweppe, an engineer, and a scientist to perfect the process of making artificial mineral waters on a large scale, with Schweppe moving the successful business to England. Patents were established there and in the United States for "means to mass manufacture imitation mineral waters." One of these means was the soda fountain, and because mineral waters originated as a health tonic, the neighborhood pharmacy became the popular place to dispense sodas. Throughout the late 1800s, American pharmacists started to add medicinal or flavor-providing herbs to the unflavored drinks. This led to cola drinks, followed by the development of soda-producing companies with trademarked names and beverages, particularly Coca-Cola and Pepsi-Cola. Table 1.1 summarizes the origins of the two cola

**Table 1.1** Origins of Cola Drinks*

| Beverage | Developed | Original ingredients | Original health claim |
|---|---|---|---|
| Coca-Cola | 1886, Atlanta, Georgia | Sugar, lime, cinnamon, coca leaves, and kola nuts | Nerve and brain tonic, headache cure |
| Pepsi-Cola | 1898, New Bern, North Carolina | Vanilla, sugar, oils, pepsin, and kola nuts | Exhilarating and invigorating digestive aid, cure for dyspepsia |

*Information sourced from official drink manufacturer websites.

giants along with their original ingredients and health claims. When launched, Coca-Cola's two key ingredients were cocaine from the coca leaf and caffeine from the kola nut, explaining its name. Shortly after the turn of the century, it moved to using "spent" coca leaves from which the cocaine had been extracted, leaving caffeine as the only stimulant. The rest, as they say, is history.

The original marketing of cola beverages focused solely on their claimed medicinal properties. Soon, however, companies realized that people enjoyed consuming these drinks, and to increase sales, they wanted to remove the stigma associated with taking medicine. The focus of advertisements moved away from the concept of medicinal elixir and more toward life enhancer. Additionally, promotion and sponsorship became the tools to market expansion. This included aligning products with sport celebrities and other high-profile members of society.

In 1909, automobile racing pioneer Barney Oldfield became the first Pepsi celebrity endorser when he appeared in newspaper advertisements describing Pepsi-Cola as "A bully drink . . . refreshing, invigorating, a fine bracer for a race" (www.pepsiusa.com/faqs.php?section=highlights). In 1928, 1,000 cases of Coke traveled with the U.S. Olympic team to the Amsterdam Olympics. Coca-Cola has continued its association with the Olympic Games to this day: It is the longest continuous corporate partner, and it is a member of The Olympic Partner (TOP) program, the top-level sponsorship awarded to a handful of sponsors with exclusive worldwide marketing rights to the Winter and Summer Olympic Games. Around the world, PepsiCo and Coca-Cola continue to sponsor a large range of regional and international sporting events and teams, seeing sport sponsorship as a natural fit.

> Over the years I've fine-tuned a caffeine protocol that works for me. I take a small dose before the start and then use caffeinated gels in the second half of the race. Overall it adds up to around 250 mg of caffeine, which is less than many people get from their daily coffee habits. I take my prerace caffeine as a tablet, and I feel a bit funny about doing this in public. I know this isn't logical because it's probably less than the caffeine in a cup of coffee, but I feel that people judge it differently when it's in a pill.
>
> *Three-time Olympic medalist, distance event in track and field*

## History of Caffeine Use in Sport

It should come as no surprise that modern athletes and coaches were first attracted to caffeine because of its ability to clear the mind of fatigue and to act as a potential muscle stimulant. In the early days of modern sport (1900 onward), mixtures of plant-based stimulants were commonly used for performance enhancement.

Indeed, as discussed previously, many of these mixtures were available as tonics and patent medicines for use in the general population. Caffeine and cocaine were particularly popular additives because they were thought to stave off the fatigue and hunger brought on by prolonged exertion.

Throughout the early 1900s, caffeine was an ingredient in cocktails for athletes that included compounds such as cocaine, strychnine, ether, and heroin. Secret recipes developed by individual trainers, coaches, and athletes were designed to provide a competitive advantage over rivals. The use of pharmaceutical cocktails by endurance athletes was so common that one author described 6-day cycling races as "de facto experiments investigating the physiology of stress as well as the substances that might alleviate exhaustion" (Hoberman 2013). This situation continued until heroin and cocaine became prescription-only substances in the 1920s and, later, when sporting organizations developed antidoping programs in the 1960s.

The earliest published studies of the ergogenic (performance-enhancing) effects of caffeine also appeared at the start of the 20th century. William Rivers and Harald Webber, colleagues at the psychology laboratory at Cambridge University in the United Kingdom, undertook a series of experiments between 1903 and 1908 on the influence of caffeine on the capacity to perform muscular work. As was common at the time, they used themselves as subjects. Their investigations included many of the elements we now consider important in sport science research, such as the use of ergometers to measure some aspect of physical activity (in this case, an ergogram, which measured the ability to lift a weight repeatedly with a finger or hand) and standardization of diet and exercise (they avoided caffeine and alcohol for months, if not years, before their experiments). Remarkably, they described the phenomenon that part of the mental and physical effects achieved by taking a compound were caused by the psychological excitement of knowing that one was indulging. This led them to employ double-blind, placebo-controlled procedures where neither the subject nor the researcher was aware of whether the experiment involved caffeine or a placebo until the conclusion of the entire study. However, today's critical eye would note that they had small subject numbers and an artificial measurement of exercise performance.

It wasn't until the 1940s that significant research on caffeine and exercise performance started to appear. American researchers from the Northwestern University medical school investigated the effects of intravenous infusions of caffeine on the capacity to perform and recover from rapidly exhausting work. These studies were significant in that they used a cycle ergometer (a more applied exercise task), had larger groups of participants (one study had 23 subjects!), and considered variables of importance such as whether subjects were trained or untrained.

John Haldi and Winfrey Wynn, from Emory University in Atlanta, Georgia, studied the influence of caffeine (250 mg) on swimming performance (91 m or 100 yd). They failed to show any influence of caffeine on performance or fatigue. Danish researchers from the University of Copenhagen investigated the effects of a range of stimulants (300 mg caffeine, alcohol, cocaine, strychnine, and nitroglycerin) on cycling performance lasting from 15 s to 5 min. Of all the drugs tested, only caffeine improved performance slightly and only in the test with the longest duration.

In the late 1970s, a series of studies from the Human Performance Laboratory at Ball State University under the wing of the father of sport nutrition, Dave Costill, investigated the benefits of caffeine intake (250-300 mg) on cycling endurance and performance. This coincided with the running boom and precipitated new interest and popular use of caffeine in endurance sports. Continued research on caffeine and exercise has intensified in three major areas: the interactive effects of caffeine and exercise on body metabolism, the effect of caffeine on prolonged exercise and sleep deprivation with relevance to military operations, and the effect of caffeine on sports performance. This is the era of the science and practice of caffeine use in sport that is covered in this book.

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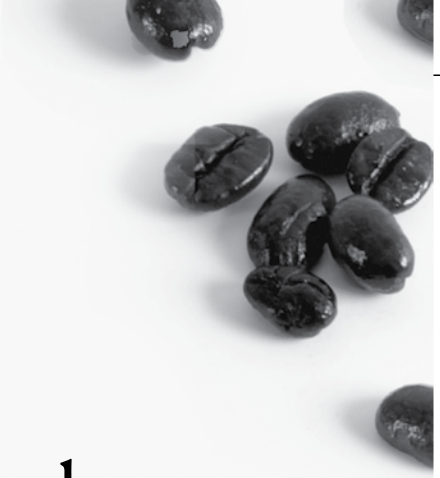

Chapter

# 2

# How Caffeine Works

As we have seen in chapter 1, caffeine is a naturally occurring chemical found in certain plants. Furthermore, as we will explore in chapter 3, it has become an additive in a range of foods and drinks. Caffeine has no nutritive value, but its druglike qualities explain centuries of use by humans to prevent or alleviate pain and general fatigue. It is also a habit-forming compound that appears to cause both physical and psychological dependencies. Withdrawal from regular caffeine use causes headaches and other symptoms, but these are relatively minor in comparison with many other habit-forming drugs such as alcohol, nicotine, morphine, cocaine, and opium.

## Metabolism of Caffeine

It is difficult to discuss the actions of caffeine in the body without some kind of immersion in chemistry and physiology. Bear with us or simply skip this chapter. In chemical terms, caffeine is an alkaloid, which means it is a basic and organic plant-derived substance, with the chemical name of 1,3,7-trimethylxanthine. It is an odorless white powder that is soluble in both water and lipids and has a bitter taste.

The chemical structure of caffeine is similar to that of adenosine, a very biologically active compound in the body. Adenosine can act alone or bound to other chemicals, most noticeably as the backbone for adenosine triphosphate (ATP), the most important form of usable energy in the body. Among its range of functions, adenosine is involved in the dilation or opening up of blood vessels and the release of hormones and fuels from tissues. It also acts as a cell-signaling molecule. Caffeine can bind to the adenosine receptors that are found throughout the body, and in most cases, as we will discuss later, this binding antagonizes (works against) the actions of adenosine.

When caffeine is consumed, it appears in the blood rapidly, with peak values reported within 45 to 90 min. Blood concentrations of caffeine are related to the size of the dose that was consumed. With drugs and many other compounds, we usually rate the dose according to the size (body mass or BM) of the person who consumes it. In the case of caffeine, the ingestion of 3 milligrams per kilogram of body mass (hereafter simply noted as mg/kg) produces blood levels of ~15 to 20 micromoles per liter (μM), while ingesting 6mg/kg produces levels of ~40 to 50 μM, and consuming 9 mg/kg results in concentrations of ~60 to 75 μM.

Examples of blood caffeine profiles after consuming such doses are found in figure 2.1. Of course, in many studies like the one that produced the results in this figure, the blood caffeine concentrations were achieved by consuming caffeine in capsule form as a single dose. If, as in real life, caffeine is ingested in a drink such as coffee, tea, or cola, it is generally spread out over a period of time. Although this would cause a delayed entry of caffeine in the blood, peak blood caffeine levels are generally still reached in 45 to 90 min.

Although the caffeine dose has been described according to the size of the person, a secondary reference point is the absolute amount that can be found in foods and drinks. Assuming the subject weighed 70 kg, the doses seen in the study would equate to about 210, 420, and 630 mg of caffeine for the 3, 6, and 9 mg/kg doses. Chapter 3 will show that the larger two doses constitute a lot of caffeine in terms of common dietary sources.

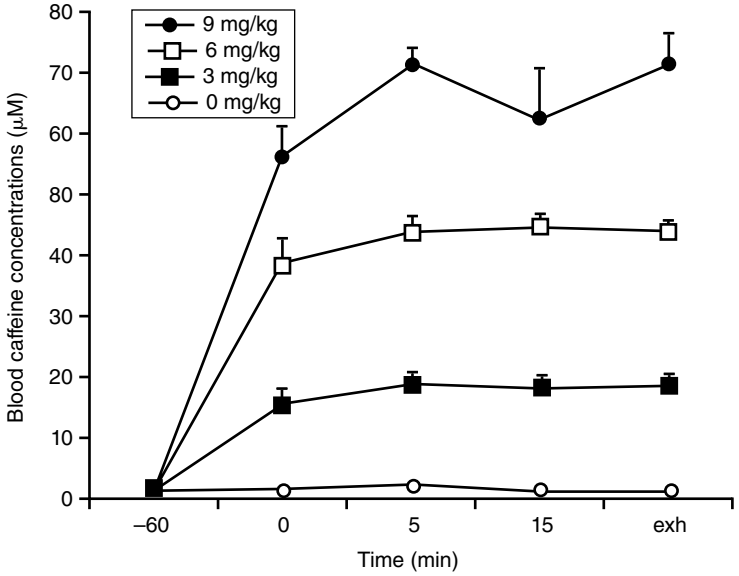


**Figure 2.1** Blood caffeine concentrations following the intake of caffeine doses equal to 0, 3, 6 and 9 mg/kg.

Reprinted from T.E. Graham and L.L. Spriet, "Metabolic, catecholamine, and exercise performance responses to various doses of caffeine," *Journal of Applied Psychology* 78(3): 867-874.

Once it is ingested, caffeine is slowly metabolized or degraded in the liver with a half-life of 3.5 to 5 hours. This means that only half of the original caffeine in the blood remains after 3.5 to 5 hours, and then in the next 3.5 to 5 hours, another half of the caffeine is gone, leaving about 25% of the original amount, and so forth. So, there still can be traces of caffeine in the blood 24 hours after ingestion. There is also a large variation in the rate at which individuals break down caffeine. Not all caffeine is broken down, however. About 0.5% to 3% of the dose is excreted, unchanged, in the urine. This is the basis of urine tests for caffeine intake (see Urinary Caffeine Concentrations: A Poor Way to Measure Caffeine Intake).

The breakdown of caffeine begins with the removal of the methyl groups by a family of liver enzymes called the *cytochrome P-450 oxygenases*. Some drugs or chemicals found naturally in food affect the activity of these liver enzymes, meaning that they can slow down or speed up the process of caffeine breakdown. There is also some genetic variability in the activity of this liver pathway. This is just one of the reasons why different people experience different outcomes from the same dose of caffeine or the same person can have a different reaction to a caffeine dose—depending on the breakdown pattern of caffeine, it may hang around in the bloodstream in high concentrations for a long time or it may be cleared quickly.

The by-products of the breakdown of caffeine appear within minutes of consumption and include paraxanthine (85%), theobromine (10%), and theophylline (5%). Why should you care about these chemicals? For one thing, they have the ability to exert their own physiological effects on the body. In addition, they are found in smaller amounts in some common caffeine-containing beverages; for instance, tea contains a reasonable amount of theophylline and chocolate contains some theobromine. If you read labels on supplements, you might also find them as ingredients in some multicomponent products sold for weight loss or as preworkout stimulants.

## General Effects on the Body

The quick release of caffeine into the bloodstream, followed by its slow metabolism, means that a dose of caffeine has plenty of time to exert its effects on the body. Importantly, it can cross the blood–brain barrier, the resistant barrier that blood vessels in the wall of the brain impose to stop compounds from moving into the cerebral spinal fluid. Therefore, caffeine should be able to interact with every tissue in the body, either by interacting with receptors on the surface of the tissue or actually gaining entry into the cell in question.

As described earlier, the most common way caffeine exerts its effects is through its ability to compete for the adenosine receptors found in many parts

## Urinary Caffeine Concentrations: A Poor Way to Measure Caffeine Intake

Both in real life and in laboratory studies, there has been a need to be able to characterize a person's recent caffeine intake. Taking blood samples always adds a level of complexity or logistical difficulty to any activity, so urine measures have become the default method. What's being measured is the caffeine that has not been metabolized within the body but has instead been excreted, unchanged, into the urine. According to pharmacokinetic studies, this accounts for about 0.5% to 3% of any caffeine dose. In the case of urine tests for caffeine use in a sporting competition, an athlete simply needs to urinate into a special jar at some time after the event. The sample goes to a lab and the caffeine concentration is measured. What could go wrong?

In fact, plenty. Both logic and experience have uncovered major flaws in the idea that such a urine test can pinpoint an individual's specific caffeine use. To begin with, there is the variability between people in the amount of caffeine that escapes metabolism. Although the difference between excretion rates might seem small, the relative differences are high. For example, if two people consume the same caffeine dose, the one who excretes 3% of the dose will produce six times as much caffeine in their urine as the person with the 0.5% loss. And that's just the start, because this caffeine is found as a concentration in urine, which has its own variability in production. Professor Don Birkett from Flinders University in Adelaide undertook a study that tracked urinary caffeine concentrations in young volunteers following a steady intake of caffeine over 6 days. Urinary caffeine concentrations varied 16-fold among subjects, sometimes exceeding 12 μg/ml, which at the time of the study was the threshold above which an athlete would be deemed to have used caffeine as a prohibited substance (see chapter 7).

Finally, there is the problem of the lack of standardization in the collection of urine samples in antidoping programs. Recent caffeine use might be better tracked if, for example, a 24-hour urine collection was undertaken to pool all the caffeine in all the urine. However, doping control is based on the collection of a spot urine sample at the athlete's convenience in the hours after an event. Depending on the type of sport, it could be just after a race lasting a minute or in the recovery from a competition lasting 8 hours. Furthermore, the athlete may have taken their caffeine dose an hour before the race or throughout the event. He or she may have urinated several times during the race (and even afterward) or not at all since getting up that morning. Are you still feeling confident that we are measuring the same thing each time?

This process might be a reasonable and pragmatic method to test for the absence or presence of substances in urine where even tiny amounts denote the absolute intake of a prohibited substance. However, the frailty of the process to be able to quantify the intake of a specific amount of caffeine is now recognized. This was one reason why caffeine was removed from the list of prohibited substances (chapter 7).

of the body. When a molecule of the caffeine binds to an adenosine receptor, it stops adenosine from binding, thereby preventing adenosine from exerting its normal effect. This is referred to as *adenosine antagonism*. By counteracting the many functions that adenosine exerts in many tissues, caffeine has profound and varied effects on our bodies. We will now examine a few of these adenosine-mediated effects.

> The England right-back Glen Johnson told BBC 5 Live after Wednesday's 1-1 draw with Poland that some of the players had taken caffeine pills before the postponed World Cup qualifier and then had trouble sleeping. "I'm not blaming that at all but it's obviously not done you any favours. . . . A lot of the lads take ProPlus [caffeine] tablets before the game and we all took that for the game [on Tuesday] then the game is off and no one can sleep."
>
> *Sam Wallace (2012)*

## Effects on the Adrenal Medulla

The adrenal medulla is the core of the adrenal gland, an important organ found near the kidney. It releases several hormones into the bloodstream that belong to a family often called *stress hormones* or *catecholamines*. The adrenal medulla is responsible for producing 80% of the body's epinephrine (also called *adrenaline*) and 20% of the norepinephrine (also called *noradrenaline*). These hormones are responsible for mobilizing the body into action in response to stress, also known as the fight-or-flight phenomenon. This includes mobilizing fuels to provide the muscles with energy, increasing the heart rate and the force of heart muscle contractions, constricting blood vessels in areas that are nonessential during exercise (such as the gut and noncontracting muscle), and increasing alertness. At lower caffeine doses (1.5-3 mg/kg), there is generally no effect on epinephrine levels in the blood, and even at moderate to high doses (5-9 mg/kg), there is little effect on norepinephrine levels. Meanwhile at the high end of this range, caffeine increases epinephrine concentrations at rest and exercise by about 50% to 100%, possibly because caffeine interferes with processes that would normally limit epinephrine release.

## Effects on Adipose Tissue

The body uses energy from a mixture of fuel sources, particularly from its fat and carbohydrate stores. How much each fuel source contributes to the mix is determined by complex factors, including how much is available and how quickly it needs to be used. Obviously, exercise is one of the conditions in which the rate of fuel use increases (often dramatically) and in which some stores can run out, especially muscle carbohydrate stores. Caffeine is one of the factors that can alter fuel use in some people. We used to think this was an important finding to

explain the benefits of caffeine on sports performance. As we shall see, however, it isn't a universal finding in all people, and caffeine enhances performance in exercise situations that aren't limited by fuel use. All in all, this finding is of interest, but it might not be as critical as we once thought.

Most of us have relatively large amounts of body fat stored in our adipose tissue, but its availability for fuel use is regulated in part by the rate at which the fat is broken down to release free fatty acids into the bloodstream for delivery to the muscles. When we are sedentary, the rate of free fatty acid release from adipose tissue is low and is arranged by the combined effects of low catecholamine levels and the presence of adenosine and insulin. Both adenosine and insulin bind to receptors on the surface of adipose tissue and inhibit the processes that break down and release fat into the blood. When fuel needs increase, for example during exercise, the rate of fat release can be greatly elevated via increases in blood epinephrine and norepinephrine levels.

In some people, caffeine can cancel out adenosine's ability to keep fatty acid levels low in the bloodstream. Sometimes caffeine actually achieves this by directly affecting the adipose tissue, independent of the work of adenosine. One way or another, in some people, caffeine leads to an increased breakdown of adipose tissue and an accumulation of fatty acids in the blood. But caffeine does not increase resting levels of fatty acids in everyone; in fact, the results vary quite a lot from person to person, and the effect is even less frequent when the caffeine dose is less than 3 mg/kg. Generally, when such variation is seen in any physiological system, we talk about dividing people into responders (those who see a large effect) and nonresponders (those who have a nonexistent or trivial outcome). When this response is examined in a study that involves a mixture of responders and nonresponders, the results of the group tend to cancel each other out so that no clear outcomes are seen. This explains the apparent contradictions among the results of various studies.

Increased blood levels of fatty acids generally lead to increased use of fat as a muscle fuel. This claimed fat-burning effect of caffeine was promoted in several ways. The first alleged benefit was as an agent for weight loss—an effect that hasn't held up to scrutiny for a variety of reasons. The second alleged benefit, heavily promoted in sport nutrition until recently, was the positioning of fat as an alternative fuel source to spare the use of the limited stores of carbohydrate fuel (glycogen) in the muscles. During the 1970s, scientists became aware of the importance of muscle glycogen as a fuel for prolonged or high-intensity exercise. It was well known that depletion of muscle glycogen was associated with fatigue and a decline in exercise performance, so efforts were made to safeguard the muscle against this occurrence. Strategies to increase muscle glycogen stores (carbohydrate loading) were shown to be effective in enhancing performance by

delaying the point of fuel depletion. A second approach was to reduce the rate of glycogen utilization. If caffeine could increase fat utilization during exercise, it would allow glycogen stores to be used at a slower rate and be available at the end of longer exercise tasks and sporting events. This became the standard theory to explain observations of better performance in marathons and other lengthy exercise activities following caffeine intake.

By the mid-1990s, however, evidence began to accumulate that glycogen sparing wasn't a major mechanism behind the ergogenic effects of caffeine. First, as we have explained, scientists realized that the fat-mobilizing and glycogen-sparing effects of caffeine are not universal. Second, it was discovered that even in people who do respond to caffeine by releasing more fat into the blood, this effect is gone after 10 to 15 minutes of exercise. Thus it would not seem to be sufficient to explain the improved performance in a long event or exercise task. Finally, an examination of individual participants in studies found that performance benefits were seen in both the responders and nonresponders to caffeine-stimulated fat release, and that caffeine is of benefit to short-duration exercise that isn't limited by the size of muscle glycogen stores.

The bottom line is that the reliable observations of work-enhancing effects during prolonged aerobic exercise could no longer be attributed to greater fat use and muscle glycogen sparing. It was time to accept that the effects of caffeine on the central nervous system (CNS) appeared to provide a more plausible theory for the ergogenic effects of caffeine, especially when consumed at low doses.

> An elite runner, a non-coffee drinker, once told me when he first heard about caffeine being an ergogenic aid, he drank two cups prerace on an empty stomach. Along the lines of if some is good, then more is better. That ruined that race!
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> *Sports dietitian and author of sports nutrition books*

## Effects on the Brain

It is widely accepted that caffeine is a CNS stimulant, causing increased wakefulness, arousal, vigilance, and alertness as well as improved mood. Because caffeine can freely pass through the blood–brain barrier, its consumption causes a rapid rise in caffeine concentration in the brain and CNS in concert with changes in other body tissues. Studies on rats show that caffeine increases the concentration of brain neurotransmitters—the chemicals released from a brain cell (neuron) to talk to neighboring neurons—increasing the firing rate of neurons in the brain and increasing spontaneous movement. The brain has high numbers of adenosine receptors, so it is generally accepted that caffeine causes the increase in neurotransmitters via the adenosine antagonism effect.

In the brain, adenosine acts as both a neurotransmitter and a chemical that affects the release of other neurotransmitters (i.e., it is a neuromodulator). Generally, the presence of adenosine and adenosine-like compounds reduces motor activity, decreases wakefulness and vigilance, and decreases the concentrations of other stimulatory neurotransmitters. Caffeine and other adenosine receptor antagonists have the opposite effect by blocking the adenosine receptors.

There are some curious issues, however. Caffeine has been shown to increase the concentration, synthesis, and turnover of all major neurotransmitters, including serotonin, dopamine, acetylcholine, norepinephrine, and glutamate. The consequences of increasing the levels of these neurotransmitters are currently unknown. However, some neurotransmitters, such as dopamine and serotonin, have been implicated in *causing* fatigue in the CNS, so it is not clear how, if caffeine increases all neurotransmitter concentrations, it could *alleviate* fatigue. One suggestion is that the caffeine-induced increases in excitatory neurotransmitters might dominate those causing fatigue, with the balance sheet leading to increased alertness and arousal, alleviating fatigue. Another possible explanation involves the existence of several types (called *isoforms*) of adenosine receptors. Each type might have different affinities for adenosine and caffeine and respond differently in terms of releasing neurotransmitters.

It is difficult to investigate what is occurring inside the brain. However, some recent work on animals has supported the argument that the work-enhancing effects of caffeine occur mainly via its actions on the CNS. A study from the University of South Carolina involved rats that had been trained to run on a treadmill and had a catheter implanted into their brain by which they could receive direct injections of chemicals into the brain. Each rat undertook four trials, each receiving a different treatment 30 min before they ran to fatigue on a treadmill. The treatments were caffeine, which was expected to block the effects of adenosine; a chemical called *NECA*, which acts like adenosine; caffeine and NECA together; and a control trial of injection fluid only.

Figure 2.2 shows the effects of the various treatments on running endurance. Compared with the control treatment, caffeine injections improved run time by about 60%, while NECA impaired run time by 68%. When caffeine and NECA were given together, they essentially cancelled each other out, producing a run time that was the same as the control trial. A particularly important finding was that measurements of activities outside the brain (muscle glycogen use and blood concentrations of fatty acids, glucose, and stress hormones) did not differ among the four trials. In addition, when the same experiment was repeated, only this time with the injection of the same four chemicals into the body cavity, there was no difference in the run times to exhaustion. Together, these results demonstrate that the important effects of caffeine occur in the brain and that performance can be improved without any metabolic effects on the muscle.