CHAPTER 9

# Walter Cannon & Self-Regulation in Animals

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## ☐ INTRODUCTION

In 1917, the United States entered World War I. Joining in a European conflict was a controversial decision for a traditionally isolationist nation, but the "Great War" also stimulated a wave of patriotism among Americans. One volunteer was Walter Bradford Cannon, a medical researcher at Harvard University. He could have easily avoided military service because of his age and his family responsibilities—at 46, he had a wife and five dependent children. Nevertheless, Cannon enlisted in the army and joined a medical unit stationed near the front lines in Belgium. Here he encountered the horrors of the modern battlefield. It was, as he later described, "a scene so awful that it seemed to me almost beyond belief that in the midst of it were *men*, with eyes and ears and sensitive nerves, who were being ripped open and mangled as they endured a maelstrom of tumult and horror."

Aside from his clinical duties, Cannon studied the causes of physiological shock. Soldiers who initially survived their wounds often died from this disorder, which is characterized by a rapid drop in blood pressure. This was particularly likely to occur in war, where casualties bled profusely. Working in the shock ward of a field hospital was a wrenching experience. Cannon vividly described the ghastly wounds, the filth, the delirious cries of injured men, and the frequent deaths. In the years before blood or plasma transfusion had been perfected, Cannon and other physicians could do little to reverse the deadly effects of shock.

These gruesome wartime experiences might impress a scientist with the frailty of life—but also its resilience. How do animals survive in an often dangerous world? Why doesn't every injury lead to a fatal disruption of vital processes? How is the normal balance of life maintained in a constantly changing environment? Such questions had interested Cannon even before World War I, and they remained the primary focus of his scientific career.

## THE IDEA OF SELF-REGULATION

On the walls of Cannon's office hung portraits of two great scientists: Charles Darwin and Claude Bernard. Like most biologists, Cannon was heavily influenced by Darwin's evolutionary theory, but he owed an even greater intellectual debt to Bernard. In a famous set of lectures delivered at about the time Cannon was born, the famous French physiologist described the difference between an organism's *internal environment* and its *external environment*. The internal environment was the blood and other fluids surrounding the body's cells. Although the external environment is constantly changing, the internal environment remains remarkably stable. Bernard concluded that the internal environment served as a kind of buffer between living cells and the fluctuating external environment.

These ideas proved to be extremely influential, and they served as guiding principles for Cannon's research. Late in his career, Cannon revised Bernard's suggestive ideas into a much more detailed form. In his popular book, *The Wisdom of the Body*, Cannon coined the term **homeostasis** for the modern concept of biological self-regulation. He based his concept on a large body of experimental evidence that he and other physiologists had gathered. In contrast to Bernard, who was unimpressed by Darwin's theory, Cannon described homeostasis as an important evolutionary adaptation. Cannon's idea became a central concept in physiology, and it was later borrowed by scientists in several other fields as well.

## THE MAKING OF A SUCCESSFUL PHYSIOLOGIST

Like many successful scientists, Cannon began doing research in college. During his senior year at Harvard, he wrote his first scientific article reporting the results of experiments on how microscopic organisms orient toward light. The next year, as a first-year medical student, Cannon began experimenting with X rays, which had been just discovered. He found that X-ray images of the digestive tract became much clearer after the patient drank a solution of barium. This innovation was quickly adopted by physicians, and it remains a standard procedure today.

Although Cannon planned to become a physician when he entered medical school, he found his clinical courses dull. His early successes in the laboratory encouraged him to pursue a career in research. Some of this research, including his wartime studies of shock, was aimed at treating seriously injured patients. But Cannon was more interested in understanding the physiology of healthy organisms. These experimental studies provided the foundation for his concept of homeostasis.

## NERVES, HORMONES, AND SELF-REGULATION

Cannon's early experiments with X rays led to an interest in digestion and how it is controlled. As a medical student, he spent hours in front of the X-ray screen observing rhythmic contractions (peristalsis) in the digestive tracts of dogs, cats, and other animals. He noticed that whenever an animal became excited, the contractions stopped. Was this response controlled by the nerves or by a hormone?

Both hypotheses were reasonable, but peristalsis turned out to be more complex than it appeared. In an early experiment, Cannon drew blood from a cat both before and after it was exposed to a barking dog. Before the stressful encounter, Cannon detected no adrenal hormones in the cat's blood. Almost immediately after exposure, however, an adrenal hormone—later called epinephrine—could be detected. Cannon then tested the two blood samples on a small strip of intestinal muscle. Isolated from the body and suspended in a dilute salt solution, the muscle continued to contract rhythmically. When blood containing epinephrine was applied to the muscle, peristalsis ceased, but when the muscle was rinsed and exposed to epinephrine-free blood, the rhythmic contractions began again.

Could this response to epinephrine be demonstrated in living animals? Was the secretion of epinephrine controlled by the nervous system? Cannon tried to answer these questions by cutting the sympathetic nerve leading to one adrenal gland but leaving intact the nerve to the other gland. After the intact nerve was electrically stimulated or after the cat was exposed to a barking dog, Cannon detected epinephrine in the cat's blood. Later the experimental cat was killed and the weights of the two adrenal glands compared. Whenever this experiment was done, the gland without neural connections always weighed more than the gland with intact nerves. Cannon concluded that the loss of weight was due to the epinephrine secreted by the intact adrenal gland.

***PROBLEM***

**What alternative conclusions could be drawn from Cannon's results? Explain whether Cannon's surgical procedure was a controlled experiment. How could the experiment have been designed differently?**

An active man who enjoyed competitive sports, Cannon turned to an athletic metaphor when he described his experimental results. Referring to the combined physiological regulation as a form of teamwork, he emphasized that the nervous and endocrine systems work together. Just how extensive was this teamwork?

Perfecting his surgical technique, Cannon and his students later removed sympathetic nerves leading to several other important organs, including the heart and the liver. Deprived of its sympathetic nerves, the heart continued to beat rhythmically. Even without neural stimulation, however, the heart responded to hormones. For example, when the adrenal glands were artificially stimulated, the heart rate rapidly increased. Conversely, injecting large amounts of insulin caused a rapid decrease in heart rate and a drop in the level of blood sugar. These effects were quickly reversed by epinephrine (and, as we now know, glucagon), which mobilized sugar from the liver and increased heart rate.

Cannon found that the liver continued to perform its function as a reservoir of sugar even when all nerves to the organ were severed. If the nerves to the adrenal glands were also cut, however, cats almost always went into fatal convulsions after being injected with insulin. Similar results occurred after chilling animals, either by placing them in cold environments or by injecting ice water into their stomachs. As long as the adrenal glands were connected to the sympathetic nervous system, cats responded adaptively to the cold stress. They shivered, fluffed their fur to increase insulation, and became more active. When nerves to both the liver and the adrenal glands were cut, the cats usually died.

The final step in this line of experimentation involved destroying the entire sympathetic nervous system. Cannon removed all of the ganglia and their interconnecting nerves (Figure 9.1). The technique had been tried before, but the experimental animals almost always died after surgery. This led many physiologists to conclude that the sympathetic nervous system was essential for survival. Cannon came to a slightly different conclusion after he discovered that his "sympathectomized" animals

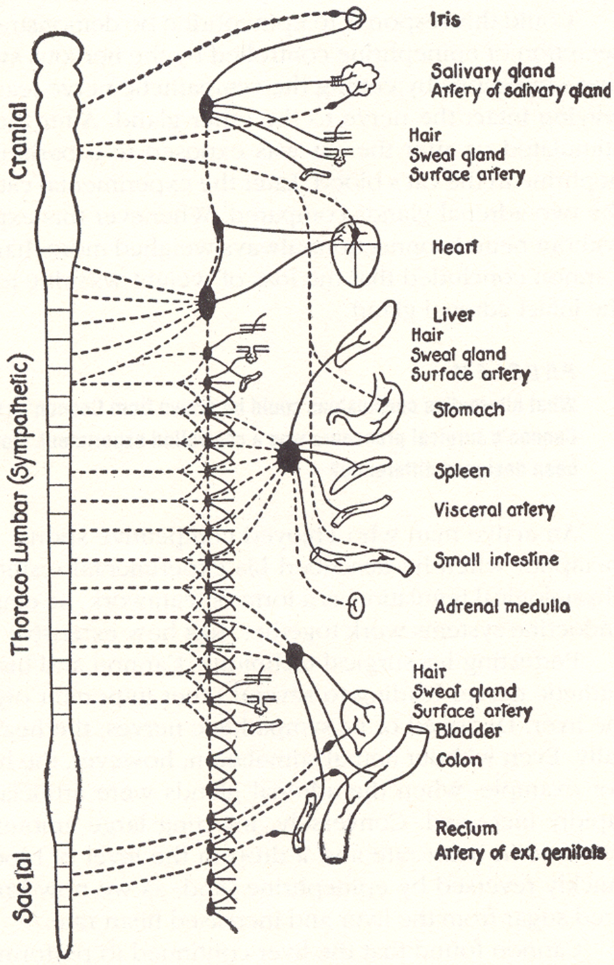


**FIGURE 9.1** A diagrammatic representation of the sympathetic nervous system. Clusters of nerve cell bodies (ganglia) lie near the spinal column. The axons of these nerves lead to nearly all of the organs of the body. By removing the ganglia, Cannon was able to destroy the action of the entire sympathetic nervous system. *Source:* from *The Wisdom of the Body*, Revised Edition by Walter B. Cannon, M.D. Copyright 1932, 1939 by Walter B.Cannon, renewed © 1960, 1967, 1968 by Cornelia J. Cannon. Reprinted by permission of W. W. Norton & Company, Inc.

often led remarkably normal lives. Several of Cannon's cats continued to live for months or even years, and at least one female gave birth to healthy kittens. If the animals were removed from the protected environment of the laboratory, however, their condition often changed dramatically. Unlike normal cats, the sympathectomized animals could not respond adaptively to stress. When forced to do even moderate exercise, the cat's heart rate often failed to increase in response to the body's demand for more oxygen. When emotionally excited—for example, by being placed near a barking dog—the cat's blood sugar level failed to increase as it would in normal individuals. When sympathectomized cats breathed an atmosphere with reduced oxygen (as might occur at a high altitude), they usually fainted. It seemed that all of the "fight or flight" responses that allow animals to respond adaptively to emergencies were under the primary control of the sympathetic nervous system. Without this protective regulatory system, experimental animals could survive only if they were artificially protected from all types of physiological stress (see Chapter 10).

## THE CONCEPT OF HOMEOSTASIS

Cannon completed this series of surgical experiments just before he wrote *The Wisdom of the Body* (1932). Although he had used the term *homeostasis* a few times before, Cannon's book made it famous. Written for a broad scientific audience, the book generated so much interest that it was revised and republished in 1939. Thirty years later, it was reprinted again in paperback form.

The title of Cannon's book may appear odd. Are subconscious neural impulses and the secretion of hormones really a form of "wisdom"? Cannon described how homeostasis had evolved through a process of trial and error. Over the course of millions of years, many species went extinct, but through natural selection successful species had evolved ways to regulate biological processes. This evolutionary process culminated in the exquisite system of hormones and autonomic nerves that allows mammals to maintain a high degree of internal stability. Virtually every important physiological function could be regulated, including body temperature, pH, amounts of water and salts, the level of sugar in the blood, and the metabolism of sugar and fat within the cells of the body. Through the course of evolution, the body had "learned" to regulate itself.

Cannon emphasized the remarkable precision of homeostasis. Underlying this optimistic theme, however, was a more sober recognition that self-regulation is not a perfect adaptation. His work as a physician, particularly his battlefield experiences during World War I, reminded Cannon that severe injuries can often overwhelm the body's self-regulatory mechanisms. His experiments on cats had also vividly demonstrated that if the endocrine or nervous systems are damaged, homeostasis is easily disrupted. How could Cannon integrate these two contrasting themes in his book?

Through the process of natural selection, Cannon believed that well-adapted species had evolved very flexible control systems. Like an engineer who designs a bridge to withstand forces greater than those normally encountered, natural selection had produced wide margins of safety in the body. Organisms could usually tolerate large fluctuations in almost any physiological function, at least temporarily. Various sense receptors acted as early warning devices to alert the body to dangerous changes. Then, through the teamwork of nerves and hormones, the body counteracted these changes. Homeostasis was never perfect, but under most conditions, the body maintained a high degree of internal constancy.

## ANIMALS, MACHINES, AND SOCIETY

Together with evolution and cell theory, homeostasis became one of the central organizing principles in modern biology. Building on the foundation of Cannon's *Wisdom of the Body*, physiologists used homeostasis to help explain the function of every organ system of the body. Homeostasis has been used by other biologists to describe self-regulation in a wide variety of living systems, including developing embryos, cancerous tumors, populations, and even ecosystems. In the years after the publication of his most famous book, Cannon's influence also stretched far beyond biology.

After World War II, the mathematician Norbert Wiener recalled how Cannon influenced his thinking about self-regulation. Wiener joined a number of young scientists who attended a weekly dinner seminar led by the famous physiologist. The seminar was a place where new ideas were presented, discussed, and criticized by the members. Wiener later helped to establish the new field of cybernetics, which studied the general principles of self-regulation. He developed the mathematical idea of **negative feedback** and applied it to machines as diverse as anti-aircraft guns, radios, and thermostats. Many biology textbooks today use negative feedback and mechanical models (for example, the thermostat) to explain homeostasis. For Wiener, who credited Cannon with inspiring some of his ideas, there was really no difference between self-regulation in animals and machines. Was such a generalization warranted? Should scientists try to extend theories from one field to another?

Cannon recognized that there is a danger in applying theories too broadly. "Nothing is easier than to let one's imagination spin fancies on the basis of slight evidence," he warned younger biologists. Yet Cannon himself was sometimes willing to go out on a limb. In the final chapter of *The Wisdom of the Body*, he left his specialty of physiology to discuss what he called "social homeostasis."

As he was writing the chapter, the nation was suffering the worst economic catastrophe in its history: the Great Depression. In some industrial cities, more than half of all workers were unemployed. Prices for agricultural products dropped so precipitously that many farmers could no longer make mortgage payments. Angry mobs attacked judges and bankers who ordered foreclosures and evictions. Radicals on both the right and left predicted the collapse of American democracy. Was the body politic suffering something analogous to the traumatic shock that Cannon had witnessed on the battlefields of World War I?

Cannon drew analogies between the economic plight of the nation and the physiological crises faced by living organisms. Like the highly adapted mammalian body, Cannon believed that industrial societies were homeostatic. Under normal circumstances, the political and economic systems were capable of regulating themselves to achieve a stable balance. Like biological homeostasis, however, social regulation came at a high cost. In order to maintain stability, societies needed to allocate economic resources to government programs that promoted harmony and social stability. Although he was a lifelong Republican, Cannon supported many of Franklin Roosevelt's New Deal programs, believing this government intervention was part of the homeostatic mechanism that would bring an end to the Great Depression and restore social harmony.

Cannon's discussion of social homeostasis is important because it serves as a reminder that laboratory life is seldom completely isolated from the broader social lives of scientists. Cannon was a cautious experimentalist who knew about the dangers of scientific speculation. Yet he was also an imaginative and creative thinker who was willing to take intellectual risks. His strong sense of social responsibility prompted him, after some hesitation, to speak out on the political and economic issues of his day. Careful experimentation and intellectual risk taking: Cannon's legacy as a great biological thinker rested on his ability to balance these two seemingly contradictory characteristics.

## ☐ EPILOGUE

Throughout his career, Cannon was forced to defend his use of cats and other animals as experimental subjects. To an even greater degree than the Great Depression, the issue of animal experimentation thrust him into the political arena. Although there is no evidence that Cannon was needlessly cruel to his laboratory animals, his experiments often resulted in their deaths. For many people, such animal experimentation was unacceptable. This "antivivisection" controversy came to a head when his friend and former teacher, William James, wrote a letter criticizing Cannon's research. Antivivisectionists publicized the letter, and it was widely read.

Although James is best known today as a philosopher and psychologist, he was trained as a biologist, and early in his career he taught anatomy and physiology. When he wrote the antivivisection letter at the end of his long career, James was one of the most respected intellectual figures in the United States. His criticism of Cannon, therefore, carried both conviction and authority.

Antivivisectionists were critical of animal experimentation for several reasons. Pain and suffering of animals was certainly an issue, but not the only one. James knew that Cannon was a careful surgeon, that he used anesthetics, and that his experimental animals were cared for properly. Of greater concern was the potential dehumanizing effects that animal experimentation might have on scientists. Routine killing, even when done humanely, might cause experimentalists to become less sensitive to pain and suffering. It might also lead some scientists to callously accept human experimentation. After all, if it was all right to experiment on nonhumans, couldn't one also justify vivisection on prisoners, the mentally retarded, or members of minority groups if the results might benefit the general public? Finally, James criticized scientists for being too authoritarian and resisting any attempts by nonscientists to oversee their work. If experimental science were really being done for the public good, shouldn't the public be allowed to regulate the types of experiments done by scientists?

Cannon considered such criticisms to be irrational, as do many biologists today. The issues have not disappeared, however. Indeed, they have become even more sharply defined. This is partly the result of the rapid growth and high visibility of science after World War II. Experimental animals are now used in research, product testing, and education on a very large scale. Reliable estimates place the number of vertebrate animals used for these purposes in the United States at 25 to 30 million per year. Public attitudes have also changed as a result of sensational cases of inhumane treatment of animals by just a few scientists. For example, in a notorious case at the University of Pennsylvania, researchers inflicted traumatic head injuries to unanesthetized monkeys and baboons. Videotapes of the experiments provided graphic evidence that some of the scientists seemed to enjoy inflicting pain on the helpless animals. Although this research was probably aberrant, it again raises the issue of whether animal experimentation may cause scientists to become callous toward their subjects. More recent revelations of radiation experiments done on mentally retarded children after World War II by doctors supported by the Atomic Energy Commission revived the antivivisectionists' long-standing fear that the widespread acceptance of animal experimentation may lead people to accept human experimentation.

The animal rights movement has seized on such cases to publicize and promote its goals. Although much of the literature of this popular movement is marked by overstatement and emotional appeals, serious ethical issues concerning the use of animals in science continue to be raised. Professional philosophers (Peter Singer and Tom Regan) and even some scientists (Richard Ryder and Mary Dawkins) have written thoughtful books and articles critical of animal experimentation. Singer argues that when the benefits of science are balanced with the suffering of experimental subjects, animals and humans must be treated equally. A benefit to humans, no matter how great, cannot justify the suffering and death of just animals alone. Only if both the suffering and the benefits are equally shared among all of the species involved can vivisection be justified. Regan makes the even stronger case that all sentient animals share certain rights, the most important of which is the right to life. These arguments have been criticized by other philosophers (Carl Cohen, Michael Leahy, and Raymond Frey), who claim that equating human and nonhuman interests is unwarranted.

These disagreements show no signs of being resolved, but they have focused attention on serious practical issues concerning the social responsibilities of scientists. Between the extreme positions in the animal rights controversy is a growing recognition that society has a legitimate role in guiding scientific research, particularly when it is supported by public funds. Even if some animal experimentation is necessary, scientists should be aware of important ethical issues raised by their work.

## QUESTIONS AND ACTIVITIES

**1.** What does this case show about the following aspects of doing biology?
— relationship between experiments and theory
— boundaries of scientific disciplines
— social, ethical, and political responsibilities of scientists

2. Cannon was primarily interested in how homeostasis maintains normal physiological balance. Describe how homeostasis can also explain pathological conditions such as the traumatic shock that Cannon encountered as a physician during World War I.
3. Discuss how your biology textbook uses negative feedback to explain homeostasis. Is self-regulation in machines and organisms basically the same, as Norbert Wiener claimed, or are there some important differences?
4. Discuss whether Cannon was justified in drawing analogies between physiological homeostasis and "social homeostasis." What are the possible benefits and dangers in this type of analogical reasoning?
5. Examine your school's guidelines for animal experimentation. To what extent do the guidelines balance public accountability with the legitimate goals of scientific research? Discuss whether Cannon's experiments would be allowed at your school. If not, could they be redesigned to make them acceptable?

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