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The Varieties of Scientific Experience

The interdisciplinary nature of neuroscience means that you, as a student entering this area, enjoy the prospect of a rewarding lifetime of learning biology, psychology, chemistry, physics, computer science, and mathematics, allowing you to be able to converse with other members of your field. You will master both the language and basic foundations of all these other sciences, and also the fundamental laboratory techniques and analysis skills of these disparate areas.

It may take time to learn all the background information that helps to make you a neuroscientist, but fortunately it is not so difficult to get started conducting research in neuroscience. If you find a mentor, choose a simple question, and master a few skills as a first focus, you can begin independent research in neuroscience. If you continue in research and have a career as an experimental neuroscientist, you will be learning new techniques throughout your lifetime; you will probably end your career using techniques not yet dreamed of. Nevertheless, how you design and analyze your experiments will still follow the principles introduced in this book.

The Savvy Research Student

To help you understand, let me tell you about the experience of a former student of mine. Stephanie had arranged for a summer internship after her second year of college. She was going to work in a laboratory studying Alzheimer's disease using a molecular approach. We discussed material that the head of the laboratory had given her, the honors thesis of a student who had just completed research in that laboratory. As we talked, I realized that Stephanie needed to sort out what was measured by a Western versus a Southern versus a Northern blot (protein, DNA, and RNA, respectively). She needed help finding the protocol books that give step-by-step directions for everything from making a stock solution to running a gel (I recommended Kathy

Barker's (2005) *At the Bench: A Laboratory Navigator;* see the end of this chapter for further information). Nevertheless, she was doing fine without understanding some of the laboratory techniques and protocols, because her experimental methods course had given her a good understanding of the scientific process. She was reading the previous student's thesis with a critical eye. She had absorbed the basic working model the laboratory was testing and focused her efforts on discovering what aspects of that model were not yet firmly supported by experimental evidence. She understood the relative strengths of correlative versus experimental designs, and she quickly grasped the reports from statistical tests. Stephanie was well prepared for this wonderful internship opportunity. She would learn many new techniques, and the fundamental understanding of experimental design and analysis from her prior course would help her plan her summer experiments to contribute to scientific knowledge.

This text will prepare you for success if you join a neuroscience research laboratory as an apprentice, an experience essential to scientific training.

The Skeptical Consumer

A research laboratory is not the only context in which you will apply the concepts discussed in this book. When you read the newspaper or browse the web, you will often encounter reports about scientific studies with results that are relevant to your life. Here is an example: If you are having trouble cramming for your final exam, should you consider staying awake all night to learn more material? One new study reports that 31 h of sleep deprivation can increase levels of a protein associated with Alzheimer's disease in the brain (Shokri-Kojori et al., 2018). This was reported in the *Daily Mail* (www.dailymail.co.uk) with the headline, "Just ONE sleepless night could spark Alzheimer's." However, another headline, reporting on a different study (Lundgaard et al., 2018) reads, "Two drinks a day can help you fight Alzheimer's, study says" (www.foxnews.com). Should you battle the effects of sleep loss with drinking alcohol to reduce your chances of developing Alzheimer's disease?

With no background in scientific method, you can at least use your common sense. If one night of sleep loss caused Alzheimer's disease, wouldn't that mean the incidence of this disease would be much higher? Pretty much every new parent suffers sleep loss, and, as you likely know, many students do as well. You are probably skeptical that the newspaper reporter was justified in jumping from "increased levels of a protein associated with Alzheimer's disease" to "could spark Alzheimer's." You might also be skeptical about the logical jump from the *association* of sleep loss and increased protein levels to conclusions about *causation* of sleep loss changing protein levels. What about the second claim that drinking alcohol reduces your chances of Alzheimer's? Could that be true?

After you gain a background in scientific methods, you will be able to find the original reports (Lundgaard et al., 2018; Shokri-Hojori et al., 2018) and analyze the studies. You will be a more competent consumer of scientific information and, given the dramatic impact scientific information has on our lives, this is an important component of educated citizenship.

What Is Science?

Before we begin exploring the process of scientific discovery, we should first define our subject. What is science? It is often hardest to define the simple terms that we use in everyday life. Can you give a definition of science? Even graduate students in neuroscience find this difficult.

- Is science a collection of facts?
- How can you distinguish science from history, which also involves a collection of facts?
- Is science a collection of facts arising from laboratory experimentation?
- What about astronomy or taxonomic classifications?

Ask yourself: How would I define science? Write down a few ideas before reading further.

I prefer this definition of **science**: "An interconnected series of concepts and conceptual schemes that have developed as a result of experimentation and observation and are fruitful of further experimentation and observation" (Conant, 1951, p. 5).

This definition stresses the important role of conceptual schemes, such as theories or models, which guide the development of scientific understanding. Both experimentation and observation are included as techniques for gaining new understanding. The last part of this definition stresses that scientific understanding is never static.

You can think of the process of science as a spiral. You enter with an idea. First, you go through a time of observation or experimentation. Second, you compare the new evidence from these observations and experiments with current scientific theories. If necessary, you begin to revise theories to take into account the new results. Third, you test these refined scientific theories by further experimentation or observations. The circle at this stage has offshoots as you have more ideas to test. This is an expansive process, leading to theories that are ever more sophisticated.

What Is the Scientific Method?

In this book, you will learn to apply the scientific method to questions of interest. But what exactly is the scientific method? Actually, there is not one scientific method. Rather, **scientific methodology** is a collection of logical rules, experimental designs, theoretical approaches, and laboratory techniques that have accumulated throughout history. Each field of science has its own history; thus, each field has slightly different scientific methods.

Scientific methods are not static. In fact, the idea of the **experiment** is a relatively new idea made popular in the 16th and 17th centuries. In an experiment, the investigator gains new information by observing results after changing one variable with all other variables held constant. Scientists before that time relied largely on one of the important tools of modern scientists, careful observation. With the addition of the experiment, a new logical analysis was possible. Because the only difference between the groups in an experiment is the one variable of interest, we presume that that variable is the cause of any difference between the groups in the outcome measures. Given the power of the logical analysis of results that an experiment makes possible, many scientific studies are experiments; however, scientists have more methods in their repertoires. In this book, we focus on the experiment, but we will also cover other, nonexperimental, scientific approaches such as case studies and correlational and observational studies.

Epistemology for Scientists

How do we know that our scientific methods are valid and our interpretations correct? Why should we even assume that we could understand nature at all? There is a long history of philosophers considering these questions, and much to gain from a consideration of their thoughts. This branch of philosophy, **epistemology**, is the study of how we know what we know.

Some of the things we accept as known we know based on **authority**. In the long period of the Middle Ages (5th–14th centuries), the church was the ultimate authority in Western culture. Church authorities had to approve new theories of the brain, which could not conflict with other church teachings. As an example, consider how the teachings of the church influenced the understanding of the ventricles, the fluid-filled caverns within the brain. Scientists thought that there were three ventricles: the first was where sensations were taken in, the second was responsible for perception, and the third was the site of reason. Why were the ventricles so important? The religious authorities taught that the soul was not material, so scientists of the time searched for a place in the brain where immaterial spirits could reside. The halls of the ventricles seemed ideal for a spacious home for spirits.

Empiricism, the idea that all knowledge arises from experience through the senses, grew in popularity in the 15th and 16th centuries. Instead of relying on the power of authority, such as the authority of the church, one could learn by observation and careful study of nature. Leonardo da Vinci's study of the ventricles is an example of the empirical approach. The human body fascinated da Vinci, a masterful observer. To better understand the ventricles of the brain, da Vinci secured an ox brain from a local butcher, assuming an ox brain might be similar to a human brain. Then he borrowed a technique used by artists, making a mold from molten wax. He poured hot wax into the ventricles of the ox brain, let the wax cool and harden, and then dissected away the brain tissue to discover the true shape of the ventricles. As Figure 1.1 shows, da Vinci discovered by empirical observation that the ventricles were not shaped as three caverns, but had a more complex architecture.

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More Information

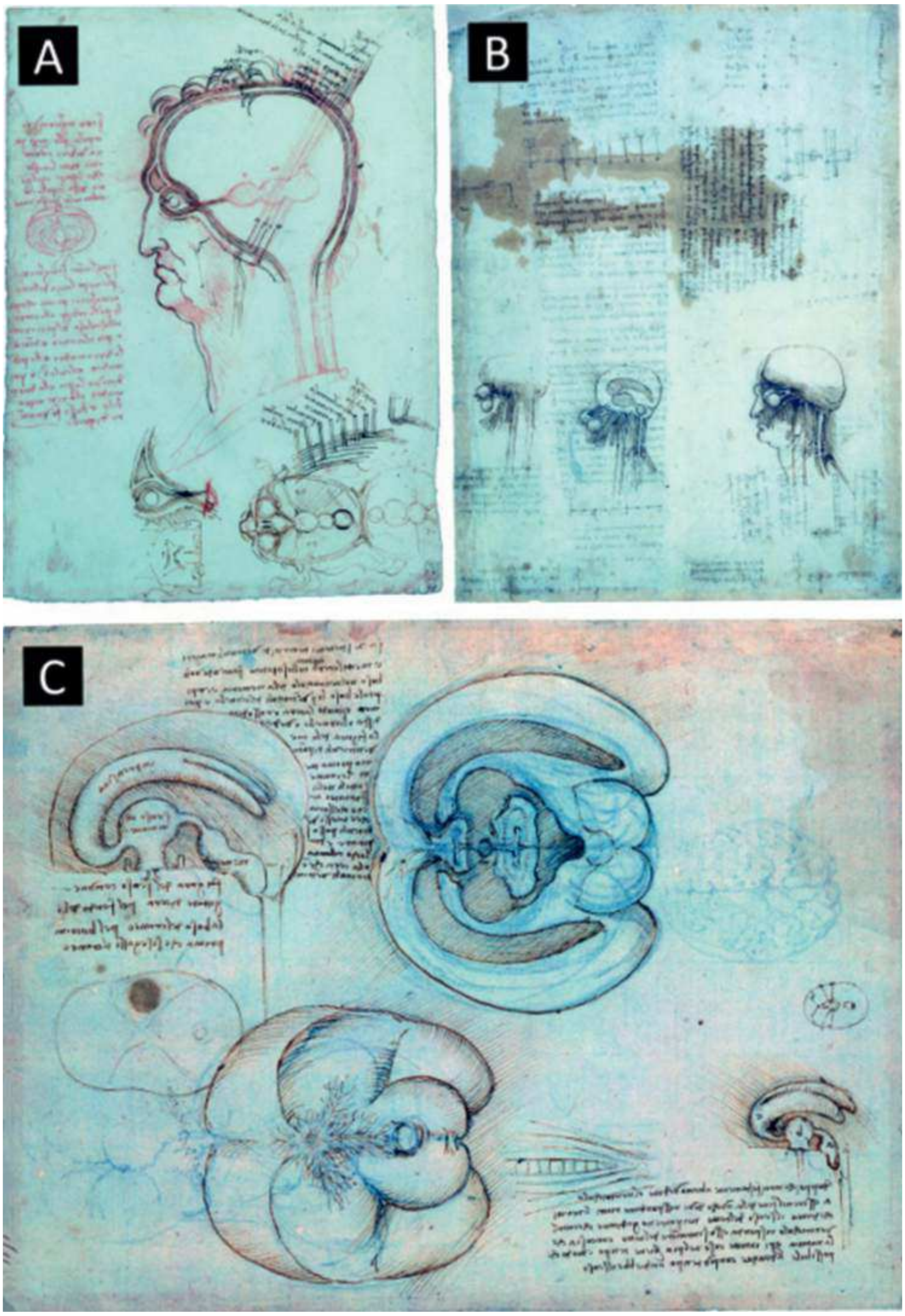

Figure 1.1 Early depictions of the ventricles in the brain. Da Vinci was influenced by ideas of his time as shown in drawing A (from 1489) where the ventricles of the brain are drawn as three chambers. In drawing B, from 1508, his understanding is developing, but still emphasizes the idea of three chambers. Following studies of the ox brain, shown in drawing C (1508–1510), his drawing is much closer to our current understanding. Source: Open-i, US National Library of Medicine.

One problem with empiricism is that we cannot totally trust our senses. Sensory perception necessarily involves active construction of theories. Thus, observed "facts" are already constructs, and our theories influence them. Visual illusions can teach us that it is impossible to observe nature without imposing our active perceptual processes.

Bias is another problem with empiricism. The ideal of an unbiased objective observer faithfully detecting nature is an ideal that is impossible to achieve. For example, look at Figure 1.2. This is an early drawing of the human cerebral cortex. Early writers described the cortex as similar to the intestines. It is obvious that this descriptive metaphor has so influenced the artist that the cortex actually resembles the intestines more than it does the true cerebral cortex (Gross, 1999). What metaphors might we be using today that blind us to the reality before our eyes?

In the 17th century, René Descartes suggested that truth and knowledge are attainable through reason, not experience. This philosophy, **rationalism**, encouraged less observation of nature and less reliance on knowledge gained through the senses. Instead, careful logical analysis would lead to a truth you could trust. Descartes was particularly interested in the question of how the immaterial soul could reside in the material body, a question that continues to fascinate many. He reasoned that the soul must consist of immaterial spirits located in the head; there must be a unitary structure associated with the soul, because the soul is unitary. Most structures in the brain are duplicated in each hemisphere; there are very few unitary structures. The pineal gland stands

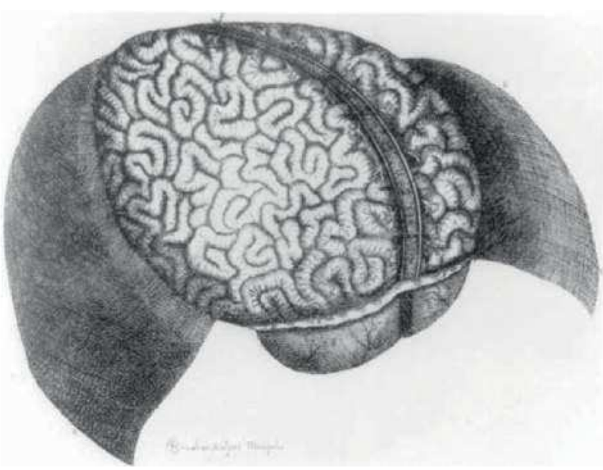

Figure 1.2 The metaphor of the cerebral cortex looking like intestines influenced the drawing of the human cerebral cortex by Raymond de Vieussens, a leading neuroanatomist in the late 17th century. Source: History & Special Collections Division, Louise M. Darling Biomedical Library, UCLA.

out as a unitary structure, and at that time, the pineal gland had no other function assigned to it. Although Descartes was probably aware that in other animals the pineal gland is located on the dorsal or topmost surface of the brain, he placed it within the ventricles of the human, so that the pineal gland might move and alter the spirits residing in the ventricles.

As you work as a scientist, the sources of your knowledge will have roots in both the empirical and the rational approach. Currently accepted forms of scientific inquiry are a product of our culture and history. In neuroscience, much of our research can be conceptualized as describing connections between phenomena described with the techniques of one field – say, chemistry – to the same phenomena described with the techniques of another field – say, psychology. Each of these disciplines must consider the others as they build explanations. E. O. Wilson (1998) describes this in a small book, *Consilience: The Unity of Knowledge*. Consilience is the linking together of knowledge from different disciplines to create a common explanation (Wilson, 1998, p. 8). An explanation of a psychological phenomenon must be consilient with (or connected and consistent with) biological findings. Similarly, biological explanations must be consilient with chemistry.

An interdisciplinary field such as neuroscience may be fundamentally different in approach from more classical fields of science, such as physics. It is helpful to apply Darden and Maull's (1977) conception of **interfield theories**, theories that bridge two fields of science. In neuroscience, we explain phenomena by building a web of links between descriptions at different levels of explanation. Our goal is to answer questions that cannot be answered using only one level of explanation or to describe a mechanism that links the various fields we draw on. Some of the phenomena we seek to explain may be unobservable, and we generally accept that we can study unobservable concepts as long as we identify observable manifestations of that concept. For example, we can study learning using behavioral changes or alterations in synaptic efficacy as the observable manifestations of the process of learning. A neuroscientific explanation of a phenomenon in the best cases is one that incorporates all of the levels of explanation, with theories bridging the many encompassed fields, such as anatomy, physiology, physics, chemistry, biology, and psychology.

Thomas Kuhn (1975) described the accepted facts and approaches in a scientific field at any one time in history as a **paradigm**. For instance, the current paradigm in neuroscience does not include questions about how the spirits move within the ventricular system; those questions belong to an earlier paradigm. Questions of that sort no longer make sense within our current shared understanding. The current paradigm is based on several key theories; for example, Ramón y Cajal's "neuron doctrine" is a key tenet in neuroscience today (Shepherd, 1991). The **neuron doctrine** is the belief that the neuron is the fundamental unit of the nervous system. Kuhn described how the paradigm for a field of science is usually rather stable, with scientists working within the same set of shared beliefs, conducting experiments to refine their theories. At other times, the paradigm appears to shift in a sudden "scientific revolution." When Copernicus proposed that the Earth revolves around the Sun, challenging the understanding of the cosmos as centered on the Earth, the suggestion of heliocentrism was profoundly revolutionary. A scientific revolution comes about when findings accumulate that are incompatible with the previously accepted paradigm. As these antagonistic findings accumulate, the scientists working with the current paradigm initially passionately resist them. Now, just because current scientists are actively resisting some radical claims, this is not proof that those claims are heralding a new scientific paradigm; those claims *could* be wrong. When one paradigm is overthrown, it is replaced by a new paradigm. Note that it is not wrong to work within the current paradigm; in fact, that is generally what each scientist should do. Only when an overwhelming weight of evidence indicates the current paradigm is incorrect or requires expansion should scientists work to change the paradigm in a scientific revolution.

Recognizing Pseudoscience

Sometimes a body of knowledge looks like science and sounds like science, but it is not science. A trained scientist recognizes it as **pseudoscience**, unscientific information masquerading as science. How can you recognize pseudoscience and distinguish it from real science? Now that you have a definition of science, this is not too difficult. Whereas pseudoscience consists of a system of ideas that either do not change or change randomly, science consists of ideas that change based on observations or experiments. Whereas pseudoscience lacks organized skepticism and the mechanisms for acquiring new knowledge are vague, the basis of science is organized skepticism through replicable experiments and observations, and there is agreement on the techniques for acquisition of new knowledge. In pseudoscience, established findings are often disregarded, whereas a new theory in science generally must always consider previously established facts. Pseudoscientific writings often stress the personal characteristics of the writer, commonly suggesting that the scientific establishment is conspiring against the writer's ideas for dubious reasons; however, this cloak-and-dagger mentality is rarely present in scientific writing (see Box 1.1 for more hints).

Box 1.1 Tools of the Trade

Rules to Help You Recognize Pseudoscience

1. Read the references. Pseudoscientific information will not often provide references, but the ones that worry me are the ones that *do* give references. Be sure you actually read those references yourself to determine if the authors of the source referenced actually support the claims.
2. Be alert for illogical leaps. For example, even if your brain waves show similarities to those from people with slight memory loss, this does not inevitably lead to the conclusion that you require a nutritional supplement to correct the "abnormality."
3. Do not be impressed by an idea's longevity. Just because an idea has been around for centuries does not indicate that the idea is valid. Pseudoscientists love to use the term "ancient wisdom" as evidence for their claim, even if scientists have long ago discarded the ideas. Scientists look for evidence to support or falsify the idea and therefore make progress beyond ancient ideas. An example here is phrenology, a long-discredited idea that the pattern of bumps on the skull indicated an individual's personality. I was surprised to discover that there are people today who ascribe to the beliefs of phrenology.
4. Do not be swayed by the degrees and awards claimed by the person promoting the pseudoscience. Diplomas or awards do not make a person a scientist – a skeptical, evidence-based approach makes someone a scientist.
5. What is the easiest way to recognize this? Nearly every pseudoscientist will offer to sell you something. Whether it is a nutritional supplement, a book that will change your life, tapes that help you breathe correctly, or electrical devices that balance your hormones, you can be sure there is some merchandise.

Neuroscience in the Service of Pseudoscience

I am appalled by uses of legitimate neuroscientific research in the service of pseudoscientific claims. They can give a patina of legitimacy to quack medical advice.

An example that intrigues me is "cranial electrostimulation." There are companies quite happy to sell you little devices that will apply an electrical current to your earlobes to electrically stimulate your brain. They claim that as you dial up the frequency of stimulation, you can achieve any desired brain wave frequency and thus an altered mental state. How will this help you? It will improve your life in countless ways – decrease anxiety, increase intelligence, improve sleep quality, lessen headaches, alleviate cancer pain… You get the picture. The companies promoting these devices suggest they would be helpful in treating headaches, anxiety, and stress – predictably, these are vague, widely reported symptoms. They also point to the ancient history of using electrical currents for therapy, even going back to when the most reliable source for electrical stimulation was electric eels.

But does it really work? A scientist cannot declare an idea wrong based simply on what I have told you so far. Look for well-controlled studies on this topic to find out. As we will discuss later in this book, these studies should be conducted with the patient, therapist, and researcher unaware of whether the patient is receiving true cranial electrical stimulation or is actually in the untreated control group. Levels of stress and anxiety are rather subjective to measure, and it is important that the measurements are collected in an unbiased manner. Such symptoms do improve spontaneously, so it is important to test a large enough sample so that you are not fooled by improvement due to chance. It would be necessary to have a control group that followed the same procedure, applying electrodes to the earlobes, experiencing a tickling sensation indicating current is being delivered, sitting quietly for an hour or two each day while treatment is delivered, and so on. This is an essential control group. Obviously, stress and anxiety might be reduced simply by relaxing for several hours each day or by the assurance that you are receiving treatment for the anxiety.

One of my favorite books – *The Monkey Gland Affair* by David Hamilton (1986) – describes the history of testicular implant treatments for the loss of libido in aging men. Another amusing angle on this story is in the film *Nuts!* (www.nutsthefilm.com/). We now know that the body immediately rejects and destroys such implants of foreign tissues. The medical establishment was fooled into accepting these treatments as legitimate, in part because of the strength of reported positive effects. Several weeks of rest and abstaining from alcohol, receiving healthy food and solicitous care from young women, were followed by an expensive operation promised to restore libido. Can you guess why the elderly male patients reported increased sexual drive?

Be a Skeptic

Your role as a scientist is to be skeptical and question everything. Ask for the evidence for the scientific "facts" your teachers present. Scrutinize that evidence with a critical eye. I can guarantee that some of these "facts" are incorrect and that scientists in your generation will correct them. Beyond the smaller "facts," perhaps there is a fundamental flaw in our current paradigm. Kuhn (1975) suggested that students training in science often accept the problems their teachers hand them, without questioning or even noticing the hidden assumptions underlying the research programs. It is worthwhile questioning the ground rules and asking for the evidence, so that you enter your career in neuroscience aware of both the strengths and the potential weaknesses in our fundamental tenets, such as the neuron doctrine.