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Neuroanatomical Foundations of Cognition: Connecting the Neuronal Level with the Study of Higher Brain Areas

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1 Introduction

In the philosophy of any science, it is important to consider how that science organizes itself with respect to its characteristic areas of inquiry. In the case of neuroscience, it is important to recognize that many neuroscientists approach the brain as a stratified system. In other words, it is generally acknowledged that there is a wide range of levels at which to investigate the brain, ranging from the micro to the macro level with respect to both anatomical scope and functional complexity. The following list of neuroanatomical kinds, for example, is ordered from the micro to the macro level: neurotransmitters, synapses, neurons, pathways, brain areas, systems, the brain, and central nervous system.

For philosophers of neuroscience, it is heuristically useful to understand that many neuroscientists view the brain in this way, because this conception of the brain helps shape the disciplinary structure of the field and helps define levels of neuroscientific research. Language, for example, is usually studied at the macro level, whereas synaptic transmission is investigated at the micro level. Although there is overlap and integration among the different levels, each level has its own methods and problem domains.

Furthermore, some levels lend themselves more easily than others to interdisciplinary involvement. Connections with biochemistry, for example, are most easily made at the micro level, whereas connections with cognitive psychology are typically made at more macro levels. Although philosophers can in principle make contact with neuroscience at any level, they have most commonly intersected at the macro levels of research. This is not surprising: it was, after all, the philosophers of mind, more so than the philosophers of science, who lead us into this particular

empirical engagement. Except for the most rabid functionalists, all cognitivists find the relevance of higher brain systems to our theories of mental function intuitively obvious.

In its central organization, this book retains that emphasis on higher-level brain research, but we also want to stress the importance and philosophical appeal of integrating work at the micro level. Unfortunately, although the philosophical gain to be had is appreciable, it is also much less apparent. Why bother with *neurons* when you really want to understand the higher operations? One of the goals of this chapter is to show that, even if one's philosophical interests in neuroscience are confined mainly to its role in cognitive explanations, understanding some important issues at the micro level can enhance one's ability to draw from this science. Another goal is to encourage the philosophical appreciation of neuroscience as a science, apart from its contributions to other fields. So, though the lowly neuron generally receives less attention than, say, the enigmatic frontal lobe, the controversy over its structural and functional elucidation is the stuff of neuroscientific legend and is of great philosophical interest.

In what follows, while I discuss both cellular and systems-level perspectives on the brain, I attempt to do more justice to the former by emphasizing the neuron doctrine (briefly, the view that neurons are physically discrete, cellular units) and the relation of this doctrine to higher-level theories. After a brief introduction to the anatomy of a neuron, I begin my account with some of the formative events in nineteenth-century biology which led to the development of the neuron doctrine. The nineteenth century is a convenient point to begin the discussion since it was at this time that the microscope (a seventeenth-century invention) really came to the forefront of scientific research. In part, this was because the microscope had undergone significant refinement in the early nineteenth century, resulting in improved clarity and range. It was at this time that microscopy at the cellular level first became sophisticated enough to be useful to biological theory. In tracing some of the most important advances from this point into the late twentieth century, I hope to show the fundamental importance of addressing micro-level research in the philosophy of neuroscience. My goal, however, is not to deny the importance of higher-level views of the brain. Rather, it is hoped that such redress will only facilitate a deeper, more informed perspective of the grosser level, the level from which philosophers most commonly draw in relating neuroscience and philosophy.

2 Basic Neuron Anatomy

In order to appreciate the issues discussed below, it is necessary to understand a few rudiments of neuron anatomy. Neurons, or nerve cells, consist of three major parts: cell body (soma), axon, and dendrites. Most neurons have only one axon, but several dendrites. Axons and dendrites are known as processes. Dendrites receive incoming signals and carry them to the cell body. Axons carry signals (action potentials) away from the cell body and toward the synapse (see figure 3.1).

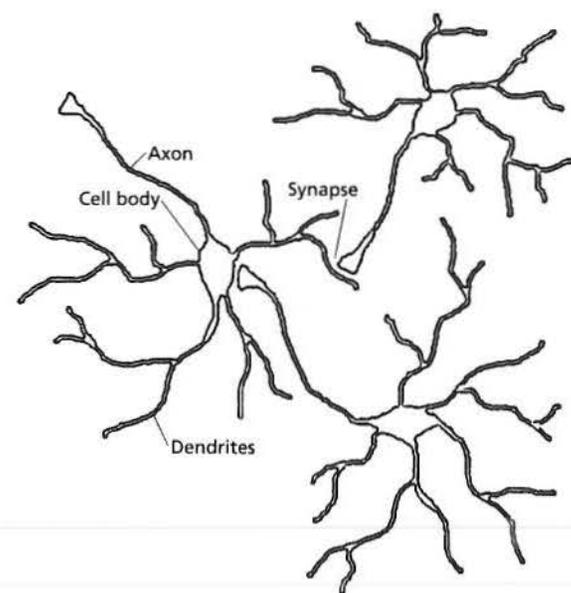


Figure 3.1 A neuron synapsing with another neuron. Note the soma, dendrites, axon, and synapse.

A synapse is a junction between two neurons, that is, between the axon terminal of the presynaptic cell and the dendrite (or sometimes, the cell body itself) of the postsynaptic cell. Synapses can be either chemical or electrical, though most are chemical. At the chemical synapse, there is no direct contact between the processes of the two cells. Instead, the signal transmission between them is mediated by chemicals known as neurotransmitters. The open space between the presynaptic cell and the postsynaptic cell is known as the synaptic cleft; this is the space into which neurotransmitters are released by the presynaptic cell.

Electrical synapses are mediated by the flow of electrical current from one cell to the next. At these synapses, the presynaptic and postsynaptic cells are linked by a very special kind of connection known as a *gap junction*, which appears to involve some cytoplasmic continuity between the connecting processes. For reasons which will be discussed below, gap junctions present a particular difficulty for the neuron doctrine.

There are several different kinds of neurons, differing according to features such as shape, number of processes, size, targets, location, neurotransmitter selectivity, and function. Estimates of the total number of neurons in the human brain vary widely, but 10^{11} appears to be a conservative estimate. Each neuron, in turn, forms an average of 1,000 synaptic connections with other neurons, resulting in at least

10^{14} synaptic connections within the brain (Kandel et al., 1991, p. 121). Altogether, we are confronted with a system of staggering complexity when looked at from the neuronal level.

For the purposes of this chapter, key concepts about neuronal structure can be summarized as follows: (1) in chemical synapses (the most common type), there is no physical contact between presynaptic and postsynaptic neurons; (2) neurons are discretely bounded, physically separate and distinct cells; (3) axonal and dendritic processes are physically integral to the nerve cell and continuous with the cell body; (4) functionally relevant differences among neuronal types can be microscopically observed (assuming the tissue has first been stained and subjected to other special treatments in order to make microscopic viewing possible). This latter feature makes it possible to use such cellular variation, otherwise known as cytoarchitectonics, as one technique for the localization and mapping of brain functions. The philosophical significance of each of these four features will become clearer in what follows.

3 The Cell Theory

That living organisms are made up of *cells*, and that neurons *are* cells, hardly seems like earthshaking news today, but at one time it was neither obvious nor uncontroversial. In fact, the establishment of the cell theory, or the theory that animal and plant tissues are composed of and generated from cells, was one of the chief advances of nineteenth-century biology. Although most historians acknowledge the key contributions of Schleiden and Purkinje, the cell theory is generally credited to Schwann, who proposed it in 1839 (Finger, 1994, pp. 43–4). Schwann's view was attractive in part because it allowed for powerful, theoretical unification. One can see him as a sort of Democritus with a biological twist: just as different material objects are composed, ultimately, of the same atomic constituents, so all living tissue is composed of the same, basic, cellular elements. What also made Schwann's theory attractive is that he proposed a general mechanism for cellular generation whereby cells are formed from the inside out, by the gradual accretion of new material, in a manner analogous to crystallization. This part of his theory proved to be erroneous, however, and by the 1850s, first Remak, and then Virchow proposed that cells are generated through cellular division. In spite of Schwann's false lead, however, the mechanism he proposed helped establish the larger idea that cells are the basic building blocks of life.

It is easy to suppose that the cell theory and the emerging structural picture of the neuron would have dovetailed so neatly as to have escaped notice. After all, given the variability of cell types found elsewhere in the body, it would seem to require very little effort to regard the neuron as just another kind of cell, and the neuron doctrine as nothing more than an extension of the cell theory. But now envision a neuron's shape and structure, and you will see an immediate problem researchers faced in classifying them as cells: neurons have long, thready processes sticking out

of them, features not found in other cells of the body. To regard the threads as part of the neuron was to be faced with two difficult alternatives. Either the concept of a cell had to be revised in order to include the irregular neuron, or the neuron had to be stricken from the cellular category.

On the other hand, it was not clear that these threads were physically integral to the neuron. Perhaps they merely played a supporting role, and, though always seen with neurons, were not themselves part of the neuron. Valentin and Purkinje, for example, both prominent, mid-nineteenth-century investigators, examined brain tissue under a microscope, and concluded that the processes were not physically continuous with the cell body. They did hold, however, that the processes played some role in the transmission of neural signals. In this case, neurons could be regarded as just "normal" cells after all, and the brain would appear to be a "normal" tissue, composed of cells just like all other tissues. The connective relation between the neuron's cell body and its processes was not clearly understood by early neuromicroscopists, and only began to take shape in the late 1830s through the 1850s, with the work of such figures as Remak and Schwann (Shepherd, 1991, pp. 19–23).

This seemingly minor issue itself makes up a philosophically rich chapter in the history of neuroscience. It ties in with such large-scale issues as materialist vs. dualist (Cartesian) views of the mind, and mechanistic vs. vitalistic explanations of natural phenomena (vitalism, or the appeal to vital forces to explain living phenomena, was still common in the nineteenth century). An extended discussion of these topics is not possible here, but they are worth a passing mention. Jacobson (1995) suggests that depicting the nerve cell body as continuous with its input and output processes conflicts with Descartes's concept of the mind, because, in this view, "There was no room for the soul between input and output in that model, and although not explicitly stated, it was implied that the soul was not required for routing the nervous activity in the brain and spinal cord. The nucleated part of the nerve cell then occupied the place between input and output formerly occupied by the Cartesian soul" (p. 181). Furthermore, if brain *tissue* were to be relegated to the lowly status of all other living tissues, not fundamentally different in kind, this demotion can be seen as yet another slap at the Rylean ghost caught within the cellular machine, and as a hopeful nod toward a reductive, mechanistic explanation.

In any event, seeing the nerve fibers as physically continuous with the cell body not only stretched the structural concept of a cell, but generated another point of tension with the cell theory. This tension centered around the nature of intercellular connection. For the cell theorist, a cell is regarded as an individual, physically discrete unit. Neural tissue, though, when prepared (stained, sectioned, fixed, etc.) and examined under a microscope, looked like a tangled net, dotted with small black blobs. So, if the long, thready processes of the nerve cell are actually part of the cell, where does one nerve cell begin and another end? *Do* they end, or is neural tissue made up of a vast, physically continuous network? (See figure 3.2.)

These seem to be questions that could easily be settled by mere observation, but there were serious limitations on what could be observed at that time.

Histological methods of staining and preparation were not nearly up to the task of settling these questions, and they would not prove to be dispositive, in fact, until the advent of electron microscopy in the mid-twentieth century. Thus we have arrived at one of the most important neuroscientific debates of the twentieth century.

4 The Neuron Doctrine

In simple terms, the neuron doctrine consists of the view that neurons are discrete, individual cells, one physically discontinuous from another; whereas the opposing, reticular theory holds that the brain consists of a continuous web, or reticulum of nerve fibers. Camillo Golgi (1843–1926) was a committed reticularist, but he invented a method of staining neurons (discussed below) which helped Santiago Ramón y Cajal (1852–1934) make a convincing case for the neuron doctrine. The debate between Golgi and Ramón y Cajal (usually referred to just as “Cajal”) is now a famous bedtime story for students of neuroscience. In the fabled version, it amounts to a heroic battle in which the great but doddering Golgi stubbornly clings to the old view ’til death, but nonetheless invents the very weapon which the brave young Spanish blade, Santiago Ramón y Cajal, uses to defeat him. Though Cajal was right and Golgi was wrong, they both won the Nobel Prize anyway, and the neuron doctrine lived happily ever after . . . or something like that.

The less condensed version of the story often flounders on just what the neuron doctrine consists of, for here things get a bit more complicated, and not all commentators agree (compare, for example, the contemporary accounts of Jacobson, 1995, and Shepherd, 1991, both with each other and with such classic sources as Clarke and O’Malley, 1968, 1996). Differences and difficulties in the precise formulation of this doctrine can be attributed to at least four major factors. First, the doctrine evolved over time and there are differences from one historical period to another. Second, its relation to the cell theory has been variously construed, and the earliest roots of the neuron doctrine were in place even before neurons themselves were widely accepted as just another kind of cell. Third, even those most closely involved with this research did not always agree on just what constituted the neuron doctrine. Golgi and Cajal, for example, articulated very different views about what constituted the neuron doctrine. For that matter, even the reticularist viewpoint is not easily encapsulated. Cajal, for example, complained in his Nobel address that the form of the reticular viewpoint “changes every five or six years” (1906, p. 241). Fourth, it was and is a very difficult matter to decide just what is to count as a part of the main doctrine itself, as opposed to the many closely related issues about neuronal structure and function.

The essence of the controversy, however, turns on whether or not the neuronal processes in the brain all run together into one vast, physically continuous network or reticulum (as Golgi and other reticularists saw it), or whether the neurons are physically distinct cells connected merely contiguously (as Cajal and other neuro-

nists would have it). Certainly the neuronists had an easier time squaring their views with the cell theory, as discussed above, but the reticularists, as we will see more clearly below, had an easier time squaring their views with certain other theories.

On the foundation of the cell theory, the neuron doctrine had been building for some time before its star combatants, Golgi and Cajal, took center stage. As it happens, it was Golgi’s development of a revolutionary, silver-based stain which laid the basis for their eventual confrontation. As noted above, it is one of the most famous of scientific ironies that Golgi himself invented the very method which Cajal exploited so successfully against him. The great advantage of Golgi’s procedure is that it stains only a small percentage of the nerve cells in a given sample (those that are stained, however, are stained completely). Previous methods, on the other hand, tended to stain samples indiscriminately, thereby making it very difficult to discern much of anything, let alone the finer structure of a single neuron (see figure 3.2). It is important to keep in mind, however, that Golgi himself did not know why the reaction worked this way, and we still do not have a clear understanding of the underlying mechanism.

Golgi developed his technique in the early 1870s and published his findings in 1873, though his work did not attract immediate attention. In 1887, Cajal first became acquainted with the complicated Golgi method and was instantly captivated by it (Ramón y Cajal, 1988, p. 3). He set to work on it immediately, attempting both to improve the unpredictable nature of the reaction itself, as well as to capitalize on the histological advantages it offered. By 1888 he had already begun to publish the results of his early work with the Golgi technique, and by 1889 was making definite assertions in print which directly opposed Golgi’s reticular theory.

From Cajal’s perspective, he simply *saw* when he looked through the microscope that his Golgi preparations supported the neuron doctrine. Yet, if it were this obvious, why didn’t Golgi come to the same conclusions? Consider figure 3.2. and it is easier to see why the debate wore on for some time even after the use of the Golgi stain. Visual observation of neural tissue did not provide conclusive warrant to decide between Cajal’s neuronism and Golgi’s reticularism. Although this kind of evidence alone would not make for decisive interpretation, the state of microscopy at that time could provide nothing better. What else was there?

Commonly, the larger theoretical structures with which the evidence coheres provides further grounds of appeal. But even when lodged within larger theoretical frameworks, neuronism and reticularism were still fairly well-matched rivals. Golgi’s reticularism harmonized well with a holistic, or non-localizationist theory of brain function, to which he was also deeply committed. Here, he explicitly notes the tension between localizationist ideas and his network theory:

Another observation occurs to me: The concept of the so-called location of the cerebral functions, should it be insisted on accepting it in a rigorous sense, would not be in perfect harmony with the anatomical data, or at the least, it should now be admitted only in a somewhat limited . . . sense. It being demonstrated, for example, that a nervous fibre is in relation with extensive groups of ganglionic cells, and that the

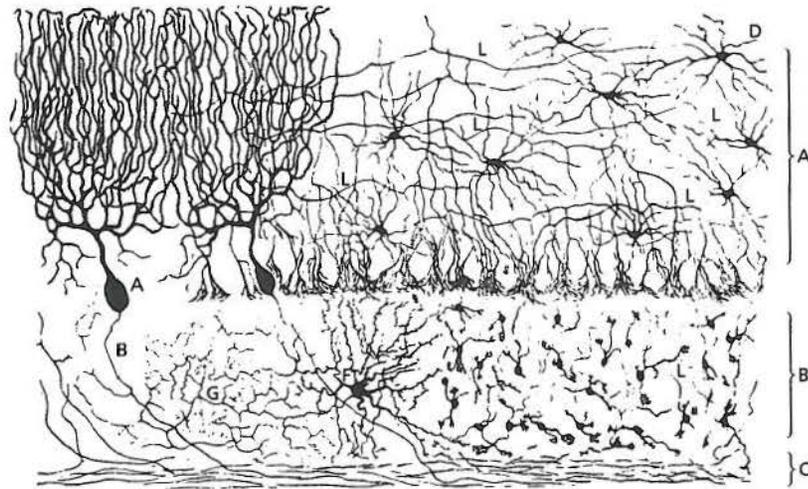


Figure 3.2 Cajal's illustration of brain tissue sample, taken from cerebellum, and prepared for microscopic observation according to Golgi method. From *Observations sur la texture des fibres musculaires des pattes et des ailes des insectes. International Journal of Anatomy and Physiology*, 5 (1888), 205–32; 253–76.

ganglionic elements of entire provinces, and also of various neighboring provinces, are conjoined by means of a diffuse network . . . it is naturally difficult to understand a rigorous functional localization, as many would have it.

(Golgi, 1883, in Shepherd, 1991, p. 96)

Placing the neuron debate within the context of the localization debate enlarges the discussion but confers no obvious advantage for either side. Just as investigators were split over the neuron question, they were split on the question of cerebral localization. More will be said about the localization controversy below, but for now it is important to note that it was also a contentious issue with an even longer history than that of the neuron doctrine. In a more subdued tone, the debate continues even to the present day.

On other grounds of appeal, when it came to explaining the transmission of neural signals from one part of the brain to the next, the reticularists clearly win the prize for parsimony. If neurons form a continuous, uninterrupted network, understanding signal transmission becomes a simple matter. Even Cajal acknowledges this point, noting that

[i]t is necessary to realize that for certain minds the reticular theory offers a most attractive and convenient explanation. Among other physiological advantages it would offer

the inestimable one of explaining in a simple manner the propagation of the nerve impulse from one neuron to another and its diffusion throughout the gray substance in a number of directions.

The important thing here is not to ponder the theoretical simplicity and facility (more apparent than real) of a theory but rather to evaluate to what extent it conforms with well-known, demonstrable facts.

(Ramón y Cajal, 1954, trans. Purkiss and Fox, 1954, p. 1)

Neuronists, by contrast, had to explain how the signal is propagated across an open space. Today, of course, we recognize this as the process of synaptic transmission, and have detailed, well-corroborated theories about its mechanism. Cajal did not.

Interestingly, though, at approximately the same time that Cajal was establishing the neuron doctrine, Charles Sherrington was developing the theory of synaptic transmission. Sherrington coined the term *synapse* in 1897, and his earliest work on the subject can be seen as providing mutual support with the neuron doctrine, as we can see from his statement below:

So far as our present knowledge goes, we are led to think that the tip of a twig of the arborescence is not continuous with but merely in contact with the substance of the dendrite or cell body on which it impinges. Such a special connection of one nerve cell with another might be called a synapse.

(Sherrington, 1897, in Shepherd, 1991, p. 228)

So, the reticularists had an easier way to account for neural signaling than the neuronists; yet even though neuronists had a more difficult story to tell, that story was already in progress, and being developed independently of Cajal's work.

Golgi never did capitulate to the neuron doctrine, though it was clear by the time they won the Nobel Prize (1906) that support had begun to sway in favor of the neuron doctrine. Even so, reticularism could not be ruled out as conclusively as one might expect. Until the development of electron microscopy the technology did not support a decisive verdict.

Even if the micrographic images themselves had presented an unambiguous case, this likely would not have settled the matter, for, as philosophers of science are wont to point out, it is not always clear what you see when you look through a microscope. Several issues arise here having to do with realism vs. anti-realism, the theory-ladenness of perception, and others, but most immediately, there is the problem of separating data from artifact.

It is a long, tortuous road from brain tissue to a thinly sliced, chemically stained and fixed slide preparation such as those on which Golgi, Cajal, and other late-nineteenth-century neuroanatomists were basing their conclusions. The transformation that takes place may not result in a veridical image of the object of study; artifacts of insertion, deletion, and distortion are all possible, and can lead to a misinterpretation of the underlying phenomena. Bechtel (1995) identifies several distinct factors underlying the difficulties separating data from artifact:

First, there are often a large number of intervening steps between the original phenomenon and the results that are construed as data. Each of these steps is potentially a point that could give rise to an artifact. Second, many procedures are extremely brutal since one often has to transform radically the phenomenon to achieve interpretable results. Third, there is often very little knowledge about how exactly the procedures work. . . . Last, it is often the case that procedures are extremely sensitive to the details of the way in which they are carried out such that slight variation in procedures may alter the results. . . .

(p. 167)

In the case of the Golgi preparation, each of these four factors is particularly striking. With respect to the first two, I have already noted some of the harsh, complicated procedures to which neural tissue is subjected in order to render images visible under the microscope. With respect to the third, for example, we *still* do not have a clear understanding of how and why the process works, and even less was understood in Golgi's time. With respect to the fourth, Golgi and Cajal were both frustrated by the capricious nature of the reaction and made constant adjustments in the process in order to attain better results. In this sense, there was no single Golgi method, but several variations on a broad technique.

Brief excerpts from Golgi's own 1875 description of his method underscore the presence of all the complicating factors identified above. Consider, for example, that *after* the samples have completed the long hardening and staining processes, they still have to undergo the following procedure in order to be made ready for the microscope:

For microscopic examination the sections are placed in damar varnish . . . or in Canada balsam after they have been dehydrated through the use of absolute alcohol and have been rendered transparent with creosote.

Time and light continually spoil the microscopic preparations obtained with my method. . . .

(in Clarke and O'Malley, 1996, p. 842)

Golgi is also indefinite about the lengths of time required for each phase of the reaction to take place and loosely remarks, for example, that the length of time he specifies can be decreased in hot weather and increased in cold weather. Finally, interspersed throughout his description are such caveats as: "I must equally declare that I have not yet succeeded in determining with certainty why under ~~the~~ same conditions . . . I have obtained very different results," and "Permit me to advise, however, that I do not find myself as yet in a position to explain with precision all the necessary procedures for the best results. They are still partly fortuitous" (in 1996, p. 845).

In time, of course, several converging factors led to the acceptance of the neuron doctrine in spite of the complications described above. Improved technology, multiple and independent confirmation, entrenchment within larger theories, all of these contributed to establishing it as one of the cornerstones of neuroscience. But many of the concerns raised in this debate, including the problem of artifacts,

retain their importance for this science; some of these will be discussed further below.

As a wry footnote to this section, recent evidence shows that we cannot quite yet consider this case closed. Shepherd's (1991) remarkable history of the neuron doctrine closes with an absorbing analysis of how some aspects of it may need to be gently revised in light of new research. The categories under which he considers challenges to the neuron doctrine are: the neuron as anatomical unit, physiological unit, genetic unit, and metabolic unit. One of the more significant developments he addresses is how the dramatic discovery of the gap junction (mentioned above) calls into question the status of the neuron as an anatomical unit. At gap junctions, there is some physical continuity, or a direct coupling between connecting neurons. Signals are carried electrically, by ionic current, rather than chemically, by neurotransmitters. Across gap junctions, aligned portals form in both presynaptic and postsynaptic neurons, creating a conduit through which ions and other molecules flow freely from one neuron to another. This direct flow of ionic current eliminates the synaptic delay found in chemically mediated transmission. For further comparison, distances across a chemical synapse (30–50 nm) are approximately 10 times greater than distances across gap junctions (3.5 nm). Both structurally and functionally there is continuity between the two neurons, which is exactly what the essence of the neuron doctrine denies. It should be borne in mind, however, that chemical synapses are in greater abundance than electrical ones. Nevertheless, if Golgi had lived to see this discovery, he would probably find some consolation in it.

5 Cytoarchitecture and Localization

We have seen how the cell theory provided support for neuron doctrine. Now I will connect the neuron doctrine with localization theory and another important progression of micro-level research: cytoarchitectonics. I will begin with localization theory.

Before addressing specific localization theories, it is useful to consider the concept of localization itself. What does it mean for a function to be localized? Early attempts to localize function were pretty straightforward, carving out a spatially defined region of the brain and correlating it with a distinct function. This is one means of analysis, and provides a convenient continuum along which to evaluate degrees of localization. Weak localizationists might be willing to attribute some functional differentiation between the two hemispheres, or perhaps among the different lobes, for example, but would not agree to specialization on a smaller scale. Strong localizationists would see functional differences among small, narrowly circumscribed regions, on the order of Brodmann's areas (discussed below), for example, or even smaller regions.

In this quantitative construal, functions are associated with a spatially defined area of the brain, and the magnitude at which functional differences are thought to arise differs from one theory to another. This also provides a convenient way of understanding the historical progression of localization theory. As Finger explains, "In the long history of the brain sciences, it is possible to conceive of the theory of localization as being applied to the whole and then to increasingly smaller parts" (1994, p. 3).

Another way to think of localization, compatible with the sense above, is qualitatively. In other words, one might begin to associate a function with a specific, neurological correlate, but that correlate might be of a given neurological kind, rather than a spatially well-defined one. In this way, we can speak about the functional specificity of different cortical layers, rods vs. cones, the purkinje cells of the cerebellum, dopaminergic pathways, etc.

It is also important to consider the function itself when analyzing the concept of localization. Some functions are considered more localizable than others, and this also helps define different degrees of localization. Many of the functions associated with the senses are considered to be more obviously localizable than consciousness, for example.

Finally, contemporary brain-mapping techniques stretch the notion of localization beyond these relatively simple analyses. In this case, a given function may correlate with repeatable activation patterns of several disparate regions of the brain. These activation patterns are neither quantitatively nor qualitatively well defined, but they are specific and regular. In many cases, it has also been possible to analyze these complex activations into the subfunctions associated with the smaller, better-defined regions of activation.

Historically, almost since the brain itself came to be seen as the seat of cognition, there have been attempts to correlate a given region of the brain with a specific psychological function. Some of the earliest localizationist theories arose in the fourth and fifth centuries, and involved metaphysically obscure, functional differentiation of the ventricles, or hollow cavities of the brain (then thought to be permeated with ethereal, animal spirits). Renaissance theories showed appreciable gain in terms of anatomical sophistication and detail, but the first modern theories of cortical localization did not appear until the nineteenth century.

One of the more influential localization schemes of this period was phrenology, developed by Gall and Spurzheim in the early 1800s (this movement is well known, so will only be summarized here). Although Gall's map delineated boundaries on the cranial surface, it was assumed that the cranial surface conformed perfectly to the underlying cortex, and it was the cortex Gall was actually mapping. He claims to have derived the map through years of human observation, correlating the most pronounced psychological characteristics of thousands of subjects with localized enlargements in the skull. Although his central assumptions were erroneous and his work widely discredited, many modern commentators agree that the essence of his project, to map the functional regions of the cortex, represented an important leap forward. Even Brodmann, a central figure of

brain-mapping research, credits him with this important conceptual contribution (Brodmann, 1909, Garey trans. 1994, p. 250). As I will explain in more detail shortly, Brodmann's most important tool in mapping the cortex was cytoarchitectonics.

Cytoarchitectonics provides a means of identifying and delineating the functional areas of the brain according to neuronal population patterns, or cellular "demographics." Of course, the overarching assumption of cytoarchitectonics is that function *can* be localized to specific brain regions; it is the *raison d'être* of this research. Another assumption behind the research has to do with the relation between structure and function, particularly at the histological level. Neurons vary according to number of processes, length of processes, degree of arborization, cell body size, cell body shape, and other structural features. Some structural features provide clues to the functional significance of a given neuron. The degree of dendritic arborization, for example, is an indication of how many input connections a cell can accommodate, and the degree of axonal arborization tells us about the number of different output sites. Not surprisingly, regions which differ cytoarchitectonically are likely to differ functionally, and this is why cytoarchitectonic variation is one of the techniques used to map the functional regions of the brain. The operative principle is that there is a close connection between structure and function, such that, when one varies, the other also tends to vary. This assumption has been instrumental in twentieth-century neuroscience, particularly in brain-mapping research.

These two assumptions behind cytoarchitectonic research, that function can be localized, and that functional boundaries correspond to cytoarchitectonic boundaries, are difficult for a reticularist to accommodate. With respect to the first assumption, it is difficult for a reticularist to explain how or why one part of a continuous, uniform nerve net should behave any differently than another. Holism is much more compatible with reticularism, and, as discussed above, Golgi subscribed to both. A localizationist, on the other hand, sees structural variation, and couples that with functional variation. With respect to the second assumption, cytoarchitectonic variation is not terribly meaningful for reticularists since, in their view, the nerve cell lacks both structural and functional independence. As late as his Nobel lecture, Golgi expressly denied the physiological "individuality and independence of each nerve element," insisting, instead, that:

nerve cells, instead of working individually, act together, so that we must think that several groups of elements exercise a cumulative effect. . . . However opposed it may seem to the popular tendency to individualize the elements, I cannot abandon the idea of a unitary action of the nervous system.

(1906, p. 216)

Golgi's remarks make it even easier to see why reticularism and holism are complementary views. Similarly, it should also be easier to see the conceptual and historical connections among the localization of function, the neuron doctrine, and cytoarchitectonic research.

The holistic view of the brain (minus reticularism), presently endures; as, of course, does the localizationist view. These two, broad research traditions, holistic and localizationist, have both made important contributions to neuroscience. Before pursuing the latter topic, below, the holistic tradition deserves some mention. At approximately the same time that cytoarchitectonic research was beginning to achieve worldwide prominence in neuroscientific research, World War I produced the practical necessity of finding effective treatments of soldiers who had sustained severe head injuries. In this sphere, holistic principles dominated therapeutic assumptions and provided more optimistic prognoses than a strictly localizationist framework. It will come as no surprise that Golgi worked at a military hospital during the war, where he created a special center for the treatment, study, and rehabilitation of soldiers with neurological injuries. The numerous cases of rehabilitated soldiers who experienced full or partial recovery of function provided some vindication for holistically oriented thinking. Kurt Goldstein was another eminent holist to emerge from this crucible, and he later helped found the Gestalt movement in psychology and neurology. Though not adamantly opposed to the concept of some regional specialization in the brain, Goldstein was holistic both in the sense discussed above and in the following sense: he enlarged the scope of information which was brought to bear in guiding his treatment and understanding of his patients. He saw the recovering patient as an organism with altered abilities attempting to cope with an environment of constantly shifting demands and challenges. The spirit of this comprehensive approach, taking into account both the patient and the world in which the patient lives, also continues to influence neuropsychiatry, and is reflected in such notable figures as Oliver Sacks. In philosophy and cognitive science, one sees a similar approach in the current shift toward "situated cognition."

6 Brain Areas and Modern Neuroscience

Although the 1990s were considered the decade of the brain, for some areas of research, it might better be seen as the *grande finale* of an entire century of the brain. In the case of brain mapping, the endpoints of the twentieth century mark a particularly important period of progress. In the early 1900s, newly developed cytoarchitectonic techniques (see above) made possible the first scientifically significant maps of the cortical surface. By the century's close, sophisticated radiographic techniques were imaging the areas where increased activation occurred as live, human subjects performed specific tasks. In this section I discuss how the acceptance of both the neuron doctrine and the localizability of function was key to these developments.

To embark on a project of mapping the functional regions of the brain, of course, requires some commitment to the localizability of function, since that is the goal of such research. As I discussed in the previous section, *cytoarchitectonic* research involves the further assumption that different populations of cells, as distinguished

at the histochemical level, perform different functions. This micro-level case is an instance of a general biological principle that physical differentiation tracks functional differentiation (and vice versa). Toward the end of the nineteenth century, Betz, and later Flechsig, published some of the earliest cytoarchitectonic work, but the method did not really come into its own until early in the twentieth century. From roughly 1905 to 1925 several researchers employed cytoarchitectonic techniques in deriving functional maps of the human cortex. Campbell produced a series of maps in 1905, Vogt and Vogt in 1919, and Economo in 1925, but the most famous and influential map (see figure 3.3) was produced in 1907 (and revised in 1909), by Korbinian Brodmann (1868–1918).

Brodmann's work and commentary provide us with a clear example of how ideas concerning neuronal structure and function became an integral part of subsequent brain cartography. Unlike many of his contemporaries, Brodmann often comments on the deeper, theoretical issues related to his research, and attempts to justify his overall approach to the problem of mapping the cortex. Possibly, this helps to explain why he had such a formative effect on future cartographic research. He makes his assumptions quite clear, for example, when he writes: "There is an undisputed axiom: physiologically dissimilar elements have dissimilar structures. Reversing this statement one may equally justifiably conclude: parts of organs that are structurally different must serve different purposes" (Brodmann, 1909, Garey trans. 1994, p. 253). He also clearly identifies his commitment to the specific case of this "axiom," which is that the level of dissimilarity which is functionally significant extends down to the cellular, or histological level: "It is a basic biological principle that the function of an organ is correlated with its elementary histological structure" (*ibid.*, p. 243). Additionally, scattered throughout his work are several attempts to support this principle. Clearly, Brodmann's work depended on a view of the neuron as a largely, if not entirely, structurally and functionally independent unit. That, of course, is exactly what the neuron doctrine was all about.

Now, to connect Brodmann's work with later brain-mapping research, it is important to realize that in addition to cytoarchitectonics (which is still in use), many other methods have been employed to chart the functional regions of the brain, and Brodmann's famous map itself has undergone some modest revisions by other researchers (see, for example, Mundale, 1998). Yet Brodmann's map has served as a common reference point since it was first published, and continues to do so for contemporary neuroscientists. It also helped to support explanations of human behavior in terms of areas of functional activation. Though Brodmann's methods and results were seriously challenged by critics from the holistic and Gestalt schools (see especially Lashley and Clark, 1946, for example), Brodmann struck a lasting blow for localizationist thinking which continues to motivate cartographic research.

Other chapters in this volume will elaborate more fully on contemporary brain-mapping methods, particularly PET scanning and other radiographic techniques. And those, in turn, will be tied to a greater understanding of such high-level

functions as perception and language. But we can also work back down to the lowly neuron, with a more connected perspective about its place in the foundations of cognition.

7 Conclusion

I began with an explanation of how researchers approach the brain as a stratified, yet integrated system in both physical and functional respects. Working within this framework, my major concern has been to show how an appreciation of several critical developments at the micro level, though often overlooked by philosophers, can greatly enhance our understanding of the brain and its functions at higher levels. To show this, I traced one particular thread from the cell theory, the neuron doctrine, the localization of function, cytoarchitectonics, and modern brain-mapping research. Although other antecedent and subsequent developments in this thread, as well as several important collaterals, remain unmentioned, it is hoped that the main example itself will provide some sense of how to enlarge the picture and draw further, conceptually useful connections between micro-level and macro-level subjects.

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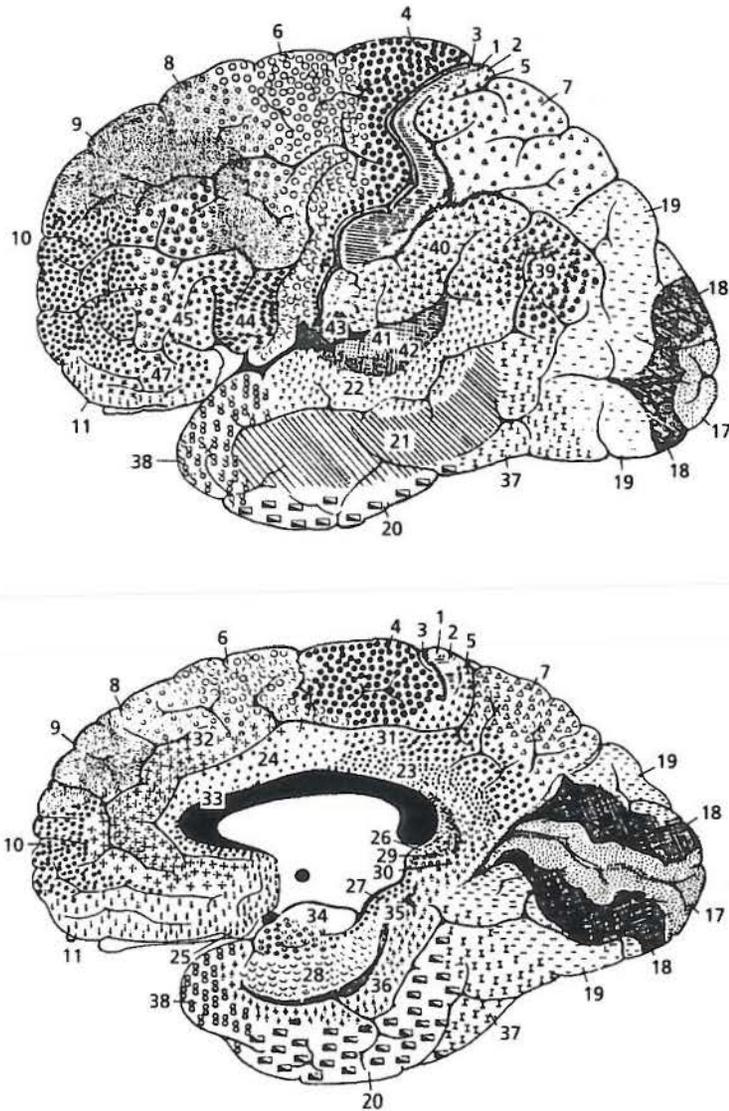


Figure 3.3 Brodmann's (1909) cytoarchitectonic map of the human cortex. Relying primarily on regional differences in cell type, density, and distribution – a method broadly referred to as *cytoarchitectonics* – Brodmann identified over 40 distinct areas of human cortex.

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Epistemic Issues in Procuring Evidence about the Brain: The Importance of Research Instruments and Techniques

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1 The Epistemic Challenge Posed by Research Instruments and Techniques

According to traditional philosophical accounts of scientific methodology, the evidence for scientific theories stems from observation, especially observation with the naked eye. These accounts portray the testing of scientific theories as a matter of comparing the predictions of the theory with the data generated by these observations, which are taken to be an objective portrayal of reality. One lesson learned by philosophers of science in the last 40 years is that even observation with the naked eye is not as epistemically straightforward as is sometimes assumed. What one is able to see depends upon one's training: a novice looking through a microscope may fail to recognize the neuron and its processes (Hanson, 1958; Kuhn, 1962/1970).¹ But a second lesson is only beginning to be learned: the evidence in science is often not procured through simple observations with the naked eye, but through observations mediated by complex instruments and sophisticated research techniques. In order to acquire evidence about the phenomena under investigation, these instruments must alter it. (For a simple, prosaic example, consider the ordinary thermometer. It requires the transformation of the temperature of the surrounding air into the expansion of a liquid or metal so as to produce a display that we can see [Hacking, 1983].) The fact that evidence consists of altered phenomena then raises a serious question: to what degree is what is taken as evidence just the product of the alteration or in what respects does it reflect the original phenomena for which it is taken to be evidence?

Since most scientific evidence is procured through instruments and research tech-