THE MORPHOLOGY AND FUNCTIONS OF THE BRAIN

*Guillermo Gutiérrez Ospina**

Understanding the relationship between the brain's morphology and function has been a fascinating and challenging scientific and philosophical enterprise Once considered a device to cool off our bodies, the brain is no longer thought of as a "cooling system" but the organ where our sensations and emotions are integrated. More important, the brain is the organ where our humanness resides and from which our individual identities emerge. But how does this extraordinary organ create illusions, expectations, ideas, obsessions, emotions, language and memories? In other words, how does it create the story of our lives? Neurobiologists believe the answer lies somewhere in the intricate and convoluted anatomy of the brain (Figure 1).

A large fraction of the brain's mass is made up of connections among nerve cells or neurons. These connections form circuits responsible for receiving, processing and storing the information we perceive through our sensory organs. It is fair, then, to think that studying how these connections are established and assembled into circuits will lead us to better understand how the structure and function of the brain interrelate. Here, I will succinctly describe current thinking on how the brain deals with the problem of assembling neural circuits. It may surprise lay readers that the prevailing view suggests that the final geometry and function of neural circuits arise after many connections among neurons are removed during brain growth. I will argue, however, that the assembling of neural circuits also involves the progressive elaboration of new connections as the brain matures. This gives rise to more complex circuits, thus providing the anatomic substratum necessary for the brain to accomplish some of its formidable functions.

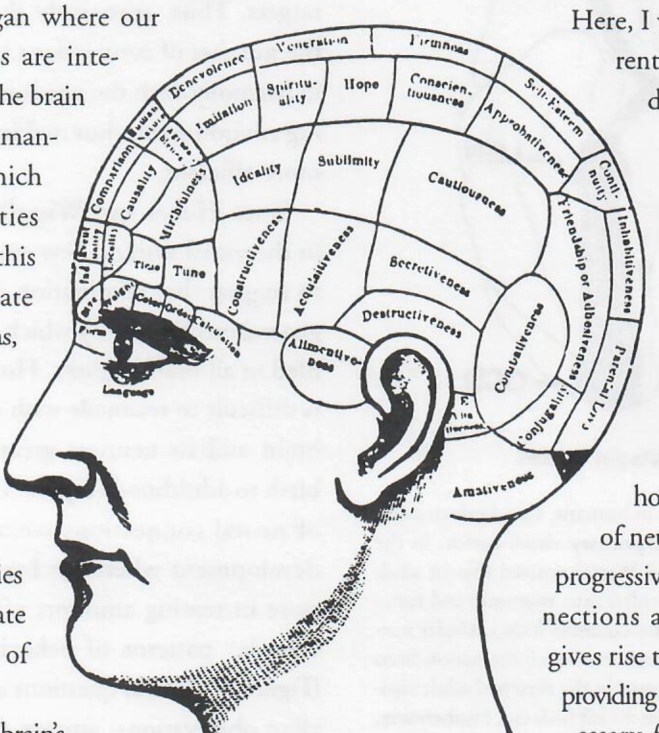

Figure 1. At the end of the eighteenth century the belief that mental functions were localized in particular regions of the brain was deeply rooted in some neurologists' minds. This way of thinking (phrenology) would later provide the basis for the "localizationist" view of brain functions that still dominates, albeit in a different context, modern neuroscience (original by Spurzheim; reproduced in P. T. Churchland, *Neurophilosophy. Toward a Unified Science of the Wind/Brain,* MIT, MA, 1992).

---

* Researcher at the University of North Carolina. Associate researcher at the UNAM's Institute of Neurobiology.

REFINING THE BRAIN'S CIRCUITRY

The brain is the organ where our humanness resides and from which our individual identities emerge.

In the 1960s, Nobel laureates David Hubel and Torsten Wiesel carried out a series of experiments that provided important clues about how neural circuits are assembled. Based on their observations of the visual system of growing cats and monkeys, Hubel and Wiesel concluded that at birth the brain has many redundant connections that are subsequently removed as we experience our surroundings during postnatal maturation (Figure 2). What could be the purpose of removing connections among neurons while the brain is still maturing? It has been suggested that this process refines the geometry and functional properties of neural circuits and decreases the number of erroneous connections between neurons and their many potential targets. Thus, apparently the final goal of reducing the number of connections is to shape neural circuits in harmony with the needs imposed by the surrounding environment, thus making the brain's functioning more efficient.

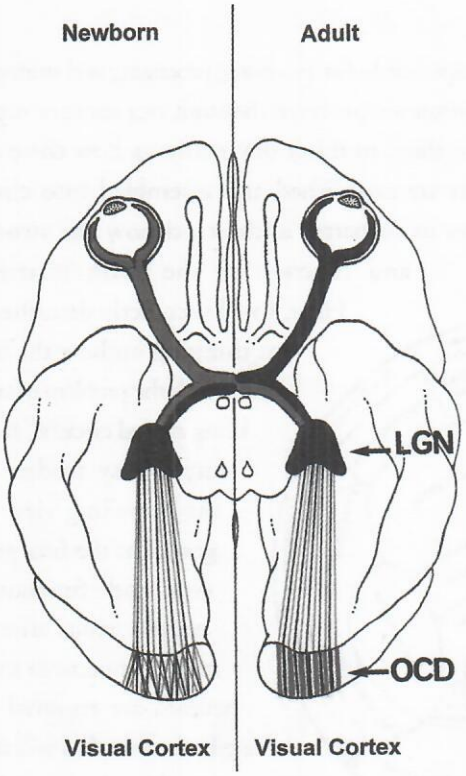

Figure 2. In the monkey brain, as in humans, visual information is transfered from the eyes to the primary visual cortex, in the back pole of the brain. Hubel and Wiesel noticed that in adult monkeys the visual cortex was divided into anatomic and functional units called ocular dominance columns (ODC). Under normal conditions, each of these columns receives information from a single eye. For instance, red columns in the sketched adult visual cortex only receive information from the left (red) eye. Furthermore, left (red) and right (black) eye-associated columns alternate throughout the adult primary visual cortex. Ocular dominance columns, however, do not exist in the primary visual cortex of newborn monkeys. At birth, neural connections associated with both eyes overlap extensively over the entire visual cortex. Ocular dominance columns in adult monkeys gradually emerge after neurons in the lateral geniculate nucleus (LGN; dark blue) remove many of their connections from the visual cortex, as the animal matures (Adapted from D. Purves & J.W. Lichtman, *Principles of Neural Development,* Sinaver, MA, 1985.

Since Hubel and Wiesel's landmark experiments in the visual system, new evidence has been gathered to suggest that elimination of connections may be a general mechanism by which neural circuits are assembled in all brain regions. However, a process like this is difficult to reconcile with at least two facts: 1) The brain and its neurons greatly increase in size from birth to adulthood (Figure 3) and 2) The elimination of neural connections seems to occur at a time in development when our brains receive, process and store increasing amounts of information, and when complex patterns of behavior progressively emerge (Figure 4). Several questions arise then from these puzzling observations, among them: How do the brain and its neurons increase their size while neural connections are removed? Why should neurons increase their size if they lose contact with their neural peers? How can the brain progressively increase its capacity to process and memorize information and generate complex patterns of behavior, while at the same time eliminating neural connections?

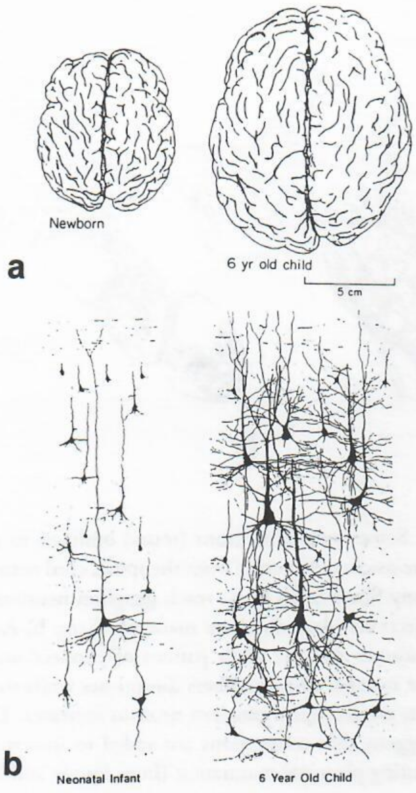

Figure 3. The human brain increases its size by about four-fold during postnatal development; a) At birth, the human brain weighs an average of 350 grams reaching approximately 1400 grams in adulthood; b) This increase in brain size not only reflects the "passive" enlargement of neurons and their connections, but the "active" elaboration of more complex circuits (Adapted from D. Purves, *Neural Activity and the Growth of the Brain*, Cambridge University Press, Cambridge, U.K., 1994).

ELABORATION OF NEW CIRCUITRY IN THE BRAIN

A mechanism whereby the brain's circuitry may be sculpted during postnatal development would be to progressively add new connections to immature neural circuits. These additions would provide the anatomic substratum necessary for the developing brain to increase its capacity to process and store novel and relevant information. Evidence supporting this possibility has been found in the peripheral nervous system, which is formed by neurons in the brain stem, the spinal cord and in small, seed-like structures called peripheral nerve ganglia (Figure 5). These neurons give rise to nerve fibers that regulate the activity of organs such as muscles and viscera. Neurons localized in some types of ganglia are themselves targets of nerve fibers from neurons in the spinal cord. Early in development, ganglion neurons receive many fibers but only a few connections are made. As postnatal maturation proceeds, the number of fibers reaching ganglion neurons diminishes. The remaining fibers, however, grow to make many connections with ganglion neurons (Figure 6). This observation suggests, therefore, that selective growth of connections also shapes neural circuits during postnatal development.

Recently, it has been demonstrated that new connections are also made in the developing brain after birth. The somatic sensory cortex is a region of the brain that contains a map representing the body's surface (Figures 7 and 8). This map in the human brain is

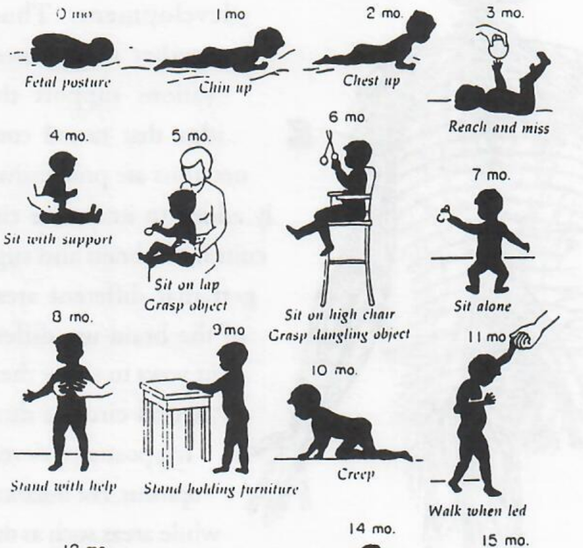

Figure 4. Human motor skills improve rapidly during the first year of life. Although the sequence illustrated here emphasizes the development of motor behavior, this phase of development is also characterized by a surprising improvement of children's cognitive abilities. Indeed, rudiments of language begin to appear by this time of development.

called the "homunculus" (Figure 7), and similar body maps exist in the brains of all mammals. The brain's body map can be readily visualized in rats and mice in which it is organized in units termed barrels because of their three-dimensional appearance. Each of these barrels represents sensory organs such as the facial whiskers on the surface of the skin (Figure 8). Studying how the pattern of connections arises in the rat barrel somatic sensory cortex, Ariel Agmon and his collaborators at the University of California, Irvine, have demonstrated that neural circuits are progressively elaborated during postnatal life, and that elimination of connections does not occur in this region of the rat brain (Figure 9). Addition of new connections to immature neural circuits has been also documented in the olfactory system, spinal cord and cerebellum during brain development. Thus, together these observations support the idea that neural connections are progressively added to immature circuits in the brain and suggest that different areas of the brain use different ways to shape their neural circuits during postnatal development. For instance, while areas such as the visual centers eliminate connections, others, like the somatic sensory cortex, appear to selectively create more.

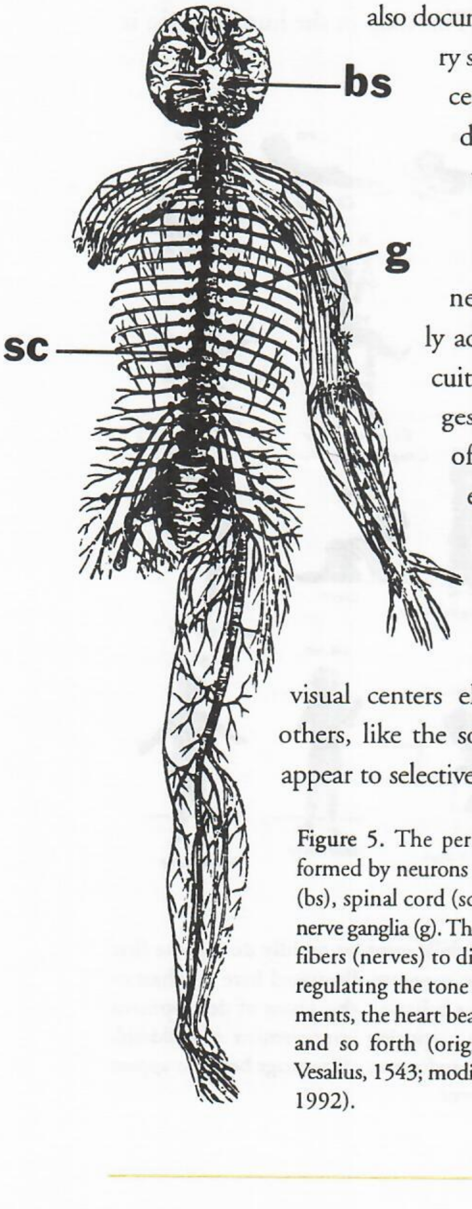

Figure 5. The peripheral nervous system is formed by neurons localized in the brain stem (bs), spinal cord (sc) and in different types of nerve ganglia (g). These neurons send their nerve fibers (nerves) to different target organs, thus regulating the tone of our muscles, gut movements, the heart beat, the pupil's reflex to light and so forth (original drawing by Andreas Vesalius, 1543; modified from P. T. Churchland, 1992).

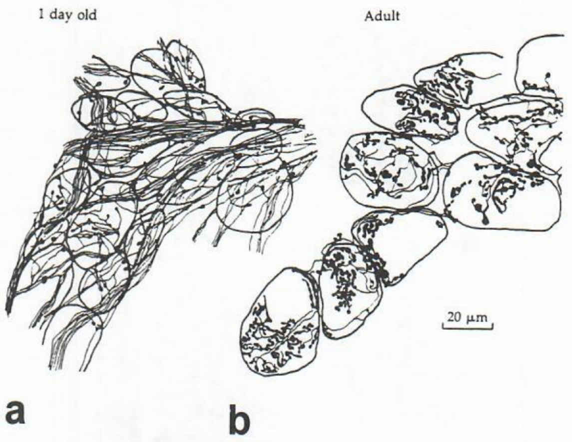

Figure 6. Some types of neurons (round outlines) in peripheral ganglia are reached by nerves from the spinal cord neurons: a) At birth, many fibers (dark lines) reach ganglion neurons but only few connections (dark dots) are made on them; b) As development continues and the adult pattern of connections is established, the number of nerve fibers diminishes while the number of contacts created upon ganglion neurons increases. This observation suggests that connections are added to immature neural circuits during postnatal maturation (from Purves and Lichtman, 1985).

SENSORY EXPERIENCE AND NEURAL CONNECTIONS

Up to this point, I have described evidence to the effect that the developing brain creates new circuitry as postnatal development proceeds. I shall turn now to an explanation as to how this might happen. I will summarize experimental data suggesting that sensory experience spurs the elaboration of neural connections in the brain.

For some time, psychologists have known that environments rich in sensory stimulation promote and improve, so to speak, the development of the brain and its functions. Experiments have demonstrated that groups of rats living in cages with "interesting objects to explore and play with" have relatively larger brains than those living in environments with poor sensory and social stimulation. Anatomic comparisons of brains from both groups of rats have shown that the number of neural connections increases in some brain regions of those animals exposed to sensory-enriched environments. Although these experiments seem to support the contention that increased sensory experience promotes the elaboration of neural connections, it is important to point out that different parts of the brain respond differently to environmental enrichment. While some regions of the brain indeed increase in size, others do not change and even diminish in their dimensions. Thus, these experiments show that the effects of enriched sensory stimulation on the elaboration of neural connections are complex and that more research is needed before advancing further conclusions.

More clear evidence supporting the role of sensory stimulation in the development of neural circuits comes from studies of the brain structure following the surgical removal of sensory organs (i.e., anatomic deprivation). For instance, deprivation of visual experience after eye removal leads to a reduction in the number of neurons, their size and their connections in areas of the brain that process visual information. However, anatomic deprivation of sensory organs probably alters interactions other than those dependent on sensory experience, making the interpretation of these results difficult. This shortcoming has been solved by depriving animals of sensory stimuli without compromising anatomical links between the brain and sensory organs. An example of this kind of experiment is sewing the eyelids closed to accomplish visual deprivation while the eyes preserve their anatomic position. These sorts of manipulation have confirmed that the absence of sensory stimuli decreases neuron number, their size and the complexity of neural circuits in the brain.

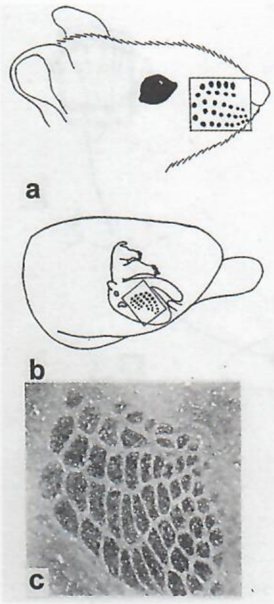

Figure 8. a) Mice whiskers provide tactile information necessary for these animals to survive in their natural environment; b) As in humans, these rodents have a body representation "imprinted" in the primary somatic sensory cortex of their brains. The head and, in particular, the whiskers occupy a large percentage of this body representation; c) The whisker representation in rats and mice can be readily seen in slices of the brain as geometric figures called barrels. Each of these barrels in the cortex represents each of the whiskers in the face. The anatomic definition of the whisker representation, among other reasons, makes it a suitable model to ask how neural connections are established during development.

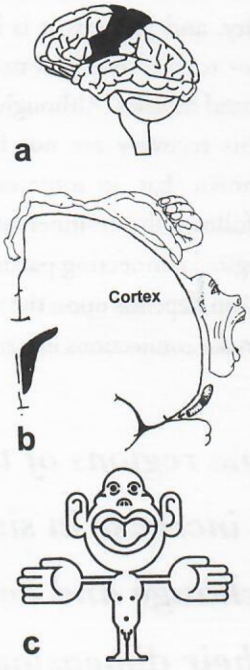

Figure 7. The human brain is divided in many distinct regions responsible for processing different types of information: a)One of these regions is called the primary somatic sensory cortex (dark area) since it receives tactile information (i.e., touch), such as vibration, temperature and pain; b) The somatic sensory cortex contains a representation of the body surface called the homunculus; c) This representation is somewhat distorted presumably reflecting anatomic differences in the sensory innervation of different parts of our bodies.

The most compelling evidence supporting the hypothesis that sensory experience regulates neural size and growth and the elaboration of new connections has been furnished by natural models of increased sensory stimulation. For instance, in lactating rats some groups of neurons and their circuits increase in size and complexity as a result of suckling, the constant

Restrictions of the neurons' ability to grow and create new circuitry might also play a role in the pathogenesis of neurodegenerative disorders.

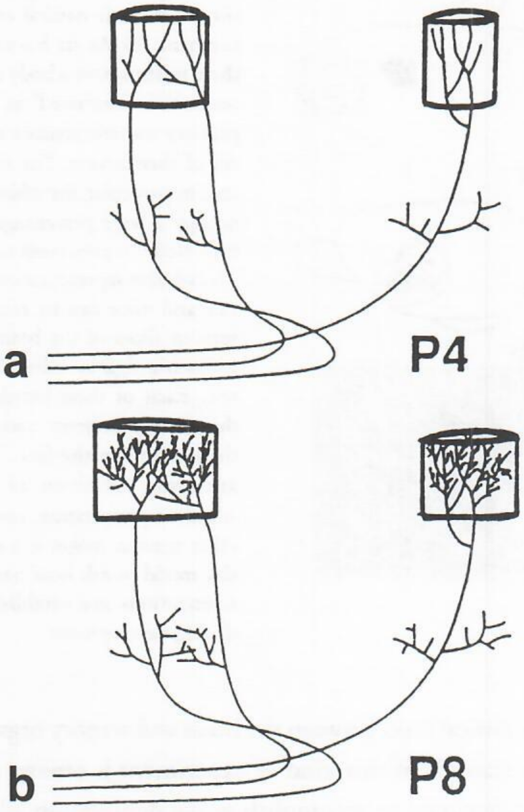

Figure 9. The development of neural circuits in the barrel cortex involves the gradual elaboration of connections: a) For instance, at day four after birth (P4), only a few branches extend from the nerve fibers to the barrel cortex; b) By postnatal day eight (P8), however, an increase in the number of branches per nerve fiber in the barrel cortex is observed. These results suggest that some regions of the brain assemble their circuits by increasing the number of connections as opposed to eliminating them.

stimulation of nipples by hungry and demanding pups (Figure 10). These changes in neural size enhance the ability of some of these neurons to secrete oxytocin, the hormone that facilitates milk secretion. These changes disappear once the suckling stimulus ends after weaning. These observations suggest, therefore, that increased sensory stimulation promotes neural growth and the elaboration of connections and that modifications in neural size and connectivity lead to striking changes in neural function.

SOME FUNCTIONAL IMPLICATIONS

Is the elaboration of connections necessary to accomplish normal brain function? Different lines of evidence document that this indeed is the case. It has been documented that neurons in different areas of the brain (including regions of the visual system!) increase their number of neural connections steadily during postnatal maturation. Conditions causing hormonal and or nutritional deficiencies, as well as some genetic syndromes that impare the formation of neural connections during brain development, lead to mental retardation in humans, and in rodents, to low performance scores in learning and memory tasks.

Restrictions of the neurons' ability to grow and create new circuitry might also play a role in the pathogenesis of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. As with humans, studies of aged animals have documented cognitive alterations associated to the degeneration of neurons and their connections in specific areas of the brain. This cognitive impairment can to some extent be reversed by treating the animals with proteins, known as neurotrophic factors, that stimulate neural growth and the elaboration of new circuits in affected areas.

The brain's capacity to modify its anatomy and function is termed plasticity, and perhaps it is best exemplified by the partial or total recovery of neural functions following severe head injuries. Although the mechanisms underlying this recovery are not fully understood, it has been shown that, in some cases, functional compensation follows the re-innervation of injured areas by their original connecting partners. This compensatory mechanism depends upon the ability of neurons to grow and make connections in a selective fashion.

> ***While some regions of the brain indeed increase in size, others do not change and even diminish in their dimensions.***

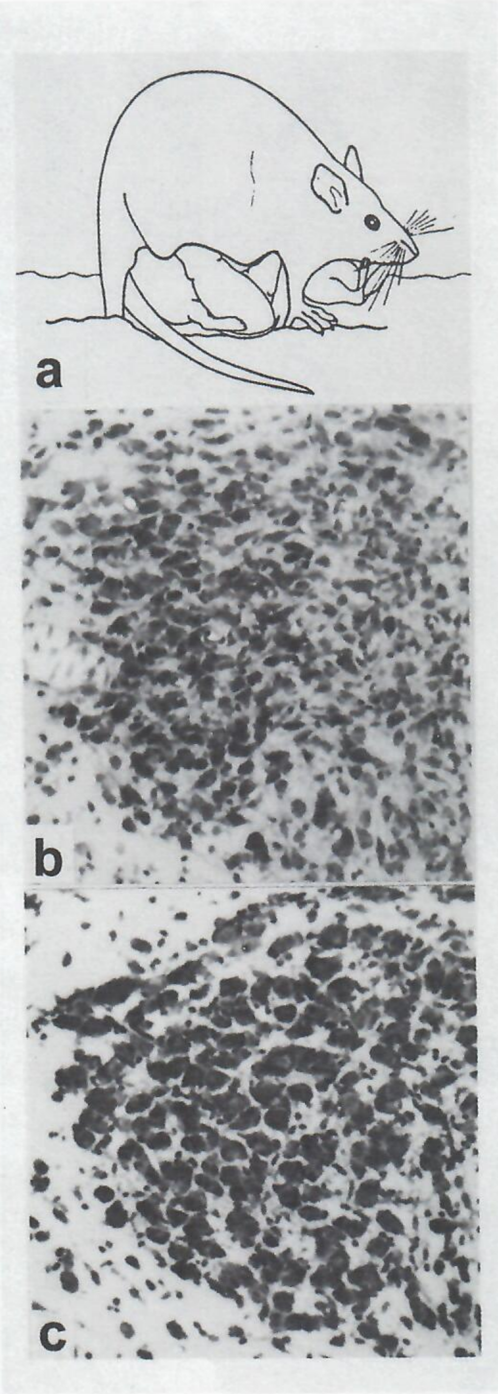

Figure 10. a) In lactating rats changes in the morphology of neurons and their circuits occur as a result of sensory stimulation. An example of these changes is illustrated by comparing the size of neurons of the paraventricular nucleus in the brain of virgin (b) and lactating (c) rats. Neurons in lactating rats are larger than in virgin rats. These differences in neural size disappear after weaning, thus suggesting that sucking stimulus (i.e., sensory stimulation) is important for the occurrence of these changes.

Neural connections and brain circuits are shaped by complex interactions of biological and environmental factors.

Addition of new neural connections have long been thought to underlie processes such as learning and memory. In support of this idea, it has been shown that certain patterns of electrical stimulation directly delivered to the hippocampus, a brain structure involved in learning and memory, not only strengthen neural connections and increase their ability to transmit information, but also induce the elaboration of new connections among stimulated neurons. Elaboration of new connections has also been reported in the cerebellum, a brain structure involved in learning some motor sequences.

Finally, evidence supporting the hypothesis that building up neural circuity increases the capacity of the brain to process and store information comes from comparative anatomic studies among different animal species. These studies indicate that the progressive increase in brain size during evolution results not only from augmenting the overall number of neurons, but from increasing the brain's volume devoted to neural connections. It is likely that this increment in neural connections, and not their elimination, led to the anatomic and functional specializations of the mammalian brain.

In summary, neural connections and brain circuits are shaped by complex interactions of biological and environmental factors. Although it has been thought that the elimination of connections mediates the effects of these factors on the neural circuitry, recent evidence suggests that the developing brain elaborates new ones as postnatal development proceeds. This addition of new connections to neural circuits may explain the increased capacity of the developing brain to process and store information, its ability to generate complex patterns of behavior and its capacity to recover after different types of injuries.