The Developing Brain

2

During fetal development, the foundations of the mind are laid as billions of neurons form appropriate connections and patterns. Neural activity and stimulation are crucial in completing this process.

• • •

Carla J. Shatz

An adult human brain has more than 100 billion neurons. They are specifically and intricately connected with one another in ways that make possible memory, vision, learning, thought, consciousness and other properties of the mind. One of the most remarkable features of the adult nervous system is the precision of this wiring. No aspect of the complicated structure, it would appear, has been left to chance. The achievement of such complexity is even more astounding when one considers that during the first few weeks after fertilization many of the sense organs are not even connected to the embryonic processing centers of the brain. During fetal development (see Figure 2.1), neurons must be generated in the right quantity and location. The axons that propagate from them must select the correct pathway to their target and finally make the right connection.

How do such precise neural links form? One idea holds that the brain wires itself as the fetus develops, in a manner analogous to the way a computer is manufactured; that is, the chips and components are assembled and connected according to a preset circuit diagram. According to this analogy, a flip of a biological switch at some point in prenatal life turns on the computer. This notion would imply that the brain's entire structure is recorded in a set of biological blueprints—presumably DNA—and that the organ begins to work only after the wiring is essentially complete.

Research during the past decade shows that the biology of brain development follows very different rules. The neural connections elaborate themselves from an immature pattern of wiring that only grossly approximates the adult pattern. Although humans are born with almost all the neurons they will ever have, the mass of the brain at birth is only about one fourth that of the adult brain. The brain becomes bigger because neurons grow in size, and the number of axons and dendrites as well as the extent of their connections increases.

Workers who have studied the development of the brain have found that to achieve the precision of the adult pattern, neural function is necessary: the brain must be stimulated in some fashion. Indeed, several observations during the past few decades have shown that babies who spent most of their first year of life lying in their cribs developed abnormally slowly. Some of these infants could not sit up at 21 months of age, and fewer than 15 percent could walk by about the age of three. Children must be stimulated—through touch, speech and images

—to develop fully. Based in part on such observations, some people favor enriched environments for young children, in the hopes of enhancing development. Yet current studies provide no clear evidence that such extra stimulation is helpful.

Much research remains to be done before anyone can conclusively determine the types of sensory input that encourage the formation of particular neural connections in newborns. As a first step toward understanding the process, neurobiologists have focused on the development of the visual system in other animals, especially during the neonatal stages. It is easy under the conditions that prevail at that stage to control visual experience and observe behavioral response to small changes. Furthermore, the mammalian eye differs little from species to species. Another physiological fact makes the visual system a productive object of study: its neurons are essentially the same as neurons in other parts of the brain. For these reasons, the results of such studies are very likely to be applicable to the human nervous system as well.

But perhaps the most important advantage is that in the visual system, investigators can accurately correlate function with structure and identify the pathway from external stimulus to physiological response. The response begins when the rods and cones of the retina transform light into neural signals. These cells send the signals to the retinal interneurons, which relay them to the output neurons of the retina, called the retinal ganglion cells. The axons of the retinal ganglion cells (which make up the optic nerve) connect to a relay structure within the brain known as the lateral geniculate nucleus. The cells of the lateral geniculate nucleus then send the visual information to specific neurons located in what is called layer 4 of the (six-layer) primary visual cortex. This cortical region occupies the occipital lobe in each cerebral hemisphere (see Figure 2.2).

Within the lateral geniculate nucleus, retinal ganglion cell axons from each eye are strictly segregated: the axons of one eye alternate with those from the other and thus form a series of eye-specific layers. The axons from the lateral geniculate nucleus in turn terminate in restricted patches within cortical layer 4. The patches corresponding to each eye interdigitate with one another to form structures termed ocular dominance columns.

Figure 2.1 SEVEN-WEEK-OLD HUMAN FETUS is about an inch long. Eyes and limbs are visible, and the emerging brain is apparent. Stimulation is needed to complete development, a process that for many neural systems continues into neonatal life.

To establish such a network during development, axons must grow long distances, because the target structures form in different regions. The retinal ganglion cells are generated within the eye. The lateral geniculate neurons take shape in an embryonic structure known as the diencephalon, which will form the thalamus and hypothalamus. The layer 4 cells are created in another protoorgan called the telencephalon, which later develops into the cerebral cortex. From the beginning of fetal development, these three structures are many cell-body diameters distant from one another. Yet after identifying one or the other of these targets, the axons reach it and array themselves in the correct topographic fashion—that is, cells located near one another in one structure map their axons to the correct neighboring cells within the target.

This developmental process can be compared with the problem of stringing telephone lines between particular homes located within specific cities. For instance, to string wires between Boston and New York, one must bypass several cities, including Providence, Hartford, New Haven and Stamford. Once in New York, the lines must be directed to the correct borough (target) and then to the correct street address (topographic location).

Corey Goodman of the University of California at Berkeley and Thomas Jessel of Columbia University have demonstrated that in most instances, axons immediately recognize and grow along the correct pathway and select the correct target in a highly precise manner. A kind of "molecular sensing" is thought to guide growing axons. The axons have specialized tips, called growth cones, that can recognize the proper pathways. They do so by sensing a variety of specific molecules laid out on the surface of, or even released from, cells located along the pathway. The target itself may also release the necessary molecular cues. Removing these cues (by genetic or surgical manipulation) can cause the axons to grow aimlessly. But once axons have arrived at their targets, they still need to select the correct address. Unlike pathway and target selection, address selection is not direct. In fact, it involves the correction of many initial errors.