# Development of the Cerebral Cortex: X. Cortical Development and Experience: II

SUSAN HOCKFIELD, PH.D., AND PAUL J. LOMBROSO, M.D.

When historians of science look closely at the pivotal issues in child psychiatry in the second half of the 20th century, one area of controversy will surely catch their attention. Few topics have displayed such major swings of the pendulum as the debate over genetic and environmental factors. Which one reigns supreme in its contribution to the normal or abnormal development of our children?

One has only to review the history of research on autism to get a feel for the intensity of the nature versus nurture debate. When Leo Kanner first described the severe syndrome of autism in 1943, he speculated that perhaps the core symptoms of these children were based in biology and that the inability to develop strong attachments was an innate feature of these children. However, he also noted that many of the parents of these children had particular personality traits. This last remark was interpreted by many to suggest that parental upbringing skills were central to the development of symptoms among autistic children. Thus, we entered an era in which the aloof-

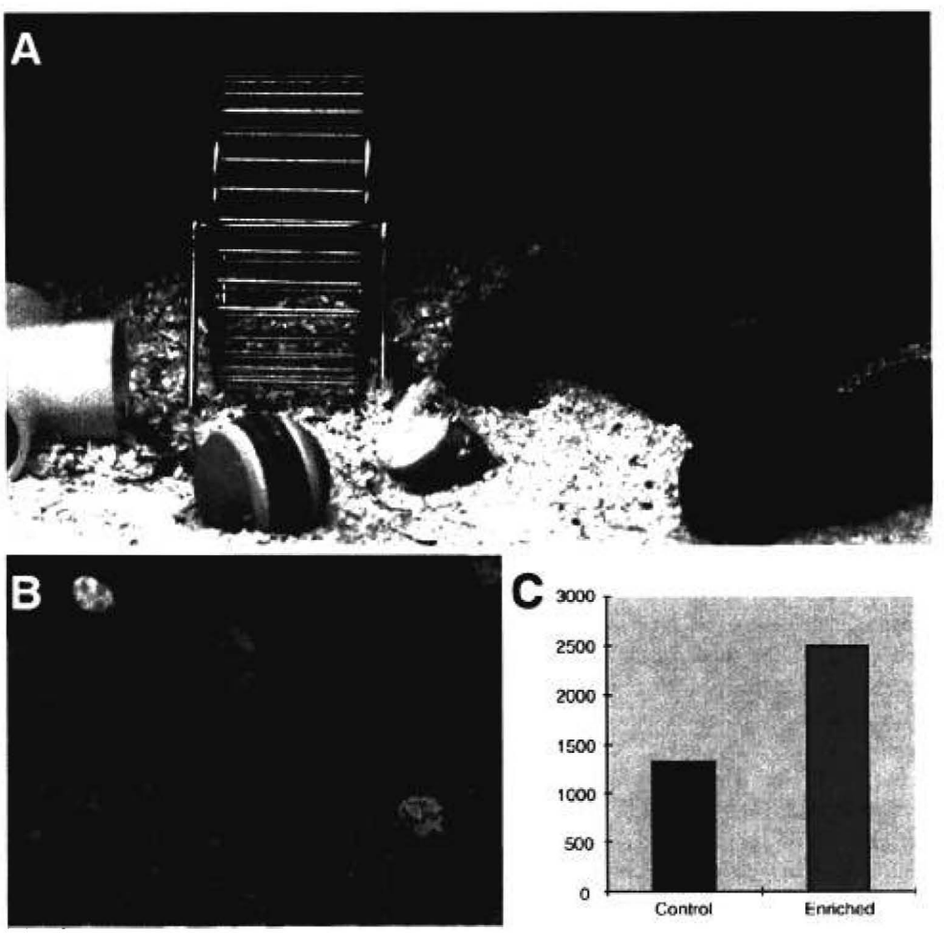


**Fig. 1** *A:* Some mice were raised in the enriched environment shown, while other littermates were not so fortunate. *B:* An example of two newborn neurons from the hippocampus of a mouse raised in the enriched environment. Scale bar 25 μm. *C:* Absolute number of newborn neurons in the dentate gyrus of 2-month-old mice. Figure courtesy of G. Kempermann, H. Kuhn, F. Gage, unpublished.

ness and coldness of "refrigerator mothers" were held responsible for the withdrawal of these children from the world. The pendulum slowly swung back during the 1970s and 1980s as studies suggested that genetic factors make important contributions to the etiology of the syndrome.

Today, the question should no longer be whether nature or nurture plays a role in the expression of childhood neuropsychiatric disorders. Both are critically important, and it is the interplay between these two factors that leads to the disruption of normal development and the expression of clinical symptoms. Occasionally, mutations occur that are so significant that the development of the CNS is affected no matter what the environmental input is. At other times, severe environmental deprivations are such that cortical development is abnormal or inadequate despite the adequacy of the genetic plan.

It is interesting that some of the strongest arguments for the contribution of both environmental and genetic factors come from twin studies. The high concordance rate among monozygotic twins compared with dizygotic twins is supporting evidence for a genetic contribution in many disorders of childhood. However, it is rare for the concordance rate to exceed 50%, and this finding provides a powerful argument that environmental factors are etiologically important.

The next decade of basic science research will continue to explore exactly how environmental factors affect the expression of certain genetic factors, and vice versa. Last month, this column reviewed the seminal studies by Hubel and Wiesel on the importance of visual input for the proper organization of ocular dominance columns in the adult visual cortex of the cat. Their work demonstrated that critical periods exist in the development of the visual cortex and that environmental input has a decisive impact on cortical growth and synaptogenesis.

Recent investigations from many laboratories provide compelling evidence that growth factors play important roles in activity-dependent modification of neuronal structure. Growth factors have long been appreciated for their ability to promote neuronal survival, as well as to direct axonal growth. Studies have demonstrated that the same growth factors that in other contexts determine whether a particular class of neuron will survive can also regulate the growth of dendrites in the visual cortex. Moreover, the strengthening of a synapse following its activation is mediated by growth factors.

The work of Hubel and Wiesel established that if you do not lay down certain synaptic connections early in development, they are less likely to become established later in life. A related question that this work did not address was what happens if you stimulate synaptic growth early on by exposure to novel or different experiences during critical periods? Are the new or strengthened synaptic connections long-lasting? Does exposing our children to "enriched" experiences early in life lead to their becoming smarter adults?

Two recent articles address these questions. The first is the latest in an ongoing series of experiments by the neuroscientist Eric Knudsen at Stanford University. His work has demonstrated directly that early experiences change the way the brain is wired and that these changes last into adulthood. Knudsen studies the visual system of the barn owl. These nocturnal hunters are known for their keen auditory and visual acuity. A region of the brain termed the optic tectum contains neurons that respond to both visual and auditory signals, permitting the brains of these animals to superimpose the two sensory systems.

If prisms are placed over the birds' eyes, the visual information is displaced to nearby neurons within the tectum. The owls must readjust their auditory maps into alignment with their visual inputs if they are to be successful hunters again. Preadolescent owls are able to readjust their maps within 3 weeks, whereas adult owls are never able to accomplish the adjustment. Just as interestingly, Knudsen's group has now shown that the cortical rearrangements are long-lasting. If the prisms are removed after the novel synaptic connections are made, the owls return to using their old neuronal pathways. If the prisms are reintroduced months later in adulthood, those owls who were trained early in their lives are able once again to adjust to the prisms, whereas other adult owls with no early training are not able to adjust to the prisms.

Kempermann and his colleagues explored the extent of neuroanatomical plasticity that occurs in the brains of mice reared in either enriched or deprived environments. They raised mice in special cages containing a number of additional items, such as wheels, toys, and tunnels (Fig. 1). There is little doubt that this type of enrichment is very different from their normal environment in the wild. However, it is a considerable improvement over the starkness of the control cages.

The brains of the animals raised in the enriched environment were compared with the brains of littermates raised in the control conditions. A number of significant morphological changes in brain growth were found in the hippocampi of mice raised in the enriched environments. These included an increase not only in the number of neurons present, but also in the overall volume of the hippocampus. The experimental animals were also found to have improved ability to learn new tasks. Other laboratories have conducted similar experiments and have also noted an increase in the extent of dendritic arborization and the number of supporting glial cells. Clearly, environmental events can have a substantial effect on how the brain develops and wires itself during critical periods of maturation.

The increasing power of molecular genetics, paired with innovations in imaging technology, promises further identification of the molecular players in activity-dependent synaptic plasticity. As these studies are published, relevant ones will be presented here as we continue our discussions of exactly

how environmental and genetic factors interact during critical periods of brain maturation.

## WEB SITES OF INTEREST

http://web.syr.edu/~jmwobus/autism/#academic
http://www.salk.edu/faculty/gage.htm
http://www.med.stanford.edu/school/Neurosciences/faculty/knudsen.html
http://nba19.uth.tmc.edu/nrc/newsltr/winter95/nrcnews2.html
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## ADDITIONAL READINGS

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*Accepted April 16, 1998.*

*Dr. Hockfield is Professor, Neurobiology, and Dr. Lombroso is Associate Professor, Child Study Center, Yale University School of Medicine, New Haven, CT.*

*Correspondence to Dr. Lombroso, Child Study Center, Yale University School of Medicine, 230 South Frontage Road, New Haven, CT 06520; e-mail: paul.lombroso@yale.edu*

0890-8567/98/3710–1103/$03.00/0

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**The Effect of Nursing on the Brain Activity of the Newborn.** Johannes Lehtonen, MD, Mervi Könönen, MSc, Maija Purhonen, MD, Juhani Partanen, MD, Seppo Saarikoski, MD, Kari Launiala, MD

*Objective:* To determine whether nursing influences brain activity in the newborn and whether there are differences in this respect between breast- or bottle-feeding and pacifier sucking. *Study Design:* Fifty unselected volunteer mothers and their healthy full-term infants, under care in the maternity ward after delivery, served as subjects. Thirty mother-infant pairs were studied in relation to breast-feeding and 20 to bottle-feeding and pacifier sucking. Breast-fed infants were studied between the 1st and 7th day after delivery (mean ± 2.7 days) and the infants in the bottle-fed group between the 1st and 8th day after delivery (mean ± 3.3 days). *Methods:* Qualitative and quantitative electroencephalogram (EEG), electrooculogram, submental electromyogram, and electrocardiogram were recorded before, during and after breast- and bottle-feeding and pacifier sucking. *Results:* The amplitude of the EEG increased significantly during breast-feeding in the posterior cortical areas in both hemispheres with a slight predominance on the right. Bottle-feeding caused a similar, but somewhat less marked change. When the breast- and bottle-fed infants were compared, a significant difference was found in only one parameter of the 84 studied. Pacifier sucking had no significant effects on EEG activity. *Conclusion:* Nursing effects a change in the brain activity of the newborn. The cortical response to nursing is most probably a result of activation of the neurohumoral mechanisms related to hunger and satisfaction, including the hypothalamic, limbic, and other brain stem structures, which also regulate the sleep-wake cycle and modulate the level of cortical activity with respect to attention and vigilance. **J Pediatr** 1998;132:646–651