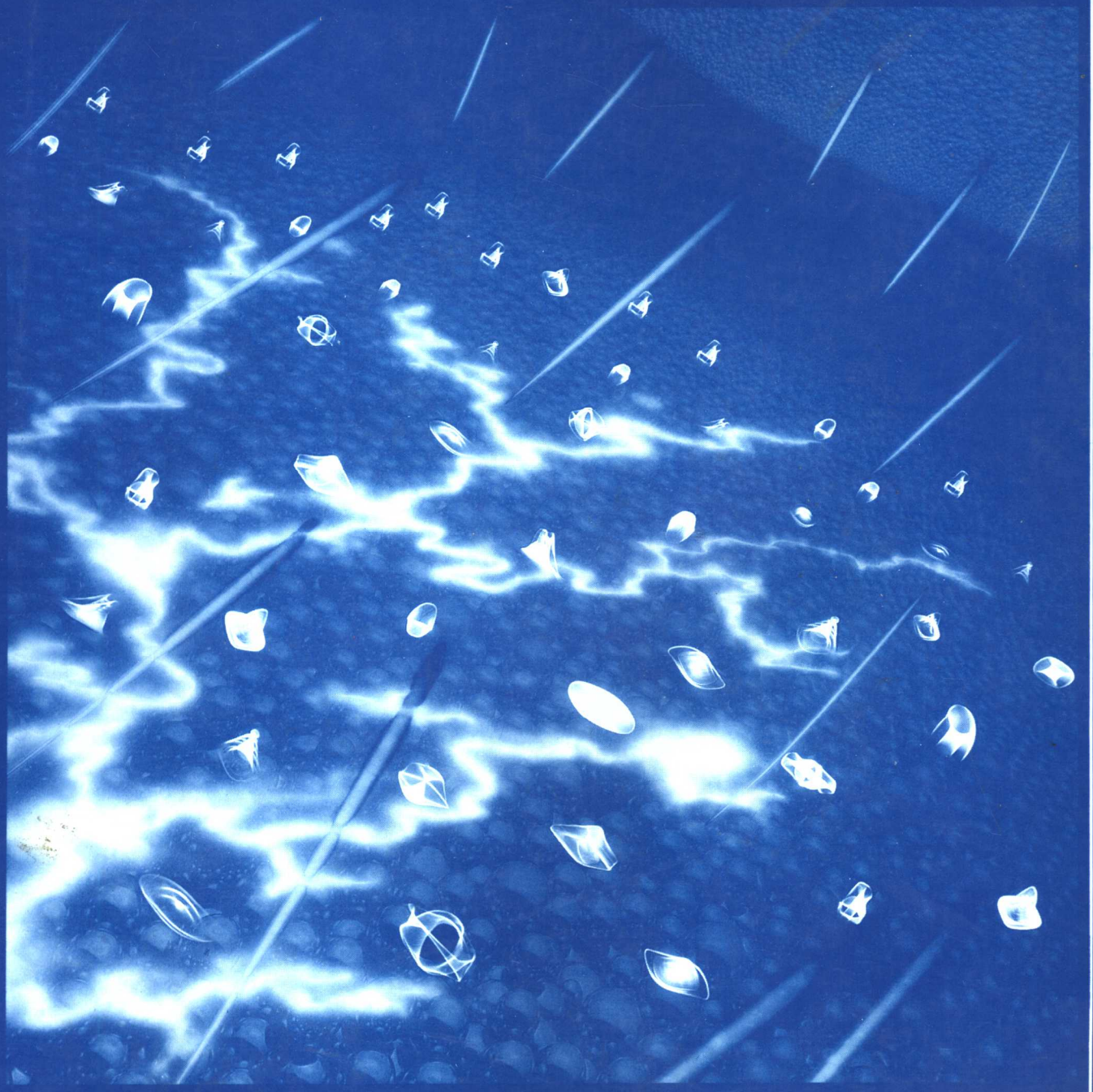
CURRENT RESEARCH IN

Biopsychology



JOHN P. J. PINEL

Current Research in Biopsychology

John P. J. Pinel

THE UNIVERSITY OF BRITISH COLUMBIA

ALLYN AND BACON
Boston London Toronto Sydney Tokyo Singapore

A Division of Simon & Schuster
160 Gould Street
Needham Heights, MA 02194

ISBN 0-205-13000-3

Printed in the United States of America

10 9 8 7 6 5 4 3 2 95 94 93 92

ACKNOWLEDGEMENTS

We are grateful to the publishers, editors, and authors who graciously permitted this facsimile printing of their articles.

Preface

These are exciting times for students and teachers of biopsychology; significant biopsychological discoveries are being reported almost daily. This book, Current Research in Biopsychology, is designed to introduce students of biopsychology to some of the most interesting and important of these current findings; it contains 24 outstanding biopsychology journal articles, all published since 1985. Current Research in Biopsychology is designed for use as a supplementary text in undergraduate biopsychology courses (variously titled Biopsychology, Physiological Psychology, Brain and Behavior, Psychobiology, Behavioral Neuroscience, Behavioral Neurobiology).

Contrary to first impressions, Current Research in Biopsychology is not just another book of neuroscience readings. It is a book of "biopsychology" readings that has been carefully tailored to the specific needs and interests of biopsychology students. The following are some of the general approaches and good intentions that guided its preparation.

Emphasizing Behavioral Research

In many biopsychology textbooks, the coverage of neurophysiology, neurochemistry, and neuroanatomy subverts the coverage of behavioral research. This prejudice is particularly obvious in the books of readings commonly used as supplements in biopsychology courses: Many of the readings in these books have precious little direct connection to biopsychological research and issues. In contrast, this book gives biopsychology top billing. It recognizes that neuroscience is a team effort and that the unique contribution made by biopsychologists to this team effort is their behavioral expertise and their interest in the neural bases of behavior—it contains only those neuroscience articles whose behavioral orientation clearly qualifies them as biopsychological.

Focusing on Primary Research Reports

Students of biopsychology receive general overviews of biopsychological research from both their textbooks and their instructors. Current Research in Biopsychology is intended to complement these two indirect sources of research coverage by introducing students to some of the best in recent biopsychology research reports. It is based on the premise that there is no satisfactory substitute for the primary biopsychological research article in the education of biopsychology students.

Increasing the Coverage of Human Research

In recent years, the field of biopsychology has become more human oriented. Current Research in Biopsychology reflects this trend; it includes several studies of human patients and of animal models of human neuropsychological disorders. One of its major themes is that major advances in our understanding of brain-behavior relations are often the result of the convergence of research involving human and nonhuman subjects.

Focusing on the Cutting Edge

Current Research in Biopsychology focuses on the best in recent biopsychological research—all the articles in it have been published since 1985, most since 1989—and all describe major new breakthroughs, ideas, or trends. The focus on current research is designed to complement the more historical treatment provided by most general biopsychology textbooks.

Selecting Articles of Particular Interest to Students

I believe that the principles of good science are best taught in contexts that are of particular interest to the students—too often they are not. All of the articles in this book meet the highest scientific

standards, but, in addition, they are all clear concise descriptions of research on topics that, in my experience, are proven student favorites.

Helping Students Learn

The articles in this book were all written by biopsychologists for biopsychologists and other neuroscientists. Accordingly, to fully appreciate these research articles, the beginning biopsychology student may occasionally need some help. I supply this help in five different forms:

Student-Oriented Introductions to Each Article

The introductions that I have written to each article are designed to generate interest, to provide any background material that students will need to understand the article and to tell students in clear nontechnical language what was done and why. The introductions pave the way.

Glossaries

A glossary is included with each article so that students have ready access to the meanings of any new terms that they might encounter. The glossaries are also useful for study and review.

Essay Study Questions

The essay study questions that follow each article are designed to encourage students to think about principles and conceptual issues.

Multiple-Choice Study Questions

Multiple-choice study questions are included to help students review the main points of each article and to prepare themselves for examinations. Answers are included at the end of the text.

Food-for-Thought Questions

The food-for-thought questions that are included with each article are designed to provoke original thought. These questions are excellent topics for classroom discussion.

Topic Areas

In selecting the 24 articles for this book, I tried to choose articles that covered as many different biopsychology topic areas as possible. As a result, I tried to select articles that are integrative: that combine approaches, techniques, and theories from more than one topic area. The following table provides an overview of the breadth and emphases of the chosen 24.

Acknowledgements

First and foremost, I thank the authors of the articles in this book and the publishers of these articles for giving me permission to reprint them here. Many of my colleagues also deserve thanks for recommending articles to me: Michael Baum, Kent Berridge, Robert Blanchard, Brian Bland, David Booth, Rod Cooper, Michael Corcoran, Verne Cox, B.G. Galef, Bill Greenough, Charles Malsbury, Morris Moscovitch, Antonio Nunez, David Olton, George Paxinos, Sergio Pellis, Ron Racine, Neil Roland, Tim Schallert, Doug Wahlsten, Neil Watson, Harvey Weingarten, Ian Whishaw, Don Wilkie, Roy Wise, Steve Woods, Eran Zaidel, and Stuart Zola-Morgan. I am also grateful to my publisher, Allyn and Bacon, and in particular to Diane McOscar, Diana Murphy, Elaine Ober, and Sandi Kirshner, who were largely responsible for designing, producing, and marketing this book. Finally, I would like to thank Liz McCririck, Rose Tamdoo, Bev Charlish, and my son Greg for their valuable clerical support.

Table 1. Topics Covered by the 24 Articles in This Collection

ABBREVIATED TITLES OF ARTICLES	Development	Brain Damage and Recovery	Perception	Motivation	Learning	Memory and Amnesia	Sleep and Circadian Rhythms	Psychopharmacology	Cognition and Language	Brain Laterality	Ethoexperimental Approach	Neuropsychology	Psychophysiology	Human Subjects	Nonhuman Primate Subjects	Avian Subjects	Case Studies	Clinical Implications	Single-Cell Recording
1. Brain Development, Plasticity, and Behavior	x	x			x							x		x			x	x	
2. Reorganization of Retinotopic Cortical Maps in Adult Mammals		x	x															x	x
3. Autograft of Adrenal Medulla to the Caudate Nucleus of Patients With Parkinson's Disease		x										x	x	x				x	
4. Knowledge Without Awareness		x	x			x						x	x	x				x	
5. Face-Responsive Potential Recorded from the Human Scalp			x										x	x				x	
6. Vision Guides the Adjustment of Auditory Localization in Young Barn Owls	x		x								x					x			
7. Studies of Sexual Reinforcement in Male Rats		x		x															
8. Feline Predation Along a Gradient				x				x											
9. Gastric Emptying Changes and CCK-Induced Satiety				x				x											
10. Sleep on the Night Shift: 24-Hour EEG Monitoring							x						x	x					
11. Transplanted Suprachiasmatic Nucleus Determines Circadian Period		x					x												
12. Female Visual Displays Affect the Development of Male Song in the Cowbird	x			x	x						x					x			
13. Caenorhabditis elegans: A New Model System for the Study of Learning and Memory					x														
14. Social Influences on the Selection of a Protein-Sufficient Diet by Norway Rats	x			x	x						x								
15. Performance of Amnesic Patients on Tests Designed for the Monkey		x				x						x		x	x			x	
16. Hippocampus and Memory for Food Caches in Black-Capped Chickadees		x				x					x					x			
17. Spatial Selectivity of Rat Hippocampal Neorons						x													x
18. Cholinergic Activity and Enhanced Memory After Early Choline Administration	x					x		x										x	
19. Alcohol Inhibits and Disinhibits Sexual Behavior in the Male Rat				x				x										x	
20. Buprenorphine Suppresses Cocaine Self-Administration by Rhesus Monkeys				x				x										x	
21. Lesions of the Nucleus Accumbens Reduce Opiate Reward but Not Context-Specific Opiate Tolerance		x			x			x										x	
22. Corpus Callosum is Larger with Right-Hemisphere Cerebral Speech Dominance									x	x		x		x				x	
23. Reading With One Hemisphere									x	x		x		x			x	x	
24. Mental Rotation of the Neuronal Population Vector			x						x						x		x		x

The Next Edition

As I write these words, Current Research in Biopsychology is not yet in press, but I am already searching for new articles for its next edition—I am planning to update Current Research in Biopsychology frequently to maintain its focus on the cutting edge of biopsychological research. I would greatly appreciate receiving your recommendations, and I would be pleased to acknowledge them in the preface of the next edition. Please send your recommendations to me at the Department of Psychology, University of British Columbia, Vancouver, B.C., Canada V6T 1Y7.

To the Student

If you have already skimmed the preface and the table of contents of this book, you will already know that it contains 24 research articles recently published in scientific journals by some of the world's best biopsychologists. For many of you, this book may constitute your first direct exposure to the primary products of biopsychology research—most of your previous exposure will have been second or third hand through your teachers and general textbooks. I can understand why you now might be regarding this book with a feeling of apprehension—it is hard to imagine how reading 24 articles that were written by scientists for other scientists could be anything other than a frustrating experience for a student. But relax, this book comes with a guarantee: I guarantee that you will find Current Research in Biopsychology to be clear, informative, and interesting—a truly worthwhile and enjoyable educational experience.

You may wonder how I would dare issue such an unqualified guarantee—and in writing yet. I feel confident in doing so because the 24 articles in this book all passed three separate tests. In addition to meeting the highest standard of scientific merit, each article is clearly and concisely written with a minimum of scientific jargon, and each article focuses on a topic, that, in my experience as a teacher, is likely to be of great interest to you. Today's biopsychologists are doing amazing things, and the articles in this book describe some of the most amazing—you are about to enter a world of brain transplants, microscopic worms that are capable of learning, birds with amnesia, drugs that improve memory, and people with only half a brain. Furthermore, if you do happen to encounter some minor difficulties along the way, I will be there to help you. To guide you through each article, I have written a stage-setting introduction, a glossary of technical terms, essay study questions, multiple-choice study questions, and food-for-thought questions.

Because my job as a producer and teacher of biopsychological research has meant so much to me, I have done everything that I can to make this introduction to the world of biopsychological research a positive one for you. I do hope that you enjoy it and that it whets your appetite for more biopsychology. If you are so inclined, please write to me at the Department of Psychology, University of British Columbia, Vancouver, B.C., Canada, V6T 1Y7. I welcome your comments, suggestions, and questions.

John P.J. Pinel

John P.J. Pinel is a graduate of McGill University and a Professor of Psychology at the University of British Columbia in Vancouver, B.C., Canada. He is the author of well over 100 research reports, review articles, and book chapters on a variety of biopsychological topics: including learning, memory, epilepsy, defensive behavior, and drug tolerance. In recognition of his research accomplishments, Professor Pinel has been made a fellow of both the American Psychological Association and the American Psychological Society, and he is a recent winner of the prestigious Killam Memorial Senior Fellowship, but his contributions to psychology have not been restricted to the laboratory. He is an award-winning teacher, and his recent textbook Biopsychology (Allyn and Bacon, 1990) has been acclaimed both for its clear, insightful, forward-looking coverage of the field of biopsychology and for its effective blend of humor, enthusiasm, and scholarship. Professor Pinel claims that he pauses from his rigorous writing schedule only long enough for the occasional afflatus.

TABLE OF CONTENTS

5. THE BIOPSYCHOLOGY OF LEARNING

6. THE NEURAL BASES OF MEMORY

7. DRUGS, BRAIN, AND BEHAVIOR

8. CEREBRAL LATERALITY AND COGNITIVE PROCESSES

ARTICLE 1

Brain Development, Plasticity, and Behavior

B. Kolb
Reprinted from American Psychologist, 1989, September, 1203-1212

Kolb and his collaborators—most notably Whishaw and Sutherland—have recently published a series of experiments that have delved into the adverse effects of early brain damage on behavioral and neural development. In this article, Kolb summarizes the results and implications of these experiments.

By blending the results of human neuropsychological case studies with the results of laboratory experiments, Kolb makes a strong case for the need to qualify the Kennard doctrine: the widely held view that recovery from brain damage is greatest when the damage occurs early in life. Kolb begins by pointing out that the Kennard doctrine has little to say about why the deficits produced by brain damage lesions occurring at one age are sometimes qualitatively different from the deficits produced by similar brain damage occurring at another age. The human nervous system continues to develop for several months after birth, and Kolb argues that the particular effects of early brain damage depend to a substantial degree on the stage of neural development that is in progress at the time that the damage occurs. The Kennard doctrine also fails to explain how the development of the brain and its recovery from brain damage are influenced by experience. For example, it cannot explain Kolb and Elliot's (1981) observation that rats with frontal cortex lesions experienced fewer deficits as adults if they were raised in an enriched homecage environment.

The most serious challenges to the Kennard doctrine come from the numerous demonstrations of cases in which greater recovery is not associated with earlier brain lesions. For example, Kolb and Whishaw (1981) found that frontal cortex lesions permanently impaired the performance of a variety of species-typical behaviors (e.g., the defensive burying of dangerous inanimate objects) in adult rats whether the lesions were created when the rats were 7 days old or when they were young adults. In contrast, the recovery of the ability of the same two groups of rats to perform various tests of learning (e.g., Morris water maze) was consistent with the Kennard doctrine; the recovery was considerably greater in the rats that had received their lesions when they were 7 days old. Clearly, the Kennard doctrine is too simple; it can account for some instances of recovery from brain damage but not others.

Recently, Kolb and Whishaw found evidence that recovery from early cortical damage might be mediated by dendritic arborization (i.e., by the growth of dendritic branches) in the remaining healthy cortex. In general, behavioral recovery from brain damage was found to be greatest in those experimental conditions that favored dendritic arborization.

Brain Development, Plasticity, and Behavior

Bryan Kolb *University of Lethbridge*

ABSTRACT: Damage to the infant brain is associated with a complex array of behavioral and anatomical effects. Recent research is leading to a new understanding of the nature of, and mechanisms underlying, recovery from brain damage.

Nearly one half million people will suffer traumatic brain injury in the United States alone this year. When one adds the people who will suffer a stroke, develop dementing disorders, or suffer from other types of brain dysfunctions such as mental retardation, cerebral palsy, or epilepsy, it becomes clear that there are a large number of people who have permanent behavioral abnormalities that may include disorders of movement, perception, or memory; loss of language; and the alteration of social behavior and personality. Thus, whereas the study of brain–behavior relationships was once restricted largely to physiological psychologists, the development of neuropsychology has moved the study of brain and behavior into the mainstream of psychology to involve significant numbers of human experimental and clinical psychologists. One problem, however, is that most of the basic work in neuroscience is largely divorced from psychology and is inaccessible to the bulk of psychologists who quite rightly have difficulty in seeing the direct relevance of this work to psychological issues. My goal in this article is to review recent work on the nature of brain development and plasticity and its relation to the understanding of behavior.

There are numerous approaches to the study of brain–behavior relationships. The first is to study how normal mature brains work. This can be done either by examining the morphological and physiological correlates of behavior or by studying the structure of cognitive processes and making predictions about how the brain must be processing information. Studies of morphological changes during learning provide an example of the former type, and psychophysical experiments provide examples of the latter. A second approach is to study the behavioral correlates of brain dysfunction, with the goal of making predictions about normal function. This has been the principle method of neuropsychology for over 100 years. A third approach is to study the manner in which the brain and behavior normally develop, with the hope of gaining insight into both how the brain comes to produce behavior and how one might gain control of the processes of development. In the latter case it is proposed that it might be possible to re-initiate developmental processes to repair injury. Indeed, because both fish and amphibian brains can do this after injury and some birds annually regrow structures necessary for song each spring, it is possible that under certain conditions, hormonal events may re-initiate neural growth in mammals. A final approach is to alter the brain during development in order to see how the anatomical and behavioral organization changes. This allows an opportunity not only to look at the processes involved in brain development but also to try to determine what rules can predict when restitution of function is likely to occur and what anatomical changes might correlate with behavioral recovery. Furthermore, this approach allows one to look at the nature of localization of functions in the brain, which is an issue that has fascinated psychologists since the time of Gall. It is this final approach that I wish to examine in detail, and I will begin with an illustrative example.

Consider the following case histories of two young women. The first, P.B., is a 22-year-old business school graduate who was struck by a car and suffered a serious head injury, requiring emergency surgery to repair her skull and to relieve the pressure from subdural bleeding. It was necessary to remove a large portion of her right posterior temporo-parietal cortex. After the accident she had a left visual field defect but was able to return to her job as a typist/clerk. Upon neuropsychological examination six years after the injury, she obtained an average IQ score, although she was relatively better at verbal tests than those requiring manipulation of pictorial information. She had particular difficulty drawing and remembering pictorial information, including faces. Her motor skills were good, and although she initially had difficulty reading because of the visual loss, she overcame this handicap and could read as well as IQ-matched controls. The second case, S.S., is an 18-year-old woman who had a difficult birth and forceps delivery and began having epileptic seizures at 14 years of age. Neurological examination revealed a right parietal cyst; this was removed surgically, and the seizures were arrested. She was an average student in school but had difficulty in 12th grade, especially with English and mathematics. Her neuropsychological assessment at age 18 revealed an average IQ, but she was relatively better at pictorial tests than verbal

 0003-066X/89/$00.75
Vol. 44, No. 9, 1203–1212

ones, which is in direct contrast to P.B. Furthermore, she had a poor vocabulary score considering her education, IQ, and socioeconomic group, and she had a difficult time with arithmetic. She also had difficulty in repeating sequences of movements shown to her by the examiner, especially those of the face, and had difficulty on tests that are typically sensitive to frontal-lobe injury. In contrast, she had no difficulty on tests of drawing or visual memory. In short, P.B. and S.S. had similar brain damage, but at different ages, and the consequences could not have been much more different. I note, parenthetically, that because P.B. had a closed head injury, one might expect some nonspecific damage, such as tearing of connections or bruising elsewhere in the brain, in addition to her focal lesions. Her symptoms were typical of patients with vascular lesions in adulthood, however, and there was some evidence of nonspecific damage on tests of interhemispheric transfer (see Kolb & Whishaw, 1985, Chapter 16, for more examples).

Several questions arise from these two cases. If functions are localized in the cortex, why are the symptoms different when the damage included the same tissue? Why did S.S. have symptoms typical of frontal-lobe injury when there is no evidence of any damage to her frontal lobe? Was the age at which brain damage was sustained responsible for her behavioral differences? Why was there a permanent loss of functions in both cases, even with years of recovery? How did the function of the remaining tissue in the two brains change after the injuries? Were the changes the same? I return to these questions later.

Brain Development

One of the wonders of human development is the manner in which the human brain, which consists of over 100 billion neurons, can develop so quickly from just a few initial neural cells. According to Cowan (1979), during the time the brain is growing in utero it must be generating neurons at a rate of more than 250,000 neurons per minute. Furthermore, once the neurons are "born," they must move to their correct locations and form connections, which have been estimated at up to 15,000 per neuron.

The gross development of the human brain is summarized in Figure 1, but these general morphological changes provide little insight into the details, most of which have been discovered in the last two decades by studies on laboratory animals, especially rats and monkeys. It is now known that the development of the cortex in any species occurs in several stages (e.g., Cowan, 1979; Rakic, 1988). These include cell proliferation, cell migration, cell differentiation, dendritic and axonal growth, cell and axonal death, and gliogenesis. I consider these stages briefly.

Like all mammalian brains, the human brain begins as a hollow tube and gradually develops the features of the adult brain. The hollow area in the tube forms the ventricular system, and the cells of the brain are generated along the ventricular wall and then migrate out to their proper locations. As the brain develops, the newly formed cells must travel farther and farther to reach their final locations. As might be predicted, the precise timing of the development and migration of cells to different cortical regions varies with the particular area in question. Once cells find their correct location in the cortex, they develop the characteristics of the cell type that they are to be (e.g., stellate or pyramidal cell) and begin to grow their dendrites and axons and to form synapses. One particularly interesting aspect of neural development is that the brain overproduces neurons, possibly by a factor of two, and the extra cells are lost by a process of cell death. Similarly, a large proportion of the cortical synapses are lost during development, perhaps as many as 50%. This cell and synaptic loss is probably not random, although the controlling factors are still unknown. Curiously, it has been suggested that a failure of cell death or synaptic loss may lead to retardation or contribute to the emergence of developmental disorders, possibly even schizophrenia (e.g., Feinberg, 1982).

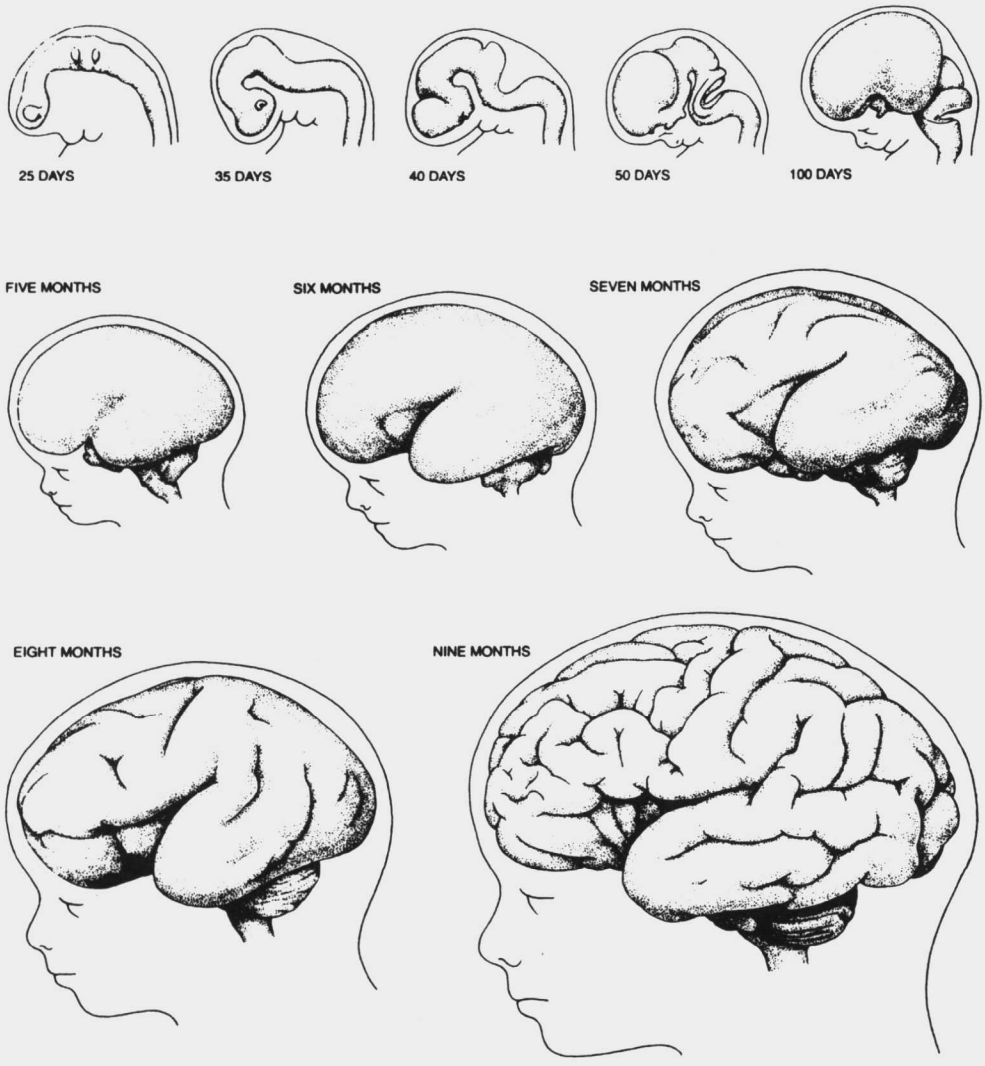
It has been possible to determine the timetable for many of these stages by labeling cells with various tracers. For example, thymidine is a compound that is incorporated into cells only during cell division. If a radioactive isotope is attached to the thymidine, the radioactivity will be detectable later only in those cells that were exposed to the thymidine during their mitosis. Cells born before or after this time will not be labeled. By labeling cells at different points in development, it is possible not only to chart the time of birth of cells but also to track their route during migration (see Figure 2). Thus, the thymidine technique has shown that cells that form the innermost layers of the cortex are born first, followed by those in the external layers. One consequence of this arrangement is that newly produced cells must migrate through the existing layers to reach their correct locations. It is also known that all cells forming a particular layer in a particular region of the cortex proliferate and migrate at the same time. Thus, brief prenatal events (e.g., drugs, toxins, or stress) that jeopardize developing cells could lead to the development of a brain without a particular cell group, the anomoly depending upon the precise timing of the prenatal event.

Detailed studies of brain development have shown that in most altricial mammals such as rats, cats, monkeys, or humans the stages of cell proliferation and migration are largely prenatal and much of the development of neuropil (axons and dendrites) and cell death are postnatal. Thus, most mammals are born with practically a full complement of neurons, and few, if any, neurons are born postnatally. One exception is the hippocampus, which continues to develop neurons throughout the life of some species. In general, however, if the brain is damaged after cell proliferation has ceased, it is obvious that any compensation will have to be accomplished by changes in the remaining cells. The fact that the growth

I wish to thank J. Vokey and L. DeLude for comments on an earlier version of this article.

Correspondence concerning this article should be addressed to Bryan Kolb, Department of Psychology, University of Lethbridge, Lethbridge, Alberta, Canada T1K 3M4.

Figure 1
The Development of the Human Brain



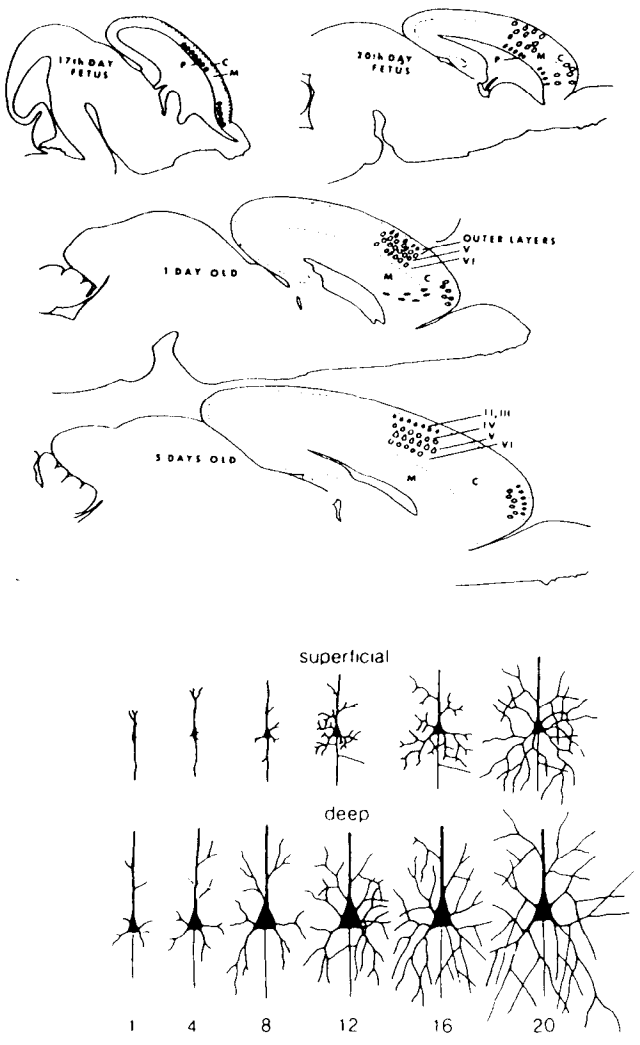
Note. Adapted from "The Development of the Brain" by W. M. Cowan. In *The Brain,* (p. 59), 1979, San Francisco: Freeman. Copyright 1979 by W. H. Freeman. Adapted by permission.

of neuropil and the loss of cells is postnatal is important for it is obvious that the extrauterine environment could have a direct influence on these processes.

Consider the following analogy. If one were to make a statue, it would be possible to do it either by starting with grains of sand and glueing them together to form the desired shape or by starting with a block of stone and chiseling the unwanted pieces away. The brain uses the latter procedure. The "chisel" in the brain could be of several forms including genetic signal, environmental stimulation, gonadal hormones, stress, and so on. Similarly, the same processes are likely to affect the development of dendrites, axons, and synapses. Cell death and neuropil development do not end in infancy but rather may continue well into adolescence. For example, it appears that cell death continues in the human frontal lobe until about 16 years of age (Huttenlocher, 1979). I should note here that cell death continues at a greatly slowed pace throughout adult life, but it is unclear what role environmental events may play in this process.

One example of the effect of environmental stimulation on brain development comes from the work of Janet Werker and Richard Tees (1984). They studied the ability of infants to discriminate phonemes taken from widely disparate languages such as English, Hindi, and Salish. Their results showed that infants can discriminate speech sounds of different languages without previous experience, but there is a decline in this ability, over the first year of life, as a function of specific language experience. One might speculate that neurons in the auditory system that

Figure 2
Migration of Cells



Note. The top panel is adapted from "Cell Migrations to the Isocortex of the Rat" by S. P. Hicks and C. J. D'Amato, 1968, *Anatomical Record, 160,* p. 621. Copyright 1968 by Allen R. Liss, Inc. Adapted by permission.

The top panel is a diagram of labeled cells that originated in the 17th (ovals) or 20th (black) intrauterine day in the rat brain. Notice that migration continues after birth.

The bottom panel is adapted from "Cellular Differentiation: Development of Dendritic Arborizations Under Normal and Experimentally Altered Conditions" by M. Berry, 1980, *Neurosciences Research Program Bulletin, 20,* p. 456. Copyright 1980 by MIT Press. Adapted by permission.

The bottom panel is a schematic illustration of the rate of acquisition of basal and apical dendrites of the pyramidal cells of the superficial and deep layers of the cerebral cortex of the rat.

are not stimulated early in life may be selected against and die, although there are other explanations.

The postnatal stages of brain development provide not only an explanation for how early experience could affect later behavior but also why brain damage at different ages might have very different effects and lead to different cerebral organizations.

Behavioral Effects of Early Brain Damage

In the 1930s Margaret Kennard was studying the effects of cortical lesions on motor performance in monkeys and reported the provocative finding that lesions in infant monkeys had less severe effects on behavior than similar lesions occurring in adulthood. This claim led to the development of the Kennard doctrine (1936), which stated that the earlier one suffers brain damage, the less severe the behavioral loss. This view was reinforced by Lennenberg (1967), who reviewed the effects of cortical lesions on language in children and concluded that left hemisphere damage in the first few years of life allowed substantial recovery of language processes, presumably because of some sort of cortical reorganization. By the mid 1970s, the Kennard doctrine was being challenged on the basis of studies using a variety of laboratory animals including monkeys, cats, and rats. For example, Patricia Goldman and her colleagues began to find that early cortical injury in monkeys was not always advantageous; the outcome depended on when behavior was assessed, the type of behavioral test employed, and the sex of the animal (e.g., Goldman, 1974). Indeed, even Kennard's experiments recently failed replication when redone using more modern behavioral methods (Passingham, Perry, & Wilkinson, 1983). Similarly, although the initial studies done by me and my colleagues on the effects of cortical lesions on infant rats supported the Kennard doctrine, we fell victim to the general principle of science that the more one studies something, the smaller the effects become (e.g., Kolb, 1987)!

Studies using children have also failed to support either Kennard's or Lennenberg's findings. Although there clearly is recovery of language after early left hemisphere lesions to the language areas and there is evidence that the language zones can shift either to the other hemisphere, if the damage is in the first two years of life (or within the left hemisphere, if the damage occurs between two and five years), children with early brain injuries suffer significant cognitive loss. For example, Woods (1980) found that the IQs of children with brain damage in the first year of life were well below average (WISC-R = ~85) as well as below those of children who suffered brain damage later in life. Similar results have been found by others, and it now appears that the period of severe IQ loss may extend as late as four to five years of age. In sum, there is little support for Kennard's original conclusions. Nonetheless, we have now identified a variety of factors that influence the outcome of early brain injury, and there is some evidence that a limited version of Kennard's principle may have some validity.

Behavioral Recovery in Rats

Over the past 15 years my colleagues and I have removed virtually every region of the rat's neocortex and have devised a neuropsychological test battery for the rat that is conceptually similar to that used for people. In contrast to the "rat studies" of the 1930s–1960s, which assumed that a rat should be used for just a single experiment, our

test battery assumes that the best way in which to study behavior in any species is to administer multiple measures of many aspects of behavior including both learned and species-typical behaviors (e.g., Kolb, 1984; Whishaw, Kolb, & Sutherland, 1983), as summarized in Table 1.

Contrasting models. To simplify the following discussion, I will focus on two of the preparations that we have used: (a) the hemidecorticate preparation and (b) the bilateral frontal preparation. In the hemidecorticate preparation, the entire neocortical mantle of one hemisphere is removed at different ages. This procedure is especially interesting in that it parallels the surgical procedure used in the treatment of children with major injuries restricted to one hemisphere, for which there is virtually no empirical basis in the primate literature (but see Villablanca, Burgess, & Sonnier, 1984, for parallel studies in kittens). In the bilateral frontal preparation, the frontal cortex that is analogous to the prefrontal and anterior cingulate region of primates is removed at different ages. We chose this preparation because the bulk of the work on infant lesions in primates has been done in animals with frontal lesions and because more is known about the frontal cortex of the rat than any other region of the rodent cortex.

Table 1
Behavioral Assessment of the Rat: A Partial Summary of Features of Behavior for Examination

Measure	Specific feature
1. Appearance	Body weight, core temperature, eyes, feces, fur, genitals, muscle tone, pupils, responsiveness, saliva, teeth, toenails, vocalizations
2. Sensory and sensorimotor behavior	Response to stimuli of each sensory modality presented both in home cage and in novel place such as open field
3. Posture and immobility	Behavior when spontaneously immobile, immobile without posture or tone; tonic immobility or animal hypnosis; environmental influences on immobility
4. Movement	General activity, movement initiation, turning, climbing, walking, swimming, righting responses, limb movements in different activities such as reaching or bar-pressing, oral movements such as in licking or chewing, environmental influences on movement
5. Species-typical behaviors	All species-typical behaviors such as grooming, food hoarding, foraging, sleep, maternal or sexual behavior, play, and burying
6. Learning	Operant and respondent conditioning, and learning sets, especially including measures of spatial learning, avoidance learning, and memory (for details, see Whishaw et al., 1983)

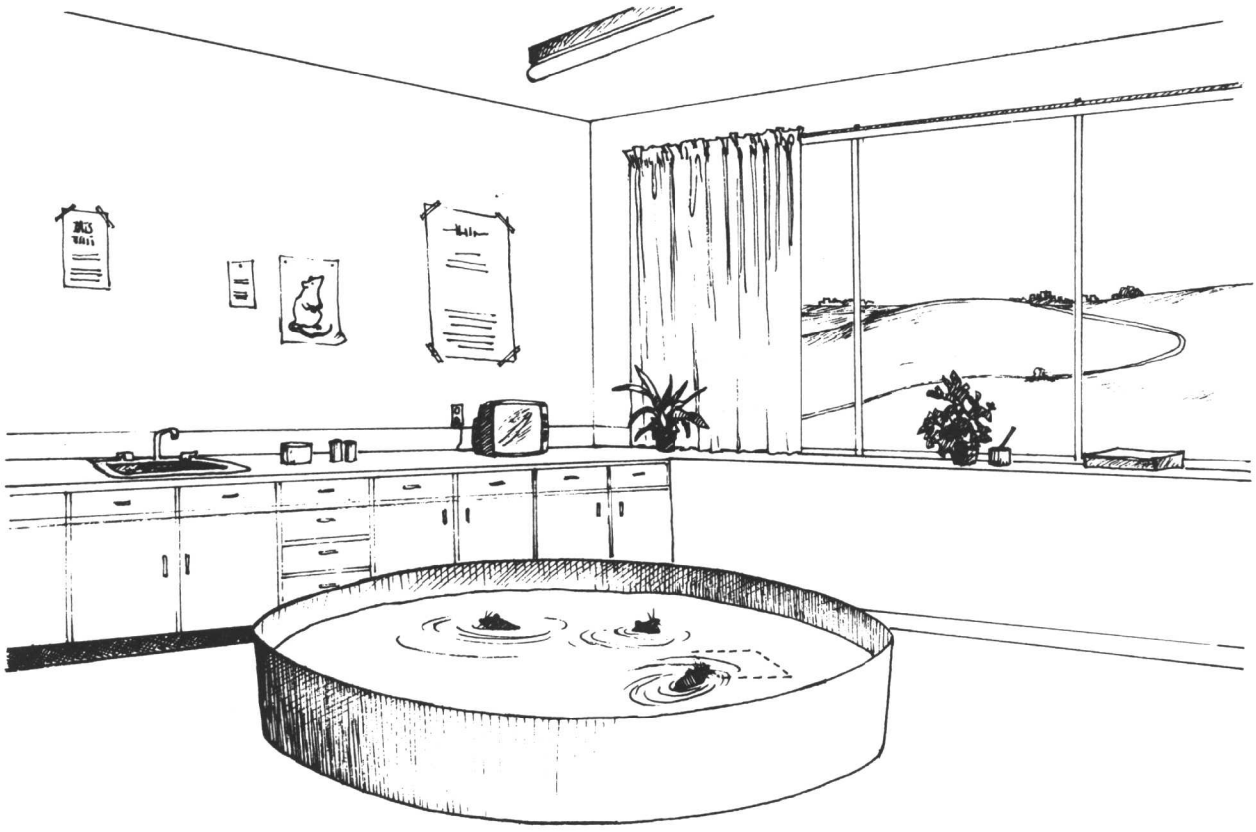
We have varied the age at lesion and found the behavioral and anatomical effects to vary with age at insult (Kolb, Holmes, & Whishaw, 1987; Kolb, 1987; Kolb & Tomie, 1988). Such a finding would be expected given the different stages of development that would be interrupted (e.g., see Figure 2). Thus, lesions on the first day of life, which we call postnatal day 1 (P1), perturb a brain in which cell migration is not yet complete and in which neuropil development has barely begun. In contrast, lesions on postnatal day 5 or 10 (P5, P10) affect a brain in which there is active development of neuropil. In human terms, the P10 lesions would be well into the first year, or even later.

Following adult rat hemidecortication there is a loss, or impairment, in a wide variety of behaviors. For example, there is a significant impairment in control of the limbs contralateral to the removal, a reduced ability to respond to stimuli contralateral to the lesion, and a deficit in most learning tasks requiring visuospatial guidance. Neonatal hemidecortication produces parallel deficits although the earliest operates (P1) were less impaired than adult operates. This advantage was not present in rats operated at P10. An example will illustrate.

Richard Morris (1981) devised an ingeneous test of spatial navigation in the rat in which an animal is placed in a large tank of water. The water is made opaque by a small amount of skimmed milk powder, and there is a hidden platform that the rat must locate to escape from the water (see Figure 3). Because rats are excellent swimmers, they need little training to learn the location of the platform on the basis of visual cues in the environment. Rats hemidecorticated as adults are impaired at this task, however, even if preoperatively trained. Although P1 hemidecorticates are also impaired when tested as adults, they are significantly superior to rats with P10 or adult lesions (see Figure 4). Parallel results are obtained from other measures, such as of motor abilities. Thus, for the hemidecorticate there is evidence that something like the Kennard principle is operating.

The effect of frontal lesions is different, however. Rats with bilateral frontal lesions at P1 are not only worse at most behavioral tasks than animals with lesions at P5, P10, P25, or adulthood, but they are also impaired on tasks at which the P10 and older animals are not. In short, they are much like those children with early lesions who have low IQs and poor recovery. The Morris water task again provides a good example. In contrast to rats with restricted lesions in other neocortical regions, rats with frontal lesions are slow to master this task. Rats with lesions at P1 are truly incapable of completing this task and never learn where the platform is. Surprisingly, however, rats with lesions at P10 are virtually indistinguishable

Figure 3
Illustration of the Morris Water Task



Note. Adapted from "Plasticity in the Neocortex: Mechanisms Underlying Recovery From Early Brain Damage by B. Kolb and I. Q. Whishaw, 1989, *Progress in Neurobiology, 32,* p. 242. Copyright 1989 by Pergamon Press. Adapted by permission.
The rat's task is to locate a submerged, hidden platform by using visuospation cues available in the room.

from control animals. If the lesions are made later in life, the deficit appears, although we do not know the exact age at which it occurs. Nonetheless, in contrast to rats with hemidecortications, in which the earliest lesions allowed the best recovery, in the frontal preparation there is a window of time around 10 days of age in which the Kennard principle holds. Similar results can be shown for other behavioral tests (e.g., Kolb, 1987).

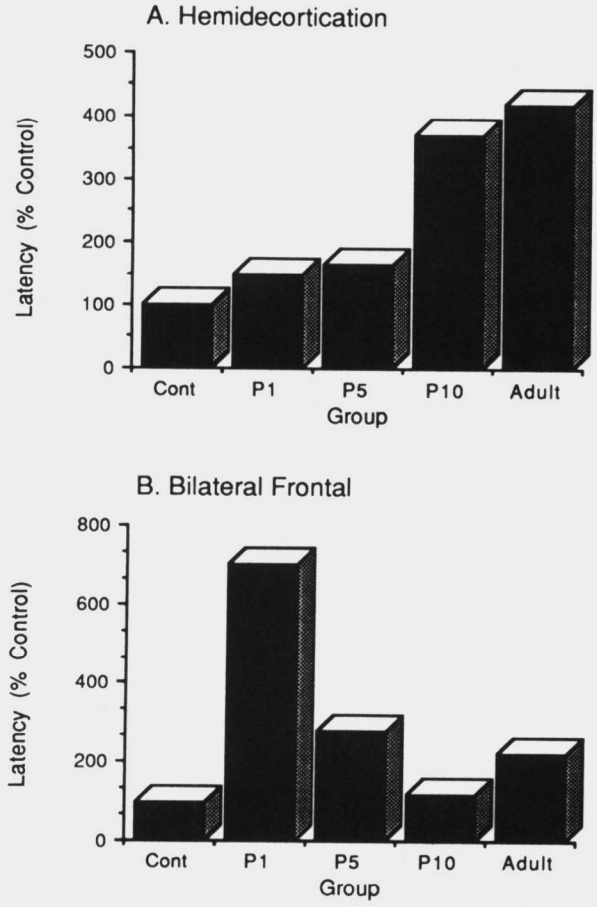
The contrasting effects of hemidecortication and frontal lesions are important because they have provided a behavioral marker that we can use to look for an anatomical correlate. Thus, the task is to find an anatomical change that occurs in P1 hemidecorticates and P10 frontals and that correlates with the Kennard effect, and an absence of this change (or possibly the onset of other changes) that correlates with the poor behavioral performance of the P1 frontal animals. Before describing such a correlate, I will consider some factors that influence recovery.

Factors Influencing Recovery

It has long been known that in different people the severity of symptoms resulting from the same brain damage varies considerably. This is presumably because of differences in a number of variables such as handedness, IQ, and personality. We have searched for modulating factors other than age that might influence the effect of neonatal (or adult) lesions in rats and have identified a large number, including sex, environmental experiences, size of brain lesion, nature of the behavioral test used, age at behavioral testing, and the level of endogenous cortical norepinephrine (e.g., Kolb & Elliott, 1987; Kolb & Sutherland, 1986; Kolb & Whishaw, 1981; Sutherland, Kolb, Whishaw, & Becker, 1982). I will briefly describe two examples.

Behavioral test. It is typical in neuropsychology to use tests of learned habits to assess behavior. When we began our studies, we also emphasized these measures, but as we expanded our tests, we were surprised to find little correspondence between the performance on tests of learned behaviors and measures of species-typical behavior such as hoarding or nest building. An example will serve to illustrate. John Pinel and his colleagues (e.g., Pinel & Treit, 1983) devised a test of natural avoidance behavior in rats in which a noxious stimulus, such as an electrified prod, was introduced into a rat's living quarters.

Figure 4
Comparison of the Effects of Hemidecortication or Frontal Lesions on Performance on the Morris Water Task

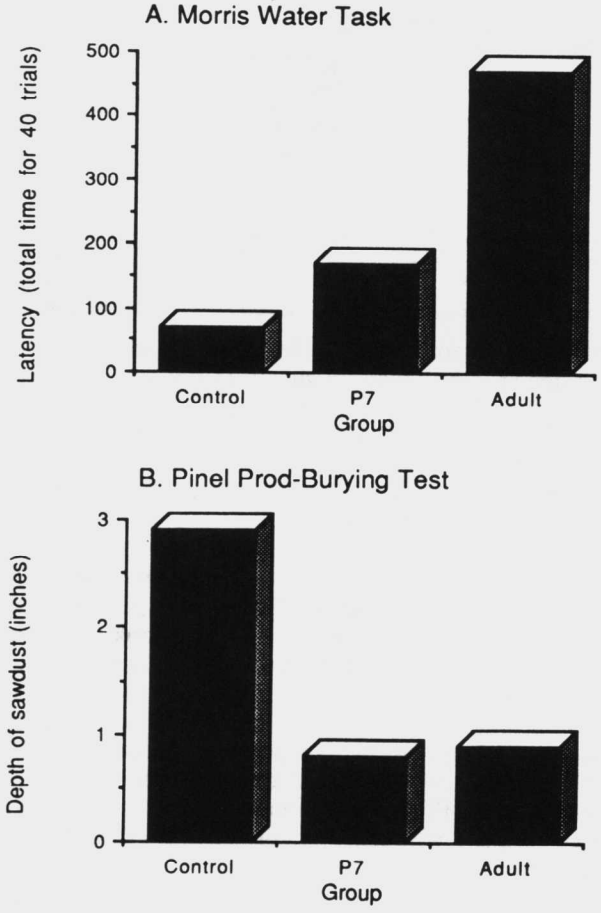


Note. The data are graphed as a percentage of control performance. All animals were tested as adults. Con = control. Ad = adult. P1 = surgery on postnatal day 1. P5 = surgery on postnatal day 5. P10 = surgery on postnatal day 10.

Pinel found that rats, being curious, approached this stimulus but once they were "stung" by it, and recovered from the immediate startle of the experience, they began to bury the stimulus. This highly reliable behavior proved simple to quantify with measures such as the depth of sawdust piled upon the electric prod. When we used Pinel's test with adult rats with frontal lesions, we found that they failed to bury the prod at all, although they clearly learned that the prod was noxious because no animal was shocked a second time; they simply avoided it. When rats with P7 lesions were tested on this task, they too failed to bury the prod. In contrast to the adult operates, however, the P7 animals showed nearly normal performance on several tests of learned behaviors, including delayed response, active avoidance, and spatial reversal learning. Further study showed that the animals that were nearly normal on a variety of tests of learned habits were as impaired at a variety of species-typical tests as were animals with adult lesions (e.g., Figure 5). Thus, it is evident that there is limited generality to the Kennard effect, even when it is present on some tests.

Environmental effects. Because it is now well accepted that environmental stimulation has major effects upon the neocortex (e.g., Greenough, 1986), it is reasonable to predict that some environmental conditions may influence the extent to which lesions influence behavior. In particular, we predicted that if animals with early lesions were housed in complex environments in which they were given considerable opportunity to move about and to explore a frequently changing world, they would show better recovery than those who were raised in standard laboratory cages. This proved to be the case: In contrast to the large impairments in isolated rats, enriched animals with P1 or P5 frontal lesions were significantly better at nearly all behaviors that we assessed, and in some cases the P5 animals were nearly as proficient as

Figure 5
Comparison of the Effects of Frontal Lesions at Postoperative Day 7 on the Performance of the Morris Water Task and the Pinel Burying Task



Note. The same animals who showed sparing of function on the learned task showed no sparing on the species typical test.