

Handbook of

# Drug and Chemical Stimulation of the Brain

Behavioral, Pharmacological and  
Physiological Aspects

**R.D. Myers**

# Handbook of **Drug and Chemical Stimulation of the Brain**

Behavioral, Pharmacological  
and Physiological Aspects

**R. D. Myers**



**VAN NOSTRAND REINHOLD COMPANY**  
NEW YORK CINCINNATI TORONTO LONDON MELBOURNE

**MEDICAL ECONOMICS BOOK DIVISION, INC.**  
ORADELL, NEW JERSEY

**Van Nostrand Reinhold Company Regional Offices:**  
New York Cincinnati Chicago Millbrae Dallas

**Van Nostrand Reinhold Company International Offices:**  
London Toronto Melbourne

Copyright © 1974 by Litton Educational Publishing, Inc.

Library of Congress Catalog Card Number: 74-10564  
ISBN: 0-442-25622-1

All rights reserved. No part of this work covered by the copyright hereon may be reproduced or used in any form or by any means—graphic, electronic, or mechanical, including photocopying, recording, taping, or information storage and retrieval systems—without permission of the publisher.

Manufactured in the United States of America

Published by Van Nostrand Reinhold Company  
450 West 33rd Street, New York, N.Y. 10001

Published simultaneously in Canada by Van Nostrand Reinhold Ltd.

15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

#### **Library of Congress Cataloging in Publication Data**

Myers, Robert D 1931-

Handbook of drug and chemical stimulation of the  
brain.

1. Psychopharmacology. I. Title. [DNLM: 1. Brain  
—Drug effects. 2. Stimulation, Chemical. WL300 M996h]  
RM315.M93 615'.78 74-10564  
ISBN 0-442-25622-1

# Preface

Ever since its inception in 1969, my intent in writing this book has been to present a comprehensive and up-to-date survey of the world's literature that pertains to the direct action of a drug or other chemical on the brain. Since experiments using the method of chemical stimulation have blossomed forth so readily in the past few years, this is indeed an appropriate time to take stock and review the exciting endeavors in this field and their present status.

Many of the research papers which are based on the application of a chemical to cerebral tissue have made substantial advances to our overall understanding of brain function. As such, they should be brought to light in the perspective of their own specific discipline. In view of this, it is my frank hope that this survey will be of value to every student interested in any of the intriguing issues of brain function, whether he be an inquisitive beginner or an established neuroscientist.

Each chapter is organized on a functional basis according to major physiological and behavioral systems. In this way, the facts which can be gleaned from the text should bring to the academician and clinician alike a keen awareness of the unique way in which a given chemical or drug can affect a distinct cerebral structure. A worker in one field of physiology, psychology, pharmacology or medicine hopefully will become cognizant of the enterprising activity of a worker in an entirely different area even though both may utilize the same experimental means to an end.

This book also seeks to point out some of the directions that a researcher may take in the future. In every chapter, the care and controls that are necessary in this proliferating field are emphasized so as to help the reader make a sensible interpretation of the series of isolated observations about a specific topic. Inasmuch as instances of controversy are not uncommon, I have attempted to evaluate critically the source of discrepancy which often rests simply in a difference in laboratory procedure.

In addition to the recent studies describing the action that a drug exerts on a specific cerebral structure, the early research reports of the German, Swiss and Japanese workers at the turn of the century are included. Since an attempt has

been made to include every pertinent paper written on this topic, any omission from the reference citations is certainly unintentional. Should the reader be aware of any paper which ought to be incorporated in the future version of this survey, I would be most grateful if the information is forwarded to me.

In general, a rule of thumb was followed to exclude from either the text or the master summary tables an abstract or summary written for the proceedings of a meeting, a conference, symposium or colloquium. Ordinarily, such an abstracted account is characterized by insufficient experimental detail, an inadequate analysis of the results or another shortcoming. Obviously, arbitrary exceptions to this rule had to be made. Although the basic reference list was completed in 1971, I have nevertheless included as many reports published in 1972 as possible.

I am deeply indebted to a great number of individuals who contributed in so many diverse ways to every aspect of this book. It is truly a pleasure to thank my professional colleagues and friends, both in England and America, who shared their valuable ideas on this subject, gave of their own personal insights and who offered the most salutary criticisms. My technicians and several other members of my laboratory staff kindly participated in the tracking down of articles, the redrawing of figures, and the reading and proofreading of the manuscript. Many authors not only gave generous permission to use their figures but often forwarded their own photographs or line drawings. The cooperation of the librarians and their various staff members of Purdue University, Indiana University Medical Center, National Institute for Medical Research (London), U.C.L.A. Brain Information Service, and University College (London) is deeply appreciated.

My secretary, Miss Jorga Fielder, typed the final draft of the book in its entirety with never-ending patience and a willingness for which I am sincerely grateful. Each of my four children always extended an amicable and helping hand whenever and in whatever direction it was needed. Finally, the cheerful and untiring efforts of my wife in typing the initial drafts, collating the references, in attending to hundreds of inconspicuous details and in offering inestimable encouragement have made this book possible.

R. D. MYERS

Lafayette, Indiana

# Contents

## PREFACE   vii

## **1 PRINCIPLES OF CHEMICAL STIMULATION OF THE BRAIN   1**

- I. INTRODUCTION   1**
- II. WHY CHEMICAL STIMULATION?   2**
  - A. Definition   2
  - B. Comparison with Ablation and Electrical Stimulation   3
- III. LEVELS OF CHEMICAL ANALYSIS   6**
  - A. Systemic Administration of a Chemical   7
  - B. Cerebral Ventricular Route   9
  - C. Direct Stimulation of Tissue   10
  - D. Iontophoretic Application   10
  - E. Tissue Analysis   11
- IV. CHEMICAL SENSITIVITY OF BRAIN TISSUE**
  - A. Sensitivity to Endogenous Factors   12
  - B. Sensitivity to a Synthetic Compound   15
  - C. Scope of Chemical Sensitivity   15
- V. CHEMICAL RECEPTORS IN THE BRAIN   19**
  - A. Receptor Criteria   19
  - B. Characterization of Neural Receptors   20
- VI. ANATOMICAL BASIS OF CHEMICAL STIMULATION   21**
  - A. Relative Position of Major Structures   21
  - B. Pathways of the Biogenic Amines   32
- VII. GENERAL CONSIDERATIONS   37**
  - A. Development of the Field   37
  - B. Usage of Master Summary Tables   40

## **2 EXPERIMENTAL METHODS FOR STIMULATING THE BRAIN WITH CHEMICALS 42**

- I. INTRODUCTION 42**
- II. CANNULA DESIGNS 43**
  - A. Infusion of Solutions 45
  - B. Application of Crystals 51
  - C. Regional Perfusion with Push-Pull Cannulae 55
- III. EXPERIMENTAL AND THEORETICAL ISSUES 59**
  - A. Diffusion of a Chemical in Tissue 59
  - B. Delivery of the Chemical into the Brain 63
  - C. The Problem of Dose or Concentration 66
  - D. Cannula Lesions and Anatomy 68
- IV. CHEMICAL TRANSPORT HYPOTHESES 70**
  - A. Chemical Transport via Blood 70
  - B. Chemical Transport via CSF 73
- V. CURRENT CONSIDERATIONS 76**

## **3 CARDIOVASCULAR, RESPIRATORY AND OTHER VITAL FUNCTIONS 78**

- I. INTRODUCTION 78**
- II. CARDIOVASCULAR CONTROL 80**
  - A. Pressor and Depressor Responses 82
  - B. Cholinergic and Adrenergic Action on Cardiovascular Mechanisms 89
- III. RESPIRATORY CONTROL 95**
  - A. Sites Sensitive to Chemical Change 95
  - B. Pulmonary Edema 100
- IV. GASTROINTESTINAL FUNCTION 101**
- V. MIXED AUTONOMIC EFFECTS 105**
- VI. CONCLUDING CONSIDERATIONS 108**
- VII. MASTER SUMMARY TABLE 109**

## **4 ADRENAL, THYROID AND OTHER HORMONAL SYSTEMS 117**

- I. INTRODUCTION 117**
  - A. Neuroendocrine Relationships 117

II. ACTH RELEASE: THE HYPOTHALAMUS	121
A. Hypothalamic Regulation of the Pituitary-Adrenal Axis	122
B. Extra-Hypothalamic Sites of Corticoid Action	130
C. Interaction with Other Hormonal Mechanisms	134
D. Putative Transmitters in the Hypothalamic Pathway	138
III. GROWTH HORMONE RELEASE	149
A. Hypothalamus and Growth Hormone	149
IV. THYROTROPIC HORMONE RELEASE: THE HYPOTHALAMUS	151
A. Anatomical Localization of Thyrotrophic Area	152
B. Action of Thyroxine on Hypothalamic Tissue	153
V. CONCLUDING CONSIDERATIONS	160
A. Feedback Loops	161
B. Biogenic Amines	162
VI. MASTER SUMMARY TABLE	164
 5 REPRODUCTIVE FUNCTIONS AND SEXUAL BEHAVIOR	 172
I. INTRODUCTION	172
A. Sex Hormones-Brain Interaction	172
B. Anatomical Relationships	173
II. CENTRAL ESTROGEN RECEPTORS	176
A. Anatomical Localization	178
B. Differential Effects of Central Estrogen	181
C. Hypothalamic Versus Pituitary Receptors	185
III. PROGESTERONE RECEPTORS	187
A. Anatomical Localization	188
B. Induced Functional Changes	190
IV. ANDROGEN RECEPTORS	191
A. Anatomical Localization	192
B. Seasonal Factors	193
V. MECHANISM OF GONADOTROPIN RELEASE	194
A. Luteinizing Hormone (LH)	195
B. Follicle Stimulating Hormone (FSH)	196
C. Prolactin	198
VI. CENTRAL ENDOCRINE EFFECTS ON SEXUAL BEHAVIOR	200
A. Mating in the Female	200
B. Mating in the Male	207

VII. INHIBITION OF SEXUAL FUNCTION	211
A. Blockade of Female Responses	212
B. Blockade of Male Responses	214
VIII. BIOGENIC AMINES IN THE HYPOTHALAMUS	215
A. Monoamines	215
B. Cholinergic Link	220
IX. CONCLUDING CONSIDERATIONS	222
X. MASTER SUMMARY TABLE	225

## 6 TEMPERATURE REGULATION 237

I. INTRODUCTION	237
A. Central Mechanisms	238
B. What are the Main Issues?	239
II. NEUROHUMORAL CONTROL MECHANISMS—AMINES	241
A. Monoamine Theory of Thermoregulation	241
B. Cholinergic Mechanisms	254
III. IONIC SET-POINT FUNCTION	262
A. Ion Balance in the Hypothalamus	263
B. Anatomical Localization of the Set-Point	264
IV. PYROGENS AND FEVER	269
A. Pyrogen and Disordered Thermoregulation	270
B. Antipyretic Agents	276
V. DRUG EFFECTS	277
A. Sensitivity of the Anterior Hypothalamus	277
B. Morphine	282
VI. CONCLUDING CONSIDERATIONS	286
A. Biogenic Amines	287
B. Temperature Control Model	289
VII. MASTER SUMMARY TABLE	290

## 7 HUNGER AND FEEDING 302

I. INTRODUCTION	302
A. Hunger and Satiety Receptors	303
B. Neuroanatomical Basis of Feeding	304
II. HYPOTHALAMIC HUNGER AND SATIETY MECHANISMS	306
A. Glucose Receptor Mechanisms	306
B. Hypothalamic Factors for Hunger and Satiety	311
C. Set-Point Mechanisms	315

III. ADRENERGIC RECEPTORS FOR FEEDING	318
A. Anatomical Aspects	319
B. Adrenergic Feeding in the Primate	325
C. Pharmacological Specificity	328
D. Destruction of Adrenergic Nerve Terminals	334
E. Palatability of Food and Other Factors	336
IV. CHOLINERGIC FEEDING	339
A. Excitation and Blockade	342
B. Cyclic AMP	344
V. INHIBITION OF FEEDING	345
A. Drug and Hormonal Effects	346
B. Toxic and Reversible Chemical Lesions	348
VI. CONCLUDING CONSIDERATIONS	350
A. Experimental Aspects	350
B. Chemical Factors	351
C. Morphological Factors	353
VII. MASTER SUMMARY TABLE	355
 8 THIRST AND DRINKING	 365
I. INTRODUCTION	365
A. Development of Thirst	365
B. Compensatory Responses	367
C. Central Pathways	369
D. Practical Issues	369
II. THIRST RECEPTORS IN THE HYPOTHALAMUS	370
A. Osmoreceptors: Evidence from Stimulation	370
B. ADH Release Mechanism	374
C. Angiotensin II Receptors	376
III. CHOLINERGIC THIRST SYSTEM	383
A. Anatomy of the Thirst Circuit	384
B. Pharmacology of the Thirst Circuit	390
C. Relation to Natural Thirst	392
D. Palatability of Fluid	397
E. Relationship to Other Functions	398
IV. ADRENERGIC MECHANISMS OF DRINKING	400
A. Destruction of Catecholaminergic Neurons	403
B. Drinking of Palatable Liquids and Nutrients	403
V. CENTRAL BLOCKADE OF DRINKING	406
A. Adipsia of Toxic Drugs	407

VI. CONCLUDING CONSIDERATIONS 409

A. Cholinergic Pathway 410

B. Receptor Sensitivity 411

VII. MASTER SUMMARY TABLE 413

9 SLEEP AND AROUSAL 429

I. INTRODUCTION 429

A. Anatomical Significance of the Brain-Stem 430

B. Neurohumoral Correlates 432

II. MONOAMINES AND SLEEP 434

A. Serotonin and EEG Synchronization 435

B. Catecholamines and Level of Arousal 436

III. ACETYLCHOLINE: SLEEP OR ACTIVATION? 438

A. Cholinergic Sleep Circuit 439

B. Cholinergic Arousal System 444

IV. IONIC BALANCE AND SLEEP 449

V. DRUGS AND AROUSAL 455

A. Local Anesthesia 455

B. Endogenous Substances and Sleep 457

VI. CONCLUDING CONSIDERATIONS 458

A. Hypnogenic Factors 459

B. Biogenic Amines 460

VII. MASTER SUMMARY TABLE 462

10 SENSORY AND MOTOR SYSTEMS 469

I. INTRODUCTION 469

A. Sensory Pathways 469

B. Motor Functions 470

II. MODIFICATION OF SENSORY INPUT 471

A. Reaction to Pain 471

B. Central Action of Morphine and Procaine 474

III. GROSS MOTOR FUNCTION 475

A. Locomotor Activity 477

B. Stereotypy Behavior 481

IV. TREMOR 488

A. Tremorogenic Substances 488

B. Parkinsonian Symptoms 494

V. SEIZURES AND EPILEPSY 499

A. Focal Epilepsy: Cortical 499

B. Subcortical Seizure Foci	500
C. Convulsant Drugs	509
D. Transitory Epileptic Episodes	513
E. Tubocurarine Seizures	519
VI. SUBCORTICAL SPREADING DEPRESSION	520
VII. CONCLUDING CONSIDERATIONS	523
A. Shift in Sensory Threshold	523
B. Cholinergic Mediation of Motor Activity	524
C. Monoamines and Sensorimotor Function	526
VIII. MASTER SUMMARY TABLE	527
<b>11 EMOTIONAL BEHAVIOR</b>	<b>552</b>
I. INTRODUCTION	552
A. Chemical Evocation of Emotion	553
B. Measuring a Change in Emotion	555
II. HYPOTHALAMIC MECHANISMS OF EMOTION	556
A. Cholinergic Rage	557
B. Blockade of Cholinergic Rage	562
C. Curare and Other Substances	564
D. Hypothalamic-Mesencephalic Emotional Axis	569
III. LIMBIC MECHANISMS IN EMOTIONAL BEHAVIOR	569
A. Hippocampus	570
B. Amygdala	571
C. Caudate Nucleus	572
IV. KILLING BEHAVIOR	574
A. Chemically-Induced Muricide	574
B. Pharmacological Blockade of Killing	576
V. TRANQUILIZERS AND OTHER DRUGS	580
VI. THERAPEUTIC APPLICATION IN THE HUMAN	583
A. Procainization of the Cerebrum	583
B. Chemical Transformation of Mood	584
VII. CONCLUDING CONSIDERATIONS	585
A. Cholinergic Emotional Circuit	585
B. Catecholaminergic Mechanisms	587
C. Clinical Application	588
VIII. MASTER SUMMARY TABLE	589
<b>12 LEARNING AND MEMORY</b>	<b>596</b>
I. INTRODUCTION	596
A. Neuronal Processes	596

B. Local Action of a Chemical on Learning	598
C. Quantification of a Change in Learning	598
II. DRIVE AND REWARD MECHANISMS	600
A. Self-Stimulation	600
B. Punishment Versus Reward	604
III. CHOLINERGIC MECHANISMS AND LEARNING	612
A. Avoidance Learning	612
B. Discrimination Learning	623
IV. HORMONES AND LEARNING	624
A. Adrenal Mechanisms	624
B. Thyroid Function	626
V. MEMORY MECHANISMS	626
A. Cortical Aspect of Retention	626
B. Hippocampus and Memory	627
C. Protein Synthesis and RNA	633
VI. CONCLUDING CONSIDERATIONS	635
A. Reward Mechanisms	636
B. Cholinergic Enhancement or Interference with Learning?	636
C. Neurohumoral Influence on Memory	637
VII. MASTER SUMMARY TABLE	639

### 13 EPILOGUE 648

I. INTRODUCTION	648
A. Anatomical Uniqueness	648
B. Basis of Anatomical Diversity	650
II. ARE FUNCTIONS OF THE FOREBRAIN AND MIDBRAIN CHEMICALLY CODED?	651
A. Concept of a Neurochemical Code	651
B. Dualism in Neurohumoral Coding	652
C. Local Release of a Humoral Factor	654
III. NEUROTRANSMITTER: CONCEPT REVISITED	660
A. Supplementary Criteria for a Neurotransmitter	661
B. Classification of Substances	664
C. How Does a Neurohumoral Code Function?	665
IV. THE BLACK BOX IS GRAY	669
REFERENCES	671
AUTHOR INDEX	731
SUBJECT INDEX	746

# 1 Principles of Chemical Stimulation of the Brain

*"To deride the hope of progress is the ultimate fatuity, the last word in poverty of spirit and meanness of mind. There is no need to be dismayed by the fact that we cannot yet envisage a definitive solution of our problem, a resting-place beyond which we need not try to go . . ."*

P. B. MEDAWAR (1972)

## I. INTRODUCTION

The incomparable challenge inherent in the manifold mysteries of brain function has led to one of the most fascinating experimental endeavors in all of the neurosciences. Essentially this widespread quest has centered on a prodigious attempt to "decode" the chemical fabric of a discrete collection of neurons. The logistics of such a decoding enterprise rests on the fundamental principle that an artificial alteration of the biochemical environment of a distinct region of the brain will produce a specific functional change in an animal. If such a change is evoked and is clearly repeatable, the response must make immutable sense in terms of the anatomy of the nervous system. In fact, the reaction to an alteration in the local chemical milieu of the brain may correspond directly with the acknowledged function of that morphological area. Or it may not correspond with the general knowledge about the structure which has been derived from the more traditional neurological approaches based on ablation or electrical stimulation.

Admittedly, any new method whereby a compound is applied directly to brain tissue, particularly of a wide-awake and behaving animal, is open to criticism. As we shall see in Chapter 2, the vast number of bench-top problems attendant to the technique itself is impressive. However, Sir Peter Medawar's statement at the heading of this chapter reflects with great insight the spirit in which the experimental evidence of an encoded functional system should be examined. The progress has been painfully slow and often obfuscated by an experimental or technical limitation rather than by an impoverished theoretical viewpoint. But the hope of understanding the neurochemical attribute of each of the complex

## 2 HANDBOOK OF DRUG AND CHEMICAL STIMULATION OF THE BRAIN

networks of neurons is notably profound, particularly if the concepts based on chemical stimulation are linked together with those derived from other experimental sources including those of histochemistry, transmitter dynamics and drug action.

In a word then, the overall purpose of this decoding endeavor is to contribute to the neuroscientist's goal of unraveling the mechanisms and even perhaps the circuitry that underlie the intricate processing of information of which the vertebrate brain is so capable. The chemical signal which triggers a response, the chemical reaction which inhibits that response, the balance and the interplay between the two, and the action which an individual substrate may have on another chemical system—all of these constitute a part of the questions raised when one stimulates the brain with a chemical substance.

### II. WHY CHEMICAL STIMULATION?

The rationale upon which the laboratory usage of chemical stimulation of the brain is based can be subdivided into two major parts. The first is concerned with the anatomical locus and cellular mechanism of any of the endogenous humoral factors. These substances that occur naturally in brain tissue include the biogenic amines, peptides, and steroids. A second and entirely different purpose centers on the localization of a possible central site of action of a chemical or drug that is administered systemically. From behavioral observations, many of these artificially synthesized compounds appear superficially to exert a direct effect on some part of the central nervous system. On the basis of these two fundamental points and because of the attractive analogies that can often be drawn with the responses evoked by electrical stimulation of brain tissue (Myers, 1971a), the theoretical principles and procedures of chemical stimulation have evolved.

#### A. Definition

In the broad context of general physiology, we shall use the term chemical stimulation to apply to any class of neuronal events that is brought about when an endogenous or synthetic substance is applied locally within a given structure of the brain. Although a multitude of compounds may affect nervous tissue in a way that is not necessarily excitatory in the sense of membrane physiology, the reaction observed by the scientist is indicative of a local perturbation of that tissue reached or touched upon by the chemical.

For example, some of the endogenous hormones, when deposited in the brain, appear to inhibit rather than stimulate neural elements in a manner similar to that of electrical current. Moreover, certain drugs act to hyperpolarize or depolarize a neuron by altering the flux of cations across the axonal membrane. Still other compounds may either block or enhance the action of a transmitter

substance or another humoral factor that is released into the synaptic cleft between two or more nerve cells. Rather than compartmentalizing the effect of a locally applied substance into functional categories, which in themselves would often be *ad hoc* and arbitrary, the term chemical "stimulation" is retained in this book for descriptive purposes.

## B. Comparison with Ablation and Electrical Stimulation

Defying all reason is a question that is argued rather vehemently in some circles by a few investigators. Is chemical stimulation "more physiological" or "less physiological" than some other laboratory procedure used in the exploration of brain function? Plainly, at the very moment when an experimental neurosurgeon enters the cranium, a nonphysiological state is created. Beyond this, the logic of the debate degenerates into a matter of relativity. The implantation or insertion of any device into any part of the brain results in a pathological circumstance. Taking the question of relative "physiological-ness" a step further, almost any neurobiological technique, except perhaps a skull X-ray, can interfere to some degree with normal function. Even the ingestion of an ordinary pill by mouth is viewed as unphysiological by certain naturopathic practitioners, who happily are in the minority.

Scientists who utilize the method of chemical stimulation ordinarily follow certain principles of neuroanatomy and exercise basic neuropharmacological controls. By staying within these principles, this approach to studying the brain can be as valid as any other that seeks a specific functional answer in the realm of an unknown cerebral process. If performed properly, the analytical exploration of a reaction of a given structure to a chemical can supplement in a very vital way the information that is already known from other studies of that region. In the broad purview of stimulating tissue that is intrinsically excitable, the topical application of a chemical does permit a fine grain resolution of the characteristics of a collection of neurons that are seemingly delegated to a specific function. Why is this so?

First, on the basis of the biochemistry of cortical and subcortical structures, we know that endogenous substances such as amines, amino acids and hormones are present in varying concentrations in separate parts of the brain (e.g., Hebb, 1970; McEwen *et al.*, 1972). Second, cytochemical studies of individual fiber systems show that individual amine pathways are laid down anatomically in unique patterns (e.g., Fuxe *et al.*, 1966; Shute and Lewis, 1967). Third, the membrane of an individual neuron that lies contiguous to another possesses a special sensitivity to different molecules, as demonstrated by the technique of iontophoresis. Logically, one can deduce that within a single collection of neurons each cell possesses: (a) distinct chemoreceptors; (b) the capacity to convey an impulse to another cell by virtue of the release of an endogenous

substance; or (c) a mechanism in the form of the release of a humoral factor for altering the depolarization threshold of an adjacent cell.

What happens when we either ablate this collection of neurons or pass electrical current through it? These events can be conceptualized by considering a schematic representation portrayed in Fig. 1-1 of a hypothetical collection of nerve cells in an unspecified area of the mammalian brain. Let us assume that three separate pathways traverse this structure. Pathway A is excitatory and mediated by an excitatory substance at synapses  $A_1$  and  $A_2$  to stimulate functional system

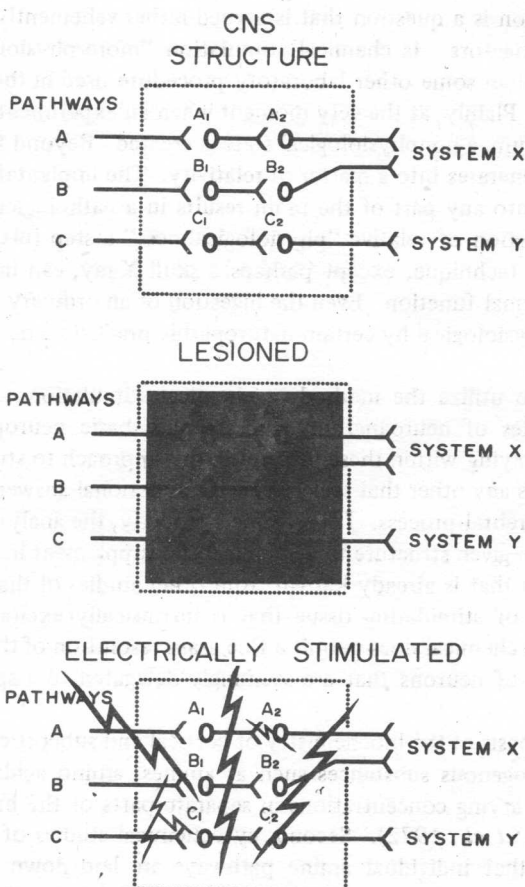


Fig. 1-1 A hypothetical structure in a mammalian central nervous system (CNS). Three separate pathways mediated by three individual sets of synapses traverse this structure. When the structure is lesioned (middle), all of the pathways are transected and the synapses are destroyed. When electric current is passed through the structure (bottom), all of the pathways are excited homogeneously in an undifferentiated manner.