

Neuropsychopharmacology and Therapeutics

Ivor S



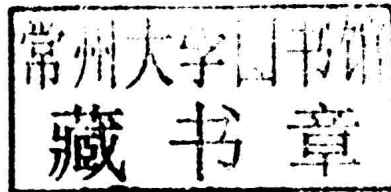
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Neuropsychopharmacology and Therapeutics

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*Dedicated to the memory of my mother, Ivy Salome Ebenezer,
and my aunt, Ellen Sophia Padayachy.*

Preface

Neuropsychopharmacology is a relatively new subject area in the neurosciences and may be viewed as the amalgamation of the principals of neuropharmacology and psychopharmacology. I have been teaching neuropsychopharmacology to undergraduate and postgraduate students for more than two decades. During this time, I have had difficulty in finding suitable textbooks that I could recommend to my students reading for the MPharm (Honours) degree in pharmacy, BSc (Honours) degree in pharmacology and related medical sciences degrees that adequately covered all the topics I teach. There are a small number of books on neuropharmacology and psychopharmacology, but they tend to cover limited areas of these topics; for example, there may be a good description of a particular central nervous system (CNS) disorder in terms of its pathology and brain dysfunction, but it may be limited in terms of therapeutics, or vice versa. In other cases, the books may only cover a small number of CNS conditions. Therefore, I have to recommend a number of textbooks to my students, as well as giving them numerous handouts to supplement my lectures. My students keep asking me if I can recommend a single textbook that reviews most of the areas covered during their neuropsychopharmacology modules because (i) they do not want to buy or borrow too many books, (ii) they find reading multiple books sometimes difficult or confusing because of different emphases or styles of writing and (iii) they complain about the lack of time when given a large reading list. Thus, many students tend to depend mainly on their lecture material and do not read adequately around the subject area. The impetus to write this book was threefold: to simplify access for undergraduate students, to enthuse them in the neurosciences and to show them how an appreciation of basic and clinical research findings can be translated into therapeutics.

Neuropsychopharmacology and Therapeutics is a textbook that had been written primarily for students reading for degrees in pharmacy, pharmacology and the medical sciences. However, it will also be useful for students on other courses where they study a module on CNS disorders. I have taught such modules to psychiatric/mental health nurses and to students reading for masters' degrees; this book will be suitable for them. The book has eleven chapters. The material covered in Chapter 1 provides an introduction to the subject area that will be beneficial when reading the other chapters. The main psychiatric and neurological disorders that are covered in most undergraduate courses are reviewed in Chapters 2 to 11. They are discussed in terms of their clinical symptoms, epidemiology, pathology, aetiology, underlying neurobiological and neurochemical mechanisms, pharmacotherapy (including information about the drugs and their recommended clinical doses, their mechanism of action, their pharmacokinetics and their adverse effects), adjunctive nonpharmacological treatments and clinical outcomes. Each chapter of the book is a 'stand-alone' chapter and is written in a style that most students will be able to follow and understand. In addition, readers may pick and choose what part of a chapter they want to read or place greater emphasis on. For example, if they are interested in the symptoms and the drug used to treat a CNS condition, then they can read those sections of a chapter. On the other hand, if they are more interested in the aetiology, pathology and the underlying neurobiological mechanisms of a CNS disorder, then they can focus on those sections.

While most texts on psychopharmacology and neuropharmacology deal with the use of drugs in the treatment of CNS conditions, they leave the reader with the somewhat false impression that pharmacological therapy alone will be sufficient to treat the symptoms of the disorder. This may be true in some cases, but with many mental illness and other CNS disorders, psychological and social-based therapies, such as cognitive behavioural therapy and psychoeducation, in conjunction with pharmacotherapy often result in better clinical outcomes. Thus, nonpharmacological treatments that can be used as

adjuncts to pharmacotherapy are discussed to give the reader a more realistic appreciation of treatment and therapeutic outcomes.

I have always been fascinated in the history of science and the manner in which scientific progress is made. As I tell my students, reading about discovery in science is like reading a detective novel. Researchers uncover clues that can lead to discovery. However, in some cases these clues can also lead scientists down blind alleyways and it may take a long time and meticulous research to find an answer to a scientific question or puzzle. This is most evident when one studies the history of psychiatric disorders. I have, therefore, endeavoured to provide brief overviews on the historical evolution of our present-day understanding of CNS disorders and the therapies that are available to treat them.

Finally, I wish to express my gratitude to former mentors and colleagues who helped shape this book by their numerous stimulating scientific discussions and their willingness to share their scientific experiences and expertise with me. In particular, I wish to acknowledge my PhD supervisor, the late Professor John W Thompson, my postdoctoral advisors, the late Professor Ben Delisle Burns, Dr Alison C Webb and Dr Bob Baldwin, my past scientific coworkers and collaborators, Dr Bob Parrott, Dr Sandra Vellucci, Dr James H. Pirch, Dr Geoffrey H. Hall, Professor John F. Golding, Professor C. Heather Ashton and Dr Rasneer S Bains, and the numerous postgraduate and undergraduate students who have worked in my laboratory. I would also like to thank Dr John C Wong, my former colleague and research collaborator, for reading some of the chapters in this book and for his helpful comments, Ms Elizabeth Renwick for convincing me to write this book, Mr Kevin Dunn (copy editor), Ms Durgadevi Shanmughasundaram (project manager), and the editorial team from Wiley, Ms Lucy Sayers, Ms Fiona Seymour, Ms Celia Carden and Ms Audrie Tan, for their help and advice.

Ivor S. Ebenezzer
Portsmouth, UK
November 2014

About the Companion Website

This book is accompanied by a companion website:

www.wiley.com/go/ebenezer/neuropsychopharmacology

The website includes:

- PowerPoint slides of all figures from the book for downloading
- PDF copies of all tables from the book for downloading

Contents

Preface	xiii
About the Companion Website	xv
1 Introduction to Neuropsychopharmacology	1
1.1 Overview	1
1.2 A Brief Overview of the Anatomy and Function of the Brain	2
1.2.1 The Brainstem	2
1.2.2 The Metencephalon	3
1.2.3 Diencephalon	4
1.2.4 The Telencephalon	5
1.2.5 The Cerebral Ventricles and Cerebrospinal Fluid	7
1.3 Important Neurotransmitters	7
1.3.1 GABA and GABA Receptors	7
1.3.2 Glutamate and Glutamate Receptors	10
1.4 Central Nervous System Stimulant and Depressant Drugs	11
1.5 Central Nervous System (CNS) Stimulant Drugs	13
1.5.1 Psychomotor Stimulants	13
1.5.2 Analeptic Drugs	19
1.6 Depressant Drugs	21
1.6.1 Benzodiazepines	21
1.6.2 Other Depressant Drugs	23
1.7 Genetics	23
1.8 Electroencephalography and Imaging Techniques	24
1.8.1 Electroencephalography	24
1.8.2 X-Rays	24
1.8.3 Computed Tomography	24
1.8.4 Positron Emission Tomography	25
1.8.5 Magnetic Resonance Imaging	25
1.8.6 Functional MRI	25
1.9 Diagnostic Criteria for Mental Disorders	25
1.10 Animals Models for CNS Disorders	26
1.11 Summary	27
2 Parkinson's Disease	28
2.1 Overview	28
2.2 Historical Background	28
2.3 Epidemiology	29
2.4 Primary Clinical Features	29
2.5 Secondary Clinical Features	30
2.6 Parkinson's Disease and the Extrapyramidal System	31

2.7	Neurotransmission in the Extrapyrarnidal System and Parkinson's Disease	33
2.7.1	Modulation of the Direct and Indirect Pathways	35
2.8	Causes of Parkinson's Disease	36
2.8.1	Genes and Parkinson's Disease	37
2.8.2	Environmental Neurotoxins	39
2.8.3	Oxidative Stress	41
2.9	Summary	42
2.10	Pharmacotherapy for Parkinson's Disease	42
2.10.1	L-DOPA (L-Dihydroxyphenylalanine)	43
2.10.2	L-DOPA Treatment	44
2.10.3	Adverse Effects of L-DOPA	44
2.10.4	Adverse Effects after Long-Term Treatment	46
2.10.5	Alternative Formulations of L-DOPA and Other Pharmacological Agents	48
2.11	Nonmotor Symptoms of Parkinson' Disease and the Development of a New Hypothesis	53
2.12	Pharmacological and Nonpharmacological Strategies for Treatment of Other Motor and Nonmotor Symptoms of Parkinson's Disease	55
2.13	Other Nonpharmacological Methods of Treating Parkinson's Disease	56
2.13.1	Lesions of the Globus Pallidus or Subthalamic Nucleus	56
2.13.2	Neurostimulation	57
2.13.3	Brain Grafts	57
2.14	Possible Future Strategies to Treat Parkinson's Disease	58
2.14.1	Stem Cell Therapy	58
2.14.2	Gene Therapy	58
2.15	Early Diagnosis for Treatment of Parkinson's Disease	59
2.16	Summary and Conclusions	59
3	Memory, Dementia and Alzheimer's Disease	61
3.1	Overview	61
3.2	Learning and Memory	61
3.2.1	Temporal Stages of Learning, Memory and Recall	62
3.2.2	Where are STM and LTM Stored in the Brain?	67
3.3	Overview of Dementia	69
3.4	Alzheimer's Disease (AD)	71
3.4.1	Clinical Symptoms of Alzheimer's Disease	72
3.4.2	Neuropathological Changes	74
3.4.3	Molecular Pathology	74
3.4.4	Staging of Alzheimer's Disease	80
3.4.5	Onset of Alzheimer's Disease	80
3.4.6	Neurochemical Changes in Alzheimer's Disease	82
3.4.7	Pharmacotherapy of Alzheimer's Disease	85
3.4.8	Future Pharmacological Strategies in the Treatment of Alzheimer's Disease	88
3.4.9	Cardiovascular Disease	91
3.4.10	Conclusions	91
3.5	Summary	92
4	Epilepsy	93
4.1	Overview	93
4.2	Background	94
4.3	Classification and Types of Epilepsy	94

4.3.1	Focal Seizures	94
4.3.2	Generalized Seizures	95
4.3.3	Epilepsy Syndromes	97
4.3.4	Epidemiology	98
4.4	Underlying Causes of Epilepsy	98
4.5	Epileptic Mechanisms	99
4.5.1	Electrophysiological Mechanisms	99
4.5.2	Mechanisms Underpinning Drug Treatment of Epilepsy	100
4.6	Pharmacotherapy	101
4.6.1	Valproate (Valproic Acid and Sodium Valproate)	101
4.6.2	Phenytoin	105
4.6.3	Carbamazepine	106
4.6.4	Ethosuximide	107
4.6.5	Gabapentin	107
4.6.6	Pregabalin	108
4.6.7	Lamotrigine	109
4.6.8	Tiagabine	109
4.6.9	Topiramate	110
4.6.10	Levetiracetam	110
4.6.11	Retigabine	111
4.6.12	Zonisamide	111
4.6.13	Benzodiazepines	112
4.6.14	Barbiturates	112
4.7	Vagal Nerve Stimulation	113
4.8	Summary	113
5	Attention Deficit Hyperactivity Disorder	115
5.1	Overview	115
5.2	Background to ADHD	116
5.3	Diagnostic Criteria for ADHD	118
5.4	ADHD and Comorbidity	119
5.5	Epidemiology	120
5.6	Aetiology of ADHD	120
5.6.1	Genetic Factors	120
5.6.2	Environmental Factors	121
5.7	The Pathophysiology of ADHD	122
5.7.1	The Prefrontal Cortex, Executive Function and ADHD	122
5.7.2	Frontocortical-Striatal Networks and ADHD	126
5.8	The Biochemical Hypothesis of ADHD	130
5.9	Executive Functional Skills, Neurodevelopment and ADHD	132
5.10	Summary of the Pathophysiology of ADHD	135
5.11	Management of ADHD	135
5.11.1	Pharmacotherapy	136
5.11.2	Nonpharmacological Management of ADHD	142
5.12	Summary and Conclusions	144
6	Affective Disorders 1: Depression	147
6.1	Outline	147
6.2	Emotion, Mood and Affective Disorders	148

6.3	Background to Depression	149
6.4	Clinical Features of Major Depressive Disorder	150
6.4.1	Subtypes of Depressive Disorders	150
6.5	Epidemiology	152
6.6	Causes of Depression	153
6.6.1	Genetic Influences	153
6.6.2	Biochemical Hypotheses of Depression	154
6.7	Stress, Learned Helplessness and Depression	163
6.7.1	Stress and MDD	164
6.7.2	What is Stress?	164
6.7.3	Stress and Depression	166
6.7.4	Brain Derived Neurotropic Factor, Neurotropic Effects and Depression	167
6.7.5	Genetics, Stress and Depression	168
6.7.6	Early-Life Stress, Depression and Epigenetics	169
6.7.7	Depression and Inflammation	171
6.7.8	Depression and Glutamate	171
6.7.9	Depression and Physical Diseases	171
6.8	Drug Treatment of Depression	172
6.8.1	Overview	172
6.8.2	Types of Antidepressant Drug	174
6.8.3	Possible Future Drugs for MDD	186
6.9	Nonpharmacological Treatments for Depression	187
6.9.1	Electroconvulsive Therapy	187
6.9.2	Transcranial Magnetic Stimulation	188
6.9.3	Vagus Nerve Stimulation	189
6.9.4	Phototherapy (Light Therapy)	189
6.9.5	Deep Brain Stimulation	190
6.9.6	Cognitive Behavioural Therapy	190
6.9.7	Interpersonal Therapy	191
6.9.8	Behavioural Therapy	192
6.9.9	Mindfulness-Based Cognitive Therapy	192
6.10	Summary	192
7	Affective Disorders 2: Bipolar Disorder	194
7.1	Outline	195
7.2	Background to Bipolar Disorder	195
7.3	Clinical Features of Bipolar Disorder and Diagnostic Criteria	196
7.3.1	Symptoms of Mania	196
7.3.2	Symptoms of Hypomania	197
7.3.3	Symptoms of Depression	197
7.3.4	Categories of Bipolar Disorder	197
7.3.5	Rapid Cycling	197
7.3.6	Mixed Features	197
7.3.7	Cyclothymia	198
7.3.8	Suicide	198
7.3.9	Course of Illness	198
7.4	Epidemiology	198
7.5	Cause of Bipolar Disorder	199
7.5.1	Genetic Factors	199

7.5.2	Environmental Factors	199
7.5.3	Neurobiology of Bipolar Disorder	199
7.6	Management of Bipolar Disorder	201
7.6.1	Pharmacotherapy	201
7.6.2	Drugs Used in the Treatment of Bipolar Disorder	204
7.7	Pregnancy and Bipolar Disorder	208
7.8	Psychological Treatments	208
7.8.1	Psychoeducation	208
7.8.2	Family-Focused Treatment	209
7.8.3	Cognitive Behavioural Therapy	209
7.8.4	Interpersonal and Social Rhythm Therapy	209
7.8.5	Lifestyle Changes	210
7.9	Summary and Conclusions	210
8	Anxiety Disorders	211
8.1	Overview	211
8.2	Background	212
8.3	Anxiety Disorders and Diagnostic Criteria	212
8.3.1	Generalized Anxiety Disorder	212
8.3.2	Social Anxiety Disorder	213
8.3.3	Panic Attack and Panic Disorder	214
8.3.4	Agoraphobia	215
8.3.5	Others Types of Anxiety Disorders	216
8.4	Neurobiology of Anxiety Disorders	216
8.4.1	Fear and the Amygdala	216
8.4.2	Anatomy and Circuitry of the Amygdala	217
8.4.3	Physiological Responses to Fear-Eliciting Stimuli	217
8.4.4	Conditioned Fear Response	220
8.4.5	Conditioned Fear Extinction	223
8.5	Worry	224
8.6	Are there Other Anxiety Circuits?	225
8.7	Neurotransmitters and Anxiety Disorders	225
8.8	Management of Anxiety Disorders	226
8.8.1	Pharmacotherapy	226
8.8.2	Psychosocial Therapies	232
8.9	Summary and Outcomes	234
9	Sleep and Sleep Disorders	236
9.1	Overview	236
9.2	Introduction	237
9.3	Physiology of Sleep	238
9.3.1	Stages of Sleep	238
9.3.2	The Ascending Reticular Activating System	240
9.3.3	Slow Wave Sleep Mechanisms	242
9.3.4	Rapid Eye Movement Sleep Mechanisms	245
9.4	Sleep Disorders	246
9.4.1	Insomnia	246
9.4.2	Hypersomnia or Hypersomnolence	254
9.5	Summary and Conclusions	257

10	Schizophrenia	259
10.1	Overview	259
10.2	Background	260
10.3	Clinical Features of Schizophrenia	264
10.3.1	Phases of Schizophrenia	264
10.3.2	Diagnostic Criteria for Schizophrenia	265
10.3.3	Violence, Self-Harm and Suicide	265
10.3.4	General Physical Health and Mortality	266
10.4	Epidemiology	266
10.5	Pathology	266
10.6	Aetiology	267
10.6.1	Genetics of Schizophrenia	267
10.6.2	Environmental Risk Factors	268
10.7	Developmental Hypothesis of Schizophrenia	270
10.8	Biochemical Hypotheses	270
10.8.1	Dopamine and the Dopamine Hypothesis of Schizophrenia	270
10.8.2	The Mesolimbic System and Schizophrenia	273
10.8.3	The Mesocortical System and Schizophrenia	273
10.8.4	Glutamate, GABA and Dopamine: A Revised Hypothesis of Schizophrenia	274
10.9	Management of Schizophrenia	277
10.9.1	Pharmacotherapy	277
10.9.2	Nonpharmacological Management of Schizophrenia	288
10.10	Summary and Conclusions	288
11	Drug Abuse and Addiction	290
11.1	Outline	290
11.2	Background	291
11.3	Neurobiology of Substance Abuse and Addiction	293
11.3.1	The Mesolimbic Reward Systems and Addictive Drugs	293
11.3.2	Extensions of the Hypothesis	298
11.3.3	Transition from Hedonic Actions to Habits to Compulsions	300
11.3.4	Summary	301
11.4	Risk Factors	301
11.4.1	Environmental Factors	301
11.4.2	Genetic Factors	302
11.5	Management of Addiction	302
11.5.1	Alcohol	306
11.5.2	Heroin	307
11.6	Summary	308
	References	310
	Index	327

1

Introduction to Neuropsychopharmacology

All things are ready, if our minds be so.

Henry V, IV, iii (William Shakespeare)

*In omnibus negotiis prius quam aggrediare, adhibenda est praeparation diligens.
(In all matters, before beginning, a diligent preparation should be made.)*

(Marcus Tilius Cicero)

1.1 Overview

Neuropsychopharmacology is a relatively new subject area in the neurosciences and may be viewed as the amalgamation of the principals of neuropharmacology and psychopharmacology. Neuropharmacology mainly deals with the effects of drugs on neurones, synapses and brain circuits and their interaction with neurotransmitters and other neurochemicals at their receptors and ion channels, both at a molecular and systems level. Psychopharmacology is the study of drugs that have the ability to alter mental states, such as emotional behaviours and cognition. Neuropsychopharmacology is, therefore, a field of study that describes the effects of drugs from the molecular to the behavioural level and requires integration and synthesis of knowledge from various disciplines, including neuroanatomy, physiology, pharmacology, molecular biology, genetics, psychology, psychiatry, sociology, biochemistry and chemistry. The principals of neuropsychopharmacology are important in (i) discovering more about the workings of the brain and the impact on behaviour, (ii) learning about the cellular, receptor and neurochemical changes that accompany brain dysfunctional states and (iii) the development of drugs to treat central nervous system (CNS) disorders and psychiatric conditions.

The authors of most textbooks on neuropharmacology and psychopharmacology presuppose that the reader has almost no knowledge of basic pharmacology, neurotransmitters and neurotransmission, receptor mechanisms, cell signalling, neuroanatomy, the fundamental principals of molecular biology and

genetics. Therefore, they spend the first few chapters of their books explaining the essential principals of these subject areas. Here, on the other hand, I will assume that the reader of this book has a working knowledge of these subjects. However, a lot of the basic information is covered in the different chapters of this book. In this chapter, some of the useful terms and concepts referred to in subsequent chapters are explained and brief overviews are given of (i) the anatomy and functions of the brain, (ii) important neurotransmitters in the CNS, (iii) some of the CNS depressant and stimulant drugs that are used in the treatment of the disorders that are discussed in subsequent chapters, and (iv) the experimental and clinical techniques that are used to obtain information on brain function.

1.2 A Brief Overview of the Anatomy and Function of the Brain

Reviewed briefly in this section are some of the important structures in the brain and their main functions. More detailed information on the anatomy and function of brain areas pertinent to specific CNS disorders are covered in the relevant chapters.

1.2.1 The Brainstem

The *brainstem* is made up of three structures, the *medulla oblongata*, the *pons* and the *midbrain* (Figure 1.1).

- The **Medulla Oblongata** (commonly referred to as the *medulla*) is a division of the brain known as the *myelencephalon*. It forms the most posterior or lowest part of the brain and is often considered an extension of the spinal cord within the skull. It is a small structure of about one inch (2.5 cm) in length and lies below the pons. It is composed largely of projection tracts carrying information between the body (via the spinal cord) and the rest of the brain. The medulla also has a network of cells that occupy the core of the brainstem, extending through the pons and midbrain, known as the *reticular formation* (reticulum means 'little net'). The ascending projections from the reticular formation project to the thalamus and cortex and play an important role in arousal and, for this reason, they are also known as the ascending reticular activating system (ARAS) (Chapter 8). Various nuclei in the medulla's reticular formation have diverse functional roles. There are cardiac, vasomotor and respiratory centres that regulate cardiovascular, circulatory and respiratory reflexes, respectively, as well as other nuclei that regulate reflexes, including vomiting, swallowing, coughing and sneezing.
- The **Pons** (which means bridge) is a structure, with a characteristic bulge, that lies above the medulla and is considered a 'bridge' between the medulla and the midbrain (which is located above it). Ascending and descending fibre tracts pass through the pons, which is also part of the reticular formation. It is a division of the brain known as the *metencephalon*. It is connected to another division of the metencephalon, the cerebellum (Section 1.2.2), by bundles of transverse fibre tracts. The pons contains centres for reflexes that are mediated by the fifth (trigeminal), sixth (abducens), seventh (facial) and eighth (vestibulocochlear) cranial nerves. The pons also has the pneumotaxic centres that, together with the medulla, control respiration.
- The **midbrain** is a division of the brain known as the *mesencephalon* and lies above the pons. Ascending and descending fibre tracts pass through the midbrain and it is also part of the reticular formation. The roof or tectum of the midbrain consists of two pairs of folds called colliculi (meaning 'little hills'); these form the upper part of the midbrain that lies immediately above the cerebellum. The two *inferior colliculi* have auditory centres and are involved in auditory function. The *superior colliculi*, which lie in front of the inferior colliculi, have visual centres and are involved in the regulation of pupillary reflexes and eye movements that are mediated by the third and fourth cranial nerves, respectively. Under, or ventral to the tectum, is another subdivision of the midbrain, the tegmentum,