

## **Marijuana and Madness**

Psychiatry and Neurobiology

---

This book provides a comprehensive and up-to-date overview of the psychiatry and neuroscience of *Cannabis sativa* (marijuana), with particular emphasis on psychotic disorders. It outlines the very latest developments in our understanding of the human cannabinoid system, and links this knowledge to clinical and epidemiological facts about the impact of cannabis on mental health. Clinically focused chapters review not only the direct psychomimetic properties of cannabis, but also the impact consumption has on the courses of evolving or established mental illness such as schizophrenia. A number of controversial issues are critically explored, including whether a discrete ‘cannabis psychosis’ exists, and whether cannabis can actually cause schizophrenia. Effects of cannabis on mood, notably depression, are reviewed, as are its effects on cognition. This book will be of interest to all members of the mental health team, as well as to neuroscientists and those involved in drug and alcohol research.

**David Castle** is Professor at the Mental Health Research Institute and University of Melbourne, Melbourne, Australia.

**Robin Murray** is Professor at the Maudsley Hospital and Institute of Psychiatry, London.

Cambridge University Press  
0521819407 - Marijuana and Madness: Psychiatry and Neurobiology - Edited by David  
Castle and Robin Murray  
Frontmatter  
[More information](#)

# Marijuana and Madness

Psychiatry and Neurobiology

Edited by

**David Castle**

Mental Health Research Institute and University of Melbourne, Australia

**Robin Murray**

Maudsley Hospital and Institute of Psychiatry, London, UK



**CAMBRIDGE**  
UNIVERSITY PRESS

Cambridge University Press  
 0521819407 - Marijuana and Madness: Psychiatry and Neurobiology - Edited by David  
 Castle and Robin Murray  
 Frontmatter  
[More information](#)

PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE  
 The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS  
 The Edinburgh Building, Cambridge CB2 2RU, UK  
 40 West 20th Street, New York, NY 10011-4211, USA  
 477 Williamstown Road, Port Melbourne, VIC 3207, Australia  
 Ruiz de Alarcón 13, 28014 Madrid, Spain  
 Dock House, The Waterfront, Cape Town 8001, South Africa  
<http://www.cambridge.org>

© Cambridge University Press 2004

This book is in copyright. Subject to statutory exception and  
 to the provisions of relevant collective licensing agreements,  
 no reproduction of any part may take place without  
 the written permission of Cambridge University Press.

First published 2004

Printed in the United Kingdom at the University Press, Cambridge

*Typefaces* Minion 10.5/14pt. and Formata *System* L<sup>A</sup>T<sub>E</sub>X 2<sub>ε</sub> [tb]

*A catalogue record for this book is available from the British Library*

*Library of Congress Cataloguing in Publication data*

Marijuana and madness : psychiatry and neurobiology / edited by David Castle and Robin Murray.  
 p. cm.

Includes bibliographical references and index.

ISBN 0 521 81940 7 (hardback)

1. Marijuana – Physiological effect. 2. Marijuana – Psychological aspects. 3. Marijuana abuse –  
 Complications. 4. Psychoses – Etiology. 5. Schizophrenia – Etiology. I. Castle, David J. II. Murray,  
 Robin, MD, M Phil, MRCP, MRC Psych.

[DNLM: 1. Marijuana smoking – psychology. 2. Marijuana smoking – adverse effects.

3. Mental disorders – complications. WM 276 M33485 2004]

RC568.C2M375 2004

615'.7827 – dc22 2003055906

ISBN 0 521 81940 7 hardback

Cambridge University Press  
0521819407 - Marijuana and Madness: Psychiatry and Neurobiology - Edited by David  
Castle and Robin Murray  
Frontmatter  
[More information](#)

---

**This book is dedicated to the memory of Frances Rix Ames, whose belief in the potential medical and environmental benefits of marijuana was never obscured by the smoke of political rhetoric.**

## Contents

	<i>List of contributors</i>	<i>page</i> ix
	<i>Foreword</i>	xiii
	<i>Preface</i>	xv
1	The cannabinoid system: from the point of view of a chemist Raphael Mechoulam and Lumir Hanuš	1
2	How cannabis works in the brain Leslie Iversen	19
3	Acute and subacute psychomimetic effects of cannabis in humans David J. Castle and Nadia Solowij	41
4	The association between cannabis use and depression: a review of the evidence Louisa Degenhardt, Wayne Hall, Michael Lynskey, Carolyn Coffey and George Patton	54
5	Cannabis and psychosis proneness Hélène Verdoux	75
6	Is there a specific ‘cannabis psychosis’? Wayne Hall and Louisa Degenhardt	89
7	Cannabis as a potential causal factor in schizophrenia Louise Arseneault, Mary Cannon, John Witton and Robin Murray	101
8	Cannabis abuse and the course of schizophrenia Don Linszen, Bart Peters and Lieuwe de Haan	119
9	The endogenous cannabinoid system in schizophrenia Suresh Sundram, Brian Dean and David Copolov	127
10	Cannabinoid ‘model’ psychosis, dopamine–cannabinoid interactions and implications for schizophrenia D. Cyril D’Souza, Hyun-Sang Cho, Edward B. Perry and John H. Krystal	142

<b>viii</b>	<b>Contents</b>	
11	Motives that maintain cannabis use among individuals with psychotic disorders Catherine Spencer	166
12	Addressing cannabis abuse in people with psychosis Wynne James and David J. Castle	186
13	Residual cognitive effects of long-term cannabis use Harrison G. Pope, Jr and Deborah Yurgelun-Todd	198
	<i>Index</i>	211

## Contributors

**Louise Arseneault, Ph.D.**  
 Social, Genetic and Developmental  
 Psychiatry  
 Research Centre  
 Institute of Psychiatry  
 King's College  
 London  
 UK

**Mary Cannon M.D. Ph.D. M.R.C.Psych.**  
 Division of Psychological Medicine  
 Institute of Psychiatry  
 King's College  
 London  
 UK

**David J. Castle M.B.Ch.B. M.Sc. M.D.**  
**DLSHTM M.R.C.Psych. FRANZCP**  
 Mental Health Research Institute  
 University of Melbourne  
 155 Oak Street  
 Parkville VIC 3052  
 Australia

**Hyun-Sang Cho M.D.**  
 Department of Psychiatry  
 Yale University School of Medicine  
 Psychiatry Service 116A  
 VA Connecticut Healthcare  
 System  
 950 Campbell Avenue  
 West Haven CT 06516  
 USA

**Carolyn Coffey B.Sc. Grad. Dip. Epi.**  
 Centre for Adolescent Health  
 Murdoch Children's Research Institute  
 2 Gatehouse Street  
 Parkville VIC 3052  
 Australia

**David Copolov**  
 Mental Health Research Institute  
 University of Melbourne  
 155 Oak Street  
 Parkville VIC 3052  
 Australia

**Brian Dean**  
 Mental Health Research Institute  
 University of Melbourne  
 155 Oak Street  
 Parkville VIC 3052  
 Australia

**Louisa Degenhardt Ph.D.**  
**M.Psychol.(Clinical)**  
 National Drug and Alcohol  
 Research Centre  
 University of NSW  
 Sydney NSW 2052  
 Australia

**Lieuwe de Haan**  
 Academic Medical Center  
 University of Amsterdam  
 Amsterdam  
 The Netherlands

**D. Cyril D'Souza M.D.**

Department of Psychiatry  
 Yale University School of Medicine  
 Psychiatry Service 116A  
 VA Connecticut Healthcare System  
 950 Campbell Avenue  
 West Haven CT 06516  
 USA

**Wayne Hall Ph.D.**

Office of Public Policy and Ethics  
 Institute for Molecular Bioscience  
 University of Queensland  
 St Lucia QLD 4072  
 Australia

**Lumir Hanuš Ph.D.**

Medical Faculty  
 Department of Medicinal Chemistry and  
 Natural Products  
 The Hebrew University of Jerusalem  
 Ein Kerem Campus  
 Jerusalem 91120  
 Israel

**Leslie Iversen Ph.D. F.R.S.**

University of Oxford  
 Department of Pharmacology  
 South Parks Road  
 Oxford OX1 3QT  
 UK

**Wynne James R.N. Dip.N.(Lond.)**

**B.Sc.(Hons)**  
 Manager  
 Next Step Specialist Drug and Alcohol  
 Services  
 26 Dugdale Street  
 Warwick WA 6024  
 Australia

**John H. Krystal M.D.**

Department of Psychiatry  
 Yale University School of Medicine  
 Psychiatry Service 116A  
 VA Connecticut Healthcare System  
 950 Campbell Avenue  
 West Haven CT 06516  
 USA

**Don Linszen**

Academic Medical Centre  
 University of Amsterdam  
 Amsterdam  
 The Netherlands

**Michael Lynskey Ph.D.**

Missouri Alcoholism Research Center  
 Department of Psychiatry  
 Washington University School of Medicine  
 40 N. Kingshighway, Suite One  
 St Louis MO 63108  
 USA

**Raphael Mechoulam, Ph.D.**

Medical Faculty  
 Department of Medicinal Chemistry and  
 Natural Products  
 The Hebrew University of Jerusalem  
 Ein Kerem Campus  
 Jerusalem 91120  
 Israel

**Robin Murray M.D. D.Sc. F.R.C.Psych.**

Division of Psychological Medicine  
 Institute of Psychiatry  
 King's College  
 London  
 UK

**George Patton M.D. FRANZCP**

Centre for Adolescent Health  
 Murdoch Children's Research Institute  
 2 Gatehouse Street  
 Parkville VIC 3052  
 Australia

**Edward B. Perry M.D.**

Department of Psychiatry  
 Yale University School of  
 Medicine  
 Psychiatry Service 116A  
 VA Connecticut Healthcare System  
 950 Campbell Avenue  
 West Haven CT 06516  
 USA



Cambridge University Press  
0521819407 - Marijuana and Madness: Psychiatry and Neurobiology - Edited by David  
Castle and Robin Murray  
Frontmatter  
[More information](#)

---

**xi****List of contributors****Bart Peters**

Academic Medical Center  
University of Amsterdam  
Amsterdam  
The Netherlands

**Harrison G. Pope, Jr M.D. M.P.H.**

Biological Psychiatry Laboratory  
McLean Hospital/Harvard Medical  
School  
115 Mill Street  
Belmont MA 02478  
USA

**Nadia Solowij B.Sc. M.A. Ph.D.**

Illawarra Institute for Mental Health  
Department of Psychology  
University of Wollongong  
Wollongong NSW 2522  
Australia

**Catherine Spencer B.Psych. M.Psych.**

c/o Mental Health Research Institute  
University of Melbourne  
155 Oak Street  
Parkville VIC 3052  
Australia

**Suresh Sundram**

Mental Health Research Institute  
University of Melbourne  
155 Oak Street  
Parkville VIC 3052  
Australia

**Hélène Verdoux M.D. Ph.D.**

University Department  
Hôpital Charles Perrens  
121 rue de la Béchade  
33076 Bordeaux Cedex  
France

**John Witton**

National Addiction Centre  
Institute of Psychiatry  
King's College  
London  
UK

**Deborah Yurgelun-Todd Ph.D.**

Cognitive Neuroimaging Laboratory  
McLean Hospital/Harvard Medical School  
115 Mill Street  
Belmont MA 02478  
USA

## Foreword

Research on the relationship between cannabis and mental health is a vivid illustration of the fact that the pace at which new scientific insights are embraced by the community is determined in an idiosyncratic, non-linear fashion. In 1987, a landmark study by Andreasson in the *Lancet* presented credible confirmation of the classic clinical observation that use of cannabis was associated with onset of psychosis. One would have expected that the link between one of the most widely used psychotropic drugs and one of the most devastating of mental illnesses would have resulted in an animated public health discussion. In actual fact, nothing happened very much. In the ensuing 15 years, however, the cumulative weight of a range of clinical, epidemiological and basic science investigations became such that by 2003 both the scientific and public health communities have gradually become aware of the potential significance of cannabis use.

Therefore, if ever a book was timely and topical, it is this one. The editors have done a remarkable job in bringing together the views of the principal experts in the field from around the world, providing a balanced summary of all the evidence that relates the use of cannabis to mental health outcomes. It includes a comprehensive overview of studies of the direct psychotropic effects of cannabis whilst in other chapters this evidence is elegantly linked to the possible neurobiological mechanisms underlying cannabis-induced mental states. The authors go on to address the question, at the population level, of whether widespread use of cannabis in many societies is associated with the onset of psychiatric disorders and, if so, whether this is because individuals with mental health problems use cannabis to help them feel better or whether use of cannabis increases the risk of onset of mental health problems. Furthermore, it addresses the question whether some individuals are more vulnerable than others to the effects of cannabis on mental health. The book includes an analysis of why some people with mental health problems would use cannabis, how it affects the course of their illness and how treatment should be tailored to take into account dysfunctional use of cannabis.

Cambridge University Press  
0521819407 - Marijuana and Madness: Psychiatry and Neurobiology - Edited by David  
Castle and Robin Murray  
Frontmatter  
[More information](#)

---

**xiv**      **Foreword**

The scientific information contained in this book not only serves clinicians, it will also help to inform public health discussions on if and how cannabis use should be regulated. Are the numerous coffee shops in the cities of the Netherlands where many young people gather on a daily basis a great good or should they be restricted? Is the rising proportion of people using cannabis a source of concern or does it show that we have learned to use the drug recreationally? In summary, does cannabis do more harm than good? Whatever the pre-existing opinion of the person when taking up this book, it is unlikely to be the same after.

**Jim van Os**

Professor of Psychiatric Epidemiology  
Maastricht University, the Netherlands

## Preface

*Cannabis sativa* (marijuana) has been used by humans for centuries, largely for its psychological effects. Currently, it is the most widely used illicit substance in the world, and there is heated public debate about whether it should be legalized, or at least decriminalized, in a number of countries. There is also considerable public and commercial interest in its medicinal properties, and in hemp as an environmentally friendly plant with numerous potential uses. This discussion needs to be informed by a consideration of the effects of cannabis on the human brain, notably its effects on cognition, and its potential to cause psychotic symptoms, particularly in vulnerable individuals. Recent advances in our understanding of the human cannabinoid system, and methodologically robust epidemiological, clinical and experimental studies of the effects of cannabis in humans, allow us to understand better how cannabis exerts both its beneficial and its adverse effects.

It has been known for many years that people who suffer psychotic illness are far more likely to consume cannabis than the general population, and there has been much dispute about the reasons for this. Unfortunately, until recently there were relatively few data available to inform this debate. The situation has changed greatly over the last decade with the publication of new basic and clinical studies. Therefore, this book provides a comprehensive and up-to-date overview of the psychiatry and neurobiology of cannabis, with particular emphasis on psychotic disorders. It outlines the very latest developments in our understanding of the human cannabinoid system, and links this knowledge to established and emerging clinical and epidemiological facts about the impact of cannabis on mental health. The clinically focused chapters review not only the direct psychomimetic properties of cannabis, but also the impact consumption has on the course of evolving and established mental illnesses such as schizophrenia.

The expert contributors explore a number of controversial issues, including whether a discrete ‘cannabis psychosis’ exists, and whether cannabis can actually *cause* schizophrenia. Effects of cannabis on mood, notably depression, are reviewed, with particular attention paid to recent prospective studies. The impact of cannabis

on cognition (both in the short- and long-term) is covered in some detail, with a careful weighing of the evidence for and against any long-term adverse effects. There are chapters on some of the ‘cutting-edge’ aspects of neurobiological cannabis research, including studies of the cannabinoid system in schizophrenia, the effect of cannabis CB<sub>1</sub>-receptor blockade on the psychomimetic effects of cannabis and cannabis–dopamine interactions.

We believe that this book provides a timely and comprehensive update on the psychiatry and neurobiology of *C. sativa*, by international experts in the field. We anticipate that the book will be of interest to those working in the mental health and drug and alcohol fields, as well as to psychopharmacologists and neuroscientists, and also to many consumers of cannabis.