Apomorphine as an alternative to sildenafil in Parkinson’s disease

I was interested in the recent paper by Hussain et al describing the efficacy of sildenafil citrate for erectile dysfunction in patients with Parkinson’s disease or multiple system atrophy (MSA). Their findings provide reassurance that this popular drug is both effective and safe in parkinsonian patients provided orthostatic hypotension is recognised as a potential side effect. Sildenafil inhibits cyclic GMP specific phosphodiesterase thereby enhancing nitric oxide mediated relaxation of the corpus cavernosum. The authors do not mention any effects of sildenafil on parkinsonian symptoms although its mechanism of action would make this unlikely.

In addition to erectile dysfunction, many factors including motor symptoms contribute to sexual dysfunction and dissatisfaction in this population. We have previously reported penile erections in a significant proportion of patients following subcutaneous injections of the dopamine agonist apomorphine to treat motor fluctuations in Parkinson’s disease. Some of these patients started using intermittent apomorphine injections specifically for erectile dysfunction. In contrast to sildenafil, dopamine agonists act centrally on dopamine receptors in the paraventricular nucleus of the hypothalamus to stimulate oxytocin release. The benefit to motor symptoms in Parkinson’s disease is mediated through dopamine receptors in the striatum. Apomorphine also benefits motor disabilities in some patients with MSA although orthostatic hypotension may be exacerbated by stimulation of peripheral dopamine receptors and its role in erectile dysfunction in this group has not been explored.

In view of the additional benefits to parkinsonian motor symptoms, subcutaneous apomorphine should be regarded as an alternative to sildenafil in treating patients with Parkinson’s disease and erectile dysfunction. Sublingual preparations of apomorphine have recently been developed for this indication. 

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References

Conflict of intentions or inner negativism?

In a recent, fascinating article, Nishikawa et al describe their encounter with “three patients with callosal lesions who sometimes could not perform whole body actions as they intended because another intention emerged in competition with the original one.” Believing “that no specific term has yet been coined for this symptom”, they “tentatively” named it “conflict of intentions.”

In fact, however, this symptom was described by Bleuler in his textbook of psychiatry, which first appeared in English translation in 1924. Bleuler termed it “inner negativism,” and noted that when “patients make an effort to start an action...a counter-impulse, or only a mere blocking appears and hinders them in its execution.” Such inner negativism could prevent “the simplest acts like eating. The spoon is arrested half way up to the mouth and must finally be put down again.” The great service of Nishikawa et al is to demonstrate the localising value of this symptom to the corpus callosum; it would be a disservice to medical history, however, to rename it.

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References

Author’s reply
We are very grateful for Dr Moore’s interest and comments on our article. We believe that the value of our study lies, firstly, in having rediscovered the significance of a symptom in some cases of partial callosal disconnection. The literature has been largely silent about this symptom manifesting itself without being noticed. Secondly, we link it to the so-called callosal disconnection syndromes by clarifying its clinical features and discussing possible pathogenic mechanisms. We gave the symptom a new label—“conflict of intentions”—because it differs from any other callosal symptom and cannot be explained by established disconnection theories, given that this symptom manifests itself without being confined to one half of the body.

Dr Moore comments that the symptom we reported has already been described in Eugen Bleuler’s classic textbook and termed “inner negativism” (“inner Negativismus” in the original). He asserts that assigning new terminology to an essentially identical symptom would be a disservice to medical history. We disagree.

We consider that the terminology used in descriptive symptomatological studies is conceptually different from that used in studies that take into account both phenomenology and pathogenesis. In Bleuler’s textbook, “inner negativism” appeared in the chapters about general descriptive symptomatology and schizophrenia. Our “conflict of intentions”, on the other hand, is a purely neuropsychological term meant to denote a particular type of callosal disconnection syndrome. We hypothesise links between psychopathological phenomena and underlying pathogenic neural mechanisms. In other words, we do not intend to equate the neuropsychological term “conflict of intentions” with the purely descriptive term “inner negativism.”

We agree that the symptom described by Bleuler has much in common with that seen in our patients. Indeed, we hope that our speculations about the conflict of intentions will help to elucidate the neural mechanisms of some well known psychiatric symptoms such as ego disturbances in schizophrenia, and ego dystonic experiences in obsessive compulsive disorders. In the future, these symptoms may be explained in terms of the dynamics among intentional, responsive, and automatic factors. It is interesting to note their respective main neural substrates—that is, the left and right cerebral hemispheres and lower neural systems—which we assume to be elements for explaining general human behaviour. Until such a unifying theory is established, we think it may not be such a disservice to medical history to preserve a distinction between the developmental processes of descriptive psychiatry and neuropsychology by retaining both terms, Bleuler’s “inner negativism” and our “conflict of intentions.”

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BOOK REVIEWS

Practical psychiatry of old age, 3rd edn


It is a curious thing that old age psychiatry is such a geographically weak discipline. There are many and excellent old age psychiatrists in Australia and Norway. The UK is arguably the home of old age psychiatry and the discipline is well established in the United States. However, in most European countries, let alone further afield, old age psychiatry as a discipline either doesn’t exist or is limited in scope.

This is a shame, as amply shown by this book. The argument in favour of old age psychiatry is well presented by Wattis and Curran. It is a discipline that is at home with physical disease as much as with that which is called functional disorders; a discipline that is perhaps the most comfortable with multidisciplinary working; a discipline that can move in the course of a day’s clinical work from molecular genetics to psychotherapy with...
demanded people. Practical psychiatry of old age, now in its 3rd edition, brings together many fields of our discipline. It is liberally scattered with useful and interesting case histories and the advice on management is sensible and up to date.

The book is clearly written for a trainee and non-specialist audience and deals with most subjects with a fairly light touch. The references at the end of the chapters serve as useful reading lists, including as they do both recent and historical papers. For students and for trainees this book will provide a useful revision and summary aid although trainees will need also to have to hand some of the works of reference whose names are scattered with useful and interesting case histories throughout this book. It is a sensible choice. To those who have yet to appreciate the joys of being an old age psychiatrist, dip into a colleague's copy—you may be pleasantly surprised.

Like the discipline itself, however, this book is very much a British affair. The sections on services have only limited international relevance and even the concept of a doctor who manages late onset psychosis, personality disorder and dementia is not so common elsewhere. The concentration on the international classification of diseases has limited application in the United States. So for those in the UK who need an introductory text to the discipline of old age psychiatry, this book is a sensible choice. To those who have yet to appreciate the joys of being an old age psychiatrist, dip into a colleague's copy—you may be pleasantly surprised.

Simon Lovestone

Brain Imaging in Schizophrenia, Insights and Applications


This is a succinct overview of brain imaging studies in schizophrenia and is well illustrated with scan photographs. The first two chapters cover the techniques of brain imaging and include several tables summarising information. The structural imaging chapter describes the techniques of computed tomography and MRI, and introduces the novel methods of diffusion weighted imaging and magnetisation transfer imaging. Complex topics such as the underlying principles of MRI are tackled in a fairly accessible manner. The functional brain imaging chapter covers PET, SPECT, fMRI, and MRS. The next two chapters cover the results of structural and functional imaging studies. These chapters are thoughtfully subdivided, and papers up to and including the year 2000 are cited. The brevity of the volume of course restricts the range of studies discussed, but generally the selection is good. Space also prevents areas of conflict from being fully resolved, for example into differing scan methodologies, data analysis protocols, and clinical populations. The penultimate chapter is titled “Other brain imaging” and describes imaging studies in twin pairs and members of multiply affected families. It includes discussion of the subtle abnormalities identified in presumed carriers. Finally there is a brief concluding chapter examining the current and future applications of the various imaging techniques in the study of schizophrenia. Overall, the results presented confirm that the complexity and heterogeneity of schizophrenia makes a single uniform underlying pathology seem unlikely. Imaging studies, with their unique ability to examine the brains of living patients, have an important role in developing our increasingly sophisticated understanding of the disorder. I would recommend this well written monograph both to academics and to clinicians keen to keep up with this fascinating and fast evolving area.

R Alexander Banitt

Parkinson's Disease in the Older Patient


This is a welcome addition to the literature. The book has been published with the help and support of the British Geriatrics Society special interest group on Parkinson's disease and the Parkinson's Disease Society of the United Kingdom. Both organisations have been at the forefront of increasing public and professional awareness of the need for a holistic approach to the care of older people with this condition. Understanding of the pathophysiology, therapeutics, and progression of the disease, as well as care, his paradigm for Parkinson's disease nurses and specialist clinics have all led to significant improvements in patients' quality of life. This well referenced publication will add to the knowledge of clinicians and geriatricians in practice as well as in training.

There are 21 chapters, in five parts, which address topics ranging from the background of Parkinson's disease, due to its diagnosis and assessment, written by Drs Macphee, Meara, and Forsyth. In the absence of a foolproof test for Parkinson's disease, these chapters go a long way to reminding readers of the importance of history, examination, assessment, and therapeutic challenge. The remaining parts include specific problems in Parkinson's disease, therapy and management, and research perspectives.

The chapter by Dr MacMahon on the organisation of services, concepts of management, and health economics builds on his theory of effective management of chronic disease, emphasising the importance of staging Parkinson's disease in terms of diagnosis, maintenance, and complex and palliative care. His paradigm for Parkinson's disease management is used by many geriatricians and is described it in greater detail for the benefit of a wider audience of clinicians.

There are also chapters on rehabilitation and the interdisciplinary team, the Parkinson's disease nurse specialist, complementary and alternative medicine, and of course drug therapy. The book is edited by Dr Playfair, one of the editors. The other editor, Dr Hindle, has written a beautifully argued chapter on the complexity of neuropharmacology in this syndrome, and automatic problems are eloquently described by Professor Kenny and Dr Allcock. Unfortunately it is impossible to acknowledge all the authors, but no aspect of Parkinson's disease is left unchallenged. The development of a properly managed, cost-effective, and evidence based service is the underlying theme throughout the book.

Without a holistic approach to the care of older people with Parkinson's disease, we will continue to offer inhumane, crisis driven care for these challenging patients and their carers. "Parkinson's Disease in the Older Patient" provides the knowledge base.

Jackie Morris

Brain's diseases of the nervous system, 11th edn


Lord Brain left us two neurological textbooks. The smaller, Brain's clinical neurology, subse-
form of bovine spongiform encephalopathy—
given under two names, “variant Creutzfeldt-
Jakob disease” in the section on dementia and
“new variant Creutzfeldt-Jakob disease” in that
on infection.

These are typographical errors, which are too many for comfort, especially in the tables, figures, and references, giving the impression that the book was rushed in its final production stages. Perhaps the most alarming was the discovery of a new cranial nerve, the 13th, in table 1.4. Figure 8.5 shows a retinal hamartoma, not haemartoma. Figure 8.4 shows the optic fundus at an unusual angle. Figure 11.3 is anatomically incorrect. Figures 3.7 to 3.9, and 29.11 are too small. The caption to figure 2.23 is incomprehensible. Many other examples could be given.

But these are mainly minor quibbles, easily rectified when the book is reprinted. Taken as a whole, Big Brain is alive and well, and safe in the hands of its new editor and his coauthors.

Lionel Ginsberg

Textbook of Clinical Neuropsychiatry


There is a certain logic to the system Moore uses in his textbook of clinical neuropsychiatry. The first half of the book essentially covers a list of causes, presenting symptoms, signs, and syndromes. For example lists are provided for causes of dementia lacking distinctive features, dementia associated with strokes, and dementia with Lewy bodies syndrome or with Parkinsonism. Confronted with a patient with dementia plus parkinsonism the reader has quick access to conditions that need to be considered. Or if the reader is looking for a list of causes of catatonia he need look no further than table 3.8. Having identified the potential causes of the patient’s symptoms the reader then goes to the second half of the book where he will find up to date descriptions of the relevant neuropsychiatric diagnoses.

The problem with such an approach is that it leads to duplication. In the first half any single diagnosis has to appear as many times as there are symptoms, signs, or syndromes that it can produce. The approach depends heavily on the validity of the classification of symptoms and syndromes; conditions with different names often seem to share more in common than they set them apart. For example it is asserted that stigmata can be distinguished from akinetic mutism partly on the basis of eye movements: in the former they are generated by the presence of comorbid conditions (the presence of comorbid conditions requiring hospital treatment), and concussion.

Multiple sclerosis: tissue destruction and repair


There can be few people still alive who came under the direct influence of Harold G Wolff before his death in 1962. (Donn Daleyess being one), but his influence on the whole of neurology has been immense and still continues. His book soon became a classic—the two editions he wrote were not long acquired only with difficulty from antiquarian booksellers. Over the years it has become slowly transformed, though perhaps some intermediate editions were a factory hybrid between the master and later developments. “Wolff’s Headache” has now emerged as a fully fledged multiauthor text in its own right, with less emphasis on the discovery of Wolff’s experimental work. We now have a 600 page authoritative book, written largely by American authors, all clearly experienced clinicians. It is comprehensively updated and more manageable than its main competitors.

In the first 100 pages the classification, anatomy, pathophysiology, genetics, and epidemiology of headache are described, with discussion of imaging techniques and comorbidity with other diseases. The core of the book covers migraine, cluster headaches, and tension headaches, including a very comprehensive review of every drug that has ever been used to treat headache, including the obscure, the ineffective, and the promising. This section on headache is also strong on the classification of chronic headache syndromes and in discussing analgesic abuse. The third section discusses every conceivable structural cause of headache, including low CSF pressure, metabolic disease, and disorders of the neck, eyes, teeth, nose, and blood vessels, including all the classic citations. The final three chapters discuss headache in children, behavioural management, and the consultation process itself.

This is an outstanding book; little of significance is omitted, and yet one is not overwhelmed with details. No doubt with the trainee entering the field in mind, it is particularly good when reviewing the literature, though some authors do occasionally lapse into the inconsistencies of older papers. It will prove to be a useful reference text for more senior neurologists confronted with a difficult patient, both for diagnostic and therapeutic options, though these are perhaps more from an American viewpoint.

Richard Peatfield

Multiple sclerosis: tissue destruction and repair


The Martin Dunitz imprint produces high quality books with catchy titles often built around European congresses of neurology. Brain disease: therapeutic strategies and repair emerged from the European Neurology Society meeting in Jerusalem (2000). Multiple sclerosis: tissue destruction and repair is the proceedings of the joint meeting of ACTRIMS (European and American Committees for Treatment and Research in Multiple Sclerosis) held in Basel in 1999. Looked at critically, neither book is much about repair. Here, the 116 contributors to three 3-motors edited by a team from Switzerland and Baltimore write on central nervous system tissue-immune interactions; in vivo assessment of tissue destruction and its consequences; multiple sclerosis fatigue; new immunological concepts and their therapeutic consequences; treatment of relapse; modern concepts of therapeutic immunomodulation; and an update of therapeutic trials. Many of the usual suspects are rounded up: magnetic resonance surrogates for various histological components of the disease process in multiple sclerosis; markers of demyelination in body fluids; treatment effects of interferon beta and its mechanisms of action; and strategies for transplantation in multiple sclerosis. Some authors take up old animal models: the use of steroids in acute episodes; and disease modifying effects of non-specific immunosuppressants. But there are also some new or emerging stories: inflammation and neuronal activity; interactions between immune mediators and growth promoting molecules; IMRI evidence for plasticity in multiple sclerosis; T helper and regulatory activity; bone marrow transplantation in multiple sclerosis; prophylactic treatment of puerperal disease activity with intravenous immunoglobulin; and a brace of preliminary clinical trials with hitherto unknown agents offering hope to watch. Multiple sclerosis: tissue destruction and repair succeeds as a statement from experts on where selected aspects of research stood in 1999 and as testimony to the deserved and sustained success of ECTRIMS (and ACTRIMS) but as a last statement on limiting and repairing the damage in multiple sclerosis, perhaps less so.

Katrina Dedman

Current management in child neurology, 2nd ed


Management includes assessment, diagnosis, and treatment. What emerges therefore is a book of clinical paediatric neurology—not a book on treatment in paediatric neurology. It is divided into outpatient and inpatient conditions and priority within these areas is apportioned by incidence. The top four outpatient neurological conditions presenting to paediatricians in Florida are attention deficit hyperactivity disorder (ADHD), seizures and epilepsy, developmental delay, and headache. The top four discharge diagnoses from hospital on the other hand are entero viral meningitis, tics, epilepsy, hyperkinetic syndrome (which the author explains by the presence of comorbid conditions requiring hospital treatment), and concussion.

The aim of this book is to provide “primary care physicians, neurologists and house staff with factual information on how to treat children with the most common disorders of the nervous system”.

There are some surprising omissions including spinal dysraphism. Movement disorders generally get short shrift. Of the 550
pages, cerebral palsy gets five (biomechanics gets five lines, prevention of secondary deformity is ignored), although there are a further eight on spasticity. There is nothing on chorea or dystonic syndromes—the latter omission is particularly surprising in view of the treatment implications.

In these days of economic scrutiny the evidence base for treatment recommendations should be referenced but is not for cerebral palsy; language disorders, or learning disability.

One hundred and nine authors contributed to this book. That so many have been induced to contribute may be because few provide more than seven pages. Thus, the most extensively treated topic is that of epilepsy with 86 pages from 13 separate authors. This leads to redundancy (treatment with antiepileptic drugs in most chapters but especially those on first choice antiepileptic drugs and recurrent seizures) and surprising omissions. A diagnostic approach to Lennox-Gastaut syndrome and progressive myoclonic epilepsies would have been useful. Nowhere are the implications of the genetics of familial epilepsies described. Genetic counselling generally is mentioned only in the chapters on neurofibromatosis and tuberous sclerosis. The concept of channelopathies is absent throughout. The target audience for this book see a lot of headaches; hence, 46 pages and seven authors. Again, redundancy and gaps. No one mentions taking the blood pressure of a child with headache. Neuroimaging is thought unnecessary unless there are abnormal neurological signs. A slightly more sensible discussion is found on page 491 in the inpatient chapter dealing with acute headache.

Prominent also is ADHD with 26 pages and five authors, reflecting the American referral patterns described above. Another curious (to the European paediatric neurologist) area of practice is outlined in the chapter “Is my child ready for school?” (by which is meant for normal school since all American children are entitled to education). At the end of four pages, which include a list 14 tests—seven of which require special training and at least five of which seem specifically designed to address the question—it is concluded that “the paediatrician or family physician can assess school readiness using a thorough, careful medical history and physical examination”.

In contrast there are five pages on inborn areas of metabolism and eight on neurodegenerative disorders. Both tend to give lists of conditions but not the screening tests including DNA analysis for those conditions. Statements such as the value of increased cerebrospinal fluid lactate are of limited value unless normal concentrations are given. Curiously phenylketonuria is not mentioned. Half a page is given to treatment of inborn errors. Enzyme replacement is not mentioned under the neurodegenerative conditions. While these conditions are individually rare, their collective burden is considerable. Many, particularly the inborn errors, are both treatable and susceptible to prenatal diagnosis. Similar comments may be made for the hereditary neuropathies (eight pages) and muscular dystrophies and myopathies (eight pages). Muscle histology gets five lines.

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DISCUSSION

A cursory look shows that the chapters on neurodegenerative diseases get far more attention than the metabolic diseases: eight pages on neurodegenerative diseases and only four pages on the metabolic disorders. But again, the reader will find useful—particularly, for example, the chapters on the economics of the health care system in the United States and advice on practice business management. Nevertheless, I think that this book sits uneasily between the needs of the general paediatrician and the needs of the neurologist. For the former there is more information—or not enough in a usable form—than is useful and for the latter the text is just not up to the standard already provided elsewhere. With the book is provided a CD-ROM, which has the text plus links to child neurology websites and the National Library of Medicine. Those who purchase this book are advised to avail themselves fully of these facilities.

Richard O Robinson

CORRECTIONS
