

PRINCIPLES OF CNS DRUG DEVELOPMENT: FROM TEST TUBE TO PATIENT. 2009. By John Kelly. Published by John Wiley & Sons Ltd. 304 pages. C\$180 approx.

Rated ☆☆☆

Neuroscience research, like most areas of biomedical research in the 21st Century, is under increasing pressure to become more “translational”. Arising from the relentless need to convert curiosity driven research into products, expressions such as “bench to bedside” or “principle to patient” are used frequently, but optimistically. Successful translational research is challenging for both basic and clinical scientists as they endeavour to take their fundamental insights and convert them into useful drug molecules or therapeutics. Accordingly, there is an important need for a brutally practical and pragmatic guidebook to take these researchers by the hand and drag them through (more hopefully over) the many potholes on the road from concept to marketable drug product. Although this book purports to be “from test tube to patient”, it is definitely not this much needed guidebook for neuroscientists – either basic or clinical. It is however a speciality textbook providing a generally excellent introductory overview (perhaps somewhat superficial in areas) for undergraduate students with little if any knowledge of neuroscience.

Over a surprisingly brief 286 pages of text, John Kelly from the Department of Pharmacology at the National University of Ireland (Galway) sets out to delineate the core processes in drug discovery and development for neurological disorders. The nine chapters of the book are divided into three principal sections. The first section (Chapters 1-4) provides an overview of major brain disorders (e.g. depression, Alzheimer’s disease, Parkinson’s disease, schizophrenia) with discussions of their global burden, neurobiological substrates and current pharmacological targets. The second section (Chapters 5-8) pertains to drug development with considerations of pharmacokinetics (i.e. absorption, distribution, metabolism, excretion; ADME), toxicology, efficacy and preclinical studies. The third and final section (Chapter 9) gives a perspective on the future of drug targets and development for neurological disorders. Finally, there is a five page collection of appendices that present a listing of drugs under development.

This is a very well written book. It is a clear and easy to follow introductory textbook. The material is straightforward and quite readable. The writing style is succinct and mercifully free of unnecessary verbal adornment. There are lots of facts presented in a logically sequential fashion. Each chapter ends with a solid collection of cited references, which reflect the literature in a comprehensive and up-to-date manner. Virtually every chapter is enhanced by the liberal use of tables. Although several of the tables present uniquely British data, in general the tables provide a wealth of useful additional data. However, unlike the tables, the figures are few in number and are of disappointing quality (below the standards of comparable books). Additional and better executed figures would have added significantly to the presentation.

The data that have been presented in this book are accurate and informative. However, the book needs to include more. For example, the test tube to patient presentation goes directly from identifying druggable targets to having drug molecules in hand for preclinical pharmacokinetics and toxicology testing. The entire area of drug design, synthesis and optimization has been completely omitted – and this certainly is a crucial component of the test tube to patient process. A chapter dedicated to the task of going from a druggable target to a drug molecule would be an absolutely essential addition to this textbook. Also, there is marked variability in the depth of presentation; for instance, the discussion of pharmacokinetics is rather sophisticated in places, whereas the discussion of neurotransmitters is very rudimentary, at a high school level at times. Moreover, for a practising neuroscientist, the descriptions of disorders such as Alzheimer’s disease or schizophrenia are annoyingly basic, lacking in both nuance and rigour.

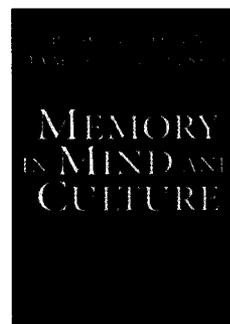
No matter how well written, no book can meet the needs of all potential readers. If I were teaching an undergraduate (or junior graduate) course on the pharmacology of neurological drug development and were looking for a reasonable introductory text, I would consider reaching for this book. If I were an at-the-bench neuroscientist looking for serious help to assist my translational research aspirations, I would probably leave this book on the shelf.

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MEMORY IN MIND AND CULTURE. 2009. Edited by Pascal Boyer, James V. Wertsch. Published by Cambridge University Press. 323 pages. C\$40 approx.

Rated ☆☆☆

There are many books on memory, most of them on the experimental and clinical aspects or episodic, instrumental and semantic memory, but this edited volume reflects the surge of interest in autobiographical memory (AM) and in the collective memories of cultures. This area of memory study seems to some the “soft underbelly” of memory research, with dubious methodology and more social, than hard core neuroscience. Autobiographical memory research began with Galton at the end of the 19th century, who used cue words to probe his own memory and found somewhat to his disappointment, that he always remembered the same things with each cue. He even concluded that his memory was impoverished. The cueing technique was resurrected by Crovitz and Schiffmann in the 70’s to elicit life stories. Initially AM had been marginalized and not considered clinically or scientifically as important as episodic or semantic memory. However AM became somewhat trendy lately as this book attests.



Pascal Boyer in his introduction, sets the stage for the importance of collective memories in the memories of the self. Williams and Conway deal with the role of memories in constructing the self and with the concept of AM networks. There is a vast depository of episodic and self related memories that are intertwined and trigger each other and play a role in developing our identity (as ancient Augustine, quoted later said). Flash-bulb memories such as the 9/11 WTC attacks, the death of Princess Diana or the assassination of JFK are culturally conditioned and are variable between countries. The age related peaks of personal reminiscences on the other hand are surprisingly similar in all cultures, where such studies are carried out. Bernstein and Bohn deals with life scripts, which are culturally shared expectations. In our society these are commonly experiences in school, with family members, marriage, children and jobs. Conflicts in this script also influence AM. This script of expectations unfolds in a stereotypic time sequence and deviations are notable. Happy and important memories have a peak of occurrence in the 15-30 life periods, while sad or anxious remembrances are more evenly distributed and increase with aging.

The specificity of memories, priming, and the role of emotions in the encoding process are the subject of Schacter at al's more traditional experimental approach, using neuroimaging to demonstrate the fine tuning of neuronal systems, when they respond to previously heard or familiar material. The memory of self has specific neural network activation in relation to structures, processing emotions. This is a stand-alone contribution.

Collective memories and the memory of history are essays comprising a major part of the book, led by Wertsch. Scholarly history has sufficient detachment and makes an effort to see the past from multiple perspectives. Collective remembering on the other hand simplifies and it is often based on myths and shaped by current political and societal considerations. History is far less static than it is conceived. Collective memories however often simplified for political reasons or through social pressures. Even official history is subject to the errors of collective remembering. Historical texts and our temples of history, the museums are repositories of interpreted memories. Many cultures enforce the traditional reiteration of past, biased as it may be, but there are revisionists and reinterpreters of the past in some other cultures such as our own, who are increasing in number and have become very fashionable. Several of the authors in this section are approaching these issues from the sociological and psychological perspective.

Repeated retrieval of collective memories becomes history. This occurs in the classrooms, in the media and in commemorations. Roediger et al review massive repetition vs. spaced retrieval, which may promote retention. Flashbulb memories are so intense and vivid that individuals remember the context for a long time. Collective flashbulb memories are not only important and shocking events, but are frequently reiterated. The subjective aspects, or context seems to be retained better than the core details of the event. Pennebaker and Gonzales also studied historical events that change the life of people and how they are shaped by various factors, such as age cohorts, culture and rehearsal. This group studied internet blogs and chatroom language after the 9/11 attacks. Another interesting study explored what various national student groups considered the ten most important events of the last 100 and 1000 years. The differences are interesting, but not surprisingly the French revolution did not make the American list.

As Ralph Waldo Emerson said : "Memory is the affection- we remember the things we love and the things we hate". The emotionality of events shape their memory and so does the time elapsed and their locale. It usually takes about 25-30 years to achieve a balance of the significance of events. Initially memorials, street names were created for JFK in Memphis, but not in Dallas and Dr. King was memorialised in Dallas before Memphis.

Historical revisionism works both ways and examples of these are studied in the last section of the book. One can learn for instance that the Canadian victory at Vimy Ridge to a large extent was attributable to "British and French artillery support and months of planning" and the quoted author felt Canadian heroism was overestimated and the battle was only part of a larger one. Early memory researchers such as Bartlett studied the "Chinese Whisper Game" effect of how stories get distorted as they are passed on. An interesting recent phenomena are the government apologies for previous injuries to other communities. It is another "reverse", politically correct, manifestation perhaps of the negative "presentism" or exegesis of history from our current perspective. It seems that historical revisionism has no end. Columbus was appreciated little at the beginning, rewarded handsomely for his discovery, than forgotten and later discovered again to become a historical giant, to be re-evaluated recently as an imperialist and the cause of ruin of native peoples.

This book is more about how history is constructed than about memory as a neurological phenomenon. It does not update or contribute to the clinical and scientific understanding of the neuropsychological aspects of memory. There are no clinical contributions, although AM has appeared in the clinical literature occasionally. Nevertheless it makes somewhat interesting general reading, while leaving the reader shaken about trusting history, historians or any recollection as a matter of fact. It will be enjoyed by sceptics and anti-establishment activists.

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NEW STRATEGIES IN STROKE INTERVENTION. IONIC TRANSPORTERS, PUMPS, AND NEW CHANNELS. 2009. Edited by Lucio Annunziato. Published by Springer. 254 pages. C\$195 approx.

Rated ★★★★★

There are currently no clinical or experimental interventions, other than thrombolysis, which improve stroke outcome, this despite great advances in an understanding of the mechanisms by which ischemia induces cell damage. Thrombolysis has major limitations including amongst others, its limited therapeutic time-window, the requirement for neuroimaging prior to initiation of treatment thereby precluding

