
BOOK REVIEWS

Functional MRI: Finally, a Textbook for All of Us

DOI: 10.1017/S1355617705220490

Functional Magnetic Resonance Imaging, by Scott A. Huettel, Allen W. Song and Gregory McCarthy. 2004. Sunderland, MA: Sinauer Associates, Inc. 492 pp., \$79.95.

Reviewed by STEPHEN M. RAO, Ph.D., ABPP-CN, *Director, Functional Imaging Research Center and Professor of Neurology (Neuropsychology), Medical College of Wisconsin, Milwaukee, WI, USA.*

Imaging the human brain at work was revolutionized by the discovery of functional magnetic resonance imaging (fMRI) in the early 1990s. Prior to this, functional brain mapping was limited to a handful of medical centers capable of conducting positron emission tomography (PET) scans of regional cerebral blood flow. With the discovery of the endogenous blood oxygen level dependent (BOLD) contrast method in 1992, fMRI “democratized” the field by expanding the number of medical centers capable of functional brain imaging. Today, over a thousand peer-reviewed fMRI articles are published each year, many in high profile scientific journals that receive additional attention by the popular press. This explosion of scientific research is relatively easy to understand: fMRI can be conducted on the majority of the 6,600 MRI scanners installed in the US alone, the technique is completely noninvasive since it does not require injection of MRI contrast agents or radiopharmaceuticals, and, as an added benefit, fMRI provides a unique combination of high spatial and temporal resolution. Not surprisingly, fMRI is the imaging technique of choice for mapping cognitive and emotional systems in the healthy brain. More recently, fMRI has been applied to clinical populations to identify the brain mechanisms governing recovery of function from stroke and head trauma, detect early brain changes in neurodegenerative conditions, and measure the effects of psychoactive medications on neurodevelopmental disorders, as examples. fMRI provides a complementary method for testing neuropsychological models of brain function derived from other methods (lesion, electrophysiology).

One should not conclude from the above discussion, however, that fMRI is “easy.” For a neuropsychologist to conduct a methodologically sound fMRI experiment, it is critical to have a fundamental understanding of the physics and physiology that underlie the functional MR signal, as well as training in image processing, experimental design, and

statistic analyses that are specifically tailored to fMRI experimentation. A variety of introductory courses offered by leading fMRI research centers have been available to neuropsychologists since the mid-1990s. Up until now, what has been lacking is an integrated textbook on fMRI that is geared to the needs of the non-physicist. With the publication of Huettel, Song and McCarthy’s textbook last year, this void has been filled.

Functional Magnetic Resonance Imaging is written in the form of an undergraduate textbook. Clearly written and entertaining in its presentation, there are abundant and well-designed color illustrations, boxes that expand in greater detail issues introduced in the text, “thought questions” designed to test the student’s understanding, and a highly detailed glossary of terms presented as a side bar in the text as well as in the appendix. Each chapter is followed by suggested readings and a bibliography of primary source references. An attached CD suggests various lab exercises and provides imaging data sets from an fMRI experiment. The authors have designed the textbook for individuals with little or no prior experience in functional imaging. As a result, the textbook is appropriate for advanced undergraduates and graduate students. The book is also valuable to faculty members who are interested in expanding their investigative methods to include fMRI. The authors have gone to great strides to clarify difficult concepts without sacrificing content. As an example, the introduction to MR physics includes equations but with sufficient verbal explanations that even the most mathematically challenged would not complain.

The 15 chapters follow a logical progression across topic areas. The first chapter provides a useful history and overview of fMRI. This is followed by a thorough and lucid presentation on MR scanner hardware and MR physics (chapters 2–5). Most importantly, the reader is introduced to the sources of potential artifacts associated with fMRI (e.g.,

geometric distortions and signal losses due to magnetic field inhomogeneities) that can influence interpretations of the data. Chapters 6 and 7 are devoted to the hemodynamic basis for the BOLD signal. Chapters 8 and 9 examine the spatial/temporal resolution and signal to noise (SNR) issues in fMRI, respectively. Chapter 10 is devoted to preprocessing issues, with comprehensive discussions of how to judge the quality of the collected imaging data, including discussions of head motion, system noise, physiological noise, and scanner drift.

Experimental design and statistical analysis issues are covered in considerable detail in chapters 11 and 12. In addition to describing the differences between block and event-related designs, there are nice discussions of the relationship between behavioral variability and the fMRI response, the use of reaction time as a covariate in image analysis procedures, and a comparison of the relative strengths of voxel wise analyses *versus* region of interest approaches. The discussion of spatial normalization is pretty much limited to the Talairach method, but alternative techniques (flat mapping) are also presented. Chapter 13 addresses various applications of fMRI, including a brief discussion of fMRI in the study of patient populations. Most of this chapter, however, provides summaries of basic cognitive neuroscience fMRI studies conducted in healthy individuals in the areas of attention, memory, and executive function. Chapter 14 discusses advanced fMRI procedures for improving spatial and temporal resolution. The final

chapter (15) integrates fMRI with other brain mapping tools, including transcranial magnetic stimulation, direct cortical stimulation, brain lesions, electroencephalography, and magnetoencephalography. The authors make a convincing case that our knowledge of the human brain function must come from a convergence of methods, since all techniques have their relative strengths and weaknesses.

Of course no textbook is without some limitations. Some chapters introduce concepts and define terms more than once. While it is conceivable that this redundancy may have been intentional, I suspect that this may have been the result of one author not being familiar with the text written by another. A discussion of the pharmacological effects on the BOLD signal transduction is not included nor is the use of fMRI to identify the localization of sites of action of short half-life CNS drugs. The discussion on experimental designs does not consider the use of free-form designs in which a continuous behavioral or physiological measure (e.g., galvanic skin response) is correlated in real-time with the fMRI signal. The book could also benefit from expanded coverage of the applications of fMRI to clinical populations. I suspect that many of these relatively minor problems will be addressed in the next edition.

In short, this book represents an essential read for any neuropsychologist considering the use of fMRI as a tool for measuring brain function. My congratulations go out to the authors for providing the field with such an outstanding contribution.

In the Spotlight or the Shadow of Alzheimer? The Role of Cerebrovascular Disease in Dementia

DOI: 10.1017/S1355617705230497

Vascular Dementia: Cerebrovascular Mechanisms and Clinical Management. Robert H. Paul, Ronald Cohen, Brian R. Ott, and Stephen Salloway (Eds.). 2004. Totowa, NJ: Humana Press, 356 pp., \$145.00, £91.00 (HB).

Reviewed by BRUCE REED, Ph.D., *Department of Neurology, University of California, Davis, CA, USA.*

Interest in how vascular factors contribute to dementia is ascendant, propelled by a number of factors. One is the widespread use of MRI, which is a highly sensitive (if not always specific) test for cerebrovascular lesions. A second is a string of epidemiological reports revealing that Alzheimer's disease shares many of the well established risk factors for cardiovascular and cerebrovascular disease (Skoog & Gustafson, 2003). Recent autopsy studies using cohorts obtained outside of the potentially winnowing influence of the Alzheimer's disease centers have reminded us that vascular lesions are common in patients with dementia (Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study, 2001). The Nun study report suggesting that infarcts create an additive or greater effect on mental function in concert with AD pathology (Snow-

don et al., 1997) received particularly wide exposure and helped revive interest in combined effects of AD and ischemic lesions. Finally, the discovery that polymorphisms of the apoE gene, long of interest in cardiovascular disease, strongly modify the risk of AD suggested the possibility of shared pathophysiological mechanisms between AD and vascular dementia (Panza et al., 2004; Strittmatter & Roses, 1995). The volume *Vascular Dementia*, edited by Paul, Cohen, Ott and Salloway, is thus a timely resource for those interested in the numerous issues surrounding the role of vascular factors in dementia.

This volume is intended as a summary of the current state of the field and as a tool for those seeking to advance it. It is not particularly oriented to the practicing clinician, and with good reason; clinical guidelines are hard to justify

when basic underlying concepts and definitions are controversial, conflicting, and inadequately validated. The depth of the controversy around vascular dementia is on striking display in the first section of the book, which contains chapters by three major figures in the field, namely Gustavo Roman, Vladimir Hachinski, and Kurt Jellinger. Roman opens with a spirited argument for his view that “cerebrovascular disease is the most important cause of dementia in the elderly.” In sharp contrast, Hachinski, with co-author Merino, presents a thorough critique of current diagnostic criteria for VasD (which, of course, underpin any prevalence data), concluding that “current [diagnostic] criteria [for VasD] are not interchangeable and are neither sensitive nor specific . . . therefore, they must be invalid.” Hopes of validating any of the clinical criteria in the near term are dealt a further blow by Jellinger. His chapter, a fine, encyclopedic review of cerebrovascular neuropathology, concedes at the outset that “one of the most controversial and incompletely understood issues is the extent to which vascular pathology contributes to dementia.” The absence of any anchoring pathological “gold standard” considerably complicates life for vascular dementia researchers.

The fundamental problems revealed in these opening chapters are relevant to nearly all chapters that follow. Any compilation of clinical findings, any attempt at diagnostic markers, any mechanistic work done on clinically defined groups must grapple with the certainty of diagnostic errors (the extent of which are unquantifiable), and the near certainty that Alzheimer’s disease is present to a variable (again, unquantifiable) degree in the living subjects under study. Further complicating the issue is the widely acknowledged heterogeneity of lesions and mechanisms associated with cerebrovascular disease. The extent to which these issues are recognized varies considerably from chapter to chapter, but having them cast so starkly at the outset helps the critical reader approach the remainder of the book.

A distinct strength of this book is the breadth of topics it covers. *Vascular Dementia* is organized into six sections: an introduction; basic mechanisms; cognitive, psychiatric and functional impacts; neuroimaging; interactions with Alzheimer’s disease; and management. Within are chapters covering topics ranging from epidemiology to pathology, from clinical features to molecular biological mechanisms, from diagnosis to the future of pharmacological intervention. The volume is thus of value to a wide range of investigators, and encourages a broad and multi-disciplinary approach to thinking about the topic.

Several chapters are particularly valuable. In addition to Jellinger’s neuropathology review there are two reviews of clinical neuropsychological findings (by Jefferson et al. and also Libon et al.), which together cover the relevant literature well. Moser et al.’s review of white matter effects on cognitive function will be a very useful starting point for anyone interested in that topic. In addition, Kumar et al. do a nice job of trying to sort out the psychiatric/behavior disturbance literature while recognizing the limitations of this literature. Salloway and Desbrien’s chapter

includes a very helpful overview of cerebral autosomal dominant arteriopathy with subcortical infarcts and lacunes (CADASIL), a relatively uncommon but potentially scientifically informative form of genetically determined vascular dementia. Gunstead and Browndyke’s compilation of the epidemiological data on mixed (vascular and Alzheimer’s) dementia, which includes much data on vascular dementia as well and which should prove a useful resource for those who want to tackle the tricky issue of prevalence (as the data there show, the oft repeated claim that vascular dementia is the second leading cause of dementia stands on shaky ground).

Other chapters present either intriguing preliminary data or discussions of potentially promising approaches to unraveling this complex knot. Moss and Jonak present a primate model for studying hypertensive effects on cognition. Mungas gives an illustration of the power of sophisticated statistical modeling to help determine the independent and combined effects of multiple pathological markers simultaneously. And, on the whole, the section reviewing possible biological mechanisms through which vascular factors may promote the pathologic changes of AD presents a wide range of stimulating ideas.

Finally, the topic of treatment is not neglected. Unfortunately, as the review by Erkinjuntti et al. makes clear, there is no well supported pharmacological approach to treating either the symptoms or underlying pathophysiology of this disease (other than, of course, the modification of vascular risk factors). However, the closing chapter by Fisher and Selim does a very nice job of cataloging the numerous promising targets that ischemia presents for intervention, leaving good reason to hope for real progress.

It has become abundantly clear that the aging brain is, more often than not, affected by multiple pathological changes simultaneously. Nothing in this volume seriously challenges the idea that Alzheimer’s disease is the major cause of dementia in old age. However, it provides ample data and discussion to stir the thinking of the Alzheimer-centric skeptic as well as that of the committed investigator of vascular dementia. There is much here to suggest that the middle ground that explores the relative contributions and interactions of these two common disease processes may turn out to be most productive.

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Expanding the Paradigm of Rehabilitation Sciences

DOI: 10.1017/S1355617705210494

Cognitive and Behavioral Rehabilitation: From Neurobiology to Clinical Practice. Jennie Ponsford (Ed.). 2004. New York: Guilford Press. 366 pp., \$50.00 (HB).

Reviewed by JANET E. FARMER, Ph.D., ABPP-RP, *Department of Health Psychology, University of Missouri, Columbia, MO, USA*.

The World Health Organization estimates that approximately 90 million people, or 1.5% of the world population, are in need of rehabilitation services at any given point in time (WHO, 2003). Many of these individuals are at risk for long-term disability due to brain injury and disease. They range from the young, who increasingly survive early brain insults, to older adults, whose independence and every day functioning may be threatened by the onset of neurologic impairments. As medical advances improve survival rates and longevity, the number of those in need of cognitive and behavioral rehabilitation services to enhance functioning is likely to grow. This situation raises pressing questions, such as, who will get better with what rehabilitation treatment, and why?

Dr. Ponsford's edited book is a scholarly effort to lay the groundwork for neuropsychologists, rehabilitation psychologists, and other health professionals to answer such questions. The book aims to integrate advances in the neurosciences with research on the clinical care of people with brain dysfunction. It is built on the premise that rehabilitation interventions may improve if they are more closely linked to emerging principles of neuronal organization and recovery processes and to theoretical models from neuropsychology and cognitive neuroscience. The contributors posit that research based on this expanded paradigm may lead to important discoveries about how to enhance human functioning following brain insult. This approach has been spurred forward by the development of interventions such as constraint-induced movement therapy (Taub & Uswatte, 2000).

The book is well organized, beginning with two chapters on brain functioning that provide a strong foundation for the remainder of the book. Kolb and Coie present an engaging overview of basic concepts underlying brain-behavior relationships, physiological events associated with brain injury, reparative processes, and variables that moderate recovery (e.g., age, type of injury). In chapter 2, Kolb adds a clear discussion of recent findings about plasticity in both the intact and injured brain. This chapter concludes with a brief review of implications for rehabilitation, such as the

idea that early intervention may be needed to promote beneficial reorganization of plastic morphological structures and to achieve adaptive rather than maladaptive functioning.

The next six chapters take the reader into the heart of what is unique about this book, an in-depth exploration of the relationship between basic research/theory and treatments for specific cognitive and behavioral domains that are affected by brain injury and disease in adults. The cognitive domains include nonspatial attention, memory, language, spatial orientation/unilateral neglect, and executive functioning and self-awareness. The authors of these chapters are experts who demonstrate breadth and depth of knowledge across diverse literatures. For example, in the chapter on memory disorders, Glisky reviews recent conceptualizations of memory as a set of overlapping systems, describes what is known about the underlying neuroanatomical substrates of these systems, presents a short discussion of the neurophysiology and neurochemistry of normal memory functions, discusses findings from studies on the treatment of memory dysfunction, and notes ways that basic research may help to refine future treatment strategies. The book illustrates findings with examples from common brain disorders such as traumatic brain injury and stroke.

In all of the chapters there is a valiant effort to integrate cross-discipline theory and research and to note where basic science informs practice. Sometimes, this reveals explanatory mechanisms for what is generally observed in rehabilitation settings (e.g., recovery is worse with more severe injury due to specific limits in reparative processes following extensive brain damage). In other cases, promising treatment approaches are identified, such as selecting the type of memory intervention strategy based on brain lesion location and the memory systems affected. The book falls somewhat short of its goal to bridge the gap between the neurosciences and clinical practice, but this is due to the size of the chasm between these fields and the immature state of these brain-related scientific disciplines.

Without a doubt, the book is thought provoking and raises key questions that must be answered to advance cognitive and behavioral rehabilitation in persons with brain insults.

It is likely to spark lively debate about the degree to which underlying neurobiology is relevant to any specific individual's recovery process, given the complexities involved in real world intervention and the number of variables that contribute to personal outcomes. Although there are other books available on current rehabilitation practices and on basic brain and cognitive research, this is the one to read to gain a glimpse of how these fields may merge and grow to benefit persons with brain dysfunction.

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