Normal-appearing White and Grey Matter Damage in Multiple Sclerosis

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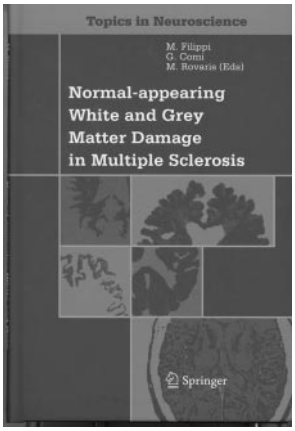
BOOK REVIEW

Normal-appearing White and Grey Matter Damage in Multiple Sclerosis

M. Filippi, G. Comi, and M. Rovaris, eds. New York: Springer; 2004, 160 pages, $109.

Multiple sclerosis (MS) has been investigated extensively by numerous researchers over the years. The curiosity for those studying MS is that so little is known of the etiology and pathophysiology of this disease. As a result, many pathologic and radiologic techniques can be and have been used in the study of MS. In essence, because of the lack of a true understanding of the disease process and the difficulty in providing biopsy or postmortem brain specimens, many new imaging techniques and hypotheses can be generated and tested without any real pathologic validation. The editors of *Normal-appearing White and Grey Matter Damage in Multiple Sclerosis* state that new imaging modalities are needed to provide more specific in vivo measures of various components of normal-appearing white matter (NAWM) and normal-appearing gray matter (NAGM) pathology in MS, and that these techniques are likely to be valuable for monitoring the natural history of MS and its modification by treatment. In general, that is the primary goal in MS research. Just as importantly, the key for the diagnostician and sufferers of this disease is finding a technique that will confirm the early diagnosis of MS from the clinically isolated syndrome (CIS) so that patient outcome can be altered by whatever therapies are available. This book provides an update of the techniques being used to make an early diagnosis and, importantly, to predict the progression of MS.

This text comprises an introduction by the editors and 13 chapters, 8 devoted to NAWM and 5 to NAGM. For a neuroradiologist with prior experience in pathology, I have been trained to always correlate imaging findings with pathology. As a result, the most intriguing and enlightening chapters for me were chapters 1, 8, and 9, which deal with the pathology of NAWM and NAGM. After all, as neuroradiologists (or neurologists), our primary focus is to image and determine issues of neuropathology, physiology, and biochemistry. In that sense, these chapters are excellent, and I would have certainly enjoyed reading more about the pathology. The photomicrographs in chapter 9 speak for themselves, and more pathologic figures would have been welcome. The ability to perform direct ultrahigh-field MR microscopy in vivo is already being realized with a number of 7T and 8T MR imagers being installed worldwide. At such high field strengths, small white matter and cortical lesions are being demonstrated in vivo. Visualization of more lesions will eventually modify our current clinical and imaging criteria (which are based on MR imaging at 1.5T) for making a diagnosis of primary demyelination, as well as probably converting the clinically isolated syndrome into clinically definite MS in the appropriate setting.



Chapters 2 through 7 cover a range of imaging techniques investigating the NAWM, including imaging blood–brain barrier (BBB) permeability, white matter volumes changes, magnetization transfer, measurements of T2 and T1 relaxation, and diffusion-weighted imaging. Chapters 10 through 13 describe imaging the NAGM, including measuring the gray matter volume, magnetization transfer effects, diffusion-weighted imaging, MR spectroscopy, and functional MRI. The references are comprehensive and current, providing a good summary of the work up to 2004. Limitations of almost every review text include the usual redundancy found in a multiauthored book, as well as the occasional unavoidable exclusions. Chapter 2 nicely describes the state of the art in terms of the pathology and technique for the measurement of BBB permeability in MS. In this and a number of other chapters, an attempt is made to correlate the perivascular lymphocytic infiltrate in the inflammatory process with BBB leakage (and other imaging techniques). There is an increasing body of work relating perfusion and blood volume measurements in the NAWM and NAGM to an underlying vasculitic/hypoxic pathogenesis to MS. This ischemic basis, in contrast to classic inflammatory pattern due to T-cell-mediated autoimmune reaction against compact myelin sheath (eg, myelin basic protein), is characterized by early loss of myelin-associated glycoprotein in the distal process of oligodendrocytes within active lesions. A number of histopathologic studies have provided evidence of vascular occlusion in MS, suggesting that there is possible primary vascular injury in MS lesions as well as the NAWM and NAGM. This has been further confirmed by advanced immunohistochemical studies demonstrating that vascular occlusion, including fibrin deposition, can occur early and perhaps prior to cerebral parenchymal reaction and demyelination. These studies indicate that an ischemic/hypoxic injury can contribute to lesion formation, disease activity, and consideration of alternative treatment strategies. Besides measuring permeability, a separate chapter describing the perfusion (blood volume and blood flow) changes in MS could have been included.

The normal-appearing human spinal cord in MS has also been imaged and studied pathologically, probably sufficiently to include a chapter describing the pathology and advanced imaging techniques used to characterize the spinal cord. There are certainly numerous references to the spinal cord in the subject index; however, it was somewhat tedious for a researcher or clinician interested in the spinal cord to search through each of the referenced pages for the appropriate text. For an imaging text, there are surprisingly few figures. For example, chapters 1, 7, 10, 11, and 13 have no figures. This seems a little odd, as there are numerous publications with exquisite figures demonstrating the imaging and pathologic correlates described in each of these chapters. On the whole, where presented, images are clearly labeled and the legends suitably descriptive.

The audience that would benefit most from this book is the clinical researcher or scientist with an interest in investigating the NAWM and NAGM. It may also have some use for the academic neurologist and neuroradiologist with access to these state-of-the-art imaging techniques. However, for most

clinical neurologists and neuroradiologists, for whom the major concern is making a definitive diagnosis of MS and accurately monitoring progression and therapy, there is limited value. As the authors state in the introduction, this text will no doubt serve to stimulate new ideas and further investigations; still, it seems that in MS, it is not so much the lack of new ideas but the lack of focus of current ideas into tools that are clinically useful. For this reason, the relevance of this book to the general neurology and neuroradiology audience is somewhat limited. Few neuroradiologists have access to the advanced imaging techniques presented. Most neuroradiologists are likely to have access only to conventional MRI, but the appeal of this book may extend to the practicing neuroradiologist who would like to read more about newer techniques and how they have been applied to MS.

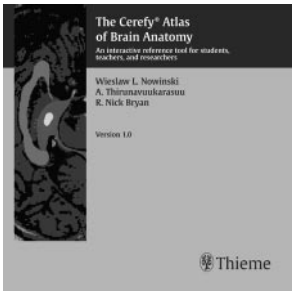
As this is a very specialized collection of chapters, there are few other texts for comparison. However, in comparison with other focused reviews, it is certainly a reasonable text with a veritable "Who's who in MS imaging research?" in the list of contributors. The audience for whom I would recommend this text and who would find it the most valuable is the neurologist and neuroradiologist with a research interest in imaging and investigating MS. For this audience, the book certainly provides a nice summary of the current work in MS.

BOOK REVIEW

Cerefy Atlas of Brain Anatomy

Wieslaw L. Nowinski, A. Thirunavuukarasuu, and R. Nick Bryan, eds. New York: Thieme Medical Publishers; 2006, Interactive CD-ROM, $69.95.

The rapid expansion of advanced functional and physiologic neuroimaging techniques is generating significant impact on the clinical neurosciences. For this development to continue, however, neuroradiologists must become facile in functional brain neuroanatomy. Techniques such as functional MRI and diffusion tensor imaging have already begun to have a significant effect on the presurgical risk assessments in patients with brain tumors and other resectable lesions. Evolving applications of brain mapping for the cognitive and neurodegenerative disorders sit close by on the horizon. Selecting appropriate treatment algorithms for stroke patients is influenced by clinical and image-based assessments of underperfused functional brain areas at risk. The integration of molecular imaging developments with other image-based functional and physiologic techniques holds great promise for the future of our field. The ability for neuroradiology to capitalize on these exciting advancements depends on our comprehension of the 3D organization of functional networks and on our capabilities of extracting information about brain pathology provided by 2D image data. This is based primarily on a thorough understanding of functional brain anatomy.



The *Cerefy Atlas of Brain Anatomy* is an electronic atlas that answers the call of functional neuroradiology training. The atlas is a CD-ROM-based interactive interface for use in neuroeducation, intended for students and residents, as well as for teachers and researchers. The atlas provides navigational capabilities in an interface of gross neuroanatomy with more than 1500 subcortical and cortical areas designated on 100 MRI images. Brain areas that are identifiable by gyral names or Brodmann's areas have been derived from the well-known brain atlas of Talairach and Toumoux and warped against MRI data using 3D Talairach transformations. Each overlaid axial, coronal, or sagittal atlas image has been warped nonlinearly against corresponding MRI sections by applying local interactive warping software. The warped atlas images have been superimposed onto MRI sections with variable blending, reshaping, and smoothing to correspond to the image data as closely as possible.

The interface is extremely user-friendly and efficient in exploring brain anatomy, including convenient features such as swapping views between axial, coronal, and sagittal planes; backward and forward operations to select the image location of interest; and a fade function that can alter the transparency of the overlaid anatomic or Brodmann's area atlas. An anatomic index uses nomenclature from the Talairach and Toumoux brain atlas and is synchronized with the main view such that pointing to or clicking on an image structure highlights the name of that structure or Brodmann's area in the index. Similarly, any structure or area clicked on in the anatomic index is highlighted in the image by blinking and changing color. In total, there are 62 subcortical structures, 31 cortical structures, and 42 Brodmann's areas identifiable in the electronic atlas. Also, a search list operation permits the user to easily find and highlight, by blinking and changing color, structures within a selected image of the main view.

The atlas application works in 2 distinct modes. First, the "Explore" mode allows the user to navigate surface or deep brain structures identified by anatomic name within the left hemisphere or corresponding Brodmann's areas within the right hemisphere on MR images. A simple right click brings forward a description of corresponding functional areas and networks. This combination of functionality is one of the best features of the electronic atlas, rapidly reinforcing the relationship between anatomy and function. Second, the "Test" mode allows the user to be tested against either the location identified on the image or by the name of an atlas structure within a compiled list. A user can be tested against the location of an atlas structure by selecting the appropriate label within the anatomic index corresponding to a highlighted structure on a given MRI section. This is extremely effective in facilitating the rapid mastery of anatomic and functional brain areas. Alternatively, users can be tested against the name of the atlas structure by clicking on the cortical or subcortical region, which corresponds to a highlighted name in the anatomic index. This latter method of testing is difficult and best suited for the more experienced individual. A score is given to each test item depending on how many attempts are required, resulting in a performance assessment.