



## Insights on Neuroimaging: Past, Present, and Future

A Review of

*Windows to the Brain: Insights From Neuroimaging*

by Robin A. Hurley and Katherine H. Taber (Eds.)

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It is not generally known that functionally induced changes in the regional metabolic rate in the human brain were first demonstrated beginning as early as the 1960s. As Raichle (2006, p. 6) noted, the introduction of X-ray-computed tomography (CT) by Hounsfield a decade later signaled the onset of high-resolution structural maps of the brain being widely available to clinicians. However, a 20-year lull between the widespread dissemination of functional methods and the first cognitive neuroscience publications in the late 1980s was due to the complexity of the development of needed quantitative methods. Interactive data languages were developed only in the mid-1970s and are binary-coded, vectorized, numerical, and interactive syntaxes that were essential to the analysis of large data sets operating on mainframe computers used in image processing.

Hurley and Taber's compilation spanning 1996 to 2006 offers a veritable plethora of concise chapters on the full gamut of neuropsychiatric disorders—a textbook that covers the majority of disorders the neuropsychiatrist is likely to see in actual practice. The chapters are geared toward differential diagnosis and sometimes get bogged down in analytical minutiae; however, on the whole *Windows to the Brain: Insights From Neuroimaging* loudly signals that image processing and interpretation are here to stay in both neuropsychiatry and neuropsychology. Skilled and knowledgeable interpretation of structural and functional neuroimaging bodes well for the future employability of neuropsychologists with their specialized knowledge of cognitive and behavioral analysis of neurological syndromes.

### The Current State of the Art

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A cursory examination of the contributing authors reveals a large contingent of experimental neuropsychologists with expertise in functional neuroimaging methods and cognitive neuropsychological task design and analysis. Currently most functional neuroimaging data analysis software packages are stripped-down versions of their former first-edition (circa 1995) matrix laboratory (MATLAB) selves, and many are now mere “black box”

instantiations run on conventional image acquisition hardware. However, this does not obviate the need for qualified postdoctoral trained experimental neuropsychologists. Neuropsychiatrists may get some training in data analysis using functional software analysis during a two-year postdoctoral fellowship; however, as a general rule psychiatrists are not as highly trained in statistical methods and experimental design compared with experimental neuropsychologists. Therefore currently many functional neuroimaging departments are overseen by neuropsychologists in senior roles, and the demands for requirements for specialized knowledge associated with the intelligent operation of such equipment is likely to increase, if anything, in the near future.

In general, these chapters, although very brief, provide enough information to convey diagnostic symptom checklists for differentials as well as adequately convey typical structural or functional findings. A strength of this text is Part 3's description of anatomy and circuits that greatly summarizes information from many different neuropsychiatric diseases and imparts the findings in terms of generalized neurological and neurophysiological systems. Major systems for sleep, fear and anxiety, long-range multisynaptic connectivity, functional disorders, corticothalamic systems, emotion regulation, pain, and hormones are applied across a range of neuropsychiatric illnesses.

Moreover, these systems are discussed in enough detail to provide a view of the functional architecture, neurophysiology, and basic neuropharmacology. Finally a glimpse of today's pinpoint-accurate psychosurgical techniques using stereotactic magnetic-resonance-imaging (MRI)-guided probes is contrasted with early biological psychiatry's medical "slasher horror shows" of the 1930s and 1940s, perhaps in the discipline's push for credible empiricism.

The first chapter on posttraumatic stress disorder (PTSD) is timely, given the inordinate numbers of U.S. and Canadian military recruits returning from combat in Iraq and Afghanistan with seriously debilitating, costly, and chronic disorders. Both PET-neuroendocrine-radioactive-labeling studies concerning the hypothalamic-pituitary-adrenal axis and the full gamut of functional neuroimaging techniques have been applied, especially within the last few years. However, limitations of this chapter are that extant studies have examined only small, isolated samples of heterogeneous veterans, clearly not the full range of tens of thousands of veterans returning in the last few years. Clearly many more studies are needed in this area using larger samples of subjects with different comorbidities and medication regimes and instituting different cognitive-behavioral treatment modalities.

Another theoretical shortcoming is an outdated comment that seems to imply that right hemispheric lateralization of linguistic functions is of necessity pathological and thereby through default associated with PTSDs. Apparently unknown to the authors, this neurolinguistic truism has been seriously challenged by large population-level studies by a German research consortium at the University of Munster (Knecht et al., 2001). Knecht and colleagues' subsequent studies (now spanning a decade), using transcranial Doppler and functional magnetic resonance imaging (fMRI) have conclusively shown that such otherwise healthy male and female right-hemisphere-dominant subjects display a full spectrum of spatial and linguistic lateralization patterns that are often mirror symmetric to normally lateralized subjects. Moreover, it appears to have been shown in subsequent reports that it is the intrahemispheric pattern of linguistic lateralization rather than the hemisphere of origin that is the sine qua non of healthy human patterns of lateralization.

## Modeling Higher Order Cognition: A Multidisciplinary Future

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The information on diffusion tensor imaging is useful and accurate, although somewhat dated already (e.g., circa 2002). More recent studies examining tractography by connecting fiber tracts in three dimensions using a combination of eigenvectors and mean diffusivity are not covered. The chapter on the prevalent disorder of schizophrenia is timely and adopts a functional connectivity approach that views the disorder as the end result of any combination of structural brain abnormalities. Such sophisticated system views of top-down prefrontal mediated networks could well benefit from some of the third-generation modeling techniques that use both diffusion-tensor-imaging (DTI) fiber tracking and vector autoregressive modeling techniques. Recent cutting-edge techniques such as Granger causality mapping are allowing for the localization of defective subsystems contributing to higher order cognitive networks (e.g., Kanwisher & Duncan, 2004, p. 439).

Unlike the classic example of the behavioral neurology of stroke, neuropsychiatric disorders are particularly fraught with methodological difficulties in that such disorders encompass the spectrum, from pure functional disorders to global brain dysfunction associated with distributed hierarchical networks. Computational modeling techniques will then be essential in understanding disorders of functional connectivity associated with schizophrenia and many of the most common mood disorders.

The chapter on autism demonstrates the superiority of localization of magnetoencephalography (MEG) due to the lack of conductivity barriers and simplistic mathematical models. This technique, aside from its excellent temporal resolution, is perhaps ideal for studying complex cognition, such as executive functions, by virtue of its decomposability yet is still strikingly underutilized almost a decade after its first appearance. However, this autism chapter again espouses a causal role for atypicality of language dominance and autism. This is perhaps a vestige of previous psychodynamic orientations still being promulgated within certain segments of psychiatry rather than the assumption of such a causal role per se (e.g., see Knecht and colleagues', 2001, criticisms of the pathologization of the right hemisphere).

Indeed, the autism and PTSD oversimplifications on the part of the authors do not readily fit with an emerging view of the right temporoparietal junction in association with right prefrontal networks as playing an essential role in theory of mind and almost all subsequent building blocks of higher level social cognition (Saxe, 2008). In this sense a renewed interest in laterality far beyond the level of sophistication of some early compilations in the field (e.g., Beeman & Chiarello, 1998) seems to be ready to begin again in earnest, especially given some of the newer statistical and imaging modalities now under development and in use.

On another level, early studies have shown that the subcortical structures do not just passively link the two hemispheres but rather coordinate and integrate hemispheric activity such as in numerical magnitudes and semantic categories (Sergent, 1990). With the emergence of the decade of the brain in the 1990s, the subcortical functionality hypothesis waned somewhat. Finally there do seem to be some vestigial remnants of Jacksonian neurological thinking in this text such that cortical is viewed in a value sense as being "better" than subcortical. Hughling Jackson's idea was rather that complexity enabled more

fully human behavior and that cortical systems were the substrate of all that was aspired to be “human.”

However, we do know that fear and instinctive as well as approach systems are largely limbic in construction and are just as important in organizing adaptive behavior at a fundamental level. Such noncortical systems have important functions in nurturing and protecting the human organism at a basic evolutionary level of understanding and are equally important in the mundane as well as the most complex of human behaviors. If such fundamentally human traits as empathy are built largely on limbic networks (Saxe, 2008) and if the most complex of semantic networks have essential and irreducible subcortical components (Mandonnet, Nouet, Gatignol, Capelle, & Duffau, 2007) then surely the distinction between cortical and subcortical evaluative judgments must be much more nuanced than either/or arguments of the past.

Many diseases covered in this text have strong indications of abnormalities in subcortical systems. Yet at the same time this text says almost nothing about what the range of normal intra- and interindividual differences in connectivity might be in the brain, nor are global paradigms for understanding neurodevelopment and neuropsychiatric theory proposed or put forward. Efforts to arrange various neuropsychiatric syndromes in similar functional systems parallel the behavioral neurologist's nomenclature of stroke lesions into lobar systems, yet neuropsychiatric causality could well prove to be even more complex than stroke neurology.

The reason for this is, again, the essential functional and effective connectivity of these disorders. Modeling and detailed lesion analysis of both brain regions and cognitive skill sets in large data sets could provide the foundations for such a theoretical approach to understanding functional neuropsychiatric systems. In such a future systems view, functional neuroimaging and computational modeling will figure prominently, perhaps painting a rosy picture for the collaborative endeavors of neuropsychiatrists and experimental neuropsychologists. Despite the shortcomings, this ambitious text is a keeper and belongs on the shelf of every aspiring neuropsychiatrist as well as neuropsychologists in clinical training.

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