Neuropsychological Functioning and Brain Imaging
Concluding Remarks and Synthesis

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As reviewed in this text, tremendous progress has been made over the past 15 years in the development of brain-imaging techniques and our ability to link imaging data with important aspects of behavior. These advances have had a great impact on both theoretical and clinical issues in the neurosciences and have greatly refined neurological diagnosties, as has been discussed by Rutledge (Chapter 2). Likewise, the greater specificity and precision of current brain-imaging techniques have provided a more complete paradigm for the study of the neurological patient in which the effects of focal, lateralized, and/or generalized neurological damage/dysfunction can be compared with neuropsychological function. Much past research in cognitive neuroscience had been hampered by the inability to study simultaneously anatomy and pathology of the brain and function. As the current generation of research unfolds, we have to rethink our understanding of the brain and its relationship to cognition and neuropsychological function. For example, as pointed out by Knopman, Selnes, and Rubens (Chapter 5), the language system of the brain may not be as localized as was once thought, and Haaland and Yeo (Chapter 8) make similar statements about motor control in their attempt to elucidate the complex factors that are involved in motor function.

A central theme of this volume is the difficulty in drawing valid structure-function relationships, a difficulty that, as Turkheimer (Chapter 3) points out, reflects conceptual as well as technological issues. Because of the unique development of each human brain along with the diversity of functional neural systems and pathways, a clinically distinct syndrome may result from several lesion sites, rendering specification of component processes and their neuroanatomic loci difficult indeed. Furthermore, there are major technical problems in determining the exact locus and extent of brain damage. For example, the physiological changes associated with structural brain abnormalities identified by CT or MRI may far exceed the boundaries of the structural deficit (see Figure 1). Pawlik and Heiss (Chapter 4) elegantly demonstrate this point in their chapter and suggest that the rigid framework of precise localization theory simply is not tenable in many brain disorders. One clear example of this is their PET work in normal subjects performing the Wis-

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focus on the ictal study, the x-ray CT is normal, but air in the ventricles from a previous pneumoencephalogram (which was also normal) is evident. The fourth patient (D) has left hemiatrophy (arrow) and diffuse hypermetabolism on the ictal study, and the fifth patient (E) has a normal x-ray CT and several hypermetabolic foci on the ictal study (from Engel, Brown, & Kuhl, 1982; reproduced by permission). These metabolic studies demonstrate the potential lack of relationship between what appears to be a structurally “normal” brain and distinctly abnormal physiological functioning. Such studies underscore the need to integrate structural, metabolic/physiological, and cognitive function in the neuropsychology of brain disorders.

The Wisconsin Card-Sorting Test, which has a long tradition in clinical neuropsychology as a test of frontal lobe function (Lezak, 1983). However, PET studies demonstrate whole-brain activation in a rather uniform fashion, not just the frontal lobes. Such brain-imaging studies indicate the need for reevaluation of traditional neuropsychological assessment techniques that aim to localize dysfunction and their implications for brain impairment.

Brain imaging and neuropsychological studies have had a profound impact on our understanding of the neurological mechanisms in emotional control and, by implication, our understanding of psychopathology. Because of the complexity of human emotional expression, it has been anticipated that the unraveling of neuromechanisms in regulating emotion likewise will be complex. Accordingly, Cullum (Chapter 10) demonstrated the difficulty of models positing a simple lesion-localization relationship in emotional control. Rather, emotional dysregulation in neurological disease or disorder occurs in a multifaceted fashion associated with numerous brain lesion sites. Neuropsychiatric disorders present a similar picture. As pointed out by Raz (Chapter 9), there are a number of anatomic brain abnormalities present in the major psychoses. It is interesting to take a historical perspective on this, as it was not too long ago that clinicians and researchers considered the neurobiological component relatively insignificant.

Neuromaging research has helped to overcome an excessive concern regarding the distinction between “organic” patients (who were thought truly to have “structural brain damage”) and “functional” patients (who were thought to have only an “emotional” illness or disorder that had no neurobiological basis). Goldstein (1986) reviews the history of this particular distinction between “organic” and the so-called “functional” schizophrenic patients. In the late 1960s and early 1970s, when clinical neuropsychology began more completely to address this problem of distinguishing between patients with “real brain damage” and those with just “schizophrenic illness,” the studies indicated that the groups really could not be separated by neuropsychological testing. We now realize, in retrospect, that the reason the “schizophrenic group” could not be separated from the “organic group” was that the schizophrenic group in fact had underlying neurological deficits, as reviewed by Raz (Chapter 9). This issue could not have been clarified without the brain-imaging technology of today (Kelsoe, Cadet, Pickar, & Weinberger, 1988). It
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is anticipated that future research in this area may facilitate the development of diagnostic markers and the identification of biologically valid subtypes. This especially may be true as imaging techniques come on line that allow in vivo measurement of neurotransmitter activity.

The diagnosis of various dementias has been greatly aided by the interface between neuropsychological assessment and brain imaging. The behavioral correlates of volumetric analyses of the human brain, as discussed by Naugle and Bigler (Chapter 7), is in its infancy. Preliminary research certainly suggests that there may be clinical and empirical applications of various volumetric procedures in the assessment and diagnosis of Alzheimer's disease and related dementias. There is a need, however, for further longitudinal studies of the degenerative process as well as determination of the neuropathological significance of cortical atrophy and ventricular dilation. As this basic neurobiological work unravels the relationship between neuronal-level degenerative changes and what is observed as cortical atrophy and ventricular dilation, it will likely pave the way for a better understanding of the degenerative processes as they relate to cognition.

For example, with improvements in MRI resolution, specific nuclei can now be identified more precisely. This has been impossible with CT scanning techniques, even with the most recent generation of technology. Recently, Kim et al. (1988) have demonstrated that the size of the hippocampus is more discriminating than volumetric measures of atrophy or ventricular dilation in assessing dementia. Luxenberg, Hasbey, Creasey, Sundaram, & Rapoport (1987) have demonstrated that it is not the size of ventricular enlargement that best differentiates Alzheimer's patients from controls, but the rate of volumetric ventricular dilation over time. Such research will undoubtedly lead to a better understanding of the clinical significance of volumetric changes identified by CT and MRI.

The relationship between individual differences and anomalous brain development presents a challenge in making generalized statements about brain function based on brain imaging. As pointed out in the chapters by Yeo (Chapter 11) and Bigler, Lowe, and Yeo (Chapter 12), there is a problem in referring to the "average" brain, as certain cognitive operations may be greatly affected by sex differences, age differences, and the prior presence of early brain insult or developmental error. These individual differences to a certain extent detract from the predictability of any type of lesion-localization theory of brain function. A number of cases were discussed in which particular lesions were clearly identified by CT or MRI technique but the lesion had little, if any, correspondence to what would have been predicted clinically. Thus, accounting for individual differences will certainly play a major role in future studies relating lesion location to function. Dimensions of differences among normal brains offer much more to neuropsychology than "nuisance" variables serving to limit generalizability. As Yeo pointed out (Chapter 11), such differences may help reveal principles of higher cortical function in terms of elucidating the advantages and disadvantages of a given design.

As a better understanding of the relationship between structure and function of the nervous system evolves, there should be at least two major effects on the clinical neurosciences. The first is improved diagnostics. We have already witnessed, in the past decade, marked refinement in the detection of space-occupying lesions, stroke, and certain degenerative disorders, to name a few (see Figure 2). Brain-imaging tests have become the diagnostic procedure of choice for determining the presence or absence of many of these disorders. The second effect, a consequence of the first, is a direct connection between diagnostic capabilities and improved treatment, particularly with respect to rehabilitation efforts in neurologically compromised patients. For example, based on current technology, the patient with Alzheimer's disease is being diagnosed at an earlier stage than ever before because of the improvements in brain imaging and neuropsychological assessment. If there is an improvement in the treatment of Alzheimer's disease, early detection is certain to be a critical variable. The biochemical and physiological abnormalities that precede the development of cognitive symptoms and neuropathological changes in brains of Alzheimer's patients occur before there are demonstrable symptoms. If we are going to be able to affect treatment of Alzheimer's disease, we will have to detect the degenerative changes at the earliest possible
FIGURE 2. Improved detection of a subdural hematoma by MRI over CT (see also Figure 9 in Chapter 1). The CT on the upper left was interpreted as being within normal limits. Obviously, in retrospect, after comparison with the MRI scans, the shadows on the lateral surface of the CT were actually bilateral subdural hematomas. The MRI scans (upper right horizontal plane; bottom coronal view) clearly depict the extent of the bilateral hematomas as well as the structural deformations caused by the position and size of the hematomas. Such improvements will likely lead to a refinement in understanding brain-behavior relationships.
stage because of the lack of regeneration within the central nervous system. There is the potential that pharmacological treatment might become available that could either slow off or actually halt progression of neuronal degeneration in Alzheimer's disease (Scheibel & Wechsler, 1986). There is also some speculation that brain grafting of acetylcholine-rich tissues may have some potential role in treating Alzheimer's disease, similar to the initial positive treatment effects of dopamine-rich tissues grafted into brain tissue in the Parkinson's disease patient (Bjorklund et al., 1987; Lewin, 1987). But for these to be effective, the diagnosis will have to be made at the earliest possible stage. Based on the work summarized in this book, and the work of others (see McGee et al., 1986), we are making progress towards earlier detection of the various dementias (see Figure 3).

Research on the diagnosis and treatment of traumatic disorders raises similar issues. As discussed by Ruff, Cullum, and Lucassen (Chapter 6), brain imaging has revolutionized the early treatment and diagnosis of intracranial pathology in the traumatically brain-injured individual. This has had a direct impact on improved recovery of function and reduced morbidity. However, the residual cognitive deficits in traumatic brain injury have a marked effect on quality of life (Bigler, 1987a,b). In this regard, tremendous interest in cognitive rehabilitation has emerged over the past half decade (Prigatano, 1987). It may be that brain imaging and neuropsychological testing will play the critical role in evaluating the efficacy of cognitive rehabilitation for a given patient and in the assessment of appropriate treatment modalities for cognitive rehabilitation training. Brain-imaging and neuropsychological research may provide further insights into the recovery process of brain injury and the adaptability of the brain to retraining. Likewise, the whole issue of recovery of function following a brain injury has been fraught with many problems until the recent generation of brain imaging has permitted a greater standardization with respect to identifying pathology and documenting structural integrity/abnormality.

Neuropsychological testing used to be done in isolation from a knowledge of underlying neuropathology. Prior to the advent of CT scanning (see Chapter 1), it was rare that the brain could be studied at a postmortem examination close to the time when the neuropsychological studies were conducted. For the most part, neuropsychological studies prior to 1975 had to infer the location and extent of cerebral damage from behavioral signs and their purported relationship to neurological examination, EEG, or pneumoencephalographic findings. For these reasons, neu-
Neuropsychology developed a tradition of localizing dysfunction independent of specific knowledge of precise areas of actual structural damage. Much has changed. We no longer have to wait for the postmortem examination to determine the structural integrity of the brain, as the various neuroimaging techniques that have been discussed in this text are widely available. It is now rare for any patient who has significant neurological abnormality not to have had one of the neuroimaging procedures. Neuroimaging diagnostics have become a standard mode of evaluation of the neurological patient, and one might predict that such procedures will be even more frequently utilized in the future. In fact, the neurological patient of the future may well receive assessment incorporating brain imaging, neuropsychological evaluation, and direct metabolic and physiological functioning (see Gibbins et al., 1987), and the data from each of these will be interfaced together to produce a composite assessment that interrelates all of this information.

Much past research in neuropsychology has been based on standardization of neuropsychometric procedures (see Yeudall, Reddon, Gill, & Stefanyk, 1987). This has been necessary because most neuropsychological diagnostic schemes are based on deviation from “normal.” Thus, some level of precision has been achieved in neuropsychology by applying statistical principles to the decision of whether a score is abnormal or not. The same process needs to take place in brain imaging. As discussed by Turkheimer (Chapter 3), a variety of quantification techniques are available, allowing researchers and clinicians to go far beyond simple rating scales. As these techniques become more and more automated, we should be able to quantify directly a variety of parameters of the brain, including the amount of white versus gray matter, ventricular volume, hemispheric nuclei, normal asymmetries, etc. These anatomic measurements may be critical parameters with respect to manifestations of certain neurological disorder states. Accordingly, the statistical emphasis that has played such an important role in neuropsychology needs to be applied to brain imaging as well.

One goal of this text is to give some direction to future research and practice in neuropsychology and behavioral neurology. It is apparent that the future of neuropsychological assessment will take a very different path than in the past. Much current research in neuropsychology is based on measures that were developed prior to 1965. As brain-imaging techniques became available, it was important first to investigate and quantify the significance of such brain abnormalities as visualized by brain-imaging methods with standardized neuropsychological measures. However, the current neuropsychological armamentarium is somewhat archaic and insufficiently related to current theories of cognitive function (Posner, 1986; Stillings et al., 1987). Further, neuropsychology has just begun to utilize the advances in computer technology. There has been a wave of enthusiasm for computerized assessment, but to date, most have simply put “paper and pencil” tests on the computer without making them adaptive, interactive, or an expert system (see Morrison, Schaeffer, & Russell, 1987; Russell et al., 1987). The assessment battery of the future likely will be, in large part, computer-based and will probably include on-line metabolic (i.e., PET or MRI) and/or physiological (computerized EEG) measurement. Such an evaluation could document anatomic integrity via specific measures of major brain structures and nuclei and integrate this with neuropsychological function and associated metabolic and physiological activity that correspond with certain cognitive states. This is the future. Such clinical advances will be paralleled by advances in the basic neurosciences, allowing simultaneous assessment of differing facets of brain activity and the development of a more integrated science of the brain.

REFERENCES


