Neuropsychological Function and Brain Imaging
Introduction and Overview

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The study of the effects of known brain lesions on behavior is crucial to progress in understanding the relationship between cognition and the brain. Before the advent of modern brain-imaging techniques, the precise effects of brain lesions could be studied only in animals. This period (circa 1930 to 1975) was extremely productive for animal model research (Kolb & Whishaw, 1985), but progress in human neuropsychology was plagued by the inability to quantify the location, size, or extent of a brain lesion in the living individual.

These particular problems are best exemplified by reviewing some of the methodologies of this past research era in human neuropsychology. For example, in the now classic symposium held in 1962 on the “Frontal Granular Cortex and Behavior” (see Warren & Akert, 1964), Teuber (1964) presented a paper on the behavioral effects of frontal lesions in man. Aspects of his research were based on patients who had penetrating head injuries, and skull x rays were used to document the location and position of entry (see Figure 1). Based on these skull films, the extent of underlying cerebral damage was inferred. Obviously, no details of the cerebral structures can be obtained from skull films, and thus, no precision could be obtained in such research in terms of the extent and location of actual damage. In 1962 this was as close as one could come in giving a noninvasive in vivo appraisal of locus of brain damage from cerebral trauma. In contrast, similar studies recently have been done by Salazar, Grafman, Vance, et al. (1986) using strict computerized tomography (CT) quantification methods which carefully outline underlying structural pathology (see Figure 2). This research (see also Grafman, Salazar, Weingartner, Vance, & Anns, 1986; Salazar et al., 1985; Salazar, Grafman, Schleselman, et al., 1986), because it permits direct quantification of areas and structures affected, has resulted in a much clearer understanding of the behavioral effects of basal forebrain lesions.

At the same symposium at which Teuber discussed the frontal cortex, Reitan (1964) presented his now oft-cited work on the effects of frontal lesions on a collection of tests that would eventually become the basis of the Halstead–Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1985). In establishing the criteria for inclusion of patients with frontal lobe damage,
FIGURE 1. Composite diagrams showing outlines of skull defects in 20 men with anterior (frontal) and 20 with posterior (parieto-occipital) missile wounds of brain (from Teuber, 1964). This illustration depicts the methodology in the pre-brain-imaging era, when one had to infer the locus of damage by the tract or trajectory of the missile by noting entrance and exit points from x-ray skull films. Although this technique provides some index of whether "anterior" or "posterior" brain regions were involved, no precision as to the actual locus or extent of the lesion can be given.

Reitan had to rely on the opinion of "fully qualified neurologists and neurological surgeons," who, in turn, based their clinical judgment on the neurosurgical findings at the time of operation or on neurological examination (i.e., physical findings such as paralysis), direct ventriculography, cerebral arteriography, or pneumoencephalography. Although such standards permitted gross distinctions, it was virtually impossible to study specific effects of discrete lesions on neuropsychological performance.

Prior to the advent of CT techniques to image the brain, one had to rely on inferential methods based on imaging techniques of the day, namely, pneumoencephalography (PEG), cerebral arteriography, and radioactive isotope brain scanning. Pneumoencephalography, introduced by Dandy in 1918 (Oldendorf, 1980), can outline ventricular structures but not image brain tissue directly (see Figure 3). Thus, in interpreting PEG results, one has to rely on inferential methods based on shifts and distortions that could be detected in the cerebral ventricles (see Figure 4). For example, a large tumor would shift the ventricular system laterally and collapse the part of the ventricle closest to the tumor. Similarly, cerebral arteriography can directly image the cerebral vasculature but not brain tissue. In interpreting cerebral arteriography results, one again relies on some distortion or change in the position of the cerebral blood vessels.

Radioisotope scanning techniques (see Oldendorf, 1980) were being developed as early as 1947, but even by the 1960s, these techniques gave only the grossest image of the brain (see Figure 5) and had only limited clinical utility. During this period, attempts were made (see Figure 6) to image the brain via ultrasonic waves. The technique, called echoencephalography (see Howard, Gallicich, & Matson, 1967), could only detect large distortions or aberrations in brain structure and yielded no information about anatomic detail. Thus, the inferential methods of angiography/arteriography or PEG were the primary imaging methods of that period, and the popularity of these techniques continued right up until the early 1970s. But, as Oldendorf (1980) states, both
Figure 2. (Left) Horizontal CT section at the level of the basal forebrain (ac, anterior commissure; amy, amygdala; ca, caudate nucleus; cb, hippocampal). (Right) Anatomic section from the same brain (scattered on the left). The anatomic section was utilized to establish a template for the lines superimposed over the CT image on the left, from the permit, a patient with Korsakoff's location. By using this technique, precise lesion-location studies can be accomplished.

(From the work of S. Steiner et al., 1983, and used by permission of Dr. Steiner.)
FIGURE 3. Schematic depictions of cerebral angiogram and pneumoencephalogram (reproduced by permission from Oldendorf, 1980).

FIGURE 4. Early brain-imaging methods. (a) Pneumoencephalogram, anteroposterior views in brow-up position, shows that right temporal horn is slightly narrower than the left. This suggests partial collapse of the right temporal horn, which was a result of compression from a tumor. (From Falconer, 1970; reprinted by permission from the Journal of Neurosurgery.) Note that with PEG the ventricular space in a single plane is relatively well defined, but no detailed image of the brain can be visualized. (b) Ventriculogram (similar to PEG except that air is injected directly into the ventricles) demonstrates a large pneumoencephalic cyst. At postmortem (c), the coronal brain section demonstrates the cyst visualized in the ventriculograms, but as with PEG, no anatomic details can be ascertained from ventriculogram studies. (From Salmon, 1970; reprinted by permission from the Journal of Neurosurgery.)
FIGURE 5. Radioisotope brain scan in an adult who sustained a closed-head injury. The image on the left was 1 week after injury and appears normal (i.e., even distribution and absorption of the isotope). The image on the right was taken 3 weeks after injury and demonstrates an abnormal distribution on the left side, which proved to be a hematoma. (From Cowan, Maynard, & Lassiter, 1970; by permission of the Journal of Neurosurgery.)

FIGURE 6. Ultrasonic-beam-generated eechoencephalogram is presented in the top view. Bottom view is a diagramatic representation of the echoencephalogram findings in relation to the head. Note that the echoencephalogram gave only the crudest image of brain structures. (From Howind et al., 1967; reprinted by permission from Neurology.)
these techniques shared two major limitations: "Both were traumatic (and as a result, not repeatable), and both showed only tissue compartments (blood and cerebrospinal fluid, respectively) that were seldom of clinical interest. Structural information about the brain tissue itself had to be inferred (p. 89)." Because of these limitations they were not very useful in doing clinical lesion location neuropsychological research.

During the same period, numerous psychological and psychodynamic theories concerning the basis of such disorders as schizophrenia, autism, major affective disorders (the so-called manic-depressive illness spectrum), and learning disorders, to name a few, continued to flourish. For example, prior to 1970, psychodynamic and psychoanalytic theories predominated the literature concerning schizophrenia, autism, and manic-depressive illness (Strauss & Carpenter, 1981). However, with the advances in the psychopharmacological treatment of these disorders in the 1950s and 1960s (Valzelli, 1973), the research focus began to switch to more biological explanations (see Flor-Henry, 1983). Rather unexpectedly, the first CT studies in schizophrenic patients (Johnstone, Crow, Frith, Husband, & Krel, 1976) demonstrated ventricular enlargement, a finding that had been suggested by PEG and postmortem studies, but as already pointed out there were severe limitations in interpreting such studies. Thus, the work by Johnstone et al. (1976) was the first in vivo documentation of possible structural brain abnormalities in psychiatric patients who were thought to lack "organic" dysfunction or deficit. Based on our current knowledge and understanding, a wide variety of diagnostic groups may have subsets of patients who demonstrate structural abnormalities or irregularities in CT or magnetic resonance imaging (MRI) scan results (see Figure 7).

In a similar vein, known neurological disorders such as Alzheimer’s and closed-head injuries were difficult to study prior to CT scanning because of the unavailability of in vivo studies. Again, research had to await postmortem investigation before structural changes in these disorders could be assessed. Even this was quite unsatisfactory because the testing would have been done prior sometimes years prior, to the death of the patient, requiring further inference to establish what the brain structure might have been like at the time of evaluation. Current technology is very different. We now have CT, MRI, positron emission tomography (PET), and related technologie

FIGURE 7. Abnormal CT scan in an 81-year-old-high-school-educated male schizophrenic. Note the ventricular enlargement, particularly of the anterior horns, and the frontal pole atrophy.
FIGURE B. (a) First-generation CT scan (circa 1974). Note the poor resolution and the size of the pixels. (b) Second-generation CT scan, which demonstrates better definition of ventricular space but still poor resolution of brain substance; however, even this poor resolution was dramatically better than that of P.E.G. (c) Improved resolution on the same scanner as in B and on the same patient 5 years later. (This patient had Alzheimer’s disease, and the second scan demonstrates atrophy.) Note the better differentiation of cerebral structures in this CT scan. These improvements relate to increased computer sophistication in signal processing and resolution. (d) Current-generation CT scan, which demonstrates some degree of white and gray matter differentiation and better subcortical identification along with ventricular and cistern spaces.
FIGURE 9. Current-generation CT scan (a), which demonstrates area of infarction (arrow). (b) Magnetic resonance imaging scan of the same patient; note the detailed resolution of the MRI results in terms of normal and abnormal anatomy and the extent of the cerebral infarction (arrow). The MRI also permits imaging in the sagittal (c) and coronal (d) planes, which allows three-dimensional viewing of the lesion (arrows). The MRI image is very close to an actual gross anatomic cross section.
FIGURE 10. (Top) Coronal anatomic section. (Middle) Similar coronal view from MRI scan. (Bottom) Schematic drawing of major anatomic sites as depicted by MRI: (1) corpus callosum, (2) anterior horn of lateral ventricle, (3) putamen/globus pallidus complex, (4) internal capsule, (5) caudate nucleus, (6) interhemispheric fissure, (7) central white matter, (8) temporal lobe, (9) gray matter, cortical mantle, (10) skull, (11) scalp, and (12) Sylvian fissure. Note the anatomic precision that can be obtained by the use of the MRI.
along with methods to quantify various brain parameters (Bottomley, 1984; Naeser, 1985; Yeo, Turkheimer, Raz, & Bigler, 1987).

The past two decades have witnessed previously unimaginable advances in nontraumatic in vivo brain imaging. We can now accomplish with humans what heretofore could only be accomplished using animal models, leading to a more precise understanding of human brain function by studying naturally occurring lesions and neurological states. An era of clinical neuroscience research is emerging that promises to provide a clearer definition of human brain–behavior relationships. In fact, in clinical neuropsychology, we have had to dismiss a considerable amount of research conducted prior to 1975. As Swierczynski and Leigh (1979) have pointed out, CT scan results provide a much more thorough and reliable indicator of actual underlying “organic” damage than electroencephalography or the neurological examination. Since the EEG and neurological examination typically provided the only criteria used in much of the clinical neuropsychological research of this period, it leaves many of the pre-1975 conclusions suspect. Also, there has been considerable refinement in the quality of the CT image (see Figure 8), and with the advent of MRI scanning even finer precision can be achieved (Figure 9 and 10), which has further advanced the use of this technique in studying structural and anatomic effects.

The goals of this text are to review the major neuropsychobiological disorders utilizing current brain-imaging techniques. We hope this endeavor will reduce some of the ambiguity in the cognitive neurosciences by providing more objective criteria for examining the relationship between in vivo abnormal brain structure and function.

REFERENCES