Abstract and Keywords

This article reviews the shared history of epilepsy and neuropsychology and highlights the clinical and scientific progress in both disciplines. It considers the role of neuropsychology in understanding the impact of the epilepsies and how cognitive studies of epilepsy and epilepsy surgery helped elucidate human brain function. It begins by focusing on the late 1800s/early 1900s, when intelligence testing became available and widely used in epilepsy and neuropsychology, before turning to the 1920s–1950s, when a clearer picture of the different epilepsy syndromes and their associated EEG and clinical seizure features emerged. It then examines surgical treatment of the epilepsies in the period beginning in the late 1940s, along with the conflict between the eugenics movement and the goal of providing better care of people with epilepsy within specialized epilepsy institutions. It also looks at the risk factors for cognitive impairment and the effects of EEG abnormalities on neuropsychological function.

Keywords: epilepsy, neuropsychology, surgery, brain function, intelligence testing, EEG, clinical seizure, eugenics movement, epilepsy institutions, cognitive impairment

Individually, the histories of epilepsy and neuropsychology are interesting in their own right. Their shared history, however, is fascinating, and the synergistic contributions of studies in these fields have contributed to meaningful clinical and scientific progress in both specialties. In this chapter, we review important components of the historical interweaving of epilepsy and neuropsychology to highlight the ways in which neuropsychology helped to better characterize the impact of the epilepsies, how epilepsy and epilepsy surgery contributed to the development and growth of the profession of neuropsychology, and how cognitive studies of epilepsy and epilepsy surgery contributed to broader insights into human brain function. Our review of this combined history is in roughly chronological order, beginning in the late 1800s to early 1900s, when intelligence testing became available and widely used in both disciplines; transitioning to the 1920s to1950s, at which time greater appreciation of different epilepsy syndromes and their associated electroencephalogram (EEG) and clinical seizure features developed; and concluding in the period that began in the late 1940s, when surgical treatment of the epilepsies became

a viable therapeutic option and yielded unique clinical data to better understand the neural substrates of memory and other cognitive abilities. The history of epilepsy neuropsychology is intimately linked to technological advances, especially in regard to imaging and EEG recording, which have contributed to more recent initiatives characterizing the neural substrates of cognitive morbidities associated with various epilepsy syndromes, as well as the behavioral effects of discharging epilepsy lesions.

Epilepsy, Deterioration, and Cognitive Testing

Conceptualization of the important cognitive abilities adversely affected by epilepsy can be found in the earliest published reports. These reports tended to be more "experimental" in approach, as they antedated the availability of "clinical" tests for the time. In fact, following the introduction of formal intelligence tests in the early 20th century, experimental approaches to assessment diminished in number.

In one of the earliest quantitative cognitive studies of epilepsy in the English literature, and using an assessment approach not unlike contemporary neuropsychology practice, Smith (1905), an assistant lecturer in physiology at the University of Liverpool, contrasted "comparatively normal" patients with epilepsy, patients with epilepsy with "marked dementia," and healthy controls (Smith, 1905). The cognitive measures tested recognition memory for words and pictures, immediate memory, sensory discrimination, reaction times involving movement and choice, as well as rhythmic movement. Patients not only performed more poorly in recognizing words than pictures, but also epilepsy patients with dementia demonstrated greater impairment in "confusion between old and new" by their greater frequency of false positive recognition errors. Commenting on the ecological validity of the findings, Smith remarked: "everyone forgets many things from day to day, while errors of confusion occur relatively seldom and are much more noticeable when they do occur."

At approximately the same time, Alfred Binet and Theodore Simon published their scale of mental development to assess the cognitive abilities of French school children in 1905, characterizing cognitive development in terms of a child's "mental age." Henry Goddard, the research director at the *Training School for Feebleminded Girls and Boys* in Vineland, New Jersey, arranged for the Binet-Simon to be translated into English in 1911. The Binet-Simon Scales, subsequently modified by Lewis Terman in 1916 (Stanford-Binet), attracted considerable attention in the emerging American psychological community (Anastasi, 1969). The earliest publications of intelligence test performance in epilepsy appeared beginning in 1912 (Wallin, 1912), and these early studies, about which we will say more later, simply attempted to characterize modal group performance.

In the early 20th century, effective treatments for epilepsy were rare, and bromides with their very adverse cognitive and somatic effects represented the primary drug treatment (Friedlander, 2000). Phenobarbital was the first "modern" anti-epilepsy medication, marketed in 1912 by Bayer (brand name Luminal), and it was not until 1938 that phenytoin, marketed by Parke-Davis (brand name Dilantin), became available. Prior to the introduc-

tion of these effective anti-epilepsy medications, epilepsy was poorly treated and controlled, with the prevailing view in the late 19th and early 20th centuries that epilepsy represented a progressive degenerative disease that eventually resulted in dementia.

The consequences of poorly controlled seizures, including the cognitive, psychiatric, and social impairments, were poorly tolerated by society. In the United States, persons with epilepsy were often relocated to the institutions of the time, which included poorhouses, insane asylums, jails, and other similar facilities. There were no specialized facilities for epilepsy. The Bethel Institution in Bielefeld, Germany was founded in 1867 as Evangelische Heil- und Pflegeanstalt für Epileptische (Protestant Institution of Healing and Care for Epileptics) in Gadderbaum, today a locality of Bielefeld. The Rheinisch-Westfälische Anstalt für Epileptische represented the first epilepsy colony in the world (Pfäfflin, 2003). Against this backdrop emerged the belief, articulated primarily by charitable and religious groups, that persons with epilepsy were very poorly cared for in general institutions and would be better served if specialized facilities for epilepsy were developed. In addition, there was a general belief that persons with epilepsy, with their seizures, were upsetting to the other institutionalized residents—making them more disruptive and difficult to manage. For the good of all concerned, it was thought that it might be better for individuals to be "housed" in separate centers.

Dedicated "epilepsy colonies" began to appear in the United States beginning in the 1880s (Friedlander, 2001; Hermann, 2010; Jubenville, 1957; Kissiov, Dewall, & Hermann, 2013; Nevins, 2009; Shanahan, 1928) with the dual goals not only to improve medical and social treatment of epilepsy, but also to facilitate research into epilepsy's causes and consequences. Research at some centers included investigations of cognition and behavior. The first centers were established in Ohio, admitting patients in 1893 (The Ohio Hospital for Epileptics), New York, admitting patients in 1896 (Craig Colony for Epileptics); Massachusetts, admitting patients in 1898 (Monson State Hospital); and New Jersey, admitting patients in 1898 (New Jersey Village for Epileptics). Typically, establishment of these centers was founded on charitable causes, economic management of a disabled populace, and hope for improving quality of life.

Epilepsy Colonies, Eugenics, and Cognitive Testing

The goal of providing better care of people with epilepsy within specialized epilepsy institutions collided with the emerging and influential eugenics movement, which was particularly powerful force in both science and policy in the early 20th century (Black, 2003). This conflict reflected the intersection of intelligence testing as first conceptualized by Sir Francis Galton and the eugenics movement, which was also popularized by Galton and defined as "the science which deals with all influences that improve the inborn qualities of a race" (Galton, 1904). Galton advocated "positive eugenics," emphasizing the importance of mating between persons with positive qualities, whereas in the United States "negative eugenics" quickly took hold. Eugenics was loosely based on genetic theory that

sought to improve society through the process of selective breeding of superior stock. In the United States, however, eugenics emphasized the blocking of reproduction of "the unfit" and their "defective germ plasm" which threatened the general populace (Nevins, 2009).

This movement was in a sense institutionalized through the establishment of the Eugenics Record Office (ERO) in 1910 in the United States, and its functions were clearly stated (Figure 1). The ERO was established through the tireless efforts of Charles Davenport (right), with Harry Laughlin (left) named its superintendent (See Figure 2). Davenport and Laughlin are also depicted at one of their training classes for "field workers" (Figure 3), who were to fan out and collect data of "eugenical import," an important activity of the ERO addressing point 3 in Figure 1.
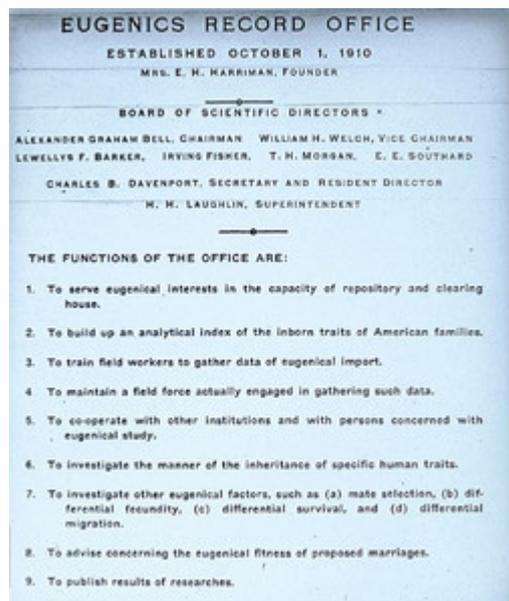

Figure 1. Listing of the Eugenics Research Office Board of Scientific Directors, and listing of the functions of the ERO.

Figure 2. Harry Laughlin (left) and Charles Davenport (right) outside the Eugenics Research Office.
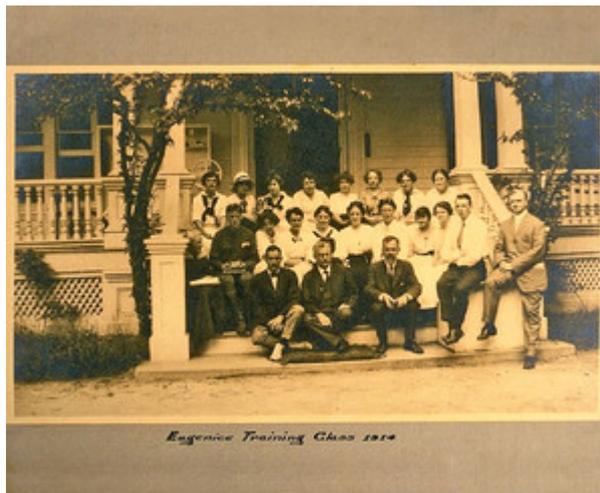
Figure 3. The Eugenics Training Class of 1914. In the front row, Davenport is third from left. Laughlin is at far right.

The "unfit" included many groups of persons, including the "feebleminded" and people with epilepsy, who represented the so-called "epileptic menace" (Black, 2003). Figure 4 provides a concrete characterization of the perceived status of people with epilepsy from the perspective of the ERO (II. "Eugenically unfit from defective inheritance." Multiple socially inadequate persons are listed, including the "epileptic").
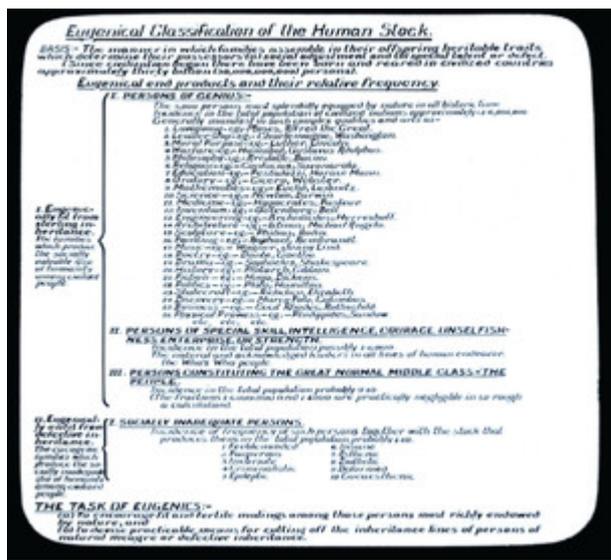
Figure 4. The eugenic perception of epilepsy, see:
"II. Eugenically unfit from defective inheritance—I.
Socially Inadequate Persons."

The ERO regularly trained so-called "field workers" (Figure 3) who were to obtain detailed "pedigrees." Among their activities, these field workers were sent to (and invited into) institutions of the time, including epilepsy colonies, and would visit the families of residents in order to secure familial patterns of target conditions. Figure 5 provides interesting details regarding the coding keys used to characterize familial patterns of undesirable traits (including epilepsy), and Figure 6 is an example of a family pedigree.
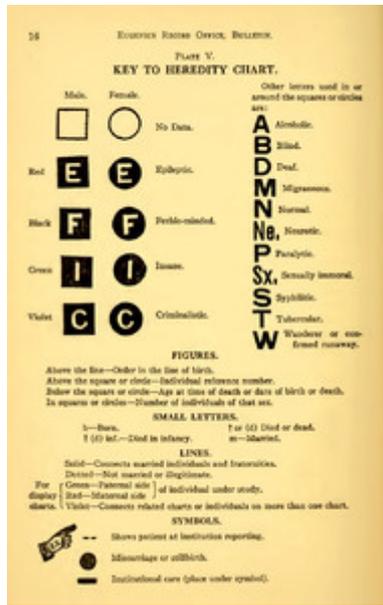
Figure 5. Coding system used in pedigree records.
This system was color coded, i.e., red denoted epilepsy, green denoted insanity, violet referred to criminality, black indicated feeblemindedness.
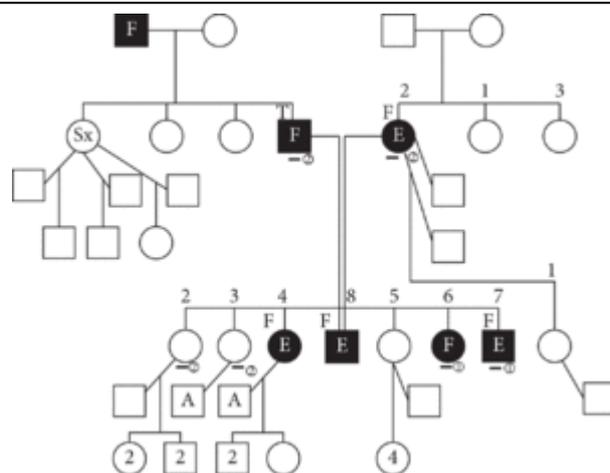
Figure 6. Demonstration of the use of genetic pedigree characterizing family from "two feeble-minded" parents.

The first study of "epilepsy inheritance," a key point for eugenicists if a group was to be targeted for limited reproduction, was performed at the *New Jersey Village for Epileptics*, and the authors concluded that epilepsy and feeblemindedness reflected a common defect of a "protoplasmic factor that determines complete nervous development" (Davenport & Weeks, 1911). In the context of the eugenics environment, the appropriate response to the genetic threat of epilepsy was obvious.

> The most effective, violating least the social ideals of our time, is the segregation during the entire reproductive period—(say from 15 to 45 years of age) of epileptics of both sexes. Such measures would be an expensive burden for the present generation of taxpayers; but if it is ever justifiable to bond a state it is for such a purpose as this; because inside of ten years the stream of defective children would be almost dry.

> (Davenport and Weeks 1911, p. 668)

In 1920, John Schwartz, an assistant physician at the Ohio Hospital for Epileptics, wrote:

> *The State of Ohio alone has between eight thousand and nine thousand recorded epileptics within its boundaries, and of this number sixteen hundred are either wholly or partially taken care of by the State, the balance are at large and a great many of these are unrestricted and allowed to propagate their species only adds to the existing misery, this is a big mistake and a gross injustice to the people of our State. And now that innumerable medicinal and dietary treatments have been faithfully carried out, also surgery and the much vaunted crotalin or snake venom have thus far been unsuccessful as to a cure, may it not be well to consider sterilization of the chronically defective as a means of preventing the propagation of their species?*

> (Schwartz, 1920)

In "Classification of the Socially Unfit from Defective Inheritance: The Cacogenic Varieties of the Human Race," epilepsy was specifically listed as targeted condition: "No clearer cases of specific hereditary degeneracy than those of epilepsy have been established" (Laughlin 1914, p. 25).

> Naturally, the first class of dependents that appeals to me that should be in State custody is the epileptic. He is probably the most dangerous defective with which the community has to deal, in that his acts are more or less impulsive and uncontrollable, and when he commits crimes they are usually brutal ones.

> (Weeks 1914, p. 59)

Reflecting this view, an **_involuntary_** sterilization law entitled "An Act to Authorize and Provide for the Sterilization of Feebleminded (Including Idiots, Imbeciles and Morons) Epileptics, Rapists, Certain criminals and Other Defectives," was passed in the New Jersey Legislature in 1911, signed by Governor Woodrow Wilson, but later overturned.

It is in this environment of heavy eugenic philosophical institutional influences that standardized psychological testing was first performed at the New Jersey Village for Epileptics (Hermann, 2010; Jubenville, 1957).

As noted previously, the Binet-Simon was translated into English in 1911, and the English version was used by Henry Goddard to study the intelligence of residents at the Training School for Feebleminded Girls and Boys in Vineland, New Jersey. While Goddard was on leave from Vineland and traveling in Europe, J. E. Wallace Wallin was invited to teach a summer course at Vineland in functional psychology in Goddard's absence. At Vineland, Wallin was exposed to and gained experience with the Binet-Simon Scale. When he was subsequently offered a position at the New Jersey Village for Epileptics, approximately 85 miles to the north of Vineland, Wallin established the Laboratory of Clinical Psychology —"the first laboratory of clinical psychology in an institution for epileptics anywhere in the world" (Wallin, 1955). Although Smith's (1905) report, published in the *British Journal of Psychology*, may have been the first formal cognitive assessment study of persons with epilepsy, the first "psychometric" report of individuals with epilepsy using standardized tests appeared in 1912 in the journal Epilepsia (Figure 7; Wallin, 1912). Wallin contrasted epilepsy patients to "feeble-minded" institutionalized patients (Figure 8). He described less overall cognitive impairment in patients with epilepsy compared to feeble-minded patients based upon classification frequencies (i.e., fewer "idiots" and more "morons," in the nomenclature of the time), concluding that that "the intellectual superiority of the epileptic defective is conspicuous," a conclusion that was inconsistent with the eugenicists' zeitgeist.

EIGHT MONTHS OF PSYCHO-CLINICAL RE-
SEARCH AT THE NEW JERSEY STATE VIL-
LAGE FOR EPILEPTICS, WITH SOME RESULTS
FROM THE BINET-SIMON TESTING*).
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The function of a clinical psychologist in an institution
for defectives, in a public school system, in a university,
in a psychiatric institute or in a juvenile court, is two-
fold: First, that of *theoretical investigation,* or the increase
of knowledge under controlled and verifiable conditions.
This is essentially the field of the research psychologist or
of pure science, so-called. Second, that of *practical appli-
cation,* or the utilization of the truths discovered in the
educational, hygienic, medical and custodial treatment of
the sufferers. This is the work of the consulting psycho-
logist as distinguished from the pure researcher, and con-
stitutes the sphere of orthogenesis, mental hygiene or ap-
plied clinical psychology. While the line of demarkation

Figure 7. Wallin (1912) publication, emphasizing both theoretical and practical aspects of clinical epilepsy research. This article appeared after his departure from the New Jersey Village for Epileptics.


	Idiots	Imbeciles	Morons	
Epileptics	5.7%	27.3%	61.5%	5.4%
Feeble-Minded	19.2%	54.0%	26.0%	0.0%
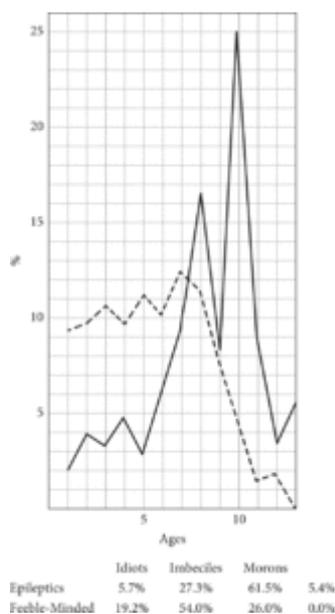
Figure 8. Results of Binet-Simon testing results comparing persons with epilepsy from the New Jersey Village to residents from the Vineland Training School for Feeble Minded. This report predates the use of quotients to characterize performance and relies on classification by mental age alone (Wallin, 1912).

Wallin's 1912 contribution is not generally recognized, but likely represented the first cognitive laboratory to study epilepsy in the United States. It was patterned, at least in part, after Goddard's lab at Vineland and was sophisticated for its time. Wallin's research occurred in the context of the eugenics movement, which was an extraordinarily stigmatizing time epilepsy patients that also advocated IQ as a means to select institutionalized patients for involuntary sterilization. Wallin worked at an institution that, although created to provide a protective and humane environment for people with epilepsy, was overseen and overrun by eugenicists with arguably hostile intentions for its residents. While Wallin benefitted from Goddard's assessment tools to characterize individual abilities, in Goddard's hands, these tools were infamous for their contributions to eugenic activities (Black 2003; Gould 1981; Nevins 2009).

Epilepsy Institutions and Beyond

A later but still early investigation of institutionalized patients with epilepsy anticipated many research trends that were to develop later and shape the neuropsychology of epilepsy. J. Tylor Fox (Fox, 1924) systematically assessed children with epilepsy who were residents in a special facility (Lingfield Epileptic Colony in the United Kingdom). Children met criteria specified in the Defective and Epileptic Children Act of 1889, which stated that practitioners approved by the Board of Education could certify that although children were not intellectually handicapped, they were unfit to attend an ordinary public elementary school because of frequent seizures or severe epilepsy.

Fox described median Binet-Simon IQs that were lower than comparative normative standards (boys IQ = 71; girls IQ = 65). Fox also assessed academic achievement using tests of reading, spelling, arithmetic, and reasoning, and also administered the Porteus Mazes to this sample. Not only were the achievement scores of the children with epilepsy lower than normal, in some cases they were even lower than would be predicted given their IQ. Fox's report is probably the first characterization of academic underachievement among children with intractable epilepsy. Many children were retested one year later and demonstrated a significant test-retest performance variability. A trend toward poorer performance was observed, reflecting cognitive deterioration, and very marked deterioration in over 8% of the children tested was described. Fox speculated that variables such as seizure type, seizure severity, or etiological considerations contributed to performance variability, and recommended that these clinical factors should more carefully investigated. Thus, Fox broadened the conception of cognition to include academic achievement and executive function and empirically tested the hypothesis of deterioration. Fox demonstrated considerable performance variability and essentially suggested that decline might represent a phenotype linked to severity of disease characteristics.

The issue of whether and why cognitive deterioration may occur as a function of poorly controlled seizures is a recurring theme and one that continues to be investigated. Multiple publications concerned with cognitive deterioration appeared in the 1920s (Dawson & Conn, 1929; Patterson & Fonner, 1928), 1930s (Barnes & Fetterman, 1938; Fetterman &

Barnes, 1934; Paskind, 1932), 1940s (Arieff & Yacorzynski, 1942; Hilkevitch, 1946; Ya-corzynski & Arieff, 1942), 1950s (Davies-Eysenck, 1952), and through the latter half of the 20th century to the present, and it was again a topic of interest at the recent meeting of the International League Against Epilepsy (2013). Unfortunately, there are multiple methodological issues that have slowed the pace of discovery in the area and that often produced discrepant findings, factors that range from an absence of longitudinal studies in a single cohort to selection bias from studying samples of convenience as specialized epilepsy care facilities (Dodrill, 2004).

In an earlier literature review, Tarter (Tarter, 1972) summarized 17 studies published between 1924 and 1968 that utilized various measures of intelligence. Over half of the studies (9/17) were conducted with institutionalized patients, however, and this overrepresentation served to decrease average IQ scores. Lennox (Lennox, 1942) previously suggested the disproportional influence of institutionalized persons in this literature and commented that the general population of persons with epilepsy was underrepresented in earlier investigations. In fact, Lennox demonstrated this point empirically by comparing the proportions of institutional versus outpatient clinic persons with epilepsy falling at various levels of the IQ spectrum, an important early quantitative demonstration of this point (see Figure 9).
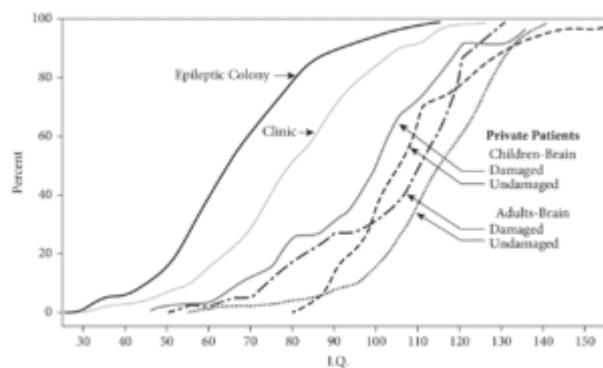

Figure 9. Cumulative frequency graph of epilepsy patients as a function of their institutional status

(From Lennox, 1942).

In a large-scale investigation of non-institutionalized children with epilepsy, Collins and Lennox (Collins & Lennox, 1947) reported an average Stanford-Binet IQ of 104, which is in the normal or average range. Similarly, the mean Wechsler-Bellevue IQ of non-institutionalized adults with epilepsy was 111. Even today, this spectrum bias confound is not always appropriately recognized by epilepsy researchers. Because groups of patients with epilepsy are available for research at selected sites facilitating research on those patients, those results are not necessarily generalizable to the entire epilepsy patient population.

Risk Factors for Cognitive Impairment

Fox's (1924) belief that clinical variables, including seizure type, seizure severity, and seizure etiology, may be related to cognitive outcomes has been firmly established over the subsequent decades using measures ranging from IQ tests to comprehensive neuropsychological batteries to measures of discrete cognitive abilities. Lennox weighed in on this issue as well and proposed the "five foes of mental competence" in epilepsy: genetic influences, organic abnormalities of the brain acquired prior to the onset of the epilepsy, the epilepsy itself and the pathological sequelae of seizures, psychosocial isolation, and overdose with sedative anticonvulsants (Lennox & Lennox, 1960). Pursuing this theme, Collins and Lennox's (1947) reported that symptomatic epilepsy resulting from an acquired brain lesion was a significant factor adversely affecting cognitive abilities, with symptomatic epilepsy patients having IQs approximately 10 points lower than those of nonsymptomatic epilepsy. They also examined a recurring theme in this literature, which was the relationship between seizure type/syndrome and cognitive ability, reporting that the highest IQ scores were present in patients with *petit mal* epilepsy and the lowest associated with having both *grand mal* and psychomotor seizures (Figure 10).
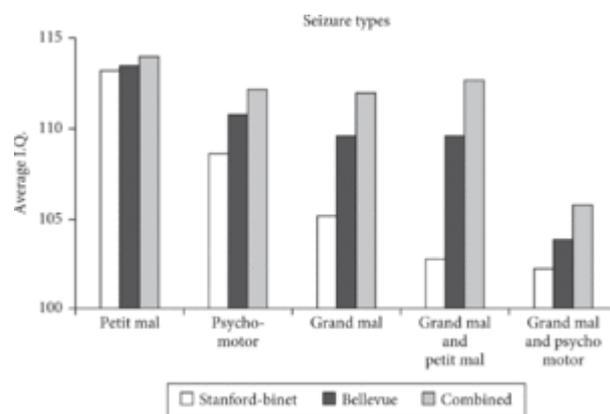

Figure 10. Demonstration of IQ variability in epilepsy patients based upon seizure type/syndrome, as well as whether Stanford-Binet or Wechsler-Bellevue IQ test was used.

From Collins and Lennox (1947).

Characterization of the general cognitive abilities of various epilepsy-patient groups proceeded over the decades. In an influential report, Matthews and Klove (1967) examined Wechsler Adult Intelligence Scale (WAIS) and Halstead performances in patients classified with major motor, psychomotor, and mixed seizures of known and unknown etiology and included, as control groups, patients with brain damage without seizures and non-neurological patients. Patients with symptomatic epilepsy tended to perform more poorly than those with idiopathic epilepsy; patients with psychomotor seizures performed better than those with major motor or mixed seizure types. Interestingly, patients with idiopath-

ic psychomotor seizures of unknown etiology were comparable to non-neurological patient controls.

Effects of EEG Abnormalities on Neuropsychological Function

Epileptiform discharges, which vary in frequency, pattern, amplitude, and other characteristics, are a defining characteristic of epilepsy. During the early 20th century, considerable efforts were devoted to identifying the EEG correlates of different epilepsy syndromes. The 3 Hz spike-wave pattern associated with *petit mal* epilepsy was first described by Gibbs and collaborators in 1935. In 1936, Gibbs and Lennox classified psychomotor seizures as a separate entity from *petit mal* and *grand mal* epilepsy based upon differences in the EEG (Gibbs, Lennox, & Gibbs, 1936). In 1937, the association between "square-shaped waves" and so-called psychomotor seizures was reported (Gibbs et al., 1937). Confirming a relationship between EEG and clinical seizure semiology was revolutionary for both neurology and epileptology and strengthened the independence of neurology as a discipline from psychiatry, medicine, and neurosurgery (Vannemreddy, Stone, & Slavin, 2012).

Given the relationship between different EEG patterns and various clinical phenotypes associated with distinct epilepsy syndromes, it was logical to begin to investigate the relationship of EEG abnormalities and neuropsychological functions. The first investigation addressing the relationship between spike-wave discharges on cognitive performance appeared in 1939 (Schwab, 1939). This report initiated one line of research in the neuropsychology EEG literature that addresses the effects of "subclinical" *petit mal* discharges on tasks of cognitive ability. Tests that have been shown to be sensitive to frequent epileptiform discharges include the Continuous Performance Test (CPT; Mirsky & Van Buren, 1965), pursuit-rotor task (Goode, Penry, & Dreifuss, 1970), decision-making measures, and other tests (Tizard & Margerison, 1963). For example, Mirsky and Van Buren (1965) compared patients with centrencephalic (*absence* or *petit mal*) seizures with those with epilepsy of focal origin on the CPT, a test of sustained attention and vigilance, and found that patients with absence seizures were found to be more impaired. In addition, during subclinical spike-wave bursts, these patients averaged 24% correct responses, while in the absence of bursts the patients performed correctly on 85% of the trials. A fuller account of the impairing effects of subclinical spike-wave discharges on cognitive functions can be found in Mirsky's (1989) review.

A second line of neuropsychology-EEG research addressed abnormal EEG characteristics such as frequency, distribution, and rate of abnormal discharges on qualitative and quantitative neuropsychological indices (Dodrill & Wilkus, 1976b; Hovey & Kooi, 1955; Klove, 1959; Klove & White, 1963; Parsons & Kemp, 1960; Pihl, 1968; Wilkus & Dodrill, 1976). Hovey and Kooi (1955) studied the relationship between "nonanswer responses," or NRs (responses which indicated a momentary deviation from an established goal idea), and patients' performances on the Wechsler intelligence tests. NRs were considered *qualita-*

tive patterns of atypical test performance. For instance, a patient might be providing correct answers, but then may suddenly make a careless error or appear as if not engaged in the task at hand, only to subsequently resume his or her previously appropriate performance. Three patient groups (epilepsy, brain impaired without epilepsy, psychiatric patients) were studied using the Wechsler-Bellevue, with a higher proportion of epilepsy patients demonstrating NRs (44%) compared to the brain impaired (17%) of psychiatric groups (9%). This variability suggested that the transient and subtle performance changes resulted from abnormal EEG discharges.

This hypothesis was subsequently confirmed via simultaneous EEG recording during cognitive performance (Kooi & Hovey, 1957). Dodrill & Wilkus (1976a) examined EEG effects relating presence, average rate, and topographic distribution of discharges. Lower IQ levels were associated with the presence of discharges, particularly for generalized discharges rather than focal discharges, and when discharge rates of more than one per minute were present. Additional work by these investigators demonstrated similar relationships to Halsted-Reitan performance (Wilkus & Dodrill, 1976) and to the relationship between other abnormal EEG patterns and neuropsychological performance (e.g., Dodrill & Wilkus, 1976b).

Similar detrimental effects of epileptiform activity on neuropsychological performance have been detected with depth-recorded interictal EEG (Rausch, Lieb, & Crandall, 1978). The term *transient cognitive impairment* is now used to refer to the cognitive changes that occur as a consequence of interictal epileptiform discharges (Aarts, Binnie, Smit, & Wilkins, 1984; Binnie, Kasteleijn-Nolst Trenité, Smit, & Wilkins, 1987).

This literature has persisted over time—most recently reviewed by Fastenau (2011). However, there continues to be a stronger relationship between prolonged reaction times and sharp wave than with atypical spikes or sharp theta activity (Aarts et al., 1984; Krestel et al., 2011). Recent investigations using driving simulators have demonstrated RT prolongation of over 100 msec—corresponding to increased breaking distance of at least 2.8 meters in a car travelling 100 km/hour (62 miles/hour)—in 40 to 50% of the sample studied (Krestel et al., 2011). In patients with hippocampal depth electrodes, interictal epileptiform discharges observed either contralateral to the seizure focus or bilateral discharges impaired multiple aspects of memory function but not reaction time (Kleen et al., 2013). Although they are beyond the scope of this review, these types of data are relevant to address the question of whether the presence of EEG spikes should be treated in the absence for seizures; clearly more research in this area is needed.

The Influence of Epilepsy Surgery on the Neuropsychology of Epilepsy (and Vice Versa)

Modern conceptualizations of focal epilepsy were introduced by John Hughlings Jackson in his 1870 pamphlet, *A Study of Convulsions*, in which he characterizes focal motor seizures as beginning in localized areas of the contralateral hemisphere rather than in

the medulla, which at time was considered to be the origin of epilepsy (Eadie, 2007). Jackson's focal motor "march" along the sensorimotor homunculus was described in 1875. Jackson considered epilepsy to result from a focal abnormality that he described as being a *discharge lesion*. Because of their focal nature, Jackson postulated that resecting a focal discharge abnormality would eliminate the seizure trigger, thus resulting in a cure (York & Steinberg, 2009).

The first epilepsy surgery was performed in 1886 by Sir Victor Horsley at Queen's Square and was based solely upon clinical findings and semiology (Horsley, 1886). Horsley's patient was a 15-year-old man with posttraumatic epilepsy that developed following a depressed skull fracture when he was 7 years old. The patient's epilepsy consisted of episodes of "Jacksonian" or simple partial status epilepticus. This clinical presentation not only matched the "march" along the sensorimotor homunculus described by Jackson, but it also corresponded to the localization based upon the patient's skull fracture and cortical scar. Horsley and Jackson hypothesized that the seizure onset must develop in the contralateral sensorimotor strip, and the patient underwent surgery, becoming seizure-free after a "vascular cortical scar" was resected. The second patient that Horsley operated on presented with seizures beginning in in the left thumb and forefinger, which Jackson noted was identical to the motor response of electrical stimulation of the motor hand area in primates. At surgery, a tuberculoma was found and removed from the location predicted by Jackson.

Other pioneering epilepsy surgeons included Fedor Krause, who operated on 55 patients in Prussia between 1893 and 1912 and developed stimulation mapping techniques to identify the "primary spasiming center" (LeBlanc, 1990); and Otfrid Foerster in Breslau, who began surgically treating posttraumatic epilepsy in veterans of World War I by identifying epileptogenic regions using galvanic cortical stimulation under local anesthesia (Sarikcioglu, 2007). These early surgical series not only demonstrated the therapeutic viability of epilepsy surgery, but they were also instrumental in establishing functional brain relationship ranging from the cognitive effects of actively discharging focal brain lesions that may be distinct from structural brain lesions to beginning to map the functional cortical specialization by using local anesthesia.

Although these early surgical series were done without diagnostic assistance other than the clinical exam or chance observation of a patient's seizures, Berger's discovery of the EEG in humans in 1929 (Berger, 1929) and confirmed by Adrain and Matthews in 1934 (Adrian & Matthews, 1934) greatly revolutionized the clinical understanding of epilepsy, with implications for characterization of epilepsy subtypes and also for epilepsy surgery. In 1937, Gibbs, Gibbs, and Lennox (1937) proposed the term "psychomotor epilepsy" to describe a characteristic EEG pattern of seizures accompanied by mental, emotional, motor, and autonomic phenomena (Gibbs, Gibbs, & Lennox, 1937). The early electroencephalographic features were characterized in the context of clinical attacks wherein "the patient, though he may perform apparently conscious acts, is not subject to command; he may exhibit involuntary tonic movements; he may display psychomotor disturbances … and on recovery he has complete amnesia for the events which occurred in the

attack." These seizures were later associated with an anterior temporal lobe spike focus, and consideration of epilepsy surgery for these "nonlesional" patients developed early on at the University of Illinois in Chicago and the Montreal Neurological Institute/McGill University based *solely* on the pattern of EEG findings.

Bailey and Gibbs at the University of Illinois in Chicago selected patients for surgery on the basis of interictal EEG criteria in association with the fact that the epilepsy had strong adverse effects on their lives (Bailey & Gibbs, 1951). From the outset, the group at Illinois (Figures 11 and 12) was concerned with the effects of surgery on the patients' neuropsychological status and behavioral and emotional adjustment. The University of Illinois surgical team was led by Percival Bailey (Hermann & Stone, 1989).
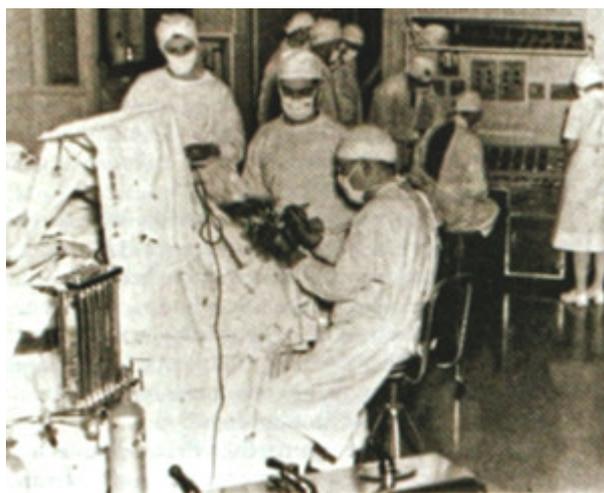

Figure 11. Bailey operating and Gibbs monitoring EEG in the operating theater at the University of Illinois Neuropsychiatric Institute.

When on the faculty at the University of Chicago, one of Bailey's residents was Paul Bucy, who described the Klüver-Bucy syndrome, consisting of visual agnosia, hypersexuality, diminished emotional responsivity, and memory impairment (Klüver & Bucy, 1939). Because damage to hippocampal gyrus and hippocampus were considered critical component results in the Klüver-Bucy syndrome, these structures were not included by Bailey in his temporal lobe resections to decrease the likelihood of post -operative Klüver-Bucy symptoms (Hermann & Stone, 1989), thus probably resulting in poorer surgical outcomes.

Figure 12. University of Illinois Neuropsychiatric Institute faculty circa 1954, including Bailey (4th from left), Gibbs (5th from left), and Bucy (6th from left) in front row.

The neuropsychological component of the University of Illinois program was performed by Ward Halstead, who had been previously been a colleague of Bailey at the University of Chicago. Following surgery, there was no generalized cognitive decline as revealed by the Impairment Index (Halstead, 1958). In addition, significant postoperative *improvements* in the Category Test, Tactual Form Board Memory, and Speech Discrimination Index were described. "An improvement in performance on most indicators is observed after anterior temporal lobectomy, but impairment in relation to normal performance is still seen on some tests." Importantly, "no *severe* deficits attributable to surgical intervention are revealed in these cases." Thus, Halstead's neuropsychological testing established that successfully surgical treatment of epilepsy was not necessarily associated with significant postoperative cognitive decline. That is, there was no significant cognitive procedural morbidity associated with surgical intervention.

Montreal Neurological Institute/McGill University

Although the contributions of Brenda Milner are well known, the systematic use of psychology at the MNI began years earlier. Penfield's desire for psychological input is reflected by his hire of Molly Harrower, who established what is probably the first clinical psychology service at a major hospital.

Recruiting psychology into a medical environment was a novel approach at that time, and it began "a totally new chapter of the kinds of things [that can be done] with a rapport with medicine." "I was really coping with really being the only woman in the hospital, the only woman fellow, the only woman on staff and the only psychologist" (http://www.uflib.ufl.edu/ufdc/?b=UF00006059&v=00001).

Prior to Milner, Penfield collaborated with Donald Hebb. Hebb's contributions to our understanding of basic brain function (e.g., Hebbian circuits, cell assemblies) are well known and anticipated many contemporary concepts, including neural nets. Hebb (1939)

distinguished the effects of epilepsy surgery on intelligence compared to more discrete cognitive abilities. In a patient who had undergone right temporal lobectomy, Hebb noted that a good postoperative IQ score was not evidence that other cognitive abilities were spared, but rather suggested that normal intelligence was a complex concept whose components could be differentiated by cerebral lesions. Hebb's patient retained good language skills (e.g., Thorndike Word Knowledge, Kelley-Trabue Language Completion) but had a concomitant disturbance of nonlanguage capacities including form perception, visual and nonvisual, and disturbance of social comprehension (e.g., Knox Cube, Seguin, Feature Profile; Hebb, 1939).

Hebb and Penfield (1940) subsequently presented psychological findings following frontal lobectomy and suggested that resection of a chronically discharging lesion might be less disruptive to cognitive function than its presence (Hebb & Penfield, 1940). Hebb was also the first to describe increased Full Scale IQ following frontal lobe resection. Prior to the 1930s, the frontal lobes were considered the seat of all that is "noble and good" about humans. Hebb demonstrated that "frontal release" neurological signs (e.g., snout, glabellar), which at that time were considered pathognomic of focal frontal lobe disease, did not result from large prefrontal lesions but, rather, occurred due to the combination of frontal lesions with diffuse pressure effects associated with expanding mass lesions. This difference from the traditional clinical dogma resulted from the MNI's early detection of tumor and more rapid referral for cognitive evaluation compared to other centers. When reporting his early findings at the American Psychological Association, Hebb's results were met with skepticism by more senior psychologists: "I don't think I was regarded as a liar, just an incompetent" (Hebb & Penfield, 1940). Although it was not widely known, one of the early patients in Hebb's series on frontal lobe lesions was Penfield's sister. In fact, it was Penfield's sister who was being described as having trouble organizing family meals when describing the real-world effects in goal-directed behavior change following frontal lobe resection (Penfield & Evans, 1935).

Description of significant memory decline following temporal lobectomy for treatment of medically refractory seizures is commonly associated with Brenda Milner, William Scoville, and patient Henry Molaison (who became known throughout cognitive neuroscience by his initials H.M. prior to his death in 2008; see Figure 13). However, there is a history of clinical discovery of memory risks associated with hippocampal resection that is described in varying detail in the 1950s. Wilder Penfield at the Montreal Neurological Institute first observed significant memory impairment following unilateral temporal lobe surgery dysfunction in 1951–1952. Two of Penfield's patients experienced significant memory decline following unilateral temporal lobe surgery, and Penfield hypothesized that both patients must have had additional pre-existing right temporal lobe damage for this magnitude of memory impaired to develop (Penfield & Milner, 1958). In contemporary nomenclature, insufficient functional reserve of the contralateral hippocampus was present to encode new memories following resection of the temporal lobe containing the primary seizure focus (Chelune, 1995). This suspicion was confirmed years later when

one of these two patients came to autopsy and a pale and shrunken right hippocampus was identified (Penfield & Mathieson, 1974).

Brenda Milner was a graduate student of Hebb, and he recommended to Penfield that she evaluate his surgical patients pre- and postoperatively. However, through her careful examination of patient H.M., as well as other patents developing postoperative amnesia following surgery by William B. Scoville at the Hartford Hospital in Connecticut, Milner demonstrated the important dissociation between episodic and procedural memory, which greatly facilitated the fractionation of "memory" into multiple and largely independent neural systems.

With the possible exception of Phineas Gage, H.M. is the most widely recognized case report in neuropsychology. H.M's development was normal until 7 years of age, when he was knocked down by a bicycle, sustained a laceration in the left supraorbital region, and was unconscious for approximately 5 minutes (Corkin, 1984). H.M. had a substantial seizure burden, averaging 10 seizures a day as well as experiencing a "major seizure" weekly. At age 27, H.M. underwent bilateral mesial temporal lobe resection on September 1, 1953 that included prepyriform gyrus, uncus, amygdala, hippocampus, and parahippocampal gyrus

> On formal testing the contrast between his good general intelligence and his defective memory was most striking. On the Wechsler-Bellevue Intelligence Scale he achieved a full scale IQ rating of 112, which compares favorably with the preoperative rating of 104 reported by Dr. Liselotte Fischer in August, 1953, the improvement in arithmetic being particularly striking. An extensive test battery failed to reveal any deficits in perception, abstract thinking, or reasoning ability, and his motivation remained excellent throughout.

> On the Wechsler Memory Scale (Wechsler, 1945) his immediate recall of stories and drawings fell far below the average level and on the "associate learning" subtest of this scale he obtained zero scores for the hard word associations, low scores for the easy associations, and failed to improve with repeated practice. These findings are reflected in the low memory quotient of 67. Moreover, on all tests we found that once he had turned to a new task the nature of the preceding one could no longer be recalled, nor the test recognized if repeated

> (Scoville & Milner, 1957, 2000).

Scoville first described H.M.'s amnesia at the Harvey Cushing Society Meeting in 1953: "bilateral resection of the uncus and amygdala alone, or in conjunction with the entire pyriform amygdaloid hippocampal complex, has resulted in no marked physiologic or behavioral changes with the exception of a very grave, recent memory loss, so severe as to prevent the patient from remembering the locations of the rooms in which he lives, the names of his close associates, or even the way to toilet and urinal (Scoville, 1954, p. 65).
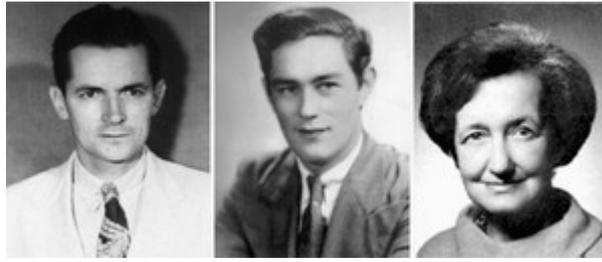
Figure 13a, b, and c William Scoville, M.D., patient H.M, Brenda Milner, Ph.D.

Wilder Penfield learned of patient H.M. in 1956 and noted the striking similarities on cognitive outcomes between H.M. and his patients developing significant memory impairment: "William Scoville, MD, described to me the psychotic patients on whom he had operated, removing both hippocampal zones in one procedure, with the untoward results similar to my own. Our talk took place during a meeting of neurosurgeons (the proper place for discussion of unhappy results!)" (Penfield & Mathieson, 1974, p. 145).

Following surgery, there has been a nearly complete inability to learn new information, with the exception of certain motor or procedural tasks, but intelligence and other cognitive abilities were well preserved. Although seizure frequency improved, H.M continued to have the smaller spells, but his generalized seizure frequency was reduced significantly, and he could go as long as a year between episodes (Corkin, 1984). Thus, by contemporary characterization of surgical outcome, H.M. would be characterized as a "double hit," that is, developed both a poor memory outcome combined with incomplete seizure control (Langfitt et al., 2007).

Scoville and Milner (1957) described two other patients with significant recent memory impairment following bilateral temporal lobectomy, although surgery in these cases was performed for psychiatric indications rather than for epilepsy (Scoville & Milner, 1957). Scoville was a pioneer of orbital undercutting, and psychosurgery was considered a viable treatment option for medically refractory psychiatric patients as well. As reported by Scoville and Milner, "In view of the known close relationship between the posterior orbital and mesial temporal cortices, it was hoped that still greater psychiatric benefit might be obtained by extending the orbital undercutting so as to destroy parts of the mesial temporal cortex bilaterally."

D.C. was a 47-year-old physician who had stopped his practice because of paranoid schizophrenia and underwent bilateral medial temporal lobectomy combined with orbital frontal undercutting. Following surgery, D.C. was outwardly friendly and nonaggressive, although paranoid thought content continued. He underwent neuropsychological testing and obtained a Wechsler-Bellevue IQ of 122 and a Wechsler Memory Scale Memory Quotient of 70. In describing the memory deficit, Scoville and Milner reported, "At the examiner's request he drew a dog and an elephant, yet half an hour later did not even recognize them as his own drawings" (p. 17).

M.B., was a 55-year-old who with normal memory who underwent bilateral temporal lobectomy to treat manic-depression; following surgery, she developed a profound amnesia involving both retrograde and anterograde components. "Her immediate recall of stories and drawings was inaccurate and fragmentary, and delayed recall was impossible for her even with prompting; when the material was presented again she failed to recognize it" (p. 17). No formal test scores were presented.

Five additional patients underwent bilateral temporal lobe resections that were associated with moderately severe memory deficits. These patients were able to "retain some impression of new places and events, although they are unable to learn such arbitrary new associations as people's names and cannot be depended upon to carry out commissions. Subjectively, these patients complain of memory difficulty, and objectively, on formal tests, they do very poorly irrespective of the type of material to be memorized" (p. 18).

Montreal's experience with significant recent memory impairment following unilateral left temporal lobectomy was published in 1958, and this series is particularly valuable, since formal neuropsychological testing is included (Penfield & Milner, 1958). The first patient presented was a 28-year-old man with a history of recurrent seizures since age 12 years. His EEGs suggested bilateral involvement that was maximal from the left side. Prior to surgery, he complained of being forgetful but could remember everyday events without difficulty, and preoperative testing revealed a Wechsler-Bellevue Full Scale (FSIQ) of 106 (Verbal IQ = 102, Performance IQ = 109), and a Wechsler Memory Scale Memory Quotient (MQ) of 94. Following left temporal lobectomy, he became aphasic and presented with a right upper quadrant field defect. Testing approximately one month after surgery revealed IQ decreases in FSIQ to 88 and VIQ to 80, with a less marked decrease in PIQ to 100. However, IQ assessed 6 months following surgery returned to baseline levels (FSIQ = 104; VIQ = 102, PIQ = 105). His MQ was 72, and this remained unchanged over the next 2 years.

The second patient was a 46-year-old man whose seizures began at age 35 and were associated with momentary lapses in his conversation; prior to onset he had experienced a single convulsion in infancy. He had undergone temporal lobe resection sparing the hippocampus 5 years earlier that was associated with transient aphasia. Psychological assessment prior to the second operation revealed a Wechsler-Bellevue IQ of 119 (VIQ = 125, PIQ = 110). Memory was not formally assessed. Following a second surgery that included the hippocampus, the patient developed a significant memory impairment in which only Penfield himself was correctly identified. One month following surgery, the patient obtained a FSIQ of 120 (VIQ = 129, PIQ = 107). Although the complete Wechsler Memory Scale was not administered, poor performances on Logical Memory and Paired Associate Learning were described. Five years later, the complete Wechsler Memory Scale was administered, and the patient obtained a Memory Quotient of 97. The patient returned to work following surgery, but was he demoted to a draftsman since he was unable to handle the administrative responsibilities associated with being a civil engineer (Milner, 1966). At autopsy, extensive atrophy of the right hippocampus was noted. Ap-

proximately 22 mm of the posterior hippocampus on the resected left side was intact at autopsy.

No other patients with marked post-operative memory impairment from the Montreal series are presented formally. However, Milner (1966) later referred to four additional patients who displayed memory impairment following temporal lobectomy (TL). One right-TL patient with right-hemisphere language dominance developed amnesia following surgery. Three patients developed moderate memory loss following dominant hemisphere temporal lobectomy, and one patient developed a moderate memory deficit following left TL in which the hippocampus was spared. Formal psychological testing was not provided. Penfield and Milner (1958) concluded that although removal of the hippocampus and surrounding tissue does not typically alter memory function, significant memory impairment may be present following unilateral temporal lobectomy if contralateral mesial temporal dysfunction is present (i.e., functional reserve). Persistent amnesia "has been seen only in patients with electrographic or radiologic evidence of damage to the opposite temporal lobe" (Milner, 1969, p. 34).

It is against the backdrop of significant memory decline following a unilateral temporal resection that the Wada test, which was initially used only for establishing cerebral language representation, was modified to include a memory component (Milner, Branch, & Rasmussen, 1962). Significant memory decline was attributed to significant bilateral disease that went unrecognized during the pre-surgical evaluation reflecting inadequate functional reserve of the contralateral hemisphere (Chelune, 1995). By introducing items to be remembered during the period of hemispheric anesthesia, the effects of surgical resection on memory could be modeled and risk for significant postsurgical decline estimated.

Wada (Figure 14) initially developed selective hemispheric barbituraization during post World War II Japan to limit bilateral seizure effects associated with electroconvulsive therapy (ECT) (Wada, 1997). By "anesthetization through a carotid route to prevent seizure bilateralization," Wada reasoned that the cognitive side effects associated with bilateral ECT would be minimized. This technique was used in epilepsy surgery evaluation to establish cerebral language representation in epilepsy surgery candidates, since epilepsy was known to potentially alter cerebral language dominance. The memory component of Wada testing was introduced several years later after multiple cases of severe memory decline were observed following unilateral TP (Penfield & Milner, 1958). The epilepsy surgery program at MNI was influential in establishing neuropsychology as a valuable diagnostic and clinical service. The goals of neuropsychological testing at Montreal were explicitly to identify specific neuropsychological deficits reflecting the integrity of focal brain regions so that resective surgery could be performed without significant cognitive morbidity.

Figure 14. Juhn Wada, M.D.

University of London, Guy's Maudsley Hospital

The University of London epilepsy program was directed by the neurosurgeon Murray Falconer, who developed *en bloc* resections of the temporal lobe the facilitated pathological studies and identified hippocampal pathology as being critical for clinical outcome (Meador, Loring, & Flaningin, 1989). Victor Meyer and Aubrey Yates were the psychology members of that program who reported a greater surgical effect for paired associated learning compared to other psychological measures, including a New Word Learning and Retention Test or 24 hour retention (Meyer & Yates, 1955). This paper indicated the sensitivity of paired associated learning to hippocampal dysfunction, which was subsequently replicated years later (Rausch & Babb, 1987), and anticipated contemporary theories of hippocampal function as a critical structure involved in "binding" associations. This group also described difficulty in establishing reliable neuropsychological change following resection of the nondominant temporal lobe. Although, "the operation on the dominant side results in a severe deficit of auditory learning, contrary to expectations, the group with operation on the nondominant temporal lobe failed to lower scores on nonverbal tests." This theme has been repeated time and time again over the decades (Barr et al., 1997).

Serafetinides and Falconer (1962) reported 34 consecutive patients who had undergone right temporal lobectomy in which memory status was characterized based upon spontaneous complaints, answers to leading questions, complaints of the informant, and, when available, formal tests. Although seven patients (21%) were described as having a recent memory impairment following surgery, four reportedly had persistent memory impairment pre-operatively. All but one of these patients had postoperative epileptiform activity recorded from the left, nonoperated, temporal lobe, which was consistent with Penfield

and Milner's (1958) postulation about the importance of the contralateral mesial temporal lobe dysfunction following unilateral temporal lobe resection.

Although Serafetinides and Falconer's patients presented with clinical memory impairment, they did not develop an amnestic syndrome. The authors concluded that "the type of memory defect we are now considering does not correlate with the more formal psychological test results" (p. 254). The authors further stated that the memory deficit was "usually compensated for," illustrating an absence of an amnestic syndrome.

Johns Hopkins University

Earl Walker described four cases of unilateral temporal lobectomy resulting in marked memory impairment (Walker, 1957), although the magnitude of memory decline did not appear to represent frank amnesia described in other series. Walker concluded that "memory disturbance occurs in not more than 10% to 15% of temporal lobe resection and may be present after removal of the lobe of either the dominant or the nondominant hemisphere" (p. 550). This is the first estimate of the prevalence of meaningful memory decline following unilateral temporal lobe resection, and these figures subsequently were used to validate results of amobarbital memory studies (e.g., Klove, Grabow, & Trites, 1969). Walker also first described the relative preservation of motor skill acquisition and retention, in addition to relatively normal digit span and remote memory, an important observation for our understanding of memory mechanisms and one for which Walker usually is not credited.

A second generation of epilepsy surgery programs emerged in the late 1970s and early 1980s. Notable programs (neuropsychologists) include the University of Washington (Carl Dodrill), Mayo Clinic (Robert Ivnik), Yale University (Robert Novelly), University of California at Los Angeles (Rebecca Rausch), and at the MNI, a passing of the neuropsychology baton from Brenda Milner to Marilyn Jones-Gotman. Important contributions to neuropsychology were made by all programs, and space does not permit a comprehensive review of each program's role in shaping neuropsychology. However, Dodrill's emphasis on psychosocial aspects of epilepsy (Dodrill, 1983) in many ways anticipated the concept of quality of life as an important construct to characterize epilepsy and its treatment (Devinsky et al., 1995). Early on, Dodrill (1978) also developed a disease-specific approach to the neuropsychological assessment of epilepsy. Rauch demonstrated subfield specialization of the hippocampus to the hard, but not to the easy, word pairs of the Wechsler Memory Scale Paired Associate Learning task (Rausch & Babb, 1993). Jones-Gotman's contribution to the understanding of temporal lobe epilepsy was unique in neuropsychology, with interests in temporal lobe contributions to noncognitive constructs of smell and taste (Jones-Gotman et al., 1997; Small, Jones-Gotman, Zatorre, Petrides, & Evans, 1997). Although Novelly moved from epilepsy to other areas of interest, his paper in the *American Psychologist* (Novelly, 1992) remains a "must read" for anyone interested in the synergy between neuropsychology and epilepsy.

Summary

The development of neuropsychological understanding of the epilepsies evolved in concert with advancements in the broader domains of cognitive psychology and epilepsy. First, early studies typically (but not exclusively) addressed intelligence. Assessment of higher cognitive functions was in its formative years and with the introduction of the Binet-Simon scales, and especially their adaption for use in the United States (e.g., the early Vineland translation and the later Stanford-Binet revision), characterization of intellectual status in epilepsy followed quickly. As greater understanding of cognition developed, and newer tests and measures were developed to assess those concepts, appreciation of the cognitive correlates of epilepsy expanded apace. Second, much of the early literature came from very limited segments of the epilepsy population, most often from specialized institutions (or colonies) serving the more complicated and severely affected individuals. Furthermore, individuals at these early facilities (and persons with epilepsy outside these institutions) were severely stigmatized by the pseudoscience of eugenics. Over time more representative portions of the population were sought out and investigated, which yielded a less biased but still imperfect characterization of the relationship between epilepsy and intelligence and broader cognitive status. Even today, research tends to study persons with epilepsy presenting to specialized tertiary care medical centers, although more representative population-based studies of cognition are available, particularly among children with epilepsy. Third, classification and taxonomy of the epilepsies developed from early rudimentary systems to the evolving and increasingly sophisticated international classification of epileptic seizures and syndromes that was recalibrated in 2010. The neuropsychological features of these syndromes and their primary cognitive signatures have developed accordingly.

Major advances in technology beginning in the 1970s have greatly influenced the care and evaluation of epilepsy. Video EEG allowed simultaneous recording of EEG and behavior, which provided a valuable tool to correlate semiology with EEG development. Imaging has rapidly evolved. The CT scan first appeared clinically in the mid-1970s and represented a significant improvement over existing imaging techniques (i.e., skull X-ray and pneumoencephalogram). In the mid-1980s, MRI was introduced and began to alter the ability to image abnormalities related to the epileptogenic focus (e.g., hippocampal sclerosis, cortical dysplasias). Additional imaging techniques and postprocessing procedures have revolutionized our ability to link brain with behavior and cognition and now include an array of functional neuroimaging techniques (e.g., PET, MEG, fMRI) and quantitative MRI metrics of gray matter, white matter, and functional connectivity. As medical technology advances, neuropsychology will continue to better characterize the neurobiology of cognitive impairment associated with epilepsy and its treatment. Neuropsychology's next frontier, however, will be to move beyond simple disease characterization and capitalize on new insights of the mechanisms associated with seizure generation and epilepsy to develop techniques that maximize brain health, thereby mitigating epilepsy's significant cognitive consequences.

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