

# NEUROLOGY IN SOUTHERN CALIFORNIA: *A Historical Perspective*



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## INTRODUCTION

Located in the far southwestern corner of the United States, Southern California was settled far later than many other parts of the country. Over the past 125 years, region has experienced tremendous population, economic, and cultural growth. Medical and neurological care has progressed from the questionable practices of the early quacks and charlatans to cutting edge therapies for previously devastating diseases. Although the early history of neurology in the area was marked by its relative late development and geographic isolation, the same historical trends that affected neurology in other parts of the country also made their mark locally, albeit in a somewhat delayed fashion. Since the end of the Second World War, Southern California has developed into important center for clinical neurology and neurological research, thanks to the visionary leadership of influential local neurologists and neuroscientists.

## MEDICINE IN SOUTHERN CALIFORNIA IN THE 19TH CENTURY

California did not join the Union until 1850, at which time the future metropolises of Los Angeles and San Diego were still small, dusty frontier towns, each with only a few thousand residents <sup>1</sup>. Although there appear to have been Americans practicing medicine in this area under Mexican rule prior to California achieving statehood <sup>2</sup>, records suggest that the first formally trained American physicians did not arrive in Southern California until in the 1850's. John S. Griffin, an alumnus of the University of Pennsylvania School of Medicine, initially came to the San Diego region during the Mexican-American War as an assistant surgeon under General Kearny, and later established a medical practice in Los Angeles in 1854 <sup>3</sup>. David B. Hoffman, an early graduate of Toland Medical College (which later became the University of California at San Francisco (UCSF)), began seeing patients in San Diego in 1853 <sup>4</sup>.

Neurology began to develop as a medical specialty in the Northeast around the time of the Civil War (1861-1865), driven by the pioneering contributions of Silas Weir Mitchell and William Hammond <sup>5</sup>. At that time, the medical community in Southern California was still in its infancy, with the first local general medical societies not established until in 1870 in San Diego <sup>4</sup>, and not until 1871 in Los Angeles <sup>2</sup>. Early concerns of these local medical societies included the emphasizing the distinctions between legitimate practitioners from "charlatans" and "quacks," establishing formal fee schedules, and promoting public sanitation <sup>2</sup>. While infectious diseases and traumatic injuries formed the bulk of the medical problems encountered by these early physicians, psychiatric disorders became increasingly common. Although part of the increased incidence of mental disease may be attributed to the rapid rise increasing population in the region, some have speculated that the unique circumstances surrounding the California gold rush may have been particularly favorable for the development of psychiatric disorders <sup>6</sup>.

The first hospital in the region was the original Los Angeles County Hospital (Figure 1), established in 1858 by six members of the Sisters of Charity <sup>3</sup>. The increasing demand for indigent care resulted in the construction of a much larger county owned hospital complex in Los Angeles by 1878 (Figure 2). A number of other small hospitals were established over the next 50 years by religious orders and private physicians <sup>6</sup>. The early hospitals were underfunded, understaffed, and relatively unhealthy destinations. Neither antiseptic nor aseptic techniques were practiced and few surgeries were performed. The quality of patient care was further limited by the absence of formally trained nurses. The



Figure 1: The Los Angeles County Hospital in 1860.



Figure 2: Panoramic views of the expanded Los Angeles County Hospital circa 1916.

primitive medical practices were exacerbated by the relative geographic isolation of Southern California, but largely reflected the dismal conditions common to the era <sup>3</sup>.

After the Civil War, Los Angeles and San Diego initially experienced steady and parallel growth and development. However, in 1872, intense political and economic maneuverings resulted in the extension of the recently completed transcontinental railroad to Los Angeles rather than San Diego. Los Angeles became the second western terminus of the railroad (with San Francisco being the first), paving the way for its development into the predominant urban center in Southern California. Encouraged by low rail fares and the promise of "terrestrial paradise," immigrants flooded into Los Angeles from the Midwest and other parts of the country by the 1880's, with the population expanding by over 350% in that decade <sup>1</sup>. The regional growth of medical care matched

the regional growth in population. The early history of neurology in Southern California was thus centered on Los Angeles.

## THE ERA OF NEUROPSYCHIATRY IN SOUTHERN CALIFORNIA

The first records of neurological care in Southern California are from the Los Angeles County Hospital. The population census from 1879 documents the treatment of 32 patients with “nervous affectations.” Both neurological and psychiatric disorders fit into this diagnostic category, which included a significant number of patients suffering from insanity<sup>3</sup>. Neurology and psychiatry were closely intertwined in the latter part of the 19th century and the early part of the 20th century<sup>5</sup>, and the early records from the County Hospital reflect this close relationship. At various times, neurology was included under a number of different departments, including the department of diseases of the mind and nervous system, the department of neuromedicine, and the department of nervous and mental diseases. The growing population of neurological and psychiatric patients treated at the County Hospital paralleled the rapidly growing population in Los Angeles. The annual census for the department increased to 72 by 1889, and to over 800 by 1910. The bulk of the service remained psychiatric in nature, with 420 patients admitted for insanity and 260 patients treated for substance abuse and its various complications. Only 179 of the patients seen in 1910 would likely fall under the purview of neurology as we define it today<sup>3</sup>.



Figure 3: Henry G. Brainerd

Prior to 1916, the only physicians in the area with experience treating diseases of the nervous system were the neuropsychiatrists<sup>7</sup>, who were primarily trained in psychiatry and had a more limited exposure to neurology<sup>8</sup>. The most prominent of the early neuropsychiatrists was Henry G. Brainerd (Figure 3). He had graduated from Rush Medical School in 1878 and served as the assistant superintendent for the insane at the Iowa Asylum for the Insane until 1886, when he emigrated west to Los Angeles<sup>3</sup>. He was an early member of the Los Angeles County Medical Association, and presented papers covering a wide variety of topics relevant to neuropsychiatry at their meetings, including brain tumors<sup>9</sup>, cerebral anatomy, post-traumatic Jacksonian epilepsy, neurosyphilis, and criminal insanity<sup>2</sup>. He served as chairman of the department of neurology, first at the University of Southern California (USC) College of Medicine and later at the Los Angeles Medical Department of the University of California<sup>3</sup>. Other neuropsychiatrists soon followed, including James H. McBride who came to Los Angeles in 1902 and assumed a position as professor of neurology and digestive diseases at the USC College of Medicine<sup>3</sup>. McBride had previously served as superintendent of two psychiatric institutions in Milwaukee, the Hospital for the Insane and the Sanitarium for Nervous Diseases. He was an early member of the American Neurological Association (ANA), admitted in 1888, and later in his distinguished career served as the president of the organization in 1919<sup>10</sup>.

## EARLY MEDICAL SCHOOLS IN SOUTHERN CALIFORNIA

The first medical school established in Southern California was the USC College of Medicine, founded in Los Angeles in 1885. Although USC, a small Methodist university established in 1881, conferred the M.D. degree, the College of Medicine itself was otherwise supposed to be a financially and academically independent institution. Unfortunately, the institution was financially strapped, lacked sufficient laboratory facilities and was only intermittently able to provide adequate clinical opportunities for its students at the County Hospital. The quality of medical education suffered correspondingly. After getting a poor rating from Abraham Flexner in his 1909 on medical schools in North America, the faculty petitioned the University of California to assume control of the school in hopes that additional state funding might improve the educational caliber of the institution. Although the petition was successful, and the school became the Los Angeles Medical Department of the University of California, funding remained scarce, and training of medical students was discontinued in 1915<sup>11</sup>.

The second medical school in Los Angeles was the College of Physicians and Surgeons, which was established in 1903. It was originally an independent institution, but after the College of Medicine terminated its relationship with USC in 1909, the College of Physicians and Surgeons established its own affiliation with USC, becoming its Medical Department. However, it too was plagued by financial difficulties and was forced to close its doors in 1919. USC would not start its own medical school until 1928, when the present USC School of Medicine began training student physicians<sup>3</sup>.

A number of other medical schools were founded in Southern California around the turn of the century. The College of Medical Evangelists (CME) opened in 1909. Preclinical instruction was conducted at the main campus in Loma Linda, while clinical training took place at the County Hospital and White Memorial Hospital. CME changed its name to the Loma Linda University Medical School in 1961, and clinical activities were shifted to the Loma Linda Medical Center in 1965<sup>3</sup>. Two early osteopathic medical schools were also established in the area. The Pacific School of Osteopathy opened in 1896 in Anaheim and the Los Angeles College of Osteopathy opened in 1904. These two institutions would merge in 1914 and were ultimately converted into an allopathic medical school, the California College of Medicine, which later became the University of California, Irvine (UCI) School of Medicine<sup>12</sup>.

## NEUROLOGY EMERGES FROM NEUROPSYCHIATRY

Los Angeles experienced another explosion in immigration after the First World War, with the population expanding

from less than 600,000 in 1920 to over 1.2 million in 1930. The new residents were attracted by the increasing industrial and commercial strength of the region, particularly the discovery of vast oil reserves, the lure of the motion picture industry in Hollywood, and the increasing shipping capacity at the Port of San Pedro <sup>1</sup>. Along with luring those seeking fortune and fame, the population boom also brought physicians with formal neurological training to the region, including Carl Rand, Samuel Ingham, Johannes Nielsen, and Cyril Courville. These four became the local leaders of a flourishing neuroscience community in Los Angeles, and played prominent roles in the growth of departments of neurosurgery, neurology, and neuropathology at the Los Angeles County Hospital, the USC School of Medicine, and CME <sup>3</sup>. Their arrival heralded the beginning of the development of neurology as an independent medical specialty in Los Angeles, separate from its neuropsychiatric origins <sup>13</sup>.

Carl Rand (Figure 4) was the first of the four to come to Los Angeles, arriving in 1916. He had trained for one year in neurosurgery under Harvey Cushing at the Peter Bent Brigham Hospital in Boston and for another year in general surgery in Chicago before joining an established surgical practice in Los Angeles <sup>14</sup>. Rand's training in the young field of neurological surgery offered him a different perspective on the brain and nervous system relative to the existing neuropsychiatrists in the region. He quickly became established as one of the leading experts in neurological disease in the Los Angeles <sup>3</sup>. Soon after his arrival, the United States was drawn into the First World War, and Cushing arranged for Rand to serve with a military surgical team that was stationed in France. During this time, he initially developed an interest in traumatic injuries to the nervous system and was part of a team that operated on 64 patients with significant head trauma <sup>9</sup>. His military experiences served him well when he returned to home after the war ended. Los Angeles in the 1920's was a hotbed of the rapidly developing Southern California car culture. The city streets were already becoming congested, and by 1924, the busiest intersection in Los Angeles saw twice the daily traffic of the next busiest intersection elsewhere in the country <sup>15</sup>. Increases in traffic volume resulted in an increased incidence of motor vehicle accidents and associated cases of head trauma. The high volume of traumatic cases that passed through Rand's operating room at the Los Angeles County Hospital helped hone his expertise and positioned him as one of the leaders in the surgical community in the management of traumatic injuries to the brain and spinal cord <sup>9</sup>.



Figure 4: Carl Rand

The first medically trained neurologists to practice in Southern California were I. Leon Meyers and Arthur E. Timme, who both arrived in 1919 <sup>13</sup>. They were followed closely thereafter by Samuel D. Ingham (Figure 5), who would later be referred to as the “dean of neurologists in Southern California” <sup>16</sup>. Prior to coming to Los Angeles for health reasons in 1920 <sup>7</sup>, Ingham had developed a successful career in academic neurology in Philadelphia at the Medico-Chirurgical College of Philadelphia and at Temple University. He authored a number of scientific articles covering a wide spectrum of neurological disease and presented several papers at the annual meetings of the ANA in conjunction with another Philadelphia neurologist, Theodore H. Weisenburg <sup>17</sup>. His earliest positions in Los Angeles were as an attending neurologist at the County Hospital and an associate professor of neurology at CME, and he later served as the chairman of the department of neurology at the USC School of Medicine from 1931 until 1950 <sup>3</sup>. Ingham was known for his unorthodox neurological examinations and his complex writings, which, amongst other topics, speculated on the neuroanatomical basis of consciousness <sup>3, 16, 18</sup>.



Figure 5: Samuel D. Ingham

One of the interns at the County Hospital who worked with Ingham shortly after his arrival was Johannes Nielsen (Figure 6). He subsequently decided to pursue further training in neurology, at the Battle Creek Sanitarium and the University of Vienna. He returned to Los Angeles in 1929, joining Ingham's private practice in neurology and psychiatry, and serving as an attending neurologist at the County Hospital. He was initially a lecturer in neurology at CME, and joined the department of neurology at the USC School of Medicine when Ingham became chairman. He later assumed the chairmanship after Ingham's retirement in 1950 <sup>19</sup>. He was also a charter member of the American Academy of Neurology (AAN) in 1948 <sup>5</sup>, and elected president of the ANA in 1955 <sup>19</sup>. While Ingham has been described as “quiet,” “philosophic gentleman” <sup>3</sup> who “dislike[d] ostentation” <sup>16</sup>, Nielsen was a “showman” <sup>3</sup> who “should have been an actor” and “could hold an audience enthralled” <sup>20</sup>. He was a prolific author on many topics in neurology, but perhaps most widely known for an influential monograph describing the clinical significance of agnosia, apraxia, and aphasia <sup>19, 21</sup>. Later in his career, he would direct a Veterans Administration (VA) treatment and research center for aphasic disorders at the Long Beach VA Hospital <sup>22</sup>.



Figure 6: Johannes M. Nielsen

Residency programs in Southern California lagged behind other programs located in the more established parts of the country. While hospitals in Philadelphia began training residents as early as the late 1700's <sup>23</sup>, the first residency program in Los Angeles (in urology) was not established until 1919 <sup>6</sup>. Formal residency training specifically geared towards neurology was sparse in the early part of the 20th century. The first compilation of American Medical Association (AMA) approved residencies was released in 1927, and shows only two neurology residency positions in the entire country, at University Hospital in Minneapolis



Figure 7: Cyril B. Courville

and Isolation Hospital in St. Louis<sup>24</sup>, although there were likely a number of informal training programs in existence at that time. The compilation also lists 360 neuropsychiatry positions, more than any other medical specialty, including 2 at the Los Angeles County Hospital and 9 in the Southern California State Mental Hospital in San Bernardino<sup>24</sup>. These numbers suggest a distinct need for specialized training in diseases of the mind and nervous system and reflect the relative emphasis on combined neurological and psychiatric training during this era. The American Board of Psychiatry and Neurology was established in 1934 to establish uniform standards for the training and certification of psychiatrists and neurologists<sup>5</sup>. However, as Freeman et al. note, the joint nature of the board, with separate emphasis on psychiatry and neurology and separate support from the American Psychiatric Association and the American Neurological Association, foreshadowed the end of the era of neuropsychiatry and the beginning of the development of the independent specialties of neurology and psychiatry<sup>25</sup>.

The first informal neurology resident at the Los Angeles County Hospital was Eugene Ziskind, who began his training in 1925<sup>7</sup>. One of his early contributions was combining neurology and neurosurgery services into a single service, and consolidating the neurology patients, who had previously been scattered throughout the medical wards of the hospital, into their own unit<sup>13</sup>. The AMA officially sanctioned the neurology residency training program at the County Hospital in 1933. The first graduates from an official neurology training program in Los Angeles were Paul Fitzgibbons, who was a former professional football player and notoriously profane; Elinor Ives, who was the first female neurologist in Southern California; and Karl Von Hagen, who later succeeded Nielsen as the chairman of the department of neurology at USC<sup>3,7</sup>. Given the combined nature of the neurology and neurosurgery services, the early neurosurgery residents were also formally trained in neurology. The first of Rand's neurosurgical residents was Leo Adelstein in 1928, who was followed by Cyril B. Courville (Figure 7) in 1929<sup>7</sup>.

Courville had been locally trained, graduating from CME in 1925, and interning at the County Hospital in 1926<sup>26</sup>. He spent the following year as a volunteer assistant on Cushing's service at the Peter Bent Brigham Hospital and developed a keen interest in neuroanatomy<sup>14</sup>. He returned to CME and pursued anatomical studies before deciding to become a neurosurgical resident at the County Hospital with the intention of specializing in neuropathology. During his residency training, he began to study the neuropathological correlates of head trauma<sup>27</sup>. After the completion of his residency, he was appointed chairman of the department of neurology at CME and established the Ramon-Cajal Laboratory of Neuropathology at the County Hospital<sup>27</sup>. His early studies of traumatic brain injury developed into a career defining research program. In his later years, Courville also made significant contributions to the understanding of perinatal anoxic brain injury. Like Nielsen, Courville was among those invited to be charter members of the AAN<sup>5</sup>.

The early centers of neurology in New York, Boston, Philadelphia, and Chicago had already established regional neurological societies by the 1890's<sup>28</sup>. As the ranks of the neurologists and psychiatrists in Southern California steadily expanded, they too began to hold meetings to review difficult cases and discuss medical and scientific topics of mutual interest. These meetings, initially informal in nature, evolved into the Los Angeles Society for Neurology and Psychiatry, which held its inaugural meeting in 1921. The wide-ranging topics discussed at the early meetings covered many disparate subjects in neurology and psychiatry, as reflected by the titles of the papers presented at the inaugural meeting: "Friedreich's Ataxia," "Some Observations after an Intelligent Survey of the Hawaiian Islands," and "Some Remarks on the Problem of Drug Addiction." However psychiatric disorders remained the primary focus of the society during its early years, mirroring the relative predominance of neuropsychiatry in the community<sup>29</sup>.

In 1932, meetings began to be held at the recently constructed new Los Angeles County Hospital (Figure 8) to encourage the participation of the academic physicians on the staffs of CME and the newly reestablished USC School of Medicine. Rand, Ingham, Nielsen, and Courville were all attending physicians at the hospital at this time, and they played an important role in increasing the emphasis on neurology at these meetings. They sought to improve the scientific caliber of the presentations, and incorporated neuropathological material from Courville's laboratory for clinical correlations. However, the shift in



Figure 8: The "new" Los Angeles County Hospital, built in 1932.

focus from psychiatry to neurology was not well received by the psychiatrists, whose influence and participation in the society's meetings was correspondingly diminished. In 1935, the society moved its meetings back to the Los Angeles County Medical Association headquarters in order to reestablish the balance between the neurological and psychiatric wings of the society<sup>29</sup>.

Undeterred, the neurology, neurosurgery, and neuropathology departments at the County Hospital continued to meet on a weekly basis, creating their own independent forum focused on the discussion of topics relevant to neurological disease<sup>29</sup>. This group was initially referred to as the Von Monakow Society, but was later renamed the Los Angeles Neurological Society and helped foster a climate of cooperation and collaboration between the different neurological services in the hospital<sup>13</sup>. In 1936, the society began publishing its own quarterly medical journal, the *Bulletin of the Los Angeles Neurological Society*, with Ingham serving as the medical editor-in-chief, Rand serving as the surgical editor-in-chief, and Nielsen and Courville serving as the managing editors. Courville later explained the impetus behind the creation of the journal:

The reason ('excuse') for a journal was (1) that because in a hospital this size there was too much valuable clinical material passing through its wards to be ignored... (2) it was also because members of the resident staff at least needed experience in learning how to put their thoughts on paper; and (3) finally it was one way for the Attending Staff to put their cogitations together in some legitimate way. It may have been because it was also a means to provide an outlet of our own, perhaps more practical, contributions to the contemporary neurological literature<sup>30</sup>.

Over time, the journal achieved a national and international circulation, and was published continuously until 1982.

Rand, Ingham, Nielsen, and Courville would remain dominant figures in the Southern California neurology community through the Second World War and the early postwar years. Aird suggests that the relative isolation of the departments of neurology on the West Coast from the more prominent departments of neurology on the Eastern seaboard may have stunted their early development<sup>8</sup>. However, the neurological services at the Los Angeles County Hospital took advantage of the unique cultural and economic trends in Southern California to develop local areas of expertise, such as traumatic brain injury. Their distinct regional viewpoint, accentuated by their geographic separation from the traditional centers of American neurology, was disseminated through the *Bulletin of the Los Angeles Neurological Society*, and would come to be known as the "Los Angeles School of Neurology"<sup>13</sup>.

## THE EXPANSION OF NEUROLOGICAL RESEARCH IN SOUTHERN CALIFORNIA

Southern California experienced another tremendous growth spurt during and after the Second World War. Most of the service personnel who served in the Pacific theatre were either stationed in California or shipped out through the ports of San Francisco, Los Angeles, or San Diego. Many of these soldiers, using the generous housing and education benefits available through the G.I. Bill, returned after the end of the war to settle in the region. The concomitant growth of defense related industries in Southern California, particularly the aviation and the apparel industries, also attracted a multitude of wartime workers from other regions of the country, many of whom would also choose to remain in the area<sup>31</sup>.

This postwar population boom in Southern California served as an impetus for the establishment of the University of California, Los Angeles (UCLA) School of Medicine in 1947. The medical school was to be situated in a new medical center adjacent to the main UCLA campus in Westwood to facilitate close interaction between the basic and clinical sciences. A nationwide recruitment process was pursued to develop the faculty of the new institution, and two of the early appointments, Horace W. Magoun (Figure 9) and Augustus S. Rose (Figure 10), established the foundation for the subsequent flourishing of clinical neurology and basic neurosciences at UCLA<sup>11</sup>.



Figure 9: Horace W. Magoun



Figure 10: Augustus S. Rose

Magoun completed his graduate studies at the Northwestern University School of Medicine Institute of Neurology under Stephen W. Ranson in 1934. He remained in Chicago after receiving his doctoral degree, working at both Northwestern and the Illinois Neuropsychiatric Institute. His early work focused on the anatomy and physiology of the brainstem reticular activating system and its role in wakefulness and arousal. However, by 1950, his research opportunities in Chicago had dwindled, and he eagerly accepted the offer to become the first chairman of the department of anatomy at the UCLA School of Medicine. Soon after his arrival, he was joined by a group of other neuroscientists, including John D. French, Donald B. Lindsey, Theodore H. Bullock, and Charles H. Sawyer. This group of investigators, who would later be referred to as the "Five Aborigines," together formed an active interdisciplinary neuroscience research group that would later become the UCLA Brain Research Institute (BRI)<sup>32</sup>.

Rose graduated from the Harvard School of Medicine in 1932, subsequently interning in medicine at the Massachusetts General Hospital (MGH) and psychiatry at the McLean Hospital. After the completion

of his training, he taught anatomy at the University of North Carolina for several years before returning to Boston in 1937, where he worked at multiple institutions, including Harvard, MGH, the Peter Bent Brigham Hospital, the Boston Psychopathic Hospital, and Boston University, and a busy private practice<sup>33</sup>. His research in Boston focused upon the treatment of neurosyphilis, but he was also beginning to develop some expertise in the field of psychosomatic medicine<sup>34</sup>. In 1950, Rose was recruited for the position of chief of the division of neurology, which at that time part of the department of medicine<sup>33</sup>. Rose found the offer quite attractive, as he was so overworked in Boston that his children did not always recognize him<sup>33</sup>. He had also wanted to increase his teaching activities, and thought very highly of Magoun, who had graciously extended the opportunity to lecture on neuroanatomy to the medical students. While still in Boston, had treated Spencer Tracy for psychosomatic symptoms and subsequently been referred to treat a number of other motion picture stars. After visiting Los Angeles in January of 1951 to serve as the on-set physician for Judy Garland and experiencing the pleasant climate and environment, Rose decided to accept the position<sup>34</sup>.

After the Second World War, academic medicine, and in particular, neurology and the neurosciences flourished across the nation, primarily due to a remarkable growth in federal involvement through the modernization of the medical programs of the VA and the expansion of financial support from the National Institutes of Health (NIH)<sup>8</sup>. These two developing trends, and the foresight of Rose and the leaders of the Brain Research Institute to exploit them, would play an important role in the rapid growth and development of neurological training and research at UCLA in the decades to follow<sup>32</sup>.

Beginning in 1945, the federal government emphasized a closer relationship between the VA and academic medicine by expanding its focus beyond the clinical care of veterans to encompass more scientific and medical research. To this end, new VA medical centers were located close to existing medical schools and teaching hospitals. Neurological disease was specifically targeted, particularly because a significant proportion of wounded war veterans were neurologically disabled, with conditions such as epilepsy, head trauma, or spinal cord injuries. These needs were addressed through the development of national treatment and research centers targeting specific neurological disorders, including Nielsen's center for the study of aphasic disorders at the Long Beach VA Hospital<sup>22</sup>. Both the division of neurology and the BRI took advantage of the closer links between the VA and the UCLA School of Medicine to secure laboratory space, since at the time of both Magoun and Rose's arrival in Los Angeles, neither the medical center nor medical school buildings had been completed (Figure 11). The investigators of the BRI were initially stationed at the Long Beach VA<sup>32</sup>, while the fledgling division of neurology found an early home at the Wadsworth VA in West Los Angeles (Figure 12)<sup>33</sup>.



Figure 11: The UCLA Hospital and School of Medicine, under construction.



Figure 12: The Wadsworth Veterans Administration Hospital, circa 1950.

Aggressive lobbying by patient groups such as the National Multiple Sclerosis Society, United Cerebral Palsy, Muscular Dystrophy Association of America, Myasthenia Gravis Foundation, and National Epilepsy League helped create the National Institute of Neurological Diseases and Blindness (NINDB) in 1950. Although the initial annual operating budget for the institute in 1951 was modest, consisting of \$1.25 million for the funding of ongoing research projects transferred from other institutes (primarily the National Institute of Mental Health), the monies available for the support of intramural and extramural research and the training of teachers and investigators steadily increased to \$10 million by 1956, \$30 million by 1959, and \$116 million in 1968<sup>22</sup>. At UCLA, both the division of neurology and the BRI deftly tapped into this growing federal resource to fund training programs, building construction, and research projects, which in turn facilitated the recruitment of highly talented faculty from around the country and accelerated the rapid development of clinical neurology and the basic neuroscience research<sup>32,33</sup>.

Arthur has suggested that the UCLA School of Medicine was optimally positioned during its formative years to reap the benefits of increased federal support for biomedical research. The first dean, Stafford L. Warren, was very familiar with the funding mechanisms of the federal government, having previously worked on the Manhattan Project and the Atomic Energy Commission. This gave him a distinct advantage in securing NIH funding over the deans of older, more established medical schools, who had little experience attracting federal funding, and had actively avoided accepting governmental grants prior to the Second World War due to concerns about academic freedom. The era of rapid expansion at the UCLA School of Medicine also coincided with the years of greatest growth in NIH funding, from the early 1950's to the mid-1960's, after which the levels of federal support leveled off significantly<sup>11</sup>.

Driven by the continually expanding population in the southern part of the state, and encouraged by the success of the UCLA School of Medicine, the University of California soon established two additional medical schools in Irvine and San

Diego. The UCI School of Medicine came into existence in 1965, when the University of California assumed control of the California College of Medicine, a private medical school in Los Angeles. In 1968, the medical school was moved to the Irvine campus<sup>12</sup>. The University of California, San Diego (UCSD) School of Medicine enrolled its first students in 1968. UCSD pursued a unique approach to developing its departments. Under the leadership of David Bonner, the institution had sought to establish integrated departments composed of both clinicians and basic scientists to foster a close relationship between the medical school and the general campus. The medical school curriculum was shaped around the “Bonner Plan,” in which first-year students were taught by basic science faculty and second-year students were taught anatomy and pathology by clinical faculty<sup>35</sup>.



Figure 13: Stanley van den Noort

The neurology divisions at UCI and UCSD, much like their counterpart at UCLA, were focused



Figure 14: Robert Livingston

upon research and academic inquiry from the time of their inception. At UCI, neurology was initially organized as a division of the department of medicine. Stanley van den Noort (Figure 13), a multiple sclerosis researcher from Case Western Reserve was recruited as the first division chief in 1970<sup>36</sup>. UCSD established the nation’s first department of neurosciences, which included clinical neurology. Robert Livingston (Figure 14), the first chairman of the department, was a former member of the UCLA BRI who had been recruited from an administrative position at the NIH in 1965<sup>32</sup>. The department of neurology at USC also began to increase its emphasis upon research, particularly after Joseph P. Van Der Meulen (Figure 15) was appointed chairman in 1971. Van Der Meulen, a specialist in neuromuscular diseases who had trained in neurology at Harvard and the Boston City Hospital under Derek Denny-Brown and completed a neurophysiology fellowship in Sweden with Nobel laureate Ragnar Granit, began to aggressively recruit basic and clinical neuroscientists into the department. This practice has continued under the subsequent leadership of Leslie P. Weiner and

Helena Chui<sup>37</sup>.

The impressive long-term dividends of these early investments in neurological research can be measured by the recent levels of federal support for the neurology departments in Southern California. In 2004, UCLA, UCI, and USC were all ranked in the top 20 medical schools nationwide in NIH funding for departments of neurology<sup>38</sup>, while UCSD was ranked first in NIH funding for departments of neuroscience<sup>39</sup>. Despite their collective youth, the medical schools in Los Angeles, Orange County, and San Diego are now internationally recognized institutions for neurological research. Active neurology training programs have also been established at the Harbor-UCLA Medical Center in Torrance, the Kaiser-Sunset Medical Center in Hollywood, and the Loma Linda University Medical Center.



Figure 15: Joseph P. Van Der Meulen

## NEUROLOGICAL ADVANCES FROM SOUTHERN CALIFORNIA

The neurology community in Southern California has contributed innumerable advances in the clinical and basic sciences over the past fifty years. While a complete compendium of the significant accomplishments of the neurologists and neuroscientists from the region is well beyond the scope of this article, we will highlight some of the regional contributions to selected neurological subspecialties, including multiple sclerosis, neuroimaging, surgical treatment of epilepsy, and dementia.

*Multiple Sclerosis.* Although Southern California is low prevalence region for multiple sclerosis, a great deal of regional interest has been focused on this disease. Multiple sclerosis was one of Rose’s main research targets when he was building the division of neurology at UCLA, and one that became particularly poignant when his son was later diagnosed with the disease. The first research scientist that he recruited was Frederick J. Wolfgram, a physiologist and biochemist, who studied myelin proteins and discovered the “Wolfgram protein”<sup>33</sup>. When Rose came to Los Angeles, there were no established therapies for multiple sclerosis, and local and national practitioners either pursued unproven treatments of questionable efficacy or embraced therapeutic nihilism<sup>40</sup>. Rose helped orchestrate the first multi-center trial for treatment of the disease, which evaluated the use of ACTH<sup>41</sup>. George W. Ellison and Lawrence W. Myers subsequently conducted additional clinical trials of immunosuppressive agents in multiple sclerosis at UCLA<sup>42</sup>. Norman Namerow came to UCLA in 1965, and he was amongst the earliest practitioners to use evoked potentials in the clinical assessment of multiple sclerosis<sup>43</sup>. Wallace Tourtellote was recruited to Wadsworth VA Hospital in West Los Angeles from the University of Michigan in 1970. At Wadsworth, he has continued his pioneering role in the study of cerebrospinal fluid in multiple sclerosis, particularly the diagnostic significance of oligoclonal bands and IgG synthesis rates<sup>44</sup>. He has also led efforts to expand the National Neurological Research Specimen Bank, which collects human neurological tissues for research into multiple sclerosis and other conditions<sup>45</sup>. Stanley van den Noort at UCI has focused for many years on the role of lymphocyte neurochemistry in multiple sclerosis<sup>46</sup>. At USC, Leslie P. Weiner has been a leader in the development of multiple sclerosis therapeutics, including involvement in the clinical trials for glatiramer acetate<sup>47</sup> and T-cell vaccination<sup>48</sup>, and studies of gene therapy in animal models<sup>49</sup>.

*Neuroimaging.* Neurologists in Southern California have played an important role in the development of modern structural and functional neuroimaging. William H. Oldendorf, who would become one of the pioneers in the field of neuroimaging, came to the Wadsworth VA hospital in 1955<sup>50</sup>. He had recently finished fellowship training at the University of Minnesota with A.B. Baker, where he had been trained extensively in performing pneumoencephalograms and cerebral arteriograms. Finding these procedures tedious, traumatic, and limited in the information that they could provide, he was driven to develop improved methods for visualizing brain structure<sup>51</sup>. In 1961, he published an article describing a technique for deriving the internal structure of objects from their X-ray absorption patterns, which would form the theoretical basis for modern computerized tomography<sup>52</sup>. Oldendorf patented the process, but could not find any commercial support for his device and further advances in the technique temporarily languished<sup>53</sup>. However, in the early 1970's, Sir Godfrey Hounsfield, inspired by Oldendorf's earlier work and aided by new mathematical algorithms derived by Allan M. Cormack and Ronald N. Bracewell, developed the first Computerized Axial Tomography scanner, which became commercially available in 1973. Hounsfield and Cormack were awarded the Nobel Prize in 1979 for their work in computerized tomography, but Oldendorf was conspicuously excluded from the award, an oversight that has been attributed to political and legal considerations<sup>54</sup>. Later in his career, Oldendorf focused upon the physiology of the blood-brain barrier and the evaluation of its differential permeability to different substances<sup>55</sup>. This work would later find clinical applications in positron emission tomography (PET) and single photon emitted computed tomography (SPECT)<sup>53</sup>. Neuroimaging has continued to be a major area of research at UCLA, under the leadership of John C. Mazziotta, who joined the Department of Neurology in 1983 and was appointed chair in 2002. He established the Human Brain Mapping Center and his work has been influential in advancing the understanding of the structure and function of the living brain, using PET and magnetic resonance imaging techniques<sup>56,57</sup>.

*Surgical Treatment of Epilepsy.* Over the past 50 years, advances in the surgical treatment of epilepsy have benefited many patients with medically intractable epilepsy. Investigators from Southern California have made important contributions to the understanding of two major approaches to surgical epilepsy treatment: callosotomy and temporal lobectomy.

Corpus callosotomy was first used for the treatment of epilepsy in 1939, but the effects of callosal transection were not well understood, and procedure was not widely performed<sup>58</sup>. However, in the late 1950's, Roger W. Sperry at California Institute of Technology began studying the procedure in "split-brain" cats and monkeys. He and Michael S. Gazzaniga then teamed with Joseph E. Bogen, a neurosurgeon at the Loma Linda University School of Medicine who was re-exploring the use of callosotomy for intractable epilepsy, and began to study the effects of callosotomy in humans<sup>59</sup>. Their work helped develop the current understanding of hemispheric specialization and the importance of interhemispheric transfer of information, which in turn has helped optimize callosotomy as a treatment for symptomatic generalized epilepsy<sup>58</sup>. Sperry received the Nobel Prize in 1981 for these contributions to field of cortical specialization.

Aided by the advances in electroencephalogram (EEG) localization of epileptic discharges, neurologists and neurosurgeons at the Montreal Neurological Institute began to use temporal lobectomy as a treatment for temporal lobe epilepsy by 1950<sup>60</sup>. Soon thereafter, in the mid 1950's, Paul H. Crandall a neurosurgeon who had trained at the Illinois Neuropsychiatric Institute under Percival Bailey, and Richard D. Walter, a psychiatrist who had completed a fellowship in neurophysiology and EEG at the Langley Porter Neuropsychiatric Institute at UCSF, were both recruited to UCLA<sup>32,33</sup>. They had a shared interest in the surgical treatment of medically intractable epilepsy, and Crandall sought to establish a center for the surgical epilepsy management, guided by neurophysiological studies, similar to existing programs at the Montreal Neurological Institute, the NIH, the University of Washington, the Barrow Neurological Institute, and the Illinois Neuropsychiatric Institute. However the variable quality of patient histories and the relatively poor sensitivity of conventional surface EEG in distinguishing unilateral onset temporal lobe discharges from independent bitemporal or diffuse frontotemporal epileptiform discharges limited the number of subjects that were suitable for temporal lobectomy<sup>61</sup>.

Crandall and Walter's efforts were aided by Jean Talairach's pioneering use of stereotactic electrodes for the study and treatment of temporal lobe epilepsy in France. The UCLA BRI, then led by John French, developed a NINDB-funded interdisciplinary program incorporating the use of deep brain electrodes in various different neurological and psychiatric diseases. Initially, this program encompassed investigations into movement disorders, intractable pain, multiple sclerosis, schizophrenia, and epilepsy, but by 1971, the goals had been shifted to focus specifically upon epilepsy<sup>32</sup>.

The UCLA group was among the earliest to use EEG telemetry and arrays of stereotactically implanted electrodes in the temporal lobes to localize specific epileptogenic foci and identify candidates most likely to benefit from surgical treatment. Surgical intervention consisted of a standard "en bloc" anterior temporal lobe resection, designed to minimize post-operative neurological deficits yet maintain proper anatomical orientation to facilitate pathological assessment of temporal lobe structures in epileptic patients. Over the years, the group incorporated sodium amytal testing, extratemporal electrodes, and structural and functional neuroimaging to further refine the candidate selection process. Additionally, their neuropsychological and neurophysiological investigations have contributed to the understanding of the underlying neuropathological substrates of temporal lobe epilepsy<sup>61</sup>. The work of this group has continued under the leadership of Jerome P. Engel Jr., an epileptologist who assumed Walter's role as chief neurologist, and Itzak Fried, a neurosurgeon who inherited Crandall's role as director of epilepsy surgery.

Over the past 45 years, numerous fellows have been trained at the program at UCLA, and many have gone on to direct surgical epilepsy centers around the nation.

*Dementia.* The evolution of dementia research in Southern California dates back to the late 1970's and early 1980's. Within a five year span, an impressive group of investigators would arrive in Southern California from the East Coast and the Midwest: D. Frank Benson, Jeffrey L Cummings, Helena Chui, George G. Glenner, Robert Katzman, Robert D. Terry and Leon J. Thal. Their work has greatly advanced the understanding of the epidemiology, behavioral abnormalities, pathology, and therapy of the various etiologies of dementia.

D. Frank Benson was already a well-established behavioral neurologist before coming to UCLA in 1979. He had worked with Norman Geschwind at Boston University and the Boston VA Hospital, where he had already made seminal contributions to the understanding of clinical-pathological correlations in aphasia, agnosia, and amnesia. After heading west, Benson continued to make substantial contributions in dementia, including the early use of PET to characterize the regional hypoperfusion in Alzheimer's disease and describing the clinical syndromes of subcortical dementias and posterior cortical atrophy. He also helped usher in the renaissance of neuropsychiatry by focusing attention on the psychiatric features of neurological disorders<sup>62</sup>. Benson recruited one of his former trainees, Jeffrey L. Cummings, from Boston University in 1980. Cummings has continued Benson's work in elucidating structure-functional relationships in dementia and extended the understanding of behavioral disturbances in dementia, creating the Neuropsychiatric Inventory, a cross-cultural measure of psychopathology that is widely used in clinical trials<sup>63</sup>. Among Benson's trainees at UCLA include Bruce L. Miller (now at UCSF) and Mario F. Mendez (now at the West Los Angeles VA Hospital), who are now among the foremost investigators in the growing field of frontotemporal dementia.

While Benson arrived in UCLA after he had already fashioned a successful career in neurobehavior, Helena Chui came to USC and the Rancho Los Amigos Medical Center in 1982 near the beginning of her career, immediately after completing a neurology residency and a neurobehavioral fellowship at the University of Iowa. She has played a significant role in the development of the Andrus Gerontology Center at USC since her arrival, and became chair of the department of neurology in 2004. Her research over the past 20 years has delved into Alzheimer's disease, vascular dementia, and the interface between the two diseases. In particular, she has investigated the natural history, neuropathological and neuroimaging correlates, and genetic risk factors for these two forms of dementia<sup>64-67</sup>.

UCSD's rapid emergence as a leading center in dementia research was catalyzed by the arrival of neuropathologist George G. Glenner from the NIH in 1982. Three emigrants from the Albert Einstein College of Medicine followed him in rapid succession: Robert Katzman and Robert D. Terry in 1984, and Leon J. Thal in 1985. The contributions of these four physician-scientists have greatly advanced the understanding of the epidemiology, pathology, and treatment of Alzheimer's disease. Each of these investigators has been awarded the American Academy of Neurology's Potamkin Prize for research into Alzheimer's disease and related dementias, which is amongst the most prestigious awards in the field. Terry was the inaugural recipient of the award in 1988 for his work in determining that the cognitive deficits in Alzheimer's disease were related to synapse loss<sup>68</sup>. Glenner was honored the subsequent year for his demonstration that the neuritic plaques that are the hallmark of Alzheimer's disease are composed of beta-amyloid<sup>69</sup>. Katzman was selected in 1992 for his seminal work in describing the epidemiological aspects of Alzheimer's Disease, particularly the role played by education<sup>70</sup>. Thal is UCSD's most recent winner, receiving recognition in 2004 for his research into experimental therapeutic agents for Alzheimer's disease through his leadership of the Alzheimer's Disease Cooperative Study and its multicenter clinical trials<sup>71,72</sup>.

## SUMMARY

Neurology in Southern California has undergone dramatic changes since its humble beginnings in the late 1800's. The early days of neurological specialization in the region were marked by a relatively delayed development and a distinct local flavor that was accentuated by the relative geographical isolation of the region. Nevertheless, the same historical trends that characterized neurology across the rest of the country also dictated the course of neurology in Southern California: the early dominance of neuropsychiatry, the formation of local neurological societies, the development of neurology training programs, and the emergence of independent academic departments of neurology. Southern California's rise to international prominence in clinical neurology and basic neuroscience was facilitated by local institutions' early recognition of the powerful role of the federal government in the expansion of biomedical research after the Second World War. Local practitioners and researchers have made valuable contributions to the understanding and treatment of neurological disease, and remain at the forefront of many new discoveries in the various fields of neurology.

## References:

1. Fogelson RM. *The Fragmented Metropolis: Los Angeles, 1850-1930*. Los Angeles: University of California Press, 1993
2. The story of the Los Angeles County Medical Association. *Bull Los Angeles Med Assoc*. 1946;75:11-96
3. Martin HE. *The History of the Los Angeles County Hospital (1878-1968) and the Los Angeles County-University of Southern California Medical Center (1968-1978)*. Los Angeles: University of Southern California Press, 1979
4. Graves CL. *The Society's first president*. San Diego County Medical Society. 1961. Retrieved July 23, 2005 from <http://www.sdcmcs.org/webpages/history.asp>
5. DeJong RN. *A History of American Neurology*. New York: Raven Press, 1982
6. Gray BB. *120 Years of Medicine: Los Angeles County, 1871-1991*. Houston: Pioneer Publications, 1991
7. Rose AS. *The western states*. In: Denny-Brown D, Rose AS, Sabs AL, eds. *Centennial Anniversary Volume of the American Neurological Association: 1875-1975*. New York: Springer, 1975:480-495
8. Aird RB. *Foundations of Modern Neurology: A Century of Progress*. New York: Raven Press, 1994
9. Keller TM. California's Cushing connection: Harvey Cushing trained California's first neurosurgeons. *J Neurosurg*. 2002;97:728-735
10. James Harvey McBride, 1849-1928. In: Denny-Brown D, Rose AS, Sabs AL, eds. *Centennial Anniversary Volume of the American Neurological Association: 1875-1975*. New York: Springer, 1975:146-147
11. Arthur R. *By the Old Pacific's Rolling Water: Birth of the UCLA School of Medicine*. Los Angeles: UCLA School of Medicine, 1992
12. *History and setting*. UCI School of Medicine. Retrieved July 23, 2005 from <http://www.ucihs.uci.edu/intmed/hypertext/hts.html>
13. Nielsen JM. *Neurological society*. *Bull Los Angeles Med Assoc*. 1946;75:167-169
14. Courville CB. *The saga of a neurosurgical service, with a few incidental remarks about its chief*. *Bull Los Angel Neuro Soc*. 1951;16:1-12
15. Starr K. *Material Dreams: Southern California Through the 1920's*. New York: Oxford University Press, 1990
16. Nielsen JM, Rand CW. *Dr. Samuel D. Ingham*. *Bull Los Angel Neuro Soc*. 1942;7:157-161
17. Tilney F, Jelliffe SE, eds. *Semi-Centennial Volume of the American Neurological Association*. Albany: Boyd Printing Company, 1924
18. Ingham SD. *Consciousness in relation to cerebral localization*. *Bull Los Angel Neuro Soc*. 1937;2:147-
19. von Hagen KO, Johannes Maagaard Nielsen, 1890-1969. In: Denny-Brown D, Rose AS, Sabs AL, eds. *Centennial Anniversary Volume of the American Neurological Association: 1875-1975*. New York: Springer, 1975:284-289
20. Ives ER. *Some personal recollections of Dr. J.M. Nielsen*. Personal communication. 1982.
21. Nielsen JM. *Agnosia, Apraxia, Aphasia: Their Value in Cerebral Localization*. Los Angeles: Los Angeles Neurological Society, 1936
22. Bailey P. *Government organization of neurological research and development in the Veterans Administration and the National Institute of Neurological Diseases and Blindness*. In: Denny-Brown D, Rose AS, Sabs AL, eds. *Centennial Anniversary Volume of the American Neurological Association: 1875-1975*. New York: Springer, 1975:509-531
23. Curran JA. *Internships and residencies: historical backgrounds and current trends*. *J Med Educ*. 1959;34:873-884
24. *Council on Medical Education and Hospitals of the American Medical Association. Hospital service in the United States*. *JAMA*. 1927;33:789-839
25. Freeman W, Ebaugh FG, Boyd DA, Jr. *The founding of the American Board of Psychiatry and Neurology, Inc*. *Am J Psychiatry*. 1959;115:769-778
26. Cyril Brian Courville, M.D. *Bull Los Angeles Neurol Soc*. 1968;33:161-162
27. Courville CB. *The Ramon-Cajal laboratory of neuropathology*. *Bull Los Angel Neuro Soc*. 1936;1:99-103
28. Goetz CG, Chmura TA, Lanska D. *Part 1: the history of 19th century neurology and the American Neurological Association*. *Ann Neurol*. 2003;53 Suppl 4:S2-S26
29. Baker RN. *The Los Angeles Society of Neurology and Psychiatry: yesterday, today and tomorrow*. *Bull Los Angel Neuro Soc*. 1966;31:2-8
30. Courville CB. *The heritage of the Bulletin of the Los Angeles Neurological Society: a historical note*. *Bull Los Angel Neuro Soc*. 1965;30:159-160
31. Starr K. *Embattled Dreams: California in War and Peace, 1940-1950*. New York: Oxford University Press, 2002
32. French JD, Lindsley DB, Magoun HW. *An American Contribution to Neuroscience: The Brain Research Institute, UCLA, 1959-1984*. Los Angeles: UCLA Brain Research Institute, 1984
33. Herrmann C. *History of neurology at UCLA: 1951-1986*. In: *History of Neurology at UCLA*. Los Angeles: UCLA School of Medicine, Department of Neurology, 1992:1-38
34. Rose AS. *UCLA Neuropsychiatric Institute and Hospital Oral History Transcript: Augustus S. Rose, 1987*. Los Angeles: Oral History Program, UCLA, 1990
35. Seybold ME. *UCSD Neurosciences History*. Personal communication. 2005.
36. Whitcomb LJ. *Stanley van den Noort, M.D., '52: MS pioneer*. *Dartmouth Medicine*. 2003;28:60-61
37. *History*. Department of Neurology, Keck School of Medicine, USC. 2005. Retrieved July 24, 2005 from <http://www.usc.edu/schools/medicine/departments/neurology/about/history.html>
38. *Neurology: NIH Awards to Medical Schools by Rank, Fiscal Year 2004*. National Institutes of Health. Retrieved July 24, 2005 from <http://grants1.nih.gov/grants/award/rank/neurology04.htm>
39. *Neurosciences: NIH Awards to Medical Schools by Rank, Fiscal Year 2004*. National Institutes of Health. Retrieved July 24, 2005 from <http://grants1.nih.gov/grants/award/rank/neurosciences04.htm>
40. Talley C. *The treatment of multiple sclerosis in Los Angeles and the United States, 1947-1960*. *Bull Hist Med*. 2003;77:874-899
41. Rose AS, Kuzma JW, Kurtzke JF et al. *Cooperative study in the evaluation of therapy in multiple sclerosis. ACTH vs. placebo—final report*. *Neurology*. 1970;20:1-59
42. Myers LW, Ellison GW. *The peculiar difficulties of therapeutic trials for multiple sclerosis*. *Neurol Clin*. 1990;8:119-141
43. Namerow NS. *Somatosensory evoked responses in multiple sclerosis*. *Bull Los Angeles Neurol Soc*. 1968;33:74-81
44. Tourtellotte WW, Ma BI. *Multiple sclerosis: the blood-brain-barrier and the measurement of de novo central nervous system IgG synthesis*. *Neurology*. 1978;28:76-83
45. Tourtellotte WW, Rosario IP, Conrad A, Syndulko K. *Human neuro-specimen banking 1961-1992. The National Neurological Research Specimen Bank (a donor program of pre- and post-mortem tissues and cerebrospinal fluid/blood; and a collection of cryopreserved human neurological specimens for neuroscientists)*. *Neural Transm Suppl*. 1993;39:5-15
46. Qin Y, Van Den Noort S, Kurt J, Gupta S. *Dual expression of CD45RA and CD45RO isoforms on myelin basic protein-specific CD4+ T-cell lines in multiple sclerosis*. *J Clin Immunol*. 1993;13:152-161
47. Johnson KP, Brooks BR, Cohen JA et al. *Extended use of glatiramer acetate (Copaxone) is well tolerated and maintains its clinical effect on multiple sclerosis relapse rate and degree of disability*. *Copolymer 1 Multiple Sclerosis Study Group*. *Neurology*. 1998;50:701-708
48. Correale J, Lund B, McMillan M et al. *T cell vaccination in secondary progressive multiple sclerosis*. *J Neuroimmunol*. 2000;107:130-139
49. Weiner LP, Louie KA, Atalla LR et al. *Gene therapy in a murine model for clinical application to multiple sclerosis*. *Ann Neurol*. 2004;55:390-399
50. Oldendorf WH. *Reminiscences on the Wadsworth VA Hospital UCLA neurology relationship*. In: *History of Neurology at UCLA*. Los Angeles: UCLA School of Medicine, Department of Neurology, 1992
51. Balshi R. *The American Society of Neuroimaging (ASN)*. *American Society of Neuroimaging*. Retrieved July 22, 2005 from <http://snap.asnweb.org/index.php?src=genidos&link=NeuroimagingHistory&category=History>
52. Oldendorf WH. *Isolated flying spot detection of radiodensity discontinuities—displaying the internal structural pattern of a complex object*. *Ire Trans Biomed Electron*. 1961;8:68-72
53. Mazziotta JC, C. CR. William H. Oldendorf, 1925-1992. *Ann Neurol*. 1993;33:331
54. Mishra SK. *The quest of brain imaging: the contribution of William Oldendorf*. In preparation
55. Oldendorf WH. *Measurement of brain uptake of radiolabeled substances using a tritiated water internal standard*. *Brain Res*. 1970;24:372-376
56. Iacoboni M, Baron JC, Frackowiak RS et al. *Emission tomography contribution to clinical neurology*. *Clin Neurophysiol*. 1999;110:2-23
57. Mazziotta JC. *Brain mapping: its use in patients with neurological disorders*. *Rev Neurol (Paris)*. 2001;157:863-871
58. Devinsky O, Laff R. *Callosal lesions and behavior: history and modern concepts*. *Epilepsy Behav*. 2003;4:607-617
59. Gazzaniga MS, Bogen JE, Sperry RW. *Some functional effects of sectioning the cerebral commissures in man*. *Proc Natl Acad Sci U S A*. 1962;48:1765-1769
60. Meador KJ. *Emergence of temporal lobe surgery for epilepsy*. *Arch Neurol*. 2001;58:1011-1012
61. Crandall PH, Babb TL. *The UCLA Epilepsy Program: historical review 1960-1992*. *J Clin Neurophysiol*. 1993;10:226-238
62. Cummings JL. *D. Frank Benson, M.D.: biography and overview of contributions*. *Aphasiology*. 1999;13:3-11
63. Cummings JL. *The Neuropsychiatric Inventory: assessing psychopathology in dementia patients*. *Neurology*. 1997;48:S10-16
64. Perlmuter LS, Chui HC. *Microangiopathy, the vascular basement membrane and Alzheimer's disease: a review*. *Brain Res Bull*. 1990;24:677-686
65. Rao VS, Cupples A, van Duijn CM et al. *Evidence for major gene inheritance of Alzheimer disease in families of patients with and without apolipoprotein E epsilon 4*. *Am J Hum Genet*. 1996;59:664-675
66. Chui H. *Vascular dementia, a new beginning: shifting focus from clinical phenotype to ischemic brain injury*. *Neurol Clin*. 2000;18:951-978
67. Mungas D, Jagust WJ, Reed BR et al. *MRI predictors of cognition in subcortical ischemic vascular disease and Alzheimer's disease*. *Neurology*. 2001;57:2229-2235
68. Terry RD, Masliah E, Salmon DP et al. *Physical basis of cognitive alterations in Alzheimer's disease: synapse loss is the major correlate of cognitive impairment*. *Ann Neurol*. 1991;30:572-580
69. Glenner GG, Wong CW. *Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein*. *Biochem Biophys Res Commun*. 1984;120:885-890
70. Katzman R. *Education and the prevalence of dementia and Alzheimer's disease*. *Neurology*. 1993;43:13-20
71. Davis KL, Thal LJ, Gamzu ER et al. *A double-blind, placebo-controlled multicenter study of tacrine for Alzheimer's disease*. *The Tacrine Collaborative Study Group*. *N Engl J Med*. 1992;327:1253-1259
72. Sano M, Ernesto C, Thomas RG et al. *A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease*. *The Alzheimer's Disease Cooperative Study*. *N Engl J Med*. 1997;336:1216-1222