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CLINTON NATHAN WOOLSEY

1904—1993

A Biographical Memoir by
RICHARD F. THOMPSON

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One of the great achievements of neuroscience in this century has been characterization of the organization of sensory and motor representations in the cerebral cortex. Rough facts of cortical localization were known from the nineteenth century and earlier, based on studies from brain-damaged humans and animals and by application of electrical stimulation. The most important contemporary scientist to pioneer the fine-grained analysis of sensory and motor representations in the cortex was Clinton N. Woolsey. In the course of his remarkable career he made many important and fundamental discoveries.

Clinton N. Woolsey was born on November 30, 1904, in Brooklyn, New York, the son of Joseph Woodhull and Mathilda Louise Aicholz Woolsey. He left Brooklyn at the age of nine months ("before developing a Brooklyn accent"). He spent his youth in Orange County, New York, and attended a one-room country school from grades 1 through 6. He described it as an interesting experience, because he "could listen to the lessons given to all the pupils." He attended grades 7 through 10 in Montgomery, New York, and moved to Schenevus, New York, for his third year of high school. There he was awarded the H. Bernard Gold Medal as the best student of the year.

In the audience during his award ceremony was Dr. Walter Allan Cowell of Olean, New York, who suggested that young Woolsey move to Olean for his senior year, which he did. Cowell was a physician interested both in the practice of medicine and in research and was studying the effects on diabetes of insulin, which had just been discovered. As a result of his association with Cowell, Woolsey became greatly interested in medicine and in research. He graduated near the top of his class and spent another year at Olean High School taking extra work in Latin, French, and other subjects.

In 1924 Woolsey entered Union College in Schenectady, New York, where Cowell had graduated. Woolsey continued his study of Latin and French and took two years of Greek and the courses needed to enter medical school. Among his most impressionable experiences at Union College was a remarkable psychology professor, Johnny March, who "described the experiments of Pavlov and Sherrington so vividly that one felt in the presence of these investigators and their experimental animals." As a result of this, Woolsey considered going to Columbia University for training in psychology. Instead, he decided to go to medical school, and was accepted by the Johns Hopkins University School of Medicine in 1928.

During his first year at Hopkins, Woolsey took courses in histology and neuroanatomy from Dr. Marion Hines. At that time Woolsey intended to become a brain surgeon, so Hines sent him to work with Dr. Sarah Tower, who was an accomplished animal surgeon. Following a special course on localization of function taught jointly by Hines and Tower, Hines invited Woolsey to work with her on the dog brain, which led to his first publication: "On the Postural Relations of the Frontal and Motor Cortex of the Dog" (1933).

Before finishing his fourth year of medical studies, Woolsey developed pulmonary tuberculosis (a not uncommon condition for medical students of the day) and had to leave school for six months to recuperate in a sanitarium. He was advised that his goal of an internship in surgery was too physically demanding and might reactivate his pulmonary lesion. Dr. Philip Bard had just been recruited to Hopkins from Harvard, and he invited Woolsey to work in his lab. Woolsey soon realized that his future lay in physiology and not brain surgery. (In later years, those of us who worked with him through all-night experiments and 14-hour brain surgeries on monkeys were amazed at his enormous energy and robust health.)

During his time at Hopkins, Woolsey married Harriet E. Runion (in 1942). They had three children: Thomas Allen Woolsey, M.D., now a leading neuroscientist; John David Woolsey, M.F.A., an artist and medical illustrator; and Edward Alexander Woolsey, Ph.D., a zoologist and teacher. Woolsey remained at Hopkins in physiology until 1948, when he accepted his appointment as Charles Sumner Slichter professor of neurophysiology at the University of Wisconsin medical and graduate schools in Madison. He remained at Wisconsin for the rest of his career and life.

I had the great good fortune to work in Clinton Woolsey's laboratory for four years from 1955 through 1959. I completed by Ph.D. thesis in 1955-56 in his laboratory (my major professor, W. J. Brogden, in the psychology department did not have facilities for my work, and Woolsey kindly allowed us to use his laboratory). I then spent three years in Woolsey's laboratory as an NIH postdoctoral fellow. It was a most exciting environment. Much of the work in the laboratory at the time focused on the organization of the motor cortex in a series of primates (including chimpanzees) using electrical stimulation and on the organization of sensory (and polysensory) cortical areas using surface-evoked potentials. P. W. Davies visited the lab during that time and described the new extracellular microelectrode technique he and Jerzy Rose had developed. Jerzy Rose visited one summer, and using this technique we completed the first single-unit recording study of the tonotopic organization of the auditory cortex (in cat) (1960).

During my time (and, of course, earlier and later, as well) there were extraordinarily talented scientists in the laboratory. Konrad Akert provided solid expertise in neuroanatomy (e.g., 1961); Joseph Hind was expert in the auditory system and all matters acoustic (1960); and W. I. Welker and Robert Benjamin were young scientists at the height of their productivity (e.g., 1957). There were many others as well (e.g., 1957). Woolsey was a very tolerant laboratory chief. If the work we did was to some degree relevant to cortical organization and functions and was carefully done, we were free to follow our own interests. Personally, Woolsey was a gentle man—I never saw him lose his temper. He was an ideal role model in that he was totally focused on the work (and his family), was objective, and never engaged in ad hominem. However, if you took a particular position on cortical organization, you had better be prepared to defend it. He had very high standards and expected the same of everyone. Morale in Woolsey's laboratory was extremely high.

Woolsey was a superb but infrequent lecturer, often teaching by demonstration. At that time textbooks stated that complete removal of the neocortex in monkeys caused virtual paralysis. In the medical student physiology course Woolsey once demonstrated a fully decorticate rhesus monkey, which he held on a stick chain while the monkey chased him around the lectern trying to bite him. This finding was, of course, much more than simply a demonstration. Travis and Woolsey (1956) showed that after bilateral removal of all neocortex in stages, monkeys could show considerable recovery of motor function and become capable of locomotion if given adequate postoperative physical therapy. Recovery of function following brain injury was of deep interest to Woolsey. I assisted Woolsey in preparation of two of the decorticate macaques (we did them in two stages) and in their postoperative care. Woolsey had developed a method of subpial surgical aspiration of cortex that made it possible to remove localized regions without damage to adjacent regions, or of an entire hemisphere of cortex with minimal bleeding. He was a superb experimental neurosurgeon.

Woolsey became the Charles Sumner Slichter professor emeritus at the University of Wisconsin in 1975, but he by no means retired from his work. He published a landmark paper on localization in somatic sensory and motor areas of the human cerebral cortex in 1979, and until shortly before his death he was hard at work bringing to completion his extensive data on cortical localization in the chimpanzee. I participated in these studies, and he called me, I believe in 1990, to check on some details.

In the course of his long and productive career, Clinton Woolsey received many honors and awards, including Phi Beta Kappa (1928); the Franklin P. Mall Award in anatomy, Johns Hopkins University (1933); National Academy of Sciences membership (1960); the Medal of Faculty of Medicine, Free University, Brussels, Belgium (1968); charter membership in the Johns Hopkins Society of Scholars (1968); an Sc.D. (honoris causa) from Union College (1968); honorary membership in the Academy of Neurosurgery (1973); honorary membership in the American Neurological Association (1975); and the Ralph W. Gerard Award from the Society for Neuroscience, with J. F. Rose (1982). He served on numerous NIH committees and was deeply involved in international scientific activities.

PROFESSIONAL HISTORY

Wade Marshall had joined Philip Bard's department at Johns Hopkins in the 1930s and had worked with the cathode ray oscilloscope in Ralph Gerard's laboratory. He and Albert Grass at Harvard built such equipment for Bard's laboratory, and Marshall, Woolsey, and Bard undertook the first detailed mapping of the somatic sensory area of the cerebral cortex of the cat and monkey, using the new evoked potential technique (1937, 1941, 1942). This formed the basis of much of Woolsey's future work. He mapped the cortical sensory areas (and motor areas) in many mammalian species in great detail. Woolsey had a deep and abiding interest in the comparative development of functional areas of the neocortex, an interest he conveyed to his student and colleague W. I. Welker, who has continued this important tradition to the present. These studies were done with great care and attention to detail and led to a general formulation in the late 1940s of the receptotopic organization of cortical receiving areas, the general plan of which is largely unchallenged to this day.

The power of this comparative approach is clear in the following passage:

> Of particular significance in the evolution of these [somatic sensory motor] fields is the central position of the hand areas of SI and MI. In the primates the hand achieves a high degree of corticalization in the precentral and the postcentral fields. Because of the central location of the hand areas, the simple basic pattern of organization seen in the rodent, where the parts are represented in relation to one another much as they exist in the actual animal, apparently becomes distorted in evolution as cortical representation for the hand increases, with the result that in chimpanzee and in man the sensory and the motor face areas lose continuity with the centers for occiput and neck, which remain associated with the trunk representations. In macaque this separation of face from occiput has taken place in the postcentral gyrus, but in the precentral field the motor pattern still hangs together as it does in lower forms. Evidence for a transitional

status in the postcentral area in the smooth-brained marmoset has been reported and illustrated elsewhere. That this separation of cortical centers for face and occiput is not the result of an *en bloc* reversal of the projections of the cervical segments upon the cortex as was once suggested (1942), but rather is due to expansion of the hand area and disruption thereby of the cortical pattern, is supported by the finding that the trigeminal nerve projects not only to the lower classical face area but also to the "upper" head area, where not only the occiput but other parts of the head and face are represented (1958, pp. 65-66).

In his initial studies Woolsey focused on the somatic sensory cortex, but he quickly extended the work to auditory and visual areas. It was known that regions of the cochlea responded selectively to different tone frequencies, but little was known about the auditory cortex. Woolsey and Walzl (1942) completed a technical tour de force by selectively stimulating localized regions of auditory nerve fibers in the cochlea and mapping the patterns of evoked responses on the auditory cortex of the cat and monkey. This was the first clear demonstration of tonotopic (actually cochleotopic) organization of the auditory cortex. They followed this by examining effects of cochlear lesions on click-evoked responses in the auditory cortex (1946).

Early in the 1940s Woolsey discovered the existence of a second somatic sensory receiving area in the cortex of the cat, dog, and monkey (1943) and subsequently discovered secondary auditory and visual areas. Both E. D. Adrian and Woolsey are credited with independent discovery of the existence of this second somatic sensory area. Actually, it appears that Woolsey was first. The following is a quote from a letter written to me by Clinton's son Thomas:

I believe Dad and his colleagues in Baltimore discovered a second somatic area independently and about the same time as Adrian. My father rarely expressed disappointments in others. However, I think this is one case where he was both very disappointed and surprised. Evidently, early during the Second World War, Adrian was in the United States and visited the laboratory in Baltimore, Maryland. As Father described it, he [Clinton Woolsey] spent a long time very carefully explaining his discovery of a second somatic area. Father said that Adrian nodded and made comments regarding the data that he was being shown, but said nothing about his own work, which Father was greatly surprised to see published several months later. I think Dad felt betrayed in his confidence. In any case, a review of the data suggests that Dad provided the first convincing evidence of an orderly sequence in a second full representation. Adrian's note had only a few points that were outside the region of what was already known to be the somatic area (SI)" (Thomas Woolsey, personal communication, Nov. 22, 1994).

Woolsey and associates carefully mapped the primary visual area of the cortex, demonstrated the detailed retinotopic organization, and mapped a second visual area (1946, 1950). In yet another series of pioneering studies, Woolsey and associates mapped the somatic sensory projections to the cerebellar cortex (1945) and the organization of projections from the cerebral cortex to the cerebellar cortex (1952).

In still yet another series of pioneering studies, Woolsey joined forces with Jerzy Rose to complete a detailed lesion — retrograde degeneration mapping of the projections from the auditory region of the thalamus (medial geniculate body) to the auditory cortex in light of the physiological organization of the auditory cortex Woolsey and Walzl had defined earlier (1949). Rose and Woolsey completed similar studies on the projections of the mediodorsal nucleus to the orbitofrontal cortex (1947) and on the relations between the anterior thalamic nuclei and the limbic cortex (1948). As noted by Clinton's son Thomas in the presentation statement for the Ralph W. Gerard Award to Woolsey and Rose in 1982, these studies demonstrated that (1) there was a direct correspondence between cortical cytoarchitectonic fields and functionally defined regions of the cortex (this structure-function concept was under attack at the time); (2) each functional and cytoarchitectonic region of cortex received a distinctive input from a specific thalamic nucleus (the concept of thalamotelencephalic dependencies); and (3) these connections either could be restricted or be distributed more widely to several functional and cytoarchitectonic areas (the concepts of essential and sustaining projections).

In an ongoing series of exquisitely detailed studies, Woolsey and associates mapped the primary and supplementary motor areas of the cerebral cortex, using electrical stimulation in a wide range of primates and other mammals (1952, 1957, 1958) and compared sensory and motor maps in both pre- and postcentral cortical areas:

> It has now been firmly established that the afferent areas are not strictly afferent nor are the motor areas entirely motor. The afferent areas (SI and SII; postcentral and "second" sensory) have well-organized motor outflows which are still functional months after complete removal of the motor areas of the frontal lobe, while at the same time it appears that afferent connections to the frontal motor areas exist independently of the parietal afferent paths (Figure 1). Thus, the concept that the rolandic region is indeed a sensorimotor system, as held by pre-Sheringtonian workers, is reaffirmed, but with the considerable difference that the region is not an undifferentiated entity but one compounded of a number of distinguishable, individually complete, though interrelated, sensory-motor and motor-sensory representations. These facts appear to us to have important consequences for studies of the role of the cortex in neurological and behavioral functions, studies which will require the close cooperation of anatomist, physiologist, and behaviorist, or the mastery of multiple techniques by single individuals (1958, p. 64).

It is perhaps fitting to close this review of Clinton Woolsey's professional history with an example of his work. Figure 1 is reproduced from Woolsey (1958). It shows the detailed maps of a portion of the postcentral gyrus of the *Macaca mulatta*, comparing the representation of the body surface on the left, obtained from evoked potential maps, to the representation of movements from the same cortical tissue,

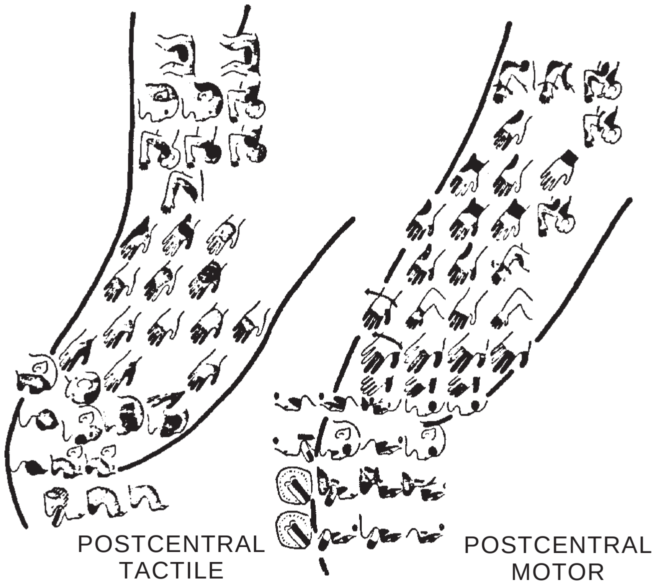

FIGURE 1: Comparison of postcentral tactile localization pattern with the postcentral motor localization pattern of *Macaca mulatta* (1958).

elicited by electrical stimulation, on the right. The figurines (a style of data representation Woolsey invented and perfected) in both cases indicate 2-mm steps along the cortex. The dark region in each figurine on the left is the region of skin surface that yields the maximum amplitude evoked potential at that cortical locus when the skin is lightly tapped. The dark regions on the figurines on the right are the cortical loci where least-intensity electrical stimulation yields the minimal movement shown. Note the exquisite detail. In the animal on the right (motor map), the cortical motor area (precentral gyrus) had been removed bilaterally, hence there is a well-organized postcentral motor system that can function independently of the frontal motor paths (see quotation just above). Woolsey also notes that these two maps are derived from different animals, yet they show remarkable similarities in their patterns of somatotopical organization.

It would be very remiss of me to conclude this biography of Clinton Woolsey without special mention of his wife Harriet. She was totally supportive of his work and career and accepted with profound good nature his incredible work schedule; he would often work all day and night and sometimes longer. Clinton was truly most fortunate. We who worked with him remember with great fondness the evenings at their home. Every summer, when the first sweet corn was ripe in southern Wisconsin, Clinton and Harriet held a corn roast for the laboratory at a local park. Perhaps it was the influence of Harriet and Clinton, but somehow corn has never tasted quite as good since.

I ACKNOWLEDGE MOST gratefully the following documents that provided information, particularly on the early phases of Clinton Woolsey's life: the autobiographical document dated April 10, 1989, that Clinton Woolsey wrote to the National Academy of Sciences; the original nomination (circa 1959) to the National Academy of Sciences; the Ralph W. Gerard Award presentation statement dated November 1, 1982, that Clinton's son Thomas A. Woolsey wrote for the Society for Neuroscience; and a letter dated November 22, 1994, that Thomas A. Woolsey wrote to me. Finally, I have innumerable personal experiences from the time I worked in Clinton Woolsey's laboratory from 1955 to 1959, the high point of my professional career.

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