10 Thalamocortical Pathways and Consciousness

CONTENTS

> O, *what a world of unseen visions and heard silences, this insubstantial country of the mind!"*
>
> (Jaynes, 1976, p. 1)

The relatively orderly series of discoveries of the functional organization of the cerebral cortex, in which anatomy and physiology often shared a certain simultaneity of discovery (as in the production of movement when precentral gyri are stimulated), did not characterize the exploration of structures beneath the cortex. On the contrary, the subcortical regions of the brain were dissected and anatomic structures described and named in profusion before any correct function was assigned to them. The major reason for the discrepancy between the rapid advance of anatomical knowledge and the slow elucidation of its related physiology was, paradoxically, the lack of a methodology to precisely locate structures deep in the living brain. Even though electrophysiologic techniques applied to peripheral nerves were advancing, their utility for investigation of the central nervous system depended on reliable localization. A second hurdle was the confused nomenclature that muddled any new information about the thalamus. In this and subsequent chapters, the history of the discoveries of some prominent subcortical structures and their functions is explored with emphasis on the novel developments in methodology that were essential for further progress.

About three centimeters long and half as wide, in the adult human the thalamus is a group of nuclei clustered into the shape of a football situated on each side of the third ventricle at the base of the cerebral hemispheres. Thirty-some separate nuclei occupy the 6–7 cm^3 of each thalamus. It is now known that all sensory fibers (except olfactory) converge there and synapse before their signals are passed on to cerebral cortex and other destinations.

IN EARLY HISTORY

The term "thalamus," meaning chamber or anteroom, was applied by Galen in the second century to the organ with which he thought the optic nerves were connected and which provided "vital spirits" for vision. A millennium later, Raimondo Mondino de' Luzzi (1275–1326) described but did not illustrate the thalami in his writings and was clear about their function. In Charles Singer's graceful translation of the text republished in Venice in 1495, Mondino declared:

> Before thou dost proceed to the mid ventricle consider the parts between the fore and the mid ventricle. . . . They are of the substance of the brain and are shaped like buttocks (*anchae*). At

Fig. 10.1. Jiri Procháska, a Czech who worked in Vienna, viewed the thalamus as a vague component of the relay station of sensory and motor impulses that resulted in "reflexion," thus providing the link between afferent and efferent limbs of the reflex arc. (From the painting [ca. 1788] by G. Kneipa; presently at the Medical Faculty of the University of Prague.)

> the side of each *ancha*, between the ventricles already mentioned, is a bloodlike substance made like a long or subterranean worm. . . . This worm can lengthen itself by constriction and block the *anchae* closing the way of passage from the fore to the mid part and contrariwise. When a man doth wish to cease from cogitation and consideration, he doth raise the walls and expand the *anchae so* that the spirit may cross over from one ventricle to the other (Singer, 1925, p. 92).

That curious description of the thalamus and choroid plexus in the ventricle must have presented a certain conceptual neatness to Mondino's contemporaries. The assignment of valve-like mechanisms controlling the flow of vital spirits persisted for more than three centuries: as noted, Descartes (1662) believed the pineal gland served the same gatekeeping function (*see* Fig. 3.10, p. 37, this volume).

After a long period of relative neglect of subcortical structures during exploration of the ventricles and gyri, some attention was accorded the thalamus in the second half of the eighteenth century. The concept of the reflex was emerging and speculation arose about where the "reflection" between afferent impressions and efferent activity occurred. Jiri Procháska (1749–1820; Fig. 10.1), a Czechoslovakian ophthalmologist who trained and worked in Vienna, designated a vague *sensorium commune*, which included the thalamus, as the intermediate agent: "[The sensorium commune] seems not improbably to extend through the medulla obligata, the crura of the cerebrum and cerebellum, also part of the thalami optici, and the whole of the medulla spinalis; in a word it is coextensive with the origin of the nerves" (Procháska, 1784, p. 115; transl. T. Laycock in Unzer, 1851, p. 430). As for function, it "changes sensory impressions into motor ones: so that external impressions that are likely to injure our body are followed by motor impressions that will produce movement. . . ." (Procháska, quoted by Neuburger, 1981, p. 244). Procháska divided the sensorium into a part for the soul and consciousness (consisting of the cerebrum only) and a part for the body.

During the first half of the nineteenth century, lines were drawn between those neurologists, especially the French, who believed the thalamus to be motor in function (Magendie and Foville, among others) and those convinced that its nature was sensory. Étienne Renaud Augustin Serres (1786–1868), in his prize-winning two-volume-plus atlas on the comparative anatomy of the brains of the four classes of vertebrate animals (reptiles, fish, birds, and mammals), was more interested in anatomy than in physiology, although he claimed his publication to be the first in the "uniting of all we know about the anatomy, physiology, and pathology of the nervous system" (1827, Preface). Regarding the thalamus, he pointed out (ibid., p. 434) that in the first three classes of animals, the "couche optique" (thalamus) remains underdeveloped, but suddenly in mammals attains its greatest volume; thus, this relatively obscure French neuroanatomist should be nominated one of the earliest comparative neurologists. Even the great Baron Cuvier (1769–1832) in his lessons on comparative anatomy (1800–1805), limited his ideas about the thalamus to the statement (vol. 2, p. 178) that, among the characteristics common to "all animals with red blood," was the fact that they possessed two each of the cerebral hemispheres, the thalami, and the cerebella.

Greater progress in the early knowledge of sensory function of the thalamus was being made outside France. Karl Frederick Burdach (1776–1847; Fig. 10.2) produced his most important contribution to neuroscience (A. C. Meyer, 1970), three volumes on the brain (1819–1826). With a Teutonic talent for diligent systematization, he took pains to report the work of others, described four nuclei in each of the thalami, and noted that of all the "ganglia" they have the greatest influence on mental expression and unify sensory impressions, "thus they allow their owner to realize that he is thinking. . . ." (vol. 2, p. 115). Burdach extrapolated the idea of the *sensorium commune* to placing the seat of consciousness in the thalami, and later wrote "they are the root of consciousness" (1826, p. 290, footnote). In his admirable *Historical Aspects of Cerebral Anatomy* (1971, p. 19), Albert Meyer makes the point that early-nineteenth-century anatomists such as Burdach, concentrated "on elaborating [the] detail of macroscopic anatomy. This entailed the need for a critical re-examination of findings which had remained controversial. . . ." and for that reason historical perspective abounds in their writings, a compulsion that seems to have persisted (cf. Tafel's 1882 annotation of Swedenborg, p. 27, this volume).

Gradually, however, the role of the thalamus as the recipient of sensory input was recognized. In the chapter on the thalamus of his great *Histologie*, Ramón y Cajal (1909, p. 295), wrote in translation: "The role of the inferior lobe of the medial geniculate body in acoustic conduction is undoubted. The results of our histological research accord perfectly with the conclusions of Monakow to prove it." Monakov's studies on sensory input to thalamus are described on p. 98, this volume.

MODERN VIEWS OF CONSCIOUSNESS

The first serious consideration of the neural substrates of consciousness appeared in two English publications, William B. Carpenter's *Principles of Mental Physiology*, published in 1842 with many successive editions and Thomas Laycock's *Mind and Brain* (1860). Although his lectures in Edinburgh were said to be dull, Laycock's influence was pervasive—Hughlings Jackson was one of his students and Laycock's three-volume treatise became widely read. Laycock developed an idea he had published earlier: "[T]he brain, although the organ of consciousness, [is] subject to the laws of reflex action, and . . . [does] not differ from the other ganglia of the nervous system" (1845, p. 298). Sechenov (*see* p. 3, 4, this volume) independently put forth (1863) the same concept of a general reflex pattern throughout the nervous system, a belief which influenced the thinking of Pavlov, Sherrington, and Freud (Amacher, 1964).

William Benjamin Carpenter (1813–1885), English physiologist, not only reaffirmed the thalamus as the center to which almost all sensations are carried but in addition proposed a close connection with cortex:

Fig. 10.2. Karl Frederick Burdach was reared by his widowed mother to distinguish the family tradition in medicine. He did so in research in neuroanatomy and in the authorship of textbooks and an encyclopedia of medical knowledge. (The impression is from Bast, 1928, p. 35 of a lithograph drawn by the artist, Kriehuben, presumably in 1832.)

> The *Sensory Ganglia* constitute the seat of consciousness not merely for impressions on the Organ of Sense, but also for changes in the cortical substance of the cerebrum so that until the latter have reacted downwards upon the Sensorium, we have no consciousness either of the formation of ideas, or of any intellectual process of which these may be the subjects (Carpenter, 1859, p. 757).

As James O'Leary (1956, p. 189) commented, "Thus a hundred years ago, albeit crudely, Carpenter already had two ideas that prevail today: those of a diencephalic center for consciousness and of a to-and-fro relation between thalamus and cortex." Recognition of the return link between cortex and thalamus is further elaborated in Chapter 12.

Arguments surrounding the involvement of the thalamus in consciousness continued along two lines—what constitutes the state of consciousness and does it have a physical substrate? Some measure of the seriousness with which those questions were regarded, especially by the psychologists, was expressed by William James, the Harvard-based propounder of "the stream of thought." In the last chapter of his introductory textbook, he wrote: "Something definite happens when to a certain brain-state a certain 'sciousness' corresponds. A genuine glimpse into what it is would be *the* scientific achievement, before which all past achievements would pale" (1899, p. 468). For himself, James offered the idea that consciousness is a "breath moving outwards, between the glottis and the nostrils . . . the essence out of which the philosophers have constructed . . . consciousness" (1904, p. 491). A half-century later, this ethereal view was echoed by the Harvard neurologist, Stanley Cobb: "It is the integration itself, the relationship of one functioning part to another, which is mind and which causes the phenomenon of consciousness. There can be no center. There is no one seat of consciousness. It is the streaming of impulses in a complex series of circuits that makes mind feasible" (1952, p. 176).

Fig. 10.3. Margaret Floy Washburn taught psychology at Vassar College for many years and was the second woman to be elected to the U.S. National Academy of Sciences (1931). She is shown in a 1927 snapshot taken at the symposium on "Feelings and Emotion" to dedicate a new psychology laboratory at Wittenberg College in Ohio, when she received an honorary degree.

At the turn of the century, American psychologists were debating the animal mind in full voice. A widely used college text on the subject was published by Margaret Floy Washburn (1871–1939; Fig. 10.3) in 1908 with new editions at approximate decades to 1936. She crisply stated her belief in how consciousness should be studied: "While consciousness exists and is not a form of movement, it has as its indispensable basis certain motor processes, and . . . the only sense in which we can explain conscious processes is by studying the laws governing these underlying motor phenomena" (1928, p. 104).

Washburn's contemporary, Robert Mearns Yerkes (1876–1956), famous for his studies of learning in apes confined in primate colonies, pointed out that Jacques Loeb, eminent biologist and student of learning in paramecia, "accepts associative memory as the criterion of consciousness, and then adds, quite safely, 'The criteria for the existence of associative memory must form the basis of a future comparative psychology' " (Yerkes, 1905, p. 145). As Yerkes was writing of animal psychology, he did not directly confront the question of human consciousness, but instead made a Jacksonian pronouncement on levels of consciousness: "[W]e may safely say that mere ability to learn is common to all animals, and that it is indicative of a low grade consciousness; ability to learn associatively . . . is a sign of a higher grade of consciousness . . . there is no one criterion of the psychic which can be accepted as a sign of all forms and conditions of consciousness" (ibid., p. 147).

The central role of the thalamus in mediation of sensation and affect in the state of consciousness was the subject of extensive discussions in the writings of that formidable team of English neurologists, Henry Head and Gordon Holmes (Fig. 10.4): "[W]e believe that the essential organ of the optic thalamus is the centre of consciousness for certain elements of sensation. It responds to all stimuli capable of evoking either pleasure and discomfort, or consciousness of a change in state. The feeling-tone of somatic or visceral sensation is the product of thalamic activity. . . ." (Head and Holmes, 1911, p. 181).

Twenty years later, another influential pair of Englishmen, George C. Campion and G. Elliot

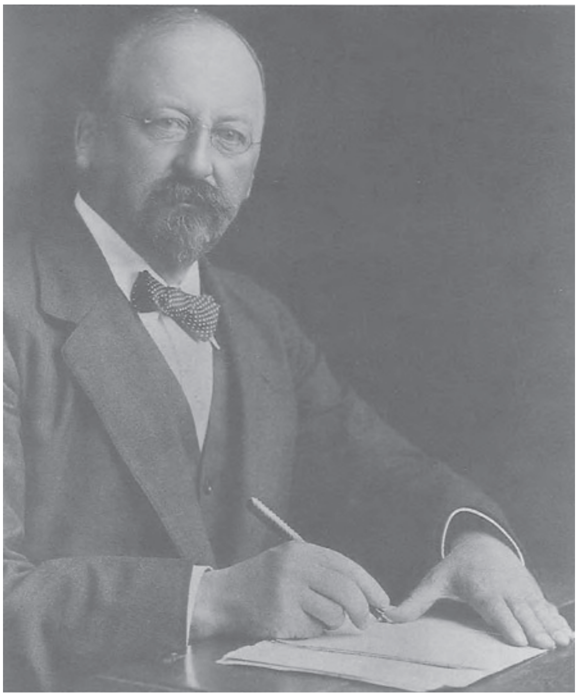


Fig. 10.4. Left—Henry Head, a Quaker, was editor of *Brain* for 15 years and made outstanding contributions to knowledge of sensory systems. He "brought order out of chaos by his vivid thought and refined clinical method" (Denny-Brown, 1970, p. 451). Right—Gordon Morgan Holmes, an Irish neurologist who had trained with Edinger and Weigert, was a meticulous observer, known especially for his description of cerebellar deficits. His attention to detail complemented beautifully the more conceptual approach of Head, and their joint paper (1911) on the sensory effects of cerebral lesions is a classic.

Smith, went further and proposed that within the thalamus resides a center which influences all thinking: "[T]he thalami which Head and Holmes regarded as the central seat of consciousness for the affective aspect of sensation, act also as central propagators of streams of neural impulse to all the 'engrammic systems' or 'neural schemata' which form the neural bases of our thought-processes. . . ." (Smith in Campion and Smith 1934, p. 107). Smith had already elevated the thalamus to prominence as an agent of evolutionary pressure, calling attention to "the neopallium [whose] expansion provoked the vastest revolution that ever occurred in the cerebral structure. It came into being to form a receptive organ for fibres coming from the thalamus, whereby . . . all the non-olfactory senses—secured representation in the cerebral cortex" (ibid., p. 25, 26).

While firm evidence of the sensory input to the thalamus accumulated, tentative statements about the importance of connections with the nearby hypothalamus came from two careful and highly respected experimentalists. Both Walter B. Cannon and S. Walter Ranson believed the hypothalamic "drive" was essential for maintenance of a conscious state of wakefulness; on the basis of close observation of monkeys with thalamic and hypothalamic lesions, the latter proposed that the "active hypothalamus discharges not only downward . . . but upward into the thalamus and cerebral cortex. The upward discharge may well be associated with emotion as a conscious experience" (Ranson, 1939, p. 18).

By midtwentieth century, observations from the clinic were expanding but not necessarily elucidating the problem. Although some neurosurgeons believed that the cortex was involved in consciousness, the extent of the involvement was unclear, whereas others were equally certain the cortex was in no way concerned (*see* Dandy, 1946). The English neurosurgeon, Hugh Cairns, in his Victor Horsley Memorial Lecture, expressed this dichotomy:

> I have the impression that some . . . overestimate the part which the cortex plays in maintaining consciousness, while others attribute to the brain-stem and thalamus degrees of consciousness which are more correctly assigned to the cortex. . . . The fact that these disturbances arise from lesions in the brain-stem and thalamus [indicates] that there are nervous pathways in these parts of the brain which are essential to the maintenance of crude consciousness. . . . A healthy cerebral cortex cannot by itself maintain the conscious state (1952, pp. 113, 141).

Similar observations and conclusions were made by G. Jefferson and Johnson (1950), French (1952), and Barrett, Merritt, and Wolf (1967).

Important as they were, most of those reports were of passing interest to their authors. There was, however, one neurosurgeon for whom the study of consciousness and the human brain was a career-long preoccupation. A year before his death, Wilder Penfield published a volume on *The Mystery of the Mind* (1975). Unlike his predecessors and critics, Penfield provided a synthesis of his half-century of studies of the exposed unanesthetized brains of more than 1000 conscious human subjects (*see* Chapter 5). In general terms, he differentiated two major systems interrelating the higher brain stem and cerebral cortex. The first was an automatic, computer-like mechanism comprising the sensory-motor regions, and the second an interpretative mind-mechanism involving the newer temporal and prefrontal cortical regions. Penfield postulated that the two are functionally related, but only the latter presents interpretations of their experiences to consciousness. As noted earlier, in the 1930s he "proposed the term 'centrencephalic system' as a protest against the supposition that cortical association or cortico-cortical interplay was sufficient to explain the integrated behavior of a conscious man" (1936, p. 68).

On completion of the manuscript for *The Mystery of the Mind*, Penfield sent copies to a philosopher, a neurosurgeon, and a neurologist. The neurologist, Sir Charles Symonds, began his reply in true British fashion:

> As Hughlings Jackson said, we are differently conscious from one moment to another. It is a function, presumably, of synaptic activity, now here and now there. It seems to me more probable that its representation is in the cortex than in the diencephalon, having regard to the relative numbers of neurons available. . . .
>
> The synaptic activity associated with consciousness is continuously present except during sleep. The explanation for this appears to be that the reticular formation in the brain stem in some way facilitates, or "drives," the higher centres, and that in sleep the activity of the reticular formation is inhibited. Here the relationship of consciousness to the brain-stem seems well-established (1975, pp. 96–97).

Many advances in brain research have been accompanied by offensive contention, but that surrounding the seat of consciousness was unusual in twice involving the same person, but on opposite sides of an issue, first at the beginning and then at the end of an intervening century. The circumstances constitute a prime example of the recycling of an idea. In 1860, Laycock complained that Carpenter had plagiarized the concepts put forth in his *Mind and Brain*, but Carpenter succinctly replied that this was impossible, because he could not understand them. In condemning Penfield's "centrencephalon of the brain stem," the irrascible British neurologist, Francis Martin Rouse Walshe (1885–1973) stated that Carpenter's concept of a dominating role of the thalamus in consciousness appeared to be the prototype of Penfield's views, that Penfield had "produced a speculative hypothesis that is virtually a replica of Carpenter's and that it might have been formulated a century ago. . . . As we read it, we find ourselves back in the intellectual climate of mid-nineteenth century, pre-Jacksonian imaginings" (Walshe, 1957, p. 538).

This persistent interest in the neural substrate of consciousness was exemplified in 1948 by an outstanding exhibit presented at the annual meeting of the American Medical Association in Chicago by

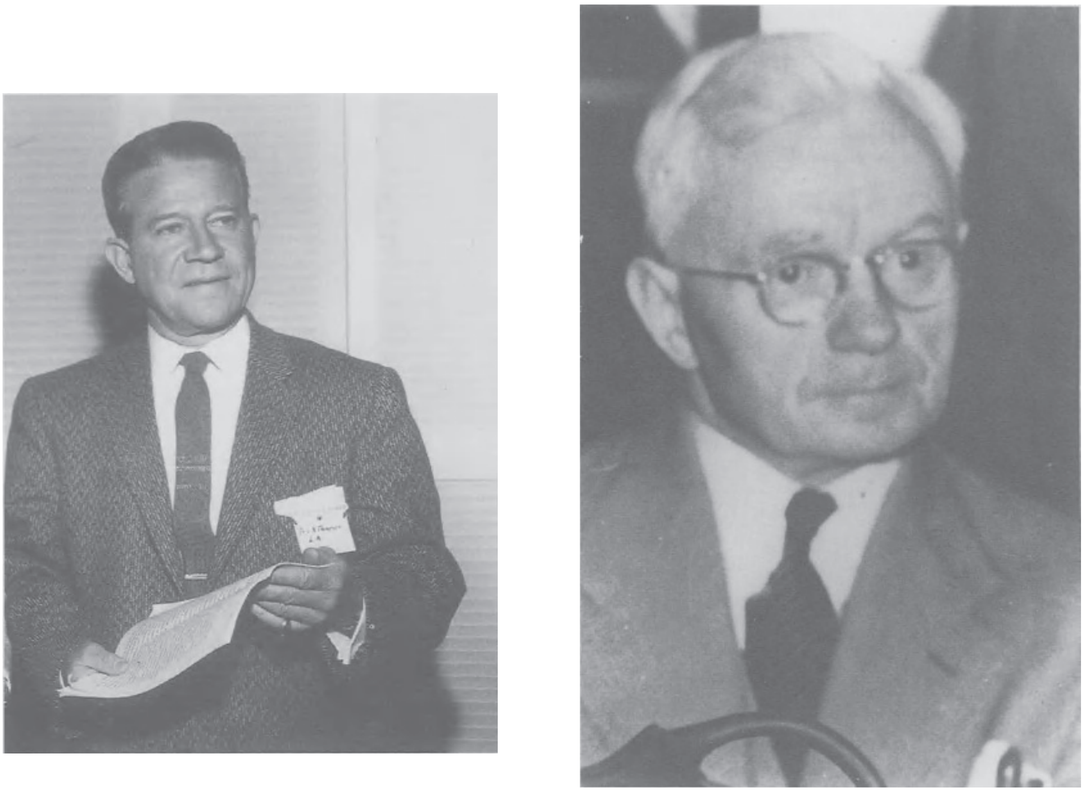
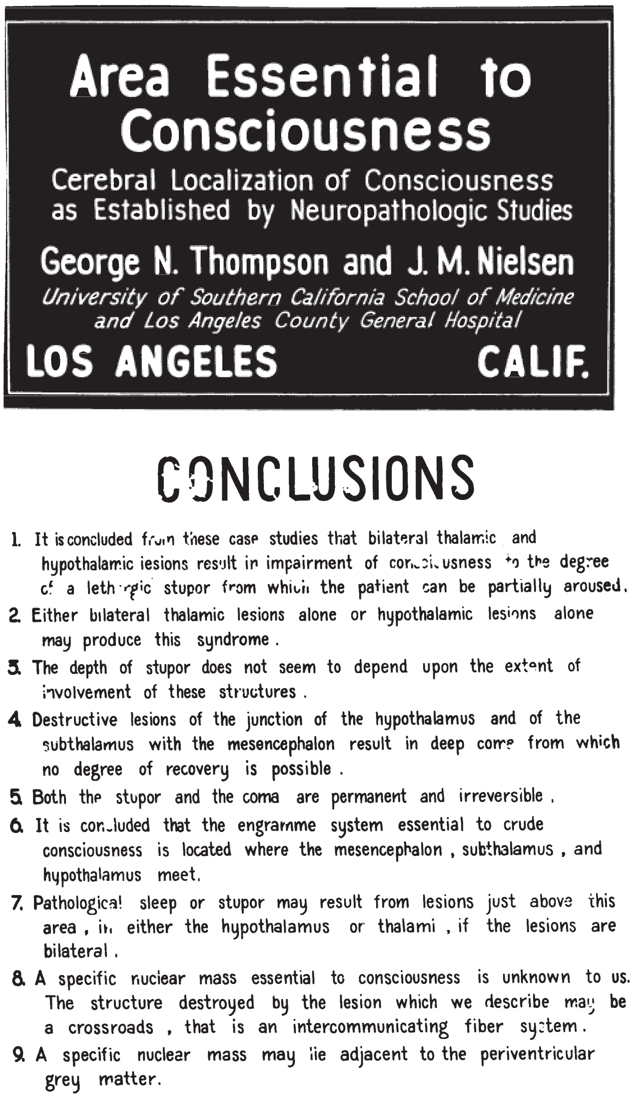


Fig. 10.5. Left—George N. Thompson, a practicing psychiatrist in Los Angeles, collaborated with Nielsen in demonstrating brain pathology associated with loss of consciousness (*see* the following figure). He is shown as president of the Society of Biological Psychiatry, of which he and Nielsen were founding members. Right—Johannes M. Nielsen was the most prominent of the early neurologists in Southern California, and director of the specialized treatment and research center for aphasic disorders established by the U. S. Veterans Administration at Long Beach after the Second World War.

two neurologist/psychiatrists from Los Angeles. Titled "The Area Essential to Consciousness: Cerebral Localization of Consciousness Established by Neuropathological Studies," Johannes M. Nielsen and George N. Thompson (Fig. 10.5) showed photographs of sagittal and coronal sections of human brains illustrating diencephalic damage associated with long-term loss of consciousness and "concluded that the engramme system essential to crude consciousness is located where the mesencephalon, subthalamus, and hypothalamus meet" (Fig. 10.6, right).

During the early twentieth century, even though the central nervous system had been pushed off center stage by an expanding interest in endocrinology and the autonomic nervous system, as historian John Burnham (1977) indicated and Cannon typified, neurologists and neurophysiologists continued to chip away at the mind/body problem. They were well aware that control of visceral processes resides in the central core of the brain—psychosomatic medicine was just around the corner. However, the "visceral" system did not fully replace the intellectual appeal of the mystery of the conscious mind and symposia on the subject continued to be organized at intervals, one of the most influential of which was the study week of the Pontificia Academia Scientiarum convened in 1964 by Sir John Eccles (*see* Fig. 10.7, right, p. 208). He brought together an international assembly of distinguished neuroscientists to talk about *Brain and Conscious Experience*, the title of the ensuing publication (1966) which he edited. Twelve years later, Eccles provided a remarkable survey and synthesis of broad topics related to the human experience of consciousness in his first series of Gifford Lectures (1979) at the University of Edinburgh. His initial concept limited commun-



Area Essential to Consciousness

Cerebral Localization of Consciousness
as Established by Neuropathologic Studies

George N. Thompson and J. M. Nielsen

University of Southern California School of Medicine
and Los Angeles County General Hospital

LOS ANGELES CALIF.

CONCLUSIONS

1. It is concluded from these case studies that bilateral thalamic and hypothalamic lesions result in impairment of consciousness to the degree of a lethargic stupor from which the patient can be partially aroused.
2. Either bilateral thalamic lesions alone or hypothalamic lesions alone may produce this syndrome.
3. The depth of stupor does not seem to depend upon the extent of involvement of these structures.
4. Destructive lesions of the junction of the hypothalamus and of the subthalamus with the mesencephalon result in deep coma from which no degree of recovery is possible.
5. Both the stupor and the coma are permanent and irreversible.
6. It is concluded that the engramme system essential to crude consciousness is located where the mesencephalon, subthalamus, and hypothalamus meet.
7. Pathological sleep or stupor may result from lesions just above this area, in either the hypothalamus or thalami, if the lesions are bilateral.
8. A specific nuclear mass essential to consciousness is unknown to us. The structure destroyed by the lesion which we describe may be a crossroads, that is an intercommunicating fiber system.
9. A specific nuclear mass may lie adjacent to the periventricular grey matter.

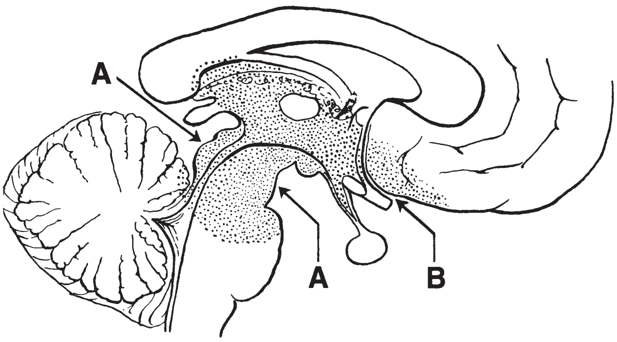


Fig. 10.6. Left—Two panels from a series exhibited at the American Medical Association meeting in 1948, showing brain sections from patients who had had long-term unconsciousness before death. (Courtesy of George N. Thompson.) Right—Diagram of monkey brain on which stippling indicates the boundaries of the region found experimentally to be essential for consciousness. (From G. Jefferson, 1958, p. 734.)

ication between the brain and the environment ("the world") to what was then called the "dominant" hemisphere (*see* Fig. 10.8, left, p. 209). In the light of the revealing work of Roger Sperry and his group on patients with commissurotomy ("split brain") demonstrating laterality of function (*see* Chapter 6, this volume), Eccles moderately revised his views, postulating that the minor hemisphere could communicate with the world, but only indirectly through the commissure to the other side (Fig. 10.8, right).

Sperry's own views on consciousness were crystallized by the thorough testing he and others carried out not only on patients with therapeutic commissurotomies but also on a case of agenesis of the corpus callosum, studies which revealed that the whole brain is more than the sum of its parts. In his words:

> Another thing to come out of all this . . . is a modified concept of the nature of mind and consciousness. . . .

Fig. 10.7. An impromptu photograph of three eminent neuroscientists of the midtwentieth century: the Australian, John C. Eccles (right) with two Frenchmen, Paul Dell (left), and Alfred Fessard (center) taken at a meeting in the 1960s.

> This is a view that postulates the presence in the brain of mental as well as physiological forces, and contends further that the phenomena of conscious awareness play an important active role in shaping and directing the flow pattern of cerebral excitation. . . . [They] interact with and largely govern the physiochemical and physiological aspects of the brain process. It obviously works the other way round as well, and thus a mutual interaction is conceived between the physiological and mental properties (Sperry, 1968, pp. 135–136).

A pioneer investigator of the neurophysiology of consciousness, Benjamin Libet at the University of California, San Francisco, and his associates applied sophisticated electronic techniques to the unanesthetized human brain and found (Libet, Wright, Feinstein, and Pearl, 1979) that electrical stimulation of the exposed sensory cortex must be maintained 500 ms to 1000 ms before subjective sensation is experienced, whereas the neural events of the evoked cortical potential are seldom prolonged beyond 25 ms to 50 ms. Such dissociation in timing of physical and mental events raised difficulties for theories of psychoneural identity, again reinforcing Cuvier's words, "Although the brain is much studied no one has not left something to be discovered by his successors" (quoted by Serres, 1827).

THALAMIC FUNCTIONS AND EFFERENT PROJECTIONS

Returning to the midnineteenth century, the thalamus was then regarded as the true visual center, an idea from Galen's time and the focus of a dissertation (1834; *see* Fig. 10.9, p. 210) by the Dane, Sophus Augustus Wilhelmus Stein (1797–1868). He listed more than 14 synonyms for "thalamus" then in use and, based on careful dissections, he described the structures in man (*see* Fig. 10.10, p. 211) and in many lower animals as the origin of the optic nerves; Stein also thought the thalami connect with the entire cerebral cortex.

DOMINANT HEMISPHERE	MINOR HEMISPHERE
Liaison to consciousness	No such Liaison
Verbal	Almost non-verbal
Linguistic description	Musical
Ideational Conceptual similarities	Pictoral and Pattern sense Visual similarities
Analysis over time	Synthesis over time
Analysis of detail	Holistic — Images
Arithmetical and computer-like	Geometrical and Spatial

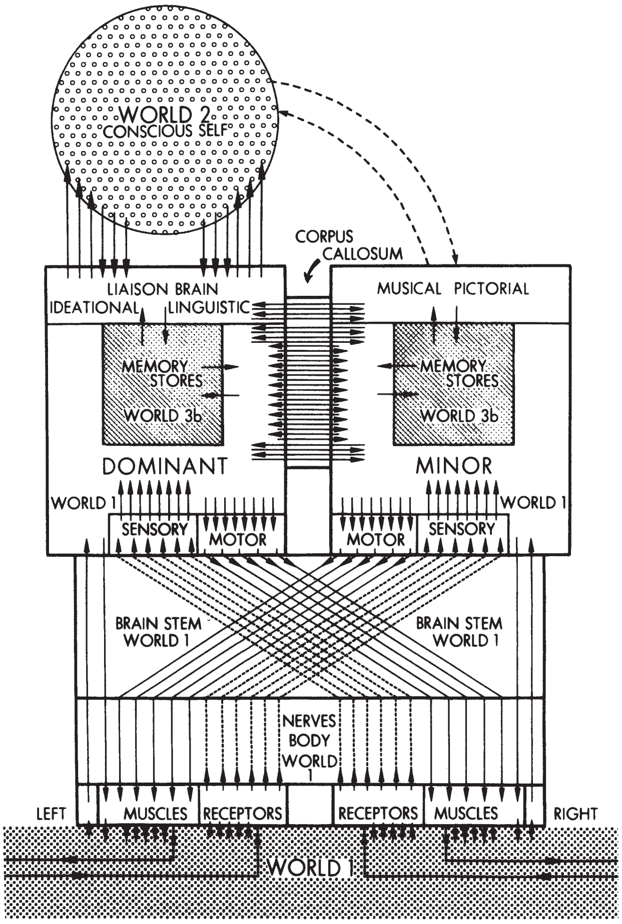
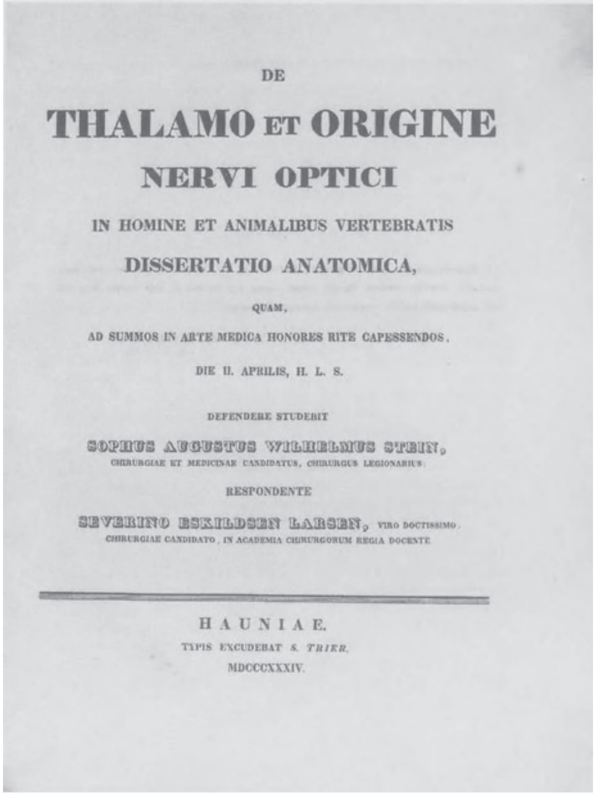


Fig. 10.8. Left—A comparison of the specific activities of the two cerebral hemispheres from the viewpoint of dominance of one hemisphere over the other, as understood during the 1970s. Right—Eccles's geometric diagram of the principal lines of commun-ication from peripheral sensors to the cerebral hemispheres, showing only a tentative participation (broken lines, top) of the minor hemisphere in consciousness. (From Eccles, 1979, pp. 222, 223, Figs. 10–7, 10–8.)

The European concept of sensory thalamic function recorded by Stein and earlier by Burdach was echoed in the English *Cyclopaedia* (1835), edited and extensively authored by Robert Bentley Todd (1809–1860). He described the optic thalami as "the principal foci of sensibility without which the mind could not perceive the physical change resulting from a sensitive impression" (vol. 3, p. 722 M). In a more sweeping context, he envisioned the encephalon as a series of centers serving intellect, volition, sensation, muscular coordination, emotion, and respiration and deglutition (ibid, p. 722 N). Although the ordering of those centers presaged Hughlings Jackson's hierarchic levels, their self-containment without interconnections precluded any idea of levels of control or inhibition.

A more substantively correct treatise on the connections and functions of the thalamic nuclei was published in 1865 by Jules Bernard Luys, a Parisian of imposing presence (*see* Fig. 10.11, p. 212). A biographer (M. B., 1897, p. 141) wrote that Luys's synthesis of what was then known about the cerebrospinal nervous system gave "une impulsion nouvelle et durable" to French thought along those lines that had been abandoned after Gall's theories were discredited (*see* Ritti, 1897). Luys's excellent three-dimensional depictions (*see* Fig. 10.12, p. 213) endeared him to a modern peer in that genre, the American neuroanatomist, Wendell J. S. Krieg, who wrote that "Luy's [sic] book . . . marks the beginning of knowledge of thalamic function" (1970, p. 56). With schemata, three-dimensional drawings, and even crude photographs, Luys presented an organized concept based on his own and others' experimental evidence and his extensive clinical observations. He revived Procháska's



DE

THALAMO ET ORIGINE

NERVI OPTICI

IN HOMINE ET ANIMALIBUS VERTEBRATIS

DISSERTATIO ANATOMICA,

QUAM,

AD SUMMOS IN ARTE MEDICA HONORES RITE CAPESSENDOS,

DIE II. APRILIS, H. L. S.

DEFENDERE STUDEBIT

SOPHUS AUGUSTUS WILHELMUS STEIN,

CHIRURGIAE ET MEDICINAE CANDIDATUS, CHIRURGUS LEGIONARIUS;

RESPONDENTE

SEVERINO ESKILDSEN LARSEN, VIRO DOCTISSIMO,

CHIRURGIAE CANDIDATO, IN ACADEMIA CHIRURGORUM REGIA DOCENTE

HAUNIAE.

TYPIS EXCUDEBAT *S. TRIER.*

MDCCCXXXIV.

Fig. 10.9. Title page of the 1834 dissertation of S. A. W. Stein in which he compared the brains of many vertebrates including humans and described the thalami as the origin of the optic nerves. That publication was the earliest of several distinguished monographs written solely on the thalamus.

appellation, *sensorium commune*, and suggested that each of the then-known four thalamic nuclei had connections to specific cortical areas and served a specific sensory modality.

The credit for initiating serious work on the thalamus held by Luys is shared by Bernard von Gudden (1824–1886) who substantiated the earlier evidence with new approaches to the problem of connections between thalamus and cortex. Familiar with the latest technical advances in tissue preparation emanating from German laboratories, Gudden's experiments on brain function were also notable in that his animals were operated neonatally and studied as adults. In 1870, his published results show that destruction of specific areas of the rabbit cortex produces atrophy of certain thalamic nuclei.[1]

One of the assistants in von Gudden's Munich laboratory was Constantin von Monakow (1853–1930; Fig. 10.13), the Russian–Swiss son of a wealthy nobleman. In his private Zurich laboratory, later associated with the university, von Monakow extended his mentor's experiments and, again in rabbits, demonstrated atrophy of the contralateral superior colliculus after enucleation at birth, and in other studies complete degeneration of the lateral geniculate body (whereas the remainder of the thalamus was intact) by neonatal removal of the occipital lobes (1882).

Each of the three preceding investigators had a modern partisan who claimed for the man he championed a preeminent role in promoting knowledge of the thalami. In *Founders of Neurology* (Haymaker and Schiller, 1970), Kreig described the discoveries of Luys (p. 56), Papez wrote of von Gudden (p. 45), and Yakovlev eulogized von Monakow (p. 487). Historians have conferred that distinction, however, on von Gudden, recognizing the novelty

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[1] For a concise review of those studies, *see* Walker (1938, p. 7).

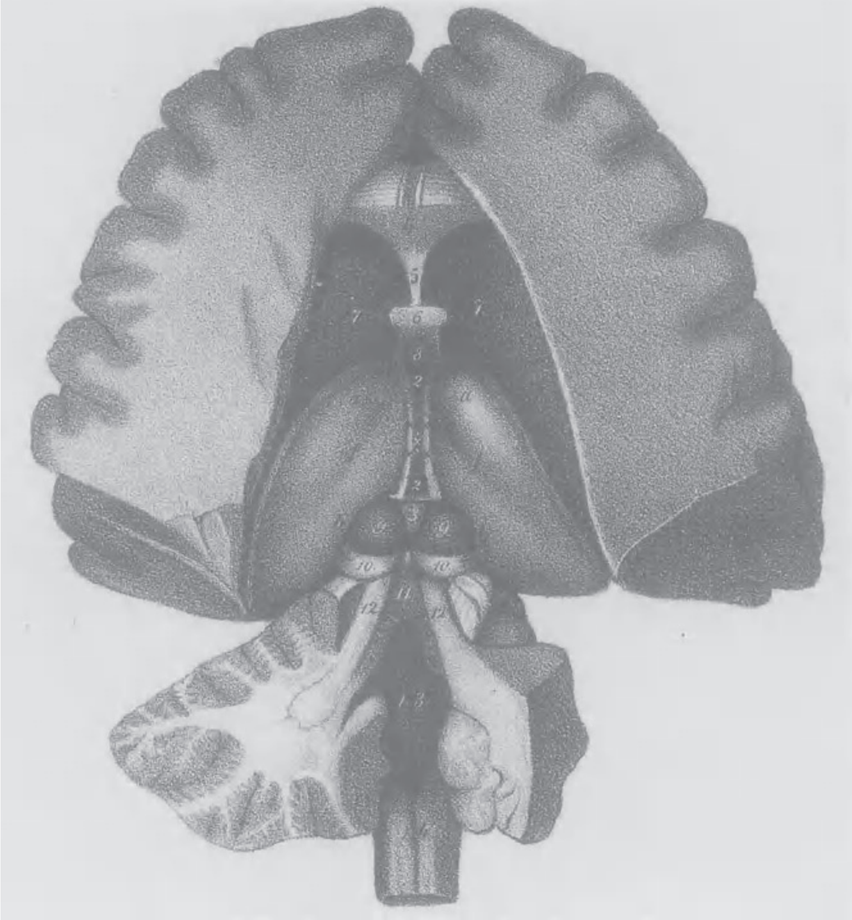

Fig. 10.10. Stein's dissection of a human brain showing it "true to nature" (ad nat. verit.). 1—Thalami nervi optici; 2—third ventricle; 3—pineal gland; 4—anterior corpus callosum; 5—septum pellucidum; 6—anterior fornix; 7—corpus striatum; 8—anterior commissure; 9,10—corpora quadrigemini; 11—valvulae magnae; 12—cerebellar peduncles; 13—fourth ventricle; 14—inferior medulla oblongata. (From Stein, 1834, Fig. 1.)

and significance of his chronic preparations (*see* Clarke and O'Malley, 1968, p. 606, passim).

The work of August Henri Forel (1848–1931; *see* Fig. 10.14, p. 215) contributed to the knowledge that the thalamic nuclei are separate in function as well as in cellular morphology. This Swiss psychiatrist-neuroanatomist made a clear statement (1887) of what was later called the neuron doctrine, based on pathological and functional evidence, within two months of that of his countryman, Wilhelm His. Additional support for the idea of thalamic nuclei as distinct units emerged when Flechsig claimed (1896) that differentiation between certain thalamopetal cells could be based on the progressive myelination of their projections, which constituted "gateways" to the brain and its functions when they continued to the cortex.

Many years later, a crucial point was raised by the Hungarian neuroanatomist, Stefan Polyak, then at the University of Chicago. He asked if those cortical projection areas were "to be regarded exclusively as 'gateways' of the cerebral cortex for the incoming impulses . . . or, do they participate likewise in higher integrative processes, . . . thus depriving the intercalated regions of the exclusive monopoly of these higher processes?" (Polyak, 1932, p. 213). Polyak's ablation experiments on monkeys had shown the unexpectedly wide extent of the somatic sensory cortex to include the precentral "motor" region.

The early microscopical studies of Luys and Forel, followed by those of Nissl (1889), demonstrating that the thalamic nuclei are distinct units, received physiological support when it became

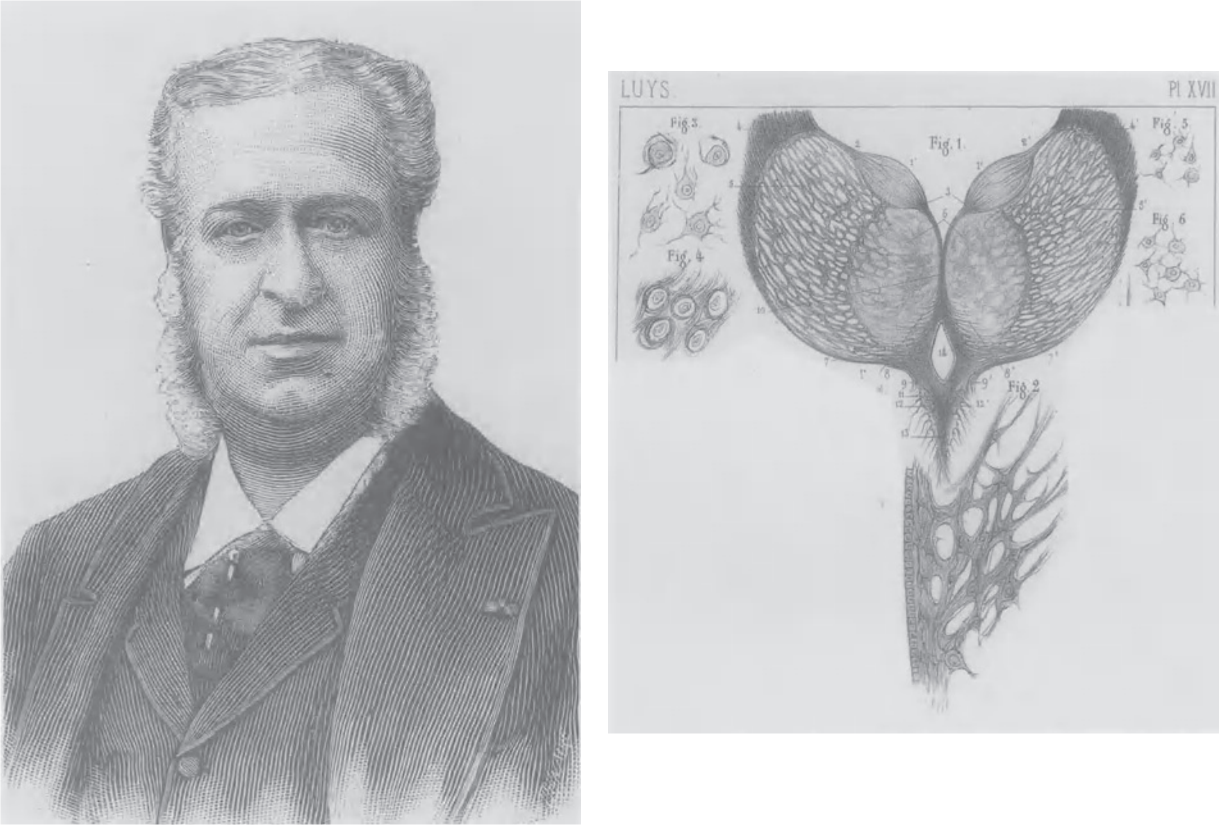

Fig. 10.11. Jules Bernard Luys's talent for draughtmanship created orderly depictions of the connections of the thalamus. 1—Anterior nuc.; 2—afferent fibers to ant. nuc.; 3—efferent fibers; 4—converging fibers from cortex to external thalamus; 5—secondary converging gray fibers which lose themselves in center (6) of thalamus; *see* original for additional legends. (Portrait from obit. signed M. B., 1897, p. 141; drawing from Luys, 1865, facing p. 39, Plate XVII, Fig. 1.)

possible to confine a lesion to a single nucleus so that the resulting behavioral deficit was relatively unaffected by damage to surrounding parts. Two French experimentalists, Sellier and Verger, used bipolar electrolysis "to study carefully with methods not used by our forerunners" (1898, p. 706) the nuclei of the couche optique. They applied (usually) a current of six milliamperes and varied the duration according to the desired size of the lesion,[2] then eight to ten days later tested the animals' perception of body position, heat, and touch. The modern nature of their experiments is striking; they also verified histologically the size of the lesions and illustrated them in the published report. The authors concluded that the "central ganglions" serve if not the same at least very similar functions as the cerebral convolutions, in other words, a specificity of function. That principle was elaborated about 30 years later from a laboratory where Dusser de Barenne had instituted the use of strychnine (neuronography) to explore thalamocortical connections. A systematic mosaic of connections constructed with von Gudden's retrograde atrophy method applied to newborn rabbits demonstrated that projections from anteroposterior sites on two medial thalamic nuclei are represented on cortex in inverse order (Stoffels, 1939; Fig. 10.15).

Coincident with the revelations about the thalami from the experimental laboratory, a scattering of clinical observations denoting thalamic involvement was appearing in the literature. The first description of a case of thalamic pathology with specific symptoms was published in excruciating detail in England in 1825 (Hunter) and a simi-

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[2] This was the first application of the method for lesion-making selected by Clarke and Horsley to use with their novel stereotaxic instrument (*see* Chapter 9).

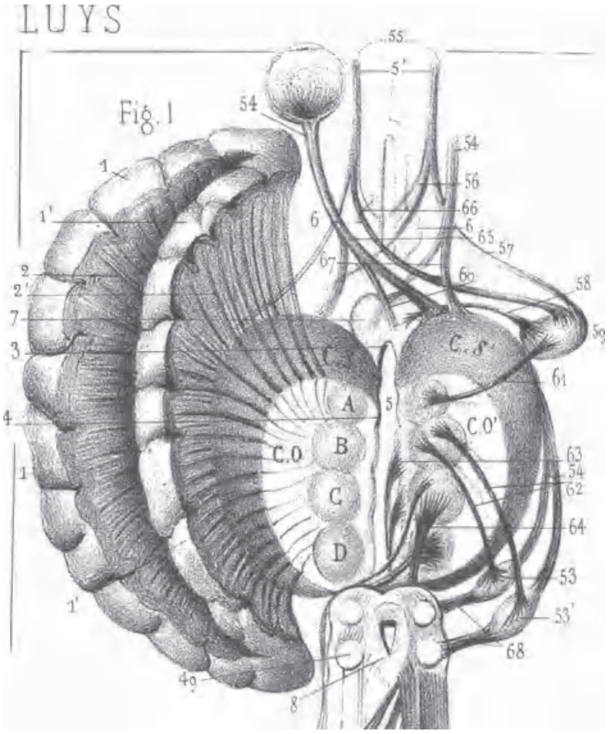

Fig. 10.12. A theoretical figure by Luys showing fibers converging on the thalamus. 1—Cerebral cortex; CS—corpus striatum; CO—couche optique (thalamus); A,B,C,D—anterior to posterior nuclei; 2,3,4—superior fibers from the cortex converging on the thalamus after passing through the corpus striatum; 5—walls of third ventricle; see original for additional legends. (From Luys, 1865, facing p. 4, Plate I, Fig. 1, ×3/4.)

lar patient was followed by Richard Bright (1837) at Guy's Hospital. Among the later neurologists with such cases, James Crichton Browne (1840–1938) stands out (Viets, 1938). This energetic and intelligent director of the West Riding Pauper Lunatic Asylum noted that the sensory cortex and the thalami share the same arterial blood supply. From observations on seven patients, he concluded that the thalami were "probably" sensory ganglia, but more interestingly he proposed a mechanism to explain the impairment of reflexes on the side opposite the lesion. Browne wrote (1875, p. 252 passim): "The sensorial ganglia . . . almost invariably consult the cerebrum before dealing with the impressions which they receive. . . ." He envisioned an "encephalic loop current" as part of a reflex pathway to explain the experimental observations made on himself: he felt pain after, not before, withdrawing his toe from a noxious stimulus, there having been a "sacrifice of time" in transmission of the loop current. It seemed to him that "undulations of nerve force are being perpetually diffused centrifugally from or through the optic thalami" and it was not difficult to understand how a lesion might create an "enfeeblement" of reflex activity.

Eight decades after Browne, George Bishop at Washington University championed the spinothalamic tracts' primitive function in pain transmission. In an unpublished talk to the Washington University Medical Center early in 1958, Bishop elaborated on his finding that the ventral lateral thalamic nuclei do not carry pain to the somesthetic cortex; in addition to experimental evidence, he invoked phylogeny, pointing out that the thalamus is the pain center in primitive brains and therefore the pain tracts are the classical spinothalamic projections situated in the more medial thalamic nuclei.

During Browne's enlightened directorship at West Riding, David Ferrier conducted experiments there on cats and dogs that disproved Meynert's (1872a) theory, concurred in by the French, that the thalamus has motor function. Ferrier's contemporary and associate at University Hospital, Queen

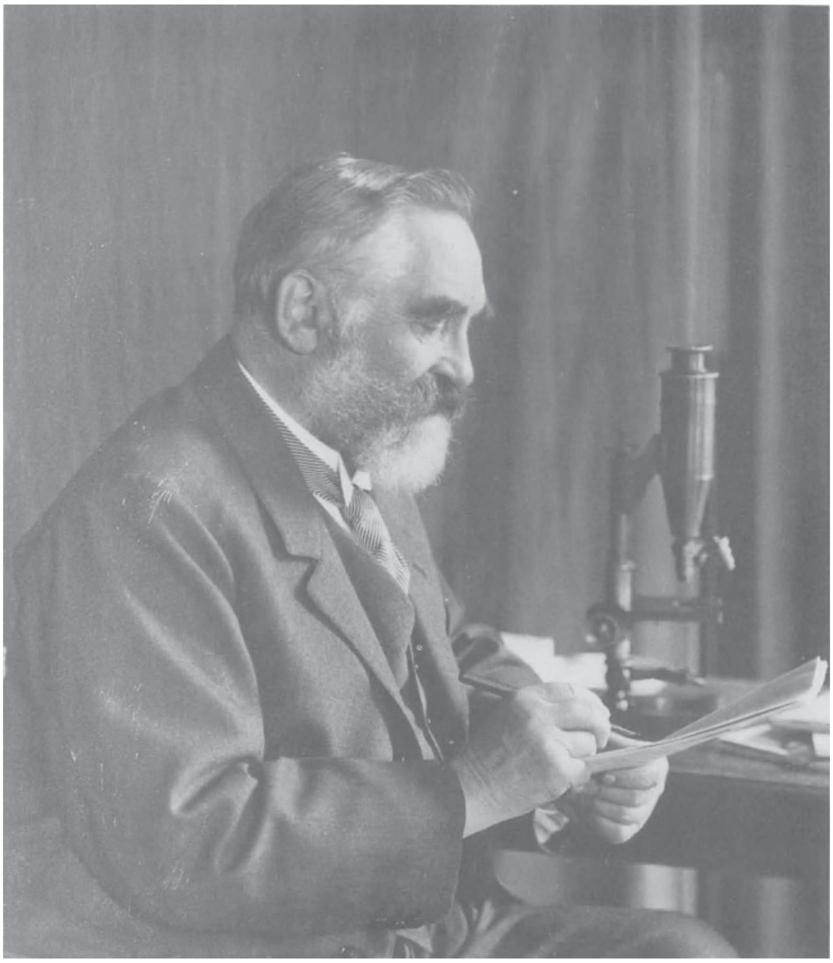

Fig. 10.13. Constantin von Monakow, photographed during the late nineteenth century, in his early career as a clinical and experimental neurologist, demonstrated the close relationship between cortex and thalamus in auditory and visual functions.

Square, Victor Horsley, like his colleague was caught up in the experimental approach to the many neurologic questions confronting them in their practices. When Horsley suggested a research topic to an American postdoctoral guest in his laboratory, it was the optic thalamus, "about which little was known" (Sachs, 1909, p. 95). Ernest Sachs, Sr. spent the greater part of two years in London, carrying out carefully executed experiments on cats and macaques with the novel stereotaxic instrument (*see* Chapter 9). His relatively discrete electrolytic lesions of the thalamus confirmed von Monakow's 1895 work showing connections between thalamus and prefrontal cortex. Although he contributed little new information, because he used the capricious Marchi stain for his histological preparations (Walker, 1938, p. 9), Sachs was among the first to electrically stimulate the thalamus. In the clinic, the thalamic syndrome, a condition also called thalamic hyperesthetic anesthesia, is the best known of the several neurologic disorders first described by Dejerine from his wide experience at the Salpêtrière and Bicêtre hospitals in Paris. He related thalamic disease or damage to a combination of specific symptoms, dissociated those due to motor deficits from sensory loss, and ascribed both to derangement of the vascular supply (Dejerine and Roussy, 1906).

The comparative and embryological studies of Edinger in Europe and the Herricks in America (*see* Chapters 1 and 9) contributed to sorting out the morphologic complexities of the many thalamic nuclei. An interest in function, however, relatively flagging during the early twentieth century, was refocused by Le Gros Clark in two lectures to the Royal College of Surgeons in 1932. Their publication in *Brain* represented the second historically significant treatise devoted solely to the thalami.

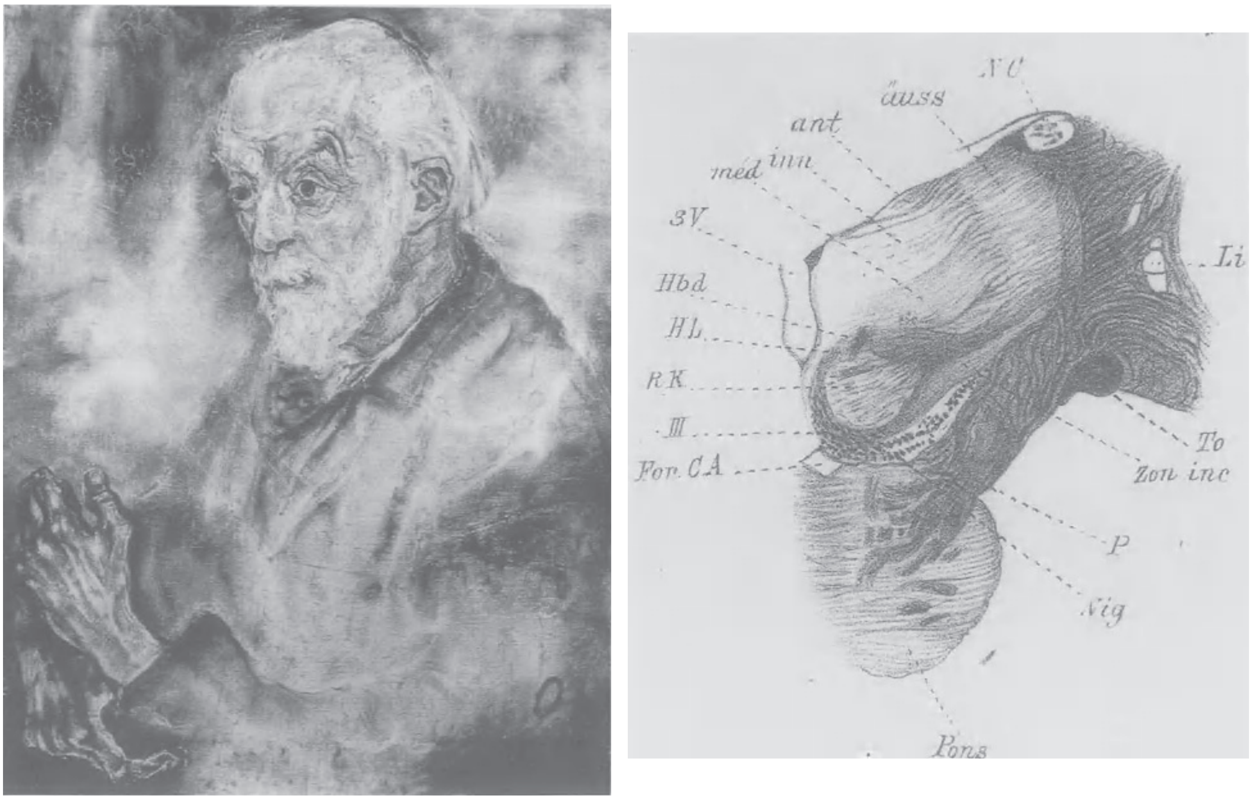

Fig. 10.14. August Forel's portrait was painted by Oskar Kokoshka and hangs in the Kunsthalle, Mannheim, Germany. Forel's drawing shows the thalamic nuclei. NC—Caudate nuc.; 3V—third ventricle; ant, inn, anss—superior, inner, outer thalamic nuc.; med—centre median; Hbd—habenula; HL—long bundle of the crest of Meynert; RC—red nuc.; III—oculomotor nerve; For CA—ant. foramen; Nig—substantia nigra; P—pes pedunculi; Zon inc—zona inserta; To—optic tract, Li—lenticular nuc. (From Forel, 1877, Plate VII, Fig. 7.)

Clark set out to "clear the terminological atmosphere," then evaluated the early work showing that thalamic fibers constitute the most direct route to the cortex, and presented evidence that the thalamus is "the anatomical equivalent of the very threshold of consciousness" (Clark, 1932, p. 407).

By 1938, thalamic cytoarchitecture and connections with the cortex were fairly well known, the former in part through Cajal's work and the latter assisted by neuronography studies (Dusser de Barenne and McCulloch, 1938). In addition, Papez had concluded, from a detailed degeneration study of serial sections of the brain of a dog from which one hemisphere had been removed six months previously, that "the dependence of the neothalamic nuclei on the cortex is evident" (1938, p. 118). The year 1938 also saw publication of the third important monograph on the subject, *The Primate Thalamus*, by the Canadian-born neurologist and neurosurgeon, A. Earl Walker. Based in part on extensive experimental studies (e.g., Walker, 1936) this milestone treatise provides an example of phylogeny being called on to "prove" an idea. Explaining that the group of midline thalamic nuclei is "relatively constant throughout the mammalian scale," Walker wrote: "Because it is present in the thalami of most primitive animals not possessing appendages, it must be related to the axial portion of the body" (Walker, 1938, p. 239). Relatedly, the author invoked phylogenetic correlations in suggesting the functions of other, nonmidline nuclei, but although the intrinsic connection between some of them with intralaminar nuclei was known, their functions were "unclear" or "even less clear" (ibid., p. 243). Among the details of the specific representation of efferent thalamic projections to cortex

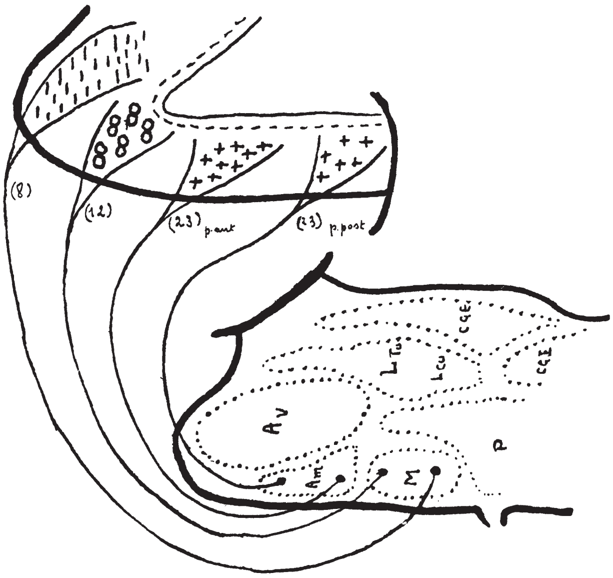

Fig. 10.15. A systematic mosaic of inverse relationships between cortical fields (top) and thalamic nuclei (bottom) was found in the rabbit after cortical ablations. P—Pretectum; Av—nuc. ant. ventralis; M—nuc. medialis; Am—nuc. ant. medialis; Ltu—nuc. lateralis, partio tuberculosa; Lcu—nuc. lateralis cuneiformis; CGI, CGE—corpus geniculatum int., ext. (From Stoffels, 1939, p. 822, Fig. 69.)

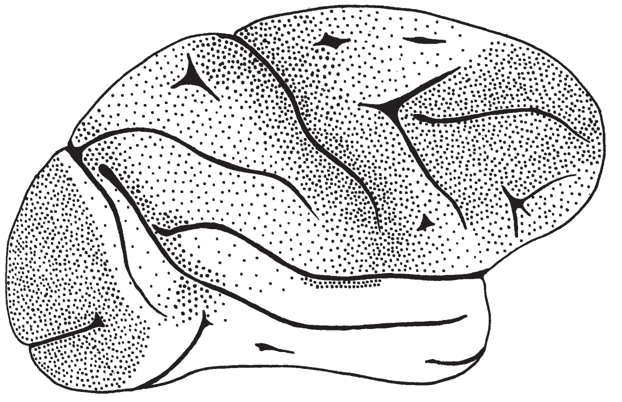

Fig. 10.16. Stylized primate right cortical hemisphere on which the relative densities of the thalamic projections to various cortical areas are depicted. Projections are most numerous in the prefrontal, pre- and postcentral, and occipital areas. (From Walker, 1936, p. 191, Fig. 68, ×4/5.)

advanced by Walker's experiments on subhuman primates, an illuminating finding was that "the intensity of the thalamic projections to the different cortical areas is not at all uniform" (ibid., p. 190), as shown in Fig. 10.16. He pointed out that functionally distinct groups of thalamic nuclei revealed physiologically in the laboratory, in many clinical cases can be correlated with specific pathological syndromes, thus merging theoretical mechanisms based on anatomical relationships with clinical applicability. Walker's volume concluded with this paragraph:

> This discussion of its pathology has emphasized the complex function of the thalamus. It is the mediator to which all stimuli from the outside world congregate and become modified and distributed to subcortical or cortical centers so that the individual may make adequate adjustments to the constantly changing environment. The thalamus thus holds the secret of much that goes on within the cerebral cortex (ibid., p. 277).

The intimacy of the association between the environment and thalamic mediation was revealed only after suitable histological methods were at hand that could bring into focus the complete picture of information transfer from the outer world to cortex. In brief mention (*see* Chapter 7 for details), the introduction of radioactive markers to trace normal pathways from retina to thalamus to specific layers in primary visual cortex showed not only the strict distribution of the projection terminals but also their correlation with the physiologically demonstrated orientation-dominant and hemispheric-dominant behavioral responses. This rare example of knowledge of function preceding the discovery of form concerns the work of Grafstein, Hubel, and Wiesel, and their associates from the late 1950s to the early 1970s.

THE DIFFUSE PROJECTIONS

Concomitant with the massive technological effort associated with the Second World War, electronic amplification and recording methods were advanced to where they could provide meaningful information in many areas of endeavor. After the horrendous, worldwide disruption of basic biomedical research, progress in electronic technology achieved during the war effort was particularly (but not exclusively) applicable to furtherance of neurophysiologic investigations. This was especially notable in studies of the central nervous system, into which the evoked potential technique

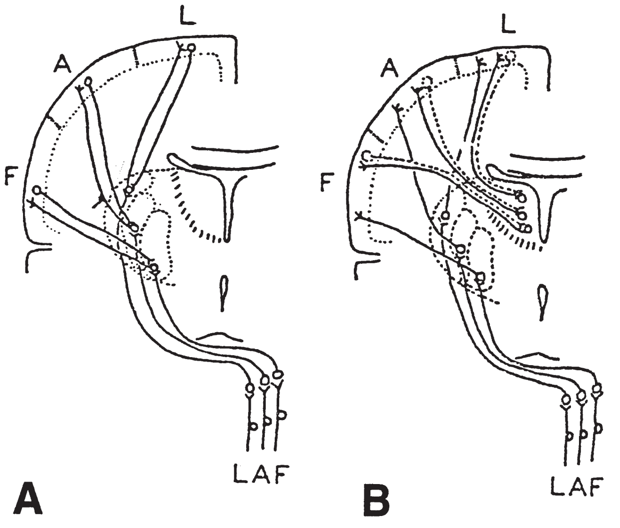

Fig. 10.17. By comparing a diagram **(A)** from Dusser de Barenne and McCulloch (1938) with their own schema **(B)**, Dempsey and Morison illustrated their conclusion that data from recruiting and spontaneous cortical potentials suggest a second and diffuse thalamocortical system involving the dorsal medial nucleus and sensory cortex (dotted lines), in contrast to the well known specific circuits between the ventral lateral thalamic nuclei and cortex. L, A, F—leg, arm, face. (From Dempsey and Morison, 1942b, p. 306, Fig. 5.)

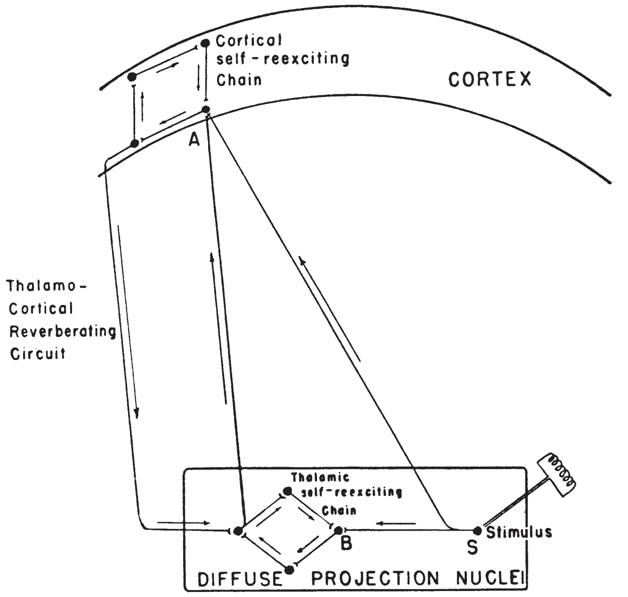

Fig. 10.18. Diagram of the mechanism proposed for development of the recruiting response, based on physiologic similarities of cortical and thalamic responses, as revertebrating circuits A and B. (From Verzeano, Lindsley, and Magoun, 1953, p. 194, Fig. 15.)

moved cephalad from the peripheral nervous system, where the axonologists had used it to great advantage. At this time also electroencephalography, a technology of proven clinical value, became a research tool essential to the demonstration of a nonspecific relationship between thalamus and cerebrum.

The groundwork for identification of the widespread influence of thalamus on cortical activity was carried out by Robert S. Morison and Edward W. Dempsey at the Harvard laboratory of physiology in the early 1940s. They found the physiologic relation between the two regions while stimulating the smaller intralaminar nuclei of the cat thalamus: a single shock produced over most of the cortical surface a train of negative potentials of gradually increasing amplitude which crested, then faded away. These spindle-shape “recruiting” responses were also obtained by repetitive stimulation, waxing and waning during five-per-second stimuli to the nuclei. Later, Morison justified the diffuse image: “I think we were the first to use the term ‘diffuse.’ We did it because there are places in this system . . . from which the entire system can be activated” (1954, p. 110). Because of its diffuseness, the response was considered to be nonspecific, in contrast to the already known specifically localized cortical response to stimulation of the larger thalamic nuclei, the augmenting response. Dempsey and Morison continued their initial observations (as did many other neurophysiologists) and soon the recruiting response was recognized as similar to the spontaneous cortical rhythm and resembled it in detail (Dempsey and Morison, 1942a,b; Fig. 10.17). Later they wrote, “Evidence is presented that a type of spontaneous effect . . . results from activity of the thalamic relay nucleus and its cortical projection” (1943, p. 296). That same year, it was proposed (Rose and Woolsey, 1943) that the nuclei reticularis thalami might serve as the distribution system for the diffuse projection (*see* below). The pursuit of the mechanism of the recruiting response became widespread among neurophysiologists; among them the active group at Northwestern University Medical School in Chicago (later at the University of California, Los Angeles), in the course of examination of the diffuse projections to cortex, diagrammed their concept of reverberating circuits (Verzeano, Lindsley, and Magoun, 1953; Fig. 10.18). Eventually, intracellular recording demonstrated that neurons participating in the recruiting response are also involved in EEG desynchronization (arousal) (Purpura and Shofer, 1963). Yet in spite of intense investigation, the recruiting response "remains as one of the largely unexplained phenomena in the electrophysiology of the cortex and thalamus" (Jones, 1985, p. 632).

A sharp focus on the diffuse projections was brought about at the midtwentieth century by the discovery in Magoun's Northwestern laboratory of the ascending reticular activating system (*see* Chapter 12). The finding that the pattern of cortical phasic activity (shown by the EEG) is profoundly altered by stimulation of the brain-stem reticular core was quickly substantiated (Jasper, 1949), but the import of an ascending arousal system was obscured by the attention accorded the other diffuse projection to cortex, the thalamic system. That situation was evident at a meeting a few months after the Northwestern work was published.

The symposium, held at Atlantic City, was presided over by Earl Walker and signaled unprecedented progress in understanding the physiology of thalamocortical relationships. The keynote paper by two prominent figures in the field who collaborated extensively—first at Johns Hopkins and later at the University of Wisconsin, Madison—the neuroanatomist Jerzy E. Rose and the neurophysiologist Clinton N. Woolsey summarized the state of knowledge of the intricate organization of the thalamic nuclei: "The available data concordantly suggest that the mammalian thalamus consists of three divisions different from each other in their phylogenetic and ontogenetic development, and in their relations to the cortex" (Rose and Woolsey, 1949, p. 402). Based on a fruitful coupling of cortical mapping using evoked potentials with histological studies of embryologic development, they characterized the epithalamus as independent of the "endbrain" and reduced in size in higher forms, the dorsal thalamus as projecting to primary sensory cortical areas which become progressively constricted in higher mammals, and the ventral division consisting of the independent ventral lateral geniculate body and the nucleus reticularis thalami as projecting "upon a large number of cortical fields" and "capable, presumably, of evoking generalized cortical activity." Reminiscent of C. J. Herrick's thesis that the increased size of the cortical association areas relate to the higher nervous functions, Rose and Woolsey stated: "[I]t appears that a very prominent feature of the phyletic development of the mammalian neocortex consists in the growth and differentiation of those sectors which are intercalated between the primary projection fields. . . . [T]hose which are so separated, drift, so to speak, farther apart the more highly the cortex is developed" (ibid., p. 401). The configuration on the cortex of primary and secondary somatosensory areas illustrated by Rose and Woolsey (Fig. 10.19) shows that in lower mammals the concentration of thalamocortical axon terminals favors the primary areas (White, 1979, p. 281). In humans, however, "the total extent of the primary visual, auditory and somatic sensory fields is relatively small and the total cortical surface of these fields together with the primary limbic fields and the primary motor area is probably less than 15 percent of the total cortical surface" (Rose and Woolsey, 1949, pp. 400–401).

Another seminal paper at the Atlantic City symposium was presented by Herbert Jasper from Montreal. He described some characteristics of the diffuse thalamocortical system which "seems well established" to exist "with independent projection to the cortex overlapping that of the better known specific . . . systems" (Jasper, 1949, p. 405). And he concluded, ". . . there exists a separate regulatory system involving thalamus and other brain stem structures which acts upon the cortex, controlling the form and rhythm of the background upon which afferent impulses must act. . . ." (ibid., p. 418). In discussing the paper, Magoun said, perhaps with a tinge of sarcasm: ". . . today, this diffuse system appears to compete seriously with all the rest of the thalamus together in its functional significance" (Magoun, 1949, p. 420). Thus did the two Titans of diffuse systems duel politely in subtle competition.

To close the symposium, Walker lamented the isolationism of thought about the thalamus brought about by nonstandard nomenclature, and offered some conciliatory remarks regarding the nice correlation between what was known about "Jasper's thalamic reticular system" and Magoun's "lower reticular centers," summarizing the proceedings thus: "There appear to be at least three mechanisms of thalamortical [sic] integration. The first is that of the well known thalamic relay systems, the second that of the thalamic elaborative or associative system and the third that of the thalamic reticu-

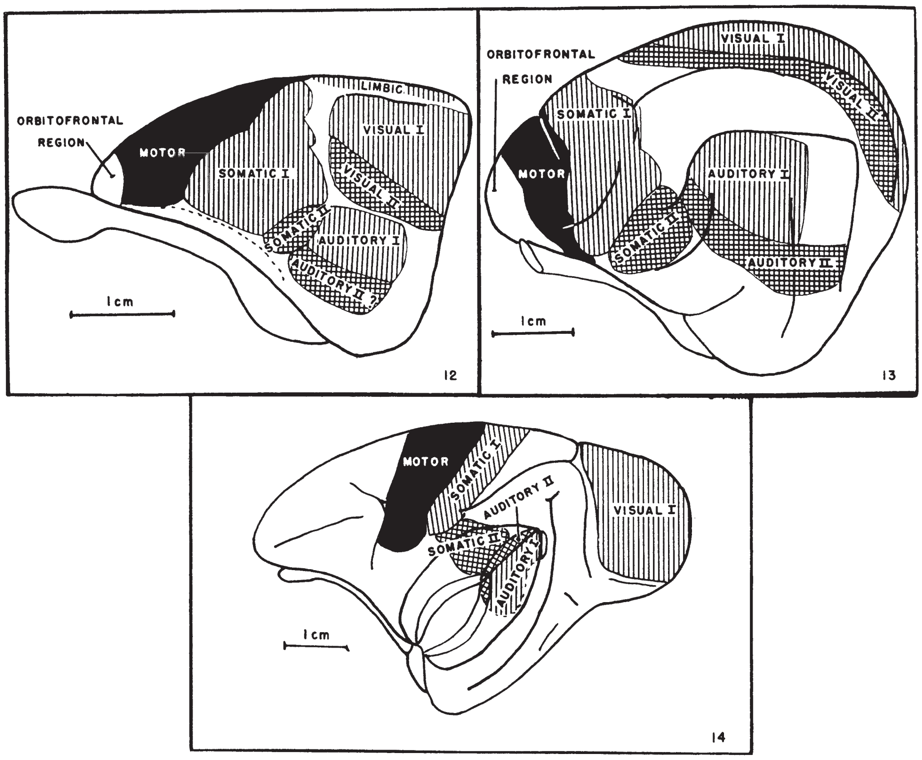

Fig. 10.19. Diagrams of the cortical fields of rabbit (left), cat (right), and monkey (below) to show primary (hatched) and secondary (cross-hatched) projection areas of visual, acoustic, and somatic afferent impulses. Note that higher position on the phylogenetic scale coincides with smaller primary sensory areas and larger secondary areas. *See* text for comparison with human brain; images not in scale. (From J. Rose and C. N. Woolsey, 1949, p. 400, Figs. 12–14.)

lar system" (Walker, 1949, p. 453). The chairman also noted the advantage conferred by the semi-independence of the thalamus and cortex manifested by thalamic spiking without concomitant cortical spikes, "since it allows the thalamus to react and adjust to extraneous stimuli without affecting cortical activity or consciousness" (ibid., p. 453).

The differentiation of thalamocortical pathways and their nuclei as specific and nonspecific in function opened at least two questions that demanded further research. The first was at what level do the linkages between specific and nonspecific systems occur? Jasper and Ajmone-Marsan (1952) found an interconnection at the cortical level for visual and intralaminar responses. Regarding a more caudal interconnection, the report (Nauta and Whitlock, 1954) of anatomic connections of intralaminar nuclei with ventralis posterior and other specific relay nuclei was welcomed as implying the possibility of a diencephalic interaction between specific and nonspecific systems: "The basal ganglia are the traditional relay points in the extrapyramidal descending paths in the motor system. The above observations suggest in addition the basal ganglia serve in much more general cerebral processes" (Magoun, 1954b, p. 114).

The second question was the reintroduction of the problem of structure that had been addressed 75 years earlier (notably by Luys and Forel), but with a new twist: Are there morphologic differences between specific and nonspecific neurons? Scheibel and Scheibel (1966) solved that problem with their Golgi-stained comparative studies of the ventrobasal nucleus of the thalamus, a specific system, and the diffuse centre median-parafascicular complex. The ventrobasal pattern of organization, which includes bushy terminal arborizations accommodating repetitive firing, implies a correlation of organization with specificity and physiological differentiation. In contrast,

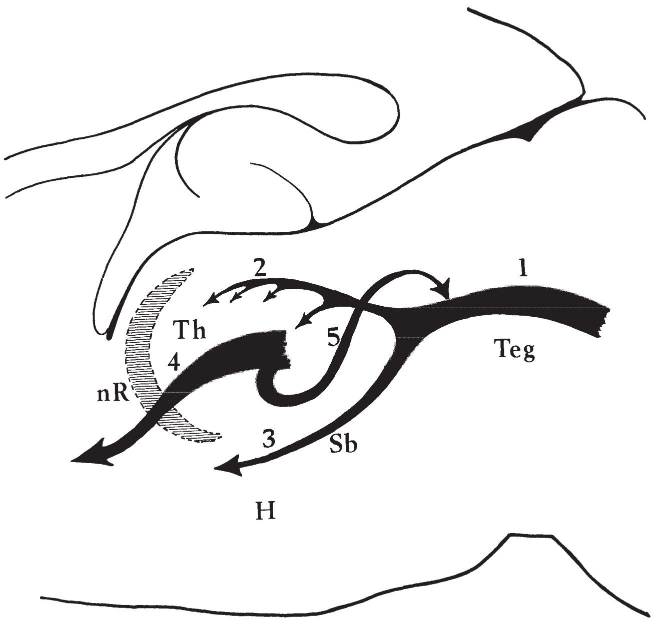

Fig. 10.20. A graceful schematic delineates the possible rostral courses of axons from brain-stem reticular core (1) and thalamic nonspecific (4) systems. Teg—Tegmentum; 2—branch passing dorsally to thalamic intralaminar (Th) and dorsomedial fields; 3—branch passing ventrally through subthalamus (Sb) and hypothalamus (H), to nuc. reticularis (nR). The thalamic system sends a caudal branch back to the tegmental level, perforates the nuc. reticularis, and continues rostrally. (From Scheibel and Scheibel, 1967, p. 84, Fig. 15.)

neurons of the nonspecific fields are homogeneous, with the afferents seeming to disappear smoothly into the neuropil matrix. This symbiosis of structure and function affirmed the individuality not only of the thalamic nuclei but also of the neurons within them.

The existence of an inhibitory action of thalamocortical neurons, as suggested by Jasper (*see* below), was supported by the Scheibels' extension (1967) of their studies on the structural organization of a specific and a nonspecific thalamic nucleus to the corticopetal projections of nonspecific nuclei. They examined the relation of intralaminar axonal and dendritic neuropils to adjacent specific and associational nuclei, as well as projections to the cortex and drew a circuit model (Fig. 10.20) that compared the pathways to cortex of the brain stem with those of the thalamic system and showed the dendrites of nucleus reticularis traversed by fibers coursing between thalamus and cortex. Their findings plus what was known of reticularis neurons led to the proposal that reticularis neurons may be inhibitory to their specific and nonspecific targets alike. Later, intracellular recordings (Schlag and Waszak, 1970) revealed that reticularis neurons discharge profusely when other thalamic neurons are silent, in striking agreement with the Scheibels' hypothesis.

The idea of possible inhibitory mechanisms operating on thalamic projections was suggested by Jasper in experiments using intracellular recording predominantly from the thalamic reticular system: Cats and monkeys habituated to a tone can be aroused by a novel tone after ablation of the auditory cortex (Li, McClennan, and Jasper, 1952).[3]

> These observations suggest the possibility that the function of the reticular system in normal adaptive . . . behavior may be more in the nature

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[3] This work was deemed a milestone contribution because it introduced cellular (unitary) studies (Steriade, 1981, p. 330).

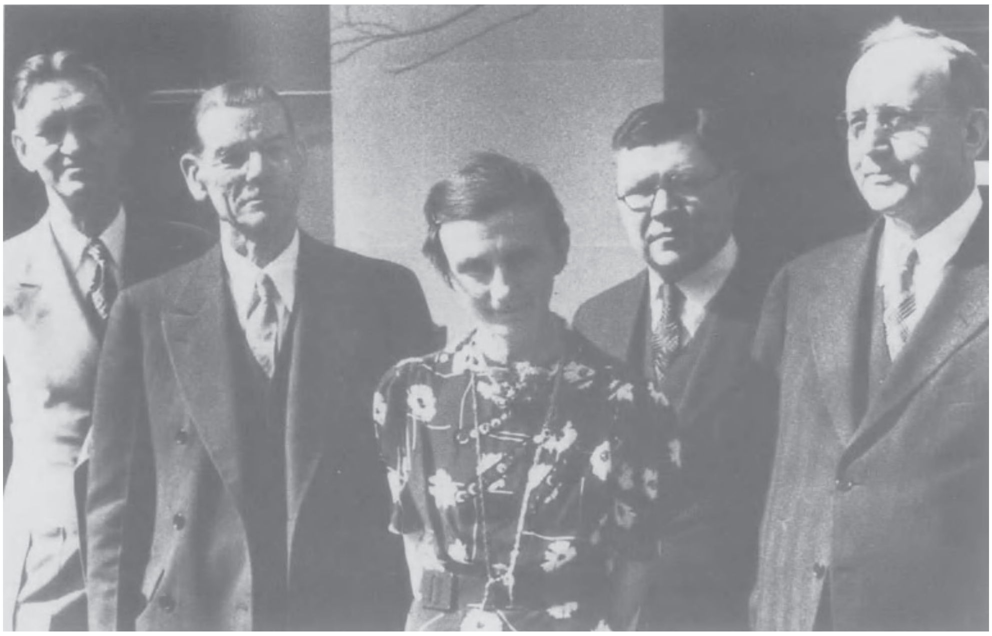

Fig. 10.21. This rare photograph of Elizabeth Crosby (center) was snapped at Northwestern University Medical School during a visit by a group of prominent neuroanatomists, about 1940–1941. From left: A. T. Rasmussen, C. Judson Herrick, Crosby, O. Larsell, and the host, S. Walter Ranson.

> of a prevention of a general arousal reaction to all stimuli, with a control of selective responsiveness to significant stimuli. . . . This implies that inhibitory rather than excitatory functions may be most important. . . . (Jasper, 1958, pp. 321–322).

The Montreal group believed that activation is characterized by varying degrees of excitation and inhibition "in a matrix" of patterns "held in the dendritic meshwork of the cortex" (ibid., pp. 330–331).

At the conclusion of the second edition of *The Waking Brain*, Magoun attempted to assimilate the focal inhibitory system into the larger concept of an integrated mechanism:

> The consequences of the action of this mechanism are the opposite of those of the ascending reticular activating system . . . for internal excitation. The principle of reciprocal innervation . . . would appear relevant to the manner in which these two higher antagonistic neural mechanisms determine the alternating patterns of brain activity manifest as wakefulness and light [nonREM] sleep (Magoun, 1963, p. 174).

A comment made by Elizabeth Caroline Crosby (1888–1983; Fig. 10.21), one of the great comparative neuroanatomists of the twentieth century, raised a relevant and thought-provoking semantic question. In her invited discussion of thalamic connections, Crosby (1972, p. 89) asked: "Would inhibition of the activity of a neuron be regarded as a supportive function? Or should such a term be applied only when there are possible excitatory effects?" The answer applies to all situations in which inhibition is a passive rather than an active event, and relates to Hughlings Jackson's dictum that the outcome of neurological dysfunction may be due to the mere absence of the removed process or it may be the effect of a new process (*see* Chapter 9).

Elizabeth Crosby's reputation as a dedicated and knowledgable authoritory on nervous systems throughout the animal kingdom is legendary. Her doctoral dissertation under C. J. Herrick at the University of Chicago, was "The forebrain of alligator mississippiensis," and became a classic publication (1917), opening doors to her internationally. She showed the reptilian representation of cortex to be the precursor of more sophisticated cortex in higher animals, a comparative approach that underwrote her life-long interest in brain evolution. Her extensive knowledge of the human brain was inspirational in her clinical work with neurologists, neurosurgeons, and psychiatrists. Perhaps more influential than personal contacts were the reference volumes, *The Comparative Anatomy of the Nervous System of Vertebrates, Including Man* (Kappers, Huber, and Crosby 1936), and a dissection guide, *A Laboratory Outline of Neurology* (Herrick and Crosby, 1918). Both works were published collaboratively, but Crosby's hand fashioned them during her seven decades of research, interpretation, and teaching.

After the two groups working on cortipetal inputs from brain stem and thalamus had reported their research in 1949, a decade of intensive activity in Chicago, Montreal, and elsewhere worldwide continued to add new interpretations and findings. Jasper's so-called thalamic reticular system did not escape scrutiny by Magoun's group. In cats and monkeys, their studies yielded "results suggesting that the . . . system is organized for mass thalamic influence upon associational cortex" (Starzl and Magoun, 1951, p. 146) and serves as a "mechanism [by which] the electrical activity of a large portion of the cerebral mantle can be brought under control by stimulation of a very tiny area of the thalamus" (Starzl and Whitlock, 1952, p. 464). Combined with the "zone of collateralization" of the brain stem reticular activating system, there was provided a "uniquely complete liaison with the external environment" (ibid., p. 464).

A definitive account of thalamic anatomy and physiology was brought to the modern period by a fourth publication focused solely on that organ. Outwriting in scope and depth Stein's dissertation, the lectures of Le Gros Clark, and Earl Walker's monograph, Edward G. Jones, a New Zealand-born neuroanatomist, contributed *The Thalamus* (1985). In more than 800 pages and with a bibliography of about 2300 references, the volume signaled the core position of research in this region of the brain. In sorting out the thalamic nuclei, Jones stated: "The hallmark of the classical system is specificity" (ibid., p. 117), in which inputs to the thalamus seek specific nuclei, are systematically distributed according to the receptor sheet they represent, and may also end on cells of a particular physiologic class.

A definition of the anatomy of the diffuse thalamocortical system is not yet possible, but there are as many versions of its function as there are investigators of what it does. An early definition spoke in generalizations: "Thus, the diffuse thalamic projection system seems to represent a mechanism for widespread simultaneous distribution of incoming impulses to large subcortical and cortical areas—a system organized, essentially, for associative and integrative functions (Verzeano, Lindsley, and Magoun, 1953, p. 183). A quarter-century later, a necessarily more sophisticated point of view regarding the nonspecific midline thalamic nuclei was that they consist of "networks of interneurons [that] form the substrate for multiple interactions that lose the labels of their specific origins and produce the convergent activities of excitation and inhibition" (Brazier, 1977, p. 205). This perspective benefited from the information that in addition to excitatory arousal impulses to cortex, the brain stem reticular formation can also forward inhibitory signals, as already noted.

OVERVIEW OF THALAMOCORTICAL PATHWAYS AND CONSCIOUSNESS

The thalamus was known in antiquity, was recognized as having something to do with vision, and therefore was named the optic thalamus. By the late eighteenth century, Procháska (1784) viewed the dual thalamus as a relay station for reflexes, the *sensorium commune* in which sensations are transformed into movement. Early in the next century, the philosopher/psychologists were in serious debate over the mind–brain question and the relation to it of sensation and consciousness and Burdach wrote that the thalami are "the root of consciousness." An argument that lasted three decades (Lacey, 1985) centered on the emotions and whether they are initiated in motor and visceral activities which feed back to the neocortex before being felt, as the James–Lange theory postulated. Or, following Cannon, are affective states translated in thalamus into central and peripheral signals for "fight or flight" (Fig. 10.22).

In the meantime, the neurologist–anatomists, represented by Luys, von Gudden, and Monakov, established the identity and independence of the thalamic nuclei, thus laying the foundation on which rests the specificity of thalamic projections to cortex. When it was realized that all sensory inputs except olfactory form synapses in thalamus, the correlation of longstanding coma with thalamic

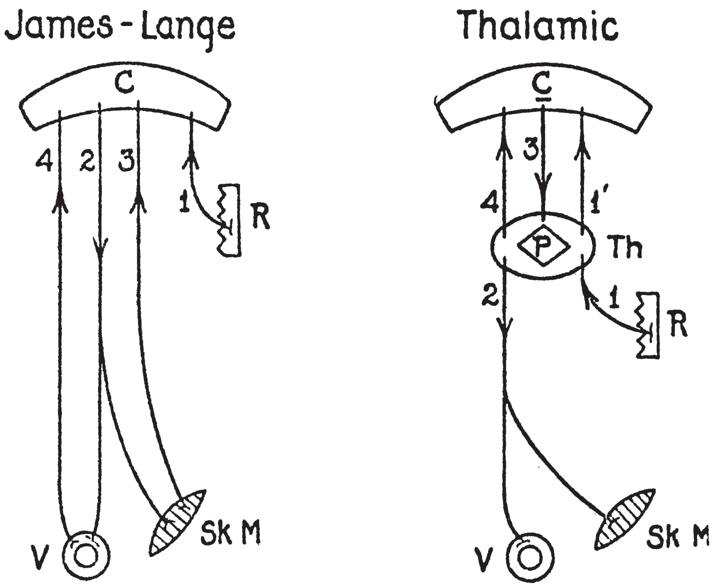

FIG. 1. Diagram of nerve connections in the James-Lange theory.

FIG, 2. Diagram of the connections in the thalamic theory.

R, receptor. *C*, cerebral cortex. *V*, viscus. *Sk M*, skeletal muscle. *Th*, thalamus. *P*, pattern. The connecting lines represent nerve paths, with the direction of impulses indicated in each instance. Cortico-thalamic path 3, Fig. 2, is inhibitory in function.

Fig. 10.22. Two diagrams of "that whale among the fishes, the theory of emotions" (M. F. Meyer, 1933), outlining the James–Lange theory and that of Cannon and Bard; *see* text. (From Cannon, 1931, p. 282, Figs. 1 and 2.)

lesions demonstrated postmortem in patients settled the question of the seat of consciousness.

In addition to the classic specific thalamocortical pathways, at midtwentieth century the existence of a diffuse system was implied by the electrophysiological studies in experimental animals (Dempsey and Morison). Clear evidence of a diffuse arousal effect on cortex of impulses from brain stem reticular core (Moruzzi and Magoun) was quickly followed by Jasper's reports of diffuse projections from thalamus to cortex and their inhibitory action. The subsequent flurry of activity produced a wealth of confirmatory and new findings and a later evaluation (Steriade) that the original observations had stood the test of time. Regarding the gaps in knowledge of thalamocortical interrelations, "only the application of a wide variety of approaches can provide the information necessary to understand how the cortex receives and processes its thalamic input" (White, 1979, p. 301). This chapter presents only a partial story; the key to the pervasive influence of the thalamus lies in the fact that the cortex projects back to it in profusion and thus establishes an effective means of control by higher centers. The discoveries of corticothalamic pathways and functions is addressed in Chapter 12 and the rewards of reading these sections in sequence is obvious.