The Thalamic Syndrome and its Mechanism
Report of Two Cases, One Due to Arteriovenous Malformation in the Thalamus

THOMAS A. WALTZ, M.D., AND GEORGE EHN, M.D.
Division of Neurological Surgery, Baylor University College of Medicine, Houston, Texas

The thalamic syndrome was defined in 1906 by Dejerine and Roussy\(^{5}\) whose original description has been little improved upon. Confusion still surrounds the true nature of many of the disorders that have since been labeled “thalamic syndrome.” As originally described, it possessed the following features: 1) continuous pain on one side of the body commonly referred to as aching, boring, gnawing, burning, icy, or crushing; 2) paroxysms of hypersensitivity to sensory stimulation, sometimes of sufficient severity to prevent adequate sensory examination; 3) elevation of the sensory threshold, generally slight in degree and selective of certain sensory modalities; 4) referral of pain over a wide area which may not include the location of the actual stimulus; 5) evocation by touch, pain, heat, and cold of similar diffuse highly disagreeable sensations more unpleasant and less definable than the effect of the same stimulus to an unaffected area; 6) a distinct lag between the time of application of a stimulus and its appreciation; 7) pain which may far outlast the stimulus which evoked it; 8) lack of association with severe motor deficit, so much so that the presence of severe paresis argues against the painful state being of thalamic origin.

Consideration of the physiology of sensation is essential in understanding the disturbances present in patients with thalamic and other central pains. Head et al.\(^{13}\) in 1905 first postulated that the afferent system incorporated double qualities to which he applied the terms protopathic and epicritic. These terms have lost popularity in the recent literature but the concept of two types of pain remains. In 1915 Ranson\(^{29}\) suggested that “protopathic” or what we now call “slow pain” sensibility was transmitted in peripheral nerves by fine unmedullated fibers. In 1930 Erlanger and Gasser studied peripheral nerve transmission by action-potential measurements and classified them by fiber size and rate of transmission;\(^{19}\) the large medullated fibers served as conductors of highest velocity impulses, small medullated fibers had an intermediate conduction rate, and the unmedullated fibers conducted at the slowest rate. Also the threshold of response varied inversely with the fiber diameter.\(^{5}\)

Attempts have been made to relate the different modalities of sensation to specific types of fibers. Most experimenters have attempted to block certain sized fibers differentially and then determine which sensory modalities have been impaired and which remain intact. Studies of neuronal asphyxiation\(^{18}\) clarified the roles of the types of fibers transmitting various sensations, for it was found, after applying an atraumatic clamp to a nerve or a pressure cuff to an extremity, that the modalities of “fast pain” and temperature discrimination were lost early whereas “slow pain” transmission persisted. During the persistence of slow pain the response to stimulus was exaggerated and the pain had many of the features of thalamic pain. Kendall\(^{17}\) performed an illuminating experiment upon himself by running water at 30°C over his elbow for one hour after which he tested sensation in the distribution of the ulnar nerve to his hand. He found complete loss of thermal discrimination in the affected area where both hot and cold stimuli were appreciated as heat having an intense, unpleasant, burning quality after approximately one second’s delay in perception of the stimulus. It thus appeared that the rapidly appreciated sensations could be divorced from the slow ones, resulting in thalamic-like pain from a subthalamic, even peripheral, level. Studies of cocainized nerves,\(^{30,31}\) in which the chemical tends to block the more slowly transmitting fibers first and the rapidly transmitting ones last, have yielded more variable results.

The various fibers which subserve pain...
sensation are intermingled in the peripheral nerves and the spinothalamic tract of the spinal cord. The larger medullated components then course superficially in the mesencephalon to the ventral posterolateral (VPL) nucleus of the thalamus. Of great interest are the separate courses taken by the fine unmedullated pain fibers to the reticular formation, central grey, nucleus intercollicularis and deep strata of the superior colliculus26,27,37 and then to the thalamic nuclei parafascicularis, paracentralis, and centralis lateralis. During axon degeneration studies in humans, Bowsher4 has found, in postchordotomy subjects, distribution to the ipsilateral lateral reticular nucleus of the medulla and bilaterally to the VPL nucleus and the medial reticular substance of the medulla. Degeneration to the VPL nucleus was seen by Biemond2 in a case of softening involving the secondary sensory area of the parietal cortex. This patient had a severe painful state of the contralateral half of his body with hemihypalgesia, though all other modalities of sensation were intact.

The study of patients subjected to stereotactic thalamotomy for relief of pain sheds some light on the physiology of the thalamus and the perception of pain. Mark et al.23-25 found their eleven patients treated for pain of advanced cancer fell into two groups. After surgery, the patients of one group experienced no relief of the pain of the disease. The pains of the malignant diseases could no longer be localized but the patients were no more comfortable than they had been prior to thalamotomy. The lesions producing these results were primarily in the VPL and ventral posteromedial (VPM) nuclei. The patients in the second group were relieved of pain and had minimal or no sensory deficits. The lesions producing this effect were found primarily in the parafascicular and intralaminar nuclei. The study of thalamic lesions produced by Hécaen et al.14 in attempts to alleviate thalamic pains is similarly instructive. Four of 5 patients in whom lesions were made in the medial thalamus were pain-free for periods up to several months. One of these 4 patients experienced paresthesias at 5 months, but had no pain. The 5th patient had recurrence of moderate pain after 2.5 months but no further worsening occurred in the next 8 months. Two other patients having lesions in nucleus VPL experienced considerable sensory deficit without satisfactory relief of pain.

Pertinent also is the result achieved by Logue21 with a small lesion in the centrum medianum. His patient suffered from recurrent pain in the left leg after bilateral thoracic chordotomy for spinal malignancy. Complete relief followed the creation of such a thalamic lesion and it endured for the patient’s remaining 8 months of life. No sensory deficit was produced by this operation. The patient’s course strongly suggested that the permanent relief of pain resulted from the thalamic lesion and not from the compression of the cauda equina by the malignant process at L-3. At post mortem the 4 mm. lesion was primarily in the centrum medianum with but slight extension into nucleus parafascicularis.

Dejerine and Roussy8 believed that the lesion responsible for the thalamic syndrome resulted from occlusion of the thalamogeniculate artery. Others31,36 have found the classical thalamic syndrome sequential to softening of the posterolateral thalamus alone. In the majority of cases the disturbances appear to have been produced by hypertension or arteriosclerosis that resulted in infarcts or hemorrhages in the thalamus; other etiologies are embolism,9,38 luetic arteritis,36 intracranial aneurysms,6 and arteriovenous malformation. However, pain having many if not all of the features described by Dejerine and Roussy8 has resulted from a variety of pathological lesions in several sites including the peripheral nerves, the spinal cord, the medulla, and the mid-brain.38 Even lesions of the cortex not involving the thalamus seem to have produced the thalamic syndrome.5,7,28,38

Neoplasms only rarely produce the thalamic syndrome.5,36 The brains of 6 patients who died of thalamic tumor were examined by Smyth and Stern32 by a technique which allowed determination of the intimate distribution of the tumor and they were able to distinguish areas entirely replaced from areas merely infiltrated by tumor. Dividing the cases in two groups, based upon whether tumor origin was in the medial or the lateral portion of the thalamus, they found the clinical manifestations varied significantly with the pathological grouping. Those in
Thalamic Syndrome and Its Mechanism

whom the tumor origin was medial had shown clinical pictures of mental impairment and iridoplegia without early sensory or motor deficits and some had never developed sensory deficits. The others with more laterally placed lesions had prominent early motor and sensory deficits with the motor losses generally preceding the sensory losses. One of these latter patients had complained of pain localized to the upper limb. This pain had been preceded by weakness and sensory deficit but not until the last 2 months of a 10-month illness was hypersensitivity to stimulus present. Their only patient having a well-developed thalamic syndrome had a lesion which originated extrathalamically, discretely destroying the posterolateral thalamus while sparing the remainder of that structure.

Thus, the evidence suggests the existence of two systems subserving pain function. These have been named the slow and the fast, or the extralemniscal and the lemniscal\textsuperscript{20} or the paleo and the neospongial thalamic systems. Slow pain has a high threshold and is mediated primarily by fine unmedullated fibers (less than 2 microns in diameter) to the medial or paleothalamus at rates of 0.6 to 2.0 m. per second. Such pain is characterized by disagreeable diffuse burning, gnawing or boring qualities. Fast pain has a lower threshold and is mediated over fine medullated fibers (2–4 microns in diameter) at rates approximately 10 m. per second. This pain is sharply appreciated as to location and type of stimulus and is less disagreeable than the slow pain.

Report of Cases

We have recently observed and studied 2 patients suffering from the Dejerine-Roussy syndrome. In one the cause was a vascular malformation of the left thalamus which, for a considerable period of time, was misdiagnosed as lower lumbar disc disease, so that the patient underwent two fruitless operations before the true cause of his suffering was appreciated. In the other patient, the disorder is more typical in origin. The results of the diagnostic spinal anesthesia and chordotomy give these cases certain interest and value.

Case 1. In 1959, L. C., a 34-year-old laborer, developed low back pain while pushing a heavy load up an incline and thereafter had intermittent attacks with tendency of the pain to extend into the right leg. In August, 1961, during another exertion, there occurred sudden extension of severe diffuse pain into the right leg. He underwent, without prior myelography, what he described as “removal of the lowest two discs and fusion of the back.” This procedure did not ameliorate the pain but was followed by some lessening of paresthesias which had been present in the hip and thigh. While walking one evening in November, 1961, prior to his return to work, he experienced a strong sensation of numbness in the entire right leg from the top of his thigh to the sole of his foot. Accompanying this numbness was burning pain in the sole which gradually extended up the leg and thence to the entire right side of the body including the head. Contact of clothing and stretching of the skin were disagreeable and he was unable to lie upon the affected side to sleep. He could not tolerate placing his bare foot upon the floor. He continued to have low back pain with extension into the right leg aggravated by coughing, sneezing, sitting, bending, and every other variety of physical activity.

On examination the cranial nerve function was normal except for altered sensation on the right side of the face, similar to that present on the remainder of the right side of the body, together with diminution of the right corneal reflex. Sensation for modalities of touch, pin prick, pain, pressure pain, position, vibration, stereognosis and recognition of figures written on the skin of the feet was everywhere acute, but the patient described light touch as feeling less acute and less ticklish while pin scratch and pin prick felt less sharp on the right half of the body, including the head, than on the left. Though the right leg and arm would flinch involuntarily as though he were appreciating pain from pin pricks, he often reported the sensation as dull. He walked about without disability and could walk on heels and toes without difficulty. The lumbar curve was flat but the back functioned well except for some limitation of flexion. Lasègue’s sign on the right was moderately positive while that on the left was negative. No motor abnormality was present except for diminution of the right Achilles reflex.

At this point, the diagnosis appeared to lie between the Dejerine-Roussy syndrome and a conversion reaction complicating an unsatisfactory operation for lower lumbar root compression. Physical signs indicating current root compression were unsubstantial but it was believed that after spine and skull roentgenography, electroencephalography and electromyography, myelographic study should take precedence over cerebral contrast examinations.

X-ray examination of the skull and chest was
normal. Films of the low back revealed slight narrowing of the lumbosacral disc with posterior fusion at this interval. The electroencephalogram was normal. Electromyograms were interpreted as showing definite evidence of fibrillation potentials in muscles served by the first sacral root. Myelography disclosed the presence of a right lateral defect at the level of the lumbosacral disc, consonant with extradural compression by herniated disc. The protein in the spinal fluid was 94 per cent.

Course. Upon exploration of the low back, some motion was found present at the lumbosacral interval. Considerable scar tissue occupied the interlaminal space under the bone graft, and after this was removed the underlying disc was found to be soft but not bulging, and an aperture could not be found in the annulus. The nuclear cavity accepted 3 cc. of saline upon test injection. The annulus was then incised and 6 gm. of cartilage removed.

Following this procedure, the patient quickly became ambulatory but continued to complain of disagreeable sensory phenomena on the right side of the body. Serial examinations following this second low back operation revealed absence of the right corneal reflex, hypesthesia and hypalgesia of the right side of the body to a line 1.0 to 2.0 cm. short of the midline, and a diminished right Achilles reflex.

Angiograms (Figs. 1 and 2) were then made which displayed a lesion in the lateral portion of the left thalamus composed of a network of abnormal vessels draining into a large vein which coursed medially and posteriorly to join the internal cerebral vein at its junction with the vein of Galen. This was regarded as a congenital arteriovenous malformation, though neoplasm was considered to be a possibility. Right carotid arteriography and pneumoencephalography were negative. Chlorpromazine, diphenhydramine hydrochloride, mephenesin carbonate, calcium

![Fig. 1. Anteroposterior view of the left carotid angiogram of Case 1 demonstrates an arteriovenous malformation in the region of the left thalamus. The lesion fills from the anterior choroidal artery and there is early opacification of the vein of Galen and the straight sinus. See Fig. 2 for lateral view.](image-url)
Thalamic Syndrome and Its Mechanism

Case 1. A 40-year-old man was admitted to the hospital on February 14, 1960, with a 10-day history of left-sided weakness. On examination he was alert and oriented but had severe expressive dysphasia and the few words he uttered were dysarthric. He had bruits over the carotid arteries and head. Right homonymous hemianopsia was present. The ocular fundi were normal except for arterial narrowing. The right pupil was slightly larger than the left but ocular movements were normal. There was right facial and tongue weakness, and severe right hemiparesis but with retention of toe wiggling and shoulder shrugging. The Babinski response on the right was extensor. Her language defect made sensory examination inconclusive but there

Fig. 2. Left carotid angiogram, Case 1. Lateral view.

gluconate, and barbibromide were administered without benefit.

The patient then underwent without benefit a 30-day course of radiation therapy utilizing a slender 2 MEV beam delivered through 8 ports to a total dose of 5,000 r. An effective lumbar sympathetic block with lidocaine failed to alter the leg discomfort. Spinal anesthesia using small doses of pontocaine was employed on two occasions and each time gave complete relief of pain in areas made hypalgesic by the injected drug. There was, in addition, distinct diminution in the arm and face pains while the lower body was hypesthetic. This was interpreted as indicating that this “thalamic pain” was capable of being diminished by reducing sensory input from the periphery and the patient was offered high cervical chordotomy. This was not done because of the patient’s reservations about accepting an experimental operation.

Case 2. T. S., a 53-year-old married housewife of American Indian extraction, was known to have been under treatment for hypertension since 1957. In January, 1960, she was suddenly stricken with right-sided weakness unaccompanied by loss of consciousness or headache.

On examination she was alert and appeared to understand questions and directions adequately but she had severe expressive dysphasia and the few words she uttered were dysarthric. She had no bruits over the carotid arteries or head. Right homonymous hemianopsia was present. The ocular fundi were normal except for arterial narrowing. The right pupil was slightly larger than the left but ocular movements were normal. She had right facial and tongue weakness, and severe right hemiparesis but with retention of toe wiggling and shoulder shrugging. The Babinski response on the right was extensor. Her language defect made sensory examination inconclusive but there
seemed to be deficits for all modalities on the right side.

Roentgen study of the skull was negative and the pineal fluid was not calcified. The lumbar spinal fluid was under a pressure of 200 mm. of water and it was turbidly xanthochromic due to the presence of 1,500 red blood cells per cu. mm. Bilateral carotid angiograms revealed good filling of the carotid arteries and their intracerebral branches without evidence of any displacing lesion. Satisfactory venograms were not obtained.

Course. The patient's recovery was unexpectedly rapid and 2 months later she was walking with a cane, doing normal housekeeping and taking long walks. Some vision returned in the right upper quadrants but body sensation remained deficient on the right. At about this time, she began to experience dysesthesias which eventually involved the entire right side superimposed upon a background of multisensory deficit with additional sensations of shocks, pins and needles. The right leg, chest, neck and face possessed, in addition, certain sensations of stiffness.

After several more months, speech became normal and she displayed only a right inferior quadrantanopsia, right corneal reflex reduction, and slight right lower facial weakness in the field of the cranial nerves. Her gait was mildly disordered by spasticity of the right leg. Strength in all limbs was good but rapid alternating movements were impaired on the right. The right limb tendon reflexes were more active than those on the left. Right ankle clonus and an equivocal right extensor plantar response were present. Sensation was reduced on the right side for all modalities with the leg being the most severely affected and the face the least. The leg was almost insensitive to touch, pin prick, position change, and vibration. Deep pressure pain was less reduced. Deficits for touch and pin prick in the right face were slight but definite.

During the next 3 years she regained slight additional sensory and motor function but most of the deficits remained as described above.

Accompanying this recovery were increasingly disagreeable feelings of stiffness in her right extremities, pressure sensations in the right side of the head and shock-like spasms darting from the tips of her right fingers into her face. The muscles of the right half of the trunk felt "balled up. " She had much difficulty describing the qualities of the various pains, which were constant except for the superimposed "spasms" or shocks. Her pains were increased by the slightest stimulus to her right side such as in walking, contact with clothing or the blowing of a cold wind. Diphenylhydantoin had been given without significant effect.

In February, 1964, intrathecal injection of 6.0 mg. of pontocaine in hyperbaric solution was made with the patient lying on her right side. She experienced immediate abolition of leg pain—even before remaining sensation for touch and motor power were impaired. As the anesthetic level ascended the body, it swept the pain before it until she was anesthetic and pain-free to the level of the costal margin on the right. Throughout out this entire area her skin could be slapped, rubbed, or pinched without her feeling any of her old pain whatever, but similar stimulation of the right arm produced intensely disagreeable sensations.

Operation. On February 18, 1964, unilateral anterolateral chordotomy was performed at the C-2 level on the left side achieving a level of analgesia to C-4 and she remained completely free of pain and hypersensitivity to stimulation of any kind until the fall of 1964. Although feelings of numbness and coldness occupied the right hand she denied having anything that qualified as pain—even in the neck or side of the head above the area made analgesic by the chordotomy. Her gait had become more free and unrestrained apparently due to diminution of spasticity that had been augmented by the preoperative hyperpathia. The pain began to reappear and has gradually increased to the present time. Centrum medianum thalamotomy is under consideration.

Discussion

The evidence from these two cases and that reported by others suggests "thalamic pain" to be the result of differential interruption at any level, peripheral or central, of fast pain input to the ventral posterolateral nucleus. It appears that with all the pathways, fast and slow, intact impulses mediated over the fast system exercise a degree of inhibition on the slow pain system, primarily at the thalamic level. Though Head and Holmes postulate that thalamic pain is a product of thalamic activity and that its suppression is effected by means of paths from the cortex to the thalamus, this fails to account for pain having all the qualities of thalamic pain which may result from lesions below the thalamus.

Little doubt can exist but that there are two sensory systems active in the transmission of pain—the slow and the fast. There is strong evidence that the slow system uses the fine unmedullated fibers and the fast system the small medullated fibers. One criticism of this view derives in part from evidence that the differences in transmission time between the systems are due to multiple
synapses in the slow system. Though multisynaptic delay contributes to the temporal separation of impulses this does not invalidate the concept of differences between slow and fast pain based upon fiber size, differential rates of transmission and thalamic targets. Indeed, if polysynapses were the sole explanation, a pain state with thalamic features could hardly result from peripheral nerve lesions.

The effect of spinal anesthesia and chordotom y in Case 2 has afforded us an opportunity to observe the result of the loss of remaining sensation (traveling via the slow system) in a patient in whom the fast system was previously impaired. From the work of Sinclair and Hinshaw\textsuperscript{20,21} it would be expected that the slow pain system would be blocked first by the anesthetic agent. Proof of the hypothesis that the slow pain system conducts the pain of the thalamic syndrome demands that the pain be eliminated immediately if at all. This was in fact the case, for it was observed that all pain was absent prior to the development of anesthesia-produced loss of remaining touch and motor power.

The case reported by Biemond,\textsuperscript{2} with a thalamic pain syndrome resultant from a cortical lesion of the secondary sensory area, offers anatomical evidence for the theory that thalamic-like pain from suprathalamic lesions may result from loss of impulses that normally inhibit the slow pain system through VPL. The literature records examples of alteration of sensory impulses by impulses from another system.\textsuperscript{20} An example of this is the experiment of Hérdandez-Péon \textit{et al.}\textsuperscript{13} in which the action potentials in the cochlear nucleus were modified by the competing olfactory or auditory stimuli. The specific inhibitory relationship between the fast and the slow pain systems has so far eluded direct proof.

It is postulated that impulses from the VPL nucleus exert an inhibitory effect on the slow pain system at the level of the medial thalamus (centrum medianum and parafascicularis) and that loss of input from either the periphery or the cortex to the VPL nucleus as well as a lesion in the VPL nucleus can cause the typical thalamic syndrome (Fig. 3).

\textbf{Summary}

The thalamic syndrome appears to result from selective loss of “fast pain” impulses to the ventral posterolateral nucleus of the thalamus. We have postulated that these impulses normally exert an inhibitory effect on the “slow pain” system at the level of the medial thalamic nuclei, principally the centrum medianum.

We have reported two patients with thalamic pain who were temporarily improved by interruption of spinal cord pain pathways.

\textbf{References}

3. Bishop, G. H., and Heinbecker, P. Correlation


5. CHEEK, W. R. Personal communication.


21. LOGUE, V. Personal communication.


36. TURNBULL, F. quoted by White and Sweet, 29 p. 529.


**Addendum to Case 2**

In July, 1965, a left thalamotomy was done aiming at centrum medianum and parafascicularis. Postoperatively, the physical findings have not changed and the patient has been free from pain.