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Phantom Limb Pain:

Implications for Treatment of Pathologic Pain

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The mechanisms underlying pathologic pain states such as phantom limb pain remain a mystery. Observations that 1) pain may persist indefinitely; 2) trigger zones may spread to healthy parts of the body; and 3) pain may be abolished by either decreasing or increasing the sensory input cannot be explained solely in terms of peripheral causes or abnormal activity restricted to the spinal cord. This paper proposes that a portion of the brainstem reticular formation exerts a tonic inhibitory effect on transmission at all levels of the somatic projection system. The loss of sensory input after amputation would decrease the tonic inhibition and increase the probability of self-sustaining neural activity. The self-sustaining activity, its capacity to recruit adjacent neurons, and its occurrence at several transmission levels would underlie prolonged pain and spread of trigger zones. Modulation of the sensory input by anesthetic blocks or intense stimulation would abolish the self-sustaining activity and produce pain relief. (Key words: Phantom limb pain; Pathologic pain.)

PHANTOM LIMB PAIN is one of the most terrible of all pain phenomena, yet its underlying mechanisms remain a mystery. The pain tends to persist for years after the stump tissues have healed. Moreover, trigger zones may spread to distant body areas. The mystery is heightened by the paradoxical observation that the pain is sometimes abolished by either decreases or increases of input from the body. Recent physiologic studies have provided valuable clues for a new concept of phantom limb pain as well as related pain states such as causalgia. The purpose of this study is to examine the properties of phantom limb pain and to explore new approaches to understanding it.

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Properties of Phantom Limb Pain

Most amputees report feeling a phantom limb almost immediately after amputation of an arm or a leg.[1] The limb is usually described as having a tingling feeling, a definite shape, and moves through space much the same way the normal limb would move when the person walks, sits down, or stretches out on a bed. At first, the phantom limb feels perfectly normal in size and shape—so much so that the amputee may reach out for objects with the phantom hand, or try to get out of bed by stepping onto the floor with the phantom leg. As time passes, however, the phantom limb begins to change shape. The leg or arm becomes less distinct and may fade away altogether, so that the phantom foot or hand seems to be hanging in mid-air. Sometimes, the limb is slowly "telescoped" into the stump until only the hand or foot remains at the stump tip.

Although tingling is the dominant sensation of the phantom limb, amputees also report a variety of other sensations, such as "pins-and-needles," warmth or coldness, heaviness, and many kinds of pain. About 35 per cent of amputees report pain in the phantom limb at some time.[2] Fortunately, the pain tends to subside and eventually disappear in most of them. In about 5 to 10 per cent, however, the pain is severe, and it may become worse over the years. It may be occasional or continuous, and is described as cramping, shooting, burning or crushing. It usually starts im-

mediately after amputation, but sometimes appears weeks, months, even years later.[2] The pain is felt in definite parts of the phantom limb.[3] A common complaint, for example, is that the phantom hand is clenched, fingers bent over the thumb and digging into the palm, so that the whole hand is tired and painful.

Phantom limb pain is characterized by four major properties:

1) The pain endures long after healing of the injured tissues. It continues for more than a year after onset in about 70 per cent of patients, and may persist for years, even decades, in patients with perfectly healed stumps.[4]

2) Trigger zones may spread to healthy areas on the same or opposite side of the body.[5] Gentle pressure or pin prick on another limb or on the head (fig. 1) may trigger pains in the phantom limb. There is also evidence that pain at a site distant from the stump may evoke pain in the phantom limb. Thus, amputees who develop anginal pain as long as 25 years after amputation may suffer severe pain in the phantom limb during each bout of anginal pain, although phantom limb pain may never before have been experienced.[6]

3) Phantom limb pain is more likely to develop in patients who have suffered pain in the limb for some time prior to amputation.[4, 7] It is relatively rare in war amputees,[8, 9] who tend to lose a limb suddenly, but more common in civilian amputees, in whom presurgical pain is a frequent accompaniment of disease of the limb.[2, 4] Furthermore, the pain may resemble, in both quality and location, the pain that was present before amputation.[7, 9-11] Thus, a patient who was suffering from a wood sliver jammed under a finger nail, and at that time lost his hand in an accident, subsequently reported a painful sliver under the finger nail of his phantom hand.[10]

4) The pain is sometimes permanently abolished by temporary decreases or increases of somatic input. Injection of procaine locally into the stump tissues or nerves[3] may stop the pain for days, weeks, sometimes permanently, even though the anesthesia wears off within hours. Successive blocks may produce increasingly longer periods of relief. Similarly, procaine injected into the lower-back interspinous tissue in leg amputees[2] produces a progressive numbness of parts of the phantom limb, and prolonged, sometimes permanent relief of pain in all or part of it. Paradoxically, *increases* in the sensory input may sometimes relieve the pain.[2] Injection of small amounts of hypertonic saline solution into the interspinous tissue of amputees (fig. 2) produces a sharp, localized pain that radiates into the phantom limb, lasts only about 10 minutes, yet may produce dramatic partial or total relief of pain for hours, weeks, sometimes indefinitely. Similar effects have been obtained by injections of hypertonic saline solution into the stump tissues.[12]

These properties define the scope of the problem that confronts us. We shall now examine possible mechanisms to explain them.

The Search for Causal Mechanisms

The mechanisms underlying phantom limb pain have been the basis of bitter controversy. The crux of the problem has been the attempt to discover a single factor as the whole explanation. Historically, the search for *the* causal mechanism has progressed from the periphery to the central nervous system, each site on the way leading to a proposed mechanism and a particular therapy to relieve pain (fig. 3). The failure of these therapeutic measures to cure all cases has led to a further explanation—that the patients are neurotic or malingering and imagining their pain. The evidence, however, is that there is not a single cause. Instead, all of these mechanisms—including emotional disturbance—may contribute to phantom limb pain.

Peripheral Mechanisms

Once phantom limb pain is under way, almost any somatic input may augment it. Pressure on tender neuromas or trigger points at the stump can evoke severe, prolonged pain. Despite the obvious contribution of sensory inputs, peripheral irritating factors such as neuromas clearly are not the main cause in most cases. Surgical section of peripheral nerves or special procedures to prevent neuroma formation frequently fail to stop pain.[4] Even dorsal root section (rhizotomy) is usually ineffective.[4, 11] A striking example is the case of a patient[11] who underwent an extensive

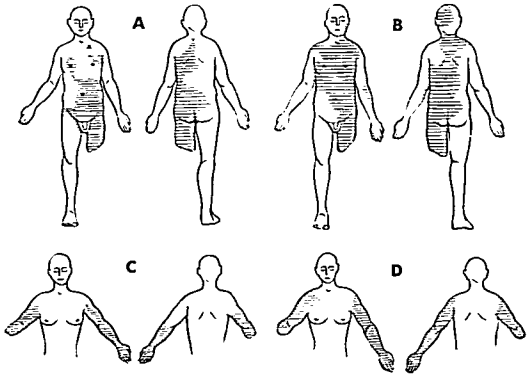

FIG. 1. Cronholm's[5] observations on stimulation sites which evoke pain sensation in the phantom limb. *Top:* 59-year-old man who received compound fractures of the lower left leg at the age of 21 years; amputation four months later. Pressure (*A*) or pin-pricks (*B*) were applied to the skin. Stimulation of effective sites (cross-hatched areas) produced severe shooting pains and other sensations in the phantom limb. *Bottom:* 34-year-old woman; amputation at the age of 14 years. Pressure (*C*) or pin-pricks (*D*) were applied to the skin. Stimulation of effective sites (cross-hatched areas) produced sensations of a diffuse, unpleasant "irritation" in the phantom hand.

rhizotomy. After surgery, he had complete cutaneous anesthesia from shoulder to umbilicus, but still felt excruciating pain in the phantom fingers which protruded from his upper arm stump.

If the cause of the prolonged pain were a chronic irritating lesion, a minor form of therapy such as injection of the affected area, nerve, or roots with anesthetic drugs could not by itself remove the pathologic cause, since the drug effects wear off after two or three hours. The fact that one or more injections may provide prolonged, sometimes permanent relief[3] rules out irritation at the stump as the major cause.[3,4] Rather, the data suggest that chronic, low-level sensory inputs *contribute* to the pain, since modulation of the input by anesthetic blocks clearly influences it, sometimes dramatically.

Sympathetic Nervous System Mechanisms

The sympathetic ganglia also contribute to the pain in some way.[3,4] There are autonomic manifestations such as excessive vasoconstriction and sweating at the stump.[3] Pain, moreover, is often triggered by autonomic functions such as urination and defecation.[9] In addition, anesthetic blocks of the sympathetic ganglia sometimes relieve pain for prolonged periods of time.[3] Sympathetic activity, however, is not the major cause of phantom limb pain. Sympathectomy, which relieves causalgic pain,[4] rarely produces lasting relief of phantom limb pain.[13] Furthermore, Li and Elvidge[14] report the case of a paraplegic who sustained a total section of the thoracic spinal cord in addition to a leg amputation, so that the sympathetic ganglia provided the sole afferent route from the stump to the spinal cord. Nevertheless, the pain in his phantom foot was not relieved during a complete bilateral block of the sympathetic ganglia.

Psychological Mechanisms

Finally, there is an obvious psychological contribution, since phantom limb pain is often triggered by emotional disturbances[15] and is sometimes abolished by distraction-conditioning,[16] hypnosis,[17] and psychotherapy.[15,18,19] These data, together with the frequent failure of traditional surgical therapy, have led to the suggestion that the patients are in pain because of psychopathologic personal needs.[15] It is true that patients suffering phantom limb pain often have emotional disturbances such as anxiety about social adjustment. Indeed,

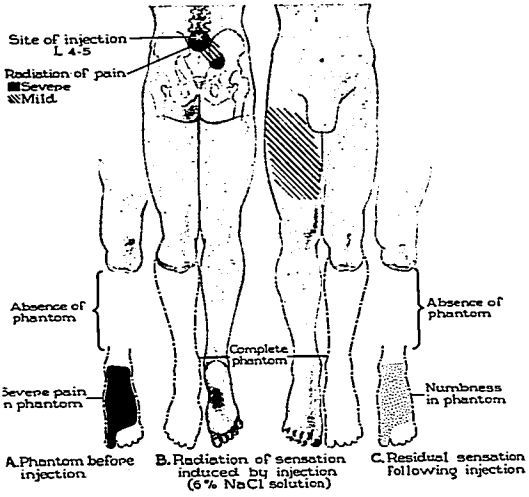

FIG. 2. Observations by Feinstein *et al.*[2] on the effect of injection of hypertonic saline solution into the L4–L5 interspinous tissues on phantom limb pain. The saline injection, in this case, produced a radiation of pain to the right hip and thigh, and sudden detailed awareness of the complete phantom limb. After injection, numbness was felt in the previously painful area. After this procedure, pain relief may last for days or weeks, and is sometimes permanent.

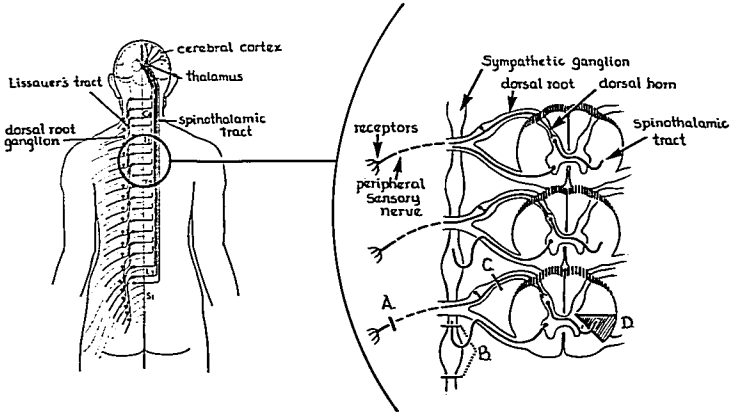

FIG. 3. Traditional concept of pain. *Left:* Larsell's[49] diagram of the pain pathway: pain fibers from the skin enter the spinal cord, ascend a few segments (in Lissauer's tract) and connect with fibers that cross the cord and form the spinothalamic tract to the thalamus. Fibers from the thalamus project to the cortex. *Right:* Diagram of spinal cord cross-sections and adjacent sympathetic ganglia, showing several neurosurgical procedures to stop pain. *A*, neurectomy; *B*, sympathectomy; *C*, rhizotomy; *D*, cordotomy.

the intense, unrelenting pain may itself produce marked withdrawal, paranoia, and other personality changes.[2, 20] However, the hypothesis that phantom limb pain always has a psychiatric basis is untenable. It cannot explain the sudden relief produced by nerve blocks.[2] It would be wrong to assume that the injections have only psychotherapeutic (or placebo) value, because injection of an inappropriate nerve fails to relieve pain, even though injection of the appropriate nerve in the same patient is effective.[3] Statistical analysis of the data presented by Ewalt *et al.*,[8] moreover, indicates that patients with phantom limb pain do not have a greater incidence of neuroses than those without pain in the phantom limb. Emotional factors undoubtedly contribute to the pain, but are not the major cause.

These data, taken together, indicate that phantom limb pain cannot be explained satisfactorily by any single mechanism such as peripheral nerve irritation, sympathetic inputs, or psychopathology. All contribute to the pain in some way. The question is: how? The most satisfactory answer so far is that traumatic or otherwise abnormal inputs may produce a change in the central nervous system itself, which is then maintained or triggered by somatic and sympathetic inputs and by brain activities.

Theories of Central Mechanisms

If the clinical data now force us to consider central mechanisms, where in the nervous system do we look? The most obvious site is the spinal cord itself. Two theories of abnormal spinal activity have been suggested.

W. K. Livingston[3] proposed that the initial damage to the limb, or the trauma associated with its removal, initiates abnormal firing patterns in closed, self-exciting neuron loops in the dorsal horns of the spinal cord, which send volleys of nerve impulses to the brain that give rise to pain. Moreover, the reverberatory activity may spread to adjacent neurons in the lateral and ventral horns and produce autonomic and muscular manifestations in the limb, such as sweating and jerking movements of the stump. These, in turn, produce further sensory input, creating a "vicious circle" between central and peripheral processes that maintains the abnormal spinal cord activity (fig. 4). In addition, emotional disturbance may evoke neural activity that feeds into the abnormal neuron pools. Once the abnormal cord activity has become self-sustaining, surgical removal of the peripheral sources of input may not stop it. Rather, clinical procedures that modulate the sensory input, such as local anesthetic injections or physiotherapy, may again reinstate normal cord activity.

Gerard[21] has suggested a theory that is similar in concept, although different in hypothetical mechanism. He proposed that a peripheral nerve lesion may bring about a temporary loss of sensory control of firing in spinal cord internuncial neurons. These may then begin to fire in synchrony, just as isolated bits of nerve tissue in an appropriate solution fire synchronously, possibly due to D.C. spread.[21] Such synchronously firing neuron pools "could recruit additional units, could move along in the grey matter, could be maintained by impulses different from and feebler than those needed to initiate it, could discharge excessive and abnormally patterned volleys to the higher centers."[21]

Although Livingston's and Gerard's concepts have considerable power in explaining phantom limb pain, they fail to account for the fact that surgical lesions of the spinal cord often do not abolish the pain. Instead, the neurosurgical evidence points to mechanisms in the brain itself. If the crucial mechanism lay in the spinal cord dorsal horns, then cutting the major sensory transmission routes through which spinal activity projects to the brain should stop the pain. Yet it is now generally recognized that, once the pain syndrome is well established, attempts to relieve it by surgical operations on spinal cord pathways are often ineffective. White and Sweet[11] report the return of phantom limb pain after cordotomy in seven of 18 lower-limb and three of four upper-limb cases. Even bilateral cordotomy may fail.[4, 11] Efforts have been made to find the "leak" in the pain projection system, and the small multisynaptic propriospinal fiber chain has been proposed as one possibility.[22] But if there is a leak, and impulses ascending the cord determine pain without further elaboration, it is hard to im-

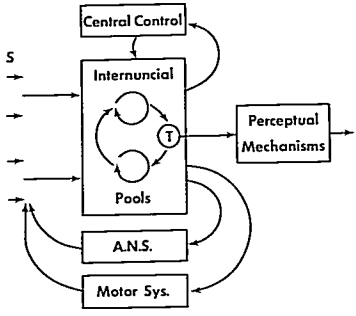

FIG. 4. Schematic diagram of W. K. Livingston's[3] theory of pathologic pain states. The intense stimulation (*S*) resulting from nerve and tissue damage activates fibers that project to internuncial neuron pools in the spinal cord, creating abnormal reverberatory activity in closed self-exciting neuron loops. This prolonged, abnormal activity bombards the spinal cord transmission (*T*) cells that project to brain mechanisms that underlie pain perception. The abnormal internuncial activity also spreads to lateral and ventral horn cells in the spinal cord, activating the autonomic nervous system (*A.N.S.*) and motor system, producing sweating, jactitations, and other manifestations. These, in turn, produce further abnormal input, thereby creating a "vicious circle." Brain activities such as fear and anxiety evoked by pain also feed into and maintain the abnormal internuncial pool activity.

agine that so small an input (after the extensive surgical cuts) can produce such massive pain.

Surgeons, therefore, have turned to the dorsal columns, the traditional "touch–proprioception pathway," particularly for cramping pains in the phantom limb. Yet the operation is ineffective here, too.[11] The frequent failure of surgery at the cord level has led to surgical operations on the spinothalamic projection pathway at higher levels. But mesencephalic tractotomy, thalamotomy, and somatosensory cortical excision have also produced variable results: some successes, but a disheartening tendency for pain to return.[11, 23]

In summary, the search for the causal mechanisms in the spinal cord or in the main somatosensory projection pathway has failed to reveal the crucial site. The pathway has been cut at every level up to and including the cortex, often without significant relief of pain. This is not to say that the projection system has no role. But it must be part of a more widespread, pervasive system. The answer must lie in some mechanism which is not on the main sensory paths, which receives inputs from multiple sources, and projects to all synaptic levels of the somatosensory pathways.

Concept of a Central Biasing Mechanism

Recent physiologic data suggest a new approach to phantom limb pain. It has been observed[24, 25] that brief (10–20 seconds) stimulation of the skin or sciatic nerve in moderately anesthetized cats produces marked, prolonged changes in the tonic, spontaneous activity at several synaptic levels of the skin sensory system, the brainstem reticular formation, and other discrete brain areas. The changes usually last 5 to 10 minutes, but may continue for as long as 30 minutes before activity returns to normal. Another brief stimulation again triggers a prolonged change. These prolonged changes occur only when the animal is moderately anesthetized, but not when anesthesia is too light or too deep. The data[24] suggest that the reticular formation plays an important role in the mechanisms underlying the prolonged changes.

The most reasonable explanation of these long-lasting changes is that an inhibitory influence which normally shuts off stimulus-evoked activity in a sensory system as soon as the stimulus is removed (fig. 5) is selectively abolished by anesthetic agents. After removal of inhibition, a stimulus which usually has only momentary effects now produces persistent activity. Recent studies suggest the kind of neural circuit that can produce long-lasting activity. Andersen and Eccles[26] and other physiologists[27, 28] have found evidence for a two-neuron closed circuit so that a single volley of impulses is capable of producing rhythmic, sustained activity for prolonged periods (fig. 5). As Andersen and Eccles[26] have noted, the inhibitory cells responsible for the self-sustaining activity could have widespread connections (fig. 5), producing rhythmic discharges in adjacent neuron pools and, with time, increasing the number of rhythmically firing neurons. The frequency of the rhythmic discharges would depend on the physiologic properties of the system, so that

the level of activity could increase or decrease compared with background tonic activity in the area. Inputs that arrive out of phase with the rhythmic activity can block it.[27]

These observations suggest a model to explain at least some of the phenomena of phantom limb pain. The model shown in figure 6 is consistent with the gate control theory of pain.[29] Briefly, the model proposes that a portion of the brainstem reticular formation acts as a *central biasing mechanism* by exerting a tonic inhibitory influence, or bias, on transmission at all synaptic levels of the somatic projection system. When a large proportion of sensory fibers is destroyed by amputation of a limb, thereby decreasing the amount of input into the reticular formation, the inhibitory influence decreases. This results in self-sustaining activity at all neural levels that can be triggered repeatedly by the remaining fibers. Pain occurs when the output of the self-sustaining neuron pools reaches or exceeds a critical level. Let us now examine the model in more detail.

After amputation of a limb, the remaining sensory nerves from the stump undergo two effects. First, there is a marked loss of fibers when the proximal end of a cut nerve is prevented from re-establishing contact with receptor organs (which occurs after amputation of a limb). Only a fraction—about 50 per cent—of the fibers in sensory nerves now project to the spinal cord.[30] Second, the remaining fibers (which eventually regenerate into the stump tissues) are not distributed across the full diameter range but tend to have small diameters and conduct slowly.[22, 31] Thus, stimulation of the stump would produce synchronous volleys rather than the complex, temporally dispersed patterns seen in a normal nerve that contains the full range of fiber sizes.

The output of the neuron pools in the cord is projected to two major systems in the brain —to the somatosensory thalamus and cortex, and to the brainstem reticular formation. It is well known that portions of the reticular formation exert a tonic inhibitory influence on synaptic transmission at all levels of the somatosensory system.[32] (Actually, inhibitory and excitatory influences are exerted, but the inhibitory effect predominates.) Conceptually, these reticular neuron pools may be considered a *central biasing mechanism* (fig. 6).

Since the tonic inhibitory influence is partly maintained by skin sensory input, a marked, prolonged decrease in the input from an area, which would occur after amputation, would decrease the centrifugal inhibition exerted at all levels of the projection system. Consequently, small-fiber volleys from the skin or deeper tissues of the stump would tend to trigger self sustaining activity in neuron pools at spinal, thalamic, and cortical levels. If this activity stopped spontaneously, inputs from the stump would again activate it. Moreover, the widespread connections of the inhibitory interneurons responsible for self-sustaining activity (fig. 5) would influence other neurons, so that adjacent neuron pools normally activated by other body areas would, with time, also begin to produce sustained activity. In this way, adjacent or distant body areas would begin to act as trigger zones. Surgical section of the pain-signalling pathways in the spinal cord—even total cord section in the paraplegic—would still permit such activity patterns to go on at thalamic or even cortical levels. Indeed, cells at higher synaptic levels have large receptive fields, sometimes half of the body surface or more,[33] so that inputs from distant skin areas could trigger sustained activity at these levels. It is proposed that pain occurs when the total output from the self-sustaining neuron pools, which project to brain areas that subserve pain experience and behavior, reaches or exceeds a critical level.[29, 34] The self-sustaining activity, its capacity to recruit adjacent neurons, and its occurrence at several levels would underlie prolonged pain, and spread of trigger zones to distant areas.

Implications of the Model

The concept that phantom limb pain results from self-sustaining activity after release from inhibition can explain the fact that one or more anesthetic blocks of tender skin areas, trigger points, peripheral nerves, or sympathetic ganglia may produce prolonged relief of pain.[3, 22] Anesthetic block of sensory input for several hours would bring about a cessation of activity in the closed, self-sustaining neuron loops. After anesthesia wears off,

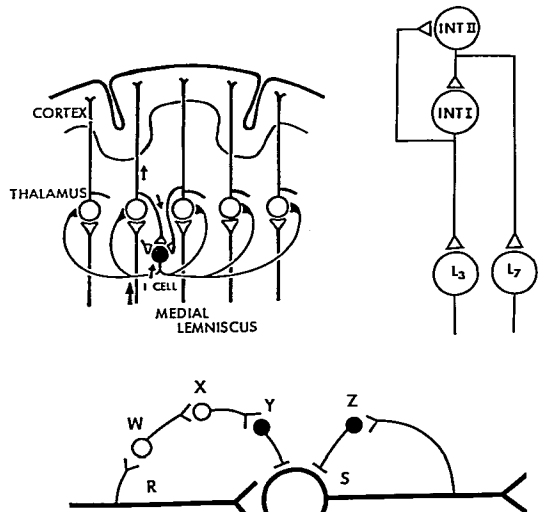

FIG. 5. Models to explain long-term changes in central neural activity. *Top left:* Model proposed by Andersen and Eccles[38] to account for repetitive, rhythmic bursts of activity in the ventrobasal thalamus. Inputs arriving along lemniscal fibers activate thalamic neurons that 1) project to the cortex and 2) send axon collaterals to an inhibitory neuron (I cell) that projects back to the thalamic cell bodies. The thalamic cells are inhibited briefly, then (after disinhibition and rebound excitation) fire spontaneously, reactivating the recurrent inhibitory loop. This repetitive activity within the closed loop could continue for prolonged periods of time in the absence of any further input. *Top right:* Schematic representation proposed by Kandel *et al.*[25] to explain prolonged activity in inhibitory interneurons in the marine mollusc *Aplysia*. A closed neuron chain (interneuron II and interneuron I) is formed by mutually inhibitory connections. The inhibition of each interneuron is followed by disinhibition and rebound excitation which leads to a sustained alternation of activity in the two interneurons. Actual records[25] of activity from L3 (a follower cell of interneuron I) and L7 (a follower cell of interneuron II) provide evidence of alternating IPSP bursts that persist for as long as 30 min. *Bottom:* Schematic model to account for prolonged activity after release from inhibition. Impulses in axon *R* normally excite neuron *S* and the neuronal side-chain *W-X-Y*. Excitation of *S* produces repetitive discharges in the recurrent inhibitory loop *S-Z*, followed rapidly by inhibition of *S* by activity in the side-chain. Moderate doses of anesthetic drugs selectively block the vulnerable multisynaptic side-chain, so that excitation of *S* leads to prolonged activity in the *S-Z* loop. Additional anesthetic doses block the *S-Z* loop, and the prolonged activity ceases.

stimulation would again trigger sustained activity, but the time necessary for it to spread to a sufficiently large number of neurons within the pools would produce pain relief that outlasts the anesthesia. Moreover, the relief of pain would permit increased use of the stump, allowing the patient to wear a prosthetic limb, to move or hold objects, and so forth. These activities, in turn, would produce patterned, temporally dispersed inputs (particularly from muscles) that would be out of phase with the rhythmically firing neuron pools and would disrupt their activity, thereby prolonging the time before self-sustaining firing starts up again.

In contrast, the relief of pain after local injections of hypertonic saline solution,[2] vibration,[35] and electrical stimulation of the skin or nerves[11,36] would be due to the increased level of inhibition produced by the input. Since hypertonic saline solution or intense, pounding vibration[35] would excite high-threshold, small-diameter receptor–fiber units it would open the spinal gate[29] and might evoke severe pain. However, because the input also projects to the central biasing mechanism, it would raise the level of inhibition and close the gate to subsequent inputs. In addition, the increased inhibition would disrupt the self-sustaining activity at all levels and produce pain relief. Inputs generated by movements of the stump would prolong the relief.

Psychological activities can also have a

powerful effect on the somatic projection system.[29, 37] The cortex is known to exert a strong influence on reticular activity.[22] It is possible, then, that the relief of phantom limb pain by distraction-conditioning,[16] psychotherapy,[15] and hypnosis[17] could be produced by cortical effects exerted on the central biasing mechanism.

The concept of a release from inhibition is consistent with the fact that phantom limb pain often resembles the pain felt before amputation.[4, 7] It is possible that prolonged pain may leave "memory" traces in the somesthetic system,[28] perhaps in the form of closed neuron loops, which are normally inhibited. The release from inhibition as a result of a peripheral nerve lesion could bring about activation of the traces to produce persistent, severe pain. The concept would also explain the astonishing observations[29] that anesthetic blocks of the lower spinal cord in amputees often produce severe phantom limb pain, even in patients who had previously suffered little or no pain. The decrease in somatic input, after anesthetic block, would lower the level of inhibition and increase the probability of self-sustaining activity.

The model also provides an explanation for the effects of dorsal column stimulation. It has been suggested[40, 41] that antidromic impulses evoked in dorsal column fibers descend to the dorsal horns and inhibit transmission from afferent fibers to dorsal horn cells (*i.e.*, "close the spinal gate"). It is now conceivable that the stimulation activates thalamic and cortical regions which, in turn, activate the central biasing mechanism. The increased level of inhibition would decrease transmission and block sustained activity at all levels, which may account for the striking pain relief that has been observed.[41]

The model proposed for phantom limb pain appears to provide a satisfactory explanation for causalgia. The loss of fibers after peripheral nerve injury would produce a prolonged, decreased input from the limb and an increased probability of sustained firing in closed neuron loops. Because the limb is not lost, the nerve fibers eventually regenerate into the skin and deeper tissues. When these fibers approach the normal number and diameter distribution for the nerve,[21] the pain would decrease spontaneously. The relief of pain, moreover, would permit increased limb movement and sensory input, which would also tend to disrupt the self-sustaining activity. This speculation accords well with the fact that causalgic pain diminishes and disappears during the first year after injury in the majority of patients.[4]

Some neuralgias, such as postherpetic neuralgia,[22] can be similarly explained. The model provides a theoretical basis for the well-known (but paradoxical) observations that several kinds of neuralgic pain can be strikingly diminished or abolished by intense tactile or thermal stimulation such as dry

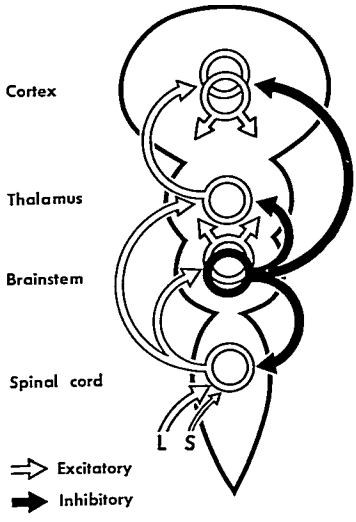

FIG. 6. Schematic diagram of the central biasing mechanism. Large and small fibers from a limb activate a neuron pool in the spinal cord, which excites neuron pools at successively higher levels. The central biasing mechanism, represented by the inhibitory projection system that originates in the brainstem reticular formation, modulates activity at all levels. When sensory fibers are destroyed after amputation or peripheral nerve lesion, the inhibitory influence decreases. This results in sustained activity at all levels that can be triggered repeatedly by the remaining fibers. *L*, large fibers; *S*, small fibers.

needling of an area, spraying the overlying skin with an ethyl chloride cold spray, or local injections of hypertonic saline solution.[12, 21, 42] Pain relief is also produced by irrigation of the spinal cord with cold, hypertonic saline solution,[43] and trigeminal nueralgia is often abolished by vigorous rubbing of the trigeminal nerve.[44] The most reasonable explanation for these observations is that the input, which at first may enhance pain, later activates a system that inhibits transmission of pain signals.

Despite the apparent power of the model, it should be noted that several important questions are left unanswered. First, the localization of pain at specific body sites may be due to 1) a general decrease in inhibition throughout the whole somatosensory system, with self-sustaining activity occurring only in those neuron pools that are deprived of input after a nerve lesion, or 2) a high degree of somatotopic localization in the input and output of the central biasing mechanism. That unilateral congenital amputees show increased sensitivity to tactile stimuli at the contralateral healthy limb as well as at the stump[45] supports the notion of a generalized decrease in inhibition. However, the evidence for somatotopic localization in the reticular formation[46] suggests the possibility of inhibitory release localized to specific projection areas of the somatic system. There is no decisive evidence so far to favor either hypothesis.

Second, there is the possibility that the self-sustaining activity would project to the central biasing mechanism, and thereby increase the level of inhibition and block itself. This would result in a decrease in inhibition, which would again provide the conditions for self-sustaining activity. An unstable, oscillatory system such as this would be highly sensitive to any change in sensory input or psychological state. In particular, it could explain the occurrence of "nerve storms"—waves of severe stump and phantom-limb pain that are intense for a few seconds, then wax and wane with a periodicity of about one per minute.[4] In view of the paucity of physiologic evidence regarding oscillatory systems,[47] it is unjustified, at this time, to speculate any further.

Third, the role of the sympathetic nervous system in pathologic pain is still unresolved. Sensory fibers from the viscera are known to travel through the sympathetic ganglia and converge onto the same spinal cord cells that receive cutaneous inputs.[48] Moreover, sympathetic efferent fibers produce changes in blood circulation and sweating, which are a source of tonic input. Sympathectomy, then, would diminish or remove a tonic discharge from viscera, blood vessels, and other deep tissues that could summate with the cutaneous input to produce pain. However, why sympathectomy is a highly effective treatment for causalgia but not for phantom limb pain[4, 11] has yet to be determined.

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