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Pain: Past, Present and Future

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Abstract Descartes' concept that pain is produced by a direct, straight-through transmission system from injured tissues in the body to a pain centre in the brain has dominated pain research and therapy until recently. The gate control theory of pain, published in 1965, proposes that a mechanism in the dorsal horns of the spinal cord acts like a gate which inhibits or facilitates transmission from the body to the brain on the basis of the diameters of the active peripheral fibers as well as the dynamic action of brain processes. As a result, psychological variables such as past experience, attention and other cognitive activities have been integrated into current research and therapy on pain processes. The gate control theory, however, is not able to explain several chronic pain problems, such as phantom limb pain, which require a greater understanding of brain mechanisms. A new theory of brain function, together with recent research that has derived from it, are described. They throw light on complex pain problems and have important implications for basic assumptions in psychology.

Résumé Le concept de Descartes selon lequel la douleur est produite par un système de transmission directe de la douleur, depuis les tissus blessés dans le corps jusqu'à un centre de la douleur dans le cerveau, a orienté les recherches sur la douleur et la thérapie jusqu'à tout récemment. Selon la théorie du contrôle d'entrée, qui remonte à 1965, un mécanisme logé dans les cornes supérieures de la moelle agit comme une barrière inhibant ou facilitant la transmission de la douleur, du corps au cerveau, en fonction des diamètres des fibres périphériques actives et de l'action dynamique des processus cérébraux. Des variables psychologiques telles l'expérience et l'attention et d'autres facteurs cognitifs ont donc été intégrés aux recherches actuelles sur les processus reliés à la douleur, ainsi qu'à la thérapie. La théorie du contrôle d'entrée ne permet cependant pas d'expliquer plusieurs problèmes chroniques, dont la douleur du membre fantôme, qui exigent une plus grande compréhension des mécanismes cérébraux. Le rapport renferme la description d'une nouvelle théorie de la fonction cervicale et des recherches effectuées récemment à partir de cette théorie. Ces recherches jettent une lumière sur les problèmes complexes reliés à la douleur et ont d'importantes répercussions sur les hypothèses de base en psychologie.

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The theory of pain which we inherited in the 20th century was proposed by Descartes three centuries earlier. Descartes was the first philosopher to be influenced by the scientific method which flourished in the 17th century, and he achieved a major revolution by arguing that the body works like a machine that can be studied by using the experimental methods of physics pioneered by Galileo and others. Although humans, Descartes proposed, have a soul (or mind), the human body is nevertheless a machine like an animal's body.

The impact of Descartes' theory was enormous. The history of experiments on the anatomy and physiology of pain during the past century (reviewed in Melzack and Wall, 1962, 1988) is marked by a search for specific pain fibers and pathways and a pain center in the brain. The result was a concept of pain as a straight-through sensory projection system. This rigid anatomy of pain in the 1950s led to attempts to treat severe chronic pain by a variety of neurosurgical lesions. Descartes' theory, then, determined the "facts" as they were known up to the middle of this century, and even determined therapy.

The power of theory was summarized briefly by D. O. Hebb (1975, pp. 5-9): "The 'real world' is a construct, and some of the peculiarities of scientific thought become more intelligible when this fact is recognized ... Einstein himself in 1926 told Heisenberg it was nonsense to found a theory on observable facts alone: 'In reality the very opposite happens. It is theory which decides what we can observe.'" Clearly, in the case of pain, theory not only determines what we observe in physiology but it determines how we treat people in pain. We now know that neurosurgical lesions to abolish chronic pain usually fail and the pain tends to return. Yet theory and so-called facts about pain fibers and pathways said they *should* work and neurosurgeons – notwithstanding their own observations on the tendency for pain to return after surgery – continued to carry out cordotomies, rhizotomies, cortical ablations and so forth. The emphasis was on the temporary successes, not on the long-term follow-up failures (Drake & McKenzie, 1953; Spiegel & Wycis, 1966). Descartes' views have so thoroughly permeated our concepts about physiology and anatomy that we still cannot escape them.

A Brief History of Pain

Descartes' specificity theory proposed that injury activates specific pain receptors and fibers which, in turn, project pain impulses through a spinal pain pathway to a pain center in the brain. The psychological experience of pain, therefore, was virtually equated with peripheral injury. In the 1950s, there was no room for psychological contributions to pain, such as attention, past experience and the meaning of the situation. Instead, pain experience was held to be proportional to peripheral injury or pathology. Patients who suffered back pain without presenting signs of organic disease were labelled as "crocks" and sent to psychiatrists. The picture, in short, was simple and,

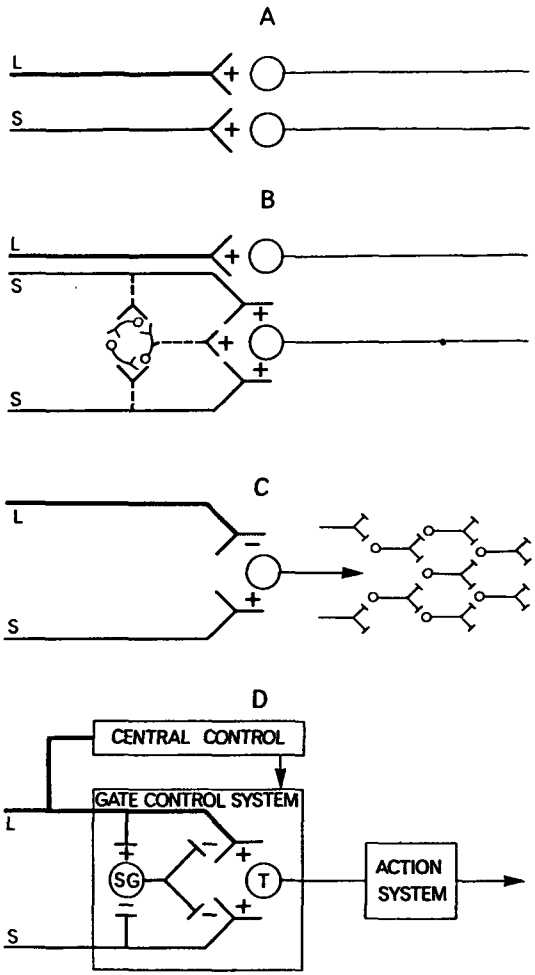

Fig. 1 Schematic representation of conceptual models of pain mechanisms. (A) Specificity theory. Large (L) and small (S) fibers are assumed to transmit touch and pain impulses respectively, in separate, specific, straight-through pathways to touch and pain centers in the brain. (B) Goldscheider's summation theory, showing convergence of small fibers onto a dorsal horn cell. The central network projecting to the central cell represents Livingston's (1943) conceptual model of reverberatory circuits underlying pathological pain states. Touch is assumed to be carried by large fibers. (C) Sensory interaction theory, in which large (L) fibers inhibit (–) and small (S) fibers excite (+) central transmission neurons. The output projects to spinal cord neurons which are conceived by Noordenbos (1959) to comprise a multisynaptic afferent system. (D) Gate control theory. The large (L) and small (S) fibers project to the substantia gelatinosa (SG) and first central transmission (T) cells. The central control trigger is represented by a line running from the large fiber system to central control mechanisms, which in turn project back to the gate control system. The T cells project to the entry cells of the action system. + = excitation; – = inhibition.

not surprisingly, erroneous. To thoughtful clinical observers, however, the theory was clearly wrong.

There were several attempts to find a new theory. The major opponent to specificity was labelled as "pattern theory", but there were several different pattern theories and they were generally vague and inadequate. However, seen in retrospect, pattern theories gradually evolved and set the stage for the gate control theory (Fig. 1). Goldscheider proposed that central summation in the dorsal horns is one of the critical determinants of pain. Livingston's (1943) theory postulated a reverberatory circuit in the dorsal horns to explain summation, referred pain and pain that persisted long after healing was completed. Noordenbos' (1959) theory proposed that large-diameter fibers inhibited small-diameter fibers, and he even suggested that the substantia gelatinosa in the dorsal horns plays a major role in the summation and other dynamic processes described by Livingston. However, in none of these theories was there an explicit role for the brain other than as a passive receiver of messages. Nevertheless, the successive theoretical concepts moved the field in the right direction: into the spinal cord and away from the periphery as the exclusive answer to pain.

When Patrick D. Wall and I began our frequent discussions that led to a new theory of pain, we were convinced that 1) brain processes had to be integrated into the theory, including feed-forward and feedback transmission, and 2) the new hypothetical spinal cord mechanism would need sufficient explanatory power to challenge spinal-cord physiologists and entice them away from the concept of specificity.

The Present Status of Pain

In 1965, Wall and I proposed the gate control theory of pain (Melzack & Wall, 1965). The theory, shown in model in Fig. 1D, is based on the following propositions:

1. The transmission of nerve impulses from afferent fibres to spinal cord transmission (T) cells is modulated by a spinal gating mechanism in the dorsal horn.

2. The spinal gating mechanism is influenced by the relative amount of activity in large-diameter (L) and small-diameter (S) fibres: activity in large fibres tends to inhibit transmission (close the gate) while small-fibre activity tends to facilitate transmission (open the gate).

3. The spinal gating mechanism is influenced by nerve impulses that descend from the brain.

4. A specialized system of large-diameter, rapidly conducting fibres (the Central Control Trigger) activates selective cognitive processes that then influence, by way of descending fibres, the modulating properties of the spinal gating mechanism.

5. When the output of the spinal cord transmission (T) cells exceeds a critical

level, it activates the Action System – those neural areas that underlie the complex, sequential patterns of behaviour and experience characteristic of pain.

When the gate control theory was published, Wall and I were astonished by the reception. The theory generated vigorous (sometimes vicious) debate as well as a great deal of research to disprove or support the theory. The search for specific pain fibers and spinal-cells by our opponents now became almost frantic. It was not until the mid-1970's that the gate control theory was presented in almost every major textbook in the biological and medical sciences. At the same time there was an explosion in research on the physiology and pharmacology of the dorsal horns and the descending control systems.

The theory's emphasis on the modulation of inputs in the spinal dorsal horns and the dynamic role of the brain in pain processes had a clinical as well as a scientific impact. Psychological factors, which were previously dismissed as "reactions to pain" were now seen to be an integral part of pain processing and new avenues for pain control were opened. Similarly, cutting nerves and pathways was gradually replaced by a host of methods to modulate the input. Physical therapists and other health-care professionals who use a multitude of modulation techniques (including acupuncture) were brought into the picture, and TENS became an important modality for the treatment of chronic and acute pain. The current status of pain research and therapy has recently been evaluated (Melzack & Wall, 1988; Wall & Melzack, 1989) and indicates that, despite the addition of a massive amount of detail, the theory remains basically intact after more than 25 years.

What was the gate theory's most important contribution to biological and medical science? I believe it was the emphasis on CNS mechanisms. The theory forced the medical and biological sciences to accept the brain as an active system that filters, selects and modulates inputs. The dorsal horns, too, were not merely passive transmission stations but sites at which dynamic activities – inhibition, excitation and modulation – occurred. The theory highlighted the central nervous system as an essential component in pain processes.

Where do we go from here? I believe the great challenge ahead of us is to understand brain function. Kenneth L. Casey and I (Melzack & Casey, 1968) made a start by trying to convince our colleagues that specialized systems are involved in the sensory-discriminative, motivational-affective and evaluative dimensions of pain. These phrases seemed strange when we coined them, but they are now used so frequently and seem so "logical" that they have become part of our language. So too, the McGill Pain Questionnaire, which taps into subjective experience – one of the functions of the brain – is widely used to measure pain (Melzack & Torgerson, 1971; Melzack, 1975). We have also

begun to understand the different pathways and neural mechanisms that underlie acute and chronic pain – again, by invoking complex spinal and brain mechanisms – and we have gained a far better understanding of the analgesic effects of morphine (Melzack, 1988).

In 1978, John Loeser and I (Melzack & Loeser, 1978) described severe pains in the phantom body of paraplegics with verified total sections of the spinal cord, and proposed a central "pattern generating mechanism" above the level of the section. We focussed more powerfully than ever before on CNS mechanisms. My own efforts now are to explore new theoretical concepts to explain phantom body experiences – from pain to orgasm – in people with total spinal sections. These experiences reveal important features of brain function because the brain is completely disconnected from the cord. Psychophysical specificity, in such a concept, makes no sense and we must explore how patterns of nerve impulses generated in the brain can give rise to somesthetic experience. It comes as a shock to conclude that "you don't need a body to feel a body", or that "the brain itself can generate every quality of experience which is normally triggered by sensory input" (Melzack, 1989). This approach seems radical and difficult to comprehend, but I am convinced that it is the only road on which we may travel.

The Future of Pain Concepts

It is evident that the gate control theory has taken us a long way. Yet, as historians of science have pointed out, good theories are instrumental in producing facts that eventually require a new theory to incorporate them. And this is what has happened. It's possible to make adjustments to the gate theory so that, for example, it includes long-lasting activity of the sort Wall (1989) has described. But there is a set of observations on pain in paraplegics that just does not fit the theory. This does not negate the gate theory, of course. All the peripheral and spinal processes are obviously an important part of pain and we need to know more about the mechanisms of peripheral inflammation, spinal modulation, midbrain descending control, and so forth. But the data on painful phantoms below the level of total spinal section (Melzack & Loeser, 1978) indicate that we need to go beyond the foramen magnum and into the brain (Melzack, 1989).

Now let me make it clear that I mean more than just the spinal projection systems to thalamus and cortex. These are important, of course, but they mark just the beginning of the psychological process that underlies perception. The cortex, White and Sweet (1969) have made amply clear, is not the pain center and neither is the thalamus (Spiegel & Wycis, 1966). The areas of the brain involved in pain experience and behaviour are very extensive. They must include somatosensory projections as well as the limbic system. Furthermore, because our body perceptions include visual and vestibular mechanisms as well as cognitive processes, widespread areas of the brain must be involved

in pain. Yet the plain fact is that we do not have an adequate theory of how the brain works.

So if I ask, "what is the future of the field of pain?", I must answer that it lies in understanding the brain. Of course there is still much to learn about nerves, the spinal cord and midbrain descending control systems. But it is the brain beyond the midbrain that needs to be explored. It represents almost uncharted territory. The revolution created by cognitive neuroscience is teaching us new facts about brain function that simply stagger the imagination. And it is to this that I shall now turn. There is no better way to enter this exciting world than to consider phantom limbs and phantom bodies: the "body-self" that is still present in experience even when input from that part of the body is gone (Melzack, 1989).

Phantom Limbs and the Concept of a Neuromatrix

My analysis of phantom limb phenomena (Melzack, 1989) has led to four conclusions which point to a new conceptual nervous system. First, because the phantom limb (or other body part) feels so real, it is reasonable to conclude that the body we normally feel is subserved by the same neural processes in the brain; these brain processes are normally activated and modulated by inputs from the body but they can act in the absence of any inputs. Second, all the qualities we normally feel from the body, including pain, are also felt in the absence of inputs from the body; from this we may conclude that the origins of the patterns that underlie the qualities of experience lie in neural networks in the brain; stimuli may trigger the patterns but do not produce them. Third, the body is perceived as a unity and is identified as the "self", distinct from other people and the surrounding world. The experience of a unity of such diverse feelings, including the self as the point of orientation in the surrounding environment, is produced by central neural processes and cannot derive from the peripheral nervous system or spinal cord. Fourth, the brain processes that underlie the body-self are, to an important extent which can no longer be ignored, "built-in" by genetic specification, although this built-in substrate must, of course, be modified by experience. These conclusions provide the basis of the new conceptual model.

OUTLINE OF THE THEORY

I will first present an outline of the theory and then deal with each of the components.

The anatomical substrate of the body-self, I propose, is a large, widespread network of neurons that consists of loops between the thalamus and cortex as well as between the cortex and limbic system. I have labelled the entire network, whose spatial distribution and synaptic links are initially determined genetically and are later sculpted by sensory inputs, as a *neuromatrix*. The loops diverge to permit parallel processing in different components of the

neuromatrix and converge repeatedly to permit interactions between the output products of processing. The repeated *cyclical processing and synthesis* of nerve impulses through the neuromatrix imparts a characteristic pattern: the *neurosignature*. The neurosignature of the neuromatrix is imparted on all nerve impulse patterns that flow through it; the neurosignature is produced by the patterns of synaptic connections in the entire neuromatrix. All inputs from the body undergo cyclical processing and synthesis so that characteristic patterns are impressed on them in the neuromatrix. Portions of the neuromatrix are specialized to process information related to major sensory events (such as injury, temperature change and stimulation of erogenous tissue) and may be labelled as neuromodules which impress subsignatures on the larger neurosignature.

The neurosignature, which is a continuous outflow from the body-self neuromatrix, is projected to areas in the brain – the *sentient neural hub (SNH)* – in which the stream of nerve impulses (the neurosignature modulated by ongoing inputs) is converted into a continually changing stream of awareness. Furthermore, the neurosignature patterns may also activate a neuromatrix to produce movement. That is, the signature patterns bifurcate so that a pattern proceeds to the *sentient neural hub* (where the pattern is converted into the experience of movement) and a similar pattern proceeds through a neuromatrix that eventually activates spinal cord neurons to produce muscle patterns for complex actions.

The four components of the new conceptual nervous system, then, are (1) the body-self neuromatrix, (2) cyclical processing and synthesis in which the neurosignature is produced, (3) the sentient neural hub which converts (transduces) the flow of neurosignatures into the flow of awareness, and (4) activation of an action neuromatrix to provide the *pattern* of movements to bring about the desired goal.

THE BODY-SELF NEUROMATRIX

The body is felt as a unity, with different qualities at different times and, I believe, the brain mechanism that underlies the experience also comprises a unified system that acts as a whole and produces a neurosignature pattern of a whole body. The conceptualization of this unified brain mechanism lies at the heart of the new theory and I believe the word "neuromatrix" best characterizes it. "Matrix" has several definitions in Webster's dictionary, and some of them imply precisely the properties of the neuromatrix as I conceive of it. First, a matrix is defined as "something within which something else originates, takes form or develops". This is exactly what I wish to imply: the neuromatrix (not the stimulus, peripheral nerves or "brain center") is the origin of the neurosignature; the neurosignature originates and takes form in the neuromatrix. Though the neurosignature may be triggered or modulated by input, the input is only a "trigger" and does not produce the neurosignature

itself. Matrix is also defined as a "mold" or "die" which leaves an imprint on something else. In this sense, the neuromatrix "casts" its distinctive signature on all inputs (nerve impulse patterns) which flow through it. Finally, matrix is defined as "an array of circuit elements ... for performing a specific function as interconnected". The array of neurons in a neuromatrix, I propose, is genetically programmed to perform the specific function of producing the signature pattern. The final, integrated neurosignature pattern for the body-self ultimately produces awareness and action.

For these reasons, the term neuromatrix seems to be appropriate. The neuromatrix, distributed throughout many areas of the brain, comprises a widespread network of neurons which generates patterns, processes information that flows through it, and ultimately produces the pattern that is felt as a whole body. The stream of neurosignature output with constantly varying patterns riding on the main signature pattern produces the feelings of the whole body with constantly changing qualities.

PSYCHOLOGICAL REASONS FOR A NEUROMATRIX

It is incomprehensible to me how individual bits of information from skin, joints or muscles can all come together to produce the experience of a coherent, articulated body. At any instant in time, millions of nerve impulses arrive at the brain from all the body's sensory systems, including the proprioceptive and vestibular systems. How can all this be integrated in a constantly changing unity of experience? Where does it all come together?

I cannot imagine how all these bits are added up to produce a whole. But I can visualize a genetically built-in neuromatrix for the whole body, producing a characteristic neurosignature for the body which carries with it patterns for the myriad qualities we feel. The neuromatrix, as I conceive of it, produces a continuous message that represents the whole body in which details are differentiated within the whole as inputs come into it. We start from the top, with the experience of a unity of the body, and look for differentiation of detail within the whole. The neuromatrix, then, is a template of the whole, which provides the characteristic neural pattern for the whole body (the body's neurosignature) as well as subsets of signature patterns (from neuromodules) that relate to events at (or in) different parts of the body.

These views are in sharp contrast to the classical specificity theory in which the qualities of experience are presumed to be inherent in peripheral nerve fibers. Pain is not injury; the *quality of pain experiences* must not be confused with the physical event of breaking skin or bone. Warmth and cold are not "out there"; temperature changes occur "out there", but the *qualities of experience* must be generated by structures in the brain. There are no external equivalents to stinging, smarting, tickling, itch; the *qualities* are produced by built-in neuromodules whose neurosignatures innately produce the qualities.

We do not learn to feel qualities of experience: our brains are built to

produce them. The inadequacy of the traditional peripheralist view becomes especially evident when we consider paraplegics with high-level complete spinal breaks. In spite of the absence of inputs from the body, virtually every quality of sensation and affect is experienced. It is known that the absence of input produces hyperactivity and abnormal firing patterns in spinal cells above the level of the break (Melzack & Loeser, 1978). But how, from this jumble of activity, do we get the meaningful experience of movement, the coordination of limbs with other limbs, cramping pain in specific (nonexistent) muscle groups, and so on? This must occur in the brain, in which neurosignatures are produced by neuromatrixes that are triggered by the output of hyperactive cells.

When all sensory systems are intact, inputs modulate the continuous neuromatrix output to produce the wide variety of experiences we feel. We may feel position, warmth, and several kinds of pain and pressure all at once. It is a single unitary feeling just as an orchestra produces a single unitary sound at any moment even though the sound comprises violins, cellos, horns, and so forth. Similarly, at a particular moment in time we feel complex qualities from all of the body. In addition, our experience of the body includes visual images, affect, "knowledge" of the self (versus not-self) as well as the meaning of body parts in terms of social norms and values. I cannot conceive of all of these bits and pieces coming together to produce a unitary body-self, but I can visualize a neuromatrix which impresses a characteristic signature on all the inputs that converge on it and thereby produces the never-ending stream of feeling from the body.

The experience of the body-self involves multiple dimensions – sensory, affective, evaluative, postural and many others. The sensory dimensions are subserved, in part at least, by portions of the neuromatrix that lie in the sensory projection areas of the brain; the affective dimensions, I assume, are subserved by areas in the brainstem and limbic system. Each major psychological dimension (or quality) of experience, I propose, is subserved by a particular portion of the neuromatrix – a *neuromodule* – which contributes a distinct portion of the total neurosignature. To use a musical analogy once again, it is like the strings, tympani, woodwinds and brasses of a symphony orchestra which each comprise a "module" of the whole; each makes its unique contribution yet is an integral part of a single symphony which varies continually from beginning to end.

The neuromatrix resembles Hebb's "cell assembly" by being a widespread network of cells that subserves a particular psychological function. However, Hebb (1949) conceived of the cell assembly as a network developed by gradual sensory learning, while I, instead, propose that the structure of the neuromatrix is predominantly determined by genetic factors, although its eventual synaptic architecture is influenced by sensory inputs. This emphasis on the genetic contribution to the brain does not diminish the importance of sensory inputs.

The neuromatrix is a psychologically meaningful unit, developed by both heredity and learning, that represents an entire unified entity.

ACTION PATTERNS: THE ACTION-NEUROMATRIX

The output of the body neuromatrix, I have proposed above, is directed at two systems: (1) the neuromatrix that produces awareness of the output, and (2) a neuromatrix involved in overt action patterns. In this discussion, it is important to keep in mind that just as there is a steady stream of awareness (even during the dream episodes of sleep), there is also a steady output of behaviour (including movements during sleep).

It is important to recognize that behaviour occurs only after the input has been at least partially synthesized and recognized. For example, when we respond to the experience of pain or itch, it is evident that the experience has been synthesized by the body-self neuromatrix (or relevant neuromodules) sufficiently for the neuromatrix to have imparted the neurosignature patterns that underlie the quality of experience, affect and meaning. Apart from a few reflexes (such as withdrawal of a limb, eye-blink and so on), behaviour occurs only after inputs have been analyzed and synthesized sufficiently to produce meaningful experience. When we reach for an apple, the visual input has clearly been synthesized by a neuromatrix so that it has 3-dimensional shape, colour and meaning as an edible, desirable object, all of which are produced by the brain and are not in the object "out there". When we respond to pain (by withdrawal or even by telephoning for an ambulance), we respond to an experience that has sensory qualities, affect and meaning as a dangerous (or potentially dangerous) event to the body.

I propose that after inputs from the body undergo transformation in the body-neuromatrix, the appropriate action patterns are activated concurrently (or nearly so) with the neuromatrix for experience. Thus, in the action-neuromatrix, cyclical processing produces activation of several possible patterns and their successive elimination until one particular pattern emerges as the most appropriate for the circumstances at the moment. In this way, input and output are synthesized simultaneously, in parallel, not in series. This permits a smooth, continuous stream of action patterns.

The command, which originates in the brain, to perform a pattern such as running activates the neuromodule which then produces firing in sequences of neurons that send precise messages through ventral horn neuron pools to appropriate sets of muscles. At the same time, the output patterns from the body-neuromatrix that engage the neuromodules for particular actions are also projected to the sentient neural hub and produce experience. In this way, the brain commands may produce the experience of movement of phantom limbs even though there are no limbs to move and no proprioceptive feedback. Indeed, reports by paraplegics of terrible fatigue due to persistent bicycling movements (like the painful fatigue in a tightly clenched phantom fist in

arm-amputees) indicate that feelings of effort and fatigue are produced by the signature of a neuromodule rather than particular input patterns from muscles and joints.

Implications of the New Concept

PHANTOM LIMB PAIN

The new theory of brain function, proposed on the basis of phantom-limb phenomena, provides an explanation for phantom limb pain. Amputees suffer burning, cramping and other qualities of pain. An excellent series of studies (Krebs et al., 1984; Jensen et al., 1985) found that 72% of amputees had phantom limb pain a week after amputation, and that 60% had pain 6 months later. Even 7 years after amputation, 60% still continued to suffer phantom limb pain, which means that only about 10 - 12% of amputees obtain pain relief. The pain is remarkably intractable; although more than 40 forms of treatment have been tried, none has proved to be particularly efficacious (Sherman et al., 1980).

Why is there so much pain in phantom limbs? I believe that the active body-neuromatrix, in the absence of modulating inputs from the limbs or body, produces a signature pattern that is transduced in the sentient neural hub into a hot or burning quality. The cramping pain, however, may be due to messages from the action-neuromodule to move muscles in order to produce movement. In the absence of the limbs, the messages to move the muscles become more frequent and 'stronger' in the attempt to move the limb. The end result of the *output* message may be felt as cramping muscle pain. Shooting pains may have a similar origin, in which action-neuromodules attempt to move the body and send out abnormal patterns that are felt as shooting pain. The origins of these pains, then, lie in the brain.

RECENT RESEARCH

Surgical removal of the somatosensory areas of the cortex or thalamus fails to relieve phantom limb pain (White & Sweet, 1969). However, the new theory conceives of a neuromatrix that extends throughout selective areas of the whole brain. Thus, to destroy the neuromatrix for the body-self which generates the neurosignature pattern for pain is impossible. However, if the neurosignature for pain is generated by cyclical processing and synthesis, then it may be possible to block it by injecting a local anesthetic into a discrete area. Such an injection would be relatively easy and harmless to carry out and could bring relief that extends beyond the duration of the anesthetic.

In the first study on this problem, Tasker and I (Tasker et al., 1987) injected the local anesthetic lidocaine into the lateral hypothalamus – an area we considered to be strategic for a neuromatrix for the body-self and pain. We found that freely moving rats that received the injection showed a significant reduction of pain in the formalin test, which produces a moderately intense

pain for one to two hours and has many of the characteristics of injury-produced pain in humans. However, the injection had no effect on tail-flick pain, which is primarily a spinally mediated reflex. Moreover, lidocaine injected into adjacent hypothalamic structures (including the medial hypothalamus) had no effect on the formalin-test pain, indicating that the analgesia was produced by local anesthesia of a specific group of neurons. Since the analgesia was bilateral, it is reasonable to assume that the lateral hypothalamus contains neurons that are important for producing the neurosignature for pain in both sides of the body.

Recently, Vaccarino and I (Vaccarino & Melzack, 1992) injected lidocaine into the cingulum bundle and other areas that seem to be strategically located in the neuromatrix for the synthesis of the neurosignature for pain. The results showed that the lidocaine produces striking decreases in pain in the formalin test as well as in self-mutilation produced by pain or dysesthesia after peripheral nerve lesions. McKenna and I (McKenna & Melzack, 1992) obtained similar results after injection of lidocaine into the dentate nucleus. These exciting results suggest a valuable new approach for the study of pain. If, ultimately, they lead to the relief of pain and suffering, the neuromatrix theory will have served at least one valuable function.

My students and I have also gathered some direct evidence supporting my suggestion that the brain – and by implication, the neuromatrix – can generate sensation on its own. The formalin pain test produces an "early" pain that rapidly rises and falls in intensity during the first five minutes after the injection, followed by a "late" pain, which begins about 15 minutes after the injection and persists for about an hour. By means of this test, Coderre, Vaccarino, and Melzack (1990) found that an anesthetic block of the paw completely obliterates the late pain, but only if the anesthetic is delivered in time to prevent the early response. Once the early pain occurs, the drug only partly reduces the later response. This observation of pain continuing even after the nerves carrying pain signals are blocked implies that long-lasting pain (such as that in phantoms) is determined not only by sensory stimulation during the discomfort but also by brain processes that persist without continual priming.

In a related study, Katz et al. (1991) showed that an injury of a rat's paw before it is totally denervated leaves a lasting memory that influences the rat's later perception of pain in the "phantom" of the denervated paw. These "pain memories" are consistent with earlier observations that the pain felt in phantom limbs in humans often resembles the pains of earlier injuries of the limbs prior to amputation (Katz & Melzack, 1990).

Because my model of brain function posits that the neuromatrix as a whole may contribute to pain, the model also suggests that altering the activity of pathways outside the somatosensory system might be important, either alone or in combination with other treatments. One place to begin work is the

limbic system. Until now, limbic structures have been relegated to a secondary role in efforts to treat pain, because injurious stimuli do not activate them directly. Nevertheless, if the limbic system contributes to output by the neuromatrix, as I have proposed, it might well contribute to the pain felt in phantom limbs. The results of the studies of the effects of lidocaine injection into the cingulum, dentate nucleus and other limbic areas, cited above, support this proposal.

The phenomenon of phantom limbs has allowed me to attack some fundamental assumptions in psychology. One assumption is that sensations are produced only by stimuli and that perceptions in the absence of stimuli are psychologically abnormal. Yet phantom limbs, as well as phantom seeing (Schultz & Melzack, 1991), indicate this notion is wrong. The brain does more than detect and analyze inputs; it generates perceptual experience even when no external inputs occur.

Another entrenched assumption is that perception of one's body results from sensory inputs that leave a memory in the brain; the total of these signals becomes the body image. But the existence of phantoms in people born without a limb or who have lost a limb at an early age suggests that the neural networks for perceiving the body and its parts are built into the brain. The absence of inputs does not stop the networks from generating messages about missing body parts; they continue to produce such messages throughout life. In short, phantom limbs are a mystery only if we assume the body sends sensory messages to a passively receiving brain. Phantoms become comprehensible once we recognize that the brain generates the experience of the body. Sensory inputs merely modulate that experience; they do not directly cause it.

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