THE NEUROMATRIX OF PAIN

Taken from "Brain Top to Bottom"

<u>The scientific search for a single "pain centre" in the brain has proven fruitless.</u> If such a centre existed, then millions of people might be relieved of their <u>chronic pain</u> by treatments to remove this centre surgically or neutralize it chemically. But no such centre has been found. Pain is a subjective phenomenon with multiple dimensions, some discriminative, some affective, and others cognitive, so it is no surprise that science has shown that any given sensation of pain is actually produced by the interactions of a <u>network of brain structures</u> that are activated by a particular nociceptive stimulus.

Science has also shown that the activity of this network is highly sensitive to "<u>top-down</u>" <u>regulatory processes</u>, which would explain phenomena such as the <u>placebo effect</u>. The way we experience a given source of pain is also influenced by our personal experience and our <u>cultural heritage</u>, which means that an even broader range of brain structures are involved.

That said, neuroscientists do now acknowledge that there is at least a partial degree of functional specialization among the brain structures involved in the various components of pain. Researchers are now attempting to associate different subsets of brain structures with these different components of pain and thereby propose an overall working model of pain. Given the complexity of the phenomenon that these models are supposed to represent, they are still the subject of much lively debate.

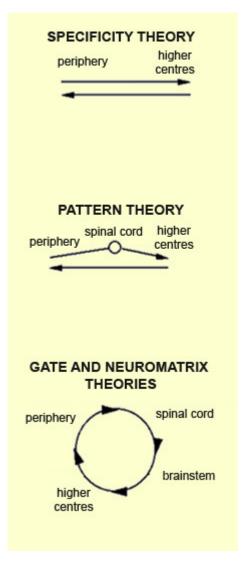
Broadly speaking, the underlying concept of <u>theories of pain has evolved over time from</u> <u>one of linear causality to one of circular causality</u>. In the early theory of intensity, pain was deemed to result from the excess activity of certain nerves that were not necessarily pain-specific. Then, in the 17th century, <u>René Descartes</u> was one of the first authors to <u>discuss pain as a specific sense</u>, just like the senses of <u>sight</u>, hearing, and smell.

In 1894, Von Frey stated an explicit theory of the specificity of sensations. According to this theory, the type of nerve ending determines the nature and quality of the sensation perceived. The resulting information then travels basically from the periphery to the higher centers, where it reaches something like a "pain centre", then travels back downward as motor control information, without having been altered in any significant way. Thus this theory does not allow for any possible changes of psychological origin, such as might result from <u>attention</u> or from past experiences that give a particular meaning to a particular situation. In this model, the brain and the subcortical relays are nothing more than passive receptors.

Unable to provide suitable explanations for phenomena such as chronic pain, specificity theory subsequently gave way to various pattern theories of pain. These theories added to the linear ascending pathway various relays that begin the process of integrating the activity of nerve fibres that have different receptive properties. Such integration would take place, for example, in the <u>gelatinous substance</u> of the spinal cord, the ventral

posterior nuclei of the thalamus, and the somatosensory cortex. Motor control signals would then be returned downward in linear fashion.

The development of the <u>gate theory of pain</u> starting in the 1960s, and of neuromatrix theory after that, was based on the finding that pain results from a multitude of interactions and information exchanges at several levels in the nervous system. The <u>ascending nociceptive information is modulated</u> at each of these multiple relays before it is integrated into a perception of pain. Perhaps the chief advantage of this circular model of pain is that it provides a better explanation of how the nociceptive, discriminative, affective, and behavioural components of pain can all influence one another.

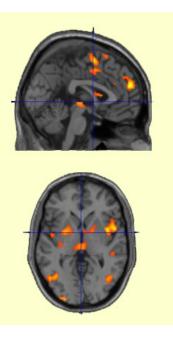


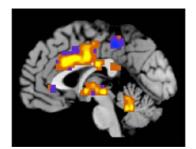
Source: Charest, Lavignolle, Chenard, Provencher and Marchand, "École interactionnelle du dos", *Rhumatologie*, 46, 221-237, (1994)

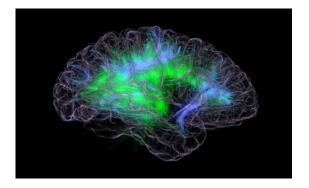
The concept of the neuromatrix of pain was first advanced by Canadian psychologist Ronald Melzack, in the late 1980s, in an attempt to explain the strange but very common phenomenon of "<u>phantom limb</u>" pain, in which people who have had a limb amputated feel very real pain that seems to be coming from that limb. This phenomenon clearly shows that pain is not generated by a one-way system. Melzack's proposed explanation was that <u>pain is actually generated by neural activity in a network composed of several different structures in the brain</u>, and that this network <u>can generate pain even when there is no sensory stimulus to trigger it.</u>

In the case of phantom-limb pain, Melzack proposed, the conflict between the visual feedback that the limb is absent and proprioceptive representations that it is present might cause confusion in the neuromatrix, and this confusion would then generate the pain. Evidence in support of this hypothesis has been provided by experiments in which mirrors were used to give amputees with phantom-limb pain the visual illusion that their amputated limbs were still present. In some cases, this measure was effective in relieving the phantom-limb pain.

This neuromatrix, or pain matrix, thus consists of all the parts of the brain whose activity fluctuates when an individual is experiencing pain—a vast neural space in which <u>various</u>, <u>distinctive types of pain</u> can be encoded. Each of these types of pain has what Melzack calls its own special neurosignature: a unique activation pattern of the neuromatrix or of some subset of it. (Other scientists use the term <u>neuronal assembly</u> to describe this kind of association of neurons.) And because the details of the connections in the brain of each individual are different, each individual's neurosignatures are necessarily different too. Likewise, <u>because synaptic connections can be modified by experience</u>, any given neurosignature in a given individual's brain will change structurally with the passage of time.







Activation of structures of the pain neuromatrix, including the insula, the anterior cingulate cortex, the periaqueductal grey matter, the medial prefrontal cortex, and the supplementary motor area

To account for all the different facets of the phenomenon of phantom pain in amputees, Melzack proposed a neuromatrix comprising <u>numerous brain structures</u> involved variously in the discriminatory, affective, cognitive, and motor aspects of this experience. Melzack's proposed neuromatrix included at least three major neural circuits whose importance has been confirmed by the numerous brain-imaging studies that followed. The first is a lateral spinothalamic ascending nociceptive pathway, which performs a discriminative function and includes the ventral posterior nuclei of the thalamus and the somatosensory cortex. The second is a medial spinothalamic pathway, which has a more affective and motivational function and involves the brainstem, the ventral medial nuclei of the thalamus, the limbic system, and the frontal cortex. The third circuit involves the associative areas of the inferior parietal cortex.

Subsequent research has shown that this neuromatrix also involves other parts of the brain, such as the orbitofrontal cortex, the prefrontal cortex (Brodmann areas 9, 10, and 44), and the motor cortex (for example, Brodmann area 6 and the <u>supplementary motor</u> <u>cortex</u>), as well as certain regions of the <u>midbrain</u>, such as the <u>periaqueductal grey matter</u> and the lenticular (or lentiform) nucleus.

Many neuroscientists have even come to regard structures such as the <u>anterior cingulate</u> <u>cortex and the insula</u> as key areas whose activation necessarily accompanies certain aspects of pain, and particularly its affective component. Without reverting to a description of these areas as "pain centres", these scientists do note that their neurons show a great deal of specificity to certain aspects of pain. This shows that the pain neuromatrix may include various nodes, and that the activity of some of these nodes may be more significant than that of certain others.

In 2004, U.S. neuroscientist A. Vania Apkarian used magnetic resonance imaging to compare the brains of healthy persons with those of people suffering from chronic back pain. In the latter group, he observed a <u>thinning of the grey matter</u> in the brain comparable to the loss of grey matter observed in 10 to 20 years of aging. And the longer

these people had been living with this chronic pain, the greater the volume of grey matter they had lost.

This loss was especially evident in the thalamus and the prefrontal cortex, an area associated with problem-solving. This finding was consistent with Apkarian's earlier observation that people with chronic pain took longer to solve certain mental-skill-testing problems than healthy people did.

Scientists are well aware of <u>the harmful effects of stress on certain neurons</u> in the brain that are particularly involved in memory. But it is still hard to say whether this stress is directly responsible for the thinning of the grey matter, or whether the stress is instead the source of chronic pain, which then in turn causes the reduction in brain volume.

Studies have shown that the <u>nucleus accumbens</u>, a key part of the brain's <u>reward circuit</u>, is activated during certain experiments that employ nociceptive stimuli. Moreover, in many cases this activation appears to be associated with a variation in the level of <u>endorphins</u> in the vicinity of the nucleus accumbens.

The fact that <u>dopamine</u> is also involved in the analgesia produced by the <u>placebo effect</u> is consistent with this finding, because the neurons of the nucleus accumbens are highly sensitive to this neurotransmitter, which they receive from the <u>ventral tegmental area</u>.

These findings tend to support the hypothesis that there are specific physiological mechanisms behind what we subjectively perceive as a continuum, from the onset of pain to its subsidence and then on to pleasant and highly pleasant sensations. This same idea that **pain and pleasure are part of a single spectrum** can be found in the writings of philosophers from past centuries, such as <u>Spinoza</u> and <u>Bentham</u>.