Neurological affects of chronic pain

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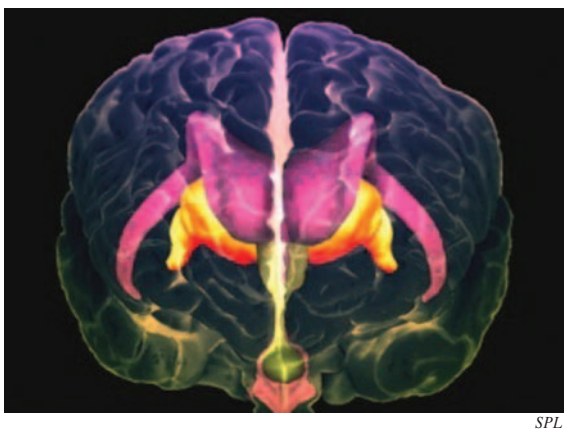
Emerging evidence suggests the brain is actively involved in interpreting chronic pain states



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Chronic pain remains one of the most indomitable medical, biological and social challenges today. During the last century, several theoretical ideas and experimental observations increased our knowledge about peripheral and central mechanisms of pain.

One of the most prominent theories that still constitutes the main framework within which brain mechanisms of pain are interpreted is the 'specificity theory'. This proposes that pain is a sensory modality conveyed by a specific pathway from peripheral pain receptors to the brain. This notion proved to be very powerful, and gave rise to most of the seminal research in pain physiology and clinical treatments for acute and chronic pain. Despite these obvious accomplishments, the role of cortical and sub-cortical areas in pain remained elusive. Their involvement was thought to be passive, reflecting spinal cord and peripheral processes.

Today, evidence from non-invasive brain imaging (positron emission tomography and functional MRI) studies support a more prominent and active role of the brain in the pathophysiology of pain, especially in patients suffering from chronic pain. There is growing evidence that chronic pain is associated with behavioural impairments and psychological disorders, in addition to cortical neurochemical changes[1] and decreased gray matter density[3]. Furthermore, data from functional imaging studies suggest that chronic pain is associated with a unique brain activity pattern distinct from that of acute pain[2]. These long-term neurological effects may provide novel targets for future therapies.

Evidence for gray matter loss in chronic pain

To understand the impact that living with chronic pain has on the brain in general, we examined brain gray matter density in 18 people suffering from chronic back pain in comparison to normal subjects[3]. We demonstrated that chronic back pain patients exhibited an additional 0.5 per cent loss of global brain gray matter density per year (equivalent to 10 to 15 years of natural aging), when compared with control subjects matched for age and sex. This gray matter density loss is localised to the thalamus and dorsolateral prefrontal cortical (DLPFC) regions (see Figure 1). The exact mechanisms leading to this atrophy remain unclear and are subject to ongoing studies. We also do not know the extent to which this atrophy is reversible.

The thalamic atrophy can be best interpreted as neural dysfunction or neuronal death due to abnormal activity within the classical spinothalamic pain pathway. This may provide an explanation for the various sensory abnormalities that chronic pain patients exhibit. The DLPFC atrophy is harder to explain within the classical framework of pain, and probably reflects complex cortical reorganisation specific for chronic pain states. This showed a specific correlation with clinical parameters for the different subtypes of chronic neuropathic and non-neuropathic pain patients examined.

Effect on emotional processing and learning

The DLPFC is involved in memory, rational thinking, and

Key learning points

- There is growing evidence that chronic pain is associated with behavioural impairments and psychological disorders.
- There was an additional 0.5 per cent gray matter density loss in the thalamus and dorsolateral prefrontal cortical (DLPFC) regions of the brain in people with chronic pain.
- Thalamic atrophy may explain various sensory abnormalities exhibited by patients with chronic pain.
- Shrinkage of DLPFC (which is involved in memory, rational thinking and reasoning) may contribute to exaggerated activity in the medial frontal cortex, augmenting the emotional dimension of chronic pain.
- Long-term chemical, functional, anatomical and behavioural modifications suggest the brain is actively involved in interpreting chronic pain states.

emotionally neutral reasoning and it is functionally inversely related with the medial frontal cortex (mPFC). The latter involves negative effect, and is activated during chronic pain. Similar evidence was presented by Lorenz and colleagues[4], who showed that the DLPFC exerts a modulatory role, decreasing the intensity of perceived pain. The implications of these results can be better appreciated within the construct of interplay between the DLPFC and mPFC in emotional-cognitive processing. The shrinkage in the gray matter density of the DLPFC may be contributing to exaggerated activity in the mPFC, augmenting the emotional dimension of chronic back pain.

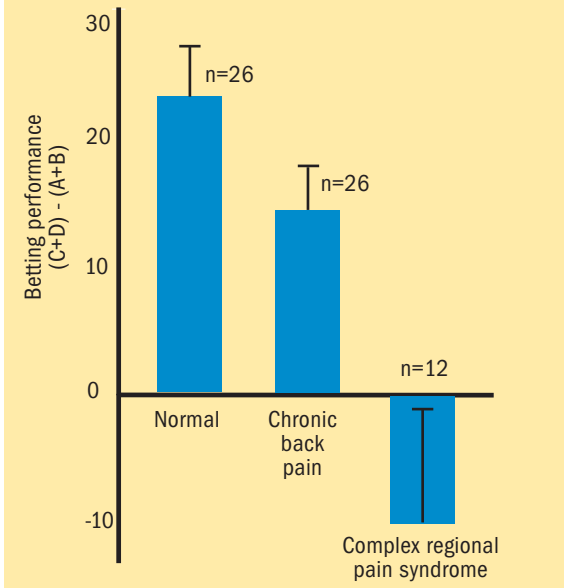
To gain further insight into the nature of this negative emotional state and its impact on behaviour, we performed a emotional decision gambling task[5]. Two groups of patients suffering from chronic back pain and complex regional pain syndrome (CRPS) were compared to people without pain[6]. The gambling task emulates in real time emotional decision making that entails monetary gain with uncertainty of the outcome.

Participants were instructed to chose between four decks of cards where two of them – C and D – yielded immediate high gain but large future losses (bad decks), and the other two – A and B – yielded low immediate gain but smaller future losses (good decks). Normal control subjects readily learned the rules as they played the game and continued to increase the frequency of choosing from the good decks. Patients suffering from mPFC lesions performed poorly in this task. Chronic back pain patients showed a delayed leaning curve. CRPS patients exhibited no evidence for ability to learn the task.

Performance in both patient groups was significantly lower than normal subjects, and CRPS patients performed worse than chronic back pain patients (Figure 2). This impairment appears to be specific to those with chronic pain, since pain intensity was significantly negatively correlated to performance in chronic back pain patients but not in CRPS. Furthermore, the outcome on the same task in normal subjects was not affected by acute thermal painful stimuli of the same intensity as the pain reported by the patient populations.

The cognitive and psychological profile of chronic pain has been extensively studied in the past. However, the emphasis of these studies was on identifying predisposing factors based on the general idea of pain disrupting attention and/or memory. In contrast, results from the gambling task provide robust evidence that chronic pain patients exhibit specific impairments as a result of long-term neurological changes specific to the clinical condition in question. This potentially links brain atrophy with brain activity and cognitive interference.

Figure 2. Effect of chronic back pain and CRPS on performance[5]



A+B = 'good' card packs with low immediate gain but smaller future losses
C+D = 'bad' card packs with immediate high gain but large future losses

Differences in performance on gambling task between chronic back pain, CRPS, and normal subjects. The more positive the score the better is performance.

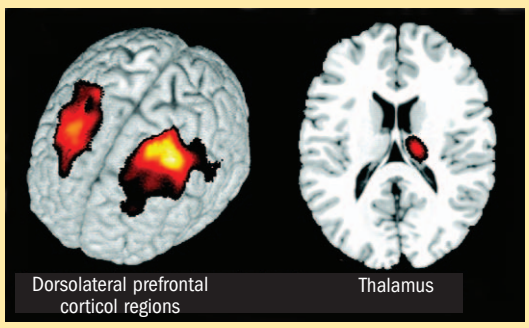
Conclusion

Our results provide new direction regarding the involvement of the cortex in chronic pain, suggesting that the brain is actively involved in interpreting pain states as evidenced by long-term chemical, functional, anatomical and behavioural modifications. Overall, these observations imply the necessity of considering brain regions beyond the classical pain circuitry to disentangle the complexity of chronic pain.

The 'specificity theory' of pain, therefore, falls short as a theoretical construct. This Cartesian viewpoint needs to be recast along the even more classical Aristotelian view of pain as an emotional drive motivating behaviour.

Figure 1.

Images of the brain indicating significant atrophy (coloured regions) in the dorsolateral prefrontal corticol and thalamus regions



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