Cognitive modulation of pain

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Pain is a highly subjective sensation with a complex and often non linear relationship between nociceptive input and pain perception. From human experimentation we know that nociceptive information processing and consequent pain perception is subject to significant pro- or anti-nociceptive modulation. Various mental processes such as attention, distraction, emotion, beliefs and feelings have been shown to influence pain perception and bias nociceptive processing in the humain brain. Studies examining brain activity during pain modulation by hypnosis induced powerful expectations one important cognitive factor interacting also with pain.

Brain areas most commonly activated in the context of pain include thalamus, somatosensory cortex S1/S2, insular and anterior cingulate cortex and prefrontal cortices, caudate nuclei, as well as amygdalae and cerebellum. This « pain matrix » is connected with a number of higher level brain areas including cingulo-frontal regions. The hypothalamus and amygdalae that may represent the basis by which cognitive and emotional variables interact with nociceptive processing.

Cognitive and affective strategies seem to rely on a descending pain modulatory system, which is able to inhibit the afferent nociceptive signal from spinal cord transmission, which are principally inhibitory in function.

Electrophysiological and pharmacological studies elaborated that descending influences on spinal nociceptive processing involves essentially the rostral ventromedial medulla (RVM), and the periaqueductal grey PAG (Fields 2000, Millan 2002). The RVM is also able to display facilitatory influences on spinal nociceptive transmission (Gebhart 2004). Therefore, central control of nociception could either alleviate pain or facilitate nociceptive processing. Facilitation of pain contributes to the maintenance of hyperalgesic states after tissue damage, which aids the patients to pay increased attention to their injury and encourages protection of this area. However, sometimes these hyperalgesic states remain beyond tissue healing time and lead to chronic pain states. The questions when and why it remains are not yet answered. The investigation of neural mechanisms underlying more complex cognitive modulation is an emerging field in pain research.

One important cognitive factor is expectation regarding pain.

Among the cognitive variables influencing pain, the brain mechanisms underlying attentional control have been probably the most extensively studied (Valet 2004,Wiech 2005, Seminowicz 2007, Hauck 2007). However, attentional processes interact with mechanisms supporting the formation of expectations about pain and reappraisal of the experience, these, in turn are influenced by prior experience. Neural mechanisms underlying learning and expectation about pain provide insights into how the brain learns about pain over time by considering the history of successful and unsuccessful learning trials (Seymour 2004, Seymour 2005, O'Doherty 2007).

Perceived control over pain decreased pain related responses in the anterior cingulate cortex (ACC), insula and SII (Salomons 2004, Wiech 2006). However, attentional control and the descending pain modulatory system are also likely to be involved in the placebo analgesia.

Placebo-induced analgesia as a clinical example of cognitive pain modulation decreases pain intensity and cerebral responses to pain in brain areas such as ACC, insula and thalamus and ventrolateral prefrontal cortex (VLPFC) (Bingel 2006). It has recently been emphasized that not only the placebo substance causes analgesia but the actual meaning we attribute to it (Moerman 2002, Liberman 2004, , Price 2008). Benedetti et al (2005) suggested that appraisals of safety might promote selfdistraction strategies, linking reappraisal processes with attentional control.

Neurophysiological bases of other mechanisms of cognitive pain modulation such as hypnosis have been addressed using neuroimaging methods (Rainville 1999, Vanhaudenhuyse 2009). They support the importance of the anterior cingulate cortex. A coupling of cingulofrontal regions with subcortical areas of the descending modulatory system has been confirmed in several strategies of pain modulation (Faymonville 2003, Wiech 2006, Wiech 2008).

Emotions have powerful effects on pain perception. The prefrontal cortex, as weel as parahippocampal and brainstem structures are involved in the emotional regulation of pain (Roy 2009). Anticipatory anxiety related to pain is regulated by he anterolateral prefrontal cortex (Kalisch 2005). Even in patients with rheumatoid arthritis, Schweinhardt et al. (2008) investigated the emotional augmentation of pain and results suggets that medial prefrontal cortex mediate the relationship between depressive symptomes and clinical pain severity.

Conclusion

From a clinical point of view, millions of people worldwide suffer from chronic pain and pharmaceutical expendit for its treatment is high but treatment efficacy remains low for many chronic pain states. Furthermore, recent findings from functional neuroimaging studies support the notion that an altered interaction of pro- and antinociceptive mechanisms may contribute to the development and maintenance of these chronic pain states. Researchers using functional neuroimaging begun to put more emphasis on the distinct neural underspinnings of pathological pain condition (Schweinhardt 2006, Moisset 2007). Future studies will need to explore how long-term exposition to psychosocial and environmental factors shape nociceptive information processing and resultant pain experience.

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