Analgesia & Resuscitation : Current Research

Opinion

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Role of the PFC in Management of Chronic Pain

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Opinion

Chronic pain is best managed employing a multidisciplinary, bio psychosocial approach. The goal isn't only the reduction of pain but also to enable patients and their loved ones to deal with their pain.

rTMS

Repetitive Trans cranial magnetic stimulation (rTMS) of the PFC or M1 may be a non-invasive strategy that would have the potential to alleviate chronic pain. rTMS stimulation of the left DLPFC in healthy subjects is found to exert a bilateral control on pain system. rTMS is additionally related to increases in thermal and mechanical pain thresholds, compared to sham treatment. Similarly, left DLPFC-rTMS delivered at 10 or 20 min after capsaicin application significantly decreases spontaneous pain in both hands, whereas no significant effect is reported after right DLPFC rTMS. It is related to increased activity within the posterior gyrus cinguli, precuneus, right superior gyrus , right insula, and bilateral central gyrus . Activity within the right superior PFC is negatively correlated with pain ratings. rTMS-induced analgesia is related to elevated blood oxygenation-level dependent (BOLD) signal in Brodman areas 9 and 10, and diminished BOLD signal within the ACC, thalamus, midbrain, and medulla. Patients with fibromyalgia who received active TMS over 2 weeks showed a 29% reduction in pain also as improvement in depression symptoms, compared to baseline. Those with chronic migraine experienced a big reduction of the frequency of attacks during treatment by high-frequency rTMS over the left DLPFC, and a short-course of rTMS over the left DLPFC was found to alleviate mild traumatic brain injury-related headache symptoms.

The analgesic effects of M1 or DLPFC rTMS also are decreased by ketamine. Since ketamine is an inhibitor of NMDA receptors, this means that rTMS-induced antinociception depends on NMDA receptors and should involve long-term potentiation (LTP) mechanisms. Lipidomic analysis of the PFC of rats after rTMS indicate loss of plasmalogen species with long-chain polyunsaturated fatty acids, with a rise in their corresponding lysophospholipids, suggesting endogenous release of long-chain fatty acids like omega-3 fatty acid (DHA) after rTMS. DHA could also be metabolized to resolvin D1 by 15-lipoxygenase-1 (Alox15), which has been shown to play a crucial role in LTP and antinociception. Results suggest that LTP-like mechanisms likely play a task within the antinociceptive effects of rTMS, possibly through the involvement of endogenous opioids and fatty acids.

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Antidepressants

A variety of medicines are wont to treat chronic pain, including gabapentin, pregabalin, noradrenaline, or serotonin-noradrenaline reuptake inhibitor antidepressants including duloxetine, tricyclic antidepressants like amitriptyline, capsaicin, lidocaine patches, tramadol, neurotoxin , and opioids. Rectal pain induces significant activation of the perigenual ACC, right insula, and right prefrontal cortex. Treatment with the tricyclic, amitriptyline is related to reduce pain-related cerebral activations within the perigenual ACC and therefore the left posterior parietal cortex, but only during stress. In another study, duloxetine treatment is related to a big reduction in brain responses to painful stimulation in major clinical depression patients in regions generally showing abnormally enhanced activation at baseline. Clinical improvement is related to pain-related activation reductions within the pregenual anterior cingulate cortex, right prefrontal cortex, and pons, but interestingly, increased baseline activations within the right prefrontal cortex and reduced deactivations within the subgenual anterior cingulate cortex predicted treatment responders at week 8. Changes associated with Regulator of G protein signaling, a sign transduction protein that controls the function of monoamine, opiate, muscarinic, and other G protein-coupled receptors, are detected within the brain, after antidepressant treatment. In another study, reductions in clinical pain scores during treatment with milnacipran, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), in fibromyalgia patients are correlated with decreased baseline functional connectivity between the insula and ACC.

Acupuncture

Acupuncture has long been used for the control of pain. Patients with painful osteoarthritis who were scanned by PET show that real acupuncture and placebo (with an equivalent expectation of effect as real acupuncture) leads to greater activation of the proper DLPFC, ACC, and midbrain, compared to skin prick (with no expectation of a therapeutic effect). fMRI analysis shows that acupuncture induces activation of the amygdala and ACC, PAG, and hypothalamus and comparatively persistent activation of the anterior insula and PFC. Patients with chronic back pain had reduced connectivity within the pain network, including the DLPFC, mPFC, ACC, and presumes, but after acupuncture, connectivity was restored almost to the amount of healthy controls, and was correlated with a discount in pain. In patients with carpal tunnel syndrome, electroacupuncture at distal acupoints leads to PFC activation and reduction in pain. The analgesic effects of acupuncture may involve the discharge of endogenous opioids within the brain.

Mindfulness

Mindfulness practitioners but not controls are ready to reduce pain unpleasantness and anticipatory anxiety during a mindful state. This is often related to increased rostral ACC activation during the anticipation of pain. In other studies, reduction in pain during mindfulness is related to activation of brain regions including the orbitofrontal, subgenual ACC, anterior insular cortex, and therefore the DLPFC.

Meditation

In contrast to mindfulness, meditation appears to possess an impact on decreasing activity in several parts of the brain. Meditators show lower pain-evoked event-related potentials within the midcingulate cortex, and lower unpleasantness ratings compared to controls, and this response is predicted by lifetime meditation experience. Pain patients who have learnt Transcendental Meditation and practiced it for five months show decreased activity within the brain, including a 40–50% reduction within the thalamus and therefore the PFC. Likewise, practitioners of Zen meditation have reduced activity in executive, evaluative, and emotion areas, including the PFC, amygdala, and hippocampus during pain, compared with controls.

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