Neurobiology: To keep pain in check, count down

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Is the heat still bearable, or should I take my hand off the hotplate? Before the brain can react appropriately to pain, it must evaluate and integrate sensory, cognitive and emotional factors that modulate the perception and processing of the sensation itself. This task requires the exchange of information between different regions of the brain. New

studies have confirmed that there is a link between the subjective experience of pain and the relative levels of neural activity in functional structures in various sectors of the brain. However, these investigations have been carried out primarily in contexts in which the perception of pain was intensified either by emotional factors or by consciously focusing attention on the painful stimulus. Now, LMU neuroscientist Enrico Schulz, in collaboration with colleagues at the University of Oxford, has asked how cognitive strategies that affect one's subjective perception of pain influence the patterns of neural activity in the brain.

In the study, 20 experimental subjects were exposed to a painful cold stimulus. They were asked to adopt one of three approaches to attenuating the pain: (a) counting down from 1000 in steps of 7, (b) thinking of something pleasant or beautiful, and (c) persuading themselves—by means of autosuggestion—that the stimulus was not really that bad. During the experimental sessions, the subjects were hooked up to a 7T magnetic resonance imaging (MRI) scanner to visualize the patterns of neural activity in the brain, which were later analyzed in detail.

In order to assess the efficacy of the different coping strategies, participants were also asked to evaluate the subjective intensity of the pain on a scale of 0 to 100. The results revealed that the countdown strategy was the most effective of the three methods. "This task obviously requires such a high level of concentration that it distracts the subject's attention significantly from the sensation of pain. In fact some of our subjects managed to reduce the perceived intensity of pain by 50%," says Schulz. "One participant later reported that she had successfully adopted the strategy during the most painful phase of childbirth."

In a previous paper published in the journal Cortex in 2019, the same team had already shown that all three strategies help to attenuate the

perception of pain, and that each strategy evoked a different pattern of neural activity. In the new study, Schulz and his collaborators carried out a more detailed analysis of the MRI scans, for which they divided the brain into 360 regions. "Our aim was to determine which areas in the brain must work together in order to successfully reduce the perceived intensity of the pain," Schulz explains. "Interestingly, no single region or network that is activated by all three strategies could be identified. Instead, under each experimental condition, neural circuits in different brain regions act in concert to varying extents."

The attenuation of pain is clearly a highly complex process, which requires a cooperative response that involves many regions distributed throughout the brain. Analysis of the response to the countdown technique revealed close coordination between different parts of the insular cortex, among other patterns. The imaginal distraction method, i.e. calling something picturesque or otherwise pleasing to mind, works only when it evokes intensive flows of information between the frontal lobes. Since these structures are known to be important control centers in the brain, the authors believe that engagement of the imaginative faculty may require a greater degree of control, because the brain needs to search through more 'compartments'—to find the right memory traces, for instance. Comparatively speaking, counting backwards stepwise—even in such awkward steps—is likely to be a more highly constrained task. "To cope with pain, the brain makes use of a recipe that also works well in other contexts," says Anne Stankewitz, a co-author of the new paper: "success depends on effective teamwork." Her team now plans to test whether their latest results can be usefully applied to patients with chronic pain.

More information: Enrico Schulz et al, Ultra-high-field imaging reveals increased whole brain connectivity underpins cognitive strategies that attenuate pain, *eLife* (2020). DOI: 10.7554/eLife.55028

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