PAIN

Less pain when you're in control?

Our responses to pain and our ability to tolerate it are known to be affected by the extent to which pain is perceived to be controllable. A study published in *The Journal of Neuroscience* now shows how differences in perceived pain control influence the activation of the insular cortex, secondary somatosensory cortex (SII) and anterior cingulate cortex (ACC), all of which are involved in pain processing.

Salomons *et al.* used painful thermal stimuli and different cues signalling controllable or uncontrollable pain to test whether subjects' perception of pain and the associated neural processing varied according to perceived controllability. Although the subjects were able to distinguish between cues signalling controllable and uncontrollable pain, there was no difference between the mean pain rating given for stimuli perceived to be controllable or uncontrollable.

The authors also used overlapping brain maps created using fMRI studies, and subtracted the activation seen in areas of interest when pain was perceived to be controllable from that seen when pain was perceived to be uncontrollable. Although parts of all three areas were activated when pain was perceived to either be controllable or uncontrollable, the degree of activation was significantly greater when pain was perceived to be uncontrollable; in particular in the dorsocaudal area of the ACC and the anterior area of the right insula. As the subjects did not give the two conditions different pain ratings, Salomons *et al.* conclude that the results of the overlap study cannot be explained by just the subjects' perception of pain.

The authors suggest that the results of previous pain studies might have been influenced by subjects' perceived lack of pain control, which, in imaging studies, could have led researchers to believe that pain itself caused exaggerated activation of particular areas of the brain. They also propose that further research be carried out to establish whether different subjects use different techniques, such as distraction, to help them cope with pain. Furthermore, they suggest that differences in perceived pain control might be used in studies of chronic pain and possible treatments for this condition.

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References and links

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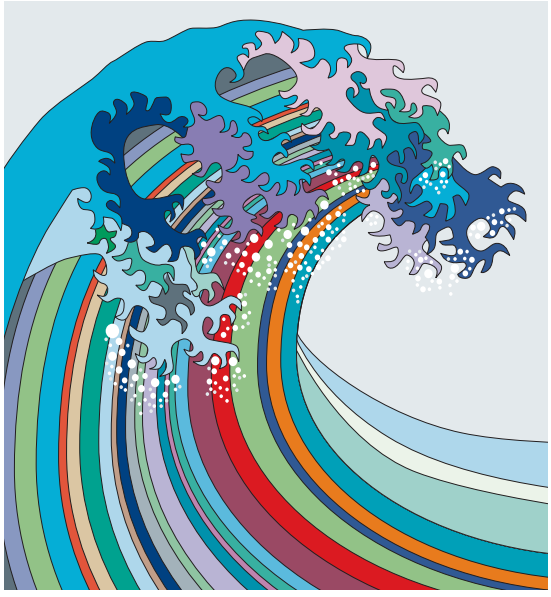
GLIA

Waves of proliferation

Radial glial cells are important in neuronal migration and also serve as neuronal progenitors, but signalling mechanisms among them are not well understood. Reporting in *Neuron*, Weissman and colleagues describe the discovery of a novel mechanism whereby proliferation of radial glial cells in the cortical ventricular zone (VZ) during development is regulated by spontaneous waves of calcium.



Using time-lapse calcium imaging, the authors first observed spontaneous calcium waves within the VZ of explants from the brains of embryonic day (E) 16–17 rats, which they could reproduce with electrical or mechanical stimulation. Calcium waves could be transmitted between two stimulated brain slices separated by up to 130 m, indicating that the propagation might be mediated by diffusible signals.

By using various receptor antagonists, the authors found that extracellular ATP was involved in spontaneous and stimulated calcium waves. Direct application of ATP resulted in an increase in the intracellular calcium concentration of the VZ cells. Initiation and propagation of spontaneous and stimulated calcium waves occurred in the absence of extracellular calcium, but were reduced when intracellular calcium was depleted, indicating that the release of calcium from internal stores might have a crucial role in the initiation and propagation of calcium waves. This is consistent with the finding that inhibitors of either inositol triphosphate or Gq-phospholipase C (PLC) significantly attenuated calcium waves.

To determine which cells in the VZ are involved in calcium waves, Weissman and colleagues stimulated the E16 coronal brain slices with ATP and monitored the calcium waves in randomly selected cells using patch electrodes. They observed that most VZ cells that displayed calcium increases in response to ATP had radial glial morphology.

The authors then assessed the functional consequence of calcium waves in radial glial cells in the VZ. They found that the cells involved in calcium waves are located in the upper third of the VZ, which represents the S-phase zone (where most cells are in the S phase of the cell cycle). The expression of spontaneous and stimulated calcium waves is maximal at E16, when neurogenesis also peaks. This developmental profile of calcium waves correlates with the sensitivity of the VZ cells to ATP. When calcium waves in E16 brain slices were disrupted by an ATP-receptor antagonist, the incorporation of 5-bromo-2′-deoxyuridine by the VZ cells — an indication of DNA synthesis in the S phase — was significantly reduced. This defect in proliferation was rescued when calcium waves were restored by a PLC activator. The authors conclude that calcium waves modulate the proliferation of radial glial cells during development and, therefore, might be important in regulating the production of neocortical neurons.

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WEBSITE

Kriegstein's laboratory:
http://www.research.hs.columbia.edu/Faculty_Profiles/profiles/kriegstein_ar.html