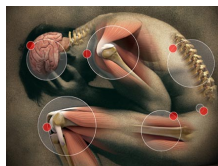


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By: Stefan Anitei, Science Editor



New Smart Painkillers

They target just the damaged tissue

Many painkillers have undesirable side effects, because they don't have the ability to target just the damaged areas. That's why researchers are trying to find a painkiller that would work just on the injured tissue, leaving the rest of the body unaffected. A new class of painkillers speculates the pH differences to accomplish this. In normal tissue, pH is around 7.4, but this decreases to 7.0 in an injured tissue, due to accumulation of carbon dioxide and lactic acid (through anaerobic respiration) as the blood supply is interrupted. The new chemicals block NMDA receptors, located in the brain and spinal cord neurons, which are involved amongst other processes in pain sensation. Previous drugs, like ketamine, also blocked NMDA receptors, but with undesirable side effects like impaired movement or hallucinations, as they affect undamaged nerve tissue also. The team at the Emory University School of Medicine in Atlanta, Georgia, has developed the chemical named NP-A, that attaches to the base of NMDA receptors and blocks glutamate and related neurotransmitters. A slight pH decrease induces a powerful increase in NP-A's activity: by 62 times from 7.6 to 6.9. "This means that NP-A gets switched on only where it's most needed, who has now set up a company called NeurOp to develop the drug further. It's a context-dependent blocking of pain, which is a new strategy for these receptors," said lead researcher Ray Dingledine. Rats injected with NP-A were much less sensitive to pain in an injured paw. Healthy rats induce with their healthy paw a force over 15 grams while with an injured paw, they will pull only 2 g. When injected with NP-A, 45 minutes after, the rats could push about 12 g. The pain was out for about 3 hours, and no side effects were observed. The team sees an application for this drug as a pain relief for patients with agonizing peripheral nerve damage (neuropathy). Standard treatment is with gabapentin, that inhibits pain through the GABA neurotransmitter, but this treatment is not effective for all the patients, as the pain cause is not GABA misfiring in all the cases. "A drug targeting NMDA receptors might help a different subset of patients who experience pain because of NMDA overactivation. GABA inhibition and NMDA firing are like yin and yang," said Min Zhuo of the University of Toronto in Canada, who studies NMDA receptors and pain.