



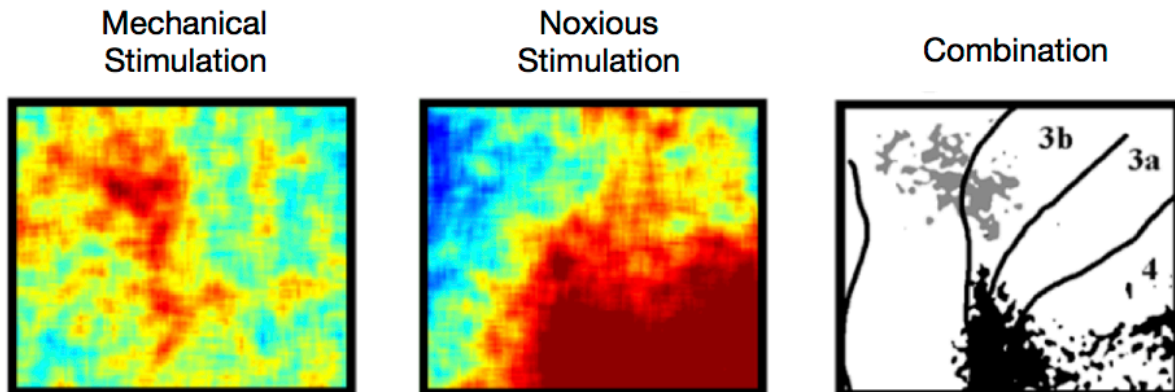
Using Brain Gauge to Study Pain

Scientific Report

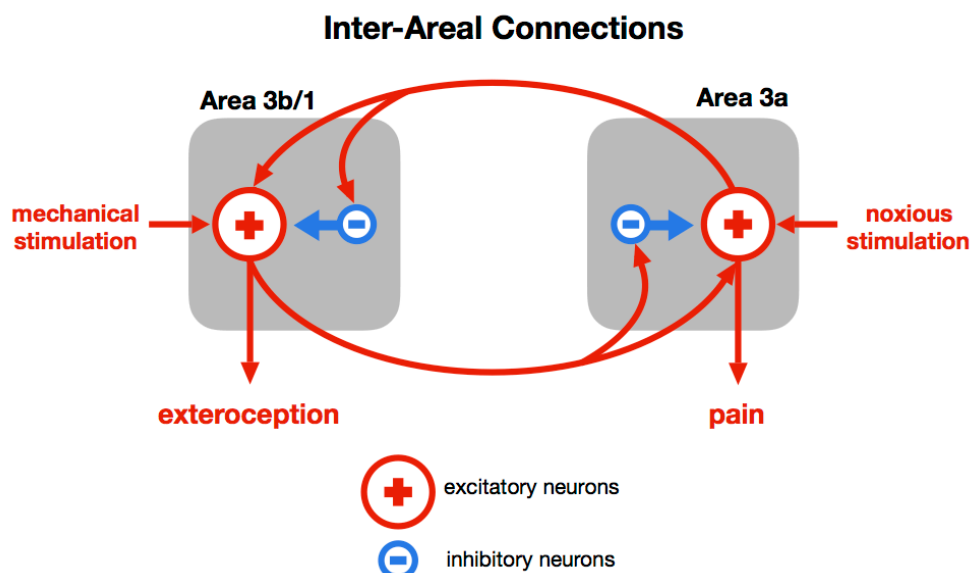
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Does Pain Influence Sensory Perception?

A few decades ago our research team discovered a significant relationship between the 3a and 3b/1 areas of the somatosensory cortex. These two areas were known to process different types of stimuli and no previous association between them had been noted. Area 3a is activated by painful or noxious stimuli, while area 3b/1 is activated by mechanical stimuli.



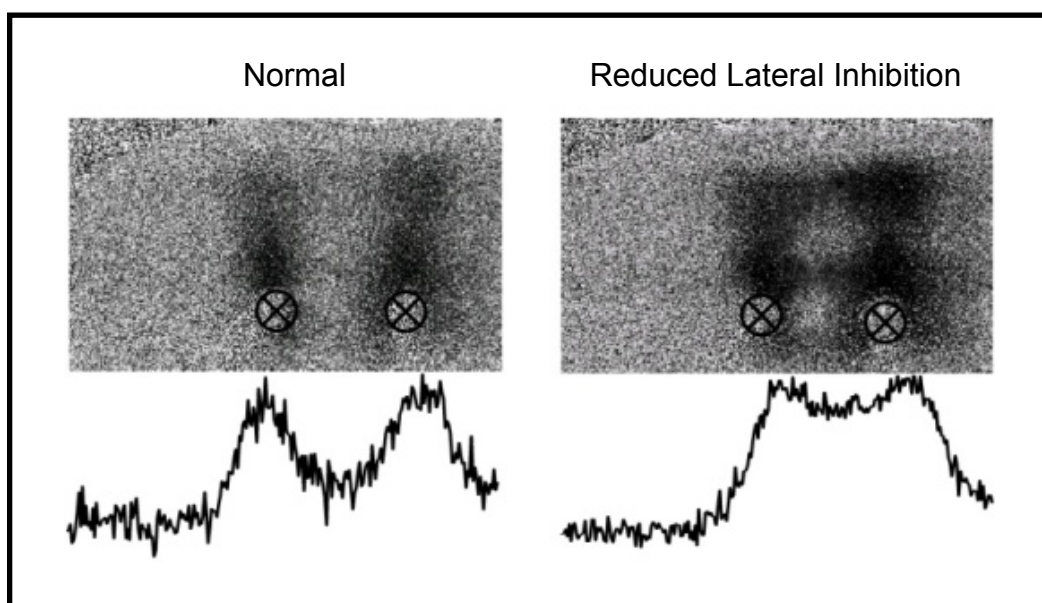
The figure above was first published in our 1998 discussion of this cortical relationship. All three images depict the region of the somatosensory cortex containing areas 3a and 3b/1. The first two panels are OIS images of the region under either mechanical or noxious stimulation, while the third panel shows the points of primary activation under each of these conditions (gray = mechanical, black = noxious). These images motivated further investigation on the interactions between the two areas.



The diagram above summarizes the results reported in numerous publications (Tommerdahl et al, 1996, [1998](#); Whitsel et al, [2009](#), [2010](#); Chen et al, 2009; [Vierck et al, 2013](#)). To summarize: (1) Noxious stimulation activates area 3a. (2) Activation of area 3a has a significant impact on stimulus-evoked activity in area 3b/1. (3) Modulation of 3a activity has an impact on pain percept and on sensory percepts modulated by areas 3b/1. Additionally, hyperactivity in area 3a most likely causes a “GABA reversal”. GABA, which is normally an inhibitory neurotransmitter, switches to an excitatory state under some conditions and thus makes the chronic pain condition worse (note that seizure-like brain activity is caused by hyperactivity).

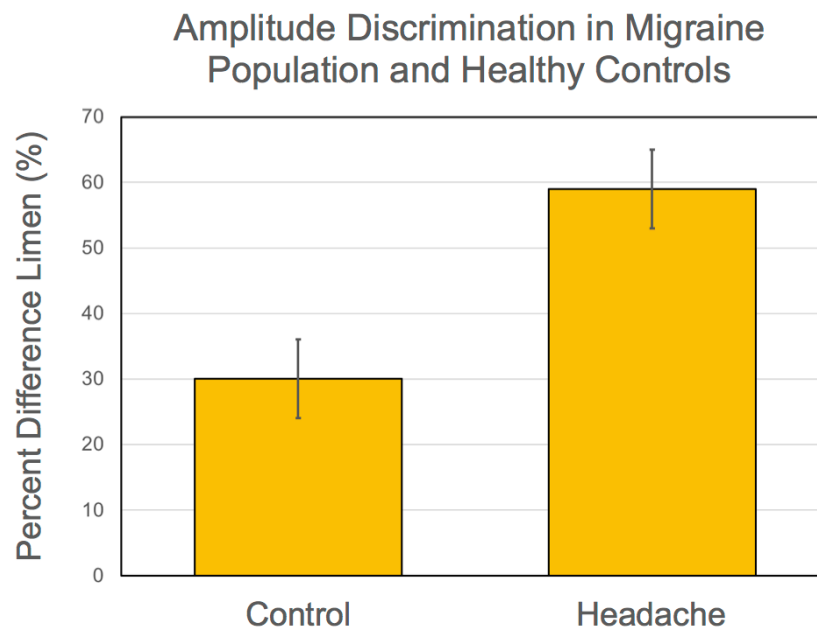
Are Sensory Percepts Modified by Pain?

Pain signals tend to significantly suppress sensory perception, and the interrelationship between areas 3a and 3b/1 is just one more example of this phenomenon. Hyperexcitability in area 3a causes suppression of 3b/1 signaling. This low amplitude also decreases the signal-to-noise ratio in area 3b/1. Thus, perception of a stimulus by the 3b/1 area is significantly reduced due to decreases in both overall excitation and local inhibition. Consider the figure below, which demonstrates the application of a drug (that reduces local lateral inhibition) makes the resolution between the two electrically stimulated sites in a slice of brain tissue much worse – In parallel, pain patients perform much worse than healthy controls on tactile discriminative tasks ([Zhang et al, 2011](#); [Nguyen, et al, 2013](#)).



How Do You Measure Changes in Sensory Percept Impacted by Pain?

Tactile-based neurosensory assessments are the most reliable way to monitor sensory perception. Unlike the visual or auditory pathways of the cortex, the somatosensory and pain systems are integrated. Both acute and chronic pain can impact activity in area 3b/1 and 3a through reciprocal connections, and thus may affect sensory perception. The Brain Gauge provides one way to measure this impact. The Brain Gauge delivers precise tactile stimuli to the finger tips, and the accompanying software queries an individual about what they perceive by using a tracking paradigm (similar to the method for conducting an eye test – questions start out easy and get more difficult as an individual reaches the limit of their discriminative capacity). One of the tests that is sensitive to pain patients asks the individual to determine which of two stimuli is larger – also known as an “amplitude discrimination” task.

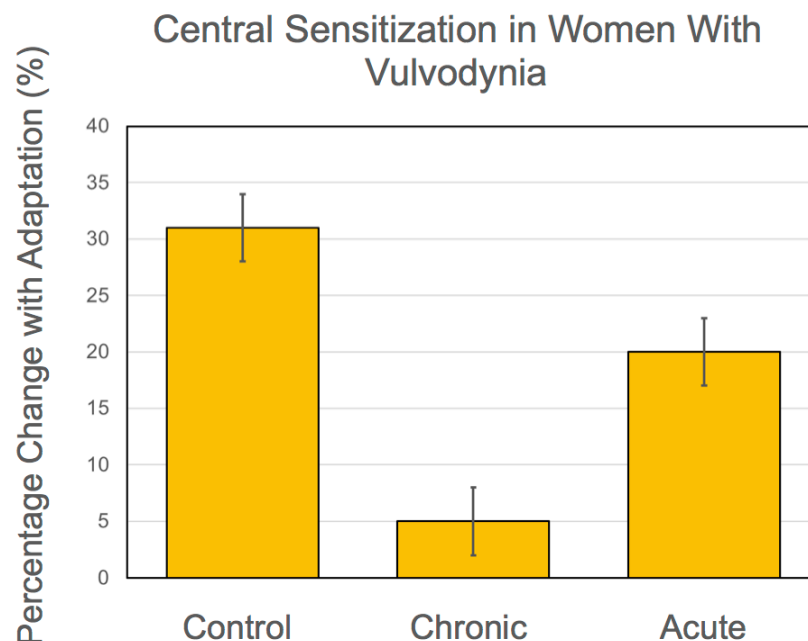


The figure above demonstrates that chronic headache patients are approximately 2 times worse than healthy controls at the amplitude discrimination task (note that the individuals tested were not experiencing headaches at the time of the test). Results of the study are described in [Nguyen et al, 2013](#). The amplitude discrimination test is hypothesized to task lateral inhibition while other tests task mechanisms of information processing (e.g., feed-forward inhibition, adaptation,

neuron-glia interactions). Multiple types of chronic pain have been studied (e.g., migraine, VVS, carpal tunnel syndrome, fibromyalgia, TMJD, IBS, focal dystonia, low back pain) and all have a sensory discriminative deficit that relates to these different mechanisms of information processing.

Acute Versus Chronic Pain

Chronic pain of the CNS is typically initiated by an acute noxious percept that arises from some injury of the periphery. If the pain persists after the tissue at the initial site of injury has healed, then the pain becomes chronic. Chronic pain can be caused by a pain-induced rewiring of the cortex. Through established methods of neurosensory testing, the Brain Gauge can be used to determine whether pain is predominantly central or peripheral. Pain that is predominantly centralized will cause an individual's plasticity score to decrease.



Note that in the figure above, there are scores for 3 groups of individuals: healthy controls and two groups of patients. The difference in the two groups of patients is that Group A, the group with the poor adaptation (or plasticity) score is chronic while Group B is not. The study is fully described in Zhang et al, 2011.

Therapeutic Potential?

Many early researchers focused on using sensory stimulation to reduce pain, however, recent studies suggest that tactile discrimination tasks are a more effective method for reducing pain than sensory stimulation alone (Mosely and Flor 2012; Mosely 2017). One possible explanation for the effectiveness of tactile discrimination is that discriminative task increases activity in 3b/1 while decreasing activity in 3a. Inhibition of 3a allows this area of the cortex to “rebalance”. Additionally, this rebalancing would reverse any GABA reversals in 3a that exacerbate the over-excitability problem. Thus, pain patients could see improvements in their Brain Gauge scores not only because their pain is being treated effectively, but because the tactile discriminative task provided by the Brain Gauge could be modulating their pain condition. This idea is consistent with several strategies that researchers are currently using to treat pain, such as TMS, tDCS, ultrasound and electrical stimulation or massive pharmacological treatment (such as ketamine comas) all of which temporarily block pain and allow the brain to shift away from its maladaptive state. We believe that a targeted approach with sensory discriminative tasks may be as effective as those treatments. We will be conducting research to determine if chronic pain states can be reversed by using discrimination tasks to target specific areas of the cortex.

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