



Published in final edited form as:

Pain. 2007 November ; 132(1-2): 8–9. doi:10.1016/j.pain.2007.09.006.

Pain and Motor System Plasticity

D Borsook

Departments of Psychiatry and Radiology, Massachusetts General Hospital

Department of Psychiatry, McLean Hospital, Harvard Medical School

Plasticity in neural systems implies a process that produces an alteration in structure or function. In the pain field, neuroplasticity has been observed in response to acute and chronic pain - plasticity of function is seen with changes in neural function in the dorsal horn and alterations in more central structures such as the thalamus and cortex 22;23;1;10;18. While plasticity has been clearly observed in sensory systems with pain, the notion of how pain may affect motor systems is relatively new.

In the paper by Boudreau et al., (this issue), the authors show that acute pain induced by capsaicin can affect acute plasticity of the motor cortex induced by a tongue task (tongue protrusion). Pain-induced by capsaicin impairs the changes in motor systems as evidence by a decreased response to transcranial magnetic stimulation applied over the motor cortex on motor evoked potentials (MEPS) measured in the tongue. While other reports exist on the effects of pain inhibiting motor cortex 19;9;7, the paper adds to this literature by evaluating changes on the effects of pain in a simple model of acute motor plasticity in a tongue 'exercise' (repeated protrusion) model. Specifically the paper raises number of interesting and important issues, including (1) the underlying neurobiology of pain affecting motor processing, (2) the rapidity of the effect of pain in altering the acute plasticity and (3) the effect of motor systems on pain and (4) the potential implications of this effect in patients with chronic pain.

Sensory-motor integration at a reflex such as a motor withdrawal reflex in response to noxious stimuli (nocifensive response) is well understood. Persistent pain generally inhibits movement, and subjects will protect the affected area to limit movement. This inhibition may 'act as a sort of motor 'decerebration' so as to allow the spinal motor system to freely develop protective responses to noxious stimulation'⁸. Interactions between pain systems and motor systems have long been integrated in traditional therapeutic approaches such as physical therapy or exercise or providing pain relief to enhance motor activity in conditions such as back pain or post-operative pain. However, these approaches have been devoid of neurobiological understandings of how motor systems may be affected by pain and vice-versa.

The second issue that the paper reports is the rapid effect of pain on cortical motor plasticity. The rapidity of plasticity of cortical sensory systems has been well documented in animals and humans following amputations or nerve blocks 5;21. In these cases, changes in synaptic inputs may alter cortical mapping. In the current issue, pain produces a rapid inhibition of motor cortex. Inhibition of motor cortex by pain has been considered to be via cortico-cortical circuits. The phenomenon is not limited to pain but also other sensory inputs such as acoustic stimulation 13. Certainly, inhibitory and excitatory cortico-cortical circuits and known and this interaction may account for an overall inhibition by pain 20. However, more complex processes involving

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

subcortical structures (e.g., thalamo-cortical and striato-cortical loops) cannot be excluded 12. Inputs via pain fibers (predominantly C-fibers activated by capsaicin) project to the primary somatosensory cortex and may produce inhibition of motor cortex via thalamo-cortical or cortico-cortical inhibitory inputs. With respect to these subcortical structures, the ventrolateral and anterior thalamic regions are the main relay for cerebellar and basal ganglia (globus pallidus) to the motor cortex 15. Direct pain afferents (a peptide class of nociceptors) to the globus pallidus from the spinal cord have been shown in animal tracing studies 6 and activation in the globus pallidus to pain has been reported in functional imaging studies in humans 3. While clearly complex, some evidence supports this, for example, stimulation of the anterior thalamus produces an alteration in motor cortex excitability 16.

As describe in the paper, there is increasing evidence on the clinical utility of modulation of motor systems on pain. Specifically, repetitive transcranial magnetic stimulation 11;14 or direct application of motor cortex stimulation electrodes 17 have been reported to improve a number of chronic pain conditions. This type of evidence further supports the notion of the interdependence of sensory and motor systems. The effects may be due to the same cortico-thalamic loops, producing inhibition on sensory systems. However, a mechanistic understanding is not currently known.

Finally, an understanding of the rapid nature of pain effects on motor cortical plasticity may be an insight into plasticity that occur throughout the central nervous system. Such plasticity may be the underpinning of the evolution of chronic pain as a result of dysfunctional circuits, loss of neurons within circuits known to be present in chronic pain 2 and the resistance to therapeutic modulation. The paper further supports the notion that pain may be a silent predator that is manifests in changes in the nervous system. Indeed, the ‘centralization’ of pain as we better understand the nature of altered brain systems derived from recent neuroimaging studies, should make us reassess our clinical approaches to chronic pain (4; Borsook et al., in press). We need to be more aggressive with early treatments and need to find ways to understand and define whether these changes are occurring after potential chronic pain producing processes (e.g., trauma, surgery) or specific diseases (e.g., chronic arthritis). Such approaches will clearly come from an improved understanding of alterations in the plasticity of multiple central neural systems.

References

1. Anderson WS, O’Hara S, Lawson HC, Treede RD, Lenz FA. Plasticity of pain-related neuronal activity in the human thalamus. *Progress in brain research* 2006;157:353–364. [PubMed: 17046675]
2. Apkarian AV, Sosa Y, Sonty S, Levy RM, Harden RN, Parrish TB, Gitelman DR. Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. *J Neurosci* 2004;24:10410–10415. [PubMed: 15548656]
3. Becerra LR, Breiter HC, Stojanovic M, Fishman S, Edwards A, Comite AR, Gonzalez RG, Borsook D. Human brain activation under controlled thermal stimulation and habituation to noxious heat: an fMRI study. *Magn Reson Med* 1999;41:1044–1057. [PubMed: 10332889]
4. Borsook D, Becerra L. Phenotyping central nervous system circuitry in chronic pain using functional MRI: considerations and potential implications in the clinic. *Current pain and headache reports* 2007;11:201–207. [PubMed: 17504647]
5. Borsook D, Becerra L, Fishman S, Edwards A, Jennings CL, Stojanovic M, Papinicolas L, Ramachandran VS, Gonzalez RG, Breiter H. Acute plasticity in the human somatosensory cortex following amputation. *Neuroreport* 1998;9:1013–1017. [PubMed: 9601659]
6. Braz JM, Nassar MA, Wood JN, Basbaum AI. Parallel “pain” pathways arise from subpopulations of primary afferent nociceptor. *Neuron* 2005;47:787–793. [PubMed: 16157274]
7. Cheong JY, Yoon TS, Lee SJ. Evaluations of inhibitory effect on the motor cortex by cutaneous pain via application of capsaicin. *Electromyography and clinical neurophysiology* 2003;43:203–210. [PubMed: 12836584]

8. Farina S, Tinazzi M, Le Pera D, Valeriani M. Pain-related modulation of the human motor cortex. *Neurological research* 2003;25:130–142. [PubMed: 12635511]
9. Farina S, Valeriani M, Rosso T, Aglioti S, Tamburin S, Fiaschi A, Tinazzi M. Transient inhibition of the human motor cortex by capsaicin-induced pain. A study with transcranial magnetic stimulation. *Neuroscience letters* 2001;314:97–101. [PubMed: 11698155]
10. Flor H, Nikolajsen L, Staehelin Jensen T. Phantom limb pain: a case of maladaptive CNS plasticity? *Nature reviews* 2006;7:873–881.
11. Fregni F, Freedman S, Pascual-Leone A. Recent advances in the treatment of chronic pain with non-invasive brain stimulation techniques. *Lancet neurology* 2007;6:188–191. [PubMed: 17239806]
12. Kaas J, Ebner F. Intrathalamic connections: a new way to modulate cortical plasticity? *Nature neuroscience* 1998;1:341–342.
13. Kuhn AA, Sharott A, Trottenberg T, Kupsch A, Brown P. Motor cortex inhibition induced by acoustic stimulation. *Experimental brain research. Experimentelle Hirnforschung* 2004;158:120–124. [PubMed: 15024542]
14. Leo RJ, Latif T. Repetitive transcranial magnetic stimulation (rTMS) in experimentally induced and chronic neuropathic pain: a review. *J Pain* 2007;8:453–459. [PubMed: 17434804]
15. Massion J. The thalamus in the motor system. *Applied neurophysiology* 1976;39:222–238. [PubMed: 1052299]
16. Molnar GF, Sailer A, Gunraj CA, Cunic DI, Wennberg RA, Lozano AM, Chen R. Changes in motor cortex excitability with stimulation of anterior thalamus in epilepsy. *Neurology* 2006;66:566–571. [PubMed: 16505313]
17. Osenbach RK. Motor cortex stimulation for intractable pain. *Neurosurgical focus* 2006;21:E7. [PubMed: 17341051]
18. Price DD, Verne GN, Schwartz JM. Plasticity in brain processing and modulation of pain. *Progress in brain research* 2006;157:333–352. [PubMed: 17167920]
19. Romaniello A, Cruccu G, McMillan AS, Arendt-Nielsen L, Svensson P. Effect of experimental pain from trigeminal muscle and skin on motor cortex excitability in humans. *Brain research* 2000;882:120–127. [PubMed: 11056191]
20. Sailer A, Molnar GF, Cunic DI, Chen R. Effects of peripheral sensory input on cortical inhibition in humans. *The Journal of physiology* 2002;544:617–629. [PubMed: 12381831]
21. Weiss T, Miltner WH, Huonker R, Friedel R, Schmidt I, Taub E. Rapid functional plasticity of the somatosensory cortex after finger amputation. *Experimental brain research Experimentelle Hirnforschung* 2000;134:199–203.
22. Woolf CJ, Costigan M. Transcriptional and posttranslational plasticity and the generation of inflammatory pain. *Proceedings of the National Academy of Sciences of the United States of America* 1999;96:7723–7730. [PubMed: 10393888]
23. Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. *Science (New York, NY)* 2000;288:1765–1769.