Brain changes and chronic pain

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Does the chronic pain change the brain?
Phantom Limb Pain:
Ramachandran, VS. 1994

Fig. 2 (A) Top view of a combined MEG and 3D surface-rendered MRI of an adult whose right arm was amputated below the elbow at the age of 11 years. The right hemisphere is normal and shows the primary somatosensory face area (red) lateral, anterior and inferior to the hand localizations (green), which are in tum lateral, anterior, and inferior to the upper arm region. The left hemisphere shows the face (red) and upper arm (blue) regions extending into the expected hand territory, reflecting reorganization of the sensory map following amputation.
• Reductions of N-acetyl aspartate and glucose were demonstrated in the dorsolateral prefrontal cortex).
Chronic Back Pain Is Associated with Decreased Prefrontal and Thalamic Gray Matter Density

A. Vania Apkarian
The Journal of Neuroscience, November 17, 2004 • 24(46):10410–10415

- 26 chronic back pain (CBP) patients to matched control subjects

- Patients with CBP showed 5–11% less neocortical gray matter volume than control subjects

- Equivalent to the gray matter volume lost in 10–20 years of normal aging

- decreased volume: 1.3 cm³ loss of gray matter for every year of chronic pain

- Brain MRI
Neuropathic Vs non neuropathic CBP
Decreased whole-brain cortical gray matter volume in CBP subjects
Different Pain, Different Brain: Thalamic Anatomy in Neuropathic and Non-Neuropathic Chronic Pain Syndromes
Sylvia M. Gustin The Journal of Neuroscience, April 20, 2011 • 31(16):5956 –5964

• subjects 21 TNP
• 20TMD
• 36 healthy controls
• no significant regional gray matter volume change in TMD patients
• volume of TNP patients was reduced in the primary somatosensory cortex, anterior insula, putamen, nucleus accumbens, and the thalamus, whereas gray matter volume was increased in the posterior insula.
Brain changes in chronic pain syndromes
Brain changes
Cause or Consequence of Pain?
Brain Gray Matter Decrease in Chronic Pain Is the Consequence and Not the Cause of Pain

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• The Journal of Neuroscience, November 4, 2009 • 29(44):13746 – 13750
32 patients with chronic pain due to primary hip osteoarthritis
Mean duration 7.35 years
subgroup of these patients (n 10) 6 weeks and 4 months after total hip replacement surgery
Prediction of Chronification

Can we Identify which patient will go on to develop chronic pain?
Corticostriatal functional connectivity predicts transition to chronic back pain


sub–acute back pain (SBP) lasting 4–16 weeks
no prior back pain for at least one year

Recovering (SBPr, n=20)
Persisting (SBPp, n=19)
Functional connectivity (links) between NAc and mPFC
Affective descriptors of McGill pain questionnaire at the day of the scan (SBPp)
Functional connectivity between insula and dLPFC/PCC
Can brain changes predict treatment outcome?
Pregabalin Rectifies Aberrant Brain Chemistry, Connectivity, and Functional Response in Chronic Pain Patients
Richard E. Harris, Ph.D Anesthesiology, V 119 • No 6 December 2013

• 17 chronic pain patients diagnosed with fibromyalgia.
• proton magnetic resonance spectroscopy, functional magnetic resonance imaging, and functional connectivity magnetic resonance imaging
• glutamate + glutamine levels within the posterior insula (pregabalin $P = 0.016$; placebo $P = 0.71$).
• Greater pre-PG levels of Glx/Cr are associated with greater subsequent reductions in evoked pressure pain ratings after PG.

• Cr = creatine; Glx = combined glutamate + glutamine.
Motor cortex stimulation outcome
Brain opioid receptor density predicts motor cortex stimulation efficacy for chronic pain

Joseph Maarrawi, PAIN 154 (2013) 2563–2568

- 15 patients, refractory NP, chronically implanted MCS
- superimposed onto a T1-weighted MRI

- 11C-diprenorphine positron emission tomography scans, opioid receptor availability
- opioid-binding in the insula, thalamus, periaqueductal gray, anterior cingulate, and orbitofrontal cortex were significantly and positively correlated with postoperative pain relief at 7 mo.

superimposed onto a T1-weighted MRI
ACC, $p<0.0001$

$p_p=0.15; P_C=0.0005$

OFC, $p<0.0001$

$p_p=0.029; P_C=0.007$
Brain changes predict intensity and duration?

Brain activity for rating spontaneous fluctuations of back pain in chronic back pain patients.

The observed correlations are strong enough that we can assert that the task can be used to predict intensity and duration of chronic back pain in individual subjects within an error of 20%.
Brain changes produce pain?

- Brain has no sensation
- Brain lesions
- Ischemic
- Infection and Inflammation
- Multiple sclerosis
- Tumors
Does therapy directed at brain change decrease chronic pain?
Cognitive modulation of pain-related brain responses depends on behavioral strategy
D.A. Seminowicza,b, D.J. Mikulisa,b,c, K.D. Davisa,b,d,*

Fig. 3. Activations associated with pain in the fixation condition compared to no stimulation in the fixation condition. Cluster size > 150, t > 3.8 (t-values shown in color bar, right side), P < 0.0001. Sagittal views show right side of brain; in the axial view, left side of image is right side of brain.
Targeting Cortical Representations in the Treatment of Chronic Pain
A Review

GL Moseley, H Flor –
Neurorehabilitation and neural repair, 2012
A Future Without Chronic Pain: Neuroscience and Clinical Research
By David Borsook, M.D., Ph.D.
*Cerebrum*, June 2012

**Figure 1: Chronic Pain and the Brain**

- Normal Brain
- Altered Brain Chemistry
- Decrease in Gray Matter
- Volume in DLPC
- Structural Changes in Nerve Tracts

**Altered Behaviors**
- Sensory (e.g., spontaneous pain at rest)
- Affective (e.g., anxiety, depression, suicide, addiction)
- Cognitive (e.g., decreased attention)
- Emotional (e.g., reward deficit state)
What does it mean to call chronic pain a brain disease?

Sullivan MD, Cahana A, Derbyshire S, Loeser JD


• Neuroimaging investigators say chronic pain is a brain disease.
• *disease" is a clinical concept”*
• negative consequences for research and clinical care of patients with chronic pain.
• should not yield to the temptation to validate pain with the magnetic resonance imaging scanner (structural or functional)
• We should not see pain as caused by the brain alone

• Pain is not felt by the brain, but by the person.
Thank you

• In this study, PET was used to examine changes in brain activity in response to an opioid drug or a placebo, administered in a double-blind fashion before the application of a tonic, painfully hot or warm stimulus, on the dorsum of the left hand in normal subjects. Placebo activation was found in the rostral ACC and in the orbitofrontal cortices (mainly in the right hemisphere) in areas that are part of the widespread activation observed in the opioid condition.
B. Example of functional MRI response to painful stimulation.
Figure a: SBPp > SBPr (visit 1) and SBPp > SBPr (visit 4).

Figure C: Number of positive links ($\times 10^4$) vs. Affective pain for Visit 1 and Visit 4.

Figure f: Number of negative links ($\times 10^4$) vs. Gray matter density (Visit 4) and Pain intensity (VAS) (Visit 4).
In summary, supplemental cognitive-behavioral management of depressive symptoms enhanced long-term rehabilitation success in patients with CLBP and co-existing depressive symptoms. The new training program seemed to reduce important psychological risk factors by addressing the specific psychological needs of this subgroup that had aggravating chronic pain. Therefore, this study suggests favorable effects of psychological treatment elements specifically targeting depressive symptoms in orthopedic inpatient rehabilitation. Our approach was unique and novel, given that comparable treatment modules have not been implemented or evaluated to date in orthopedic inpatient rehabilitation of CLBP.