Neuroplasticity and spinal control: Latest evidence of sensorimotor involvement in low back pain.

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Neuroplasticity and spinal control: Latest evidence of sensorimotor system involvement in low back pain

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Low back pain represents an important medical and socio-economic problem [Hoy et al. 2012]. Currently, treatments provide modest short-term success due to insufficient knowledge of the mechanisms of non-specific low back pain [Costa et al. 2013]. Impaired sensorimotor control is suggested as a likely mechanism of developing and/ or sustaining low back pain [van Dieën et al. 2013, Claeys et al. 2015]. Until recently, most studies focused on the "*end organ dysfunction*", i.e. on the structural and functional abnormalities within the musculoskeletal system [Robinson & Apkarian 2009]. However, patients with low back pain might also have structural and functional changes within the central nervous system. Moreover, clinical interventions increasingly aim to drive neuroplasticity with treatments to improve sensorimotor function and pain.
This short communication comprises three parts. The first section briefly defines neuroplasticity in relation to spinal control & low back pain but also argues the finite potential of the system to adapt. The second part explores the different research approaches to neuroplasticity & low back pain and succinctly reviews the structural and functional brain changes as it relates to non-specific low back pain and sensorimotor function. The final section presents the clinical implications.

1. Defining neuroplasticity in relation to spinal control & low back pain

Neuroplasticity refers to the capacity of the nervous system to undergo functional and structural change modulated by activity and reinforcement [Chang 2014]. The adult nervous system retains an enormous capacity to change and these changes may underpin adaptations in the sensory system, the motor system and the widespread changes in neural processes associated with the low back pain experience. Neuroplasticity could underpin the development of spinal control changes that precede low back pain, or could underpin changes after the development of low back pain.
On the other hand, neuroplasticity is an old concept and so broad that it is almost meaningless, differentiating an alive neuron or nervous system from a dead one (Lindley 1897). Therefore, functional neuroelasticity**,** referring to condition and time dependent characteristics of the brain, could be more preferable, whereby the brain can be considered as a mass of neural networks- "*neurotags"* that compete for influence. Subsequently, influence is determined by the number of neurons (mass) and inhibitory interneurons (precision). These neural representations, or neurotags, refer to the idea that networks of brain cells, distributed across multiple brain areas, work in synergy to produce outputs such as movement or pain [Wallwork et al. 2016]. All together, we have to exercise caution interpreting results of brain studies considering the huge complexity of the central nervous system and despite the enormous capacity of the brain to adapt this system has no infinite potential.

2. Different research approaches to low back pain & neuroplasticity and the structural & functional brain changes in patients with low back pain

In the last decade a vast body of knowledge is developed on structural and functional brain changes in patients with chronic low back pain. However, one should know that in these studies chronic low back pain is used as a *persistent pain model* to study pain processing. For instance, to perform data analysis of fMRI brain imaging often *a priori region of interest* has to be selected. This selection is determined by the experimental hypothesis (e.g. *pain matrix* versus *sensorimotor network*) and consequently will differ between the research interests (e.g. *pain processing* versus *sensorimotor control*).

Structural gray and white matter alterations have been observed in e.g. the dorsolateral prefrontal cortex, temporal lobes, insula, primary somatosensory cortex, corpus callosum and internal capsule. Functional connectivity during rest seems to be altered with an enhanced activation of medial prefrontal cortex, cingulate cortex, amygdala, insula and sensorimotor integration regions, together with a disrupted functional connectivity in the default mode network [Baliki et al. 2012, Apkarian et al. 2013, Hashmi et al. 2013, Mansour et al. 2013].

For excellent reviews on chronic low back pain and changes in the "*pain matrix"* and the "*emotional brain"*, the reader is referred to Apkarian et al. 2011, Baliki & Apkarian 2015, Vachon-Presseau et al. 2016.

In contrast to the vast body of literature on chronic low back pain and changes in the "*pain matrix"* and more recently the "*emotional brain"*, few neuroimaging studies exists on low back pain as a symptom of a functional spinal control/ sensorimotor impairment [see Wand et al. 2011, Kregel et al. 2015]. For instance, Flor et al. [1997] showed a reorganization of the primary somatosensory cortex in patients with chronic LBP based on tactile stimuli. More specifically, a shift of the back area in medial and inferior direction and an expansion of the sensorimotor cortical representation of the leg were demonstrated. Other studies showed a loss of discrete cortical organization of the back muscles in patients with recurrent LBP compared to healthy controls, more specifically a posterior and lateral shift of motor cortical representation of trunk muscles and an overlap of the longissimus erector spinae and deep multifidus [Tsao et al. 2008, 2011, Schabrun et al. 2015]. In addition, manually applied posterior-anterior pressure to the lumbar spine revealed a blurring of the somatotopic representation of the lumbar spine in secondary somatosensory cortex in patients with chronic low back pain [Hotz-Boendermaker et al. 2016]. Motor imagery driven activity showed reduced brain activation within the left supplementary motor area and the right superior temporal gyrus and sulcus while the functional connectivity within the motor imagery network was enhanced in patients with chronic low back pain compared to healthy individuals [Vrana et al. 2015].

Our research group demonstrated a relation between a reduced white matter integrity of the superior cerebellar peduncle and a weak proprioceptive weighting capacity for standing postural control in patients with recurrent low back pain [Pijnenburg et al. 2014]. Furthermore, a significant reorganization of the sensorimotor resting-state network is shown in individuals with recurrent low back pain compared to healthy controls. In addition, patients with recurrent low back pain were observed to have decreased functional connectivity in brain areas related to the integration and processing of sensory and motor signals for adequate movement. This decreased functional connectivity of the sensorimotor network was associated with the slower performance of a dynamic sensorimotor task (i.e. five times sit-to-stand-to-sit task) [Pijnenburg et al. 2015]. Moreover, we have shown a disrupted network organization of white matter networks in patients with recurrent low back pain, which may contribute to their persistent pain and sensorimotor impairments [Pijnenburg et al. 2016a]. Lastly, patients with recurrent low back pain showed alterations of cortical thickness in brain regions that play an important role in the cognitive regulation of pain, as well as an impaired sit-stand-to-sit performance compared to healthy controls. Cortical thickening was associated with increased pain intensity in these individuals. In addition, slower sit-stand-to-sit performance on unstable support surface was correlated with decreased cortical thickness of the rostral anterior cingulate cortex [Pijnenburg et al. 2016b].

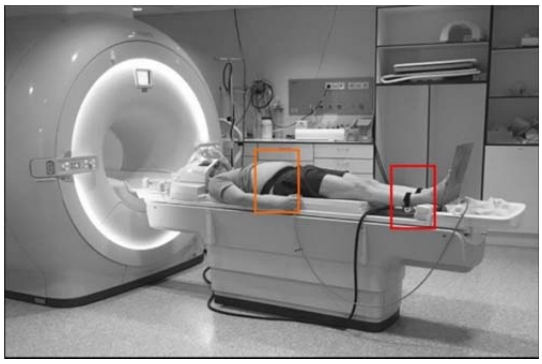

Figure 1. Participant is placed supine and head-first in the fMRI scanner. Air-driven fMRI-compatible muscle vibrators are attached to the back at lumbar level L5 and at the ankle muscles.

At this moment, preliminary fMRI scans with muscle vibration have been performed in three patients with low back pain who have a dominant ankle-steered postural control strategy during standing (Figure 1). The preliminary results show that several sensorimotor and higher-order processing brain areas are involved in the processing of muscle spindle afferent signals ($p < 0.05$ FWE-corrected) (Figure 2). During ankle muscle spindle stimulation, increased activation was found bilaterally in the primary somatosensory cortices, superior parietal lobules, inferior frontal gyri, middle and superior frontal gyri, including orbitofrontal cortices and cerebellar lobules VI and VIII. Moreover, activation was found in the right primary motor cortex, supplementary motor area, basal ganglia (putamen and caudate nucleus) and parahippocampal gyrus and in the left insula. In contrast, back muscle spindle stimulation elicited less activation than ankle muscle vibration, more specifically activation was observed bilaterally in middle and superior frontal gyri and in inferior frontal gyri. Right-sided activation was found in the cingulate motor area, cerebellar lobule VI, insula and basal ganglia (putamen and caudate nucleus), whereas left-sided activity was seen in the primary somatosensory and motor cortex and in cerebellar crus II.

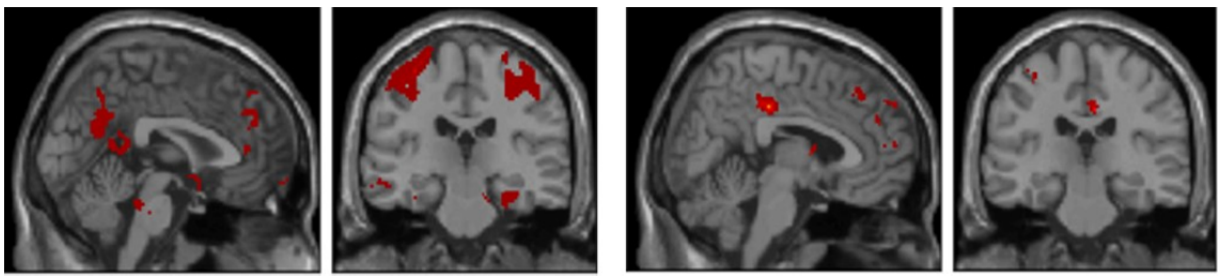

Figure 2. More brain activation during ankle muscle (left) compared to back muscle (right) spindle stimulation in three patients with low back pain ($p < 0.05$, FWE-corrected).

Perhaps the most important message here is that, in spite of the expanding body of knowledge of structural and functional brain changes in patients with recurrent and chronic low back pain, again we have to be very careful interpreting neuroimaging results and further longitudinal studies are warranted.

3. Clinical implications and conclusions

Depending on the point of view on low back pain: i.e., as a *persistent pain processing problem* versus a *symptom of an underlying sensorimotor impairment*, respectively, different interventions and modalities are suggested.
Cortical pain processing can be changed from emotional motivational (anterior insula) to sensory discriminative (posterior insula) in patients with chronic low back pain by extinction training. Visual

feedback of one's own back may reduce the perceived intensity of acute nociceptive pain stimuli applied to this site and reduces habitual pain [Diers et al. 2016].
On the other hand, treatment of patients with low back pain may focus not on distraction and analgesia but on precisely encoding the painful event by reducing the influence of protective neurotags, through eliminating danger cues and differentiating safe cues and by increasing the influence of performance neurotags [Moseley & Vlaeyen 2015, Wallwork et al. 2016].
Involvement of corticolimbic (central dopaminergic) circuits in low back pain chronification may be targeted by a combination of L-DOPA and NSAID treatment [Vachon-Presseau et al. 2016].
Neuromodulatory therapies such as transcranial direct current stimulation and peripheral electrical stimulation may be utilized to enhance a priming mechanism that ameliorates pain sensitivity, normalizes cortical organization and improves posturomotor control in patients with low back pain [Massé-Alarie et al. 2013, Schabrun et al. 2014, Pelletier et al. 2015].
Specific motor control training can reverse reorganization of neuronal networks of the motor cortex in people with recurrent low back pain while general exercise such as walking does not [Tsao et al. 2010].
So, neuroplastic changes may be addressed by top-down cognitive-based interventions (such as education, cognitive-behavioral therapy, motor imagery) and bottom-up physical interventions (such as sensorimotor learning, peripheral sensory stimulation, manual therapy). An integrated contemporary neuroscience and clinical approach may combine intensive pain neuroscience education with cognition-targeted sensorimotor control training [Hodges et al. 2013].

In conclusion, people with recurrent and chronic low back pain have been observed to have both functional and structural changes in the "*pain matrix*", the "*emotional brain'*, but also in the "*sensorimotor networks*". Addressing these neuroplastic changes more specifically may lead to better outcomes in patients with recurrent and chronic low back pain.

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