

Editorial

Pain, brain imaging and physiotherapy—Opportunity is knocking

What is brain imaging?

Brain imaging refers to a range of technologies that describe the structural and functional anatomy of the brain. There are several different technologies, each with advantages and limitations. This editorial will focus on magnetic resonance imaging (MRI). MRI uses a very strong magnetic field to align our body's molecules and then uses a second field to invert (or 'flip') some of them. Because each type of molecule has a unique rate at which it flips back (or 'relaxes'), it is possible to 'tune' a radiofrequency receiver within the MRI machine, to detect a particular molecule. The molecule to which the MRI is 'tuned' determines, after sophisticated data processing, the resultant image. Tuning it to water provides a structural image, because water content varies between tissues. Tuning it to oxygenated haemoglobin provides a functional image (fMRI) because neuronal activity causes an increase in oxygenated haemoglobin.

fMRI can provide very precise information about *where* neuronal activity occurs (spatial resolution), but not about *when* it occurs (temporal resolution). Electroencephalography (EEG), for example, better tells us when, but not where. Rapid technological progress means that fMRI can now delineate areas (called 'voxels') smaller than 1 mm³. In fact, the spatial resolution of fMRI is limited not by technological limitations, but by the brain's circulatory network. Bearing in mind, however, that 1 mm³ of the brain contains about 25,000 neurons and 200 trillion synapses, fMRI can only give us information about a very large number of neurons. In this sense, it is a blunt tool.

What has brain imaging told us about brain activity during experimentally induced pain?

Despite its limitations, brain imaging has told us a great deal about *where* brain activity changes when someone is in pain. Most experiments involve healthy volunteers, who receive noxious stimuli and their brain

activity is compared between the period directly after each stimulus and that during a control, or rest period. These studies, and there are many of them, yield a reasonably consistent result—that the dorsolateral prefrontal, insula, anterior cingulate, primary and second sensory cortices, and the thalamus, constitute a kind of human 'pain matrix' (Ingvar, 1999; Apkarian et al., 2005).

Unfortunately, however, it is not quite that simple. First, whether the participants in these studies are in fact normal people, even though their very participation in a study that inflicts sometimes severe pain, repeatedly, might suggest otherwise, is seldom questioned. Nor is the external validity of these studies: How realistic are the stimuli and the context in which they are delivered? That is, how many patients attend for physiotherapy having sustained multiple stimuli of a known temperature and duration, delivered under the assurance that the stimuli are not, in fact, dangerous, and with the approval of a multidisciplinary ethical review board? Second, the results are variable—seldom do we get the pain matrix, the whole pain matrix and nothing but the pain matrix. So what is the truth? Our current understanding is that the neural network activated during pain is unique to the individual, although there are some areas far more likely to be activated than others. However, imaging the brain during pain is not simply neophrenology—exciting material emerges when scientists start comparing within and between people.

Within-subject comparisons of brain activity associated with pain

By manipulating the context of a noxious stimulus, scientists have uncovered neural correlates of, for example, attention, anxiety, expectation, empathy, placebo analgesia, mood, body ownership, somatic monitoring, and drug-induced modulation (see Tracey and Mantyh (2007) for review). The findings are consistent with the neuromatrix theory of pain: experimentally manipulating activity of the neural network representing, for example, anxiety, can modulate the neural network representing, for example, pain, via

synaptic connections between the two (see [Moseley \(2007\)](#) for review).

Between-subject comparisons of brain activity

As yet, no-one has tracked the changes that occur in the brain as pain persists. However, the brain of someone with persistent pain has been compared to the brain of someone with acute pain, and to that of someone who is pain free and (supposedly) normal. Three intriguing results, each with profound implications, consistently emerge from these comparative studies. First, persistent pain is associated with upregulation of the pain matrix and downregulation of endogenous antinociceptive mechanisms ([Apkarian et al., 2005](#)). This means that the relationship between pain and input from the tissues becomes less predictable. Second, the representation of body parts and movements, held within the primary sensory and motor cortices, becomes reorganised. This means that perceptual and motor mechanisms that are based on these maps, can become disrupted (see [Lotze and Moseley \(2007\)](#) for review). Third, the density of gray matter in several parts of the pain matrix, for example, the thalamus and dorsolateral prefrontal cortex, may decrease ([Apkarian et al., 2004](#)), which potentially means a reduction in brain performance. These changes may provide new targets for intervention, targets that physiotherapists are well resourced to pursue.

Physiotherapy, brain imaging and pain

Physiotherapy-induced analgesia

Many physiotherapists make a living out of decreasing pain. Aside from the staple strategies, like movement, joint mobilisation and TENS, we now also know that motor imagery and mirror therapy ([Brodie et al., 2007](#); see also [Moseley et al. \(2008a\)](#) for a review of mirror therapy for analgesia and also [Moseley et al. \(2008b\)](#) and [Gustin et al. \(in press\)](#) for examples of motor imagery increasing pain), and carefully explaining the biology that underpins someone's pain state, can decrease pain ([Moseley, 2002, 2004](#); [Moseley et al., 2004](#)). What we do not know, however, is how the brain contributes to these effects. Collaborative studies, between brain imagers, pain scientists and physiotherapists would stand to bridge this substantial gap in our knowledge. Such studies could, for example, elucidate the relative contribution of increased inhibition and decreased facilitation, of opiate and non-opiate systems, of higher-order cognitive processes. We could tease out effects on sensory-discriminative and affective-motivational mechanisms. I contend that these are indeed exciting prospects—we stand to discover not only new

interpretations for established effects, but also new effects, which in turn will provide fresh targets for physiotherapy-induced analgesia.

Cortical organisation

Persistent pain and cortical reorganisation are related, but we do not know whether one causes the other (see [Flor et al. \(2006\)](#) and [Moseley \(2006\)](#) for reviews). That said, there is emerging evidence that treatments that aim to normalise cortical organisation, also reduce pain and disability in people with chronic pain. For example, sensory discrimination training for phantom limb pain ([Flor et al., 2001](#)) and tactile discrimination training for complex regional pain syndrome ([Moseley and Wiech, 2008](#)), both target body maps in primary sensory cortex and both show a clear relationship between increased tactile acuity, which is a marker of primary sensory cortex organisation, and decreased pain.

At present, the effects of physiotherapy interventions on body and motor maps are unknown. Clearly, however, opportunity is knocking. Again, appropriate collaborations might make us reinterpret established effects—perhaps body maps hold the key to why some patients respond better to a comprehensive physical examination than they do to the subsequent treatment. Is it possible that the physical examination, with its exhaustive and often repetitive provocation of specific joints, with specific mobilisations, which require the patient to carefully attend to and discriminate the location, quality and intensity of the percept works via similar mechanisms to discrimination training? Is it possible that learning precise and sometimes subtle motor skills, which require the patient to attend carefully to specific body parts and to discriminate the contraction of one muscle from the contraction of its immediate neighbour, has a similar effect? Is it possible that exploiting the brain's predilection for congruent multisensory input, via manual and tactile or visual feedback, could enhance this effect? Such suggestions are speculative, but by no means are they outrageous.

Conclusion

The wealth of data already uncovered concerning pain and the human brain raises questions directly relevant to physiotherapy practice. The challenge will be to establish strategic collaborations between pain scientists, brain imagers and physiotherapists. Clinicians must talk to scientists, and importantly, scientists must listen. Indeed, all stakeholders must be sufficiently open-minded to consider new explanations for old effects, and sufficiently alert to pursue new and better treatments.

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