The Brain in CRPS—More Barriers or New Opportunities?

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From a biological perspective, I find CRPS very perplexing. So do many other people—the community of scientists that are pursuing better treatments, through a better understanding of the basic mechanisms, or by developing better animal models of CRPS, or by undertaking clinical investigations and clinical trials, stretches across many countries and many scientific and clinical disciplines. With all of those supposedly-clever people working on it, one might expect that by now there would be better ways to prevent and treat this debilitating disorder. For many people with CRPS, and for many clinicians trying their darndest to help them, the situation can feel a bit hopeless. That is one place where organizations like RSDSA play a crucial role—reminding patients and clinicians that significant gains are being made, and that there is hope. In fact, all of those supposedly-clever people are, in fact, developing a better understanding of the mechanisms and possible treatments of CRPS.

When Jim Broatch asked if I would write an article for this newsletter, he suggested that I provide an update of my own research and what it might mean for people with CRPS and the clinicians who treat them. From where I sit, my own research looks rather simple, compared at least to the very sophisticated work going on elsewhere.

I get a little bamboozled with the molecular biology—just remembering what the acronyms stand for seems an arduous task. The thing that interests me is what it is like to have CRPS, what goes wrong in the way the limb feels, how the brain might contribute to this, how these changes might contribute to the problem, and what we can possibly do about it. In this article, I will concentrate on the things that, at first glance, seem a little daunting because they involve changes in the way the brain works, but, at second glance, are actually opportunities because the brain, more than any other organ we have, is very responsive to training. These are the things I have been a part of that I think are important for people with CRPS and their team.

People with chronic CRPS tend to think that their affected limb is bigger than it really is[1-2]. I first wondered about this when I noticed that patients would describe their limb as feeling swollen, and describing the size of the limb in a way that made me think, "Hang on! It's not *that* big!" Now, if someone is saying that their arm feels big when it is not, they are either lying or it does actually feel bigger than it really is. I don't think many people, patients or otherwise, are liars, so we set up an experiment. In short, we took a photograph of both limbs and then manipulated the photograph so that the affected limb looked bigger or smaller than it really was. We then asked patients to select the photograph that they thought was the real photograph. People without CRPS tend to pick the correct one. People with chronic pain that is not associated with CRPS tend to make more mistakes but still get it about right. People with chronic CRPS tend to pick the photograph that shows the affected limb to be slightly bigger than it really is. We have done subsequent experiments to confirm this phenomenon.

Movement causes a bigger increase in pain and swelling when the visual image of the painful body part is magnified[3]. On the basis of the above, we decided to see if this distortion of perceived size of the painful limb might contribute to pain and swelling. We did an experiment with 10 people with CRPS of one hand. They did a set of movements while they looked at their hand under three conditions: normal, through a set of glasses, through a set of magnifying glasses. Remarkably, when they watched through the magnifying glasses, the increase in pain and swelling was significantly worse. So, when a painful limb looks bigger, it actually gets more painful and more swollen. The groovy and unexpected finding was that when the magnifying glasses were inverted, the increase in pain and swelling was reduced! We don't know why that happened, but we have started to think about how to use this clinically.

The brain's map of the affected body part shrinks[4-5]. This is a little tricky to understand, but give it a go because if you can understand this bit, you will understand how we go about treating it. The brain holds maps of the body so that it can tell you where exactly you are, where you end and the space around your body begins. These maps are really important for the feelings that we have of our own body—that it is ours and that we own it. The group of brain cells that holds the map of a specific body part— let's say your arm—is reasonably consistent between people and it is kept accurate and precise by a very complex system of brain cells influencing brain cells. For some reason, in CRPS something goes wrong with this system so that fewer brain cells are responsible for the map and the map becomes 'smudged'—the outlines are not as clearly delineated, which really means some brain cells become part of two or three maps instead of one). It is not only CRPS in which this happens. It also happens in people with phantom limb pain after amputation. The opposite thing happens in people who use a body part a lot. For example, more brain cells are involved in the map of the left hand of a violinist, or—*get this*—Braille readers have more brain cells involved in the map of their index finger during the week than they do on weekends! Those discoveries are very important because they show that you can train the brain to change the maps.

Training the map of the body decreases pain and swelling[6-8]. The first three discoveries are all related and all contribute to the idea that we might be able to reduce symptoms by training the brain. A neuroscience superstar in Germany, Herta Flor, PhD, did exactly that in amputees with phantom limb pain. She showed that with just two weeks of training, amputees could discriminate between different types and locations of electrical stimuli delivered to the stump, which significantly reduced pain AND returned the map in the brain back to normal. This was a profound finding. We did a dumbed-down version of this in people with CRPS. We used a wine cork and a pen lid to touch the affected limb in one of five places. The patients had to discriminate between the two stimuli and between the five places. Again, in two weeks, there was a significant reduction in pain and swelling, but only if patients had to discriminate between the stimuli—not if they were just touched and didn't concentrate on it. We did a subsequent study that showed that this effect increases if you use a mirror, so that you can look at the mirror image of your opposite limb while doing the training.

The brain gets better at producing pain and swelling as CRPS progresses[9-10]. CRPS affects many brain functions. A key change occurs with the sensitivity of the mechanisms that cause the symptoms. We have shown that people with CRPS get worse when they just think about moving the body part, even if they don't even move it a whisker. We have also shown that if we trick patients into thinking that we have touched their painful arm by getting them to watch us touching their other arm, in a mirror placed between their arms, it hurts just like it would if we touch their painful arm.

People with CRPS find it difficult to recognize whether a pictured hand is a left hand or a right arm, if the pictured hand is the same side as their own affected hand[11-12]. The same is true for feet. We have done a range of studies exploring this intriguing finding and have found that the effect is not due to pain and is not confined to people with CRPS. However, in testing it, we noticed that people with CRPS could improve on this task with practice. We decided then to see if we could use this task as a stepping stone to other treatments.

Graded motor imagery reduces pain and swelling in chronic CRPS[10,13-14]. Graded motor imagery involves three stages: (i) recognizing pictured hands (or feet, depending on the affected limb) as being left or right, (ii) imagined movements, and (iii) mirror movements. Each stage lasts about two weeks and patients practice hourly. Noigroup Australasia (www.noigroup.com) produces a *Motor imagery pack,* which includes access to resources, an online recognition program (*Recognise*), and a mirror box. We have undertaken subsequent investigations that show that frequent practice is essential—we saw nearly no effect when patients practiced only once or twice a day. Graded motor imagery is the only treatment for chronic CRPS for which there is both strong evidence of efficacy and no known risks and minimal side effects.

Discussion

An important aspect of all of this research is that clinical interventions are always undertaken within the context of resourcing patients with as much *accurate* information about pain, about chronic pain and about CRPS, as we can give them. I don't mean that we just bombard them with information—I mean that we take seriously the role of educating patients about these things so that they understand it, so that they 'get it' in the marrow of their bones. There is a whole body of literature that clearly shows that empowering patients in pain, with an understanding of how pain *really* works—the biological processes that underpin it and what changes when pain persists—improves outcomes[15]. This is not a trivial task, but I think it is a terrifically important one.

It is critical to make it really clear in any article like this, that although the results of clinical trials are promising, the treatments don't work for everyone. It is also very important to emphasize that in the treatments I have described, the role of the physical therapist, doctor or other medical or health practitioner is really important. However, this person is more like a coach or supervisor, since all the real work is done by the patient. As I say to patients—patience, persistence and courage. If you can muster each of these in good measure, I believe you will more than likely make it through.

Finally, my research is only a small proportion of all the work that is being done to better understand, manage, and treat CRPS. To provide an overview of all that is being done is beyond the scope of Jim's request. It is also beyond me and would constitute a very large book with very small writing. I have cited the key papers relating to what I have written about in the reference list. In addition, I have provided some relevant links or sources for further information.

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Additional Resources

Motor Imagery Program Products. Available at: www.noigroup.com

Butler DS, Moseley GL. *Explain Pain.* Noigroup publications; Adelaide: 2003. Available at: www.optp.com

Moseley GL. *Painful yarns. Metaphors and stories to help understand the biology of pain.* OPTP: 2007. Available at: www.optp.com ■