

## **CHAPTER X: THE PLACEBO EFFECT**

Well, I don't think I can finish a talk on acupuncture and the neurobiology of acupuncture without raising this specter, you know, not the ugly specter, but you know, the question of placebo effects. Because it certainly is a question on many people's minds, how much of what we see when we perform acupuncture may be related to what we know to be one of the most powerful therapeutic effects there are and that's a placebo effect.

In fact, a recent paper by a wonderful colleague of ours, Ted Kaptchuk, at the Osher Center at Harvard who's been working with us and helping us perform our acupuncture studies, looked at a sham acupuncture device relative to another way to perform a placebo effect and that's with an inert pill and just compared two shams to see whether they each would have an effect. And his conclusions were that indeed, both the pills and the sham acupuncture, in this case with a straight Berger needle - it's a needle that looks like it's going into the tissue, but actually has a retractable tip. So for the novice acupuncture subject, they don't really know what's going on, most will report that they felt that they had real acupuncture.

And in fact, in his data, he suggests that the sham acupuncture not only had a comparable placebo effect, but might in some ways have an even greater placebo effect than the oral placebo pills.

Of course, he also showed, and that's very important, that many of these effects, including potential adverse effects, were intimately linked to the kinds of information that the patients were provided, in other words to the expectations that patients had when they came into the experiment.

It was this interest in studying the effects of a placebo and effects of expectation that led Ted to work with Dr. Randy Gollub in our lab and Kong Jang, who are studying acupuncture effects using a variety of tools. And they performed this very interesting study where they were comparing real acupuncture and sham acupuncture.

Here, the important point that I want to bring out in this rather complex line is the fact that even with the sham acupuncture alone, that when the patients were provided a reason to expect that the acupuncture worked - In this case, Randy performed a little

trick. She used a heat probe, something that gave a short painful heat sensation. Then she performed a sham acupuncture, repeated the heat, but actually turned the heat down and didn't tell the subjects that, so they were led to believe, of course, that the acupuncture worked. In the experiment with the magnet, this time she didn't turn the heat down, and wanted to see whether there was a part of the brain that was responding. Behaviorally, most of the patients reported an effect of just this so-called sham acupuncture.

Interestingly, however, she saw parts of the brain that were -- first, there were broad regions of the brain that responded to the pain. We knew that, we've seen that previously. What she showed, however, was that some focal areas of that network actually showed an increase in signal following this expectation manipulation greater than just the response pre- and post- to the high pain versus lower pain condition.

So in other words, there was actually a part of the brain that seemed to be -- part of the pain network that seemed to be increasing as the patients were then reporting that they were getting a decrease in pain. It was working harder to somehow generate this placebo effect. And interestingly enough, she found other parts of the brain outside the pain network that had that same behavior. In other words, the placebo effect seems to actively recruit parts of the brain.

It's interesting, folks like Richard Davidson have actually shown that the placebo effects can modulate and actually decrease certain sensations, but other parts of the brain, as Randy showed, seem to increase with that placebo effect -- certainly pause for hesitation as we think about understanding our acupuncture data.

And I'll just show this quick summary. And of course, her conclusion based on comparisons of her data with those of others is that there may indeed be multiple pathways by which placebo may work.

No surprise in the end. What does this relate to? There's an old Chinese saying, "it's futile to treat a patient who doesn't want to be treated." Expectations bear a lot in terms of underlying treatment effects.

But I wouldn't want to leave you with the downer that everything that we're seeing is strictly related to sham effects. I think that there are some very important

studies that we need to do to understand the biology of placebo and then related to what we see with acupuncture.

But in this particular study, another very sophisticated study performed by Randy Gollub and her team, they combined MFRI and an opioid bonding study with pets, because of course of many generations of reports, especially out of China, have shown increases in endogenous opioids following acupuncture treatment.

And indeed, in careful conditions where they directly compared real acupuncture to sham acupuncture, they did see areas of activity with FMRI and modulations increase in opioid, endogenous opioid transmission, highlighted by a displacement of this opioid analog that's labeled with a positron emission tracer.

And quite remarkably, the same small areas of the brain seemed to be highlighted with these two very distinct techniques, one a neurochemical change, one an underlying hemodynamic change, even when very carefully controlling for these sham and expectation effects.