Dynamic Chiropractic

CHIROPRACTIC (GENERAL)

Understanding the Placebo Effect: Different Strokes for Different Folks

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The popular American idiom, "Different strokes for different folks," is believed to have emerged from the American South in the 1950s[1] before it was practically immortalized as Sly & the Family Stone's top-selling single recording about a decade later.[2] What is becoming more and more apparent, however, is that a new lease on life for that slogan has emerged as evidence-based medicine becomes more and more cognizant of patient expectations and values as part of the evidence base.

Nowhere is this more reflected than in the growing recognition of the placebo effect, once dismissed by the medical community as a bothersome confounder of clinical outcomes research. Now it is understood to represent more a function of patient individuality, such that – depending upon the patient's emotions – the substance of the intervention itself often seems to become all but submerged in a sea of patient emotions and accompanying responses.

Strictly speaking, the word *placebo* derives from the Latin, "I will please," from a biblical translation by Jerome.[3] The placebo treatment itself is traditionally defined as inert, assuming that it contains no active components. This inertness remains as long as the patient is totally blinded from what is being given, or whether something has been given at all. But if patient affect should come into play, all bets are off.

Expectations and Conditioning

Patient expectations then become one of the pathways characterizing one's response and could be primed by such factors as the affect and enthusiasm of the health care giver or appearance of the placebo itself. *Classical conditioning*, on the other hand, appears to have a longer-lasting effect[4] and may affect earlier stages of information processing.[5] What this simply means is that patients display varying amounts of positive responses to *anything* that is given to them, simply because attention has been paid to the participants.

Just knowing that they were receiving some kind of treatment in a trial – active or inert – led headache sufferers in a systematic review of 119 studies to report recovery rates anywhere from 0-80 percent when they were, in fact, receiving the placebo intervention.[6] This has commonly been known as the Hawthorne Effect.[7]

Regardless of the reactive pathway taken, there is a wealth of information that supports the reality of the effect. From the perspective of pain perception, Bergmann's research group nearly 20 years ago was able to track changes in the Visual Analog Scale after naproxen or placebo was administered to cancer patients either given or lacking the information that they were enrolled in a crossover,

randomized trial. Simply possessing the information that they were included in the study led patients who were given the placebo to report improvements in pain approaching *90 percent* of those in patients given the live naproxen. Patients who lacked such information of enrollment showed a more classical response, in which the pain-reduction differential between live and inert treatments was more substantial.[8]

The role of expectation in treatment looms even larger when one considers a trial in which medications were either revealed or hidden from the individual. In the treatment of patients with pain, anxiety, and Parkinson's disease, Colloca, et al., demonstrated that pain reductions usually *doubled* when the patient was aware of any one of three opioids (morphine, buprenorphine, tramadol) or two NSAIDs (keterolac, metamizol) administered in treatment, offering a substantial demonstration of the psychological context (expectation) of health care.[9]

Physiological Response

But where the placebo effect really comes down to brass tacks is when we demonstrate that an indisputable, objective physiological response has occurred. Such a hypothesis was fulfilled by the recent finding of Zubleta in a study that tracked the activation of brain neurotransmission, as seen by the binding of carfentanil, a radiolabelled tracer to the mu-opioid receptor. Here, this binding was shown to correlate strongly with decreased pain intensity and sensory pain qualities, found when groups of patients were told that they were receiving an agent which may or may not relieve pain – while in fact, the agent was nothing more than saline.

This was the first experiment to report that a placebo with nothing more than implied analgesic properties regionally activated a specific pain and stress inhibitory neurotransmitter system, supporting the hypothesis that a patient's simple belief in treatment may enhance the therapeutic effect of any intervention.[10] Earlier evidence demonstrating the molecular basis of the placebo response was offered by Grevert, et al., who demonstrated that placebo responses evoked by conditioning and expectancies were fully or partially reversible by the opioid antagonist naloxone.[11]

In the realm of surgical and physical medicine, the placebo effect must be reckoned with as well. In surgery, a well-known trial recently demonstrated that patients with osteoarthritis of the knee receiving a sham procedure (skin incisions plus simulated debridement without insertion of the arthroscope) reported no deficiency in pain and functionality recovery when compared to those who received a full arthroscopic debridement.[12] And in chiropractic, many sham procedures have been tried with the fact remaining that a placebo manipulation by hand is a virtual impossibility, leading too many to a disastrous interpretation of outcomes.[13]

Ten years ago, a Danish meta-analysis attempted to demonstrate that the placebo effect was minimal, if existent at all.[14] By combining so many disparate trials for different conditions for different patients in a mixed salad, this investigation has endured several criticisms[15] and simply emphasizes the fact that lumping disparate treatments and methodologies together in a "one size fits all" paradigm flies in the face of recognizing individual, patient-centered therapies.

Future Direction of Clinical Research and Practice

Therefore, with so many elements of the patient's response coming into play, where does this take us in clinical research and practice? Are therapeutic approaches hopelessly muddled by our current findings of the placebo effect? As Ted Kaptchuk, director of the Program in Placebo Studies and the Therapeutic Encounter at Harvard, has stated, "I've always believed there is an important component of medicine that involves suggestion, ritual, and belief."[16]

The defeatist approach would lead us to throw in the towel and follow an axiom that was often repeated by one of my chemistry professors years ago: "Under conditions of constant temperature, pressure and volume – variables behave as they damn well please." The more activist of us have been rapidly revising the paradigms of clinical research design and evidence-based medicine, as I've discussed at length elsewhere.[17]

But in the management of patients, it is becoming increasingly obvious that both patient diversity and the patient's entire emotional, nutritional and belief systems must come more into play in order for many health care interventions to be successful. Outside of traumatic injuries or emergency treatment, far more attention needs to be paid to how nutritional,[18] hormonal[19] and emotional[20] elements influence neural function and immunity.

This is precisely where more ecumenical approaches to health care such as applied kinesiology[21] come into play, in its attempt to embrace the broader spectrum of the human experience in health management. It all raises the bar on how meaningful research that captures a more significant scope of the human experience needs to be designed. In this respect, far more attention to broad-spectrum approaches needs to be paid.

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