Hooked on a Feeling

This is your brain on a placebo.

BY SHARON BEGLEY

AS FAR AS THE BODY is concerned, a placebo is nothing—a sugar pill, a sham treatment, an inert compound. But try telling that to the brain, as scientists led by Daniel Cherkin of Group Health Center for Health Studies in Seattle recently saw. They assigned 638 adults with chronic lower-back pain to receive either standard acupuncture therapy, customized acupuncture (tailored to the individual, such as by using nonstandard acupuncture points), sham acupuncture (toothpicks in acupuncture-needle guide tubes that mimic the feel of real acupuncture) or standard back-pain care, such as anti-inflammatory drugs and massage. As the scientists reported this month in Archives of Internal Medicine, pain diminished significantly for 60 percent of the people in all three acupuncture groups—but for just 39 percent of patients receiving usual care. On average, both fake and real acupuncture reduced pain more than twice as much as standard care. Weirdly, this is being spun as "acupuncture is better than standard medical care for back pain!" I say "weirdly" because the key finding is that sham acupuncture delivered as much benefit as real acupuncture. And the most parsimonious explanation for that finding is inescapable: it is possible to think yourself out of pain.

In fact, the power of thought to relieve pain has been known since 1978, when neuroscientists began studying placebo responses in earnest. Now they have even mapped the brain processes that underlie it. When people expect their pain to diminish, typically because a doctor tells them that a little pill or other treatment will do so, that mere expectation produces activity in the prefrontal cortex, site of higher mental function, which in turn activates other regions to release the brain's own homemade opioids, says Fabrizio Benedetti of the University of Turin Medical School, a pioneer in placebo research. (A big advance in understanding placebo was showing that a drug that blocks the effects of opioids also blocks the placebo effect on pain, prima facie evidence that the brain's endogenous opioids are in play.) The higher the expectations, the greater the pain relief, too. When scientists led by Dan Ariely of Duke University gave volunteers identical dummy pills before and after an electric shock, and told some of their human guinea pigs that the pills were analgesics costing $2.50 and others that they cost 10 cents, more of those getting the expensive placebo than the cheaper one reported pain relief (85 percent vs. 60 percent).

It's not just pain anymore, either. If neuroscientists have learned anything about placebo, it is that there is not a single placebo effect, but placebo effects, plural, each with different mechanisms and each shedding light on how ethereal, high-level mental functions control the nitty-gritty of lower-level brain processes. For one thing, what Benedetti calls "mind over matter" (matter being the body) turns out to be effective in conditions having nothing to do with pain. Injecting an inert saline solution reduced the symptoms of Parkinson's disease. For instance, when patients were told that they were receiving medication, many of them began to move more fluidly and had less rigidity, scientists at the University of British Columbia found. What seems to happen is that expecting a treatment to be effective releases dopamine, which is both the brain's reward molecule and the precise chemical that is scarce in the brains of Parkinson's patients. That dopamine surge from the striatum calms the chaotic neuronal firing that causes the spasms and rigidity of Parkinson's, as Benedetti showed in the first study of the placebo effect on individual neurons. "Verbal suggestions of clinical improvement changed the activity of neurons in specific brain areas," says Benedetti. It doesn't work on everyone, and the effect typically fades after a while—two of the many remaining mysteries about placebo responses.

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Remarkably, placebo effects occur through physiological pathways that have nothing to do with expectations and the release of opiates or dopamine. Instead, they work because the brain has learned that a particular experience is followed by a particular response—Pavlovian conditioning. Morphine, for instance, is notorious for depressing respiration, which is why it can be dangerous. In one 1999 study, after patients had received several doses of a morphinelike drug for post-op pain, a placebo produced the same respiratory depression: the brain had learned, at the neuronal level, that injection equals slow, shallow breathing and responded that way even to an inert compound. "The response is completely unconscious," says Benedetti. Similarly, when he and colleagues gave volunteers a cortisol-lowering drug twice, and then a placebo, the placebo mimicked the cortisol-decreasing action of the drug, regardless of what patients expected. Pavlovian conditioning also seems to be behind placebo effects on the immune system. When scientists repeatedly gave the powerful immune suppressant cyclosporine (used to prevent rejection of transplanted organs) along with a flavored drink, and then the drink alone, the patients' immune systems were as quiet as when on the drug. It was like finding that Kool-Aid can prevent transplant rejection. Mind over matter had struck again.

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CHRIS WAHLBERG—PHOTOGRAPHER'S CHOICE—GETTY IMAGES

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Experiments and Observational Studies

ARTICLE: "ADHD linked to lead and Mom's smoking"
http://www.nbcwashington.com/news/health/ADHD_Linked_To_Lead_and_Mom_s_Smoking.html

Based on this article, can we conclude that smoking or lead exposure *causes* ADHD?

When it is impossible to tell which of 2 or more factors is causing a change in the response variable, we say the factors are ___________________.

Studies like this one are called __________________________________ because researchers don't assign subjects to do one thing and other subjects something else. In an observational study, we CANNOT conclude that changes in the explanatory variable *cause* changes in the response variable because of the presence of confounding variables.

Is there any way we can show that smoking causes ADHD?

An ___________________ investigates how a response variable behaves when the researcher manipulates one or more factors to determine if changes in those factors *cause* changes in the response variable. In an experiment we study the specific factors we are interested in, while controlling the effects of lurking variables.

The primary difference between an experiment and an observational study is the way in which the groups are formed. If groups are formed based on the choices of the subjects, then a study is observational. If a researcher assigns groups at random, then the study is an experiment.

If humans are being experimented on, they are called _________________. Other individuals (tomato plants, mice, loads of dirty laundry) are commonly referred to as _________________________. An experimental unit is the smallest unit to which a treatment is applied.

The specific values that the experimenter chooses for a factor are called the _____________ of the factor.

The combination of specific levels from all the factors that the experimental unit receives is known as its ____________________.

A recent study declared that people who go to church have longer life expectancies than people who don't go to church.

- Do you think this was an observational study or an experiment? Explain.

- Assuming there is an association between church attendance and longer lives, can we conclude that going to church is the cause?

Section 5.2: Designing Experiments

Suppose we wanted to design an experiment to see if caffeine affects pulse rate.

What is the explanatory variable (factor)?

What is the response variable?

Who will be the experimental units?

Here is an initial plan:

- measure initial pulse rate
- give each student some caffeine
- wait for a specified time
- measure final pulse rate
- compare final and initial rates

What are some problems with this plan?

Some problems, such as telling a joke while waiting for the caffeine, can be easily solved by including a ________________ which does not receive caffeine. In our experiment, we can accomplish this by using 2 ____________ of caffeine: no caffeine and some caffeine. For example, we could assign each member one of two __________________: Regular Coke or Caffeine Free Coke.

Why don't we give Coke to one group and nothing to the other group?

Often times applying *any* treatment can create a change in the response variable. For example, when a child gets hurt, they feel better when their wound is kissed or covered with a band-aid, even though neither of those treatments actually take away the pain.

In our study, if only one group got a treatment, the fact that they were chosen to receive free soda might make their pulse increase before the caffeine even hits their bloodstream!

The ______________________ occurs when subjects in an experiment know they are receiving a treatment. This knowledge may cause a change in the response variable which _______________ the effect of the treatment. In other words, we will not know which caused the change in the response variable: the explanatory variable or the placebo effect.

Def: A ______________ is a treatment known to have no effect, administered so that all groups experience the same conditions. In this case, caffeine-free Coke is a placebo.

Having every subject receive a similar looking treatment ensures that the placebo effect will treat both groups the same. Then, any difference between their pulse rates can be attributed to the ____________ ______________ (factor) and not the excitement of being in an experiment.

Of course, it is essential that the subjects do not know which treatment they are receiving! When a person doesn't know who is receiving which treatment, that person is ___________.

There are two classes of individuals who can influence the results of an experiment:

- those who could influence the results (subjects, treatment administrators, etc.)
- those who evaluate the results

When every individual in one of these classes is blinded, the experiment is called ________________.
If every individual in both classes is blinded, then the experiment is __________________.
Can our Coke experiment be run in a ______________ manner?

<u>Key Principles of a Good Experiment</u>: THE BIG IDEA--Our goal when designing an experiment is to make the treatment groups are as similar as possible, with the exception of the treatments. Then, if there is a change in the response, it can be attributed to the explanatory variable (factor) and not any other extraneous variables.

An ____________________________ is one that is not of interest in the current study but is thought to affect the response variable. We need to be aware of extraneous variables for two reasons:

1. Extraneous variables have the potential to become confounding variables.
   - For example, sugar is an extraneous variable since it may affect pulse rates. If one treatment group was given regular Coke (which has sugar) and the other treatment group was given