



*Society for the Anthropology of Consciousness  
Distinguished Lecture:  
Consciousness, “Symbolic Healing,” and the  
Meaning Response*

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ABSTRACT

*Symbolic healing, that is, responding to meaningful experiences in positive ways, can facilitate human healing. This process partly engages consciousness and partly evades consciousness completely (sometimes it partakes of both simultaneously). This paper, presented as the Society for the Anthropology of Consciousness Distinguished Lecture at the 2011 AAA meeting in Montreal, reviews recent research on what is ordinarily (and unfortunately) called the “placebo effect.” The author makes the argument that language use should change, and the relevant portions of what is often called the placebo effect should be referred to as the “meaning response.”*

KEYWORDS: meaning response, placebo effect, consciousness, medicine, surgery



INTRODUCTION

I’ve never been quite sure what “consciousness” was.

I think I get the idea of “conscious” (the adjective, not the noun), which means something like “awake and aware.” It has some nice clear antonyms, like *unconscious*, or *subconscious*, or *preconscious*. Got those. But “awake and

aware” seems to cover most of the world’s animal critters, if only in that they try to escape danger and find prey or other stuff to eat. Surely apes and monkeys, whales and dolphins, spiders and mosquitoes, and lots of others are “awake and aware” to some degree. My vegan friends have all made this point clearly enough that it would be hard for most of us to object even if we do continue to prefer chicken salad to hay. And remember Darwin’s masterful book, *The Power of Movement in Plants* (Darwin and Darwin 1880), where he shows us a sleeping clover (perhaps unconscious; but then if, as Darwin says, they are asleep, perchance to dream?) and an awake, aware, and conscious clover. With alterity? Who knows.

But those are all adjectives. They all take some subject, like “mind” or some other word I never use. Can you have a “subconscious soul”? Or can you have a “conscious brain”? What other words can they modify? “Body”? Can you have a conscious body? Or maybe leg? Can you have a conscious knee?

I guess for me, “consciousness” means something more than *conscious*. To have *consciousness*, you have to be—sort of—conscious of yourself, a sort of metaconscious condition. Jensen and Overgaard (2011) asserted, “We, like several others in this field of research, take the concept to mean subjective or phenomenal experience.”

The more I think about it, the more conscious I seem to be. *Whoa! I do have a left leg!* Not something I’d think about very often unless I had just broken it or experienced “restless leg syndrome”—that is, if my leg were acting on its own, not just mindlessly, or deliberately, walking me (well, half-walking me) across the lawn or gone and I had some sort of “phantom limb pain” where the leg, long lost as a casualty of war, felt itself to be wrapped around my neck, trying to choke me to death. In all these cases, my leg is sort of living a life of its own, even if it isn’t there. And damned if it isn’t living its life inside of me! A sort of parasitical meta-leg. All this leads me to think that consciousness is something better left unthought about. Let it alone, or it might choke me to death with my own left leg.

So, here I am, an honored guest of the Society for the Anthropology of Consciousness, suggesting that thinking about consciousness is generally a bad idea. Regardless, I’m going to look at the role of consciousness in healing the sick. This will necessitate a look at a number of cases where it’s pretty clear that while such healing occurs there is often no consciousness involved at all.

In 1979, 33 years ago, I published a paper with the grandiose title “Anthropology of Symbolic Healing” (Moerman 1979) In it, in fumbling fashion, I tried to show that symbolic or meaningful experiences could directly affect health or illness. As a broadly educated three-field anthropologist, this seemed like a really interesting way to understand something about the

character of human beings as symbolic, meaningful creatures and also as biological organisms, the product of millions of years of evolution.

The problem with this for my task tonight is that I generally think that much of what goes on here involves, well, nonconsciousness. Let me give you a few examples of the sort of thing I'm thinking about.

First let me recount for you a few details of a fascinating study carried out a few years ago by neurologist and neuroscientist Fabrizio Benedetti (Amanzio et al., 2001). Benedetti reported on an experiment where surgery patients were treated with four different drugs appropriate to their conditions; however, half the patients received their drugs openly, with an injection by a

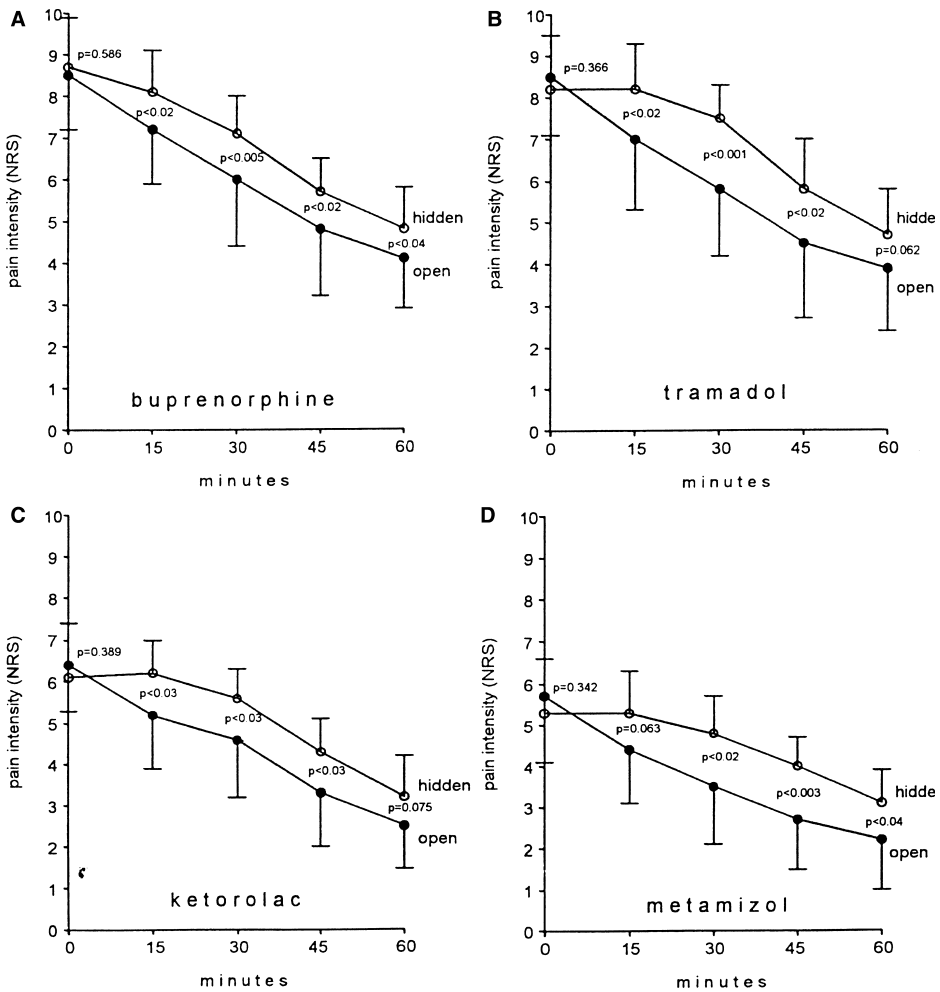


FIGURE 1. OPEN INJECTION IS MORE EFFECTIVE THAN HIDDEN INJECTION OF ANALGESIC. PAIN SCORES AFTER OPEN INJECTION ARE SHOWN BY THE LOWER LINES; EACH GRAPH INDICATES A DIFFERENT ANALGESIC (AMANZIO ET AL., 2001).

clinician, while half received equivalent doses of the same drugs by hidden infusion through an intravenous line. The results are shown in Figure 1.

Pain intensity is reported on the vertical axis, at 15-minute intervals shown on the horizontal axis. Patients receiving the medication openly, who were told they were about to receive it (the lower lines on the graphs), reported more pain relief than those who received equivalent amounts of drugs secretly (the upper lines in the graphs). Pain researcher Don Price, in an accompanying editorial, described this study as “assessing placebo effects without placebo groups” (Price 2001:202). As much as I respect Don Price, this is an unfortunate use of language. There were no placebos here. So obviously, there weren’t any “placebo effects.” What differentiated the separate groups in this study were *words*.

Price did, however, recognize this: he noted that, although the increase in pain relief in the study was probably not, by itself, clinically significant, “both pain research scientists and the pharmaceutical industry go to the ends of the earth to make improvements of this magnitude [to existing drugs]. Adding one or two sentences to each pain treatment might help to produce them” (Price 2001:201). Placebos are inert, but language is not! And, in this case, since the event involves a conversation, it clearly has a cognitive, or conscious, dimension. Simply being aware that you are getting an analgesic enhances its effectiveness.

Figure 2 represents the components of the human healing process. This figure isn’t quite right since it suggests that meaning responses and drug responses are independent and distinct. They aren’t. But I couldn’t quite figure out how to make the figure show that. The key thing is to indicate that there are many factors besides drug effects that occur in any medical intervention. Note that in Figure 2 I didn’t use the term “placebo effect.” Why? I found the term to be imprecise, used by people to cover all sorts of odd things, using it very different historically than in a contemporary context. “The history of medicine is the history of the placebo effect until the

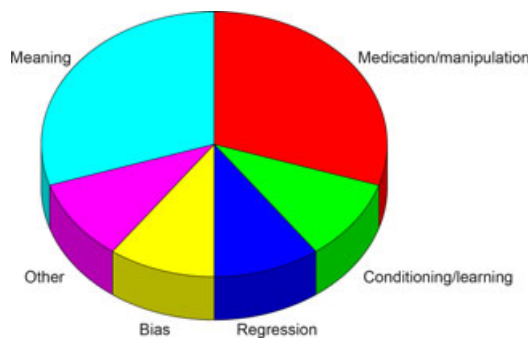


FIGURE 2. COMPONENTS OF THE HEALING PROCESS.

discovery of penicillin,” and so on. No two of the classic writers—Shapiro, Frank, Beecher, and so forth—used the same understandings and definitions for it; and I thought that historian Sissela Bok had forever ruined the term when she equated it with deception, and damned it, quoting St. Augustine, and arguing that, “little by little ... and by gradual accessions [deception] will slowly increase until it becomes such a mass of wicked lies that it will be utterly impossible to find any means of resisting such a plague grown to huge proportions through small additions” (Bok 1974:23).

Wow. This approach focused all attention on the “placebo” itself, privileging the deception in a pill that was inert. This had the effect of mystifying what was going on—as, I’d argue, did reference to St. Augustine—fine for a magic show, but not much good for science.

One of the biggest difficulties in all this follows from the confusion of what is happening with the placebo treatment. Imagine that patients in some mythical trial are given inert tablets called placebos. A week later they are different than at baseline; this difference is the “placebo effect.”

Of course, it’s not. Placebos are inert; they don’t do anything. That’s what a placebo is—something inert. One reason people may be different is regression to the mean. Regression to the mean *is not caused by placebos* but by study selection criteria. Placebos don’t cause changes due to natural history, and they don’t cause conditioning. For conditioning to occur, you have to train the subject with an active drug, one that has an unconditioned response.

But it’s also the case that people *can* and *do* respond to language and meaning. Benedetti has replicated his open/hidden drug experiment in three other areas: diazepam in anxiety state, stimulation of the subthalamic nucleus in Parkinson’s patients, and administration of beta-blocker (propranolol) and muscarinic antagonists (atropine) in healthy volunteers (Benedetti et al. 2003). In all these cases, when the treatment was given openly, it was more effective than when given secretly.



#### THE MEANING RESPONSE

Given that there are no placebos anywhere in these experiments, it seems unwise to call these responses “placebo effects.” And so I define the *meaning response* as “the psychological or physiological effects of meaning in the treatment of illness, and elsewhere.” Much of what is called the placebo effect—the really *interesting part*—is meaning responses elicited with inert medications or other treatments, or the evil twin of the meaning response, that is, much of what is called the “nocebo effect” (Hahn 1997).

I am interested particularly in the responses that people have to what things mean or to what they know, to what others often call their expectations or expectancies. I don't use these terms since they seem to me as an anthropologist insensitive to culture; I anticipate before the fact that people in different parts of the world with different cultural backgrounds will know the world differently and might construct different meanings of apparently similar objects or experiences. I would suggest that, more often than not, expectancies are the outcome of a complex play of meanings. The two approaches are not fundamentally different but have a different emphasis. And note that in these cases of hidden/open administration we are dealing with (at least in part) conscious processes. The people who know—are conscious of, are aware that—they are receiving treatment respond more than those who don't, those who only receive drugs.

It is also important to note that these matters, where meaning has an influence on health and even mortality, can occur well outside the ordinary bounds of the clinic. Dr. David Phillips, a sociologist at UCSD, and colleagues have shown that, in the presence of a broad range of diseases in Chinese Americans in California, those who are understood by Chinese traditions of astrology to be particularly susceptible to these conditions—by virtue of the year of their birth—die significantly earlier than those with the same conditions born in other years (Phillips et al. 2001). Here are two examples that Phillips described.

Chinese with lymphatic cancer who are born in “earth years” (that is, years ending with the numeral eight or nine like 2008 or 1949 and, consequently, deemed by Chinese medical theory to be especially susceptible to diseases involving lumps, nodules, or tumors) die (on average) four years sooner than Chinese with lymphatic cancer born in other years. Those with lung diseases born in “metal years” (years ending in the number zero or one—in Chinese theory, “the lung is the organ of metal”)—die (on average) five years younger (roughly 7% of length of life!) than those born in other years. There were no such differences found in a similar examination of the mortality of thousands of non-Chinese Californians. These are very compelling examples of “meaning responses.” Throughout much of Asia, there is also a complex of meaning regarding the number four. The Chinese word *four* and the Chinese word for *death* sound a lot alike. Four is thereby an unlucky word in much of Asia. Like the U.S. concern for the number 13, Asian hotels often don't have a fourth floor (or perhaps floors numbered 40–49). Phillips showed that Chinese–Americans and Japanese–Americans were more likely to die on the fourth day of the month than any other because four is an unlucky number; however, if 13 is an unlucky number for Californians in general, it's not unlucky enough to increase the mortality rate (Phillips et al. 2001).

At least some of the time, biological processes can be “activated,” or perhaps “suppressed,” by that system of meanings we call culture, and we may have no awareness of it at all. Although these effects occur widely in human life, they are often most clearly and visibly displayed in the clinic. People bring to their engagements with physicians many things; patients are not blank slates. But one of the most powerful influences on patients is their doctors. Dozens of studies have demonstrated this.

Physician attitudes can be conveyed to patients in extremely subtle and delicate ways. Rick Gracely has described a phased experiment in which dental patients about to have wisdom teeth removed were told they would receive either placebo, naloxone, or fentanyl and that these might increase, reduce, or do nothing for their pain. Subjects were all recruited from the same patient stream, with consistent selection criteria by the same staff. In the first phase of the study, clinicians (but not patients) were told fentanyl, a powerful and fast acting narcotic, was not yet a possibility because of administrative problems with the study protocol, yielding the PN group. In the second phase, clinicians were told that now patients might indeed receive fentanyl, yielding the PNF group (although in fact no one was ever treated with fentanyl in the study). Placebo-treated patients during the first phase of the study received no relief from it, and, after an hour, their pain reports increased significantly. In the second phase of the study, placebo-treated patients experienced significant pain reduction from their inert treatment. The only apparent difference between the two groups was that the clinicians knew that no one in the first would get fentanyl while the patients in the second group might (although none represented in the figure actually did; they all received only placebo). It is not at all clear how physicians elicited these effects from their patients in a double blind trial. But they did (Gracely et al. 1985). Note that while there was some deception in this study, those deceived were clinicians, not patients. In this study, patients were unaware of their clinician’s knowledge, and their clinicians were unaware that they were influencing their patients. It seems to me that in this case, it was only Rick Gracely who was conscious of what was happening, and he never saw a single patient.

Clinician knowledge shapes drug experiences. This seems to be a fairly broadly applicable principal that can be seen in a number of different contexts. It has been shown that old treatments become less effective as new ones come along. It is, for example, a commonplace in medicine that one should use drugs quickly before they lose their effectiveness. This quip has been attributed to William Olser, among others. These data come from a meta-analysis of treatment of ulcer disease. As shown in Figure 3, the healing rates of drug groups in endoscopically controlled trials of two antisecretory drugs are plotted by year of publication of the study (Moerman 2000).

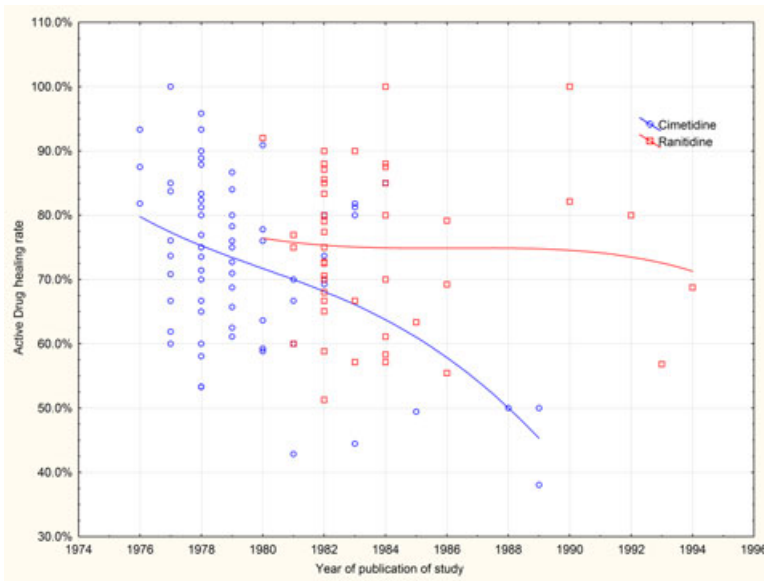


FIGURE 3. OLD DRUGS BECOME LESS EFFECTIVE AS NEW ONES COME ALONG.

At least in the pre-Internet world of the 1970s and 1980s, it was doctors, not patients, who knew what the hot new drug was. And, apparently, old drugs become less effective as new ones come along.

Meaning responses occur throughout medicine, in surgery as well as in internal medicine. A fascinating study showed the effects of inactive versus active pacemakers in obstructive heart disease. Three months after installation of pacemakers, randomly activated or not, all patients were better than at baseline. Shaded bars in Figure 4 show activated pacemakers; clear bars show inactivated ones. Sham and active pacemaker patients were better on most dimensions of the study: (from right to left on the figure) palpitations, dizziness, shortness of breath, chest pain, self-perceived health, and so on. While pacemakers worked better when they were turned on, they weren't much better; they certainly don't seem to help "cognitive functioning" (Linde et al. 1999). Everyone knew they had new pacemakers; no one knew if it was turned on or not.

And, in a recent wrinkle in heart surgery called laser transmyocardial revascularization [TMR], there are significant meaning responses as well. In this procedure, lasers cut channels (sometimes called "bloodlines") thru the wall of the left ventricle, presumably to create the equivalent of new arteries. I have emphasized the word "suggests" and "believed" in these texts but otherwise not changed them at all. In a variation of this operation a laser catheter is inserted in the femoral artery, guided into the left ventricle, and shoots holes in the heart from the inside out. These surgical procedures are reserved



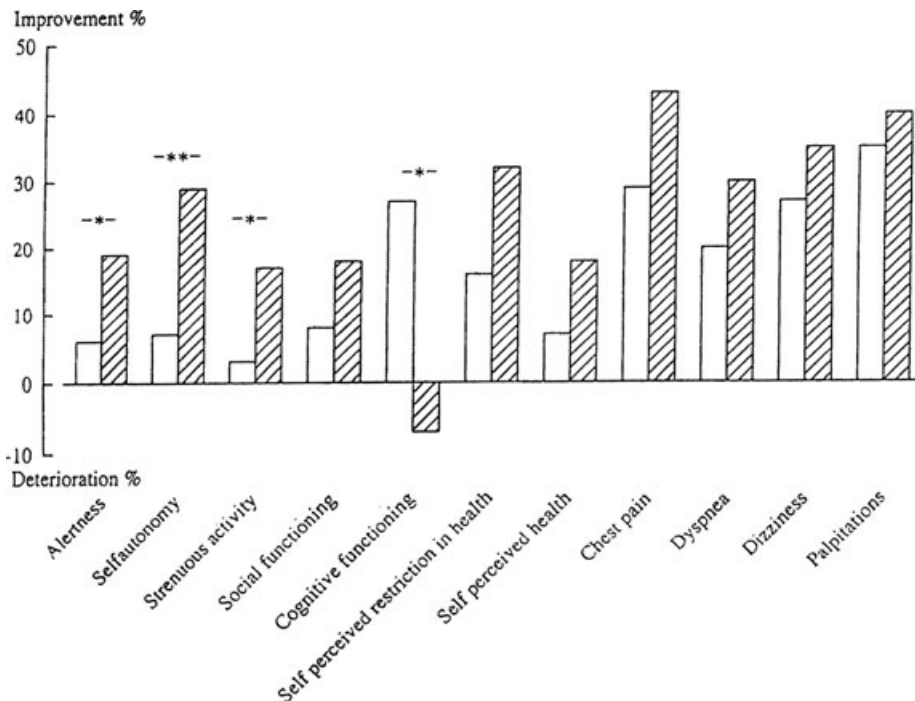


FIGURE 4. IMPROVEMENTS AFTER IMPLANTATION OF PACEMAKERS, ACTIVE AND INACTIVE. THE PERCENTAGE DIFFERENCE FROM BASELINE IN QUALITY OF LIFE PARAMETERS AMONG PATIENTS ASSIGNED TO INACTIVE AND ACTIVE PACING (LINDE ET AL. 1999).

for patients with the most severe and otherwise untreatable angina. In a quite remarkable study, 300 patients with very serious angina were randomly assigned to high dose, low dose, or no dose of TMR. At baseline, all patients were rated as class III or IV on the Canadian Cardiology Society Angina Class scale, a physician assessment that was the primary outcome of the study. Two thirds of the patients improved two or more grades on the CCSS. Improvement was substantial, and the same, after three and six months for patients who received high dose, low dose, or no treatment with laser catheter inserted but not fired (Leon et al. 2000). Disease perception was dramatically improved, as were a broad range of other secondary outcome measures.

Alan Johnson made a prescient observation in 1994; “Electrical machines have great appeal to patients [and doctors] and recently anything with the word ‘laser’ attached to it has caught the imagination” (Johnson 1994:1141). What we know, what we think, what we are led to believe, or what we understand can have a significant effect in the context of medical care.

These things also happen in Complementary and Alternative Medicine (CAM). A nice example involves acupuncture of point P6 on the inner wrist; known in China as *neiguan* (*nei* means median, or central; *guan* means pass,

as a pass between two mountain peaks, or tendons in this case). Traditionally, needling this spot is understood to minimize nausea and vomiting, among other things. A lot of research has been done on this point in order to try to reduce: (1) postoperative vomiting and (2) nausea of pregnancy. The former has been more successful than the latter. In 33 studies, the acupuncture was done after anesthesia four times. Results? It didn't work. In 29 studies, it was done before anesthesia so the patient knew it was happening. Results? It worked in 27 of the 29 studies (Vickers 1996). In this treatment, apparently the patient must know that it has happened, be conscious of it, in order for it to work.

Now, a caveat. While I believe that it is always prudent to imagine that some substantial portion of every medical intervention includes some portion of the meaning response, it isn't always the case. One study shows a very classic dose response rate: eight groups of patients were given increasing doses of a statin, from 0 to 80 mg per day; the larger the dose, the more ldl dropped. However, the group with 0 mg had no response. This is unusual, and very interesting; it suggests that the liver operates in a way somehow insulated from cognitive influence. Odd, but possible. What this also shows is that we are dealing with a complex form of physiology here, not magic. If it isn't magic, what is it?

I would argue that it is at this point where we confront one of the biggest and most interesting challenges in this whole arena; and I would suggest that they are very big, very important, and very interesting challenges. *Nobel Prize-worthy challenges*. One of the classic ways that people have dismissed these matters in the past has been by saying, "Well, it's all in your head." It turns out they are right, but not in the dismissive way they intended.

Parkinson's disease has long been known by clinicians to be susceptible to influence by inert treatments. Imaging studies by a group from British Columbia have shown a neurological basis for this common clinical observation.

Figure 5 shows the increased occupancy of D<sub>2</sub> receptors with dopamine in the striatum after an injection of saline solution in a Parkinson's patient; the increased dopamine crowds out the radioactive dye. These effects are similar in magnitude to the effect of amphetamine in healthy people; the authors note elsewhere that an area of the nucleus accumbens is also susceptible to the meaning response in Parkinson's (de La Fuente-Fernandez et al. 2001). So, it's all in your head.

A similar case involves placebo and depression. Although the clinical response of drug and placebo patients was, effectively, identical in this study, drug response in brain activity was somewhat more general than placebo response: "Active fluoxetine treatment was associated with additional and unique changes in the brainstem, striatum and hippocampus" (Mayberg et al. 2002:730). This may help to account for why it is that, while placebo treatment

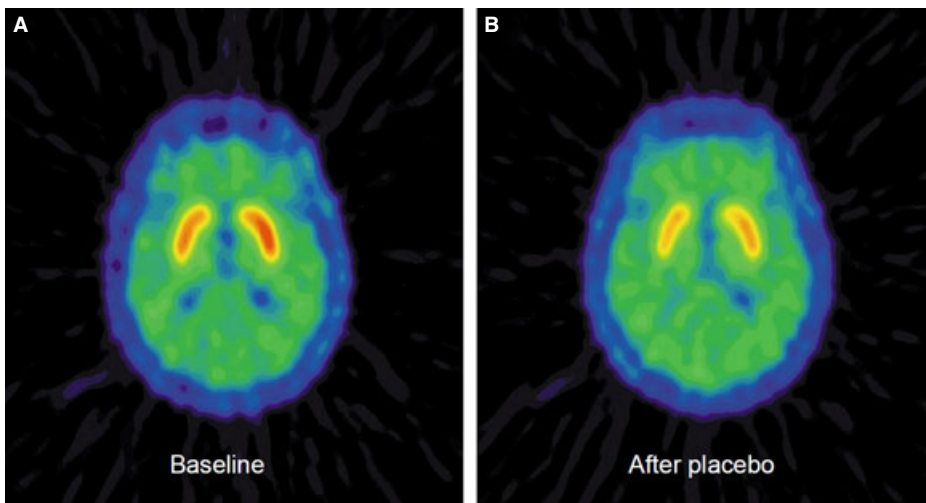


FIGURE 5. PLACEBO TREATMENT REDUCES SYMPTOMS OF PARKINSON'S DISEASE: "THE LOWER RADIOACTIVITY OBSERVED IN THE STRIATUM AFTER PLACEBO (SALINE INJECTION) REFLECTS INCREASED OCCUPANCY OF STRIATAL D2 RECEPTORS [WITH DOPAMINE] (I.E. PLACEBO INDUCED DOPAMINE RELEASE)" (DE LA FUENTE-FERNÁNDEZ ET AL., 2002:88).

of depression is often very nearly as effective as is treatment with SSRIs, there is often substantially less evidence of unwanted side effects with placebo (Leuchter et al. 2002).

■

#### VARIABILITY IN THE MEANING RESPONSE

Given this, that it's "all in your head" and that it involves language, it seems reasonable to imagine that cultural factors—different ways of knowing the world through language and meaning—will shape different responses to the same "placebos" around the world. There is a great deal of variability in the response to meaning in medicine, which I wish to look at briefly now.

Meaning responses are highly variable. If there is a single shibboleth in the world of the effect of meaning or of placebos, it is that "placebo effects occur about a third of the time." I can't address the history of this idea here, but I can assure you that it is wrong. Figure 6 displays the four-week endoscopically verified healing rates in 126 *control groups* in trials of antisecretory medications prescribed for peptic ulcer disease. They range from 0 to 100% (Moerman 2000). Meaning responses can be extremely variable. I am convinced that the study of this variability can be a key to developing a fundamental understanding of how meaning interacts with human biology.

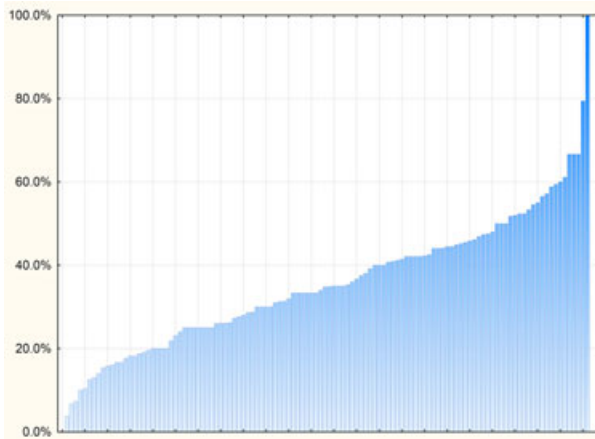


FIGURE 6. PLACEBO GROUP HEALING RATES IN 126 TRIALS AGAINST PEPTIC ULCER DISEASE RANGE FROM 0% TO 100% (MOERMAN 2000).

Such variability might be accounted for in many different ways. Color makes a difference: changing the color of a pill can change its effects in a variety of ways. In one particular case, a dozen or more studies have shown that, in western nations, red pills tend to act as uppers/stimulants while blue ones tend to act as downers/sedatives. Moreover, although they probably don't realize they are doing it, drug manufacturers tend to follow suit, coloring their drugs to match these cultural expectations. DeCraen and his colleagues did a study of 49 medicines available for sale in Holland that affect the nervous system. They found that stimulant medications tend to be marketed in red, orange, or yellow tablets, while depressants or tranquilizers tend to be marketed in blue, green, or purple ones (de Craen et al. 1996).

There are some interesting exceptions to this pattern. In a series of experiments in Italy, it was shown that blue sleeping tablets, or blue placebos presented as sleeping tablets, worked better than did tablets of other colors—but only for Italian women. In contrast, blue tablets tended to have a stimulating effect on men! Checking with an Italian-American anthropologist friend, we came up with this speculation: my friend explained that many Italian women have a special relationship with the Virgin, who is the protector of women; the Virgin Mary is almost always shown in blue, and the relationship to women seems to be particularly strong in Italy although it may be so elsewhere as well.

What about men? *Azzuri* (blue) is the name (and the color) of the Italian national football team. Blue, for many Italian men, is not a color of solace but of excitement and stimulation, of joy and madness, of exhilaration and, too often, of catastrophe. It's hardly the color of sleep. (Let me note that I have a certain sympathy for this proposition since a good translation of

“*Forza Azzuri*” chanted by Italian fans is “Go Blue,” the chant of the University of Michigan Wolverines who wear maize and blue colors while running onto the field in Michigan Stadium in front of 110,000 screaming fans. Not a soporific sight.)

But note as well that these matters are not simple and straightforward. Consider the color of a very famous drug, Viagra. Viagra is almost always shown as an oblong object, usually pointing upwards to the right. And it seems always to be blue. In English, while blue has long had an association with “low, down, depressed,” or with “having the blues,” it can also mean mildly salacious, sexy, or sexually inappropriate, as in “blue movie.” The OED quotes a dictionary of slang from 1864 indicating “*Blue*, said of talk that is smutty or indecent” (Hotten 1870).

We are all, I suppose familiar with Picasso’s “blue period,” which lasted from about 1901 to 1904, when many of his paintings were suffused in a general blue color. Picasso was a young man, about 21, when he painted “*Erotic Scene*” (which shows him receiving fellatio from a prostitute); his interest in the erotic and his use of blue to frame it continued on for many years. In 1932 (when he was about 51), he painted “*Nude, Green Leaves and Bust*,” which shows his mistress, Marie-Therese Walter, with leaves and a statue. It also shows the same blue as in “*Erotic Scene*.” Art historians squabble about what the blue in Picasso’s blue period means. Now you know. (Google these paintings to see the colors; both are available in high quality images online.)

I’m also fond of a particular ad for Viagra in Arabic. It shows the standard oval blue pill pointing to the upper right, with a line of text below. A literal translation is something like, “Make a gubba out of a hubba.” A “hubba” is a little seed, or grain, or pit. A “gubba” is a dome, as on a mosque. So, “make a dome out of a pit,” or more colloquially, “Make a mountain out of a molehill.” The details vary, but the sensibility is obvious. And, in Arabic, it rhymes! And it’s blue. (If you are over 21, Google images “Viagra Arabic.”)

So, in complex, polysemic, cultural ways, colors can modify the effects of medication. So can the form of medication. For example, Ton de Craen has shown that injected placebo is more effective than oral placebo in the treatment of migraine headache (de Craen et al. 2000). When the drug sumatriptan (known in the United States as Imitrex, and as Imgran elsewhere) was first introduced, it was only available in the form of an injection; today it is still available that way but also as tablets and nasal spray. De Craen did a meta-analysis of 35 trials. In placebo-treated patients, among those treated with a pill taken by mouth, after two hours 26% of patients reported that their headache was better (it was gone, or mild). Of those treated with a placebo injection, 32% of patients were better. This difference is small (about 6%) but it is statistically significant ( $\chi^2 = 9.4$ ,  $p = .002$ ). In studies like this, no one involved, from funder to subject, has any idea at all that factors like

this are in play; they are utterly out of consciousness. We will come back to this example in a moment, but from a different direction.

So, color and form can make a difference, and so, too, the number of pills taken can make a difference. In a very subtle meta-analysis, De Craen showed that, in some 80 studies of several antisecretory medications for duodenal ulcer, there was a significant difference in the endoscopically verified healing rates for those who took two placebos per day (36%) compared to those who took four placebos per day (44%), a difference of 8%. Everyone knows that  $4 > 2$ , but who knew this?

Finally, for the anthropologists, cultural factors can make a difference. There are also cultural factors, which are associated with some variation (in addition to color!). In addition to the Italian difference with respect to “blue,” there are other cultural differences in the meaning response. Recall the study of inert injection versus inert tablet for migraine where shots worked better than pills. The bars on the left in Figure 7 represent the numbers I mentioned earlier for injected versus tablet for Imipramine. However, in studies that were carried out in the United States, the same pattern appeared: 22% oral versus 34% subcutaneous placebo relief rate. In studies done in Europe, however, the difference disappeared: 27% oral versus 25% subcutaneous placebo relief rate (de Craen et al. 2000:186). Injections work better than pills, but only in the USA. There are cultural differences shaping the placebo effect. In my work with peptic ulcers, the mean placebo healing rate (again, four-week, endoscopically controlled) in six German studies is 59%; the rate in three Brazilian studies is about 7%. Perhaps Brazilians and Germans have fundamentally different kinds of ulcers (although this seems doubtful). Comparing the six German studies to five studies from Germany’s

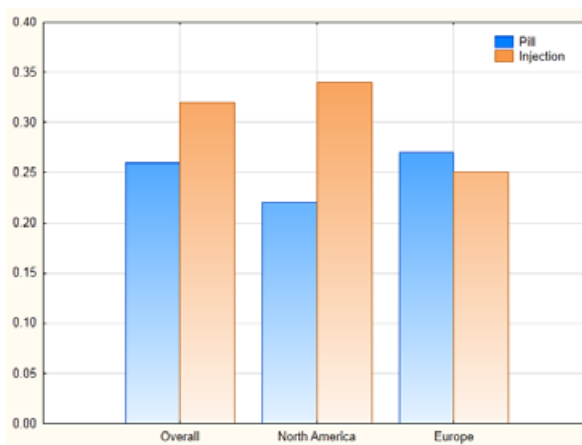


FIGURE 7. INERT INJECTION IS MORE EFFECTIVE THAN INERT TABLET FOR MIGRAINE, BUT ONLY IN THE NORTH AMERICA, NOT EUROPE.

northern low-country neighbors in Denmark and the Netherlands, the German placebo healing rate is 59% compared to the Danish/Dutch rate of 22%. Note that the situation is not a simple one and that these differences seem to vary by illness: the control group healing rates in treating *hypertension* are lower in Germany than in other Western nations. These are not generic cultural factors but seem to involve specific cultural conceptualizations, understandings, or constructions of illness in different cultures, which seem to have a real impact on health and healing.

Finally, it seems as if, sometimes, there are historical factors that can shape these forces. Indeed, these kinds of differences can be seen not only between different cultures but through time as attitudes and understandings change. Walsh and colleagues (2002) reviewed 75 trials of various antidepressants: tricyclics (like Elavil and Tofranil) and SSRIs (like Prozac and Zoloft) compared with placebo. The effectiveness of drug treatment for depression has trended up substantially between 1981 and 2000, so that the proportion of patients responding to tricyclic antidepressants and to SSRIs had increased from about 40% to about 55%. Over the same period, the proportion of patients responding to placebo increased from about 20% to about 35%. The proportion responding was strongly correlated with the year of publication of the study for both drug and placebo treatment. The authors concluded that, "Some factor or factors associated with the level of placebo response must therefore have changed significantly during this period. Unfortunately, we were not able to identify these factors" (Walsh et al., 2002:1844).

However, the matter doesn't seem too complicated to me. Over the past generation, there has been a clear shift in consciousness among doctors, patients, friends, and, generally, everyone, to the effect that depression can be treated with drugs. This was simply not the case (or at least not broadly shared) 20 or 25 years ago. As recently as 1970, for example, Goodman and Gilman's *Pharmacological Basis of Therapeutics*, one of the standard reference sources was clearly more enthusiastic about electro-convulsive therapy (ECT) than it was about treatment with imipramine or amitriptyline, which were said never to be more effective than ECT (Goodman & Gilman, 1970:186–192). Today, while we practically never hear of ECT, we all "know" that drugs are effective for depression; we read it in the newspapers, in the scientific journals, we see it on TV dramas, and, in the US at least, we see it in drug company advertisements everywhere, both in professional media and on TV commercials, and, of course, in our spam e-mail.

Antidepressant drugs are available in the drugstore and, in the form of St. John's Wort, at the OTC drug section of your local supermarket. As we change our views of the effectiveness of drugs, their effectiveness changes, as do their placebo mimics in trials. Meanings change and so do meaning responses. I have never been able to figure out just how much the pharma-



Company	Fine	Drug	Date
Bristol Myers Squibb	\$515 million	Abilify	2007
Eli Lilly	\$1.4 billion	Zyprexa	2009
Pfizer	\$2.3 billion	Bextra	2009
Astra Zenica	\$520 million	Seroquel	2010

TABLE 1. A COST OF DOING BUSINESS. FINES PAID TO THE FDA FOR ADVERTISING TO DOCTORS FOR UNAPPROVED (OFF-LABEL) USES OF DRUGS (WILSON 2010).

(AUTHOR'S NOTE: ON JULY 2, THE JUSTICE DEPARTMENT ANNOUNCED A \$3 BILLION FINE AGAINST GLAXOSMITHKLINE FOR ILLEGAL ADVERTISING FOR PAXIL, WELBUTRIN, AVANDIA AND "OTHER DRUGS". THE ARTICLE MENTIONS IN PASSING THAT ABBOTT LABS SETTLED FOR \$1.6 BILLION FOR ILLEGAL MARKETING OF DEPAKOTE IN MAY; AND AN AGREEMENT PENDING WITH JOHNSON AND JOHNSON COULD RESULT IN A FINE OF AS MUCH AS \$2 BILLION FOR ILLEGAL MARKETING OF RISPERDAL.[http://www.nytimes.com/2012/07/03/business/glaxosmithkline-agrees-to-pay-3-billion-in-fraud-settlement.html?\\_r=1](http://www.nytimes.com/2012/07/03/business/glaxosmithkline-agrees-to-pay-3-billion-in-fraud-settlement.html?_r=1))

ceutical industry spends on advertising, but it is said to be about the same as, or more than, the amount spent on research. Most of this advertising is directed to physicians, but in the United States and New Zealand, what is called "DTC; Direct To Consumer" advertising is legal; it's unlikely that this can't have some effect on perceptions and understandings of people regarding particular drugs or drugs in general, and it is certainly possible that it is enhancing the general understand people have of how effective drugs must be.

Table 1 seems an interesting proxy for this advertising. It is a list of some recent fines paid for illegal advertising to physicians of unapproved uses of drugs (sum of the four amounts is \$4.7 billion dollars). The money spent on drug promotion is enormous. And it probably has effects well beyond what the drug companies intend. It would be among the richest of ironies if drug company advertising were responsible for such an increase in the meaning response that the companies could no longer show their new drugs to be superior to placebo!



## CONCLUSIONS

What we know, understand, think, and feel; what we are told and believe; our cultural background; the TV and sports cultures we know; the newspapers and magazines we read; the relationships we have with our clinicians (our doctors, residents, interns, nurses, aids, orderlies, and probably receptionists and parking lot attendants), our families (our moms and dads, siblings, cousins, spouses, children, especially grandchildren), and our friends (jogging or fishing companions, drinking buddies, knitting clubs, coffee club pals) can



very directly or, maybe, more often *indirectly*, affect our responses to medicines, inert or otherwise. Some of this is conscious and clearly the result of cognitive interactions; much of it is not at all conscious and is completely off our ordinary radar. These matters are, these days, largely left to chance, or to ideology, or to market forces, but are rarely subject to robust science, although that's less true today, thankfully, than it was a decade ago. The clinical, analytical, and scientific implications of these matters are clearly rich and full and virtually unexamined.

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