

Nocebo: The Power of Suggestibility

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INTRODUCTION

To get a modern perspective on the placebo-nocebo phenomenon we are obliged to acknowledge the pioneer concepts of Adolf Meyer's "psychobiology" [1] and its extension by George Engel into a "biopsychosocial" paradigm [2]. Meyer postulated that illness needs to be examined in the context of an individual's psychobiological development and history. Engel worked toward a systems approach that takes all factors of one's life into account as part of any diagnostic and treatment picture. He postulates a complex series of interactions that includes the impact of social and emotional relationships as well as influences of individual personal and family history, current social situation, beliefs, needs, and fears on any biological insult [3].

A story is told that Dr. Engel [4], conducting hospital rounds, examined a woman with cancer. She asked him: "Doctor, is my cancer a male cancer or a female cancer?" He responded: "Why do you ask?" She said: "I've been told that you suffer more pain with a male cancer than with a female cancer." He answered her query: "You have a female cancer."

The implications of Engel's reply are enormous. He accepted a patient's psychological reality as a significant part of treatment responsiveness. He reacted as a compassionate physician striving for therapeutic effect and healing. Such a physician welcomes a placebo influence as additive and interactive with biological treatment. This is in stark contrast to many who are baffled by or ignorant of this powerful interpersonal feature.

MEDICINE: ART OR SCIENCE?

In the 19th century, the field of medicine adopted chemical and biological principles causing a shift from the "art" of healing to a "science" of therapeutics. "Placebo" became an epithet to identify drugs and ministrations that pleased but could not be considered the cause of a specific benefit nor could be scientifically measured to explain effect. In the 20th century, the biomedical paradigm, representing the core of mainstream medical thinking, regards a placebo effect as a

contaminant in research and a pejorative factor in clinical care. The placebo deflates and confuses the importance of biochemical discoveries by those who consider the biomedical model the highest standard of care.

With Pasteur's discovery of bacteria, biological reductionism became *the* pathway for medicine to develop into a scientific discipline. Causes of diseases could be analyzed into single identifiable parts, which could then be specifically targeted and treated. Dazzling achievements ensued in the cure and prevention of bacterial diseases. The record of success has had the effect of convincing the mainstream of medicine that biological reductionism is the *only* appropriate approach to understanding and coping with health and disease. Yet this paradigm has not yielded the same measure of success in the treatment of illnesses related to aging, allergies, immune diseases, and cancer as it has with bacterial diseases.

PAIN MODEL

Consider pain as a model. There is the physical stimulus that causes the irritation and there is the person reacting to the stimulus. The tremendous variation in the way different persons under different circumstances react to a similar pain stimulus is at times awesome and even baffling. Beecher [5] found that men who were wounded at the Anzio beach invasion in WWII required significantly less morphine than civilians who had suffered similar injuries in accidents.

Beecher's work addresses the reactive component to pain. When an injury was severe enough to save a man from life-threatening combat experience, but not so severe as to impair his function in civilian life, the wound was associated with freedom and survival. The same degree of injury in civilian life was not interpreted as a welcome pathway to survival but rather as an unexpected catastrophe, usually accompanied by anger at whomever or whatever was to blame. Reactive components can minimize or maximize pain sensations and thus are additive to the physical irritation. This was reflected in Beecher's study by measuring patient requests for morphine.

When the pain is not one's own, there can still be a pain response. Particularly in pediatric medicine, it is not unusual to watch parents hold their children as the

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child gets ready to receive an injection. The baby may be calm, not knowing what is going to happen, while the parent's face reflects agony and pain. This is a vivid example of the difference between a painful stimulus and an emotional reaction to it.

The dichotomy between the physical insult and the psychological reaction to it suggests two separate aspects of any medical condition: first, the disease itself, and second, the illness behavior [6,7]. The disease is the actual physical dysfunction or trauma and the illness behavior is the person's response to the event.

IMAGINATION

A unique feature that distinguishes the human being from all other animals is his imagination. Humans and animals share the autonomic mind, but the cognitive self-aware mind is uniquely human. It is only the human being that has evolved and developed art forms to create explanations and meaningful narratives to make sense of the universe.

Without control or appropriate focus, imagination can lead to anxiety, confusion, and panic. With relevant control, imagination can lead a person to find meaning, motivation, and inspiration in what transpires. Specific meanings can produce a sense of relative security or insecurity about what is going on which, in turn, influences expectations, actions, and outcome. Individuals use their assumptions, beliefs, knowledge, and fears to arrange, rearrange, and interpret events to develop a story line through which day to day living is perceived.

Imagination reflects the operation of the brain-mind. Body sensations caused by events outside and inside the body signal *upward* to the brain. Conversely, thoughts and feelings that the brain generates move *downward* to influence the body. For example, the thought of sucking on a lemon can evoke salivation, a worry can prompt the stomach to secrete acid or lead to a tension headache, and thoughts can provoke or prevent sexual arousal.

In one experiment on controlled imagination, I hypnotized an army corporal and gave him the instruction that he would be touched on his forearm with a hot iron. When I touched him with a pencil point, he reported pain and within a few minutes a blister formed. Several days later the scab that had formed fell off. This experiment was repeated four times during the following month with the same response. However, the fifth time this experiment was repeated, it was in the presence of a high-ranking officer who voiced doubts about the genuineness of the experiment. After being belittled and humiliated by this authority figure, this subject never again responded to the hypnotic suggestion.

The pain model and this simple experiment illustrate the power of upward and downward causality as

well as the leveraging effect of interactions with the outside world. These examples argue for an inevitable recognition of all three domains—biological, psychological, and social—as relevant to understanding the many factors that are constantly interacting to influence a person's health and illness.

ECOLOGICAL SENSITIVITY

Studies of hypnotic phenomena indicate that individuals differ considerably in their range of pliability, suggestibility, and responsivity to external influences. The concept of hypnotizability offers a useful perspective to identify this spread. Hypnosis is controlled imagination, or, to put it another way, it is a state of attentive, receptive concentration [8]. As a measurable phenomenon, three interactive components are identifiable as dissociation, absorption, and suggestibility.

(1) *Dissociation* is imagined activity that generates a vivid experience from a fragment or construct of reality. This is especially useful in the presence of painful experiences related to physical injury, medical treatments, and natural phenomena such as child birth. The degree to which one can dissociate on command is determined by a biological ability reflected by the relative mobility of the external ocular eye muscles. This is identified as the Eye Roll Sign, i.e., the ability to look upward on a 0–4 scale while closing the eyelids. It is a fixed biological marker that indicates the degree to which one is able to separate memory, perception, or motor response from the mainstream of awareness, which may at the same time manifest some influence on lifestyle and conscious flow.

(2) *Absorption* is the degree to which one can focus on a single theme, image, idea, or instruction. The goal is to constrict peripheral awareness to facilitate greater focal attention. This biopsychosocial phenomenon is like a psychological “zoom” lens that shifts back and forth between diffuse and finely focused attention. As attention becomes more intense and focused, there is less awareness of external signals that would distract from the task at hand.

(3) *Suggestibility* is a proneness to perceive and accept new information with a relative suspension of customary critical judgment. Motivation, personality style, context, belief systems, fear, and trust will influence the degree to which an individual edits, filters, or accepts influence and direction from another. The more hypnotizable, the greater the suggestibility and the greater the likelihood of uncritical compliance.

These features are an inherent part of the personality style of each person and are operational *with or without* formal identification and *with or without* formal hypnotic inductions. The style manifests itself with each challenge of day to day living but it is most dramatically evident within a formal trance state or *in a situation such as a hospital or traumatic event that*

acts as an external force causing a person to dissociate, become absorbed, and maximize suggestibility to the utmost degree of his particular style.

These three components underlie malleability, vulnerability, and degree of responsiveness to placebo-nocebo. In the presence of authority figures with expertise, such as physicians, a person is more likely to separate from the mainstream of his own experience, become totally absorbed in external factors, and suspend his own critical judgment to accept all that is communicated as hypnotic suggestion.

CASE EXAMPLE

A 24-year-old woman hospitalized with Hodgkin's disease was given Demerol for abdominal pain relief. A consult was called to see if her pain could be controlled with self-hypnosis to allow her to function outside the hospital with mental clarity. When I arrived, she was surrounded by medical students and residents. She said: "I don't want to embarrass you doctor, but I don't believe in this." Despite her verbal objections, I asked her to look up toward an imaginary spot at the top of her head and then to close her eyes. She easily went into trance and accepted suggestions to feel tingling numbness *more* than the pain and to allow this numbness to filter the hurt out of the pain. She came out of the trance free of pain and declared it to be a miracle. I gave her a posthypnotic suggestion to have one of the residents rehypnotize her each day. I would see her the following week.

For 5 days she was off all medication for pain. On the 6th day, the resident repeated the same induction procedure in an attempt to hypnotize her, but this time the patient failed to go into trance and the pain returned. When I saw the patient 2 days later, she reentered trance and was able to regain control over the pain.

The resident, who was in psychoanalytic training, had been told by his training analyst that there must be something immoral or unethical about hypnosis because Freud, himself, had given it up. The analyst ordered his trainee to stop using hypnosis. This so rattled the resident that the patient sensed his anxiety and ambivalence. Consequently, during their treatment session, the patient did not respond to the hypnotic induction instructions and the pain perception returned.

Such is the sensitivity of hypnotizable people that they pick up cues whether or not one is consciously aware of the message being conveyed. In this instance, the patient complied with the ambivalence of the resident and accommodated him by not going into trance.

The proper balance of biopsychosocial factors includes motivation, caring, and trust. When these factors are in a proper equilibrium, we get a placebo effect; when these factors are out of balance, we get nocebo.

PLACEBO

The placebo effect can occur when conditions are optimal for hope, faith, trust, and love. When morale is high, conditions for healing are enhanced. In military combat, for example, motivated soldiers endure unbelievable stress and even surprise themselves with their own ingenuity and performance [9].

J.C. was a platoon staff sergeant who had been with his outfit several years and had much battle experience. For 2 months, he had been on night patrol duty in the Ousseltia Valley (Tunisia). One morning, after launching an attack with his platoon, he reached his objective—a hill that had to be held for further operations. Shortly after he took the hill, the enemy counterattacked. Shells from the mortars began coming in. Several landed near him, one very close. He was stunned, but not hit. He managed to continue the fighting; however, he soon became tremulous and unable to hold his rifle.

Helped by another soldier, he came to the aid station with gross tremors and a sickly smile.

"Don't send me back to the rear, I'll be all right!" he insisted. In an effort to salvage him, he was sent to the kitchen area for 2 days and nights. When he came back, his tremors were gone but he had developed a facial tic. Still, he was eager to rejoin his outfit.

For 3 months, he carried on in active combat with a high degree of efficiency. Once, when his company was launching an attack, all the officers were killed or wounded in the first half hour. As the ranking noncommissioned officer in the outfit, he led the company until a relief officer assumed command.

Despite prolonged stress with physical symptoms, his motivation and unit loyalty was such that he had refused evacuation to stay with his men. His inner commitment yielded a powerful placebo effect.

In civilian life, inner conviction and social support can produce the same kind of momentum that we see in combat. For example, although there are disturbing exceptions, many Christian Scientists endure and often recover from sickness and trauma without conventional medical ministrations. The Christian Science approach reminds us that many diseases have a natural course. Often, recovery from illness occurs spontaneously if not interfered with [10].

When there is a total reliance on biological medicine, the professional may suffer concern and anxiety about the limitations of care. Some years ago Dr. J. E. Jesseph, a surgeon at the Brookhaven Laboratory Hospital, was conducting research on radiation therapy for breast cancer. Aware that the treatment program offered little more than minimal palliative care, Dr. Jesseph buffered himself with five cups of coffee in the morning to delay facing his patients. When he did arrive, he was concerned that his despair was transmitted to the women under his care [8].

Serendipitously, he received a brochure announcing

a course on the use of hypnosis for pain control. Four months after taking the course, he reported: "I have taught my patients to use self-hypnosis. There's been a 90% drop in nightmares, a 30% drop in the use of medications for pain control, and I'm back to one cup of coffee for breakfast."

This experience reflects the impact of the doctor-patient interaction from the physician's perspective. When psychological issues are addressed knowledgeably, it provides hope, optimism, a boost to morale, and a sense of mastery, enhancing the healing atmosphere between the doctor and the patient. This leads to improved biopsychosocial function in those who give as well as those who receive care.

The placebo effect is dependent on an interaction between the doctor, the treatment, *and* the psychological malleability of the patient. At the Columbia-Presbyterian Hospital we studied acupuncture with 98 cases of chronic pain [11]. A Chinese acupuncturist treated these patients for pain relief. Another physician, blind to the individual responses with various degrees of pain relief, measured for hypnotizability (psychological malleability). Outcome was measured by patient report in three categories: 90-100% relief, partial relief, and no relief at all. The breakdown shows that there were no low hypnotizables in the 90-100% relief group, 1 had partial relief, and 12 had no relief at all. The highly hypnotizables and those in the mid-range constituted most of the 90-100% relief group. These results are consistent with the spectrum theory of hypnotizability, which would predict that the more hypnotizable the person, the more ability there is to use dissociation, absorption, and suggestibility to alter biopsychosocial variables involved in the experience of chronic pain.

This suggests that we are measuring not just the needle, but also the person's capacity to accept the procedure and respond. The treatment procedure is an interactive process between the ceremony and the patient's motivation, responsivity, and inherent malleability.

NOCEBO

There are at least three different ways in which the nocebo effect is activated: (1) negative messages from the health care environment, (2) negative messages from the patient's social and psychological milieu, and (3) secondary gain. Nocebo can be identified as the absence of conditions that promote placebo as well as a direct insult.

(1) The first, the imposition of a negative message by the health care system or an individual in the system, takes the form of a direct insult. To illustrate, when I was an intern in a Catholic hospital, a cardiologist observed that one patient on a large cardiac ward had taken a turn for the worst and was about to die. We

immediately called for a priest to administer last rites. By mistake, the priest went to the patient who was in the bed next to the patient who was dying. He gave this patient last rites with an impressive air of authority and a very brusque voice. Within 15 minutes, that patient died. The man we wanted the priest to see lived for another 4 days.

It seems you do not have to go to Africa to see the equivalent of a Voodoo death. It can happen anywhere. It is simply a matter of recognizing it when it occurs. This was a nocebo effect caused by an institutional mishap.

Another example of a nocebo effect involved a hospitalized woman with such severe back pain she could not walk. She was scheduled for surgery to remove a disc. The resident doctor, who had been assigned to her case, had just learned to use hypnosis. He taught her self-hypnosis with suggestions to imagine cool, tingling numbness instead of the pain. In a few hours, she was able to get out of bed. She walked for the first time in weeks. The nurses on the ward had tears as they watched this wonderful scene.

The day before surgery was scheduled, the surgeon heard that she was walking as a result of self-hypnosis exercises. He came to her room and impatiently reprimanded her: "Look young lady, you have real pain and this hypnosis nonsense is not going to work. You are going to get your operation tomorrow." After he left, her pain returned and she was unable to walk. She had her surgery the next day.

(2) A second type of nocebo comes from the social and medical environment of the patient. One study done by Marcia Greenleaf [12] at Albert Einstein College of Medicine discovered the effects of mixed messages on coronary artery bypass patients during their recovery period in the intensive care unit (ICU). Thirty-two patients were tested for their suggestibility (hypnotizability). Patients in two groups were taught formal hypnosis with different treatment strategies; patients in the third group were not taught formal hypnosis.

Independent of experimental treatment with formal hypnosis, the patients' degree of hypnotizability (suggestibility) predicted physiological recovery in the ICU. Measures included the amount of medication required to control blood pressure and the amount of time to achieve cardiopulmonary stability.

The highly hypnotizable patients were the most unstable in the first 48 hours in the ICU. Those in the midrange of hypnotizability stabilized more rapidly than the "highs" or "lows." When the patients were removed from the atmosphere of the ICU and in the protective environment of the cardiac care unit, the highs caught up with the recovery pace of the midrange but the lows lagged behind. The lows' total length of stay in the hospital averaged 5 days longer than those in the midrange and the highs.

People who are highly hypnotizable have an exqui-

site vulnerability to all messages from external authority sources. Under stress, the highs tend to suspend their critical judgment, whereas the midrange maintain their editing function and can be more selective about what they respond to. The lows are comparatively less sensitive to the nuances of the external environment because of their fixed commitment to their internal beliefs, and, therefore, are less suggestible and less responsive to negative or positive cues.

When the highs were moved out of the perplexing high-tech milieu of the ICU, they quickly mobilized their resources and caught up with the pace set by the midrange. The nocebo effect of the ICU on the highs was neutralized by the quiet supportive atmosphere of the cardiac care unit.

In studying the effects of group support for women with metastatic breast cancer, David Spiegel and his colleagues at Stanford University [13] have been able to measure the impact of the intervention on a variety of placebo-nocebo effects. The study started in 1977 and consisted of 86 patients who were randomly assigned to either a treatment group or a control group. The treatment group consisted of 50 patients who attended weekly support group meetings for 1 year, in addition to the usual medical treatment. The control group consisted of 36 patients who received the usual medical treatment only.

On analysis, Spiegel et al. found that 4 years later, all patients in the control group had died, while one-third of the patients in the treatment group were still alive. The last two survivors died in 1994. During the first year of the study, assessments demonstrated an immediate effect for the treatment group. They experienced significantly more comfort, less pain, and less depression than the control group. At 10-year follow-up, statistical analysis revealed that the treatment group lived an average of 18 months longer than the control group.

In the process of replicating his findings, Spiegel [14] reports an outstanding feature of women who attend the support groups is their sense of learning how to deal with the inevitable feeling of powerlessness: "Why me" or "Why does this happen to me." By developing a meaningful group cohesiveness, they discover that: (a) they are not alone with their calamity and (b) they can learn to negotiate thoughtless, careless, or uninformed comments from family, friends, and often from doctors, who may make unwise predictions about how long they're going to live. Morale is enhanced when the women learn to negotiate insults, misunderstandings, and alienating communication from health care givers, family, colleagues, and friends. It becomes "us" dealing with "them."

Learning to evaluate and neutralize a vast array of comments converts nocebo possibilities into placebo possibilities. With new perspectives, patients can give their bodies a more favorable atmosphere for healing

and muffle unwitting psychological insults. In David Spiegel's study, the control group did not have the benefit of a program that systematically provided psychological protection. One can hypothesize that those in the control group were more vulnerable to nocebo effects from internal and external expectations.

(3) A third factor for nocebo influence is secondary gain. If a patient senses that new status, new attention, and new power within his social network emerges as a result of the disease or trauma, and if the support and network permit or encourage the new status to develop and stabilize, dire consequences can ensue. Invalidism and victimization can become a new theme for survival. A way of life based on illness may evolve, relieving and depriving the patient of previous responsibilities. If insurance money or legal compensation become factors, the nocebo effect transforms the sick role into an illusion of achievement—even success.

Ironically, while an apparent gain develops, an insidious process of secondary loss emerges. The process is so insidious that it is not often detected soon enough to alert the patient about the loss of self-esteem and self-mastery. Backing into invalidism this way frequently leads to regret, depression, alcoholism, and drug addiction.

On the encouraging side, many patients refuse to let illness and infirmity take over their sense of identity and, instead, mobilize their healthy resources in a timely manner and restructure a whole new way of living productively [15,16].

SUMMARY

A useful way to summarize the placebo-nocebo theme is to consider the tension and interaction between conviction and responsibility. With the conviction of the mainstream biomedical paradigm prevalent today, it would be tempting to say to Dr. Engel's patient: "That question is nonsense. Cancer pain is not classified as 'male' or 'female.' Pain varies with location in the body and other factors." This response is technically honest but, in effect, it would have the impact of a nocebo. It would impair the patient's hope and morale. The doctor's honesty and conviction would serve as blinders to the patient's suffering. This type of honest statement results in a diminished sense of responsibility for the patient's well-being.

Taking the biopsychosocial context into account, Dr. Engel achieved a balance between conviction and responsibility. The patient's question was understood within the meaning and metaphorical terms of her belief system. He answered in a manner that respected her private point of view toward pain and tapped her suggestibility, guiding her toward a probable placebo effect. "Female cancer" resonated with her personal beliefs and wish for less pain. Engel was both true to his convictions and responsible for providing the highest

standard of care by understanding the patient's convictions and needs for comfort.

The biopsychosocial concept provides a blueprint to bring the old-fashioned medical art of "humanness" to modern scientific care. Identifying the interactions of the problem, the person, and the totality of resources permits a focus on therapeutic strategies to promote placebo effects and prevent the consequences of nocebo.

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