

Assignment #1 for MrBrown

This Assignment will look at the concept of **Placebo** and the **Placebo Effect**.

Read and study the several articles in this document. Two of them support the idea of Placebo Effect and two of them do not. Search on line for more ideas to support the ideas in these articles.

Write a point/counter point summary about **Placebo** and the **Placebo Effect**.

Share with jbrown for partial credit.

Print and give to MrBrown for full credit.

A Study Casts Doubt On the Placebo Effect

In a new report that is being met with a mixture of astonishment and disbelief, two Danish researchers say the placebo effect is a myth.

The investigators analyzed 114 published studies involving about 7,500 patients with 40 different conditions. The report, published in *The New England Journal of Medicine*, found no support for the common notion that, in general, about a third of patients will improve if they are given a dummy pill and told it is real.

Instead, the researchers theorize, patients seem to improve after taking placebos because most diseases have uneven courses in which their severity waxes and wanes. In studies in which treatments are compared not just with placebos but also with no treatment, they said, participants given no treatment improve at about the same rate as participants given placebos.

Some doctors say the findings of the study ring true. Others are not prepared to abandon their belief in the placebo effect just yet.

Article, Page A20.

ARTICLE II

Placebo Effect Is More Myth Than Science, Study Says

By GINA KOLATA

In a new report that is being met with a mixture of astonishment and sometimes disbelief, two Danish researchers say the placebo effect is a myth.

The investigators analyzed 114 published studies involving about 7,500 patients with 40 different conditions. The report found no support for the common notion that, in general, about a third of patients will improve if they are given a dummy pill and told it is real.

Instead, the researchers theorize, patients seem to improve after taking placebos because most diseases have uneven courses in which their severity waxes and wanes. In studies in which treatments are compared not just with placebos but also with no treatment at all, they said, participants given no treatment improve at about the same rate as participants given placebos.

The paper appears today in *The New England Journal of Medicine*. Both authors, Dr. Asbjorn Hrobjartsson and Dr. Peter C. Gotzsche, are with the University of Copenhagen and the Nordic Cochran Center, an international organization of medical researchers who review randomized clinical trials.

Dr. Hrobjartsson said he had been telling other investigators what he found and watching their responses.

"People react with surprise, but also with a kind of satisfaction," he said in a telephone interview. "They start reflecting."

Experts interviewed this week had a range of responses from ready acceptance of the conclusion to great surprise to a skepticism and the desire to see the details of the analysis.

Dr. Donald Berry, for example, a statistician at the M. D. Anderson Cancer Center in Houston, said: "I believe it. In fact, I have long believed that the placebo effect is nothing more than a regression effect," referring to a well-known statistical observation that a patient who feels particularly terrible one day will almost invariably feel better the next day, no matter what is done for him.

Another physician, Dr. Jonathan Moreno, director of the Center for the Biomedical Ethics at the University of Virginia, said it rang

true to him. "Maybe it is one of the urban legends of medicine," he said.

But others, like David Freedman, a statistician at the University of California, said he was not convinced. Professor Freedman said the statistical method the Danish researchers used, pooling data from many studies and using a statistical tool called metanalysis to examine them, could give misleading results.

"I just don't find this report to be incredibly persuasive," he said. "The evidence of a placebo effect is maybe a little bit less than I thought it was, but I think there's a big effect in many circumstances. This doesn't change my mind."

The researchers said they saw a slight effect of placebos on subjective outcomes reported by pa-

tients, like their descriptions of how much pain they experienced. But, Dr. Hrobjartsson said, he questions that effect.

Finding what may simply be a disease's natural course.

books asserted that placebo effects were so powerful that, on average, 35 percent of patients would improve simply if they were told that a dummy treatment was real. The investigators began asking where this assessment came from. Every paper, Dr. Hrobjartsson said, seemed to refer to other papers. And those papers referred him to other papers. He began peeling back the onion, finally coming to the original paper. It was written by a Boston doctor, Henry Beecher, who had been chief of anesthesiology at Massachusetts General Hospital in Boston and in 1955 published a paper, "The Powerful Placebo" in *The Journal of the American Medical Association*.

In his paper, Dr. Beecher, who died in 1976, reviewed about a dozen studies that compared placebos with active treatments and concluded that placebos had medical effects.

"He came up with the magical 35 percent number that has entered placebo mythology," Dr. Hrobjartsson said.

But, Dr. Hrobjartsson said, diseases naturally wax and wane. And no matter how sick the person is, a truly bad spell will almost inevitably be followed by a period in which the condition seems to improve. What if the natural variation in a disease's course is behind the placebo effect, they asked?

"Of the many articles I looked through, no article distinguished between a placebo effect and the natural course of a disease," Dr. Hrobjartsson said. "This is a very banal error to make, but sometimes banal errors are made."

He and Dr. Gotzsche began looking for well-conducted studies that divided patients into three groups, giving one a real medical treatment, one a placebo and one nothing at all. That was the only way, they reasoned, to decide whether placebos had any medical effect.

But they worried that there might be so few such studies with a treated, untreated and placebo group that they would never be able to answer the question. "We thought if we could find 20, that would be a huge success," Dr. Hrobjartsson said.

To their surprise, they found 114, published between 1946 and 1998. The conditions included from med-

Among some scientists, a belief that a report is unconvincing.

ical disorders, like high blood pressure, high cholesterol levels and asthma; behavioral disorders and addictions, like alcohol abuse and smoking; neurological diseases like Alzheimer's disease, Parkinson's disease, and epilepsy, and infections, like bacterial infections and the common cold.

When they analyzed the data, they could detect no effects of placebos on objective measurements, like cholesterol levels or blood pressure.

Dr. John C. Bailar III, an emeritus professor at the University of Chicago who wrote an editorial accompanying the placebo paper, said the findings called into question some mind-body beliefs. These are arguments that use the placebo effect to conclude that the mind can so profoundly affect the course of a disease that people should be able to harness this power and think themselves well.

The findings should also give doctors pause in prescribing treatments they know are useless, like a glass of warm milk at bedtime for patients with insomnia or futile drugs for patients in the late stages of fatal diseases, Dr. Bailar said.

"I think what this ought to do is bring about a very sharp reduction in the use of placebos," he said. "My guess is that it will bring about a modest reduction and that it will take a second or third penetrating paper to bring about a real change."

But, Dr. Bailar said, he understands the reluctance many will feel to abandon their belief in placebos. He, too, is hesitant to wrench himself completely away from what he now thinks is largely a myth.

"I'm not ready to give up on placebos entirely," Dr. Bailar said. "I hope there will be a lot more research on how they work." Or, he said, "if they work."

For Chronic Fatigue, Placebos Fail the Test

ARTICLE #2

By NICHOLAS BAKALAR

Many doctors believe that sugar pills are likely to be effective for patients with chronic fatigue syndrome, trusting that a placebo will help relieve the mental and physical exhaustion that characterize the illness.

But a new study has found that people who have the syndrome respond at a lower rate to placebos than patients with other diseases. The paper was published in the March-April issue of *Psychosomatic Medicine*.

Studies suggest that placebos relieve the symptoms for about 30 percent of patients suffering from a wide variety of illnesses. Migraine headaches, for example, respond at a rate of about 29 percent to placebo treatment, major depression at about 30 percent and reflux esophagitis at about 26 percent.

In some diseases, placebo treatments are even more effective — 36 to 44 percent of patients with duodenal ulcers improve on placebos, depending on how many of the treatments are offered each day.

But by pooling results from more than two dozen studies, the researchers, led by Dr. Hyong Jin Cho, a professor of psychiatry at King's College London, found that, among people with chronic fatigue syndrome, only 19.6 percent responded to placebos, not the 50 percent found by previous, less systematic studies.

To Dr. Cho, the results were both unexpected and disappointing: he says he believes placebos can be a legitimate and useful form of medical treatment. He concluded not that placebos were unhelpful in treating chronic fatigue but that their use should be perfected.

"At the clinical practice level," he wrote, "the overall low placebo response emphasizes the need to enhance" the placebo effect in treating the illness.

To many doctors, chronic fatigue syndrome seems like a perfect candidate for placebo treatment, Dr. Cho and his colleagues write. Its symptoms are often indistinct: in addition to general fatigue, patients complain of muscle and joint pain, headaches, memory impairment and mood disturbances. Moreover, the symptoms frequently fluctuate over time, and they are more acute when the patients are paying close attention to them.

The illness has no cure, and the Centers for Disease Control and Prevention estimates that as many as 500,000 Americans suffer from it.

Dr. Cho and his colleagues speculate that the skepticism about the illness on the part of health care professionals may damage the trust between doctor and patient — a factor that may influence the effect of a placebo.

According to the study, placebos presented as medical or alternative-complementary treatments have a greater effect with chronic fatigue patients than do those offered as psychiatric interventions. The researchers suggest that this may be because most patients have a firm prior belief that the illness is physical. They make no judgment about the accuracy of that belief.

But Dr. Brian Fallon, an associate professor of psychiatry at Columbia University, offers a different interpretation. The fact that chronic fatigue syndrome responds so poorly to placebo treatment, he said, provides evidence that the

Can a sugar pill trick your symptoms?

syndrome has a physiological basis, though one that is still poorly understood.

"The finding by Dr. Cho and colleagues will come as no surprise to patients with C.F.S. who experience debilitating fatigue despite numerous treatment interventions," Dr. Fallon said. "That the placebo response in C.F.S. was far lower than in primary psychiatric disorders such as depression highlights the distinct nature of C.F.S. and how little we know."

Whatever conclusions may be drawn from the study's results, Dr. Cho says he sees placebo treatments as important.

"Many alternative therapies may provide a cure that depends on this powerful placebo effect," he said in an e-mail message. "I'm not using the term pejoratively, since empathy and time spent with the patient by the professionals in this area are indeed of important therapeutic value."

The New York Times

Placebos Prove So Powerful Even Experts Are Surprised

New Studies Explore the Brain's Triumph Over Reality

By SANDRA BLAKESLEE

Many doctors know the story of "Mr. Wright," who was found to have cancer and in 1957 was given only days to live. Hospitalized in Long Beach, Calif., with tumors the size of oranges, he heard that scientists had discovered a horse serum, Krebiozen, that appeared to be effective against cancer. He begged to receive it.

His physician, Dr. Philip West, finally agreed and gave Mr. Wright an injection on a Friday afternoon. The following Monday, the astonished doctor found his patient out of his "death bed," joking with the nurses. The tumors, the doctor wrote later, "had melted like snowballs on a hot stove."

Two months later, Mr. Wright read medical reports that the horse serum was a quack remedy. He suffered an immediate relapse. "Don't believe what you read in the papers," the doctor told Mr. Wright. Then he injected him with what he said was "a new super-refined double strength" version of the drug. Actually, it was water, but again, the tumor masses melted.

Mr. Wright was "the picture of health" for another two months — until he read a definitive report stating that Krebiozen was worthless. He died two days later.

Doctors who know this story dismiss it as one of those strange tales that medicine cannot explain. The idea that a patient's beliefs can make a fatal disease go away is too bizarre.

But now scientists, as they learn that the placebo effect is even more powerful than anyone had been able to demonstrate, are also beginning to discover the biological mechanisms that cause it to achieve results that border on the miraculous. Using new techniques of brain imagery, they are uncovering a host of biological mechanisms that can turn a thought, belief or desire into an agent of change in cells, tissues and organs. They are learning that much of human perception is based not on information flowing into the brain from the outside world but what the brain, based on previous experience, expects to happen next.

Placebos are "lies that heal," said Dr. Anne Harrington, a historian of science at Harvard University. A placebo, Latin for "I shall please," is typically a sham treatment that a doctor doles out merely to please or placate anxious or persistent patients, she said. It looks like an active drug but has no pharmacological properties of its own.

Until fairly recently, nearly all of medicine was based on placebo effects, because doctors had little effective medicine to offer. Through the 1940's, American doctors handed out sugar pills in various shapes and colors in a deliberate attempt to induce placebo responses.

Nowadays, doctors have real medicines to fight disease. But these treatments have not diminished the power of the placebo.

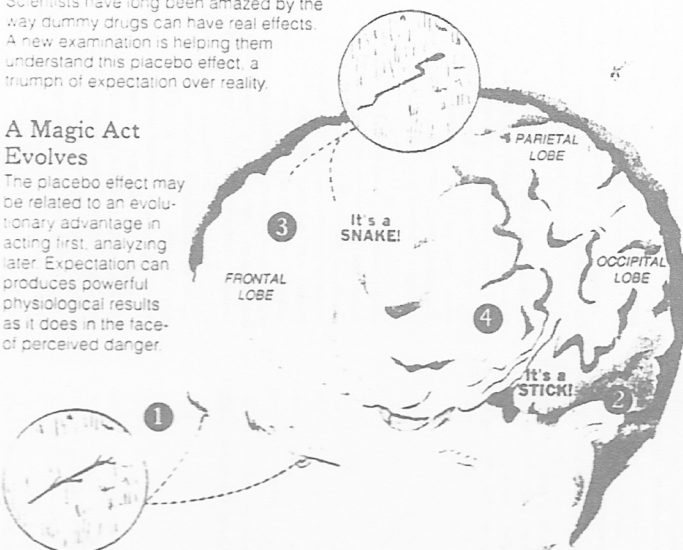
Doctors in Texas are conducting a study of arthroscopic knee surgery that uses general anesthesia in which patients with sore, worn knees are assigned to one of three operations — scraping out the knee joint, washing out the joint or doing nothing. In the "nothing" operation, doctors anesthetize the patient, make three little cuts in the knee as if to insert the usual instruments and

A Medical Mystery

Scientists have long been amazed by the way dummy drugs can have real effects. A new examination is helping them understand this placebo effect, a triumph of expectation over reality.

A Magic Act Evolves

The placebo effect may be related to an evolutionary advantage in acting first, analyzing later. Expectation can produce powerful physiological results as it does in the face of perceived danger.



1 OBSERVATION

A man walks through the forest and spies a long, thin brown object in the high grass.

2 INTERPRETATION

The lower brain processes sensory input: there is no sound or movement, the object has a dark exterior. It looks like a stick.

3 EXPECTATION

Simultaneously, the upper brain, drawing on experience, interprets information from the senses and comes to a different conclusion: snake!

4 RESOLUTION

The brain may give equal weight to input from the internal and external worlds. But if expectation wins out, the body will produce stress hormones in response to the stick.

Jim McManus/The New York Times

Doctors uncover mechanisms that can turn belief into an agent of biological change.

then pretend to operate. Two years after surgery, patients who underwent the sham surgery reported the same amount of relief from pain and swelling as those who had had the real operations.

A recent review of placebo-controlled studies of modern antidepressant drugs found that placebos and genuine drugs worked about as well. "If you expect to get better, you will," said Dr. Irving Kirsch, a psychiatrist at the University of Connecticut who carried out the review. His findings were met with a great deal of skepticism.

And a recent study of a baldness remedy found that 86 percent of men taking it either maintained or showed an increase in the amount of hair on their heads. But so did 42 percent of the men taking a placebo.

Some studies are specifically designed to explore the power of placebos rather than drugs. On Coche Island in Venezuela, asth-

The Body Heals Itself

New studies show the placebo effect at work from head to toe in different cultures around the world.

Hair Growth

Forty-two percent of balding men taking a placebo either maintained or increased the amount of hair on their heads.

Asthma

Smelling a placebo helped asthmatic children in Venezuela increase their lung function by 33%.

Allergies

In a Japanese study, people exposed to fake poison ivy developed real rashes.

Joint Repair

Doctors in Texas studying knee surgery found similar levels of pain relief whether surgery was real or feigned.

Pain

When told a heavy object was about to hit their foot, people in a study exhibited the kind of brain activity researchers associate with pain perception.

The Power of the Placebo Amazes Medical Experts

ARTICLE
#3

Continued From First Science Page

extremely specific effects. For example, a study was carried out in Japan on 13 people who were extremely allergic to poison ivy. Each was rubbed on one arm with a harmless leaf but were told it was poison ivy and touched on the other arm with poison ivy and told it was harmless. All 13 broke out in rash where the harmless leaf contacted their skin. Only two reacted to the poison leaves.

Studies have shown, time and again, that placebos can work wonders. Like "real drugs," they can cause side effects like itching, diarrhea and nausea. They can lead to changes in pulse rate, blood pressure, electrical skin resistance, gastric function, penis engorgement and skin conditions. The question is, why? Explanations of why placebos work can be found in a new field of cognitive neuropsychology called expectancy theory — what the brain believes about the immediate future.

'We are misled by dualism or the idea that mind and body are separate.'

Like classical conditioning theory (Pavlov's dogs salivate at the sound of the bell), expectancy involves associative learning. The medical treatments you get during your life are conditioning trials, Dr. Kirsch said. The doctor's white coat, nurse's voice, smell of disinfectant or needle prick have acquired meaning through previous learning, producing an expectation of relief from symptoms. Each pill, capsule or injection is paired with active ingredients, and later, if you get a pill without active ingredients, you can still get a therapeutic effect, he said.

Such conditioning shows how expectations are acquired, Dr. Kirsch said. But it does not explain the strength and persistence of placebo effects. These responses occur almost instantly, with no apparent conscious thought, and are therefore wired firmly into the brain, he said.

Response expectations are strong because the world is filled with ambiguity. A long thin object seen in dim light could be a stick or a snake. But it may not be safe to take the time to find out. So people evolved a

mechanism to anticipate what is going to occur. This expectation speeds the perceptual processing at the expense of accuracy.

As in the outside world, people's internal states have inherent ambiguity. That is why, when people in an experiment were given a drug that produced a surge of adrenaline, they interpreted the feeling as anger, euphoria or nothing at all, depending on what they had been told to expect.

Critics of alternative medicine say its enduring appeal is explained by the placebo effect. When conventional therapies fail to help chronic or poorly understood conditions, the acupuncturist, homeopathist or chiropractor steps into the breach with a potent belief system ready-made to help the suffering patient. "If a guy in a white coat or a guy dressed in feathers can induce a patient's immune system to fight back, who is to say which is better?" said Dr. Dan Molerman, a medical anthropologist at the University of Michigan at Dearborn.

Support for the expectancy theory emerged about 10 years ago, when many scientists realized how closely the brain, the immune system and the hormone production of the endocrine system are linked. Chronic stress sets into motion a cascade of biological events involving scores of chemicals in the body — serotonin, cortisol, cytokines, interleukins, tumor necrosis factor and so on.

Such stress lowers resistance to disease and alters gene expression. When people are under stress, wounds tend to heal more slowly, latent viruses like herpes erupt and brain cells involved in memory formation die off. The precise molecular steps underlying all of these changes have been mapped out.

But what about the opposite? Can a thought or belief produce a chemical cascade that leads to healing and wellness? Researchers studying placebos think the answer is yes, and they offer several ways it might work:

¶A placebo might reduce stress, allowing the body to regain some natural, optimum level called health.

¶Special molecules may exist that help carry out placebo responses. For example, a recent study found that stressed animals can produce a valium-like substance in their brains, but only if they have some control over the source of the stress. People almost certainly have similar brain chemistry.

¶Placebos may draw their power from the way the brain is organized to act on what experience predicts will happen next.

Dr. Marcel Kinsbourne, a neuroscientist at the New School for Social Research in New York, explains it this way. The brain generates two kinds of activation patterns, which arise from networks of neurons firing

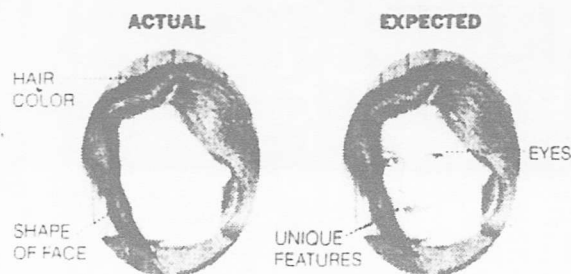
Expectancy Theory Fills in the Blanks

In addition to the medical miracles of placebos, the brain's reliance on expectancy affects many aspects of ordinary life.

EXAMPLE 1

Say, isn't that...

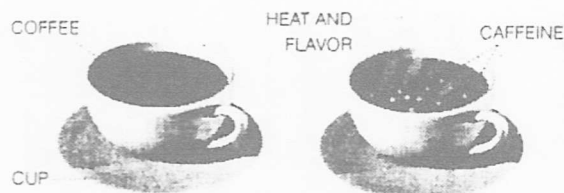
When seeing someone partially or from a distance, the brain fills in unclear or unseen elements, turning the stranger across the room into a familiar face.



EXAMPLE 2

Ah, a hot cup of Joe...

The sight of the first morning pick-me-up conjures expectations of warmth, flavor and the stimulating effects of caffeine regardless of actual content.



EXAMPLE 3

Hey, where's that step?

When the brain's expectation doesn't jibe with the reality, as when one expects an additional step on a staircase, a quick sense of surprise and confusion results.



The New York Times

together. One type is set in motion by information flowing into the brain from the outside world — smells, tastes, visual images, sounds. At the same time, the cortex draws on memories and feelings to generate patterns of brain activity related to what is expected to happen.

The top-down patterns generated by the cortex intersect smoothly with the bottom-up patterns to inform us about what is happening, Dr. Kinsbourne said. If there is a mismatch, the brain tries to sort it out, without necessarily designating one set of patterns as more authoritative than another.

The expectations that result are internally generated brain states that can be as real as anything resulting purely from the outside world. For example, recent experiments with monkeys show that if they expect a reward like a sip of apple juice, cells in their brains fire 20 to 30 seconds before they actually receive it. In other words, expectancies are embedded in the brain's neurochemistry.

"We are misled by dualism or the idea that mind and body are separate," said Dr. Howard Fields, a neuroscientist at the University of California at San Francisco who

Examining the remarkable power of the placebo effect — lies that heal.

studies placebo effects. A thought is a set of neurons firing which, through complex brain wiring, can activate emotional centers, pain pathways, memories, the autonomic nervous system and other parts of the nervous system involved in producing physical sensations, he said.

Morphine will alter brain patterns to reduce pain. So will a placebo. Obviously, placebos have limits. Mr. Wright's miraculous remission aside, most people cannot think, hope or believe their way out of cancer or AIDS.

As Dr. Howard Spiro, a gastroenterologist at Yale University, put it: Some diseases are unleashed with the power of a firehose. Others unfold at a trickle, and perhaps those are the ones amenable to placebo effects.

ARTICLE
#3

Enthusiasm Of Doctor Can Give Pill Extra Kick

ARTICLE #4

By SANDRA BLAKESLEE

Though some people respond more strongly to placebos than others do, it seems that everyone responds at some time or other. And doctors seem to play a large role in the degree of that response.

"The thing that trumps everything is the enthusiastic physician," said Dr. Dan Molerman of the University of Michigan. For example, one study offered the same drug to patients with identical symptoms, with one difference. Some were told by their physicians, "This drug has been shown to work," while others were told, "I am not sure if this treatment will work — let's just try it." The first group of patients did much better, Dr. Molerman said. "The physician is an agent for optimism and hope and a great inducer of beliefs."

Physicians can even fool themselves. Years ago, researchers carried out controlled studies of a drug for angina or heart pain and found it was no better than a placebo, Dr. Molerman said. Once doctors knew that, its effectiveness fell.

While doctors and patients affect one another's expectations, both are swept up into a wider context of culture and biology, said Dr. David Morris, an adjunct professor of medicine at the University of New Mexico in Albuquerque. The brain circuits through which placebos act, he said, are activated through the experience of living in a particular culture.

To explore the importance of cultural context, Dr. Molerman, in an analysis forthcoming in the journal *Medical Anthropology Quarterly*, compared 122 double-blind placebo-controlled ulcer studies from all over the world. Doctors used the same techniques, the same drugs and the same placebo pills and studied an image of the stomach lining before and after treatment to see what worked. The drugs worked 75 to 80 percent of the time, Dr. Molerman said, whereas the placebos worked from zero to 100 percent of the time, depending on the country. The placebo healing rate for ulcers in Germany was 60 percent, almost double the world average of 36 percent, which is about where the United States fell. But in Brazil, the mean placebo healing rate was a startling 6 percent.

"I don't have hint of what is going on here," Dr. Molerman said. "I can only say that cultural differences affect ulcer treatments, even though ulcers are the same the world over."