

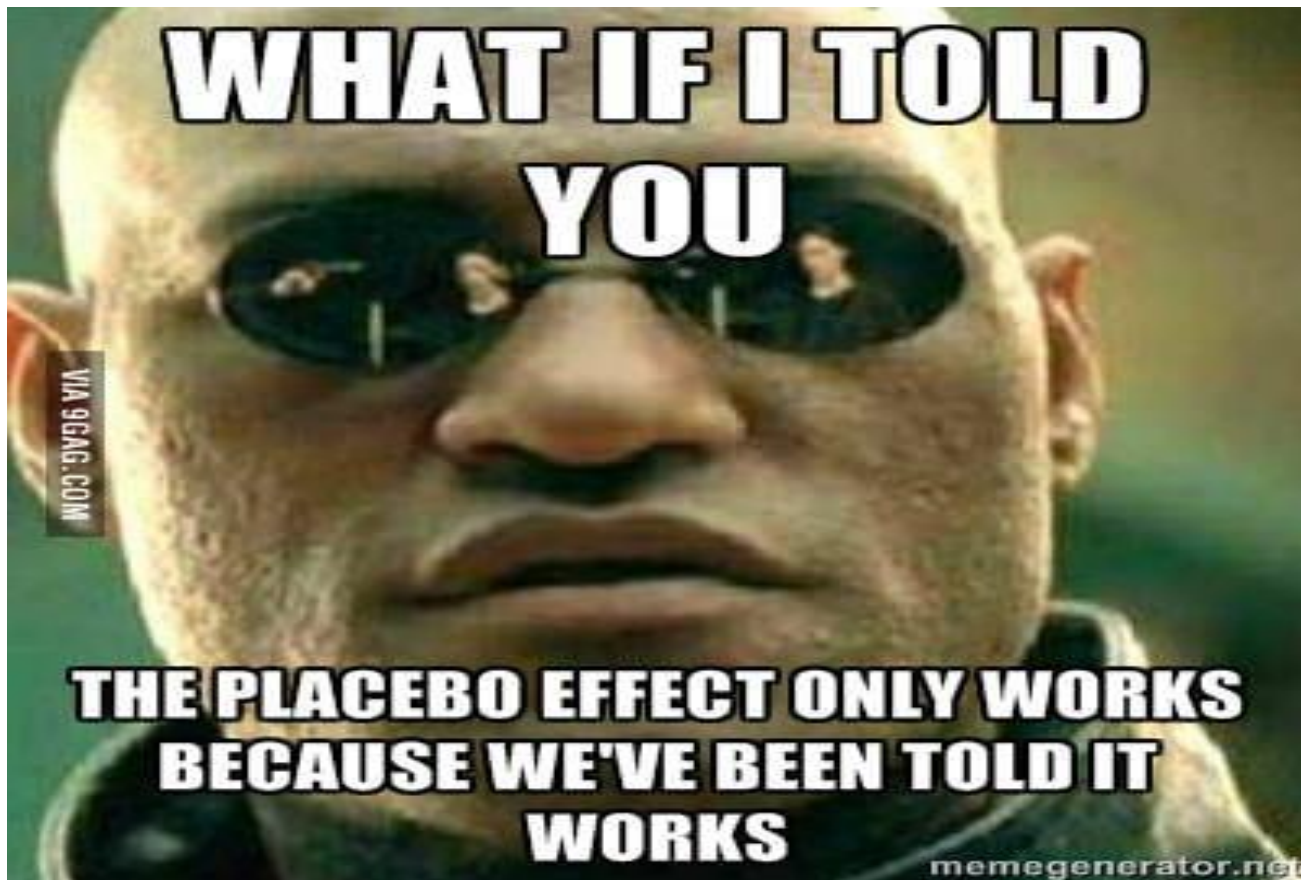
Placebo effect in clinical practice

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Definitions

- Latin for I shall please .
- An inactive substance /preparation given to satisfy the pt's symbolic need for drug therapy and used in controlled studies to determine the efficacy of a medicine , also a procedure with no intrinsic therapeutic value .

Placebo



Definitions continue...

- A placebo is any therapeutic procedure which is given deliberately to have an effect on a patient's symptoms, but objectively without specific activity for the condition it is given for
- The placebo must be differentiated from the placebo effect, which may or may not occur and which may be favorable or unfavorable.
- The placebo effect is defined as the changes produced by placebos.

Placebo effect

- As defined in research trials, any difference in outcome between a placebo-treated group and untreated control group in an unbiased experiment (Ernst 2001).
- Placebo could be pharmacologically active or inert substances , most commonly the latter.
- Active placebo has some activity inherently, but not against the treated condition.

Definitions continued...

- The placebo is also used to describe an adequate control in research .
- A placebo is some thing , which is intended to act through psychological mechanism , it is an aid to therapeutic suggestions, but the effect which it produces , may be either psychological or physical .

Definition continue...

- Observer – oriented definitions , on the other hand , tend to be broader : “placebo” refers to that aspect of any treatment which is effective through symbolic rather than instrumental means . In this view , the placebo is “an active ingredient in practically every prescription” indeed, any thing offered with therapeutic intent may be a placebo even words!

Definition continue

- Placebo effect may also be viewed as a subset of a larger group of mind-brain-body effects such as the psycho-immunological effects of religious beliefs, cultural and social systems

Nocebo

- When a substance administered for placebo effects produces prominent side-effects, it is known as nocebo (I shall harm).
- The term 'nocebo effect' refers to the negative consequences, adverse reactions and intolerance resulting from the administration of a placebo.
- It is generally non-specific; nausea and headache

Placebo sag

- The decrease in the placebo effect with repeated or chronic administration of placebo.

Placebo effect

- Placebo work best for pain, disorders of autonomic sensations, and disorders of factors under the control of neuro-hormones ; nausea, blood pressure and bronchial asthma
- Psychiatric disorders: depression 25-60 %, mania 25%, schizophrenia 25-50% (depending on the criteria) and panic disorder 70 %
- More chronically ill patients show lower placebo response rate

Placebo effect

- It fails in hereditary degenerative disorders, toxic and metabolic syndromes or vascular events.

Placebo

- Placebo effects are not unique to placebo preparations; they are seen with active drugs too. e.g. a substantial proportion of patients responding to analgesics or antidepressants do so due to the placebo effect. Hence, the net effect of a given drug is thus the sum of the drug's pharmacological effects and the placebo effect.

Placebo

- Physiological changes in opioids and GABA have been proposed to explain some aspects of placebo action; this neuropeptide hypothesis holds good for placebo analgesia, but not proven to operate in other conditions e.g. depression.

Further information

- A placebo can be a procedure and not a medication e.g. sham ECT, and sham surgeries with the only skin incision.
- The placebo response is higher in trials with more than 2 arms compared to those with two arms only (placebo vs. active arms). In a three-armed trial, participants are aware that they have $\frac{2}{3}$ chance of receiving active treatment compared to $\frac{1}{2}$ chance in 2 armed study –hence there is a higher placebo response.

Further information

- Capsules are perceived to be stronger than tablets, producing more placebo effects. Larger pills have stronger placebo effect than smaller pills. The number of pills also influences the perception of pill strength. Multiple pills have stronger placebo effect than single pills.

Further information

- Anxiety symptoms responded better to green tablets and depressive symptoms responded better to yellow tablets. These are examples of the relative potency of medication varying with pill colour (Schapira et al. 1970).
- Injections elicit a stronger placebo effect than oral medications. Surgery is likely better than the others in terms of eliciting placebo effects.

The negative connotations of placebo

- The placebo effect is a neglected and berated asset of patient care .
- The more the doctor viewed medical practice as a scientific exercise , the more disparaging he was about placebo therapy .

More negatives

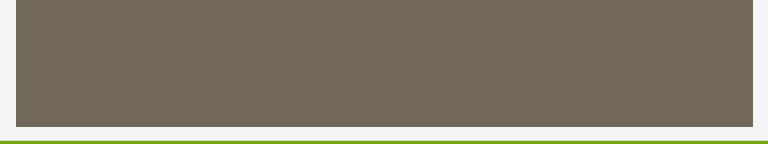
- Doctors definition tend to suggest that the placebo is an inert preparation ,or form of therapy , which has little or no specific medical effect , but is given “to humor rather than cure . “ Definition of this type always imply that the practitioner knowingly exploits such technique to gratify the patient .

However

- Even though on an official basis , the medical community disdains the use of placebo and is trying to get it out of the way so they can prove the efficacy of the therapeutic agents they use , placebos are there front and center

Doctors attitude toward placebo (Jean Comaroff)

- Dr A “ I would say that I prescribe it in 95%of my consultations .That sound high , it is high, not all these of the prescriptions are warranted in medical terms . When people go to doctors they expect a prescription , even if given Aspirin it would have therapeutic value .You can't always call this placebo, I would say the placebo effect was 50% , it is very important that every body get a prescription , most of the thing I give have therapeutic effect of some kind .But for some of them it's the placebo effect rather than the therapeutic effect that is more important .



Others are beginning to recognize that there is something to it

- Too many studies have found objective health improvements from placebo to support the notion that the placebo effect is not entirely psychological .

How big is placebo effect

- In 15 studies involving 1082 pts , placebos were found to have an average significant effectiveness of about 35%, a degree not widely recognized .
- About 75% of the apparent efficacy of antidepressants may be attributable to placebo effect .
- Wolf and Pinsky (1954) found that 30% of 31 anxiety patients improved on placebo(lactose) .

How big is the placebo effect...

- In 1946 DuBois stated “ although scarcely mentioned in the medical literature, placebo is more used than any other class of drugs .
- Many effective drugs have power only a little greater than that of placebo .
- Many of the drugs have been extolled on the basis of clinical impression when the only power they have is the placebo effect .
- In recent years in a lot of studies done by drug companies, sugar pills have done as

How big placebo effect

- A study of 500 patients undergoing dental procedures , those who were given placebo injection and reassured that it would relieve their pain had the least discomfort – not only less than the patients who got placebo and were told nothing but also less than the patients who got a real anesthetic without any reassuring comment that it would work .

How big is the placebo effect ...

- The world average of for placebo effect in peptic ulcer studies is about 36%, results in USA is close to this , in Germany about 59% but 22% in Denmark and the Netherlands , and in Brazil only 7% .

What part of an active drug effect is real

- The placebo effect of active drug is masked by their active effects . The power attributed to Morphine is then presumably a placebo effect plus its drug effect .The total drug effect is equal to its active effect plus its placebo effect
- Of a group of severe postoperative pain 75% are satisfactorily relieved by large doses of Morphine , But 35% are relieved by placebo .
- What counts more in reality Is what is going in the brain/mind not the

It may be hard to tell how much of the effect is “real”

- In their studies in the university of British Columbia ,researchers found that comparable levels of Dopamine are released in the brain after an injection of either a drug or a placebo IF the patient expect to get the drug .
- In one blind study, researchers found that patients with Parkinson’s disease who were given placebo released Dopamine in their brain , just like those who were give active drug .

Patterns of discovery

- Three phases :

1 – It's new. It'll cure every thing . And of course there are no side effects .

2 – Oooops! Maybe we were wrong. The honeymoon is over .

3 – Is it actually better than any thing we have ? Is it actually better than placebo .

Patterns of discovery.....

- Honigfeld show that drs communicate a subtle enthusiasm to pts in clinical trials and clinical situation .
- Many temporarily successful new surgical procedures owe their success to placebo effect alone .
- In a recent study in arthroscopic knee surgery, matched against sham surgery, 2 yrs later 35% of pts said they felt less pain ,were better able to get around , whether they were operated upon or not .

Changes in Medicine

- Medical science has improved so much and so fast in the last 40 yrs that it is easy , perhaps, for drs to neglect the part of medicine that is not a science at all .
- The ready and lavish display of sympathy , the laying on of hands, the projection of a slightly mystical authority, are now more often the province of alternative medical practitioners .

Important factors in placebo effect

- The placebo effect seems to be derived from a combination of factors involving the pt. the Dr and the relationship between the two . A meaningful Dr-Pt interaction is extremely important , allowing the transfer of the pt's concerns to an acknowledged scientist and healer, the physician .
- The physician's beliefs in the intrinsic worth of his medicine has always rivaled that of the patient .
- The psychological state of the pt. , pt's expectation and conviction all affect his response to treatment wither active or placebo .

Factors continue...

- Physicians who have faith in the efficacy of their treatments allow that enthusiasm to be communicated, have strong expectations, and are self-confident and attentive are the most successful in producing positive placebo effect.
- The length of time spent with the patient and the demeanor of the physician are pertinent factors.

Factors continued...

- Nature of the disease treated

Why does a placebo work?

- **Natural remission theory** states that the disorders for which placebo works are inherently episodic (i.e. natural cycles show periods of remission and relapse). Hence even without treatment an improvement would have occurred, and placebo use is merely coincident.

Why does a placebo work?

- **Measurement regression:** When a continuous variable is measured repeatedly in a sample, with each subsequent measurement the mean of the sample will move from extreme values and become closer to the population mean, the central value. This might explain why there is an apparent placebo response in control groups.

Conditioning theory

- According to classical conditioning models of placebo effects active medications are Unconditioned Stimuli and the vehicles in which they are delivered (i.e., the pills, capsules, syringes, etc.) are Conditioned Stimuli. The medical treatments that people experience during their lives constitute conditioning trials, during which the vehicles are paired with their active ingredients leading to the unconditioned response of therapeutic benefits initially. These repeated pairings endow the pills, capsules, and injections with the capacity to evoke therapeutic effects as Conditioned Responses later on.

Conditioning theory

- During placebo treatment, the belief of the patient in being treated may result in selective attention to symptom improvement and expectation. The momentary experience of symptom improvement may then act as a reward and positively reinforce preceding changes of autonomic function. Thus, visceral learning due to a mechanism similar to operant conditioning may occur, in which the reward is internally provided.



Thank you