

Peter Bügel

University of Groningen, The Netherlands

The Many Meanings of Placebo

Key Words

Placebo response · Doctor-patient relationship · Situational factors · Cross-cultural difference

Summary

Physicians throughout medical history knew three possible ways to explain the association between treatment and cure: 1. the beneficial effect of the treatment itself, 2. the healing power of nature, and 3. the placebo effect. In the modern definition by Grünbaum, a treatment is a placebo when the effect cannot be explained by the theory that describes its activity. In clinical practice the placebo phenomenon is commonly misunderstood. Placebos are given to prove the patient wrong or to punish him. Nevertheless, most clinical pain can be reduced to at least half of its intensity by placebos. Also cough, headaches, asthma and other ailments can thus be relieved. Explanatory theories are often much narrower in focus than the phenomenon they seek to explain. A Meaning Model could offer new possibilities, as it includes the doctor-patient relationship, belief systems, social support, and feelings of mastery over the symptoms. One way to make such a model visible is the exploration of the deep-seated cultural assumptions about illness in different countries.

Schlüsselwörter

Plazeboeffekt · Arzt-Patient-Beziehung · Situationsrelevante Faktoren · Interkultureller Unterschied

Zusammenfassung

Die vielen Bedeutungen von Placebo

Während der gesamten Medizingeschichte wussten die Ärzte von drei Möglichkeiten, die Beziehung zwischen Behandlung und Heilung zu erklären: 1. den heilenden Effekt der Behandlung selbst, 2. die heilende Kraft der Natur und 3. den Plazeboeffekt. Nach der modernen Definition von Grünbaum gilt eine Behandlung als ein Plazebo, wenn die Wirkung nicht durch die Theorie erklärt werden kann, welche ihre Wirkungsweise beschreibt. Im klinischen Alltag wird das Plazebophänomen häufig missverstanden. Plazebos werden dem Patienten gegeben, um ihm zu zeigen, dass er irrt, oder um ihn zu bestrafen. Dennoch können viele in der Klinik auftretende Schmerzen in ihrer Intensität um mindestens die Hälfte reduziert werden. Auch Husten, Kopfschmerzen, Asthma und andere Unpässlichkeiten können so gelindert werden. Erklärende Theorien sind meist viel enger angelegt als das Phänomen, welches sie zu erklären suchen. Ein Bedeutungsmodell könnte neue Möglichkeiten bieten, da es die Arzt-Patient-Beziehung, Glaubenssysteme, das soziale Umfeld und das Gefühl der Beherrschbarkeit der Symptome miteinschließt. Ein Weg, ein solches Modell aufzuzeigen, ist die Erforschung der tiefstehenden kulturellen Annahmen über Krankheit in verschiedenen Ländern.

History

The role of psychology in medicine is not only a contemporary issue. Jerome Garb, a professor of medicine and chemistry at the University of Leyden, wrote in 1747:

'In his thoughts, to be sure, the physician can abstract body from mind and consider it separately in order to be less confused in the marshalling of ideas. Yet in the actual practice of his art, where he has to do with man as he is, should the physician devote all of his

efforts to the body alone, and take no account of the mind, his curative endeavours will pretty often be less than happy and his purpose either wholly missed or part of what pertains to it neglected.' (Garb, quoted in [48]).

Physicians throughout medical history have been confronted with the problem of explaining why a patient gets better after a particular healing intervention. Besides therapeutic theories, two alternative general explanations seem to have remained from the days of Hippocrates to the present.

One account was the '*vis medicatrix naturae*', or the healing power of nature [43]. It calls attention to the recuperative power of the organism and its ability to restore balanced function in the face of illnesses. Another account could be labelled as the healing power of the imagination. This can be traced back to Plato [37]. It is argued that the positive emotions in the mind of the patient, prompted by the intervention of the physician, and not the specific properties of the treatment, make the difference in the outcome of the disease. Burton wrote in 1621: 'There is no virtue in folk remedies, but a strong conceit and opinion alone, as Pomponatius holds, 'which forceth a motion of the humours, spirits, and blood, which take away the cause of the malady from the parts affected.' ... An empiric often times, or a silly chirurgeon, doth more strange cures than a rational physician ... because the patient puts his confidence in him.' (Burton, 1621/1924, [15]).

In the 18th century, Franklin's inquiry into animal magnetism revealed that the emotional effect of the treatment, and not the postulated physiological properties, accounted for the observed changes [12]. At that time the first definitions of placebo began to appear in medical dictionaries. They reveal an ongoing tension between the '*vis medicatrix*' and the imagination hypotheses in favour of the first to explain why diseases could be cured by bread pills. Placebo, Latin for 'I will please', was taken literally, as a remedy given to please the patient, without any hope that it would exercise curative powers [49].

In the twentieth century the opinion swung over to the imagination camp. It could be demonstrated that placebos could indeed change the natural history of an illness via psychological or psychophysiological mechanisms. In the late 1940s, the double-blind controlled study emerged as the golden standard of medical research, and with it the modern age of placebo research was born.

It has thus only been recently that the placebo effect has been viewed as a variable, open to direct experimental manipulation.

Definition

The definition of a placebo is subject to discussion. A simple solution was to define a placebo as an inert or neutral substance or procedure that elicits a therapeutic response [7, 29, 30, 50].

The problem here is that the sugar pill and penicillin alike have placentogenic efficacy. Penicillin, for instance, can work faster than is pharmacologically explainable.

A detailed discussion of the problems of definition of the placebo was given by Grünbaum. He maintained that the decision whether or not a therapy is a placebo should be related to a disease as well as to a theory about the characteristic effect of the therapy on that disease. In an abbreviated form, Grünbaum's definition held that a therapy was a non-placebo if it could be objectively demonstrated that its effect on a disease depended on its characteristic factors, i.e., if the therapy operated according to the theory that described its activity. If a treatment had an effect that did not depend on the characteristic factors, but on other elements, for which Grünbaum introduced the term 'incidental' factors, then the therapy should be

called a placebo for this disease. Grünbaum's definition calls for process rather than outcome studies in order to empirically demonstrate the non-placebo nature of a treatment [33–35].

Clinical Relevance

In clinical practice the placebo phenomenon is commonly misunderstood. Placebos are often administered to show that there is nothing really wrong and that the patient's purported pain is rather 'all in the mind'.

Placebos may be given not only to prove the patient wrong, but also as punishment, thus not to please but to hurt. Physicians may give placebos to vent their own frustrations at the recalcitrance of patients themselves or their problems [32].

Paradoxically, in doing so they could be helpful. Reviews of 26 double blind studies covering 1991 patients found that 35% had their clinical pain reduced by a placebo to at least half of its original intensity [29].

Placebo effects are not limited to chemical treatments, but include surgical and psychological therapies. In his classical paper: 'Surgery as a Placebo', Beecher [8] investigated the results of the once popular internal mammary artery ligation for angina pectoris. Two independent teams [17, 19], using a single-blind procedure, performed a bilateral skin incision on all patients, and in randomly selected patients the internal mammary artery was ligated. Dimond et al. [19] found that 100% of the non-ligated and 76% of the ligated patients reported decreased need for nitroglycerin and increased exercise tolerance. All non-ligated patients showed improvement for more than 6 weeks, and the patients remained improved 6 to 8 weeks later. Neither the ligated nor the non-ligated group showed any improvement on electrocardiography. Cobb et al. [17] reported that 6 months after surgery 5 ligated and 5 non-ligated patients reported more than 40% subjective improvement. Two non-ligated patients showed dramatic improvement in exercise tolerance, and one non-ligated patient even showed improved electrocardiographic results after exercise. These studies demonstrated that ligation of the internal mammary artery was no better than a skin incision, and that skin incision could generate a dramatic and sustained therapeutic effect.

Placebo effects are not limited to the relief of acute pain. Placebos may be useful in the therapy of cough, headaches, asthma, multiple sclerosis, the common cold, diabetes, ulcers, arthritis, emesis, seasickness, cancer, parkinsonism and other ailments [6, 24, 26, 27, 59].

There seems to be little evidence that the efficacy of placebo therapy can be correlated with a particular personality type [13, 14]. The only consistent findings seem to be that patients who are more communicative, more socially responsive, and more trusting of their physicians seem to benefit more from placebo therapy. Social isolation, scepticism about other people's motives and competencies, and a general sense of uneasiness, doubt and mistrust are reported as significantly more frequent in non-reactors [25, 39].

Theories

Many hypotheses have been advanced to explain the mechanism of the placebo response. Barber [5] and Shapiro [50] favoured a suggestion hypothesis, and Evans [29] an anxiety-reduction hypothesis. Frank [31] and Streubel and Glueck [51] stressed the role of expectancy in potentiating therapeutic response.

Wickramasekera [58] describes the placebo effect as a conditioned response. He proposes that a variety of inert, neutral or non-specific substances, procedures, persons or places can come to function as conditioned stimuli for the alleviation of anxiety, pain, dysfunction, trauma and disease, if such stimuli have been repeatedly associated with the onset of powerful therapies (e. g., penicillin, nitroglycerine, insulin, morphine, etc.) that reliably relieve the symptoms of illness.

Also, placebo effects in animals can be explained in this way. A possible physiological mechanism was suggested by animal and clinical experiments, which showed that endogenous opioid and antiopioid peptides in the brain mediated some types of pain [22, 56]. In a double-blind experiment, patients were given placebos followed by intravenous naloxone after tooth extraction. The naloxone blocked the placebo effect which the subjects had earlier experienced. Naloxone is a partial opioid antagonist that binds the same receptors in the brain as endorphin, the natural opioid neurotransmitter. Later studies, however, contradicted these results. Even if opioids and antiopioids explain some cellular aspects of placebo action, the construct does not explain how symbolic input, that is a thought or an emotion, releases neurotransmitter peptides. Moreover, the neuropeptide hypothesis appears to be valid only for the analgesic effect of the placebo, and not its ability to improve well-being in other ways.

It is stated that an important element of placebo action is faith [44]. The contexts within which placebo effects have been found to be strongest are also those that one would expect to be most faith-enhancing. Doctors perform archaic rituals at hospitals, where amazing cures occur. Investigative, operating and intensive care units are places of limited access. Physicians use tasteless though powerful drugs, they use spectacular machines that whirl, flash lights or emit invisible but powerful rays. Surgeons perform dramatic operations, in which they literally kill the patient to resurrect him afterwards.

The family doctor, however, does not work at a disadvantage. In a classic study, two matched groups of patients facing abdominal surgery received different types of care [28]. The anaesthetist told one group about the operation but did not mention the post-operative pain. He spent more time with the other group, discussed the pain they would experience and assured them that medication was available. The patients who were thus prepared needed only half the analgesic and left the hospital two days ahead of the others. This study shows that the humanity of doctors is a driving force behind the placebo effect, not their medical skill by itself.

Pills and potions are not a necessary condition of the placebo effect. K.B. Thomas, a Southampton general practitioner, investigated the value of placebo prescribing in 200 of his patients. He

identified those patients who had symptoms, such as a headache, vague abdominal pain, backache, sore throats, cough and tiredness, but in whom he was unable to make a specific diagnosis [54]. He created two groups: one group received a 'positive consultation', that is, they were offered a firm 'diagnosis' and strong reassurance that they would speedily recover. The second group was told, 'I cannot be certain what is the matter with you, but if you are not better within a few days please return'. At the end of two weeks, 64% of those who had received a positive consultation were better as compared to only 39% of those who were offered uncertainty.

The Groningen Research Group on Placebo Effects (GROPE) tried to duplicate this famous study of Thomas. A group of 50 general practitioners, trainers of the department of general practice of the University of Groningen, were interested to cooperate in this experiment.

Patients who presented symptoms of cough, belly-ache or back-pain, who had no abnormal physical signs and in whom no definite diagnosis was made, were randomly selected for one of the two consultations. In the first type of consultation the doctor made no diagnosis and gave no positive prediction. In the second type one of three diagnoses was given: Postviral Syndrome (PVI), Irritable Bowel Syndrome (IBS) or Ischias. For reasons of control, we asked the physicians to videotape these consultations. The patients were asked to fill in a questionnaire about their recovery from these complaints and to send it to us two weeks after the consultation. Although we trained the doctors in both consultation modes, the majority found the 'no diagnosis, no prediction' mode too difficult; a minority had problems with the other mode. All of them found videotaping problematic. Finally, only two out of the original fifty participants completed the total of 10 patients per complaint per mode. Although our results point in the same direction as the Thomas study, it is not possible to draw scientific conclusions from these data. Important factors associated with earlier recovery were: a positive prediction and agreement with the patient about the origin of the complaints.

Now, in just assuming that diagnosis, positive expectancy and agreement are the principal behavioural aspects of the placebo effect, we were interested in the opinion of general practitioners about these factors, as well as their appearance in the actual consulting behaviour of GP's. We conducted three studies to investigate this. I will give a brief impression. In the first study, simulated patients and role-playing practitioners were used to produce video-taped consultations with and without the afore mentioned characteristics. We asked doctors to evaluate these consultations. We also asked them whether they used these tactics with their own patients (fig. 1).

We sent questionnaires to more than a hundred teaching doctors (GP-teaching) to obtain their opinion about these modes of behaviour. In addition, we asked them to estimate whether, and how often, they used these tactics (fig. 2).

Finally, we made live videorecordings in the consulting rooms of a group of ten doctors from this cohort to evaluate the behaviour modes in real-life consultations, as well as the reactions of the patients (fig. 3).

It is possible to identify more variables for a theory of the placebo

bo response. White et al. [57] made a summary of the biopsychosocial placeboogenic variables that are known today. The list comprised 30 concepts derived from cultural influences, social-psychological theory, cognitive theory, classical conditioning, and psychophysiology. They state: 'An appreciation of the significance of placebo effects may serve as a departure for an integra-

tive theory leading to a sustained programme of research in which mechanisms will become specified and magnitude of effects will be delimited.'

The placebo phenomenon poses a dilemma: Though there is ample evidence of its existence, there is almost no place where it fits easily and comprehensively within established scientific contexts. Nei-

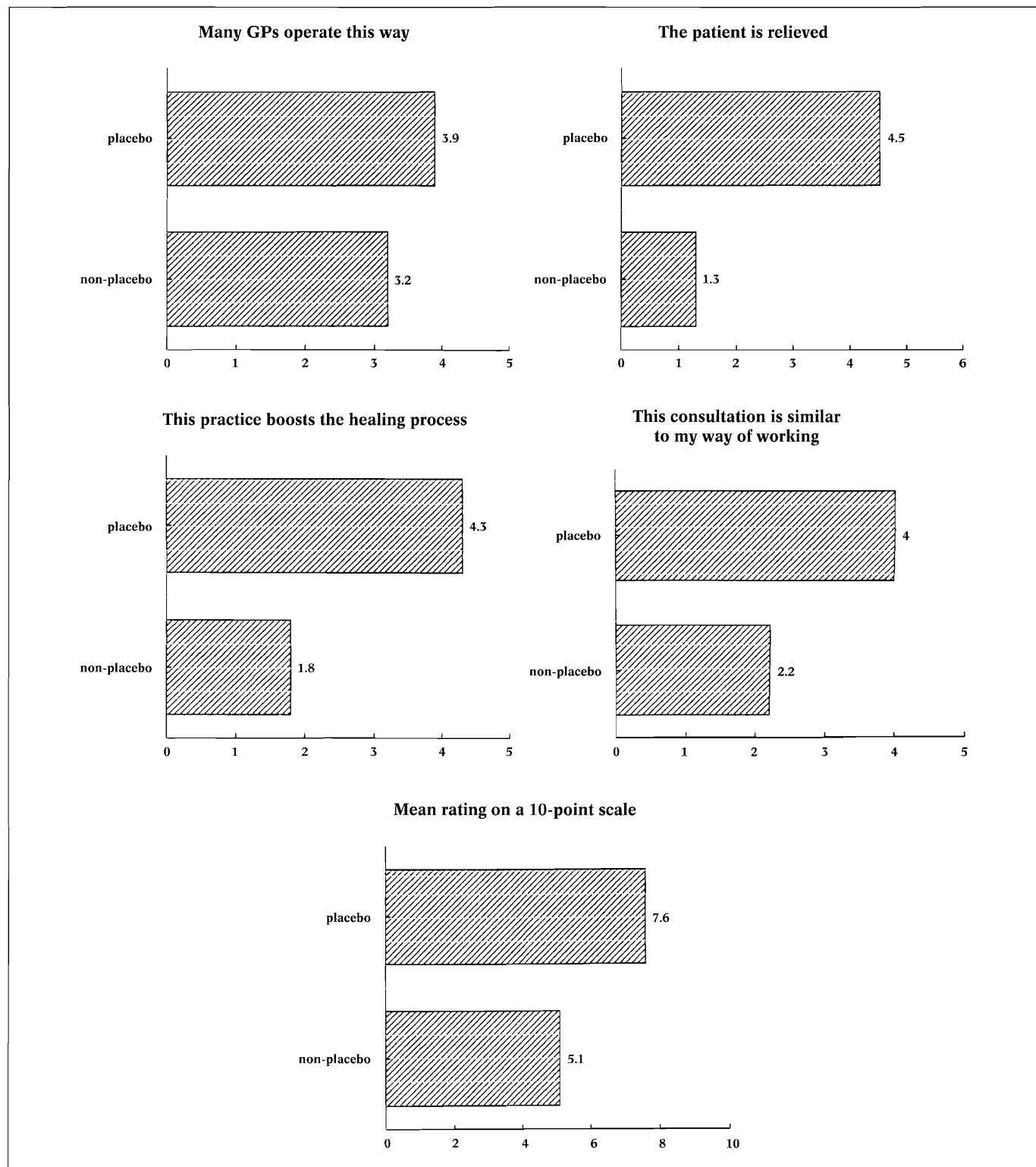


Fig. 1. Evaluation of a simulated consultation by GPs (means on a 5-point scale).

ther is there a satisfactory metaphysical position developed for the mental-physical duality problem. One can, however, argue that this is unnecessary [3]. Progress in science can be made without solving the ultimate questions first. Biology, for instance, has made great progress without solving the problem of what life is.

The Meaning Model

It seems that the placebo effect is a very broad phenomenon, that is in important ways dependent upon the entire context of the physician-patient relationship, including both the cultural as well as the personal belief systems of the two individuals involved.

The explanatory theories that have appeared so far, such as classical conditioning, transference, expectation and suggestibility, are much narrower in focus than the phenomenon they seek to explain.

Two studies of the physician-patient relationship are quoted by Brody [12] in this context [1, 16]. He concludes that they point to a Meaning Model. A positive or negative placebo effect would occur

when the meaning of the illness experience was changed for the patient, in either a positive or a negative manner.

This meaning was postulated to hinge on three major elements. First, whether an explanation was offered that made sense in terms of the patient's accepted world view; second, whether the patient experienced the immediate social group as expressing care and concern; and third, whether the patient achieved a sense of mastery or control over the symptoms or the illness.

In this Meaning Model the distinction between diagnosis and treatment breaks down. Not only is the search for diagnosis itself a form of active response, but it is widely recognised that naming a problem offers the sufferer and his family a degree of control through certainty, that must itself be considered therapeutic. The names of the illnesses change over time. Premenstrual syndrome, chronic Epstein-Barr virus infection and hypoglycaemia are medical reformulations of complaints that in other historical epochs may have been otherwise defined or may not have been defined as requiring active response. The chronic fatigue syndrome, characteristic of the Epstein-Barr infection, is strikingly similar to that associated with neurasthenia in the nineteenth century, but

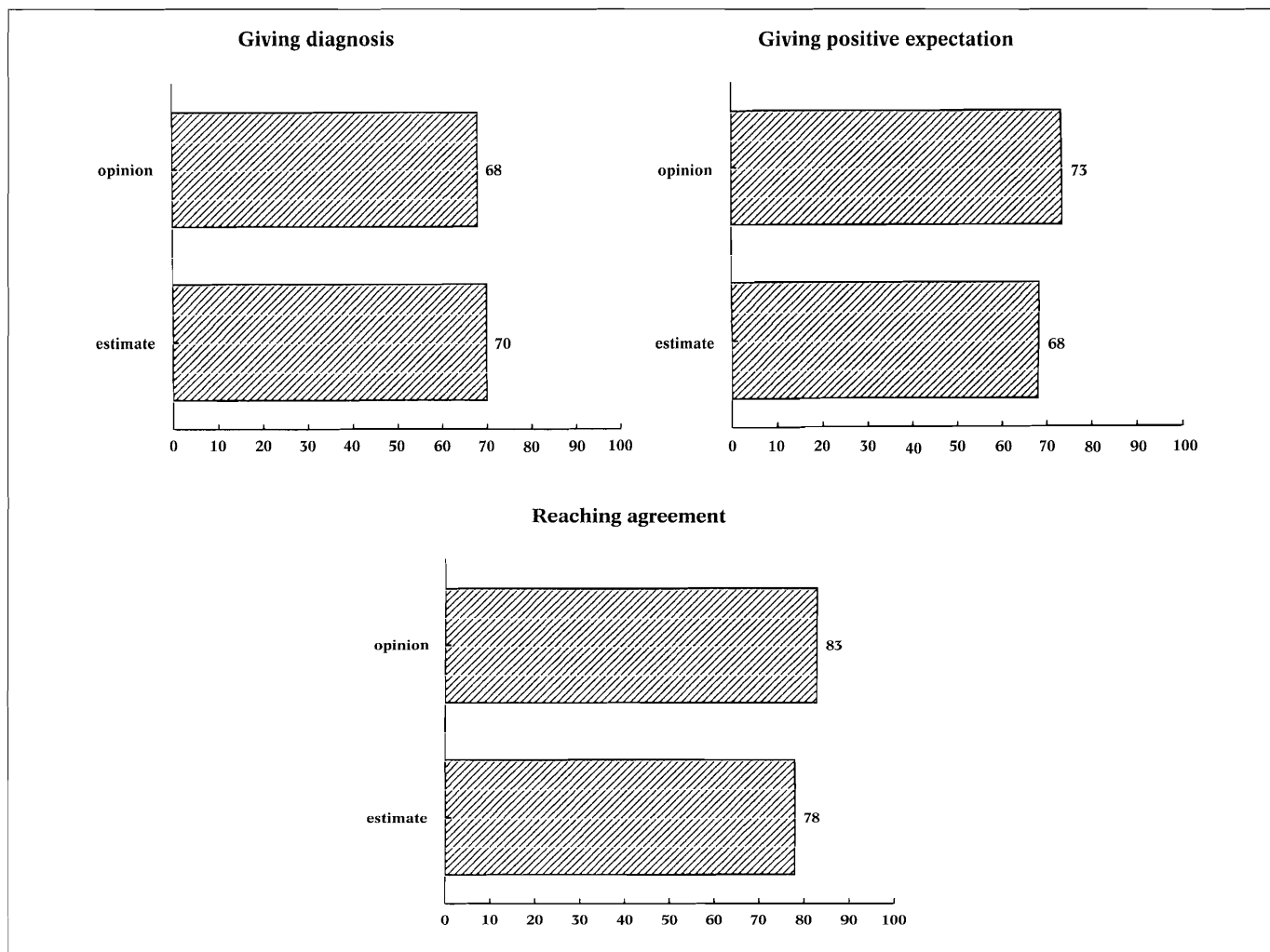


Fig. 2. Estimate and opinion of placebo behaviour (percentage consultations). Estimate: 'How often do you use these tactics?' Opinion: 'How often do you think these tactics are necessary?'

carries a different cultural meaning insofar as it is conceived as a virus infection instead of a nervous disorder. Bulimia, or the binge-purge syndrome, is now identified as pathological behaviour, whereas it was a refined aristocratic practice in the Roman Empire [18].

In the Meaning Model, the therapeutic procedure can be seen as the unfolding of a ritual. For anthropologists the idea of therapeutic process is analogous to the idea of 'rite de passage' [55].

The shaman may go into trance and take a mystic journey to retrieve the soul of the afflicted, or suck on an afflicted part of the patient's body in order to remove an intrusive spiritual object. The psychoanalytic patient is instructed to say whatever comes to mind, and this free association is expected to bring important repressed contents of the unconscious into the scrutiny of the clinical gaze. The surgeon grafts a portion of a vein from the leg into the patient's aorta and coronary arteries, and this coronary bypass is expected to renew the restricted blood flow to the patient's heart. The patient at the temple of Asclepius in ancient Greece offered sacrifices and fell into a sleep during which the god appeared. This 'incubation' was expected to heal the person or reveal instructions to follow for a healing.

A distinction can be made between discursive and presentational forms of therapy [38]. Discursive form is that of language, understood as a succession of interrelated concepts with consistent internal logic and rationality. Presentational form is characteristic of symbol and metaphor, wherein the meanings are simultaneous and integral.

Therapeutic process can be conceived along a continuum between these forms, with, for example, the talking cure of psychoanalysis occupying the discursive pole and healing based on electroconvulsive shock therapy occupying the presentational pole.

Moerman [41] defines treatment empirically as a field of symbols perceived by the patient, created by a healer in terms of the relationship between mind and body, symbol and substance. He cites research on psychosomatic illness, biofeedback and immunology, as well as links among the body's neural, endocrine, and autonomic systems, to suggest not only the existence of pathways linking body and mind, but that these pathways are the locus for broad-based influence of metaphor and symbol on biological processes.

The placebo effect can thus be understood as an effect of interpersonal communication, activating endogenous healing processes [36, 42, 47].

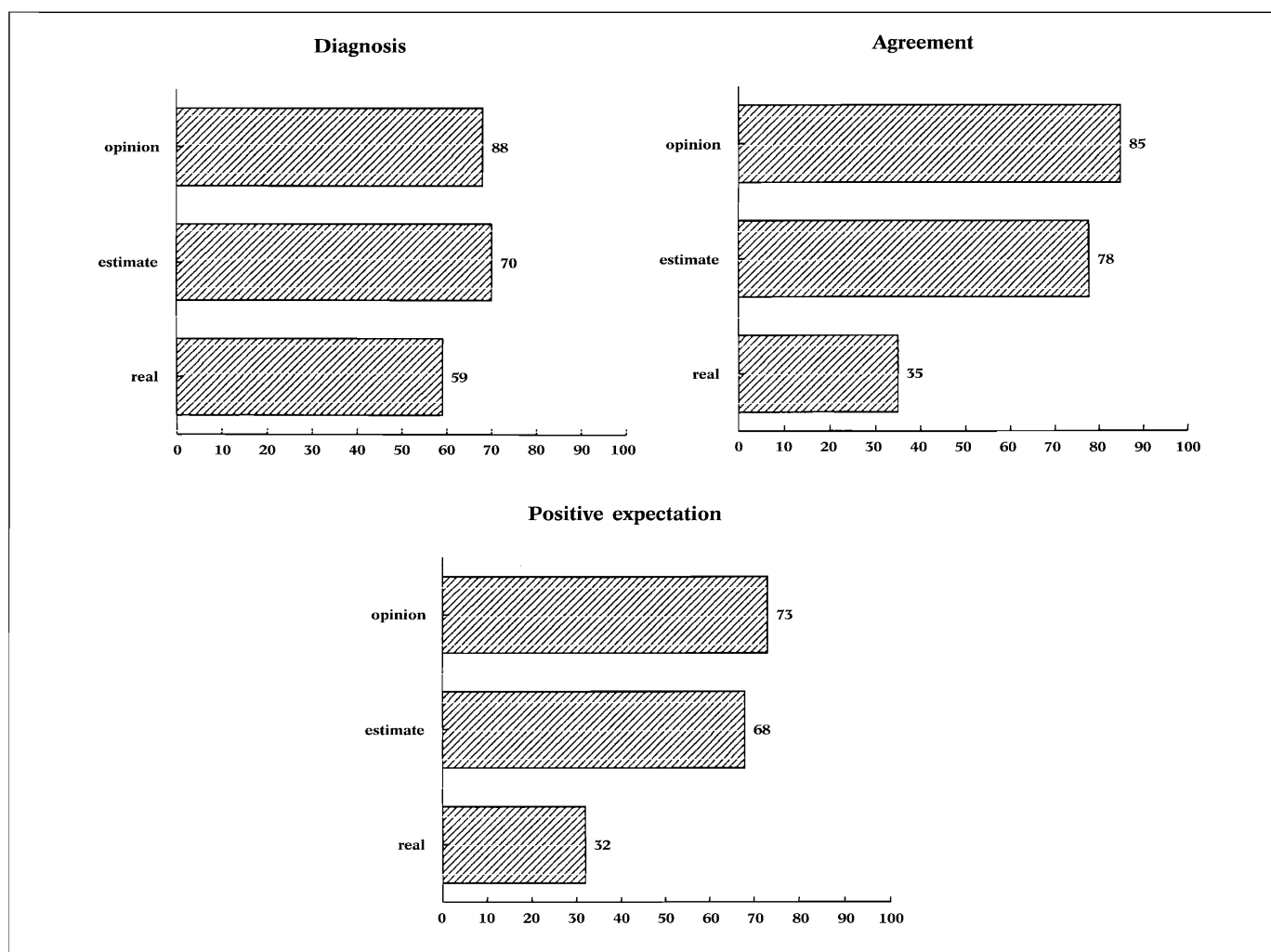


Fig. 3. Opinion, estimated and real use of placebo-consultations (percentage consultations).

In Western society, biomedicine is generally believed to operate in a realm of facts. This realm is often perceived to be quite separate from other cultural and social domains. 'To a degree perhaps unique to segmented Western society, the participants of this biomedicine emphatically distinguish their medicine from other aspects and institutions of their society. Illness is thought of as a 'natural' occurrence' [36]. Given this assumption that nature and the body exist in a directly apprehendable realm of fact, the problem for a cultural analysis of the placebo effect is vast. As Martin points out [40], it takes a 'jolt' to see the 'contingent nature' of biomedical description.

Several recent explorations of biomedicine undertake specific and deliberate strategies to provide this jolt by making visible the culture of medicine. One strategy is historical contextualisation, highlighting the 'arbitrariness of institutions' [21].

Another strategy is to uncover, through analysis of metaphor, ways in which social meaning is embedded in biomedical categories [2]. For instance, it can be enlightening to compare the differences in theories of illness in various European cultures [45].

In the Meaning Model, a shared world view between healer and patient is necessary. This is very important, as the healer must be able to name that which is wrong with the patient. In some cultures 'catching a cold', in others 'violation of a taboo', are believable as the cause of an illness. This is called the principle of Rumpelstiltskin of diagnosis.

In the studies of Grimm [23] this principle illustrates the magic of the right word. Even in the Western world there are big differences to be distinguished in diagnoses that will reassure the patient.

A liver crisis will reassure a French patient, while it would alarm an American one; the diagnosis of 'a virus' would probably have opposite effects on each. The vague digestive troubles that the French would call a liver crisis, is a food allergy for doctors and patients in the United States. In Germany, there is no word for 'chest pain', only words for 'breast pain' and 'heart pain'. In fact, heart pain is the seventh most common reason for contact with general practitioners in Germany, resulting in the diagnosis '*Herzinsuffizienz*'. As a result, the Germans use about six times the amount of heart drugs as do the French and the English. The American, on the other hand, regards himself as naturally healthy. It therefore stands to reason that if he falls ill, there must be a cause for the illness, preferably one that comes from without, and which can be dealt with quickly, like a bacteria or a virus. The doctors share the belief that disease is some wild and hairy monster to be locked up in the neat medical grids of differential diagnosis and treatment. The idea that disease must be caused by something in the environment, probably a germ, can explain the American penchant for cleanliness.

When the patient accepts the explanation that makes sense in his world view, his expectations are influenced positively. Feelings of hope and trust are generated. Again, the meanings of these feelings are different.

Each culture has its distinctive ways of looking at health and illness. In some cultures, like in France and Germany, there seems to be more trust in the body. In the Anglo-Saxon world, fighting the bad forces from the outside takes preference.

The 'fragile liver' in France, as opposed to a liver being over-

whelmed by food and drink, illustrates the importance of the '*terrain*' in French medical thinking. As a translation the word 'constitution' may be used. While the English and the Americans tend to focus on the insult, the French and Germans focus on the reaction, and are more likely to try and find ways to modify the reaction as well as fight off the insult.

Focus on the terrain shapes French and German medicine. It skews drug consumption away from antibiotics, which fit the English and American theories of disease as an invader, towards tonics, vitamins, and more recently towards ways to stimulate the immune system.

In the social system of the patient the doctor plays an important role. As a rule healers around the world have personality characteristics that are admired in their culture. Physicians in all countries tend to be authoritarian, but they may in fact be even more so in Germany. When German doctors were asked what their patients usually thought was wrong with them, they replied that German patients did not think anything because they had been taught it's not up to them to make the diagnosis. Dutch research [10] shows that a combination of clinical competence and empathy are benevolent.

The third basic component of the Meaning Model of the placebo effect is an acquired sense of mastery, i. e. the knowledge, competence, insight and understanding necessary to master life's adversities, be it in the form of a virus or an ancestral spirit.

This knowledge is also culturally determined. In France even serious infections are not taken that seriously, because one trusts the power of the *terrain*. Also in Germany, doctors consider that the body can get rid of a fever on its own. In the States, however, a patient feels more confident with an aggressive therapy.

In the classic concept, the placebo is seen as a process whereby the patient is made feel better after taking an inert potion given by the doctor. As we have seen, this is not strictly true. The placebo effect can be produced by any action intending to heal. It has been shown [52] that a consultation in which no treatment is given can have healing effects. Also a procedure, such as admission to a hospital ward, or any contact between doctor and patient, even a few words exchanged in the street [53], can produce these effects.

The real importance of the placebo at present and during the thousands of years of medical history is that it demonstrates the power of the doctor to make the patient feel better.

Since much of the success of medicine, and to some extent the success of surgery, depends upon the placebo effect, it is puzzling that medical textbooks have little or nothing to say on the subject. Perhaps 'the giving of the placebo seems to be a function of the physician, which like certain other functions of the body, is not to be mentioned in polite society' [46]. Most probably it represents a reluctance within the profession to face an embarrassing reality.

A better appreciation of this power would change doctors' attitudes and would result in the making of less illness, the prescribing of less medication, and a better understanding by the patient of his condition.

In 1957 Michael Balint wrote his widely known book '*The doctor, the patient and his illness*' [4]. He claimed that the most important drug in medicine was the doctor himself.

Now we know that we can split this drug into three parts: the world view of the doctor, which he has to share with his patients and which gives him the ability to enhance the expectations of the patients; the social group, including the doctor; and last but

not least, as Jerome Frank argued in 1974 [20], the power to change the patient's image of himself, from a person who is overwhelmed by his symptoms to one who can master them.

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