

Beyond the placebo:

understanding the therapeutic context

THE DOCTOR DRUG

An old but still relevant study by Thomas, conducted in 45 different general practice settings, explored 200 British patients in whom no definite diagnosis could be made. All patients were randomly selected for one of two procedures: either they were given a symptomatic diagnosis and medication, or they were told that no treatment was required as there was no evidence of disease. No differences were found in outcomes with respect to reported symptoms and number of new contacts to the GP within a month.¹

Thomas later wrote in the *Lancet*:

*'The placebo effect in general practice is the power of the doctor alone to make the patient feel better, irrespective of medication. It is one of the most important factors in the consultation, yet generally it is neglected, unrecognized, and untaught. A better appreciation of this power would change doctors' attitudes to the consultation and would result in the making of less illness, the prescribing of less medication, and a better understanding by the patient of his or her condition.'*²

CONTEXT IS THE PLACEBO

More than ever, Thomas's study and the statement are relevant. New research has documented the therapeutic power of placebo defined as the effect of the meeting between the doctor and the patient, and the context in which the specific treatment is given.³⁻⁵ Nevertheless, three major obstacles seem to prevent a more targeted use of the placebo effect in general practice.

The first obstacle is the term 'placebo'. In basic scientific training, we learn that placebo is inert: a fake pill or something to do with deception. This impact must be eliminated when we study the specific treatment effects. We do not like to be 'merely' placebo physicians. Yet, the goal in daily clinical practice of ensuring maximum symptom alleviation is gained as a result of both specific evidence-proven treatment and non-specific context-mediated factors, including the impact of the interpersonal encounter between the doctor and the patient.³ Therefore, it might be better to simply forget the word 'placebo' and replace 'placebo effect' with 'context-mediated effect' when we define this effect or describe the effect of the total care experience

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encompassing the treatment, for instance, the specific effect of analgesics.^{4,5}

SYMPTOMS AND THE BRAIN

The second obstacle is the lack of clarity and precision with respect to where context should, or should not, be used as a relevant treatment modality. Obviously, we cannot treat a severe infection, a fracture, a cancer, or any other biological failure through context-mediated factors. Let us appreciate the progress in high-tech treatment within modern health care. However, the main focus of most treatment, especially in general practice, is alleviation of symptoms, including symptoms caused by (mechanical) biological failures. But symptoms are complex. They are influenced by culture and personal factors, and appear as the result of conscious and non-conscious emotional and cognitive processing of cerebrally perceived signals. These may be expressed as pain, nausea, tiredness, dizziness, anxiousness, depression, and several other conditions in which cerebral signal processing is an essential part of the expression of the disease. We treat the diseased organ with evidence-based drugs and procedures, but the primary focus is to treat the patient who experiences symptoms caused by a diseased organ. Often, we may even treat symptoms without being able to identify the presence of a specific disease.⁶ Symptoms are strongly modulated by the patient's expectations and beliefs, and the clinical context surrounding the specific treatment. Essential components of the total context are the doctor's attitude, especially his or her communication skills, the doctor-patient relationship, the way the doctor

applies therapeutic procedures or rituals, and, ultimately, the doctor's ability to create trust.³⁻⁶

RESEARCH IN SYMPTOM PROCESSING

The third obstacle is a severe lack of translational research in cerebral processes and ways to manipulate these. Over the past 20 years, much empirical research has shown impressive symptom-modulating effects, not only from the placebo pill, but also from the context surrounding the encounter between patient and therapist (including therapists practising complementary and alternative procedures, for example, acupuncture).^{4,5,7} In addition, new types of scanning technology have allowed us to study the biological processes in the brain intensively during the past 10 years, and these processes have been demonstrated to be strongly influenced by a variety of contextual factors. The biological processes and the variations in the context-mediated effects in the brain have now been scientifically proven.⁷

For decades, clinicians have known that drugs can influence brain processes. It is now time to realise in clinical practice that placebo, or context, in the modern and broad definition of the concept, may influence brain processes — and thereby also the experienced symptoms — just as much, or possibly even more, than symptom-alleviating drugs. It is also time to realise that doctors may actively modulate the total context surrounding the encounter with the patient. The next step is to realise that 'nocebo', the opposite of placebo, understood as anxiousness, mistrust, and lack of relationship or contact, may aggravate symptoms and thus outperform,

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in part or in total, the effect of, for example, analgesic drugs.⁸

NOCEBO

The recent development in the field has considerable implications for our understanding of the importance of continuity and patient involvement in the complicated clinical pathways that characterise modern health care. In particular when the aim is also to ensure appropriate management of symptoms and not only to repair a (mechanical) organ failure. The new understanding also has implications for the way we inform patients about possible side effects of drugs and treatment, where nocebo effects may be induced; most people tend to experience more severe symptoms if the clinical encounter or setting fosters mistrust, anxiousness, and lack of continuity.⁷⁻⁹

MEDICAL TRAINING

General practice will be particularly affected by this new understanding. The placebo effect, or the context-mediated effect, also referred to as the ‘doctor drug’, forms a crucial part of daily clinical symptom management in general practice, where the goal of maximum symptom alleviation is based on a combination of randomised controlled trial-documented treatment and the doctor drug. We must use these effects wisely and precisely — and we must train doctors to do so.

The pre- and post-graduate teaching community is currently facing a challenge to convey this message and to train students and young doctors in the use and dosage of these effects. Young doctors should learn about the scientific evidence base of context-mediated effects, including their clinical limitations. We must make doctors aware of the negative associations that are incorrectly attached to placebo.

CLINICAL RESEARCH

The new knowledge about context-modulated symptoms has important implications for all clinical research. The classic randomised controlled trial, where we try to eliminate or neutralise the placebo effect, has severe limitations when it comes to trials for which the outcome measure is perceived symptoms as these

are modulated in the brain. The processing of symptoms is influenced by the patient’s daily life and the context in which treatment is given. Experimental effects may be very different from effects in daily life. Context and its effect are a hidden and often uncontrolled part of the intervention, which may cause severe positive or negative bias when we attempt to translate efficacy studies to daily clinical practice. Are producers of Cochrane reviews and so-called evidence-based clinical guidelines fully aware of these limitations in the current research designs, for instance, when procedures are recommended or the effect of antidepressants are discussed?^{7,10}

Efficacy studies cannot always simply be translated into daily clinical practice. The clinical research community in primary care needs to create elegant studies that can identify and document the best ways to precisely use the context-mediated effect in combination with specific treatments in ordinary clinical practice.^{5,7,10}

CONCLUSION

The time is ripe for a stronger promotion of research and training on symptom interpretation and treatment based on our current knowledge about context-mediated symptom modulation.

The core message is that we now have a scientific understanding that can explain the observations experienced by doctors since Hippocrates; the power of the encounter between doctor and patient should not be ignored.^{3,6} We are finally ready to translate Thomas’s wise words into research, teaching and daily clinical general practice.²

Frede Olesen,

Professor, University of Aarhus, Research Unit for General Practice, Aarhus, Denmark.

Provenance

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ADDRESS FOR CORRESPONDENCE

Frede Olesen

University of Aarhus, Research Unit for General Practice, Vennelyst Boulevard 6, DK-8000 Aarhus C, Denmark.

E-mail: fo@feap.dk

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