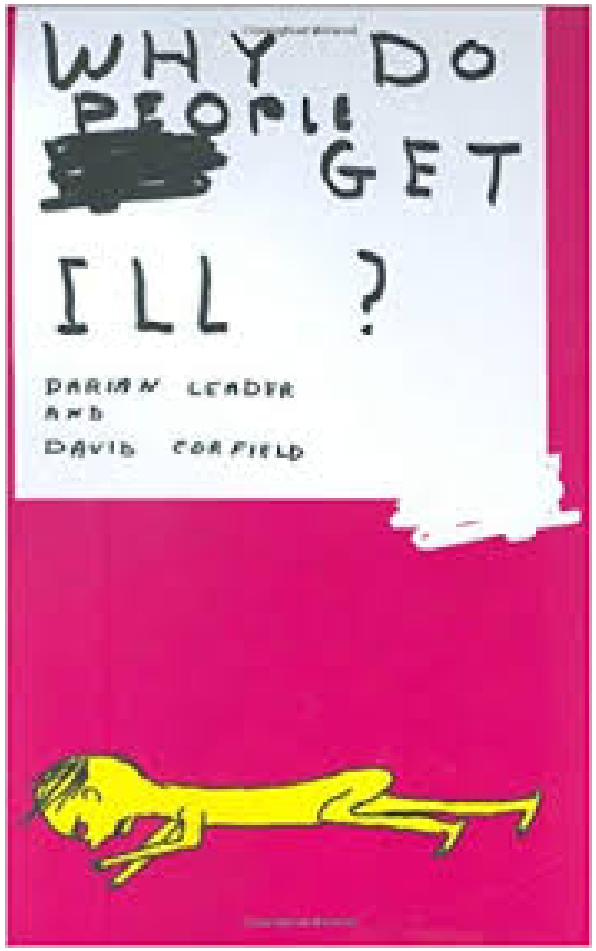
Health methodology and the psychosomatic approach to medicine

11 June, 2019

Why do people get ill? Hamish Hamilton 2007



The term ‘psychosomatic’ qualifies an approach to medicine, rather than a kind of illness.

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It turned out that as a 9 or 10 year-old boy, he had been whipped for the offence of peeking through the window of a girls' dormitory. The recurrence of these lesions ten years later took place immediately after he had been apprehended loitering on the grounds of the nurses' dormitory at the military post where he was stationed. He had hoped to see a nurse he was interested in, but was caught by an officer and reprimanded. Within an hour the skin lesion had developed.

- Plausible story.
- Highly particular detail, but with some generalisability.
- Far from amenable to testing by double-blind RCT.

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- Decades of research on hypnosis, especially on skin disorders, including warts.
- Older idiographic work in the "psychosomatic" tradition, continued by, e.g., Nick Read in *Sick and Tired* (though largely limited to 'functional' illnesses).

There are plenty of reasons to be critical of RCT-methodology, not least its conceptualisation of the *placebo effect*.

First, let's see how dangerous they can be, even the placebo wing.

Overdosing on placebo

Mr. *A* was pale and diaphoretic with a blood pressure of 80/40 and heart rate of 110. He was tremulous, and respirations were rapid. Examination was otherwise unremarkable. An intravenous line was inserted, blood drawn and infusion of normal saline begun. Acetaminophen and salicylate levels were zero, urine drug screen was negative and other laboratory studies were within normal limits. After receiving 2 L of normal saline, blood pressure rose but again dropped when the infusion was slowed. Over 4 h, he was given approximately 6 L of fluid. He remained lethargic with a blood pressure of 100/62 and heart rate of 106. At this point, a physician from the clinical trial arrived and determined that Mr. *A* had taken placebos. When informed of this, the patient expressed surprise then almost tearful relief. Within 15 min, he was fully alert, blood pressure was 126/80, heart rate was 80. (Reeves, R. et al. 2007)

Howick on placebos

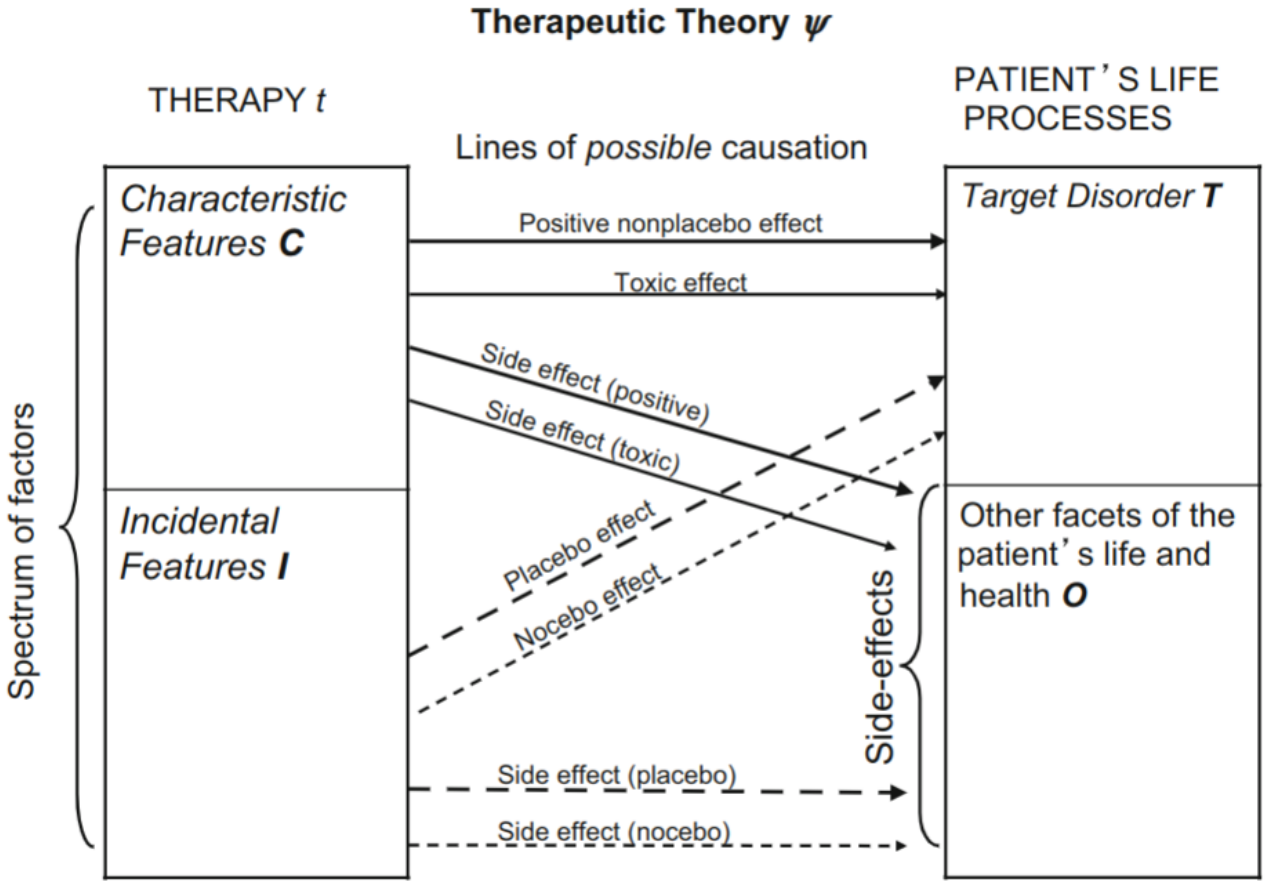

Fig. 3 Revised illustration of the therapeutic theory, used in clarifying definitions of 'placebo', nonplacebo, harmful intervention, placebo effects, and nocebo effects

Placebo effect: a placebo effect is either (a) one produced by the incidental features of some treatment (even when the treatment as a whole is a nonplacebo), or (b) any effect of a generic placebo (treatment process for which none of the characteristic treatment factors are effective (remedial or harmful) for the disease).

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The therapeutic theory is needed to say which components are characteristic. Then we design trials so that both arms share all the incidental features.

Theoretical decisions

- In acupuncture, is pressure on the skin characteristic?
- In psychotherapy, is the supportive manner of the therapist characteristic?
- In surgery, is making an incision in the relevant place characteristic?
- When prescribing medication, is a positive attitude towards it characteristic?

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Is it justified to believe that subtraction works?

Real open − Placebo open = Real hidden − Placebo hidden

Lancet. 2010 February 20; 375(9715): 686–695

Cholecystokinin antagonist proglumide was shown to be better than placebo, which was in turn better than no-treatment for post-operative pain. According to methodology used in classical clinical trials, these results would indicate that proglumide is a good analgesic which acts on pain pathways, whereas placebo reduces pain by activating placebo analgesic mechanisms (through expectancy pathways).

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However, this conclusion proved to be erroneous, as a hidden injection of proglumide was completely ineffective. If the drug was an effective modulator of pain pathways, such a difference between open and hidden administration should not be seen. In this instance, the drug achieves a response by interacting with and enhancing placebo mechanisms (expectancy pathways), not by acting on pain pathways, and therefore it is only effective when combined with the placebo mechanisms inherent in the clinical encounter.

All too linear?

A patient has been invited onto the trial, its protocol is explained and a pill is given.

Features: *Ingredients of pill, being entered for the trial, the way the pill is spoken about and delivered, location, the way patients' concerns are received, bulking agent, colour and size of pill, side effects, amount of deblinding for patient and staff,...*

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What if small nonplacebo effect could be responsible for large placebo effect through such a feedback loop?

Few studies report whether blinding is successful.

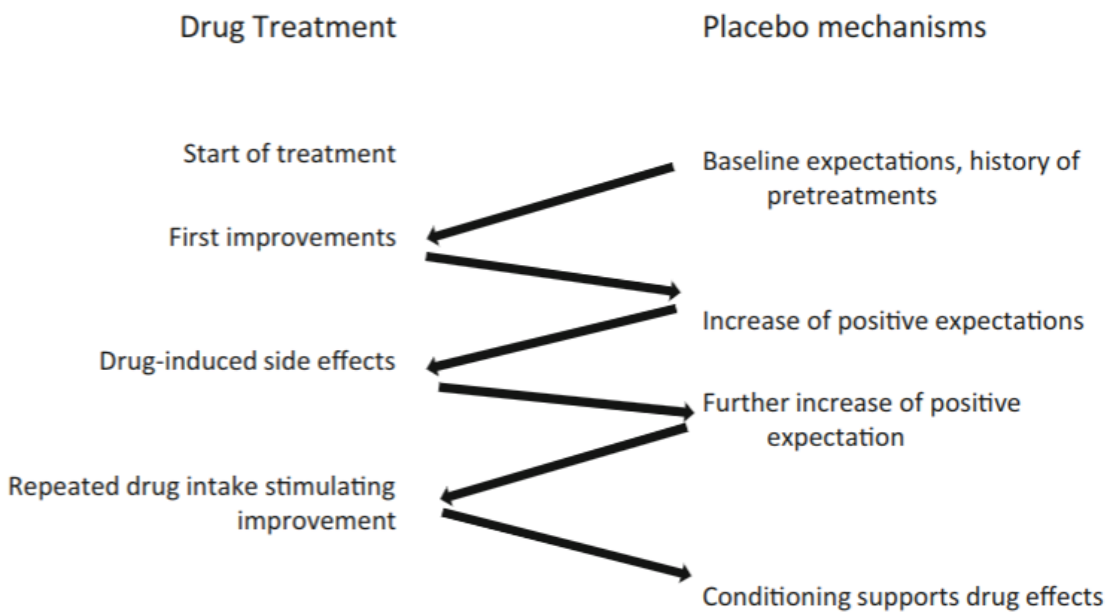
Out of 300 studies, twenty-four trial publications explicitly reported the risk of unblinding, of which 16 publications reported compromised blinding; and 8 publications intact blinding. The reporting on risk of unblinding in the 24 trial publications was generally incomplete. The most common mechanism for unblinding was perceptible physical properties of the treatments, for example, a difference in the taste and odor of a typhoid vaccine compared with its placebo. (Bello et al. 2014)

Some point out that correct hunches about trials may result from the real effectiveness of a drug, as though this is only an effect not a cause and so the deblinding unproblematic. But why can't there be a feedback loop?

Some studies suggest the whole verum/placebo difference is due to successful guessing. (p. 299)

Dynamic model – Doering et al.

Fig. 1 Complex interaction of placebo mechanisms with specific treatment effects. Therefore, in this example, nonspecific effects in placebo and drug groups can differ



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Pain systems (endogenous opioid, endocannabinoid), autonomic nervous system, endocrine system, immune functioning, dopamine system, cardiovascular system, gastro-intestinal system (gastric, bowel motility), and pulmonary functions can be affected by placebo interventions.

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"The phenomenon of learned placebo responses in neuroendocrine and immune functions is a fascinating example for the communication between the brain, the endocrine, and peripheral immune systems." (Wendt et al. p. 172)

Benedetti, F. et al. (eds.) 2014. Placebo, Handbook of experimental pharmacology 225, Springer.

Even the heart

"After the completion of routine diagnostic catheterization, patients with biomarker-negative chest pain were randomized to either a verbal suggestion group or a control group and received an intracoronary saline injection via the catheter. Only in the verbal suggestion group, however, patients were informed by the cardiologist that a pharmacological drug to improve coronary perfusion was going to be administered.

Patients and physicians were blinded with regard to the study medication. Angiograms were performed immediately before and after the intervention. In addition, blood pressure and heart rate were repeatedly assessed, and patients were asked for acute chest pain and perceived stress just before and after the coronary injection. Remarkably, the coronary diameter was significantly affected by the verbal suggestions. Contrary to our expectation, however, we observed a coronary vasoconstriction in the verbal suggestion group as compared to controls.

This vasoconstriction was accompanied by a reduction of chest pain. This study was the first to show a direct placebo response on the coronary arteries. The pain reduction in the verbal suggestion group indicated a positive expectation toward the "drug." The coronary vasoconstriction could not be explained by stress, since heart rate, blood pressure, and perceived stress did not change differentially between groups. Possibly, the verbal suggestions reduced the sympathetic outflow to the coronary arteries, thereby reducing oxygen demand, and thus coronary perfusion (Ronel et al. 2011)" (Meissner, 189).

Is RCT ideology behind the restriction to conditioning and expectancy?

Is it that we must restrict ourselves to existing RCT techniques to establish efficacy of 'placebo' features now taken as characteristic, and only expectancy and conditioning provide suitable cases for RCT exploration?

Then, only this RCT evidence warrants placebo intervention?

Alfano

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Or, for a broader, integrated approach, go 'Continental' – Frenkel, Ongaro-Ward.

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- RCT-methodology is blinkering. Take seriously a wide range of forms of evidence, even idiopathic.
- An opportunity to rethink the body-mind relation.