The Nocebo Effect: Impact, Mitigation and Prevention.

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Abstract

The nocebo effect is the induction of a symptom perceived as negative by sham treatment and/or by the suggestion of negative expectations. Recent evidence has mounted in support of the notion that the nocebo effect may be influenced by themes of language used by healthcare practitioners. The importance of the nocebo effect may be exaggerated in the chronic disease population, particularly in those at an advanced age. Using a clinical vignette to illustrate, this piece elucidates the nature of the nocebo effect in practice and explores potential areas of future consideration for physicians and physicians–in–training.

Consider the following scenario: patient GS, a 25–year–old male, receives a radiograph of the right hip and pelvis for sharp pain. The pain resolves without intervention shortly thereafter. The radiograph, however, captures the lumbar vertebrae and shows mild osteoarthritic–type changes in the L3-4 and L4-5 disc spaces. GS has no history of back pain and is active, well–muscled, and otherwise healthy.

In the interest of disclosure, his general practitioner explains that the radiograph demonstrated evidence of osteoarthritis, an irreversible, degenerative joint condition that causes pain and joint stiffness. GS, considerably more anxious than when he arrived, leaves without much further explanation. Two weeks later, when friends ask GS to go on a long hike—similar to ones they've done before—GS is hesitant and eventually turns down the invitation, fearing aggravation of the "joint problems" his doctor told him about. What has happened?

Amongst a host of other potential reasons for his refusal, the general practitioner's language may have primed GS to experience the nocebo effect.

Closely related to its cousin the placebo effect, the nocebo effect is the induction of a symptom perceived as negative by sham treatment and/or by the suggestion of negative expectations.[1] In other words, patients may perceive what they expect to perceive, either positive (placebo) or negative (nocebo).[2] To illustrate, a 2010 study demonstrated that using gentler, more reassuring language to describe pain during local anesthetic administration (e.g., "We are going to give you a local anesthetic that will numb the area and you will be comfortable during the procedure") was associated with significantly less patient–reported pain compared to the traditional preamble (e.g., "You are going to feel a big bee sting; this is the worst part of the procedure").[3]

Given that language can palliate or potentiate the nocebo effect, it is reasonable to postulate that the words physicians and physicians–in–training use may have tangible effects on a patient's behaviour, expectations, and subsequent clinical outcomes.[4,5] Building off of emerging evidence, physicians must ask themselves: how can we minimize nocebo–induced harm?

In the current evidence–based practice model, healthcare practitioners must be cognizant of potential biases in interpreting evidence. Certain study designs may not provide the insight required to deduce or predict an individual patient's disease history.[6] Thus, projecting a biased interpretation of evidence may only serve to worsen patient experience, since individuals may exhibit disease without symptoms or symptoms without disease. This may prove especially difficult for medical students, who are bred in a preclinical system of automatic association between symptom and disease.

Furthermore, it is essential to recognize that a patient's disposition and situation may affect his or her interpretations of medical counseling. Is this patient generally anxious at baseline? Is the patient already living with a substantial disease burden? Did the patient lose a parent to the condition the physician is speaking about? For some patients, enumerating all potential adverse effects of a medication may be more harmful rather than informative. As the medical profession becomes increasingly patient–centered, physicians must reconcile their obligation to provide nonbiased information with an understanding that patients often present to physicians for their opinion and guidance above all else. Indeed, perceptions and expectations of pain and/or other symptomatology generally predict an increase in frequency and severity thereof.[7,8] To accept this may be to accept that ethical practices such as informed consent may need to be contextualized within the confines of an individual patient's needs, rather than viewed as absolute and uniform for all patients, as highlighted by the questions above.[9]

Patients with chronic disease, particularly those at an advanced age, may be especially susceptible to the effect of "nocebogenic" language. While skipping a hike with friends may not precipitate any long–term sequelae for GS, a reluctance to engage in biweekly walks to the grocery store may be tremendously impactful for the otherwise sedentary, sarcopenic, 76–year–old woman with hypertension, chronic kidney disease, and diabetes, whose radiograph looks like that of GS. This clinical picture vividly illustrates the importance of encouraging patients to maintain self–efficacy and activity in light of a potentially morbid diagnosis. A physician's language, thus, must foster and encourage a patient's sense of self–efficacy and autonomy to optimize outcomes.[10,11]

The argument here is not that physicians should aim to withhold information about patients' health conditions or taint patients' perceptions with rose–coloured glasses. Rather, physicians should aim to present information so as not to disproportionately limit patients, thereby maximizing their potential and improving or maintaining quality of life reliably. Projection of negative expectations about a patient's course may engender confirmation bias and subsequent behaviour modification that ultimately worsen the patient's clinical outcome in accordance with the physician's original and not entirely reasonable expectations. Prevention begins with the recognition that physicians can "nocebo" patients into symptoms that were previously absent.

Returning to the clinical encounter, one can recognize how the suggestion of negative expectations may have rendered GS unnecessarily fearful, anxious, and hypervigilant of osteoarthritic

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symptoms, causing a modification in behaviour that, unbeknownst to GS, may precipitate the symptoms that do not yet exist. By contrast, the same 10–minute office visit may have been better spent reassuring GS that the correlation between osteoarthritic symptomatology and radiographic evidence is imperfect and does not represent the constellation of patient experiences, and that weight–bearing exercise can reduce the symptom burden associated with osteoarthritis.[12-14] This dialogue is considerably less likely to "nocebo" GS into excessively precautious behaviours that will not improve his prognosis. Further, if GS's condition did truly require lifestyle modifications, informing him of these would not constitute a nocebo.

While the cognitive processes affecting a patient's decision–making are complex and multifactorial, the nocebo effect can play a key mediatory role. Mitigation of "nocebogenesis" requires subtle but significant modifications in the explanations physicians provide to their patients; focusing on self–efficacy, autonomy, and maintenance of existing healthy behaviours makes for a win–win for the patient and the physician. Nonetheless, the burden of action remains in the hands of the individual physician, be he or she a family practitioner or a general surgeon.

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