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A REVIEW ON THE SCIENCE OF NEGATIVE EXPECTANCY EFFECT EVIDENCE AND CLINICAL RELEVANCE THE NEGATIVE NOCEBO EFFECT

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ABSTRACT

The nocebo effect is a clinically important phenomenon in which negative expectations, previous experiences, or beliefs about a treatment contribute to the occurrence or intensification of adverse symptoms, independent of the treatment's pharmacological action. Increasing evidence suggests that nocebo responses have a substantial influence on patient outcomes by increasing the reporting of adverse effects, reducing treatment adherence, and limiting therapeutic success. This review examines the underlying psychological and neurobiological mechanisms responsible for the nocebo effect, including expectancy, conditioning, observational learning, anxiety, and stress-related pathways. It also discusses the role of healthcare communication, informed consent, and the therapeutic environment in shaping patients' expectations and influencing clinical outcomes. Research from experimental studies and clinical trials demonstrates that negative information and poor communication strategies can significantly increase perceived side effects and contribute to premature discontinuation of treatment. Recognizing the impact of nocebo responses is essential for healthcare professionals to optimize patient care, improve treatment compliance, and maintain ethical standards while providing accurate medical information. Greater awareness of this phenomenon can support the development of communication strategies that minimize unnecessary harm while preserving patient autonomy and informed decision-making.

KEYWORDS: Nocebo effect, negative expectations, adverse drug reactions, patient communication, treatment adherence, placebo, anxiety.

1.INTRODUCTION

Laboratory research on the nocebo effect — which refers to harmful effects caused by expectations — has shown that this is a neurobiological phenomenon that can lead to measurable changes(1) in the body and result in negative health outcomes.In clinical trials that compare treatments with placebos, patients who receive placebos often report side effects similar(2) to those experienced by patients receiving actual treatment.These side effects may be due to the way potential adverse effects are communicated during the informed consent process. (3) The nocebo effect is not only about negative reactions to inactive treatments, as seen in placebo-controlled trials and lab experiments. It can also happen in clinical practice when patients have negative expectations about possible side effects of prescribed treatments (4). For example, informing a patient that a drug might cause a side effect can lead to the same side effect occurring, regardless of the drug's actual properties. In this article, the term "side effect" refers to any signs or symptoms that are not the intended effect of the treatment. Just as positive aspects of the (5-8) clinical interaction can be beneficial, negative elements in the clinical encounter can lead to nocebo effects. In everyday medical practice, these effects can arise from interactions between healthcare providers and patients, as well as from the overall psychological and social environment the patient is in Negative outcomes may also be linked to how serious illnesses and their prognosis are communicated, as well as the (9,10) sources of health information. This article focuses on nocebo

effects that occur during the sharing of medical information in clinical settings. After briefly covering some methodological aspects and key findings from research on the mechanisms of the nocebo effect, we will examine clinical research that explores the relationship between negative expectations — including social, psychological, and behavioral factors — and changes in the (11) body and overall well-being. Translating knowledge about the mechanisms of the nocebo effect into practical observations and real-world clinical settings poses a unique challenge for healthcare providers.Doctors have a responsibility to provide accurate and truthful information so patients can make informed healthcare decisions.However, the act of providing information can also lead to(12,13) negative expectations and unwanted side effects.We will explore this contradiction and consider relevant factors in medical care.Understanding the nocebo effect can help the medical community recognize its impact on patient care and develop strategies to reduce nocebo effects in a way that is ethical and acceptable. Definitions and methodological considerations It important to clearly define what is meant by the "nocebo effect" and the methods used to identify nocebo responses within the context of mechanistic studies and randomized, placebo-controlled trials. Although the biological pathways involved in nocebo effects are different from those involved in placebo effects, the term "nocebo effect" was originally introduced to represent the negative counterpart of the placebo effect, distinguishing it from the beneficial effects of placebos. The term "nocebo" has been used to describe an inactive substance or treatment meant to create negative expectations, such as giving a placebo along with verbal suggestions of worsening symptoms.The former refers to the negative psychological and social environment surrounding a patient and the treatment, along with its neurobiological basis, while the latter refers to the changes in a patient's mind-body system(14,15) caused by negative expectations.It is clear that negative expectations can lead to nocebo responses without the use of any inert substance.For example, words or elements of the clinical encounter can trigger nocebo responses that worsen a patient's condition.Nocebos are used in research, but unlike placebos, they are not used in clinical practice.While promoting placebo responses may be a desirable and intentional part of clinical practice, clinicians do not intentionally produce nocebo responses, as this would go against the ethical principles of beneficence and non-maleficence. Methodologically, in the context of clinical trials, Ernst and Resch distinguished between apparent and true placebo effects. The apparent placebo effect is the response seen in the placebo group of a randomized controlled trial, which may be due to factors like the natural progression of the condition or regression to the mean, rather than the placebo itself.Detecting a true placebo effect requires comparison with a no-treatment control group.This distinction is also relevant to the nocebo effect.Apparent nocebo effects are adverse reactions observed in the placebo group of a randomized controlled trial, such as reports of agitation or sexual dysfunction in patients with depression randomized to a placebo, which could be symptoms of depression or the result of expecting side effects.Only the latter represents a true nocebo effect.A true nocebo effect in the context of clinical trials is a negative effect that(16-18) can be attributed to the placebo intervention, including the informed consent process that mentions potential side effects of the study treatment.These can only be accurately identified in specific clinical trials by comparing them to a natural history control group.Therefore, nocebo effects can be properly identified in three-arm placebo-controlled trials that include a no-treatment group, which does not receive expectations of side effects related to a treatment intervention. Assessing side effects and determining whether they are caused by nocebo effects also raises methodological challenges. In many studies, patients are simply asked if they have experienced any side effects since their last visit Inother studies, they are given a list of possible adverse events to choose from. The method used to identify side effects can influence what patients report, indicating the need for standardized assessment procedures. Mechanistic research on nocebo effects Most studies on the nocebo effect come from the field of pain processing in healthy individuals because of the ease of delivering controlled painful stimuli and the availability of advanced brain imaging techniques. (19,20) The basic psychological mechanisms behind the formation of negative expectations that lead to nocebo effects involve various aspects related to how individuals interpret and respond to potential harm.

Prior experiences of negative therapeutic outcomes (20, 21), along with observations of other patients facing similar negative results (22), have been noted.In controlled studies, healthy individuals who were given a fake radiofrequency treatment and told that an electric current was going through their heads reported headaches (23).This suggests that expectations can lead to discomfort and even pain (24,25).Additionally, mental processes can influence how medication works in unexpected ways.For example, the usual pain-relieving effect of 33% nitrous oxide (N2O) (26) was changed to increased pain sensitivity—where a mild level of pain was felt as more intense—when participants were incorrectly told they might feel more pain.Verbal statements of negative information can transform harmless stimulations into painful experiences and cause nocebo responses that are as strong as those triggered by actual negative experiences (27). These behavioral changes are supported by objective findings from psychopharmacology (28) and brain imaging (29). One example is proglumide, a drug that blocks both CCK type-A and B receptors.When given along with a placebo and a suggestion that pain would increase, it stops nocebo-related pain sensitivity, suggesting that the cholecystokinergic system plays a key role in nocebo effects.Another finding is that just one piece of information about an increase in pain can affect how pain is perceived over time, causing the insular cortex to become more active for as long as 8 to 90 days.These findings have been supported by brain imaging studies.The pain-reducing effects of remifentanil, a μ-opioid agonist, were completely canceled out when participants were told that the drug was stopped, even though it had not been.This shows that negative expectations can interfere with how drugs work (30). Overall, these experimental results in the study of pain are important for people suffering from chronic pain and might also be relevant to other medical situations where mental factors significantly impact treatment outcomes.

Different side effect profiles offer evidence that can suggest nocebo effects.For example, Amanzio and his team conducted a systematic review of adverse effects in anti-migraine drug trials that used placebos.The final analysis included 69 studies, with 56 focusing on triptans, 9 on anticonvulsants, and 8 on non-steroidal anti-inflammatory drugs.They found that the placebo groups often experienced a high rate of adverse effects, similar to those seen with the actual drugs being tested.For instance, anticonvulsant placebos led to issues like appetite loss, memory problems, tingling, and upper respiratory infections, all of which are also reported as side effects for this class of drugs.This connection between reported side effects in the placebo groups and known side effects of specific drugs suggests that nocebo effects can occur due to the informed consent process. Similar findings have been reported for antidepressants. A large meta-analysis of 143 placebo-controlled trials for antidepressants, which included 21 trials for tricyclic antidepressants (TCAs) and 122 for selective serotonin reuptake inhibitors (SSRIs), found that the placebo groups in TCA trials had higher rates of adverse effects than those in SSRI trials.This was true for both active drug and placebo groups.For instance, patients receiving TCA placebos reported more dry mouth, vision problems, fatigue, and constipation than those receiving SSRI placebos.This shows that information about drug side effects can shape patient expectations, which in turn can affect how they experience side effects and influence the results of clinical trials. Another common issue in clinical trials is the withdrawal of treatment due to nocebo effects. In one study, researchers looked at the impact of consent forms that either mentioned or did not mention gastrointestinal side effects.The study was conducted at two of three centers involved in a trial testing aspirin, sulfinpyrazone, or both in patients with unstable angina.They found that when consent forms included information about possible gastrointestinal side effects, there was a significant increase in reported gastrointestinal symptoms and a six-fold rise in patients stopping their treatment on their own. More recently, Rief and colleagues studied the occurrence of adverse effects and the reasons for stopping treatment in trials involving statin drugs. Although varied methods of assessing adverse effects made it hard to estimate accurate dropout rates, the researchers found that between 4% and 26% of patients in control groups of large statin trials stopped using the placebo because they believed they were experiencing side effects.These examples show that nocebo responses can be identified retrospectively, but some studies have been designed to look at this effect prospectively.For instance, a study on finasteride showed that patients who were informed about

possible sexual side effects reported more of these issues than those who were not warned.This demonstrates the influence of expectations on actual experiences. Nocebo effects are also seen in other contexts. For example, women undergoing epidural analgesia or cesarean delivery were given either a negative or a reassuring description of the procedure. Those told to expect pain reported higher levels of pain than those who were given a more positive description. This shows how information can affect how people perceive and experience pain. Repeated painful experiences can lead to anticipatory pain behaviors and conditioned nocebo hyperalgesia. One study found that infants of diabetic mothers showed more pain during venipunctures and even anticipated pain when their skin was cleaned, even without actual pain. This is an example of a conditioned nocebo response. Nocebo effects are also involved in allergic disorders and severe symptoms, such as nausea in cancer patients, which are often related to verbal and conditioned negative expectations. These effects can reduce quality of life and make it harder for patients to follow treatment plans. Physicians traditionally controlled how much information patients received, but now, both law and medical ethics support informed consent and limit therapeutic privilege. It is important for doctors to provide truthful and complete information so patients can make informed decisions about their healthcare.

2.ETIOLOGY OF THE NOCEBO EFFECT :

The etiology of the nocebo effect is multifactorial ,involving complex interactions among psychological, neurological , social and contextual factors .

2.1 NEGATIVE EXPECTATIONS

It is considered as the primary factor in the development of the nocebo effect .When patients anticipate adverse effect from a treatment ,these expectations can influence symptom perception and physiological responses.

2.2 PSYCHOLOGICAL FACTORS

Psychological characteristics such as anxiety, stress, depression, somatization, and heightened health-related concerns increase susceptibility to nocebo responses. Individuals with elevated anxiety levels are more likely to interpret normal bodily sensations as treatment-related adverse effect

2.3 CONDITIONING AND PREVIOUS EXPERIENCES

Prior negative experiences with medications, medical procedures, or healthcare interventions can condition patients to expect adverse outcomes(31). Through classical conditioning, previously experienced side effects may reoccur when similar treatments are administered, even in the absence of a pharmacological cause

2.4 HEALTHCARE PROVIDER COMMUNICATION

The manner in which healthcare professionals communicate information about potential risks and adverse effects can significantly influence patient expectations.(32) Emphasis on side effects or the use of negative language may unintentionally contribute to the development of nocebo responses.

2.5 SOCIAL AND OBSERVATIONAL LEARNING

Patients may develop negative expectations by observing adverse experiences in others or through (33)exposure to information from family members, peers, social media, or mass media. This phenomenon, known as observational learning, can enhance susceptibility to nocebo effects.

2.6 NEUROBIOLOGICAL MECHANISMS

Neurobiological processes involving the central nervous system play a crucial role in nocebo responses. Brain regions associated with pain perception, emotional processing, and anxiety regulation, including the prefrontal cortex, anterior cingulate cortex, and amygdala, have been implicated. Neurotransmitters such as (34)cholecystokinin (CCK), cortisol, and other stress-related mediators contribute to symptom generation.

2.7 PATIENT–PROVIDER RELATIONSHIP

A lack of trust, poor therapeutic alliance, and inadequate communication between patients and healthcare providers may increase uncertainty and anxiety, thereby facilitating nocebo responses.

Negative Communication

+

Previous Negative Experiences

+

Psychological Factors

(Anxiety, Fear, Stress)

↓

Negative Expectations

↓

Conditioning & Symptom Monitoring

↓

Neurobiological Responses

↓

Increased Symptom Perception

↓

NOCEBO EFFECT

MECHANISM OF NOCEBO EFFECT

Negative Expectations

↓

Anxiety and Anticipation

↓

Activation of Brain Regions

(Amygdala, Hippocampus, Prefrontal Cortex)

↓

Neurochemical Changes

↑ Cholecystokinin (CCK)

↑ Cortisol Release

↓ Dopamine Activity

↓ Endogenous Opioid Activity

↓

Enhanced Pain/Symptom Perception

↓

Manifestation of Adverse Effects

3.MANAGEMENT OF NOCEBO EFFECT

1.Patient Education & Positive Communication clear and balanced counselling . Building trust between healthcare professional and patient Avoiding unnecessarily frightening information.

2. Psychological Interventions Cognitive Behavioral Therapy (CBT)

Stress management techniques Relaxation therapy and mindfulness.

3. Treatment of Associated Anxiety or Depression

There is no specific pharmacological treatment for the nocebo effect.(35) Management primarily focuses on effective communication, patient education, psychological support, and treatment of underlying anxiety or depression when present."

4.CLINICAL MANIFESTATIONS OF THE NOCEBO EFFECT

The nocebo effect manifests as the appearance, worsening, or perception of adverse symptoms resulting from negative expectations, fear, anxiety, or prior negative experiences rather than from the pharmacological action of a treatment. (36,)These manifestations can significantly affect patient well-being, treatment adherence, and therapeutic outcomes.

Common clinical manifestations

4.1PAIN RELATED SYMPTOMS

Headache and migraine

Musculoskeletal pain

Exacerbation of chronic pain condition

Increased pain intensity

4.2 GASTROINTESTINAL SYMPTOMS

Abdominal discomfort

Diarrhea

Loss of appetite

Nause and vomiting

4.3 NEURILOGICAL SYMPTOMS

Fatigue

Weakness

Difficulty concentrating

Sleep disturbance

4.4 PSYCHOLOGICAL SYMPTOMS

Anxiety and fear

Depressed mood

Heightened concern about treatment related adverse effect

4.5 CARDIOVASCULAR MANIFESTATION

Palpitations

Increased heart rate

Elevated blood pressure

Sensation of chest discomfort

4.6 DERMATOLOGICAL SYMPTOMS

Itching

Skin rashes

Tingling or burning sensation

4.7 TREATMENT RELATED CONSEQUENCES

Reduces medication adherence

Reduced treatment effectiveness

Increased reporting if adverse drug reaction

FACTORS INFLUENCING THE NOCEBO EFFECT

Negative Expectations(37)

+

Previous Negative Experiences

+

Psychological Factors (Anxiety, Fear, Stress)

+

Healthcare Professional Communication

+

Social & Media Influences

+

Symptom Monitoring (Hypervigilance)

↓

Enhanced Perception of Symptoms

↓

Neurobiological Responses

↓

Clinical Manifestations

↓

NOCEBO EFFECT

5.DRUGS

5.1 STATINS

Statins are a group of lipid-lowering medications widely used to reduce blood cholesterol levels and prevent cardiovascular disease. (38-40)They act by inhibiting the enzyme HMG-CoA reductuctase in the liver, which plays a key role in cholesterol synthesis. This results in decreased low-density lipoprotein (LDL) cholesterol and helps reduce the formation of atherosclerotic plaques.

Statins are considered one of the most effective and commonly prescribed treatments for preventing heart attacks, strokes, and other cardiovascular complications.(41-43) Beyond lowering cholesterol, they may also improve blood vessel function and stabilize existing plaques

Statins are **lipid-lowering medications** that primarily reduce **LDL cholesterol ("bad cholesterol")** in the blood.

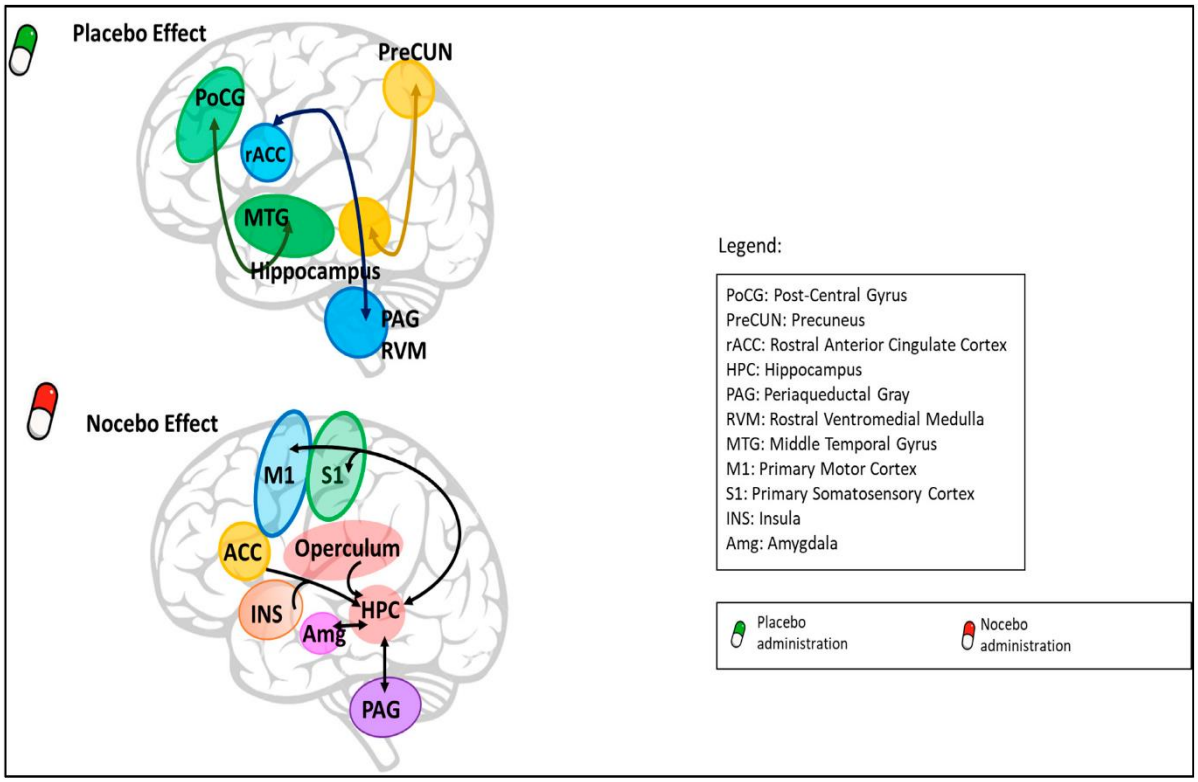
High LDL can build up inside arteries and form plaques (atherosclerosis), narrowing blood vessels and increasing the chance of(44):

- Heart attack
- Stroke
- Peripheral artery disease

6. MECHANISM OF ACTION

The nocebo effect occurs when a person expects a treatment to cause harmful effects. This negative expectation increases anxiety and activates the brain's stress response. The brain releases stress hormones and neurotransmitters, which increase pain and discomfort. As a result, the person experiences real symptoms even if the treatment is harmless.

The **placebo effect** occurs when a person expects a treatment to produce beneficial effects. This positive expectation activates the brain and releases natural chemicals such as **endorphins** and **dopamine**. These chemicals reduce pain, improve mood, and promote healing. As a result, the person feels better even though the treatment has no active medicine.



CLASSIFICATION OF STATIN DRUGS

Statins (HMG-CoA reductase inhibitors) (45) can be classified based on their origin and potency.

6.1 BASED ON ORIGIN

A. NATURALLY DERIVED STATINS

Lovastatin

Pravastatin

Simvastatin

B. SYNTHETIC STATINS

Atorvastatin

Rosuvastatin

Fluvastatin

Pitavastatin

6.2 BASED ON LIPID LOWERING POTENCY

High intensity statin – Rosuvastatin,Atorvastatin

Moderate intensity - Simvastatin,Pravastatin,Lovastatin,Fluvastatin,

6.3 ADVERSE EFFECTS

Musculoskeletal ,hepatic effect,GIT effect, metabolic effect,neurological effect.

6.4 THERAPEUTIC USES

1.Hypercholesterolemia

2.Dyslipidemia

3.Prevention of cardiovascular disease

4.Stroke prevention

7. ROLE OF STATIN IN NOCEBO EFFECT

Statins play an important role in the study of the nocebo effect because they are among the most commonly prescribed medications in which perceived adverse effects may be influenced by patients' expectations rather (46-48)than the pharmacological action of the drug

The role of statins in the nocebo effect is primarily associated with the reporting of statin-associated muscle symptoms (SAMS), such as myalgia, fatigue, and weakness. When patients are informed about potential side effects or exposed to negative media reports, they may develop negative expectations regarding statin therapy. (49-50)These expectations can increase symptom awareness and lead to the perception or amplification of adverse effects.

Clinical studies have demonstrated that muscle-related symptoms are reported more frequently in open-label settings than in blinded randomized controlled trials, suggesting that psychological factors contribute significantly to symptom occurrence and reporting.

As a result, the nocebo effect may lead to:

Increased reporting of muscle pain and fatigue

Reduced adherence to statin therapy

Premature discontinuation of treatment

Poor cholesterol control

Increased cardiovascular risk due to treatment interruption

8. BETA BLCOKERS

Beta-blockers are widely prescribed cardiovascular medications used in the management of hypertension, angina pectoris, cardiac arrhythmias, heart failure, and myocardial infarction. Although generally well tolerated, patients receiving beta-blockers frequently report adverse effects (51-53)such as fatigue, dizziness, weakness, sleep disturbances, and sexual dysfunction. Evidence suggests that some of these reported symptoms may be influenced by the nocebo effect, where negative expectations regarding treatment contribute to the perception or amplification of adverse events

8.1 MECHANISM OF ACTION

Beta-Blocker Prescription

+

Information About Side Effects

↓

Negative Expectations

↓

Anxiety and Fear

↓

Increased Symptom Monitoring

↓

Enhanced Perception of Bodily Sensations

↓

Reported Adverse Effects

(Fatigue, Dizziness, Sexual Dysfunction)

↓

Nocebo Effect

↓

Reduced Adherence or Drug Discontinuation

8.2 ROLE OF THE NOCEBO EFFECT IN BETA-BLOCKER THERAPY

The nocebo effect occurs when patients anticipate adverse outcomes after receiving information about potential side effects(54-56). In beta-blocker therapy, awareness of possible adverse reactions may increase symptom monitoring and anxiety, leading patients to attribute common physical sensations to the medication. Studies have demonstrated that adverse effects, particularly fatigue and sexual dysfunction, are reported more frequently when patients are informed about these possibilities, highlighting the contribution of psychological factors to symptom development

8.3 CLINICAL MANIFESTATIONS

Common symptoms associated with the nocebo effect during beta-blocker therapy include:

Fatigue

Dizziness

Weakness

Sleep disturbances

Sexual dysfunction

8.4 ETIOLOGY OF BETA-BLOCKER–ASSOCIATED ADVERSE EFFECTS

The etiology of beta-blocker–associated adverse effects is multifactorial and involves pharmacological, patient-related, disease-related, and psychological factors.(57-58) These factors influence the occurrence, severity, and perception of adverse reactions during beta-blocker therapy.

8.4.1 PHARMACOLOGICAL FACTORS

Excessive β-adrenergic receptor blockade

Non-selective beta-blocker activity

High drug dosage

Lipid solubility affecting central nervous system penetration

Drug-drug interactions

8.4.2 PATIENT-RELATED FACTORS

Advanced age

Female sex

Renal impairment

Hepatic dysfunction

Genetic variability in drug metabolism

Pre-existing cardiovascular disease

8.4.3 DISEASE-RELATED FACTORS

Heart failure

Bradyarrhythmias

Asthma or chronic obstructive pulmonary disease (COPD)

Diabetes mellitus

8.4.4 LIFESTYLE AND ENVIRONMENTAL FACTORS

Physical inactivity

Smoking

Alcohol consumption

Poor nutritional status

Stress and anxiety

8.4.5. PSYCHOLOGICAL (NOCEBO) FACTORS

Negative expectations about treatment

Previous adverse drug experiences

Fear of side effects

Negative media exposure

THERAPEUTIC USES

Beta-Blockers

↓

Block β-Adrenergic Receptors

↓

↓ Heart Rate

↓ Blood Pressure

↓ Myocardial Oxygen Demand

↓

8.5 CLINICAL USES

- Hypertension
- Angina Pectoris
- Myocardial Infarction
- Heart Failure
- Arrhythmias
- Migraine Prophylaxis
- Hyperthyroidism
- Anxiety Disorders
- Glaucoma
- Essential Tremor

CONCLUSION

The nocebo effect is a clinically significant phenomenon in which negative expectations, beliefs, and psychological factors contribute to the perception or occurrence of adverse symptoms following a therapeutic intervention. It is mediated through complex interactions between cognitive, emotional, and neurobiological mechanisms, including anxiety, conditioning, and heightened symptom monitoring. The nocebo effect can adversely affect treatment adherence, patient satisfaction, and overall therapeutic outcomes, particularly in chronic conditions requiring long-term pharmacotherapy.

Recognition of the nocebo effect is essential for healthcare professionals, as effective communication, appropriate patient education, and a strong therapeutic alliance can help minimize its impact. By addressing patients' concerns, providing balanced information about treatment benefits and risks, and promoting shared decision-making, clinicians can reduce nocebo-related adverse effects and enhance treatment adherence. Therefore, understanding and managing the nocebo effect is crucial for optimizing patient care and improving clinical outcomes in modern healthcare practice.

REFERENCES

1. Benedetti F, Lanotte M, Lopiano L, Colloca L. When words are painful: unraveling the mechanisms of the nocebo effect. Neuroscience. 2007;147(2):260
2. Barsky AJ, Saintfort R, Rogers MP, Borus JF. Nonspecific medication side effects and the nocebo phenomenon. JAMA. 2002;287(5):622–627.
3. Myers MG, Cairns JA, Singer J. The consent form as a possible cause of side effects. Clin Pharmacol Ther. 1987;42(3):250–253.
4. Flaten MA, Simonsen T, Olsen H. Drug-related information generates placebo and nocebo responses that modify the drug response. Psychosom Med. 1999;61(2):250–255.
5. Lancman ME, Asconape JJ, Craven WJ, Howard G, Penry JK. Predictive value of induction of psychogenic seizures by suggestion. Ann Neurol. 1994;35(3):359–361.
6. Luparello TJ, Leist N, Lourie CH, Sweet P. The interaction of psychologic stimuli and pharmacologic agents on airway reactivity in asthmatic subjects. Psychosom Med.
7. Mondaini N, Gontero P, Giubilei G, Lombardi G, Cai T, Gavazzi A, Bartoletti R. Finasteride 5 mg and sexual side effects: how many of these are related to a nocebo phenomenon? J Sex Med. 2007;4(6):1708–1712.
8. Colloca L, Lopiano L, Lanotte M, Benedetti F. Overt versus covert treatment for pain, anxiety, and Parkinson's disease. Lancet Neurol. 2004;3(11):679–684.
9. Miller FG, Kaptchuk TJ. The power of context: reconceptualizing the placebo effect. J R Soc Med. 2008;101(5):222–225.
10. Lamont EB, Christakis NA. Complexities in prognostication in advanced cancer: "to help them live their lives the way they want to". JAMA. 2003;290(1):98–104.
11. Sakala C. Letter from North America: understanding and minimizing nocebo effects in childbearing women. Birth. 2007;34(4)
12. Grimes DA, Schulz KF. Nonspecific side effects of oral contraceptives: nocebo or noise? Contraception. 2011; 83:5
13. Kennedy WP. The nocebo reaction. Med World. 1961;95
14. Kissel P, Barrucand D. Placebos et effet placebo en medecine. Paris: Masson; 1964.
15. Ernst E, Resch KL. Concept of true and perceived placebo effects. BMJ. 1995;311(7004).
16. Tracey I. Getting the pain you expect: mechanisms of placebo, nocebo and reappraisal effects in humans. Nat Med. 16(11).
17. Colloca L, Benedetti F. Nocebo hyperalgesia: how anxiety is turned into pain. Curr Opin Anaesthesiol. 2007;20(5).
18. van Laarhoven AI, Vogelaar ML, Wilder-Smith OH, van Riel PL, van de Kerkhof PC, Kraaimaat FW, Evers AW. Induction of nocebo and placebo effects on itch and pain by verbal suggestions. Pain. 2011;152(7).
19. Colloca L, Sigaudo M, Benedetti F. The role of learning in nocebo and placebo effects. Pain. 2008;136(1–2).
20. Colloca L, Petrovic P, Wager TD, Ingvar M, Benedetti F. How the number of learning trials affects placebo and nocebo responses. Pain. 2010;151.
21. Mazzoni G, Foan L, Hyland ME, Kirsch I. The effects of observation and gender on psychogenic symptoms. Health Psychol. 2010;29(2).
22. Schweiger A, Parducci A. Nocebo: the psychologic induction of pain. Pavlov J Biol Sci. 1981;16(3).
23. Oftedal G, Straume A, Johnsson A, Stovner LJ. Mobile phone headache: a double blind, sham-controlled provocation study. Cephalalgia. 2007;27(5).
24. Stovner LJ, Oftedal G, Straume A, Johnsson A. Nocebo as headache trigger: evidence from a sham-controlled provocation study with RF fields. Acta Neurol Scand Suppl. 2008;188.

25. Dworkin SF, Chen AC, Leresche L, Clark DW. Cognitive reversal of expected nitrous oxide analgesia for acute pain. Anesth Analg. 1983;62.
26. Benedetti F, Amanzio M, Vighetti S, Asteggiano G. The biochemical and neuroendocrine bases of the hyperalgesic nocebo effect. J Neurosci. 2006;26(46).
27. Doganci B, Breimhorst M, Hondrich M, Rodriguez-Raecke R, May A, Birklein F. Expectations modulate long-term heat pain habituation. Eur J Pain. 2011;15(4).
28. Bingel U, Wanigasekera V, Wiech K, Ni Mhuircheartaigh R, Lee MC, Ploner M, Tracey I. The effect of treatment expectation on drug efficacy: imaging the analgesic benefit of the opioid remifentanil. Sci Transl Med. 2011;3(70) .
29. Amanzio M, Corazzini LL, Vase L, Benedetti F. A systematic review of adverse events in placebo groups of anti-migraine clinical trials. Pain. 2009;146(3).
30. Reuter U, Sanchez del Rio M, Carpay JA, Boes CJ, Silberstein SD. Placebo adverse events in headache trials: headache as an adverse event of placebo. Cephalalgia. 2003;23(7).
31. Rief W, Nestoriuc Y, von Lilienfeld-Toal A, Dogan I, Schreiber F, Hofmann SG, Barsky AJ, Avorn J. Differences in adverse effect reporting in placebo groups in SSRI and tricyclic antidepressant trials: a systematic review and meta-analysis. Drug Saf. 2009;32(11).
32. Cairns JA, Gent M, Singer J, Finnie KJ, Froggatt GM, Holder DA, Jablonsky G, Kostuk WJ, Melendez LJ, Myers MG, Sackett DL, Sealey BJ, Tanser PH. Aspirin, sulfinpyrazone, or both in unstable angina. Results of a Canadian multicenter trial. N Engl J Med. 1985;313(22).
33. Rief W, Avorn J, Barsky AJ. Medication-attributed adverse effects in placebo groups: implications for assessment of adverse effects. Arch Intern Med. 2006;166(2).
34. Cocco G. Erectile dysfunction after therapy with metoprolol: the Hawthorne effect. Cardiology. 2009;112(3).
35. Silvestri A, Galetta P, Cerquetani E, Marazzi G, Patrizi R, Fini M, Rosano GM. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo. Eur Heart J. 2003;24(21).
36. Varelmann D, Pancaro C, Cappiello EC, Camann WR. Nocebo-induced hyperalgesia during local anesthetic injection. Anesth Analg. 2010;11
37. Taddio A, Shah V, Gilbert-MacLeod C, Katz J. Conditioning and hyperalgesia in newborns exposed to repeated heel lances. JAMA. 2002;288(7).
38. Liccardi G, Senna G, Russo M, Bonadonna P, Crivellaro M, Dama A, D'Amato M, D'Amato G, Canonica GW, Passalacqua G. Evaluation of the nocebo effect during oral challenge in patients with adverse drug reactions. J Investig Allergol Clin Immunol. 2004;14(2).
39. Lombardi C, Gargioni S, Canonica GW, Passalacqua G. The nocebo effect during oral challenge in subjects with adverse drug reactions. Eur Ann Allergy Clin Immunol. 2008;40(4).
40. Colagiuri B, Zachariae R. Patient Expectancy and Post-chemotherapy Nausea: A Meta-analysis. Ann Behav Med. 2010; 40:314
41. de la Cruz M, Hui D, Parsons HA, Bruera E. Placebo and nocebo effects in randomized double-blind clinical trials of agents for the therapy for fatigue in patients with advanced cancer. Cancer. 2010;116(3).
42. Bovbjerg DH, Redd WH, Jacobsen PB, Manne SL, Taylor KL, Surbone A, Crown JP, Norton L, Gilewski TA, Hudis CA, Reichman BS, Kaufman RJ, Currie VE, Hakes TB. An experimental analysis of classically conditioned nausea during cancer chemotherapy. Psychosom Med. 1992;54(6).
43. Roscoe JA, O'Neill M, Jean-Pierre P, Heckler CE, Kaptchuk TJ, Bushunow P, Shayne M, Huston A, Qazi R, Smith B. An exploratory study on the effects of an expectancy manipulation on chemotherapy-related nausea. J Pain Symptom Manage. 2010;40(3).

44. Shelke AR, Roscoe JA, Morrow GR, Colman LK, Banerjee TK, Kirshner JJ. Effect of a nausea expectancy manipulation on chemotherapy-induced nausea: a university of Rochester cancer center community clinical oncology program study. J Pain Symptom Manage. 2008;35(4).
45. Stockhorst U, Wiener JA, Klosterhalfen S, Klosterhalfen W, Aul C, Steingruber HJ. Effects of overshadowing on conditioned nausea in cancer patients: an experimental study. Physiol Behav. 1998;64(5).
46. Katz J. The Silent World of Doctor and Patient. New York: Free Pr; 19
47. Berg JW, Appelbaum PS, Lidz CW, Parker LS. Informed Consent: Legal Theory and Clinical Practice. 2nd ed. New York: Oxford Univ Pr; 2001.
48. Miller FG, Colloca L. The placebo phenomenon and medical ethics: Rethinking the relationship between informed consent and risk-benefit assessment. Theor Med Bioeth. 2011;32(4).
49. Edwards A, Elwyn G, Covey J, Matthews E, Pill R. Presenting risk information--a review of the effects of "framing" and other manipulations on patient outcomes. J Health Commun. 2001;6(1).
50. O'Connor AM, Pennie RA, Dales RE. Framing effects on expectations, decisions, and side effects experienced: the case of influenza immunization. J Clin Epidemiol. 1996;49(11).
51. Dworkin G. The Theory and Practice of Autonomy. Cambridge: Cambridge University Press; 198
52. Egbert LD, Battit GE, Welch CE, Bartlett MK. Reduction of Postoperative Pain by Encouragement and Instruction of Patients. A Study of Doctor-Patient Rapport. N Engl J Med. 1964;270.
53. Gracely RH, Dubner R, Deeter WR, Wolskee PJ. Clinicians' expectations influence placebo analgesia. Lancet. 1985;1(8419).
54. Greenfield S, Kaplan S, Ware JE., Jr Expanding patient involvement in care. Effects on patient outcomes. Ann Intern Med. 1985;102(4).
55. 57.Kaplan SH, Greenfield S, Ware JE., Jr Assessing the effects of physician- patient interactions on the outcomes of chronic disease. Med Care. 1989;27(3 Supply.
56. Brewin TB. Three ways of giving bad news. Lancet. 1991;337(8751).
57. Petrie KJ, Muller JT, Schirmbeck F, Donkin L, Broadbent E, Ellis CJ, GambleRief Effect of providing information about normal test results on patients' reassurance: randomised controlled trial. BMJ. 2007;334(7589).
58. Enck P, Benedetti F, Schedlowski M. New insights into the placebo and nocebo responses. Neuron. 2008;59(2):195–206.