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PERSPECTIVE ARTICLE

# Complementary action of nocebo and placebo effects

**Claude F. Touzet***

Department of Neuroscience, Faculty of Biology, Aix Marseille University, Marseille, France

## Abstract

The placebo effect exists and is accounted for by regulatory agencies, which require new medications to demonstrate efficacy beyond a placebo. The person-dependent nature of the placebo effect has made it challenging for practitioners trained solely in allopathic medicine—often focused on the suppression of symptoms without accounting for the uniqueness of patients—to fully grasp its significance. Advances in cognitive science have shed light on how memories are stored and how they interact with an individual's interpretation of the world situation, effectively generating the placebo effect as a byproduct of this processing. Neuroscience further reveals how cortical maps involved in cognition interact with lower-level neural networks responsible for homeostatic regulatory loops, enabling an "idea" to produce physiological changes. In the context of optimization theory, the placebo effect can be understood as a straightforward hill-climbing strategy. Conversely, the nocebo effect is just the opposite strategy. However, both effects can be harnessed therapeutically to promote positive outcomes. Although this may seem counterintuitive regarding the nocebo effect, it can nevertheless prove valuable, particularly for patients who do not respond to a placebo.

***Keywords:*** Placebo; Nocebo; Homeostasis; Artificial neural networks; Optimization tool

***Corresponding author:**
Claude F. Touzet
(claude.touzet@univ-amu.fr)

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## 1. Introduction

The placebo effect improves a patient's condition, while the nocebo effect exacerbates it.[1] These effects are usually considered complementary, and great efforts are made to avoid the nocebo effect. Both placebo and nocebo are patient-dependent, relying heavily on the individual's (memorized) previous experiences.[2] This study focuses on these two effects.

Any health condition is essentially the result of a homeostatic loop that operates outside the boundaries of good health, which, at a minimum, requires the absence of symptoms.[3] A health condition is abnormal and arises because the mechanisms responsible for feedback control are no longer optimal. Each homeostatic loop is, at least in part, regulated by a neural network devoted to this function.[4]

Given that homeostasis involves neural networks and their dynamical behavior, this study introduces the concept of basins of attraction—borrowed from artificial neural networks and optimization theory—to explain placebo and nocebo effects and to clarify how cortical activations induced by memory events affect the neural networks governing

various homeostasis loops.[5] This framework allows us to conceive the placebo and nocebo effects as two sides of the same coin, both capable of improving patient health through a shared mechanism—a conclusion that may appear counterintuitive but holds practical significance.

Section 2 presents the concept of the basin of attraction, a central component in the dynamics of artificial neural networks. Section 3 demonstrates that the placebo effect emerges as a side effect of the automatic and perpetual memorization that occurs within the hierarchy of cortical maps. Optimal dynamics—characterized by escaping local minima (chronic condition) toward a global minima (good health)—underpin the placebo effect. Section 4 describes how the opposite strategy—escaping local minima toward states opposite the global minima—characterizes the nocebo effect. Section 5 explores the therapeutic application of the nocebo effect through the Law of Similars, a pillar of homeopathic medicine. It also provides explanations for the influence of belief, optimism, and hypnotism on the placebo and nocebo effects. Section 6 concludes by advocating that a better understanding of both effects may advance the development of personalized medicine.

## 2. Using the framework of computational neuroscience and optimization methods

In biology, homeostasis refers to the steady internal physical and chemical conditions maintained by living systems.[6] It represents the state of optimal functioning for the organism and involves keeping numerous variables, such as body temperature and fluid balance, within defined physiological limits (the homeostatic range).

Homeostasis is maintained through a natural resistance to change when conditions are already optimal, and equilibrium is preserved by several regulatory mechanisms. It is thought to be the central motivation for all organic action.[7] All homeostatic control mechanisms have at least three interdependent components: a receptor, a control center, and an effector.[5]

In many cases, control centers include neurons distributed across various regions. For example, the hypothalamus regulates core body temperature[8] and fluid balance,[9] while the medulla oblongata contains centers that regulate arterial blood pressure[10] and levels of blood gases (including blood pH).[11] The neuroendocrine system provides further evidence of neural involvement in systemic regulation.

Neurons operate in ensembles, processing input and generating output signals. Their connectivity continually self-organizes through synaptic plasticity mechanisms, succinctly summarized by Hebb's rule.[12] Adjustments in synaptic efficacy shape neural network behavior by reinforcing effective connections and pruning those that are unnecessary.[13]

A neural network is a dynamical system whose states evolve within a phase space and tend to converge toward stable configurations known as attractors. The region of phase space from which trajectories converge to a given attractor is called the basin of attraction.[14] Neural behavior thus consists of either exploring the interior of a basin of attraction or transitioning between basins.

The collection of basins structuring dynamics may be conceptualized as a 3D map, with hollows representing basins of varying width and depth (Figure 1). The deeper and broader a basin, the more likely the system is to remain within it.

The validity of this attraction-based framework for neural dynamics is supported by the development of efficient computational methods such as the Monte Carlo method and simulated annealing.[15] Originating in the 1980s, both methods enabled numerous industrial applications and relied solely on stochastic search to explore the solution space and identify global optima. By contrast, the later emergence of efficient learning strategies, such as error-gradient backpropagation[16] and reinforcement learning,[17] uses local information relative to the current position within a basin of attraction to iteratively reduce error and move the dynamics toward more optimal states. Backpropagation, despite being more than half a century old, is central to the development of

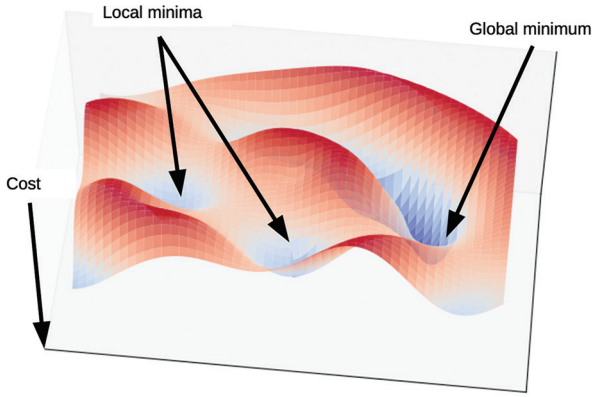


**Figure 1.** Basins of attraction that are available to the dynamics of a given neural network. Assume that "good health" is the deepest basin (the global minimum), while all other basins represent sub-optimal health conditions (local minima). The dynamics of the system are dependent on the regulatory mechanisms that push the system evolution toward the attractor at the center of whichever basin it currently occupies. Escaping a basin requires climbing its walls—i.e., moving against the direction imposed by regulatory mechanisms.

current artificial intelligence (AI) systems,[18] including large language models such as Grok and ChatGPT.

Returning to the clinical domain, this study proposes that the largest basin of attraction corresponds to good health (the symptom-free state), whereas the other basins of attraction correspond to various symptomatic or pathological conditions. As time passes, neural dynamics reinforce the structure of the basin in which they reside. When the system occupies a sub-optimal basin, ongoing reinforcement makes escape increasingly difficult, leading to chronic health conditions.

The placebo effect is clinically observed as a transition from poorer health to better health. In the context of basins of attraction, the placebo effect is moving from a sub-optimal basin of attraction toward the optimal basin, following a trajectory of progressively diminishing symptoms. Conversely, the nocebo effect corresponds to movement toward basins associated with worse health—an increase in symptoms and a shift toward even more sub-optimal attractor states.

## 3. Placebo effect

A placebo is a substance (e.g., sugar pill) or a sham procedure that should have no therapeutic effect, as it "*is objectively without specific activity for the condition being treated.*"[19(p471)] Nonetheless, placebos are effective in a tremendous number of health conditions, as evidenced by the requirement that new pharmaceutical drugs must demonstrate efficacy beyond that of a placebo to be considered effective.[20]

The placebo effect is highly individualized; one may respond to one placebo but not another, and the magnitude and consistency of the response vary widely. Studies have shown that factors such as a placebo's form, color, and price—and even the patient's country of residence—modulate placebo responsiveness.[20] A compelling argument that individual experiences shape placebo responsiveness is the observed rise in placebo effects among the United States population following the legalization of direct-to-consumer pharmaceutical advertising (DTCPA) in 1997.[21] This phenomenon has prompted many contemporary placebo-controlled trials to be conducted in locations where DTCPA is prohibited or ineffective, such as rural India or Iran.

To say that the placebo effect is "highly individualized" means that it depends on personal experiences, which, by definition, are not shared universally. These experiences are encoded in the cortex and distributed across as many cortical maps as dimensions present in the original situations.[22] A memory is the joint activation of several cortical columns, each belonging to a particular cortical map; together, these activations form a distributed pattern spanning the cortex.[23] This cortical activity pattern interacts with lower-level neural networks, i.e., neurons that do not belong to the cortex. Although the cortex occupies approximately 80% of brain volume, it only accounts for 20% of the neurons.[24] Therefore, the majority of neurons lie outside the cortex, many directly or indirectly connected to cortical circuits and involved in homeostatic regulation.

It is appropriate to conceive of the nervous system as a whole, with no neuron acting in isolation or independent of the activity of others (either directly with neurotransmitters, or indirectly with neurohormones). This continuity implies that Hebb's rule applies not only to cortical neurons but also to all the other neurons. Consequently, a memory is not restricted to the cortex; rather, it extends to all neural networks co-activated repeatedly within a narrow temporal window of a few milliseconds.[25]

Such a memory process explains why "naïve" patients do not exhibit a placebo effect—or only a small one—compared to patients who are already acquainted with the drug (to be replaced by the placebo). One of the earliest documented studies of the placebo effect demonstrated how placebo-induced endorphins mimic the action of morphine by binding opioid receptors, inhibiting ascending pain pathways, altering pain perception, and producing central nervous system depression.[26]

When are the neural mechanisms responsible for endorphin synthesis and release encoded? As soon as a patient starts receiving intravenous (IV) morphine, new patterns of neural activities—those corresponding to the transition to a pain-free state—are formed and consolidated. Despite being altered in their functioning, neurons continue to follow Hebb's rule,[12] reinforcing the synapses involved in this new activity pattern. The subsequent placebo effect (associated with a fake "morphine" IV) is simply the reactivation of this memorized neural pattern.

Since a neural network is an associative memory,[27] it can reconstruct an entire neural activity pattern from a partial cue or probe (Figure 2). If the cue is merely an IV of physiological saline (a placebo), the system can nevertheless recruit the full pattern, including the components responsible for inhibiting ascending pain pathways, allowing the patient to experience pain-free despite receiving no active drug. In this way, a cognitive expectation—*I am going to be pain-free thanks to this IV of morphine*—is instantiated physiologically through the reactivation of the neural activity pattern previously associated with actual morphine-induced analgesia.

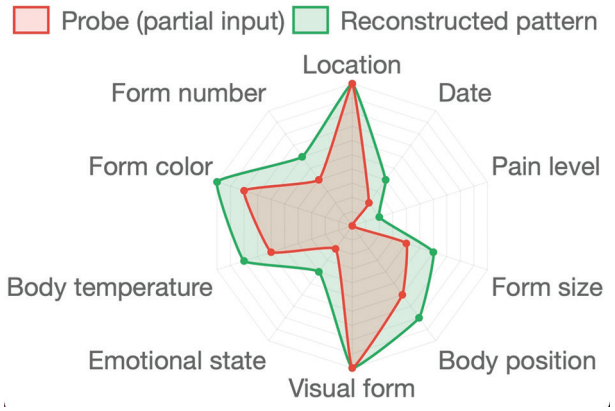


**Figure 2.** An associative memory, i.e., a neural network allows the reconstruction of an entire activity pattern using a probe that is only a subset of its features. The number of dimensions shown here is 10. The cortex comprises 360 specialized cortical maps, each constituting a distinct dimension. However, not all 360 cortical maps are implicated for a single remembrance.

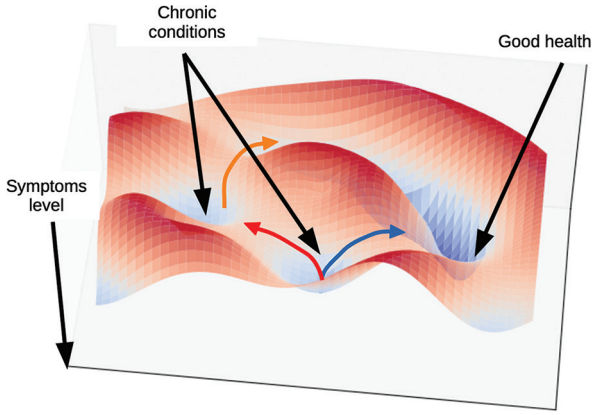


**Figure 3.** Blue arrow: the placebo effect drives the dynamics of the system toward the global minimum (good health), enabling it to escape the local hollow and continue moving toward the desired symptom-free hollow. Red arrow: the nocebo effect shifts the dynamics in the opposite direction—away from "good health"—until escaping the local hollow. From this new location, the system may be able to find an alternative way (in orange) to reach the global minimum (good health) more easily.

## 4. Nocebo effect

The example presented in the previous chapter, the case of pain management with morphine, illustrates the placebo effect well, but it is not representative of a chronic health condition. In chronic disorders, regulatory mechanisms actively maintain the system within a sub-optimal basin of attraction. Looking at the map showing the various hollows (Figure 3), the "good health" basin may lie nearby, yet remain inaccessible: whenever the system attempts to climb in the desired direction, regulatory mechanisms pull it back into the "chronic condition" hollow.

Escaping a local minimum corresponding to a non-optimal hollow is a classical problem in local search methods used in mathematical optimization.[28] Heuristic methods attempt to infer a direction that will allow the system to escape the local minimum and approach the global minimum.[29] The heuristic may be a score, such as the depth of the hollow, exploring only moves that reduce this score.

Figure 3 translates these concepts into the clinical domain. The placebo effect can be viewed as moving the neural dynamics toward the desired symptom-free basin, while the nocebo effect moves dynamics in the opposite direction. In doing so, the nocebo effect may ultimately allow the system to exit its current basin and arrive at a new position from which movement toward the healthy basin is possible—and sometimes easier.

The difference between placebo and nocebo effects is that, in escaping the local basin of attraction, the nocebo pattern of neural activities does not guide the neural dynamics toward the healthy basin. Therefore, it is normal to observe worsening of symptoms—even the development of new symptoms. However, this deterioration does not necessarily imply a poorer long-term prognosis. The previous health condition was chronic in the sense that the dynamics were trapped within a specific basin of attraction. The nocebo effect may dislodge the dynamics from that basin and move it into a new location. Even if this new position initially worsens the health condition, it may reduce the dominance of the chronic attractors and increase the relative influence of the healthy attractor.

Attractors are neural-based; their efficiencies depend on how frequently they have been reinforced through learning. Therefore, the length of time spent in a condition defines the number of neural co-activations retained in memory, thereby influencing the depth and size of the associated basin of attraction. In general, the healthy condition has a longer learning history compared to the chronic condition. Therefore, once the system escapes a chronic basin of attraction, there is a substantial chance that the dynamics will drift toward a better condition.

## 5. Therapeutic application of and factors affecting placebo and nocebo effects

Having matured over 40 years, the framework of computational neurocomputing and optimization is useful in explaining the placebo and nocebo effects. In particular, it presents the similarities and differences: opposite escapes of local minima, with (placebo) or without (nocebo) guidance toward the global minimum once escaped.

There may be cases where no placebo effect is able to escape local minima. In such a case, an efficient nocebo

effect is beneficial. One can even envisage that once escaped from local minima with a nocebo effect, the placebo effect kicks in to guide the dynamics toward the healthy minimum. In this case, nocebo and placebo effects are no longer opposed but complement each other, achieving results neither can achieve alone for the betterment of the patient.

It seems that the Law of Similars[30] may be—at least partially—based on this observation. At first sight, using ingredients known to induce symptoms similar to those targeted for treatment appears counterintuitive. However, there is logic in recruiting the nocebo effect in specific situations.

The Law of Similars has been integrated into the proposal of Hahnemann[31,32] and is a pillar of homeopathic medicine. It is well known that the homeopathic remedy is selected because it produces the same symptoms as those of the patient (i.e., pathogenesis). The patient is therefore well informed of a potential nocebo effect, but he (or she) also has faith in the homeopathic practitioner and believes in a positive outcome (placebo effect). In conclusion, homeopathy—whatever its intrinsic effectiveness—is also calling on the complementary action of a nocebo effect followed by a placebo effect.

Kent's 12 Observations[33] are a set of guidelines formulated by the renowned homeopath James Tyler Kent in 1900. These observations serve as a valuable framework for assessing the progress of a homeopathic case and making informed decisions at the second prescription. Mastery of Kent's 12 Observations is fundamental for homeopathic clinicians to interpret complex remedy reactions accurately, thereby enhancing the precision and success of homeopathic treatment.[34,35] Each observation focuses on specific aspects of the patient's response to the initial remedy and provides crucial insights into the dynamic nature of the case. Two of these observations (Numbers 2 and 3) describe situations in which the remedies initially worsen the condition before improvement occurs. If one remembers that a patient using a homeopathic remedy may be well informed of the Law of Similars, it is legitimate to conclude that the situations following Kent's second and third observations could be concrete examples of situations where a positive harnessing of the nocebo effect is summoned.

It is worth mentioning that the Law of Similars was already referred to in the writings of ancient healers[30] such as Charaka, the Indian father of medicine (c. 1000 B.C.), Hippocrates, the father of Western medicine (Greece, c. 400 B.C.), and Paracelsus, the father of toxicology (Europe, 1493–1541).

The connection between our description of the placebo and nocebo effects and homeopathy, specifically the Law of Similars, is potentially controversial, particularly for advocates of an evidence-based-only medicine. This medicine only targets symptoms (i.e., allopathy) and denies the benefits of personalized medicine. One could argue that homeopathic medicine is more than 200 years old and practiced worldwide, such as in India where there are more than 300,000 homeopathic registered practitioners[36] (to be compared to 1,386,136 registered Indian allopathic doctors[37]), and therefore the number of patients that fall into Kent's second and third observations over the last 200 years is anything but small. It is important to note that this work does not have to rely on the efficacy of homeopathic remedies. On the contrary, the most informative case for demonstrating the usefulness of this study's framework is to assume that homeopathic remedies are ineffective and that homeopathy relies only on placebo and nocebo effects.

Numerous applications of the placebo/nocebo effects target conditions that evolutionary medicine (or Darwinian medicine[38]) points out to be body responses adapted to the current health situation. Since many of these responses are unpleasant, many people (aware or unaware of evolutionary medicine) prefer to avoid them as much as possible, despite the fact that these responses help them return to a healthy state. Many of these body responses involve symptoms that have a neural origin. It is, for example, the case after an infection or injury with symptoms such as fever,[39] pain,[40] or sickness behavior.[41] Given their neural origins, it is easy to understand why these conditions are also prone to placebo/nocebo effects.

Clinical results demonstrated that dispositional optimism predicts placebo analgesia.[42] It is clear that if a person does not believe in the remedy, it forbids his visualization of good health, and the change in neural activity patterns toward a healthier state does not occur. People with such a pessimistic attitude may be more prone to exhibit a nocebo effect, which could be useful.

Belief is a major component of the placebo effect because it accounts for the number of neurons activated by the same "idea."[43] When a huge number of cortical neurons embed an "idea," a vast number of lower-level neurons get activated and act on the regulatory loops.

Hypnosis is a similar procedure for belief manipulation. Using movements unknown to the patient (i.e., ideomotor movements) but predicted by the hypnotist, the patient's belief in his own ability to correctly interpret reality declines. On the other hand, the patient's belief in the hypnotist's "power" increases until the hypnotist states new ideas that are not questioned, nor challenged and

verified by the patient anymore. Hypnosis silences pain, often more effectively than other recognized treatments,[44] and is part of treatment programs used against many chronic psychological and physiological conditions.[45] In the context of the work presented here, hypnotism may be seen as a method to boost optimism and belief, allowing a significant placebo effect.

## 6. Conclusion

The explanations presented in this study are hoped to demystify the placebo/nocebo effects and promote their conscious use by therapists.[46] It is counterproductive that placebos are still not officially prescribed in cases that would benefit from them.[47] Some therapists even consider placebo prescription as unethical and call for "deceptive medicine."[48] As presented here, even a nocebo effect may be beneficial for the patient's health.

A placebo or a nocebo is a trigger that evokes memories. The cortical map activations encoding these memories are linked to low-level neural circuits responsible for homeostatic regulation through feedback loops. The cue that summons the full memory pattern must include at least one dimension relevant to that memory—activation of the entire pattern follows automatically since our brain is an associative memory. This cue need not be a pill of a particular color, size, or price. It could be as simple as a word, a sentence, or advice, greatly simplifying therapeutic application. It is believed that demystifying placebo/nocebo effects will foster their adoption, transform patient care, and advance personalized medicine without moralizing or stigmatizing their use.

The potential limitation of the framework presented here is the simplification inherent in Figures 1 and 3, which depict a 3D surface to represent patient health. The actual number of dimensions associated with health is much bigger. The same consideration applies to Figure 2, which shows only 10 dimensions related to a memory. Here again, the actual number of dimensions is much bigger but should not exceed 360.

How could our description of the placebo and nocebo effects be tested? As with any intervention deeply intertwined with a patient's personal history (i.e., patient's memories), the gold standard of evidence-based medicine, which relies on group statistics, can be challenging to yield meaningful results. Nonetheless, evidence-based clinical trials on placebo effects do exist.[49] To validate the mechanisms of action of placebo and nocebo effects, a study of the benefit of a nocebo effect should be conducted only among patients who are not responding to a placebo. If health improvement occurs, it could be taken as evidence in favor of validating our description.

Last but not least, the framework of health as a multidimensional landscape—with optimal and sub-optimal basins of attraction governing the dynamics of health over time—is of tremendous importance. It encourages viewing the medical history of a patient as a trajectory, recognizing that there is a hierarchy/chronology to the diseases. For example, approximately one-third of children with eczema will develop asthma.[50] Conventional allopathic medicine, which tends to treat diseases as isolated entities, might consider eczema and asthma as distinct psychosomatic pathologies. In contrast, the framework presented in this study clarifies that the "eczema basin" of attraction lies between the "good health basin" and the "asthma basin," indicating that asthma reflects a further deterioration of health compared to eczema. Allowing allopathic physicians, accustomed to a one-drug-fits-all model, to recognize a hierarchy among pathologies is one of the required steps toward the development of personalized medicine.

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## Author contributions

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## References

1. Häuser W, Hansen E, Enck P. Nocebo phenomena in medicine: Their relevance in everyday clinical practice. *Dtsch Arztebl Int*. 2012;109(26):459-465.

   doi: 10.3238/arztebl.2012.0459

2. Colloca L, Barsky AJ. Placebo and nocebo effects. *N Engl J Med*. 2020;382(6):554-561.

   doi: 10.1056/nejmra1907805

3. Kroenke K. A practical and evidence-based approach to common symptoms: A narrative review. *Ann Intern Med*. 2014;161(8):579-586.

doi: 10.7326/M14-0461

4. Berne RM, Levy MN. *Physiology*. 6th ed. United States: Mosby; 2004.

5. Modell H, Cliff W, Michael J, McFarland J, Wenderoth MP, Wright A. A physiologist's view of homeostasis. *Adv Physiol Educ*. 2015;39(4):259-266.

doi: 10.1152/advan.00107.2015

6. Cannon WB. Organization for physiological homeostasis. *Physiol Rev*. 1929;9(3):399-431.

doi: 10.1152/physrev.1929.9.3.399

7. Cannon WB. *The Wisdom of the Body*. New York: W.W. Norton and Company; 1932.

8. Morrison SF, Nakamura K. Central mechanisms for thermoregulation. *Annu Rev Physiol*. 2019;81:285-308.

doi: 10.1146/annurev-physiol-020518-114546

9. Zimmerman CA, Leib DE, Knight ZA. Neural circuits underlying thirst and fluid homeostasis. *Nat Rev Neurosci*. 2017;18(8):459-469.

doi: 10.1038/nrn.2017.71

10. Guyenet PG. The sympathetic control of blood pressure. *Nat Rev Neurosci*. 2006;7(5):335-346.

doi: 10.1038/nrn1902

11. Nattie E, Li A. Central chemoreceptors: Locations and functions. *Compr Physiol*. 2012;2(1):221-254.

doi: 10.1002/cphy.c100083

12. Hebb DO. *The Organization of Behavior: A Neuropsychological Theory*. Hoboken: Wiley; 1949.

13. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ, editors. *Principles of Neural Science*. 5th ed. United States: McGraw-Hill; 2013.

14. Weisstein EW. *Attractor*. *MathWorld--A Wolfram Web Resource*; 2020. Available from: https://mathworld.wolfram.com/attractor.html [Last accessed on 2025 Dec 11].

15. Vanderbilt D, Louie SG. A Monte Carlo simulated annealing approach to optimization over continuous variables. *J Comput Phys*. 1984;56(2):259-271.

doi: 10.1016/0021-9991(84)90096-8

16. LeCun Y, Boser B, Denker JS, *et al*. Backpropagation applied to handwritten zip code recognition. *Neural Comput*. 1989;1(4):541-551.

doi: 10.1162/neco.1989.1.4.541

17. Watkins CJCH, Dayan P. Q-learning. *Mach Learn*. 1992;8(3-4):279-292.

doi: 10.1007/BF00992698

18. LeCun Y, Bengio Y, Hinton G. Deep learning. *Nature*. 2015;521(7553):436-444.

doi: 10.1038/nature14539

19. Moerman DE, Jonas WB. Deconstructing the placebo effect and finding the meaning response. *Ann Intern Med*. 2002;136(6):471-476.

doi: 10.7326/0003-4819-136-6-200203190-00011

20. Waber RL, Shiv B, Carmon Z, Ariely D. Commercial features of placebo and therapeutic efficacy. *JAMA*. 2008;299(9):1016-1017.

doi: 10.1001/jama.299.9.1016

21. Ventola CL. Direct-to-consumer pharmaceutical advertising: Therapeutic or toxic? *P T*. 2011;36(10):669-684.

22. Gallistel CR. *The Organization of Learning*. United States: MIT Press; 1990.

23. Buzsáki G. *The Brain From Inside Out*. Oxford: Oxford University Press; 2019.

24. Herculano-Houzel S. The human brain in numbers: A linearly scaled-up primate brain. *Front Hum Neurosci*. 2009;3:31.

doi: 10.3389/neuro.09.031.2009

25. Markram H, Lübke J, Frotscher M, Sakmann B. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. *Science*. 1997;275(5297):213-215.

doi: 10.1126/science.275.5297.213

26. Beecher HK. The powerful placebo. *JAMA*. 1955;159(17):1602-1606.

doi: 10.1001/jama.1955.02960340022006

27. Kohonen T. *Self-Organizing Maps*. 3rd ed. Germany: Springer; 2001.

28. Russell SJ, Norvig P. *Artificial Intelligence: A Modern Approach*. 4th ed. United Kingdom: Pearson; 2021.

29. Kirkpatrick S, Gelatt CD Jr., Vecchi MP. Optimization by simulated annealing. Science. 1983;220(4598):671-680.

doi: 10.1126/science.220.4598.671

30. Jonas WB. The homeopathic therapeutic relationship: The role of the consultation in healing. *Homeopathy*. 2012;101(1):4-7.

doi: 10.1016/j.homp.2011.10.002

31. Hahnemann S. *The Homœopathic Medical Doctrine, or "Organon of the Healing Art"*. Dublin: W.F. Wakeman; 1833.

32. Hahnemann S. *Organon of the Healing Art*. 6th ed. England: W. Headland; 1921.

33. Kent JT. *Lectures on Homoeopathic Philosophy*. Uttar Pradesh: B. Jain Publishers; 2004.

34. Soni A, Ali SA, Das A, Dey S. Kent's twelve observations: A doctrinal legacy of Hahnemann for clinical prognosis. *Int J Hom Sci*. 2025;9(3):501-506.

doi: 10.33545/26164485.2025.v9.i3.H.1699

35. Ullman RW, Reichenberg-Ullman J. *The Patient's Guide to Homeopathic Medicine*. Amsterdam: Picnic Point Press; 1994.

36. *Lok Sabha Unstarred Question No. 1768. Ministry of AYUSH*; 2022. Available from: https://sansad.in/getFile/annex/257/AU1768.pdf?source=pqars [Last accessed on 2025 Dec 11].

37. *Lok Sabha Unstarred Question No. 1887*. Ministry of Health and Family Welfare; 2019. Available from: https://sansad.in/getFile/loksabhaquestions/annex/182/au1887_xrgu06.pdf?source=pqals [Last accessed on 2025 Dec 11].

38. Nesse RM. How is Darwinian medicine useful? *West J Med*. 2001;174(5):358-360.

doi: 10.1136/ewjm.174.5.358

39. Evans SS, Repasky EA, Fisher DT. Fever and the thermal regulation of immunity: The immune system feels the heat. *Nat Rev Immunol*. 2015;15(6):335-349.

doi: 10.1038/nri3843

40. Wall PD. *Pain: The Science of Suffering*. Weidenfeld and Nicolson; 1999.

41. Dantzer R. Cytokine-induced sickness behavior: Mechanisms and implications. *Ann N Y Acad Sci*. 2001;933(1):222-234.

doi: 10.1111/j.1749-6632.2001.tb05827.x

42. Kang H, Miksche MS, Ellingsen DM. Association between personality traits and placebo effects: A preregistered systematic review and meta-analysis. *Pain*. 2023;164(3):494-508.

doi: 10.1097/j.pain.0000000000002738

43. Camerone EM, Tosi G, Romano D, *et al*. The role of pain expectancy and its confidence in placebo hypoalgesia and nocebo hyperalgesia. *Pain*. 2023;164(4):834-845.

doi: 10.1097/j.pain.0000000000002760

44. Patterson DR, Jensen MP. Hypnosis and clinical pain. *Psychol Bull*. 2003;129(4):495-521.

doi: 10.1037/0033-2909.129.4.495

45. Yerzhan A, Ayazbekova A, Lavage DR, Chelly JE. The use of medical hypnosis to prevent and treat acute and chronic pain: A systematic review and meta-analysis. *J Clin Med*. 2025;14(13):4661.

doi: 10.3390/jcm14134661

46. Colloca L, Miller FG. The nocebo effect and its relevance for clinical practice. *Psychosom Med*. 2011;73(7):598-603.

doi: 10.1097/PSY.0b013e3182294a50

47. Finniss DG, Kaptchuk TJ, Miller F, Benedetti F. Biological, clinical, and ethical advances of placebo effects. *Lancet*. 2010;375(9715):686-695.

doi: 10.1016/S0140-6736(09)61706-2

48. Foddy B. A duty to deceive: Placebos in clinical practice. *Am J Bioeth*. 2009;9(12):4-12.

doi: 10.1080/15265160903318350

49. Hróbjartsson A, Gøtzsche PC. Placebo interventions for all clinical conditions. *Cochrane Database Syst Rev*. 2010;2010(1):CD003974.

doi: 10.1002/14651858.CD003974.pub3

50. Van der Hulst AE, Klip H, Brand PL. Risk of developing asthma in young children with atopic eczema: A systematic review. *J Allergy Clin Immunol*. 2007;120(3):565-569.

doi: 10.1016/j.jaci.2007.05.027