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Biosemiotic medicines: Symbolic formulations for placebo enhancements

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Abstract:

The healing response is a complex and multiform procedure that involves many physical and symbolic interactions and synchronizations. In the clinical research model, certain factors are abstracted during which contextual elements, such as placebo responses and communicative factors, are excluded to reveal the pieces of evidence that are necessary for the mass production of clinical materials and methods. On the other side, clinical practice is a singular and chaotic communicative action in which we should include contextual and discursive factors for prompting proper biological as well as behavioral responses. Placebo responses, personal history and attitudes, and clinical relationships and communication are some of the contextual and individual factors that can be changed effectively if we can communicate with the symbolic and reflective matrices of clinical practice. In this article, the author introduces a biosemiotic formula for healing responses that include symbolic and reflective factors of healing response aligned with the related biological procedures. Not only are psychological interventions beneficial in mental health problems and symptom control but they could also be used as co-treatments to reinforce placebo responses and improve illness behavior and treatment narratives.

Keywords:

Biomedicine, mind–body, nocebo, placebo, psychosomatic medicine

Who Cares about Placebo Enhancement?

The placebo effect size is usually so big that it casts out on the effectiveness of many common drugs.^[1,2] Occasionally, we overlook that placebos are not malevolent forces that diminish our understanding and ability to control healing. As emphasized by Mitsikostas *et al.*^[3] in their 2011 study, nocebo is the enemy, not the placebo. It is a common belief that we should only remove the unintentional effect of placebos to reveal the pure verum effect—our pure power of control.

In the control game, placebos are our rivals, but once we change our game to integrity and harmony, placebo responses appear as our allies and a natural tendency to recreate

balance that is always eagerly awaiting an opportunity to put salutogenic procedures into action. We spend billions of dollars each year to maximize the effectiveness of therapeutic remedies and procedures, but how much do we expend to enhance placebo responses and reduce nocebo responses?

It is not very hard to imagine that placebo and the unconscious power of salutogenesis sometimes felt as a threat to our ego and selfish hunger to know and control. It seems that our narcissistic attitude and materialistic approach lead us to neglect or exclude placebo effects instead of reinforcing these natural medicines. The bitter truth is that nobody can monopolize this ever-present natural power so it is predictable that no powerful institution will make continuous efforts to promote and sell it. Can we hope that pharmaceutical and medical equipment companies will use placebo boosters in addition to their product launches?

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Despite an exponential rise in placebo studies, there is currently still an aura of myths and misconceptions around its image. Some of the most influential myths are “placebo is a nonspecific/constant effect” and “placebo has no therapeutic use.”^[4]

Is Placebo the Constant of Healing Equation?

When we talk about placebos, before everything, we imagine sugar pills. Of course, the sugar molecules in that amount, or any other inert materials used for placebos, have no specific effects. Therefore, we supposed that the placebo effect is the constant of the healing equation. A bizarre illusion!

Placebos are not inert materials or sham procedures, but are the sets of symbolic signs that we suggest to, or incept in, the patient’s mind that modify their healing expectation. That is why Moerman^[5] and many other scientists prefer the term “meaning effect” instead of the placebo effect. The placebo responses are semantically specific, considering the gender, types of personality and disease, doctor–patient relationship and communication, and other symbolic and relational factors.^[6-8]

Whereas verum effects rely on physical and chemical pathways to modify bodily structure and functions, placebos run neurocognitive pathways that can regulate physiologically. Every form of treatment takes place in a symbolic and communicative environment, which creates certain expectations of betterment via explanations, rules, rituals, instructions, and narratives.^[9,10] These symbolic signs run a neocortical-sympathetic-immune axis that can induce positive or negative physiological changes.^[11] The bottom-up effects of the physical and chemical interventions are always affected by the top-down effects of the symbolic and reflective elements of the therapy context.

Biosemiotic Formulas

While we rigorously formulate therapeutic agents, the meaning effect of symbolic agents is mostly implicated and, therefore, left to chance. To reduce adverse and nocebo responses and reinforce the placebo responses, we need to accurately formulate the symbolic components of the treatments. In other words, we should synchronize the chemical and physical signs with the symbolic and reflective signs to create a synergetic healing response.

From a biosemiotic perspective, even the material interactions and energetic flows are interpreted in a lived body, and the vital functions are indeed the meanings that form the physical as well as the mental.^[12] Molecules and cells and different types of energies are information

carriers for their molecular or cellular receivers; better to say interpretants, similar to the propositional or self-reflective signs that make meaning by connecting and synchronizing certain neuronal circuits.

It is time to abandon the old debate of dualism and reductionistic materialism since both of them have a hard scheme of the matter, but one of them illustrates the mental as a parallel soft world by ambiguous connections whereas the other exhibits it as the shadow of the material.

In the book *Anticipation and Epigenetics*, I propose a biosemiotic formula that integrates all the physical and symbolic aspects of healing in response to any form of therapeutic intervention [Figure 1]. This formula summarizes a body of knowledge on the elements that determine our responses to drugs and surgeries, as well as psychotherapy and placebos. I explain the pieces of evidence and reasons for this formula in the chapter “Body, Meaning, and Time: Healing Response as a Transtemporal and Multimodal Meaning-Making Process.”^[13]

Our current clinical trial paradigm is focused on the elimination of all contextual and individual factors to exclusively reveal the verum effect of the generalizable factors. This strategy is completely reasonable for the mass production of treatment materials and methods but, in the live and singular context of life and clinical acts, it is very poor and insufficient. If we want to have more control over the healing response, we should consider the contextual matrices of the person, illness, care setting, and other symbolic and reflective signs, in the presence or absence of the biomedical interventions.

It seems that we need a new generation of psychosomatic medicines and guidelines for the clinical and personalized treatment plans that include all the real factors of healing in the clinical act which have been excluded in the process of clinical research. Medical practice is chaotic and eclectic by nature, whereas clinical research aims to simplify the complex act and relational context of care and cure. Obviously, the will to know is superior to the will to heal. We need to rescue the practice from the exclusive hegemony of research.

$HRp = Ecs + Cx + Mn + Ba + Vr$ <p>Ecs = RTM + PRE</p> <p>Cx = NH + PH + HE</p> <p>Mn = PR – NR</p> <p>HRp: Perceived Healing Response, Ecs: Cognitive-statistical Errors, RTM: Regression to the mean, PRE: Patient Recall Errors,</p> <p>Cx: Contextual factors, NH: Natural history of the disease, PH: Personal history, HE: Hawthorne effect,</p> <p>Mn: Meaning induced responses, PR: Placebo response, NR: Nocebo response, Ba: Bodily awareness, Vr: Verum effects.</p>

Figure 1: Perceived healing response elements^[13]

Towards a Live Practice for the Live Body

Life is a network of complex meaning systems that feed on information.^[14,15] You may think that you feed on material foods, not information. Let us have a short imaginary experiment. Imagine you can analyze your lunch to its basic elements: carbon, oxygen, hydrogen, nitrogen, and so on. Now, you may inhale the gas elements and eat something like charcoal powder. How many calories can you take from this meal? How many essential nutrients? The answer is nothing. We open all the energetic nodes, the informational network that makes the organic matter usable and interpretable for the body. Now, it is more tangible how we assimilate information of resources into our informational network of the body and maintain our energy.

Energetic, material, symbolic, and reflective signs form and lead the vital information flows.^[12] The more coherent meaning systems and the more synchronized meaning-making processes, the healthier and more resilient we are. Thus, we need to formulate integrated semantic-mechanical treatment protocols to optimize the healing responses. Thus, it is reasonable to design a sort of active placebo that is used clinically with, not instead of, verum interventions. We can name these complementary semantic agents as biosemiotic medicines.

Biosemiotic medicines can be defined as symbolic formulations for synergizing clinical communications, visualizing the healing mechanisms and other fact-based beliefs, and moderating adverse and nocebo effects.

Biosemiotic medicines can be used as treatment-specific programs that use instructions and mind-body techniques like imagery, hypnosis, and mindfulness to enhance placebo responses.^[16] These placebo boosters can moderate psychoneuroimmune functions/meanings that align with the verum effects of remedy or procedure-based treatments.

The symbolic and reflective co-treatments are currently used in many psychosomatic and integrative medicine settings. However, I mean biosemiotic medicines in a narrower sense of mind-body interventions that focus on clarifying and calibrating the healing expectations we can have from a certain therapeutic intervention.

For instance, we can use a mind-body package for increasing nonjudgmental bodily awareness and a pain and inflammation reduction imagery exercise to boost the pain control effect of a drug or device. The script of guided imagery or self-hypnosis in this type of mind-body intervention should be very minimalistic and just a visualization of the evidence-based mechanisms of the related treatment.

These symbolic formulations could also be used in an individualized manner by moderating personal factors affecting placebo responses such as gender, temperament, attachment, emotion regulation, and cultural and personal health beliefs. Considering these factors, we can maximize the coherence of the healing narrative and responses.

Every Treatment Is a Narrative

We should remember that each treatment presents in a certain discourse of in/direct advertisement and in a sort of clinical relationship, communication, and education. These symbolic interventions are interwoven into the chemophysical agents and what we assess is the effectiveness of such psychophysical cocktails. Thus, it is quite reasonable to consider ourselves responsible not only for the modular and biomedical interventions but also for the singular phenomena and clinical narratives.

For the last 20 years, I have been working on reframing biomedical interventions for my patients to change their treatment narrative, especially for those clients who have negative attitudes toward their prescribed treatments. Some of them have obsessive-compulsive traits and some of them simply do not expect a healing response from that treatment. Some of them experienced terrible nocebo responses to different types of drugs and created unwelcome barriers in the path of recovery. In parallel, we usually practice different types of mind-body interventions to set their healing expectations and coordinate their psychoneuroimmune system.

Both treatment-specific and individualized biosemiotic medicines can be helpful in reducing chaotic responses to treatments and low adherence to medical instructions and prescriptions. Integrating non-cognitive and cognitive meaning-making systems about treatments may evolve our understanding and effectiveness in healthcare systems.

Several studies on open placebos show that even the ritual of receiving treatment can moderate the physiological functions and bodily sensations and feelings.^[17,18] Even such minimal symbolic and reflective signs can activate salutogenesis.

Based on the specific and even singular context of treatment, caregivers and patients can participate in the co-construction of more synergetic anticipations, beliefs, and narratives that work as symbolic and reflective boosters of biomedical interventions or even distinct therapeutic agents that can induce our epigenetic changes.^[19]

In this biosemiotic approach to health and healing, caregivers are more authentic and innovative than the

mechanical role of the executors of clinical guidelines, whereas patients are much more active in formulating their biosemiotic medicines.

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