

## RESEARCH ARTICLE

# How placebo shapes sensory data

## *From signs and memory to the embodiment of living beings*

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**Abstract**

The placebo phenomenon is observed on the basis of two main assumptions, at the intersection between biological, semiotic and epistemological fields. 1. A placebo response is induced by many pretexts in different contexts, none of them being regarded as a cause, but as a catalyst. 2. This response is an interpretation by the body of how to adapt during the coming times.

To tackle it in an interdisciplinary approach, we did not aim at a homogenous understanding, but assembled different considerations from the psychophysiology, semiotic or phenomenology, in order to find the *signature* of placebo. We propose that this unique *signature* appears in the particular way sensory data are shaped in a configurative meaning suggesting future body adaptive requirements.

The placebo effect refers to the meaning of a treatment for the subject himself, a meaning the body can grasp. This very grasp can be enlightened by the transcendental understanding of the body and its bodily language developed by Merleau-Ponty. Such language is addressed by the body to the body. This language is also approached by psychosomatic, and might be analyzed both in more general and more specific ways at the same time. Its epistemological dimension can be related to the logic of abduction.

**Keywords:** placebo - conditioning - memory - meaning - expectancy - anticipation - embodiment - epistemology

## Introduction

Placebo is widespread in the everyday language, and yet it remains very difficult to define. To have a grasp on such a multifaceted phenomenon, we managed an interdisciplinary perspective, more likely to account for the cultural as well as biological aspects of placebo, encompassing its memory and communication dimensions. First, we considered memory as a fundamental property of living organisms, in its contribution to adaptation strategies evident in placebo responses. In a second step, we analyzed placebo as a sign, following C.S. Peirce semiotic model, and we extended this perspective to the molecular description of intra and intercellular signalling mechanisms. In a third step, we tackled the twofold direction of memory as a trace of the past experience (trace of) to be integrated in the elaboration of future oriented strategies (trace for). This is recognized as the heart of the abduction concept, to make it an embodied epistemology concept. Finally, we revisited Merleau-Ponty's transcendental phenomenology in an attempt to bridge what remains a gap between the reading of signs and a coherent bodily response.

In spite of the obvious complexity of the word placebo, recent advances in neuroscience provided the everyday language with very simple statements about human behavior, such as "this is certainly a placebo effect", or "it is in her DNA". These statements are often made with an almost perfect assurance. They are frequently considered key explanations with a scientific basis because they rely heavily on the use of technical words. However, the word "placebo" has a fickle meaning, and its underlying mechanisms are still in question as well as its scientific basis is far from being clearly established. In pharmacological studies, placebo is technically defined as a difference between

the therapeutic effect of a known pharmacological substance and the observed response to an inactive agent in a double-blind experiment but such a definition does not shed much more light on the phenomenon.

Yet, the placebo response provides fascinating evidence that animals, including humans, are permanently expressing anticipatory adaptation responses to what is likely to happen. A placebo response entails a communication between an environment and a subject, relates to mental and somatic processes, combines past and future adaptations in response to the interpretation of signs. Disciplinary approaches, such as psychophysiology, pharmacology, semiotics or statistical analysis, seem to fall short when dealing with an issue of such a complexity. This is why we combined our efforts in an 'undisciplinary' line of research in which no specific explanation is a priori favoured: on the contrary, we entangle various disciplinary perspectives in order to provide an 'enriched' view that might better account for the placebo phenomenon.

However, our purpose is not to mix specific description in a more general language, it is to combine these approaches to respect the multidimensionality of an object such as the placebo phenomenon. In other words we would like to find how specific disciplinary approaches tackle similar processes and yet enrich their signification.

First, we will focus on the biological perspective of memory as a fundamental issue. Secondly, we will consider producing and interpreting signs as the essential activity of living structures whatever the complexity of their biological organization is. Third, we will tackle the epistemological issue of how the placebo response illustrates the effort of an organism to tame the future in a proactive stance, possibly

compared with the effort by which a scientific approach aims at elaborating laws. Finally, we will question to what extent the phenomenological perspective developed by Merleau-Ponty concerning the issue of transcendence might help to understand how placebo responses are in a continuity, from physiological reflex responses to cognitively adjusted adaptive ones

### **1. Memory as a basic property of living beings**

Placebo responses rely on memory as a fundamental property of living organisms, from elementary cellular activities to cognitive abstractions. In this perspective, we assume that different specific brain systems have different memory properties, which contribute to a multiplicity of memory systems. In the brain, a federation of structures enables us to project a possible narration, often starting with a conscious statement, such as «I remember», but memory as an overall process has many different faces, not all of them declarative.

The writings of Marcel Proust (1919) provide one of the most famous examples of a rich multi-sided memory. First, the contact with cake crumbs in a sip of tea triggers a delicious pleasure with no evident cause (p.46). Later on, following the successive activation of different memory components, a broader context reached Proust's consciousness: Combray and its neighborhood emerged from his tea cup (p.49). This description reflects a sequence of specific memory components. First, an emotional reaction links a deep pleasure with a surprise due to the lack of identified cause relating to this memory reactivation. A search effort follows, involving successive steps, until hitting the heart of the recollection, its exact context, i.e. the room of aunt Leonie, a place inserted in a geographic context, Combray. Such an

instance illustrates what is defined as episodic memory. It does also insist on the fact that reactivation need not be voluntary. Automatic processing was triggered by a reminder cue, the sip of tea, and was further assisted by an active supervision. As we know from personal experience, automatic search processing may support prolonged unconscious activations, until a name, missing some time ago in a conversation, suddenly comes up loudly.

Any of the memory systems studied by the neurosciences during the second half of the 20th century (Squire, 2004) are possibly included in placebo responses, though none is specifically implied. Beside a broad concept called «expectancy», specific conditioning responses have been related to placebo responses in experimental procedures (Colloca & Miller, 2011). The association of conditioning and expectancy accounts for the frequent dualism of memory categories, i.e. implicit or explicit, procedural or declarative, knowing how and knowing that... In a biological perspective, and also following Proust description, we consider that conscious strategies are mainly useful in reinforcing some memory processes, like the phonological loop contributes to reinforce a working memory process through voluntary reactivations and repetitions.

For our purpose, the most important issue is how to harness placebo responses as a component of positive treatment issues rather than a strategy aiming at deceiving the patients or the subjects. To cut a long story short, a placebo, or possibly a nocebo, response inevitably participates in therapeutic issues.

In the following, we examine some memory dimensions contributing to the placebo phenomenon: 1) this adaptive physiological response is experience-dependent, much like a change in cardiovascular responses

following living in low gravity; 2) as a reaction to an on-going situation, it requires an interpretation, either provided by active perception or by the extraction of its meaning, the purpose of the treatment and the intention of its provider; 3) placebo response can also be triggered by a speculative conviction as how the subject's situation might evolve from now on; 4) no consideration of a possible future can be dissociated from an embodied simulation of this future, as in a hypothesis testing process. This need not be voluntarily oriented.

### ***1.1. Placebo facilitates adaptive responses***

At first sight, a placebo response might not look like a very successful adaptation strategy, because it seems easy to deceive. It is like a gamble based on the hypothesis that the future is likely to repeat past disturbances taking place in « similar circumstances ». Reactivating past adaptive strategies, from molecular reactions to sophisticated anticipation, might thus be relevant. This is why a conditioning response has been considered first to account for the underlying mechanisms (Price & al, 2008; Benedetti, 2014). In this view, conditioning favors an early and accelerated adaptation process, reducing the effect and cost of a repeated disturbance.

According to a general biological definition, memory brings together the traces of previous adaptation efforts made by a living organism. This accounts for the growth of muscle fibers following physical activity, the reinforcement of neuronal circuits after prolonged activation (plasticity), the production of new granular cells following activation of the hippocampus and numerous other obvious or subtle functional changes. In other words, living organisms undergo a structural and functional development to be ready to adapt more efficiently to a future

situation similar to those faced in the past, as if trained to current selection processes

In this sense, memory facilitates a sequence of actions in which each step increases the probability of the next one. Eating requires the detection of food, and serial activation of the digestive tract. This can be triggered by the smell of food as well as other neutral cues in the environment following proper conditioning. On a higher organizational level, the pavlovian conditioning illustrates how the vegetative and behavioral components of an adaptive response such as food consumption or fear responses are activated as soon as precursors of such opportunity can be detected, even to the mere thought of it. Memory prepares for future scenarios in simulating their possible consequences through associated sensorimotor reactivation. Early salivation and activation of the digestive tract when food is likely to be available is certainly time saving, as it bypasses the extensive sequence of reflex responses that ought to be triggered by the actual presence of food in the mouth or stomach. Anyone familiar with the speed of a dog swallowing a piece of meat understands that any advanced preparation facilitates earlier digestion processes.

In brief, all systems in an organism have to satisfy an adaptive issue, which contributes to an overall homeostatic memory, combining cognitive and emotional responses. Non lethal strategies are likely to be repeated in similar circumstances. Responses too costly to prolong biological maintenance in certain contexts would promote allostasis (Koob & Le Moal, 2001), a situation from which return to homeostasis is unlikely. On the long term, these responses cost more in terms of energy dependent processes with regard to the main benefit of what they prevent.

### ***1.2. The meaning of the «treatment» participates in the placebo response***

Moerman & Jonas (2002) proposed that deconstructing the placebo effect reveals the role of the «meaning response». In other words, patients' responses express how they interpret the treatment and the meaning of a treatment can be compared to its aim, according to his or her expectation and to the intentions of the prescribers and other caregivers. Following Gallagher (2008), understanding intentions is mediated by active perception. It might thus not require any additional cognitive machinery - based on the theory of the mind (TOM) or on simulation theory (ST) - to elaborate sophisticated inferences about what this treatment means. An active perception (Gallagher, 2008) includes the simultaneous coding of the partner's intentions. This is merely embedded in action perception or enaction (Varela & al, 1993), and prepares the perceiving subject to engage in some action compatible with this perception. This is not to say that conscious cognitive representations are not contributing to placebo. We do simply suggest that «meaning» assessment does not require the subject to be fully conscious. The meaning can also stem from faith, in medicine, God, scientific explanations or from unidentified body sensations, or merely enhanced comfort.

Placebo is thus related to social perception in the intersubjective context and this would also account for possible nocebo effects related to patients (mis)understanding how clinicians comment on their situation. No conscious effort would be required from the ill or even comatose patients to benefit from any additional placebo effect that would enhance any real treatment (Colloca & al, 2004). The meaning can be simply evoked by a physician reporting some comments of patients treated with such an inactive pharmakon (Kaptchuk & al, 2010). This

view insists on the fact that the meaning, like any placebo phenomenon, is elaborated by the patient or subject itself in his relation to the social or physical environment. It is not directly due to whatever placebo treatment is provided as such.

Pain has largely been considered to be vulnerable to placebo suggestions. This emotional response induces a negative effect and reduces motor activity or any motivation for risk taking in general. It contributes to the assessment of how serious the situation is, and of how it might get worse. Any reduction of pain, whatever its origin, thus may affect the meaning response. As emphasized by Humphrey (2002), there is no clear explanation as to why auto-analgesia is not activated in any painful situation, except that this would inhibit a functional signal. Nor is it clear which factors may activate or prevent this inhibition. Except a devaluation process of the pain signal from unknown origin, among which placebo inducers.

### ***1.3. Placebo as a working hypothesis***

The main motivation mediated by pain is to contribute to its reduction, by any means. Any decrease in pain is actively expected from a treatment and is likely to enhance the meaning of a treatment. So that the first effect of a treatment, well before its physical action, might be an auto-induced pain reduction, mediated by endorphines, thus buffering the emergency. Since pain and pleasure share common neurological networks (Leknes & Tracey, 2008; Leknes & al, 2013) these changes are likely to trigger dopaminergic activation (Schultz, 2007) in the healing context (Miller & Kaptchuk, 2008). Conversely, this may also enhance context meaning and suggests that pain reduction and placebo effect interact in circular loops, able to enhance the expected and effective pain reduction. An explicit declaration that a powerful antalgic

treatment such as morphine is being administered has an impressive placebo effect, as if encouraging the patient's body to contribute directly to analgesia (Colloca & al, 2004).

A recent vision of the individual, based on brain properties is that it tries to anticipate whatever is likely to happen (Bar, 2007; Bar, 2011). This is accompanied with a revival of the efference copy concept by Von Holst & Mittelstaedt (1950) leading to the statement that action perception is hypothesis testing (Donnarumma & al, 2017). It has also been encouraged by a proposition that pain was enhanced by the failure of hypothesis confirmation (Harris, 1999). In other words, the confirmation of an expected increase in well being might engage in a positive feedback loop, thus enhancing the placebo effect. Acknowledging for the gamble dimension underlying placebo responses suggests that an expected hit, even a small one (*l'hypothèse suffisamment bonne*, Schenk & Tarditi, 2012) should enhance the placebo effect.

The perspective of a proactive brain supports the view that remembering the past contributes to imagining the future (Schacter & al, 2007; Büchel & al, 2014) and that the placebo response mediates a homeostatic imagination. It emphasizes the essential role of signs reading, as discussed in semiotics.

## 2. The Semiotics of Placebo

Nowadays some doctors prescribe placebos to their patients with full knowledge of their lack of direct therapeutic effect (Tilburt et al. 2008). Such a practice aims at maximizing the chances of healing, inasmuch as the context of healing gathers multiple signs that orient the subject being healed towards the horizon of getting better.

This orientation towards getting better is qualified hereafter as the placebo effect.

Thus, we assume that the placebo effect stems from the interpretation of biological and cultural signs in a context animating their therapeutic action. In order to grasp these cultural and biological processes of signification, we based our interdisciplinary perspective on the semiotic theory of Charles Sanders Peirce (1931-1966). Such a theory enables us to consider placebo as an indexical sign (a clue) and to explain the foundations of its interpretation.

### 2.1. Collecting signs

According to Peirce, a sign is “something which stands to somebody for something in some respect or capacity” (Peirce: CP 2.228). In other words, a sign is a sign because it is “read”: it is always integrated in an interpretative process. In human communication, a sign can be a word, a gesture, a text or a posture read by an interpreter. In the biological context for example, a sign can be a neurotransmitter read by a membrane protein with which it is temporarily in synchronisation. For Peirce, the signs can be apprehended according to three functions: as a symbol, an icons and an index<sup>1</sup>. Let us consider placebo through the prism of each of these functions:

- as a word (which means by convention), it is a symbol;

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<sup>1</sup> Those three functions – symbol, icon and index – are understood through the relation between the *sign* and the *object* that it designates (Peirce 1931-1966): a symbolic *sign* is associated by convention to its object. The word “fire” thus refers to the *object* “fire”; the *sign* of an index has a relation of existential contiguity with its *object*, thus smoke is a clue of fire. An iconic *sign* resembles its *object*, a drawing of a fire resembles a fire. We will come back to this instance.

- as a pill (which looks like a drug), it is an icon;
- as a possible effect (which generates expectations), it is an index.

It appears that those three functions can be associated to a single sign.

Taken out of context, every sign potentially implies these three functions. Put into context, a sign is always construed as an indexical sign (indexical value <sup>2</sup>): notwithstanding its main function, it orients the reader's attention in a specific direction. In the context of a placebo response, all the signs – words, wordings, gestures, pills, white blouses – acquire the qualification of indexical signs. This qualification is what leads to the placebo effect.

Why is there a relation between the indexical value of a sign and the placebo effect? The answer is in the definition of the function of an indexical sign. To define this function, let us take the example of the relation between smoke and fire. Smoke is an indexical sign, a clue, for fire inasmuch as they are in an “existential continuity”, in an “association by contiguity” (Peirce: CP 2.306) and in a “dynamic connection”. Smoke implies the existence of fire. Even more so, smoke is traced back to fire, which is the very condition of its existence: where there is smoke, there is fire. It is our experience that brings us to establish this relation between the sign (smoke) and its object (fire): seeing smoke compels us to find fire.

Regarding placebo, in a medical context, a comforting utterance, a pill or a white gown

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<sup>2</sup> This indexical value is somewhat of an arch-functionality of signs (Berthoud 2006; Merminod, forthcoming) relative to the generalized indexicality of the signs (Garfinkel 2007 [1967]; Levinson 1983; Heritage 1984): a sign acquires its sense in and through its use.

functions as indexical signs, they are the clues of a possible recovery. They indicate a direction, as they are oriented, and therefore they create an expectation of recovery. As a consequence, our experience of the world, *i.e.* our memory, associates those signs with the possibility of feeling better. Thus, in a medical context, they act as an operating order, which invites the interpreter to a potentiality into an actuality, as we will explain it in further details *infra*.

## 2.2. A theory to relate signs to one another

Quite reasonably, the interpretation of those signs is inserted in the patients' vernacular theory regarding their modes of recovery or symptoms reduction. Among those symptoms, the main one would be pain.

In the case of placebo, it is easy to detect vernacular theories that may underlie the placebo effect:

- The syringe of the healer contains a liquid that should be effective;
- The hospital is a place gathering multiple experts wearing white gowns, it is therefore logical to go there in case of medical emergency;
- Doctors do not indulge in small talk, they are neither charlatans nor liars: should they tell me that I will heal, it means that I will heal... In that case, I might play my part in it.

Concrete imagination (sensory, through familiar objects or encountered situations, for instance) but also moral imagination framed by normative systems (Geertz, 1973) and shared representations are the main supports of vernacular theories (J.C. Usunier, personal communication). Vernacular theories are also called folk, popular

or cultural theories. Kempton<sup>3</sup>, in Quinn and Holland (1987), suggests the following definition:

« Human beings strive to connect related phenomena and make sense of the world. In so doing, they create what I call folk theory. The world folk signifies both that these theories are shared by a social group and that they are acquired from everyday experience or social interaction. To call them theories is to assert that they use abstractions that apply to many analogous situations, enable predictions, and guide behavior. I contrast folk theories with institutionalized theories, which are used by specialists and acquired from scientific literature or controlled experiments » (Kempton, 1987, 222).

The theory described by Kempton operates through its abstract structure. In other words, it is a *mnemonic theory*, a theory as memory (Volken, 2005).

The theory operates through its epistemological cognitive and mnemonic aspects, but also through its semeiological nature. Indeed, by mentioning that a theory not only allows to classify or categorize (given that its « abstractions » apply to « *many analogous situations* ») but also emits predictions and guides conducts, Kempton mobilises an entire semantic field that refers to the semeiological notion of *index*: traces, indications, hypothesis, orientations, directions, expectations, anticipations. In physiological terms, those signs are marked as traces in the memory. They are then refreshed according to the necessities of the context of action in which

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<sup>3</sup> Kempton (1987) uses the vernacular theories of heating a home. (i. e. how to spend as little fuel as possible while heating one's self as well as possible). The vernacular theories concern nearly every aspect of life: from the roundness of the Earth to healing processes and the origin of HIV.

the “subject” is. Those traces shaped as scripts are ready to be used under the condition that they can be adapted to the current case, thus always operating *in concreto*, but not without a certain “memory” of the past.

Let us take the example of a traffic sign. It has the specificity of being both an *event-sign* and an *action-sign*. As an event-sign, it is something of and in our world - a sign in our case -, a reality that we can concretely, “pragmatically”, experience. As an action-sign, it gives a direction to the on-going action, a “projection”: a *direction* relating to space and a *direction* relating to meaning. The indexical sign thus enables the implementation of such an action. Are the traffic signs not sometimes called “indicators” or “sign-posts”? Theory and practice are therefore strongly linked, *entangled*, in order to give us a direction. The placebo effect can base itself on such a twofold direction.

### 2.3. *Actions are for the future*

As an indexical sign, placebo is at the same time a *trace of* and a *trace for*, linking past and future. From a condensed past (*trace of*), it looks onto a future (*trace for*).

The indexical sign thus appears as a “*thick sign*”, implicitly containing a rule of extension such as: « If A, then... ». Every sign, and the indexical signs in particular, refers to a reality (material or immaterial) other than itself: if smoke then fire, according to a conjectural inference, based on experience or “common sense”. and deprived of any absolute necessity. This sign can be called “*thick*” because it acts according to and in a temporal window: it takes time, it is not instantaneous. It opens a time window during which particular reactions, biological ones, are easily triggered.. This cognitive structure could be expressed as follows: a past apprehended by

the future during a complex cognitive operation, a future that became possible thanks to this past and that is oriented, led, anticipated by this dynamic sedimentation.

Thus, placebo as an indexical sign – that is to say, as a *trace of* and *trace for* both in *theory* and *practice* – prompts the subject to interpret actively. This interpretation has to be understood as the subject's integration of the suggestions made by the context to anticipate the phenomena that would trouble or favor its project of living being.

This perspective is clearly related to a contemporary understanding of the brain structures involved in episodic memory such as the hippocampus. There is growing evidence that the later structure is taking an active participation, together with anterior cortical regions (among which the prefrontal cortex) when subjects imagine the future (for a review, see for ex Berthoz & Debru, 2015).

### **3. When past means future: an epistemological consideration**

As stated above, the placebo effect manifests itself in two ways. Firstly as « trace of » (past-oriented) and secondly as « trace for » (future-oriented), both of which create the space for a « present ». This present integrates past experiences and previous personal knowledge, all of which create expectations for the future. These expectations, while directing our actions, remain quite flexible in terms of understanding the first signs of their (possible) inadequacy, which in turn induces a modification of the expectations or a change of strategy.

As « trace of », placebo construed as a clue mainly refers itself to an entire medical scenario made of prototypical depictions such as being taken in charge in a hospital (an indication of professionalism), by

people wearing white gowns (an indication of appropriate knowledge) and carrying drugs or syringes (indications that the therapeutic strategy will be successful).

As a « trace for », placebo generates positive expectations: When a living organism anticipates an effect, this anticipation has some components of what will happen, it is a simulation. As Plato says: if I know everything there is to know about an object I am aiming at, such a research becomes useless. That being said, if I have absolutely no knowledge regarding said research, it becomes just as pointless, given that I do not know how and where to start it. Contemporary epistemology corroborates this argument: « [...] there is no such thing as an unprejudiced observation. All observation is an activity with an aim (to find, or to check, some regularity which is at least vaguely conjectured); an activity guided by problems, and by the context of expectations (the “horizon of expectations” [...]). » (Popper, 1974).

#### **3.1. Testing the simulated future**

Based on this horizon of expectations, we formulate a rule taken as a hypothesis. If what we observe with our own eyes is indeed an occurrence of such a rule, the situation does not have anything surprising: it is tamed and thus integrated in the corpus of ideas that are proven and accepted by the relevant community (the scientific one in our case). Epistemologists are well aware of this anticipated rule which, if properly selected (thus showing the confrontation with the « real »), will explain the occurrence through deduction (albeit always incomplete) of this anticipated rule. This method is called « hypothetico-deductive » or abduction.

This figure is well-known in Anglo-Saxon semiotics and popularized by Umberto Eco,

in his thriller novels in particular. Indeed, police investigations, like medical examinations, proceed by stringing clues, traces or symptoms with one another. Clues are at the heart of the legal methodology as seen in judgments, which are not based on the truth but on convictions, the « inter-subjective » agreement between members of the concerned community. Such an agreement can be put in doubt, but this incertitude will be so confined that it will not hinder one's claim to the truth, the « veri-similitude » (plausibility) and not the truth itself: « beyond reasonable doubt ».

As soon as reality escapes binarity (nearly always), knowledge cannot logically search for an « absolute » truth, given that not proving the danger of a certain substance is not the equivalent of proving its innocuousness. Truth thus reveals itself as properly « relative », not relativist but probabilist, according to the highest « veri-similitude » (plausibility) of the alternative chosen *in relation* to the other possible ones. This sends back to a problem of choice, thereby of conviction, belief and trust. The placebo effect does not require anything more.

The scientific epistemologist recognizes in the placebo effect the very structure of abduction, which does not require solid bases (as it is hypothetical), rather a « sufficiently good » base to voice anticipations and direct our everyday knowledge like our scientific experiments: « The empirical basis of objective science has thus nothing 'absolute' about it [This assertion is based on an analogy between science and law, which is taken as the model. More precisely, the analogy is made between science and the judgment procedure of the jury in which our peers determine the facts and give a decision that is beyond reasonable doubt]. Science does not rest upon solid bedrock. The bold structure of its theories rises, as it were,

above a swamp. It is like a building erected on piles. The piles are driven down from above into the swamp, but not down to any natural or 'given' base; and if we stop driving the piles deeper, it is not because we have reached firm ground. We simply stop when we are convinced [*beyond reasonable doubt*] that the piles are firm enough to carry the structure, at least for the time being. » (Popper, 1935).

We therefore *really* know the world, but only within the aspects to which our body grants us access, meaning, *aspectually*. Because we are embodied, we know first through our body, physiologically, according to the pragmatic intimacy between this body that we are and the nature that we question in the *act* of knowledge: "The act of who is currently feeling and what is currently felt is one and the same" (Aristote De anima 425 b 25-27, our translation).

### 3.2. Placebo questioning the future

This *act* of knowledge differentiates itself from *knowledge*, which is built *from* this aforementioned act, by repetition, by abduction and analogy, using in turn memory and imagination according to Aristotle. The « continued » cognitive process (considered in the perspective of duration), viewed from a temporal window, therefore includes simultaneously the unity of the Subject and the Object in the *act of knowledge* and their duality, or separation, in the *knowledge* and its abstract ascent in the mind of the Subject, momentarily freed from the presence of the Objects.

This « *complex monism* », combining unity and duality, is set against modern dualism, which separates the mind from the body all the while asserting the superiority of the mind, like the spirit or soul (*res cogitans*) and the scope (*res extensa*) for Descartes. They are seen as situated in different

worlds, despite the fact that the pragmatic realities force them to closely interlock.

We wish to have a «sufficiently good» knowledge of these pragmatic realities for us to maintain ourselves *alive* in them, i.e. in movement in physico-physiological terms, and in action in ethical terms, body and soul: «*Among* all animals, only the human...» as Aristotle repeatedly says. Could this be the most fundamental (re)discovery of neurosciences?

The observation of this «sufficiently good» encompasses the «everything is equally valid» of relativism, the «we know nothing» of skepticism, as well as the «we will know everything someday» of scientism.

It is through acceptance that the human *is* a body that the clue (the most corporeal function of semiotics), is at the heart of every human cognitive undertaking, in particular the placebo, that we will understand that the general texture (*princeps*) of science is the anticipation under a certain hypothesis (the future) based on real-life cases (the past), i.e. the very operation of everything living, i.e. abduction. We understand that science is literally embodied, induced by the body.

#### 4. Merleau-Ponty's transcendental account explaining placebo

Our interdisciplinary investigation regarding placebo emphasized its multiple components and the necessity to convene multiple perspectives to genuinely picture the placebo phenomena. We insisted on the convergence of physiological, semantic, and cultural levels of explanation, which in their turn require an “embodied” conception of subjectivity. This diversity of perspectives provided a systematic and descriptive collection regarding placebo phenomena. However an absolutely crucial

issue still remains unsolved, namely, how is the “existential continuity” between the “indexical sign” and physiology claimed by Peirce even possible? In other words, we need to establish a conceptual framework, to genuinely think of such a continuity. That is to say, a theory, which actually accounts for this “existential continuity”, not merely describes or points at it. The Peircian sign, as we saw, does necessarily bring memory into play as the fundamental ability of the living to anticipate<sup>4</sup> “through an interplay between ‘trace-of’ and ‘trace-for’”. Hence, we still need to face up the following question: how is it possible for the sign to be conditioning regarding physiological organization of the organism which interprets it? It seems to us, in this respect, that the transcendental phenomenology of Maurice Merleau-Ponty could be a way to “embody” this constituting ability of the sign regarding the organism.

Let us first things notice that the physiological description of memory as an anticipatory ability is completely in line with what Merleau-Ponty described of the living organism in the *Phenomenology of Perception*, namely, that the organism, if it actually receives stimuli from its environment, is always “meeting” them while organizing itself and stimulus reception in advance. This very (auto)organizational ability characterizes the Merleau-Pontyan understanding of the transcendental as always embodied (as underlined in Barbaras 1990 or Gallagher

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<sup>4</sup> The endeavor consisting in seeking to go “beyond mere correlates” (Forest 2016: 100) is actually a traditional one in philosophy of mind (see for example “beyond the gap” by Roy *et al.* 1999). Maurice Merleau-Ponty's phenomenology has by the way often been proposed as a solution to such an issue (Bimbenet 2012, Gallagher 2005, Varela, Thompson & Rosch 1993, Petitot *et al.* 1999).

2005). Drawing on Stein, Merleau-Ponty writes<sup>5</sup>:

“The ‘sensible quality’ [...] are not de facto effects of the situation outside the organism but represent the way in which it meets stimulation and is related to it. [...] The function of the organism, in receiving stimuli is, so to speak, to ‘conceive’ a certain form of excitation. [...] The excitation is seized and reorganized by transversal functions which make it resemble the perception which it is about to arouse.” (Merleau-Ponty 2005: 86-87; emphasis original).

For our present purpose, nothing forbids us to hypothesize that the organism could organize its own physiological disposition to “meet”, not a stimulus in this case, but a medical treatment. Indeed a medical treatment is, in principle, nothing radically different from a stimulus: it is actually a physico-chemical phenomena interacting with an organism and appealing to a reaction of this organism. The Merleau-Pontyan statement according to which “the excitation [perceived by the organism] is seized and reorganized by transversal functions which make it resemble the perception which it is about to arouse”, seems, according to this parallel drawn between stimulus and medical treatment, easy to paraphrase as follows: when one takes a (supposedly medical) substance, his organism is reorganized by transversal functions which make it resemble the

medical treatment which it is about to arouse (if the taken substance were actually a medical one). If we take this statement into account and consider the Merleau-Pontyan analysis of organic anticipation of stimuli (the embodied transcendental allowing the organism to “resemble” what is “about to” happen), it will then be serious to think of the organism as having the ability to resemble (by anticipation) the treatment it is going to receive. This could be an explanation of what we generally call a placebo effect.

However, one would probably object that this could only explain a placebo effect in the case where the organism would have experimented, in the past, the treatment it will try to “resemble.” Regarding a placebo effect occurring with a treatment entirely new to the organism, or, occurring to a subject because of a mere explanation one gave him of the effects a medical substance is supposed to have, things are quite different: the subject thinks he will take this substance but actually does not take it and never took it in the past, how does one explain a placebo effect in these very cases? In other words, how does one understand and explain that a mere explanation (linguistic and therefore semantic) can result in a placebo effect, that is to say, that a mere explanation can put the organism in a position to anticipate an effect which is actually not even embedded in the substance he will take and which he never experienced before? This opens the possibility for language to take part in physiological anticipation. Merleau-Ponty himself, by the way, suggests that language has an important role to play regarding this process when he writes that “the function of the organism [...] is so to speak to ‘conceive’ a certain form of excitation.” The question is therefore to know whether the function of the organism regarding placebo phenomena would not merely be to “conceive” (that is to say to embody, by

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<sup>5</sup> For a general definition of the “transcendental”, the reader can rely on the one provided by Dan Zahavi : “Transcendental phenomenology [...] is interested in the constitutive dimension of subjectivity, that is, it is interested in an investigation of consciousness in so far as consciousness is taken to be a condition of possibility for meaning, truth, validity, and appearance” (2010: 10). Zahavi did not intend this definition as specifically applying to Merleau-Ponty in his article but it is in our opinion sufficiently general to provide the reader with an idea of what a transcendental perspective is. For more details about the transcendental, see Zahavi 2014. About the difference between transcendental perspective and “empirical science” and the importance of the former, see Zahavi 2010: 8.

organizing itself) a certain form of physiological effect, effect triggered by taking a substance. This question leads in turn to the question to know what could be the status of language when a mere process of conception would be capable of organic anticipating effects, as Merleau-Ponty nearly explicitly suggests it here.

In other words, our attempt to explain the placebo phenomena in a Merleau-Pontyan way left out the question of the relationship between language and the “transversal functions” of the organism emphasized by Merleau-Ponty. Fortunately, the work of Merleau-Ponty actually widely addressed this issue. Indeed, as Renaud Barbaras emphasized, despite the difficulties he encountered all his work along, Merleau-Ponty tried to account for the transcendental perspective and mental life in general from the perspective of their embodiment within the concept of “living body.” This logically led Merleau-Ponty to an embodied conception of language (Barbaras 1990, 1998, 2008; see also Bimbenet 2004). And yet, this understanding of language, providing its translation within the theoretical framework we are currently trying to set up, allows one to account for the semantic features of the placebo phenomena we are trying to explain. The following quote can indeed be a response to the question to know what could language be for a transcendental anticipating body as the one described by Merleau-Ponty:

“I do not need to visualize the word to know and pronounce it. It is enough that I possess its articulatory and acoustic [essence] as one of the modulations, one of the possible uses of my body. [...] The word has a certain location in my linguistic world, and is part of my equipment.” (Merleau-Ponty 2005: 210; emphasis added, translation slightly modified)

Bimbenet clearly comments: “Speech is therefore originally a bodily acting and the meanings it is aiming at, before being objective and conceptual, are gestural and

existential” (2004: 199; our translation). Further, Merleau-Ponty specifies this conception of language as an “equipment” of the body in the following way:

“The word ‘sleet’, when it is known to me, is not an object I recognize through any identificatory synthesis, but a certain use made of my phonatory equipment, a certain modulation of my body as a being in the world. Its generality is not that of the idea, but that of a behavioral style ‘understood’ by my body in so far as the latter is a behaviour-producing power, in this case a phoneme-producing one. One day I ‘caught on’ to the word ‘sleet’, much as one imitates a gesture [...]” (Merleau-Ponty 2005: 468-469; emphasis original).

In other words, as Merleau-Ponty also writes: “expression is everywhere creative” and “there is no analysis capable of making language crystal clear and arraying it before as if it were an object.” (Ibid.: 455).

If we now try to articulate this Merleau-Pontyan conception of language to our attempt to account for placebo phenomena and to the particular question of the role played by language in the placebo phenomena, things become far more clear. Given that language, as Merleau-Ponty understands it, could refer to the indexical function of the peircian semiotics we developed in section 2, and that it is therefore “part of my equipment” as “one of the possible uses of my body, (and language in Merleau-Ponty’s work is more or less equivalent to “semiotic” as we used it before), therefore, given that this use is characterized by Merleau-Ponty with the notion of “behavioral style”, nothing forbids us any more to understand the placebo effect as the product of a bodily reorganization triggered by the anticipation of the effects of a medical treatment. This reorganization could actually be ensured by the same “transversal functions” operating within perception, inducting in this case a resemblance of the bodily state to the treatment which would normally occur, treatment the subject can picture through

the explanation given to him even if he never actually experienced it before.

We thus understand, in other words, how it is possible that placebo can occur even though there are, so to speak, only mere words at stake in the process: we saw that Merleau-Ponty thinks of this physiological reorganization with the category of “conception”, which appears now completely legitimate given his understanding of language as “one of the possible uses of my body” as being “a behavior-producing power.” Therefore, placebo effect, as a reaction to an explanation (given by the doctor who will give the patient the fake treatment) is a conception by the body – a bodily behavior in a very strong sense of the term –, that is to say, a physiological anticipative organization conceived by the body to “meet”, namely, “resemble,” the treatment “which is about to arouse”. The new feature of the treatment is no longer an issue given that, its effect being explained to the subject within language (by the doctor), it is therefore “caught on” to by the body as “one of [its] possible uses” and thus anticipated by the body as it anticipates, in perception, an excitation to “resemble the perception it is about to arouse”. It seems to us in this respect that his Merleau-Pontyan theory of language has demonstrated its explanatory power to understand how semantic realities can dictate a physiological reorganization to the body. Frenkel (2008) also takes this issue into account but, in our opinion, in an unsatisfactory way.

Let us moreover precise that this perspective which tries to show the physiological implications of Merleau-Ponty’s phenomenology is inspired by (and tries to be in line with) recent works (Bimbenet 2012, Gallagher 2005, Gallagher & Zahavi 2012, Petitot *et al.* 1999, Thompson 2007, among others). Let us also

note that our attempt ends up being frankly different from Frenkel’s Merleau-Pontyan understanding of placebo (2008), because Frenkel simply ignores the transcendental perspective, even though he sometimes quotes the same extracts we relied on (69-70), even though he characterizes placebo as being part of “the family of bodily activities we would label skillful and unreflective” (65) and tries to “generalize this idea to a bodily understanding of socially and biologically determined space” (68), and even though we are in line with some of his important claims, for example when he writes “that we need a way to discuss embodied meanings” (67). He nevertheless does not emphasize enough the anticipatory ability of the body, as a result – in our view – of the complete absence of the transcendental perspective in his article: this ability is, according to our argumentation, the only way to explain rigorously what he points at as the “ability” of “meaning” “to influence physiology” (74).

## **5. An interdisciplinary perspective to consider a placebo signature**

In this work, we found that placebo has many of the features requiring an interdisciplinary approach. This phenomenon has a different echo in different disciplines, each contributing to establish the multimodal perspective to account for what is commonly considered as « placebo ».

Placebo is a phenomenon within a material context. It develops in a physical environment and has obvious effects on living beings. However, like in the coding of a place in space, no specific sensory information is prevalent (Jacobs & Schenk, 2003). As developed by John O’Keefe, a place unit animates the meaning of just « being there », among other places, i.e.,

those that you come from and those where you might aim at. Such a concept was difficult to catch before O'Keefe and Nadel (1978) proposed to concentrate on the hippocampus, a crossroad in the memory circuitry. In the same time there was a risk to forget that the hippocampus, thus considered, remained an active structure in a living organism and that space representation required a distributed activity.

Similarly, the placebo concept, like pain itself, is difficult to capture within a specific disciplinary perspective, whether among the biological or the human sciences. Our review proposes that placebo is situated at the border between biology, semiotic and epistemology. It is thus an interpretation by the subject itself of what might be its coming future. Of course this «trajectory towards the future» is not explicit, even though scientific or magical/mystical explanations of expected effects attempt to outline this transformation process. It is a bodily knowledge, a simulation emerging from a guess to facilitate anticipated adaptation. It is a process that appears somewhat transcendental, in the sense proposed by Merleau-Ponty.

To discuss placebo in an interdisciplinary perspective, we assembled different lines of analyses from the psychophysiology, semiotic or phenomenology, in order to extract a specific and dynamic signature of placebo. We find this signature in the particular way sensory data are shaped in a configurative meaning prescribing future body adaptive requirements. This signature mediates a passage from past to future, hence the title of our paper.

From a semiotical point of view, placebo is related to traces, which also suggests a role in crossing temporal gaps. The *trace-of* is also a *trace-for*, based on memory associations. It mediates the passing of time

and links past experience with an near future of the body. This temporarily circular link is indeed a dynamic signature, it corresponds to the necessarily moving view of the present. This function does meet the recently accepted role of memory in mediating future adaptations, in anticipation. The hippocampus, a central structure at the heart of spatial and episodic memory, is also actively involved in anticipating future actions and events. Perhaps the still frame imposed by a word such as placebo in a verbal description diverts our understanding toward a more sterile acceptance of this phenomenon. At least, it fixates the meaning dimension of placebo as a signature or a keyword of a living being.

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terms of quality as well as originality and creativity.

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