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**Can and should the placebo effect be used in osteopathic treatment?**

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## **Foreword**

With thanks to Professorr Stephen Tyreman for his guidance and his knowledge in this field.

A.M.D.G.

*All my deeds for God*

Robert McMorrow, Vinterbro, 16.05.2015

## **Abstract**

This paper conducts a qualitative literature search to answer the questions of can and should the placebo phenomenon be used in osteopathic treatment? Papers studied drew mainly upon randomised controlled trials, pain studies, neuropsychobiology, systems theory and consciousness studies. Despite a lack of literature in the osteopathic field which is seen as one study weakness, strong evidence exists for the placebo phenomenon. Ethical concerns about “deception” can be superseded by seeing the placebo phenomenon as contextual healing with the application of systemic thinking. Inducing the placebo response in osteopathic treatment however should be seen as augmentative and not a replacement for proper osteopathic treatment planning and implementation. It is hoped that these conclusions can be explored further in future studies.

**Keywords: osteopathy, placebo, effect, research, understanding, systemic, medicine, consciousness.**

## **1. Introduction**

The placebo phenomenon, in one of its better known definitions, has been defined by Shapiro as **(1)**:

" any therapeutic procedure which is given either 1. Deliberately to have an effect or  
2. Unknowingly;  
and which has an effect on a symptom, syndrome, disease, or patient but which is objectively without specific activity for the condition being treated. The placebo is also used as an adequate control in research. The placebo effect is defined by the changes produced by placebos. "

Moerman **(2)** however is amongst those who have criticised this definition. He indicates that the phenomenon is not caused by a placebo as the placebo is by definition an inert thing or substance.

The disagreement here is an indicator of the confusion that exists around the phenomenon.

The ambivalence around it can be seen when one understands that it has been suggested that the "effect" should be minimised in a successful randomised control trial (RCT) but maximised in treatment. **(3)**

The phenomenon has been known since the time of Hippocrates **(4)**. Moerman informs that the term in Latin means "I shall please." However in the early middle ages the word's meaning had a negative connotation of that of a sycophant who pleased others with artifice rather than substance. In Chaucer's "Canterbury tales", a character called "Placebo" gives advice to a lecherous man who wants to marry a young girl. The term morphed in early 19<sup>th</sup> century to mean any medicament given more "to please than to benefit the patient." With

advances in biology it's meaning changed again in the 20th century to have the meaning of a substance which doctors think has a good effect but which later research proves to be inert (2). Thus the perception of the phenomenon has changed over time.

What is the placebo phenomenon's relationship with osteopathy? Osteopathy is a school of manual medicine.. A.T. Still, the founder of osteopathy stated that the osteopath's job is "to find health," (5, p4) by a knowledge and application of complete anatomical principles which involve the body as a whole and involve all it's processes (5, p16-28).

In relation to osteopathic medicine, Still's main concern was anatomy. Still stressed the importance of unimpeded fluid flow and nerve supply n the human body, and proper motion of body parts in all their anatomical relations. One of Still's maxims was that "life is motion," and that the part that is moving the least in the human body (in regard to it's anatomical connections) is the biggest barrier to health. However, Still also made observations about the relationship between the mind and the soma. Stone (6) describes health from an osteopathic perspective. One model is that the balance between chemical, physical and *mental/emotional* environments of the body is also related to the intersection and balance between the physical, chemical and environmental factors external to the body.

As osteopathy thus deals with the mind as well as manipulation of the body, an understanding of the placebo phenomenon is necessary. This study uses a critical qualitative literature review to answer the question: "can and should the placebo phenomenon be used in osteopathic treatment?" This study may serve as a pre-cursor to a future study of either Norwegian or UK osteopaths' use of the placebo phenomenon in osteopathic treatment.



## 2. Method

Literature searches were conducted using databases Pubmed, osteopathic research web, Ostmed Dr, PsycNET, and Google scholar to define the parameters of the study.

The first two searches used the keywords;

“Placebo effect research understanding”

“Osteopathy placebo effect”

Benedetti’s ( a noted researcher in the field) detailed book published last year on the phenomenon, was also reviewed.

Due to findings a later 3<sup>rd</sup> search was done to deepen the knowledge field using the keywords “systemic medicine placebo.”

Key research areas were noted and findings/concepts were qualitatively linked together logically under these areas with the help of the techniques of Buzan (mind mapping). In summary this entailed a process of transcription, familiarization with data, clustering and checking. (7) Important concepts were further explored using references found in the papers found in the study. As questions about the nature of mind arose, literature on neurosurgical brain research was also reviewed.

This allowed an answer for the two questions that are inherent in this study:

Can the placebo phenomenon be used in osteopathic treatment? That is, does it exist and is it compatible with osteopathic treatment? If so, should the placebo phenomenon be used? In other words to question two, are there ethical objections?

This study did not require special approval from the ethics committee.

### 3. Results

#### 3.1 Can the placebo be used? What is the evidence for the phenomenon?

There is a limited amount of direct osteopathic research into this phenomenon. Results thus for the most part draw on other disciplines.

##### 3.1.1. History.

The history of medicine has been seen as the history of the placebo. **(1)**. Shapiro gives the examples of many medicines and procedures used in the past which today are not held by mainstream medicine to have any effect. He gives the example of the antidotes used against poison such as the bezoar, a hard indigestible mass of material found in the stomach of animals, which according to legend was the crystallised tear from the eye of a deer bitten by a snake. These were claimed however to be *believed* to be effective at the time. **(1, 8 p6)** As time progressed an understanding developed that imagination and belief seemed to be the cause of the effect, giving rise to the first historical account of scientific trials. King Louis XVI in 1785 commissioned a study into mesmerism which was headed by Benjamin Franklin. They had a control group of blindfolded patients with the treatment and concluded that the postulated healing fluid of “animal magnetism” could not exist and that the effect seemed to be more in the patient’s imagination. **(8. p6)** The respected French internist Trousseau in 1834 in his researches into homeopathy found a positive effect from bread pills with patients attributing this in his paper due to the natural course of disease and imagination. **(8. p6, 9, 10)** Such understanding and with the development of chemistry and physiological understanding leading to a desire to directly test drug effects gave rise to the modern Randomised Control Trials (RCT) first developed in the 1950s.

### 3.1.2. Modern definition of the placebo.

Benedetti reports that the term placebo, specifically when used in RCTs is often inexact and subject to confusion. **(8)** The true placebo response, which is *attributable purely to psychosocial factors* should be separated from other reasons for improvement, these being listed as: spontaneous improvement, statistical regression to the mean, biases and co-interventions. The word response is preferred to “effect.” This is perhaps best argued by considering that the imagination plays a major role in therapeutic outcome as the patient’s mind controls a number of physiological functions. **(8. p16, 11.)** Thus the phenomenon is a response of the mind, not a strict mechanistic effect which is predictable (as in say a chemical reaction.) Benedetti summarises this concisely as **(8):**

*“The patient’s mind really matters.”*

3.1.3 Nocebo. This phenomenon is the opposite of placebo where there is a clinical deterioration in an individual. The term means in latin “I shall harm.” **(8)**

### 3.1.4 RCTs. .

In an RCT it is desired to show that an active treatment (physiologically) is better than imagination as an addition to measuring against no treatment. In general the modern RCT can have 4 phases. Phase 1 measures drug excretion, which is not concerned with the placebo response. Phase 2 uses healthy volunteers to test side effects of the drug being tested. Phase 3 is where there is a particular focus to compare active treatment with a patient group versus a control. (Phase 4 studies themselves are usually studies done after a drug is launched on the market.) It is phase 2 and 3 where drug companies are most focused on showing the superiority of their treatment to a placebo group. **(8)**

Blinding involves not telling either participants or the researchers which group is the active group and which is the control. The double blind study (where both researchers and patients are “blinded”) was probably first used in 1918 by Bingel **(8, 12.)**

Randomisation was also considered another important development, attributed to Hill in 1948 with his study into the antibiotic streptomycin. **(8)**

With these trials, there is no desire to actually know how the placebo works, but in fact a desire to eliminate it. There are a great many variations in the RCT which attempt to minimise placebo. “Active placebos” are sometimes used to mimic side effects of active treatments to “fool” participants they are having active treatment. Researchers often also can mimic placebo effect by timed drug release methods, were participants do not know the exact time when they are actually receiving a drug or not. **(8)**

An example of such an RCT is the “balanced placebo design.”

Table 1 “The balanced placebo design” **(8., p13)**

PARTICIPANT	GETS PLACEBO	GETS ACTIVE TREATMENT
TOLD THEY RE GETTING PLACEBO	= BASELINE MEASURE “NO EFFECT”	=ACTIVE TREATMENT MEASURE ***
TOLD THEY RE GETTING ACTIVE TREATMENT	= PLACEBO RESPONSE MEASURE ***	= ACTIVE TREATMENT + PLACEBO RESPONSE MEASURE

The boxes above marked with the stars give differential information about drug and placebo response effects. **(13)** . Some studies aim to reduce the amount of deception in the above model by agreeing to allow participants to have a combination of placebo and active treatment, however this causes problems with interactive effects. **(8.)**

It can thus be argued that *the best direct evidence for the existence of the placebo response is that drug researchers go to such great lengths in RCTs to try to eliminate it.*

Against this, Hjrobjartssons study **(14)** and his Cochrane review metastudy **(15)** compared other studies where some participants had placebo and some no treatment. His findings were that there was no significant difference in these groups with the exception of studies 1.

Involving subjective outcomes and 2. involving pain and nausea measurement.

Hjrobjartssons's conclusions have however received criticism from other researchers **(8. p30)**

His suggestion that bias was often a real source of the perceived measurement in placebo response can now be evaluated more realistically by the use of modern brain imaging techniques **(8).**

#### 3.1.4.1 RCTs in osteopathy.

The RCTs which are used in osteopathy use "sham" treatment as the control (placebo response) group. Noll et al. argued with a small sample size **(16)** that sham treatment could be used to mimic real treatment. However the challenge of this was summarized (and thus the problems surrounding it) as follows:

" The goal of using a sham protocol is to control for the potentially therapeutic effects of touch and belief, which are components of the placebo effect. When participants are blinded to group assignment, the placebo effect can be controlled. However, it is challenging to design a sham protocol that is both *ineffective* (carries little or no therapeutic value) and *plausible*.

### 3.1.5. Methodological studies particularly in applied psychology (neuropsychobiology) and pain studies.

#### 3.1.5.1 Recent UK General Practitioner (GP) study

Bishop's recent study of GPs in the UK s views on the placebo found respondents stating that pain, irritable bowel syndrome and depression were the most responsive conditions to the effect. **(17)**

#### 3.1.5.2. Pain studies

This is the most studied aspect of the phenomenon and also the chief reason why a patient will consult an osteopath. **(18)** Benedetti states the interest in placebo pain studies developed following the work of Beecher in World War II using the phenomenon in battlefield surgery when "active" drugs were in short supply and also because of the development in understanding that pain is modulated by psychosocial factors. **(8)** This is something which has correlates with the work of Melzack **(19)** on the neuromatrix theory of pain.

Neuroscience has now shown that there is no specific pain area in the brain. Mechanisms are spread over the cortex and there are two main postulated pathways: 1 Lateral, which runs from the lateral thalamic nuclei to other parts of brain including the primary and secondary somatosensory cortices 2. Medial, which runs from the medial thalamic nuclei to other parts of brain including the prefrontal and anterior cingulate cortices. Further, there is postulated two main neurotransmitter systems which modulate pain (descending inhibition) : 1. opioid and 2. non-opioid (endocannabinoid) which are distributed differently over the medial and lateral systems. **(20)**

Pain should also be broken into its sensory localisation component and its emotional component. **(21.)** Stress, particularly fear related anxiety, can increase or decrease pain dependent on the patient's area of attention, particularly if focusing on the emotional component of pain. **(22)** The prefrontal cortex is linked with suppressing affective responses. **(8)**

Placebo response Studies have shown a drop in Visual Analogue (pain) Scale (VAS) of an average of two points, with much stronger drops in some patients. **(23, 8)** The placebo response to verbally induced expectation in one study was as strong as the clinical response to lignocaine. **(24)** A nocebo response (hyperalgesia) has been shown to be mediated by cholecystokinin . **(25)**

### 3.1.5.3. Psychology

It can be stated that the phenomenon is psychobiological where the mind expects a clinical benefit. Psychologists consider the placebo effect as an example of the mind body interaction, where the mind modulates physiological functions. Thus psychosocial context is very important as is an understanding of the mind. **(8)**

The anthropologist Moerman has demonstrated that the placebo phenomenon is a meaning response. **(2)** Moerman reports ten studies which convinced him of the reality of the phenomenon as a response to meaning.

Brody places an emphasis on symbolic meaning with the phenomenon. **(26)** Jung in "Man and his symbols" affirms a twofold premise based on clinical experience that "symbols are used to represent concepts that we cannot define or fully comprehend (conscious component)...but that man also produces symbols unconsciously and spontaneously, in the form of dreams" (unconscious component.) **(27)**

#### 3.1.5.4. The clinical encounter

Ross cites the following elements as being present in the placebo phenomenon clinically **(28)**:

- Physician patient relationship.
- Patient expectation and needs.
- Patient personality and psychological state.
- Severity and discomfort of symptoms
- Type of verbal instructions given
- Preparation characteristics
- Environmental milieu (clinical setting)

Kapchuk states in addition **(29)** :

- Nature of illness
- Type of treatment
- Kramer adds the importance of
- Cultural setting.. **(30)**

Miller cited by Sinclair, adds that

- The patient taking responsibility enhances the response. **(31.32.)**

In summation, the clinical encounter, in its totality, should be thought of as a potential therapeutic medium. Miller in fact proposes an important term: *contextual healing*. **(31. , 8.. p34.)** The clinical encounter is loaded with potential meaning. The above factors can be set so as to maximize therapeutic benefit. **(28)** In a sense, there is a ritualistic component to the clinical encounter (symbolic meaning being a component of ritual.)



### 3.1.6. Neuroanatomy

The anterior frontal lobe has been shown in studies to be associated with both memory and expectation. Neuro-scans have also shown this area to be highly active in depressed individuals. **(33)** The frontal lobes are also connected with suppressing emotion.

In conditions where the frontal lobes have a lesion, for example Alzheimers disease, the placebo response has been demonstrated to be diminished or absent. **(8)**

### 3.1.7. Consciousness

As the placebo phenomenon is a phenomenon of mind, it is important to understand consciousness. Rangel has defined intelligence as degree of awareness, i.e. degree of consciousness. **(34)**

#### 3.1.7.1 “Classical” neurosurgical research into consciousness

Some insights into consciousness were gained by study of individuals who have Agenesis Corpus Callosum (ACC). This is a congenital condition where the two hemispheres of the brain are severed and only have a very limited lower brain communication between each other. These individuals however do not show two selves, or a split self, but have one. Kim Peek, made famous by the film “*Rainman*” which was loosely based on his character/life was such an individual. Eccles citing Sperry **(36. p356-)** concluded that self-consciousness in commisurotomy patients only arose in relation to activities of the dominant hemisphere.

Penfield found that the human cortex could be mapped by patients conscious during brain surgery reporting their perceptual experiences from cortical stimulation (CS) **(35)**

Neurophysiological parsing or refractory period is held to be about 200mS to 300mS, which is conceptualised as the minimum time taken for consciousness “to make a decision.”

Surprising unexpected effects, postulated as antedating affects - have been found in consciousness. Libet did experiments where a patient having neurosurgery had both sensory stimulation (SS) to their skin and repeated stimulation directly to their cortex (CS) using electrodes to allow a perceptual experience at various times with varying gaps between these.

**(36)** It is important to realise that a threshold must be met to elicit a conscious experience with stimulation of the cortex and that it must be applied over a period of time. Sensory stimuli require only a short pulse.

What was found firstly was that a sensory stimulus on its own was perceived relatively late, after 0.5 s (despite on average signals getting to brain after 0.15s). Similarly, a CS on its own is perceived roughly 0.5 s later, which is when “neuronal adequacy is thought to occur.” However when a SS was given to patient about 0.2-0.3 s after the beginning of a CS, the person became perceptually aware of the SS before the CS and further, there was almost no delay with the perception of the SS. This effect did not occur when an SS was applied after subcortical stimulation. **(36-38)**

It was hypothesised by Eccles and Popper **(36)** that this represents a delay in cerebral production combined with a subjective antedating of a conscious sensory experience (i.e. that the mind dates a signal backwards in time from when it is processed). Eccles and Popper also postulated dualism (a split between the mind and its brain.) **(36)**, Eccles also hypothesised that only specialised parts of the brain was in liaison with the self conscious mind.. He postulated that the prefrontal areas along with Brodmann areas 38,39 are the most important liaison areas for mind-brain interaction. **(36)**

Libet also demonstrated strongly that readiness or action potentials in the human cortex are generated *before* the conscious perception of the desire to act, suggesting many actions are at first triggered unconsciously. **(39)**

### 3.1.8 The “motor” of the placebo response

The main motor of the placebo response seems to be threefold from the literature:

- \* A Reward system (motivational system)
- \* B expectancy (or beliefs) and also
- \* C classical conditioning (which is involuntary.)

#### 3.1.8.1 Reward system .

The hypothesised motivatory/reward system, the mesolimbic dopaminergic system, is a drive towards homeostasis or placating a negative emotional state. This is closely linked with the sympathetic and parasympathetic nervous system. **(40)** It is a learned response **(8. p115 )** which corresponds with planning and the emotion of hope. **(41)** It can be argued that any repetitive treatment can be seen as ritual (i.e. the encounter is weighed with meaning within the reward system.) Placebo analgesia had been found to be part of the dopaminergic reward system in the brain. **(8, p133)**

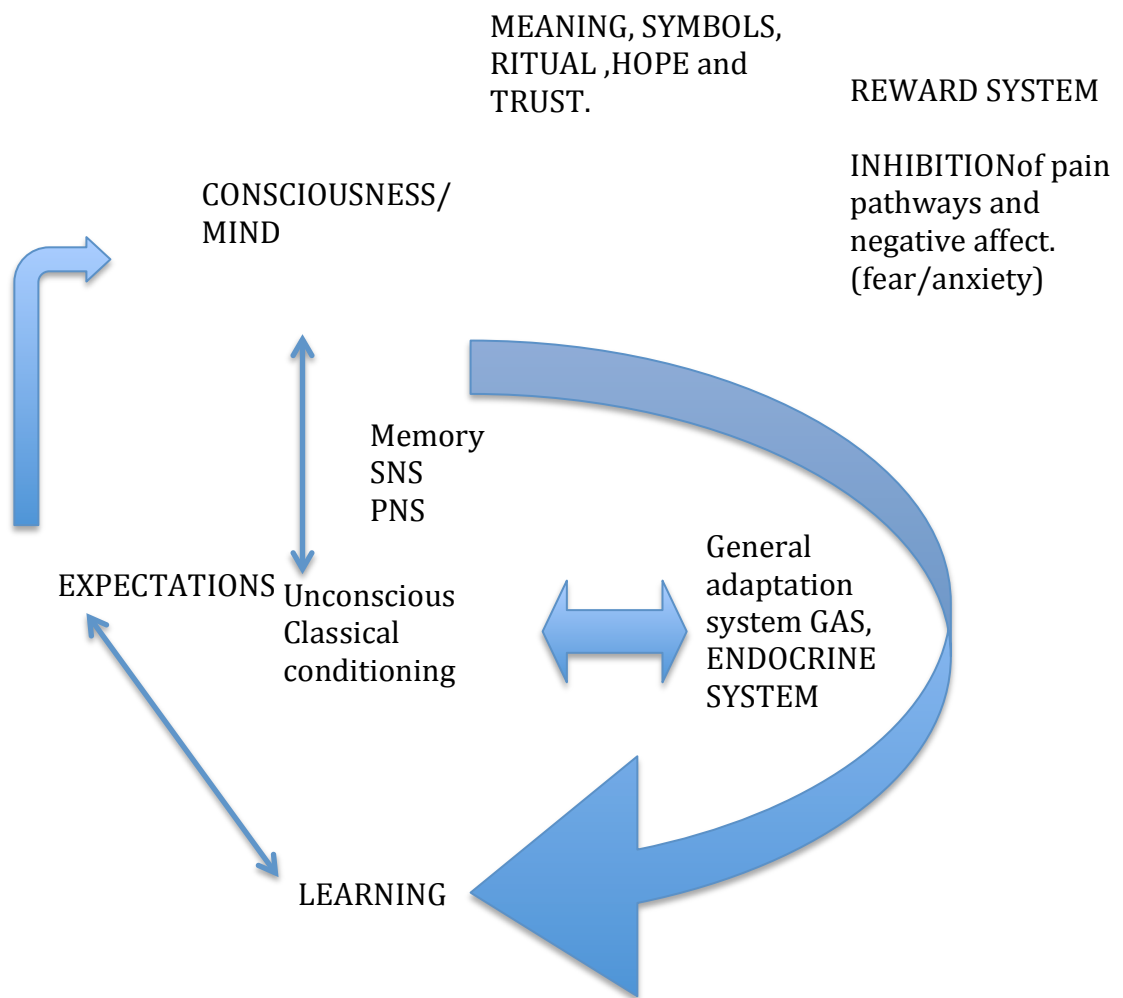
#### 3.1.8.2 The patient’s expectations

These can be positive or negative. They are meaning induced. These seem to be at a level below the reward system, where the rewards system role is to try to minimise negative emotions and reward positive affect. High suggestibility to hypnotism correlates with a strong placebo response. **(8)** White et al. **(42)** has proposed a social model of nocebo and placebo which can affect expectation. Finiss et al. demonstrated that Opioids mediate expectancy and placebo response and could be reversed by the antagonist naxolone.. **(40)**

### 3.1.8.3 Classical conditioning.

Leuchter states that endocrine responses from placebo in the body are based on classical conditioning not on expectation, although they are subject to long term control of consciousness. **(19. , 8. p49)** Woods demonstrated insulin levels could be strongly affected by placebo response (the effect being measured in animals ) via a conditioning mechanism. **(43)** A conditioned nocebo response can induce anxiety, which activates the hypothalamus pituitary adrenal axis (Adrenocorticotrophic Hormone/cortisol. **(22)** which triggers the General Adaptation System (GAS). The emotion of trust has found to be mediated by the hormone oxytocin. **(44)**

Diagram 1. Schematic of the motor of the placebo phenomenon. NB/ classical conditioning can induce both placebo and nocebo. SNS = sympathetic nervous system, PNS = parasympathetic nervous system



### 3.1.9. Embodiment effect

It is shown in the medical anthropological literature that in individuals with post traumatic stress disorder (PTSD), consciousness can be bypassed with regard to accessing traumatic memories of events but that “residue” emotional impressions can also be “imprinted” on parts of the body. That is the emotional component of a trauma can link itself to parts of the body. This phenomenon seems to share a similar neurological mechanism to the placebo response. (45) This may correlate with clinical experience in osteopathy whereby certain parts of the human body often have an emotional component attached to them during a release technique, the diaphragm being an example.

### 3.1.10 Children:

The effect has generally demonstrated to be stronger in children. It has been postulated that this is due to several factors. Children also use the mechanisms of imitated learning/instrumental learning which may strengthen the response particularly when they are exposed to strong parental expectations and the associated related behaviours. (46)

### 3.1.11 Osteopathic Diagnosis and treatment

There is a debate generally in medical literature about whether diagnosis promotes nocebo (47) or placebo phenomenon. Osteopathic diagnosis however is related to the current epistemological and paradigmatic debates.

In regards to treatment, Still states:

“Definition of the word ‘treat:’ ...has but one meaning- that is, to know you are right, and do your work accordingly... Your osteopathic knowledge has surely taught you that, with an

intimate acquaintance with the nerve and blood supply, you can arrive at a knowledge of the hidden cause of disease, and conduct your treatment to a successful termination. Tis not by your knowledge of chemistry, but by the knowledge of the anatomy of man, and of what is normal and what abnormal....” (5)

Thus there is a danger that too much focus on use of the placebo response may trivialise the osteopathic focus of getting a direct response of the body to manipulation. From this viewpoint, the placebo should be seen as augmentative. (22)

On a side note, Sinclair argues that a well executed HVLA with the “pop” can be construed in a ritual manner by patients inducing a placebo response. (32)

### 3.2. Should the placebo be used?

#### 3.2.1. World Medical Association (WMA) definition of Helsinki declaration 33

This declaration addresses placebo use:

*“ The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven interventions, except in the following circumstances:*

*where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention.*

*And the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention*

*Extreme care must be taken no to abuse this option. “ (48)*

Hjrobarsson states that the effect should only be used in RCTs. (14) He stated in another study that the placebo is used to avoid confrontation with patients. (49) Rangel, in opposition,

states that the WMA definition is unethical and that the effect must be cultivated and not eliminated. (34)

3.2.2. Bishops 2014 study of GPs (17) addressed many ethical areas related to allopathic medicine. GPs differentiated between pure and impure placebos. The former have no known clinical effect, whereas the latter do but are not specific for the patients condition. An example of the latter would be a GP administering an antibiotic for a viral infection. It was found that GPs often used a cost benefits analysis if using placebo. There was also a trade off between two principles: *1. do not harm and 2. do not lie*. Arguing that pure placebos are ethically acceptable prioritises the first principle whereas impure placebos can be argued as ethically acceptable by prioritising the second principle.

A high number of GP s felt the practice of placebo was deceptive. However, a smaller number of GPs indicated that placebo effects were inherent in medical practice. (17, p362)

Some GPs stated that the boundary between pure and impure placebo was an artificial one.

Bishop also discusses a conflict between four ethical principles in medicine with the use of the placebo, these being malifience, beneficence, respect for autonomy and justice.

With the assumption of inherent lying in using the effect, there is a conflict between the principle of benifience and autonomy. Miller et al. challenges this view however in his paper on “the placebo without lying.” (50) Indeed, by shifting paradigm and understanding the placebo response a new way, it can be explained to a patient whilst maintain both principles of benfience and autonomy.

### 3.3 Epistemological debate

Heidegger (who as a proponent of phenomenology) criticised any systematic thought that considers the problem of the nature of being as something extrinsic or "out there," that is that



successful understanding in any field can only be tackled by tying it intrinsically to the nature of being. **(51)** He stated that a "science" could be considered healthy if it can have a "crisis" of thought. **(51, p23-24)** This corresponds to Kuhn's theory of scientific revolutions. **(52, 53)**. This states that the anomalies in normal science are not anomalies but processes that cannot be described in the current paradigm. Still in his "Philosophy of Osteopathy" gave his observation that the body was driven by mind and had an intelligence behind it's creation. From a phenomenological perspective it can be argued that Still did not separate the nature of being from health. This is in contrast to allopathic medicine which itself takes no position on the nature of being. **(54)**

### 3.31 Paradigm change

*“ It is not clear whether we should differentiate the placebo responses based on the basis of mechanism or rather on the basis of the disease, this will be a future challenge in placebo research. “* **(8., p44)**

Engel stated in relation to the phenomenon that there is the need for a new model (biopsychosocial model.) **(64)** This has been realised in part by the advent of neuropsychobiological research and procedures.

Placebo is the patient's anticipation of a cure. **(54)** A chief finding of this study is the “paradox” of the place response whereby although an acknowledgement that it exists is agreed upon by most researchers - there is a focus on suppressing it.

Ivanavos argues in this regard that the placebo response is non-specific. That is, it is not directly related to a disease or any one mechanism. He states that a soon as a systemic approach is used, all paradoxes disappear. Thus the uncertainty around the placebo effect is not due to lack of knowledge, but to lack of a suitable epistemological tool. **(54)**

### 3.3.2 Two ancient views of understanding “disease”

Two main rational healthcare approaches are rooted in the history of ancient Greece, these being the Cnidian and Coan traditions/schools. Cnidians were the forerunners of conventional biomedical reasoning – where diseases are seen as distinct from each other and are independent of who is suffering from it. (This was the approach of the Greek physician Galen ca 129-200 AD in the Roman empire) . The Coans (of which Hippocrates was a member) emphasised the unity of all disease and believed that disease presented differently *depending on personal and environmental factors*. The clinical method for the Coans was to understand the patient in his or her family and social context – and describing the particularities of how disease affected this person “in this context and at this time.” **(55)**

It can be seen that modern Evidence Based Medicine (EBM) approaches comes from the Cnidian school. In the modern context, Ivanavos states that it is a medicine strictly based on controlled trials, neglecting personal impression or experience, or even other types of understanding the patient” **(54., p80)** He lists (among others) the following criticisms of EBM:

- The human factor (cheating e.g. for commercial advantage.)
- Problems with evaluation and validity, and consequences for clinical practice.
- Lack of significance and predictability.
- Surrogate (wrong) parameters can easily be measured mistakenly.
- Rare side effects are not taken into account enough.
- Arbitrary causality.

As an alternative, modern systemic approaches draw on the Coan approach.

#### 4. Discussion

In attempting to understand the placebo result, an understanding of systemic approaches is necessary. (54. , 56) This it can be argued comes naturally to Osteopaths, due to treatment being inherently systemically based.

In interpreting results it is argued that the importance of the receiving system's structure, that being the human body including the mind must be taken into account in understanding how the placebo phenomenon operates. This means understanding that the human body is a living system, and also trying to make sense of the nature of how the human brain operates and consciousness itself.

##### 4.1 General Systems Theory(GST)

An approach to studying the complexity in biological systems was by the development of systems theory first attributed to Von Bertalanffy in 1928. (57)

A system's purpose is to reach equilibrium (22). They can be classified as being composed of a non-linear interaction of components. It can either be controlled (cybernetic, that is able to deal with feedback) or uncontrolled. In fact systems can be evaluated by 3 general approaches: holist, reductionist and functionalist. The first examines the system as a complete functioning unit, the second looks downwards and examines the subsystems whilst the latter looks upward and looks at the part a subsystem plays in the complete system.

A system can have a detector, selector and effector, detection and effecting being interactions between two systems. "Selection" consists of the rules that a system uses to make decisions.

## 4.2. Living systems in more detail

The basic concepts or shared features behind living systems are as follows (54):

- Closed and open systems: A closed system is sealed from the external environment. By definition, if we know its starting state then its end state should be predictable. Living systems are by definition open systems, as they interact and take materials in from their environment and expose waste. Their end states are not predictable due to this interaction:
- Struggle between parts.
- Centralisation.
- Circadian rhythms. Of interest, Hippocrates observed a healing rhythm in the human body. He stated for example that fevers generally reach a crisis on certain days. He listed days 4,7,11,14,17,20,34,40,60 after the beginning of a fever.
- Achieving goals.
- Self regulation
- Equifinality: This means that different routes can be used to get to the same final state. This is significant in osteopathy, for it demonstrates that treatment approaches can differ and yet lead an individual back to the same state of health.
- Emergence : elements which are structurally interconnected produce a new behavior not inherent in their parts.
- Recursion: is a somewhat difficult concept to explain and manifests somewhat differently structurally (organically) and phenomenologically (the latter being how a recursive unit expresses itself.) A simple practical example is holding two mirrors up to one another and looking at the reflections stretching into infinity – this is an example of a recursive process. Recursive units are complete in themselves, but hold

also other recursive units which are complete in themselves. Recursive units are directly linked to cybernetic cycles.

- Cybernetics: Most if not all biological and physiological processes are integrated into cybernetic cycles e.g. regulation of the thyroid gland. **(54, p165)** First order cybernetics is “the cybernetics of observed systems.” **(54, p168)** Second order cybernetics involve the observer as well as the observed. This is an important point in the placebo response. A simple example is an osteopath who decides to use verbal instructions to give a placebo effect before manual treatment. If he says the instructions without conviction (purpose) then this may affect system two (the patient’s trust.) A nocebo response may then ensue in the patient thus in turn affecting the osteopath’s confidence/conviction as his patient is not getting better, a negative recursive process in action.
- Trivial and non-trivial systems: A trivial system is “linear, expressed mathematically as  $f(x)=m*y + k$ . A non-trivial system occurs as soon as three cybernetic cycles are inter-related. The normal reductionist approach investigates trivial machines. In a chemical reaction, very often the process is linear. However in the human body, due to the signals being interpreted which includes the intake of substances; it can be seen that response is complex and based on the systems overall purpose.
- Synergy means directly “non-trivial.” It implies an interaction between components which do not exhibit non-linear behaviour. A medical example of a non-synergistic drug response is the protein alpha-synuclein which might contribute to Parkinsons Disease in a higher concentration but protect against it in a lower concentration. **(58)**

#### 4.3. Hermeneutical principle.

In summary, hermeneutics are the science or art of interpretation. Von Forsters principle is that it is the hearer who determines the meaning of an utterance. **(54. p143)** In relation to the human being, the implication is that each patient, despite a similar “input” or sensory signal being given; will however have a different response based on the subsystems of that person, but most importantly: due to the regulation by the person’s mind and consciousness and it’s unique interpretation of the signal or input. This fact is rarely taken into account in EBM, and actually serves as a criticism of RCT studies. Information is thus the interpretation of the signal and not the signal itself. Information in it’s simplest form can also be defined as the smallest recursive unit.

#### 4.4 Criticism of GST.

It has been described as non-teological in that most GST approaches do not take purpose into account. **(34. , 54)** GST assumes organization as a spontaneous phenomenon and not an act of mind or intelligence and neglects the human systems purpose of survival. GST has difficulties defining it s paradigm as there is not complete agreement on what a system is. **(59)**

#### 4.5 Viable systems model (VSM) an example of a purposesful systems model.

An example of an application of systemic thinking was performed by Beer. **(60)** who as a manager in British Steel in the 1950 s designed a model to help manage organisational work structures by studying the human body’s arrangement as a suitable model for designing an intelligent system.

*“We will seek the source of effective organization in the cybernetics of natural processes – the brain itself.”*

VSM is a “whole systems” theory. Beer’s studies saw the human as five main interacting systems:

1. All the muscles and organs. The parts that do something, or the operation.
2. The peripheral nervous system which monitors the muscles and organs and ensures their interaction is kept stable
3. System 3 the base brain which oversees the entire complex of muscles and organs and ensures that their interaction is kept stable.
4. System 4 the mid brain. The connection to the outside world through the senses.  
Future planning
5. System 5 higher brain functions. Formulation of policy decisions. *Identity*.

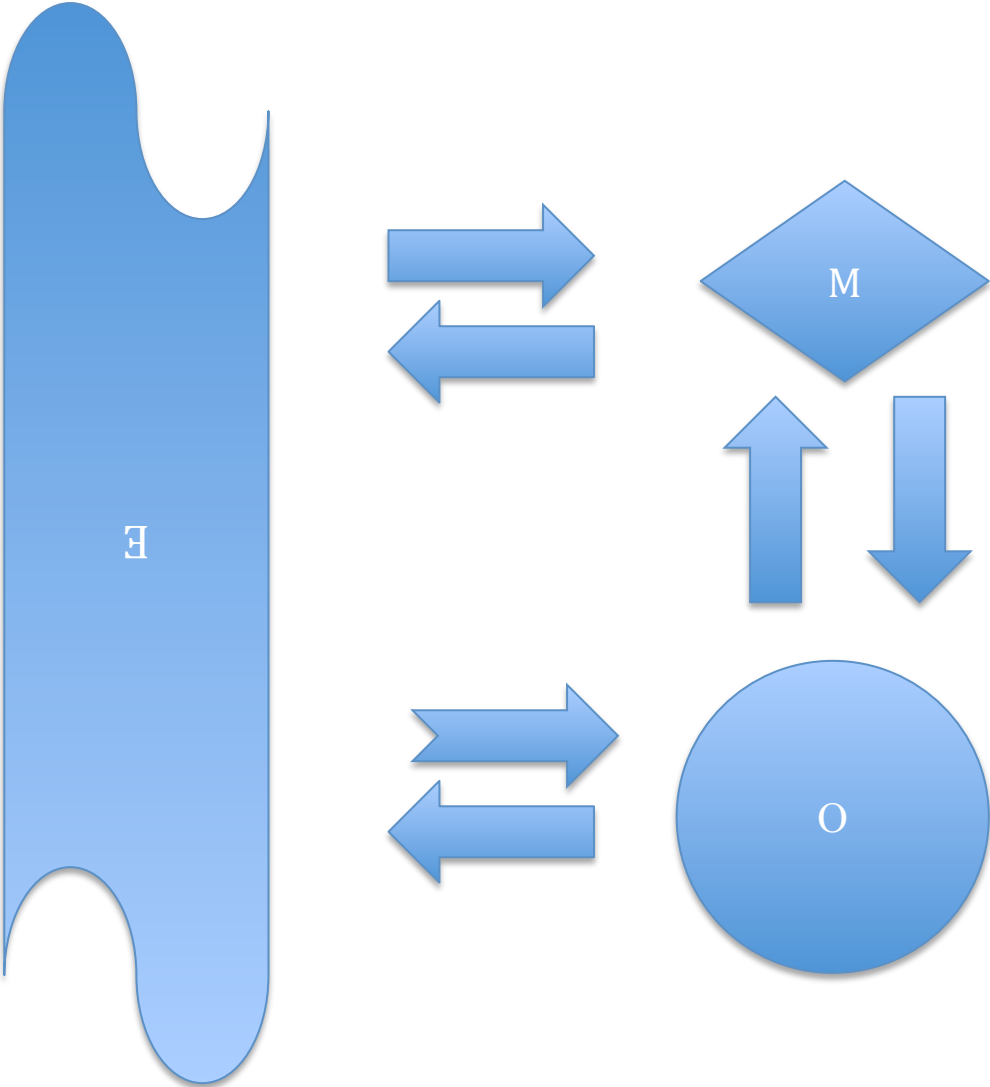
He then identified elements:

The operation (muscles and organs in human body), the metasystem (the brain and nervous systems in human body which ensure various operational units work together in an integrated and harmonious manner) and the environment (all the parts of the world which are of direct relevance to the system as follows.) *All systems must be in balance or disorder arises.*

An example of recursion in organisation in the social world is that when organisations grow in size they generally organically spread out into smaller units which specialize in certain functions whilst communicating with the command structure. **(60)** It is postulated that the brain operates in a similar manner. Recursion means that at all levels, the same principles of organization “recur.”

Beers studies are very instructive in that he applied the organisation of the human being to the social level - in the process of which he identified conceptually key components of the human system.

Diagram 2. The Viable Systems Model VSM



O = operation (viscera and soma), M= metasystem lower brain, mid brain and higher brain (mind), E = environment



#### 4.6 Network pathology and disease as a state of entropy:

Rangel complains that modern biophysics concepts are missing in both orthodox and complementary alternative medicine (CAM). He argues that true systemic approach is differentiated from others by incorporating the concepts *of intelligence, energy and the objective to survive*. **(34)** This places consciousness itself in a central footing in understanding the placebo response.

*“ According to reasoning, organization in “far from equilibrium” systems cannot be reached or attained without a modulating intelligence and an adaptive energy generator within the system. Intelligence to be understood should be defined on a scale of consciousness...it exists in a gradient scale of awareness i.e. from the very aware to the unaware. Intelligence is the central controller of a system. It is also the genesis and causative entity. ... Without intelligence there can be no living system.” (34)*

Illness in this model is due to increasing entropy in a system (disorder.) From this, it can be inferred that health is a promotion of negative entropy, that is order in the system. Pathology must thus be considered as a systemic cascade due to elements of disorder in the system.

#### 4.7 The problem of consciousness

The “hard” problem of consciousness is the explanation of how physical processes can give rise to conscious phenomenal experience, **(61)** which from our own experience, is intuitively characterised by free will. In a related sense, a thought experiment is this: when one sees a face one recognises, how does the brain remember who it is? Firstly, the brain has to find the memory with the picture of the person it recognises. But then, how does it remember where this memory is stored? And where does it remember how to find a memory? How does it remember the “location” of where the procedure of finding a memory is situated *ad infinitum*? Ivanavos states that if the findings of neurophysiology (on their own) were to be

taken seriously, it leads to the assumption that there is no self. (54. , p64) Chalmers himself argues that no reductive problem of consciousness can solve it and that the “hard” problem of consciousness is insoluble. (61) However, It seems that the problem of consciousness can be partly tackled by looking at it as an active, not a passive process. (62)

Libet, in addressing Chalmers, stated that solutions to the “hard” problem must accept conscious experience as a fundamental non reducible phenomenon in nature (as Chalmers suggests.) Libet proposed a “conscious mental field” as an emergent property of appropriate neural activities *with the attributes of integrated subjective experience and a causal ability to modulate some neural processes*. He took no firm stand on whether such a field would be monist or dualist. (63) In either case, there is a general view that recursive processes and structures play a large part. (54)

#### 4.7.1 Libet’s research into consciousness/perception: “antedating”.

Popper and Eccles stated Libets research on antedating gave strong evidence for the dualist thesis, that mind is separate from the brain. (36)

They listed this as one of four serious reasons to argue against a purely materialist view of consciousness (that is against a purely “psychoneural” identity):

1. The phenomenon of the focus of attention, focus on thoughts. Unitary character of mind.
2. The relationship of the self conscious mind with neural events in the brain – there is a degree of correspondence but they do not give an identity.
3. Libets findings of the temporal discrepancy between neural events and the experiences of the self conscious mind – antedating.
4. There is a continual experience that the self conscious mind can act on brain events.  
For example: recall of memory, a word, a phrase.

Significantly, these views correlate with Still's own observations that man is "triune." (5. , p16)

"...we are forced by reason to conclude there is a superior being who conducts the material man, sustains, supports, and guards him against danger; and after all our explorations, we have to decide that man is triune when complete.

First there is *the material body*, second the *spiritual being*; third a *being of mind* which is far superior to all vital motions and material forms, whose duty is to wisely manage the great engine of life. This great principle, known as mind, must depend for all evidences on the five senses, and on this testimony all mental conclusions are based, and all orders are issued from this mental court..."

These views are however disputed by other researchers. (39) Libet himself states that his findings did not directly disprove monism, however they did demonstrate the great distinction between the phenomenological subjective content of an experience and of the observable neuronal features that give rise to it (the action potential for example.) (63)

#### 4.7.2 Libet's research into volition

Libet, suggested that volition has an inhibitory aspect to it, postulating that many decisions are not directly initiated by consciousness due to it being too time-consuming. Instead there is a window of time where the mind has a "veto" on what the brain is planning to do.(39) The surprise however of his findings however, is that we are probably not aware of how many of our actions are not directly attributable to direct consciousness but more to our unconscious minds. We are aware that we are acting but not perhaps that the brain decided it for us.

#### 4.8. General osteopathic consideration of placebo response

The findings of this literature study show strong evidence for the placebo phenomenon, despite some opposition to this in the literature. It shows the strong link between soma and mind. Such findings necessitate osteopaths to take seriously patients' minds and how they think.

In summary, much is still unknown about the human brain and mind and its interaction physiologically with the systems of the body: however evidence seems to suggest that the brain makes many decisions unconsciously with only "the final say" being given to consciousness.

It can be argued that the main function of consciousness is to make sense of meaning, which is closely tied to the phenomenon of the placebo as a response to meaning. Given that the purpose of the human system is to survive, it seems that meaning and survival are intimately connected. When our minds start to evaluate our circumstances as negative, it has an effect on our health due to the promotion of the GAS ("flight, fight or freeze") which if prolonged in the long term makes exacting demands on health leading to disease. As an alternative, positive life situations lead to reward in the brain encouraging us to lead positive lives to keep us in health.

On historical grounds and based on a tension between paradigms, it is argued that the placebo response must be seen using systemic approaches. Removing the barriers to health needs an understanding of the patient's mind.

In osteopathy, the clinical encounter should be seen as an avenue for contextual healing and as a strong augmentation to manipulation but not replacement. It follows from the results listed, that Osteopaths should also consider that patients who do not respond to treatment, if not due to a "red flag," that a nocebo response is a possibility. The area of "diagnosis" should also be strongly thought about as to whether this will help or hinder the patient via placebo or

nocebo responses – this cannot be answered prescriptively but thought about in each unique case.

#### 4.9. Limitations of this study

This study due to its consideration of an alternative paradigm did not use formal quality scoring systems of papers. Due to limited time and resources, no “inter rater” approach was done with the literature research findings in the data pooling process. A lot of studies in the relation of neurological conditions to the placebo response, due to time, were not able to be studied. A wide pool of information can still be untapped to aid understanding of the placebo phenomenon, however particularly productive insights will be garnered from applied neuropsychobiological studies. A lack of osteopathic literature on the phenomenon is also considered a study weakness.

#### 5. Conclusion

Despite a lack of literature in the osteopathic field, it has been demonstrated that the placebo phenomenon exists from a wide front of studies in related fields in health. Ethical concerns about “deception” can be superseded by seeing the placebo phenomenon as contextual healing with the application of systemic thinking - which is naturally a part of osteopathic treatment approaches. Inducing the placebo response in osteopathic treatment however should be seen as augmentative and not a replacement for proper osteopathic treatment planning and implementation. The use of a diagnosis should also be considered carefully with a view to the danger of a nocebo response. It is hoped that these conclusions can be explored further in future studies.

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