A Qualitative Study of Placebo Effects in Osteopathic Practice

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A Qualitative Study of Placebo Effects in Osteopathic Practice

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Reflections: beliefs and knowledge about the placebo phenomenon

- Subjective vs. objective?
- ‘Real’ vs. imaginary?
- Is deceit necessary?
- Unintended/unexpected outcomes?
- Is it still a placebo effect if it is intentionally derived?
- Do placebo effects occur in clinical practice, OR are they a construct of research?
- Influence on disease processes and health?
Historical Concept

https://www.psychologytoday.com/blog/ulterior-motives/201103/your-beliefs-affect-the-strength-the-placebo-effect

http://www.skepticink.com/gps/2014/05/02/the-placebo-effect-and-alt-med-is-it-magic-or-pseudoscience/
Placebo Effect Research

Psychosocial Context
- Brain
- Course of disease
- Response to therapy

Physiology

Variables

Methods of amplifying
An inert treatment plus the context that tells the patient that a therapeutic act is being performed.

(Benedetti, 2009, p. 35)

The way the therapeutic (psychosocial) context influences the patient’s brain, body, and behaviour.

(Finniss, Kaptchuk, Miller, & Benedetti, 2010)


Translation of research into practice?

Neurobiological phenomena influencing patient health

Conceptual confusion and misleading terminology

Osteopathic literature?

Translation of research findings → osteopathic practice
Purpose of the Study

Elaborate on factors (i.e. determinants) stimulating placebo effects in osteopathic practice

Relate the physiological basis of placebo effects to an osteopathic concept of healing

Create a framework for understanding placebo effects that can be applied in osteopathic practice as an adjunct tool
Qualitative Study Design

Research Questions

1) Mechanisms (physiological basis)
2) Determinants
3) Osteopathic conceptualization
4) Relating placebo effects to healing
5) Framework for osteopathic practice
RQ1: Physiological Basis (Mechanisms)

Neurological Mechanisms

- Opioids (Benedetti, 1996; Petrovic, Kalso, Petersson, & Ingvar, 2002; Scott et al., 2008; Zubieta et al., 2005)
- Descending inhibition of pain (Bingel, Lorenz, Schoell, Weiller, & Buchel, 2006)
- Cannabinoids (Benedetti, Amanzio, Rosato, & Blanchard, 2011)
- Dopaminergic systems (de la Fuente-Fernandez et al., 2001)
- Specific modulation of ANS activity
  - Respiratory (Kemeny et al., 2007)
  - Gastric (Meissner, 2009)
  - Cardiovascular (Meissner & Ziep, 2011)
RQ1: Physiological Basis (Mechanisms)

Oxytocin-Mediated Mechanisms

- Oxytocin-enhanced placebo analgesia \(^{(Kessner, Sprenger, Wrobel, Wiech, & Bingel, 2013)}\)

Immune and Endocrine Responses

- Classical conditioning \(^{(Albring et al., 2012; Benedetti et al., 2003; Goebel et al., 2002)}\)
- Positive social interaction \(^{(Barrett et al., 2011; Kokkotou et al., 2010; Rakel et al., 2011)}\)
RQ1: Physiological Basis (Mechanisms)

- Opioids
- CB
- Dopamine
- Oxytocin
- ANS
- Immune
- Endocrine

Resiliency and Adaptability Mechanism
RQ2: Determinants

**Expectations**
- Verbal suggestions (Benedetti, Arduino, & Amanzio, 1999)
- Prior experience (Colloca & Benedetti, 2006)
- Somatic focus (Geers, Helfer, Weiland, and Kosbab, 2006)
- Social observational learning (Colloca & Benedetti, 2009)

**Conditioning**
- Conditioned responses = ‘learned placebo responses’ (Pacheco-Lopez, Engler, Niemi, & Schedlowski, 2006)

**Motivation**
- Motivational concordance (Hyland & Whalley, 2008)

**Perceptions and meaning**
RQ2: Determinants

- Patient Factors
- Disentangling Placebogenic Factors
- Practitioner Factors
- Patient-practitioner Interaction & Communication
- Treatment Characteristics & the Therapeutic Ritual
**RQ2: Determinants**


- **Optimism/pessimism + certain expectations** *(Geers, Helfer, Kosbab, Weiland, & Landry, 2005; Geers, Kosbab, Helfer, Weiland, & Wellman, 2007)*

- **Stress resiliency and interpersonal function (opioids)** *(Pecina et al., 2013)*

- **Novelty seeking, behavioural drive, fun seeking (dopamine)** *(Schweinhardt, Seminowicz, Jaeger, Duncan, & Bushnell, 2009)*
RQ2: Determinants

- Professional status, mannerisms, physical appearance (Moerman, 2002)

- Significant variation in placebo responding depending on treating practitioner (Kelley et al., 2009)

- Beliefs about the illness and the treatment (Gracely, Dubner, Deeter, & Wolskee, 1985)
RQ2: Determinants

- Colour/shape/brand/price of medication, route of administration, type of device, procedures, manual maneuvers

- Multisensory therapeutic rituals (Kaptchuk, 2002, 2011)

- Influence outcomes via symbolic meaning (Moerman, 2000)

Placebo injections > pills (de Craen, Tijssen, de Gans, & Kleijnen, 2000)
Branded pills > unbranded (Branthwaite & Cooper, 1981)
Sham acupuncture > inert pill (Kaptchuk et al., 2006)
‘Tylenol’ (placebo) > sham acupuncture (Kong et al., 2013)
4 pills/day > 2 pills/day (de Craen et al, 1999)
RQ2: Determinants

- **Cognitive and emotional care**
  - Pain, blood pressure, asthma (*Di Blasi, Harkness, Ernst, Georgiou, & Kleijnen, 2001*)

- **Effective communication**
  - Subjective and objective measures (*Griffin et al., 2004; Stewart, 1995*)

- **Overt/covert paradigm of drug administration** (*Colloca et al., 2004*)

- **Empathy**
  - HbA1C and LDL-C (*Hojat et al, 2011*)
  - Interleukin-8 and neutrophils (*Rakel et al., 2011*)
RQ2: Determinants

- Determinants can be separated and progressively re-combined to create graded clinical improvements in IBS \((Kaptchuk \ et \ al., \ 2008)\)

- Open label placebo \((Kaptchuk \ et \ al., \ 2010)\)
  Positively framed persuasive rationale + supportive patient-practitioner relationship + engagement in therapeutic ritual
Mechanisms

- Opioids
- Dopamine
- Oxytocin
- ANS
- Immune
- Endocrine

Determinants

- Disentangling Placebogenic Factors
  - Treatment Characteristics & the Therapeutic Ritual
  - Patient-practitioner Interaction & Communication
  - Patient Factors
  - Practitioner Factors

Resiliency and Adaptability Mechanism
How do osteopaths conceptualize placebo effects as a phenomenon in clinical practice?

RQ3: Osteopathic conceptualization

RQ3: Osteopathic conceptualization

“You can’t call it a placebo if there is a measurable physiological effect.” #10

“You don’t think placebo – the way people want to define it – I don’t think it exists.” #18

“...what is underlying the placebo effect, I believe, is at the root of how the body heals itself.” #14

“...whether you call that placebo or not, I don’t know.” #12
RQ3: Osteopathic conceptualization

The challenge of defining placebo effects
(no consensus)

- Psychosocial/context/relationship effects
- Unintentional outcomes
- A construct of research
- ‘Not real’ effects
- A purely subjective phenomenon
- A subjective or objective phenomenon
- A demonstration of self-healing
RQ3: Osteopathic conceptualization

The challenge of defining placebo effects (no consensus)

The whole clinical encounter (consensus)

The patient’s mental constructs (all except #18)

The therapeutic relationship (all except #10, #14)

Shaping mental constructs through framing (all except #6, #18)
RQ3: Osteopathic conceptualization of placebo effects: Placebogenic or foundation of treatment?
Osteopathic concept vs. placebo literature

Concept

Mechanism

Resiliency & Adaptability (Homeostasis)

- Oxytocin
- ANS
- Immune
- Endocrine
- Opioids
- Dopamine
Does engaging placebo mechanisms result in clinically meaningful improvements in health?

Extent of Placebo Effects

Conditions

Outcomes
Placebo-Sensitive Conditions

- **Pain**
  - Petrovic et al., 2002
  - Colloca & Benedetti, 2006
  - Ronel et al., 2011

- **Parkinson’s Disease**
  - Benedetti et al., 2004

- **IBS**
  - Kaptchuk et al., 2008
  - Kaptchuk et al., 2010

- **Immune Function**
  - Ader et al., 2010
  - Albring et al., 2012

- **Endocrine Function**
  - Benedetti et al., 2003

- **Common Cold**
  - Rakel et al., 2011
  - Barrett et al., 2011

- **Nausea**
  - Horing et al., 2013

- **Asthma**
  - Kemeny et al., 2007

- **Hypertension**
  - Amigo, Cuesta, Fernandez, & Gonzalez, 1993
  - Meissner & Ziep, 2011

- **CVD & Mortality**
  - Padula et al., 2012
  - Yue et al., 2014
Placebo-Sensitive Outcomes

**Subjective Measures:** The ‘illness’ experience

- Pain scales (VAS)
- QOL
- Perception of motor function
- Disease-specific symptom scales

**Objective measures:** Evaluation of ‘disease’

- Neurological
  - fMRI
  - MRI
  - PET (+/- radiotracers)

- Biochemical
  - Blood serum markers (Interleukin-8, Neutrophils, Osteoprotegerin, Growth Hormone)

- Functional
  - Accelerometers
  - Spirometry (FEV)
  - EGG
  - ECG, HR, BP
Towards an osteopathic understanding of healing

Healing is a natural inherent *restorative process* of finding balance, equilibrium and/or *homeostasis* within the body.
RQ4: Relating placebo effects to healing

- Subjective
  - Spiritual Healing
    - Psychological/emotional/mental Healing
    - Sociocultural Healing

- Objective: Neurological

- Objective: Biochemical

- Objective: Functional

Physical Healing (Form and Function)
RQ4: Relating placebo effects to healing

Resiliency & Adaptability Mechanism (Homeostasis) + Healing is a natural inherent restorative process of finding balance, equilibrium and/or homeostasis within the body. = Placebo effect mechanisms reflect the inherent capacity of restoring homeostasis and health.
RQ5: Framework for Osteopathic Practice

Sources of conceptual confusion

1. Historical definition
2. Cross-paradigm and cross-context translation issues
   • what is considered a placebo (and subsequent effect) is contingent on:
     a) guiding theoretical framework and understanding of causality
     b) whether (or not) the effect was intended
3. Application of reductionist scientific principles to a therapy believed to be effective through a multitude of different factors
RQ5: Framework for Osteopathic Practice

A new conceptual framework: Therapeutic Ingredients

Process of health promotion in osteopathic practice

(generated by content from informant interviews)
RQ5: Framework for Osteopathic Practice

Theoretical framework

- Definition
- Treatment elements (therapeutic ingredients)
- Mechanisms
- Determinants
  - Effect on healing processes
  - Evidence based method of promoting health
  - Defining element of osteopathic practice
## RQ5: Framework for Osteopathic Practice

### Practical guidelines

<table>
<thead>
<tr>
<th>What it is</th>
<th>What it does</th>
<th>How to do it</th>
</tr>
</thead>
<tbody>
<tr>
<td>Build trusting partnerships</td>
<td>Utilize strategies of effective communication</td>
<td>Provide a framework</td>
</tr>
<tr>
<td>Recognize placebo-sensitive individuals and conditions</td>
<td>Create unique and comfortable environments</td>
<td>Engage in personal development and self-care</td>
</tr>
<tr>
<td>Recognize the role of ritual and meaning</td>
<td>Maintain honesty and ethics</td>
<td>Recognize the potential and know the limits</td>
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Use these strategies as an adjunct tool in the provision of comprehensive patient care.
Conclusion

• Placebo effect mechanisms reflect inner healing processes
• Mechanisms can be encouraged ethically and honestly
• Conceptual confusion needs to be addressed
• The guidelines outlined in this paper provide a method potentiating the intrinsic health-restoration resources of an individual as a complementary tool in osteopathic practice
Conclusion

“...in my life, in my relationships with my fellow man, I really try to bring love. Agape. A love of God, you know, in what I do. And we, in Osteopathy, are so blessed to convey this, with your eyes, with your hands, and your heart.”
Thank you for listening!


References


References


References


References


Supplemental information
Strategies of effective communication

- See supplemental handout

Adapted from Derksen et al., 2013; Griffin et al., 2004; Hojat et al., 2011; Kaptchuk, Kelley, Conboy, et al., 2008; Rakel et al., 2011; Stewart, 1995; and content from informant interviews.
Mechanism of placebo analgesia

- Same brain regions active in placebo and opioid analgesia (rACC, pons, and PAG) (Petrovic, Kalso, Petersson, & Ingvar, 2002)
- ↑ endogenous opioid neurotransmission in pain sensitive regions (rACC, NAC, insula, DLPFC, amygdala, and PAG) (Scott et al., 2008; Zubieta et al., 2005)
- Opioid antagonist partially blocks placebo analgesia (Benedetti, 1996)

Placebo analgesia = changes in CNS nociception processing
Determinants of Resiliency

• Close relationships with parental figures who are caring and competent
• Ability to self-regulate behaviour
• Positive views of self
• Self-efficacy and self-determination
• Executive functions of problem solving, foresight, and future orientation
• Optimism and positivity
• Perceiving stressful occurrences in less threatening ways and being able to reframe adverse experiences in a positive vein
• Spirituality
• Being able to find meaning amidst adversity