

A Qualitative Study of Placebo Effects in Osteopathic Practice

OsEAN Open Forum – April 22, 2016
Vienna, Austria

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Thesis defended at the Canadian College of Osteopathy
Diploma of Osteopathic Manual Practice
Toronto, Ontario, Canada (November 2015)

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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/>

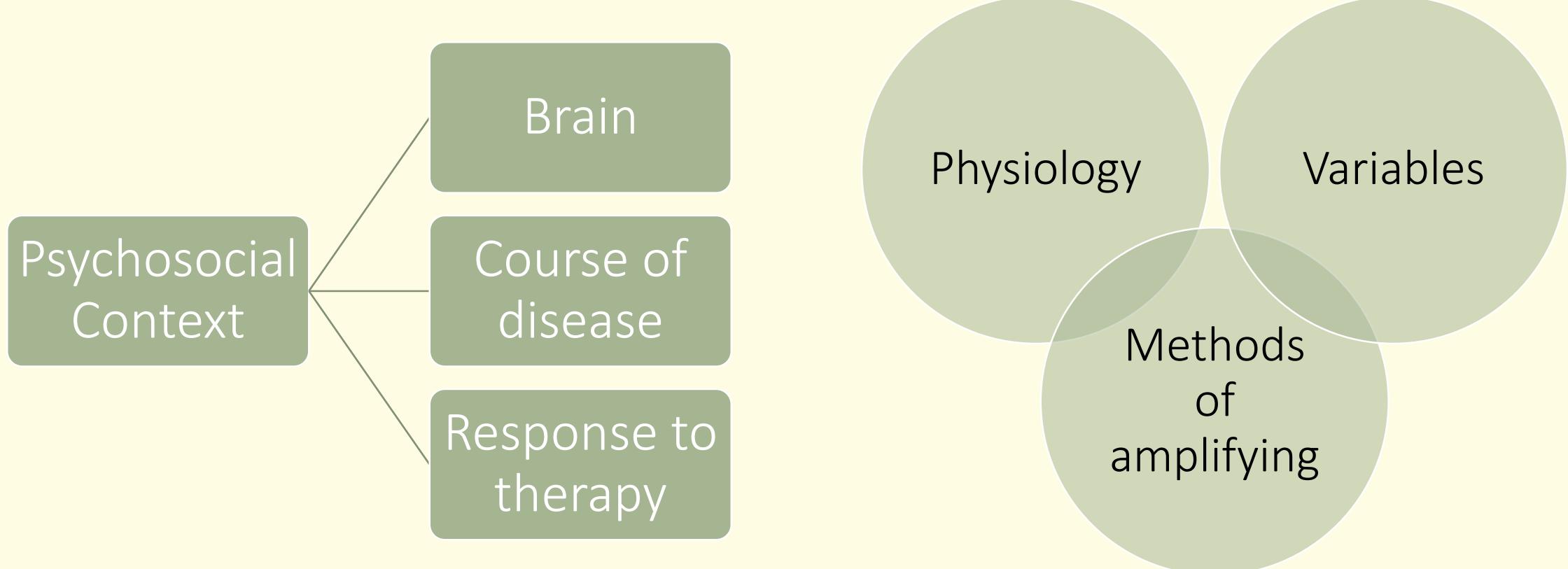
T H E

PLACEBO

P A R A D O X

<http://mentalfloss.com/article/51789/understanding-placebo-effect>

Placebo Effect Research



Contemporary Definitions

Placebo

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

(Benedetti, 2009, p. 35)



Placebo Effect

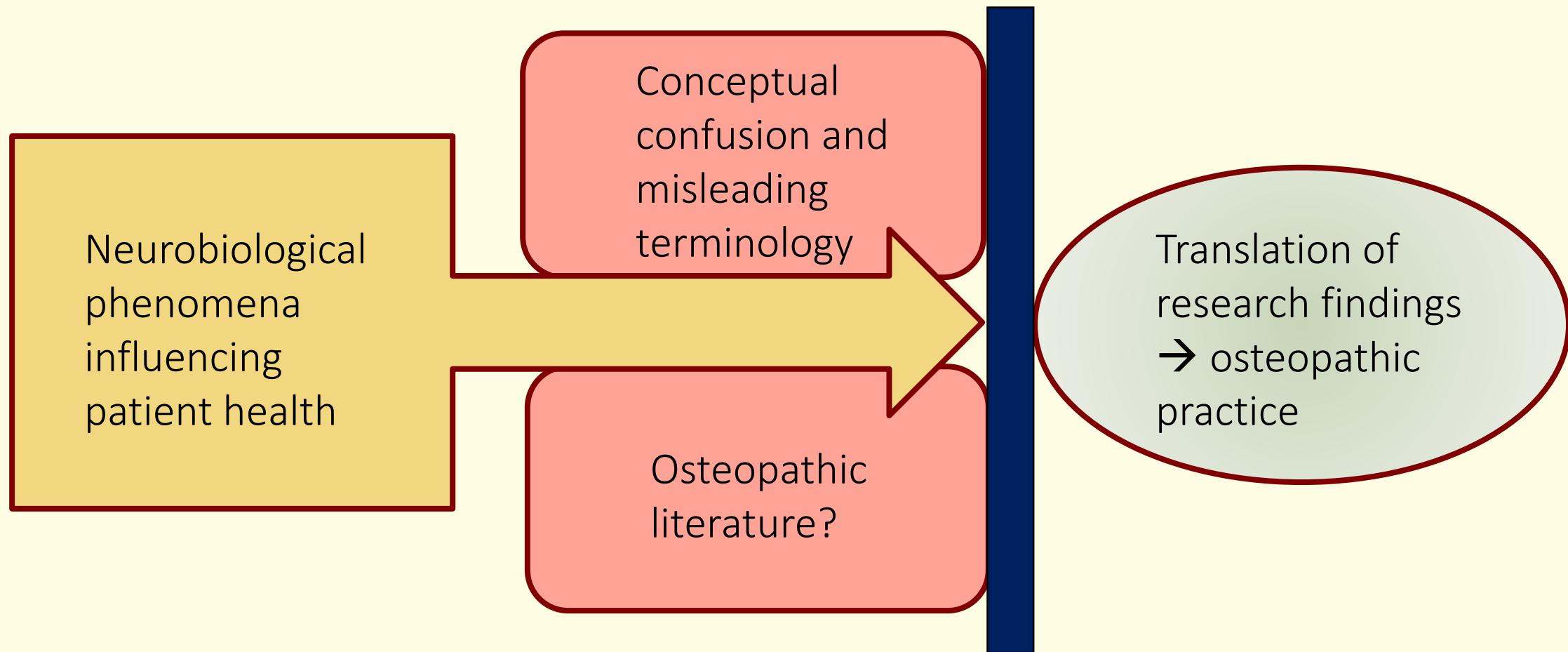
The way the therapeutic (psychosocial) context influences the patient's brain, body, and behaviour.

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

Benedetti, F. (2009). *Placebo Effects: Understanding the Mechanisms in Health and Disease*. New York, NY: Oxford University Press.

Finniss, D. G., Kaptchuk, T. J., Miller, F., & Benedetti, F. (2010). Biological, clinical, and ethical advances of placebo effects. *Lancet*, 375(9715), 686-695. doi: 10.1016/S0140-6736(09)61706-2

Translation of research into practice?



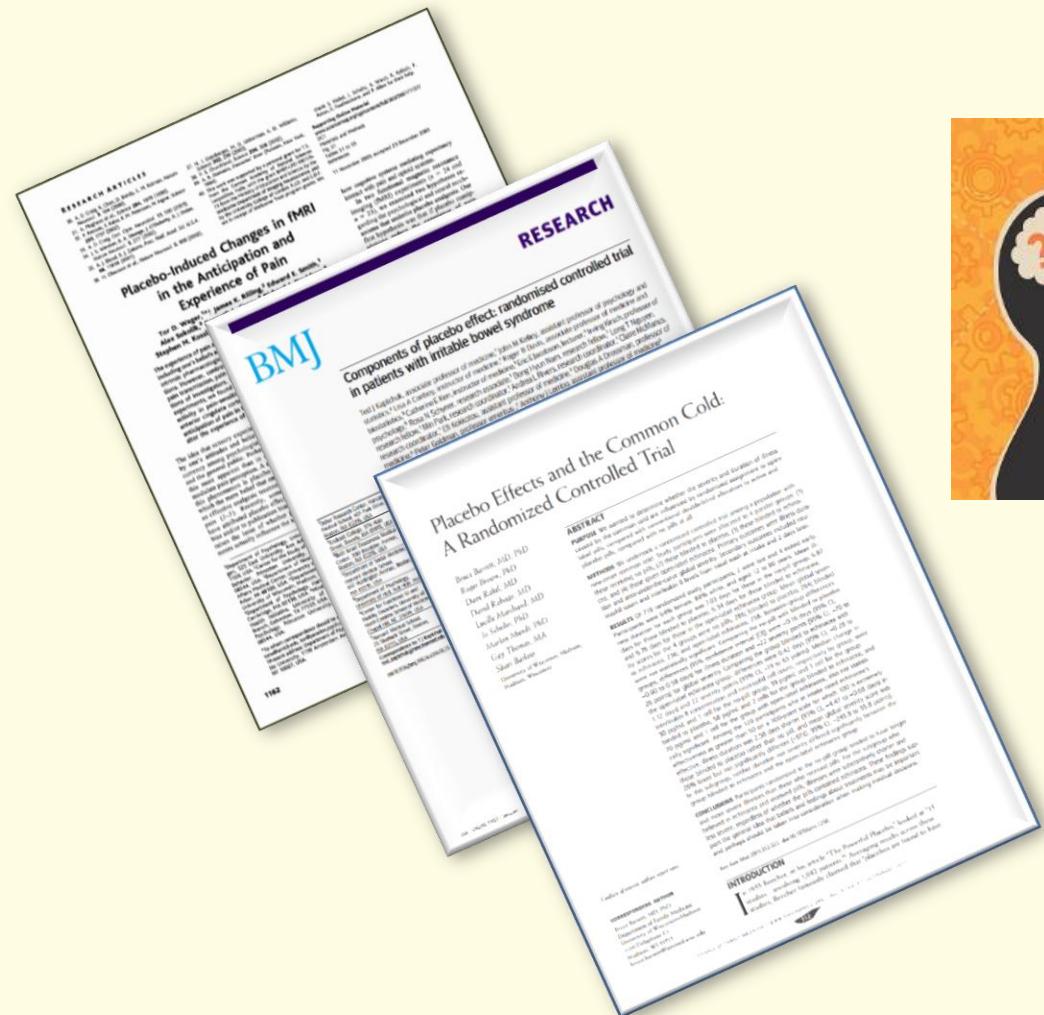
Purpose of the Study

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

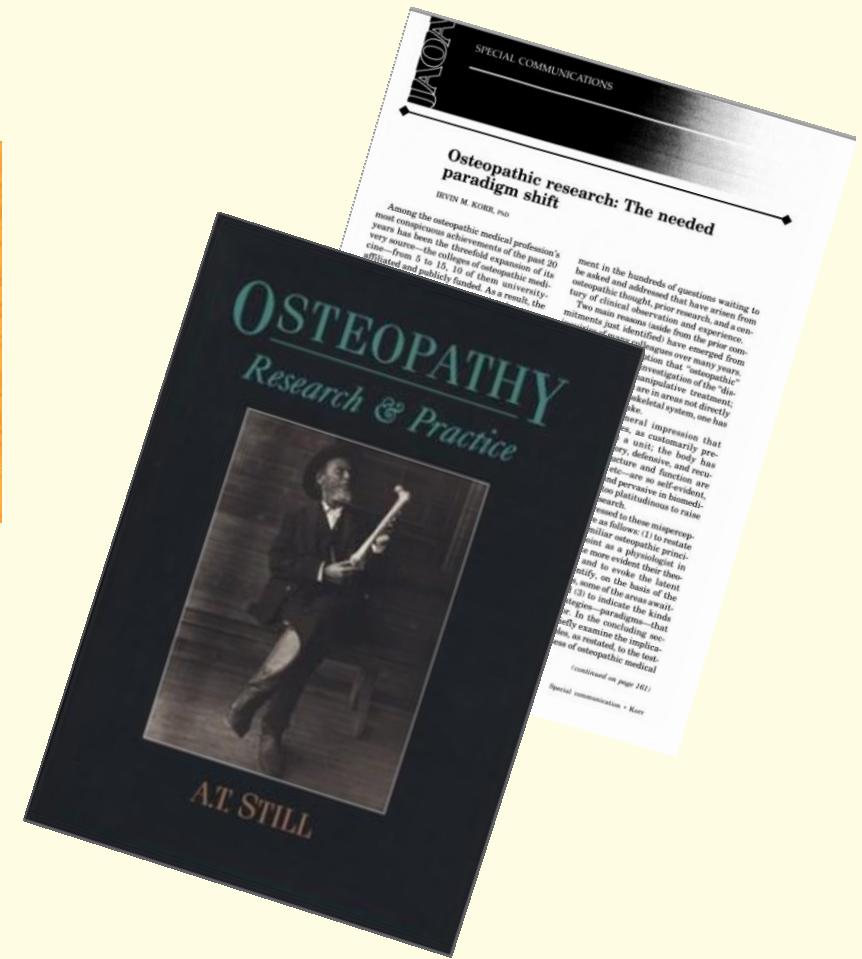
Relate the physiological basis of placebo effects to an osteopathic concept of healing

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

Qualitative Study Design



<http://study.com/academy/lesson/problem-solving-skills-for-kids.html>



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)

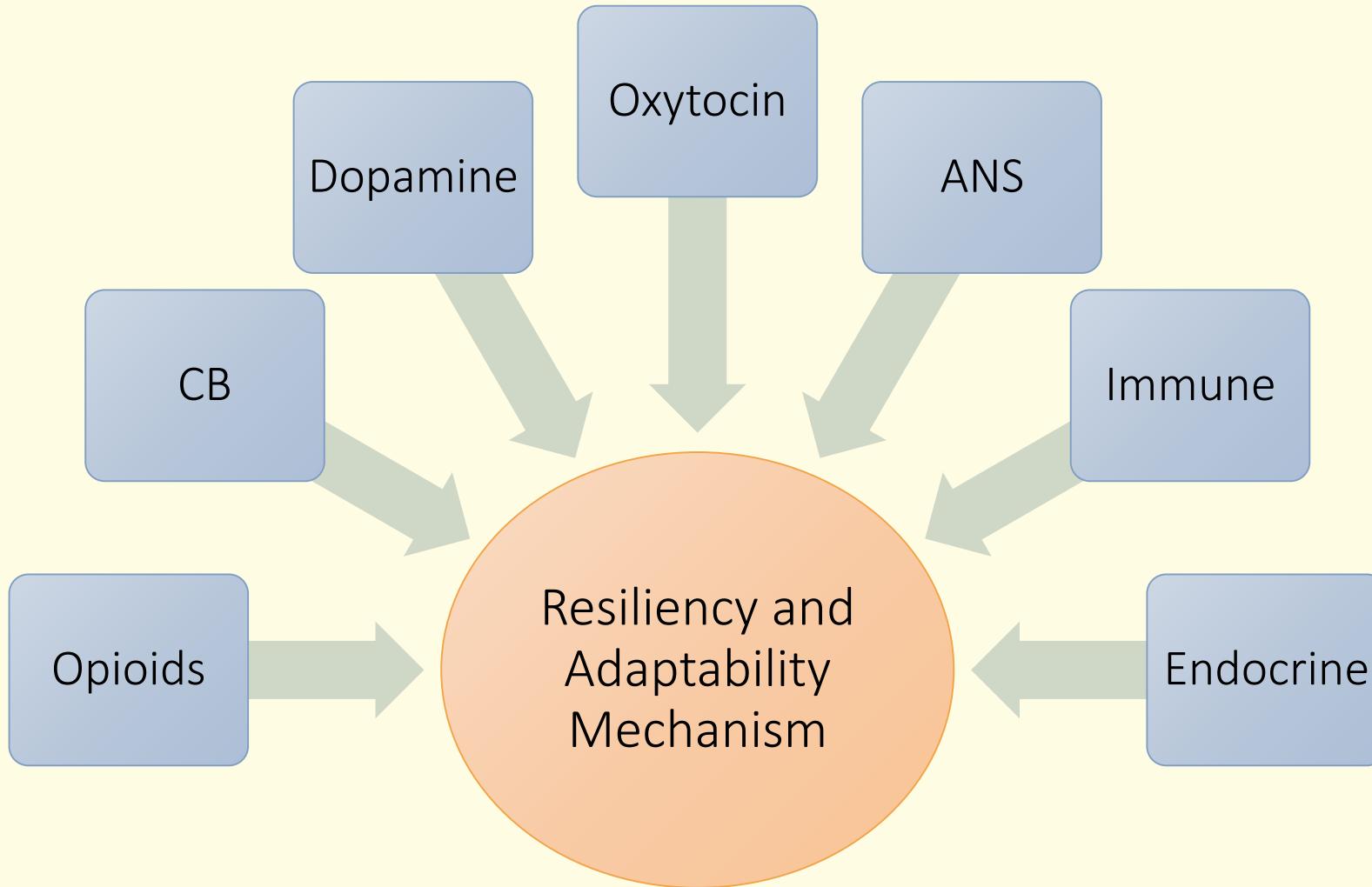
Oxytocin-Mediated Mechanisms

- 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)



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

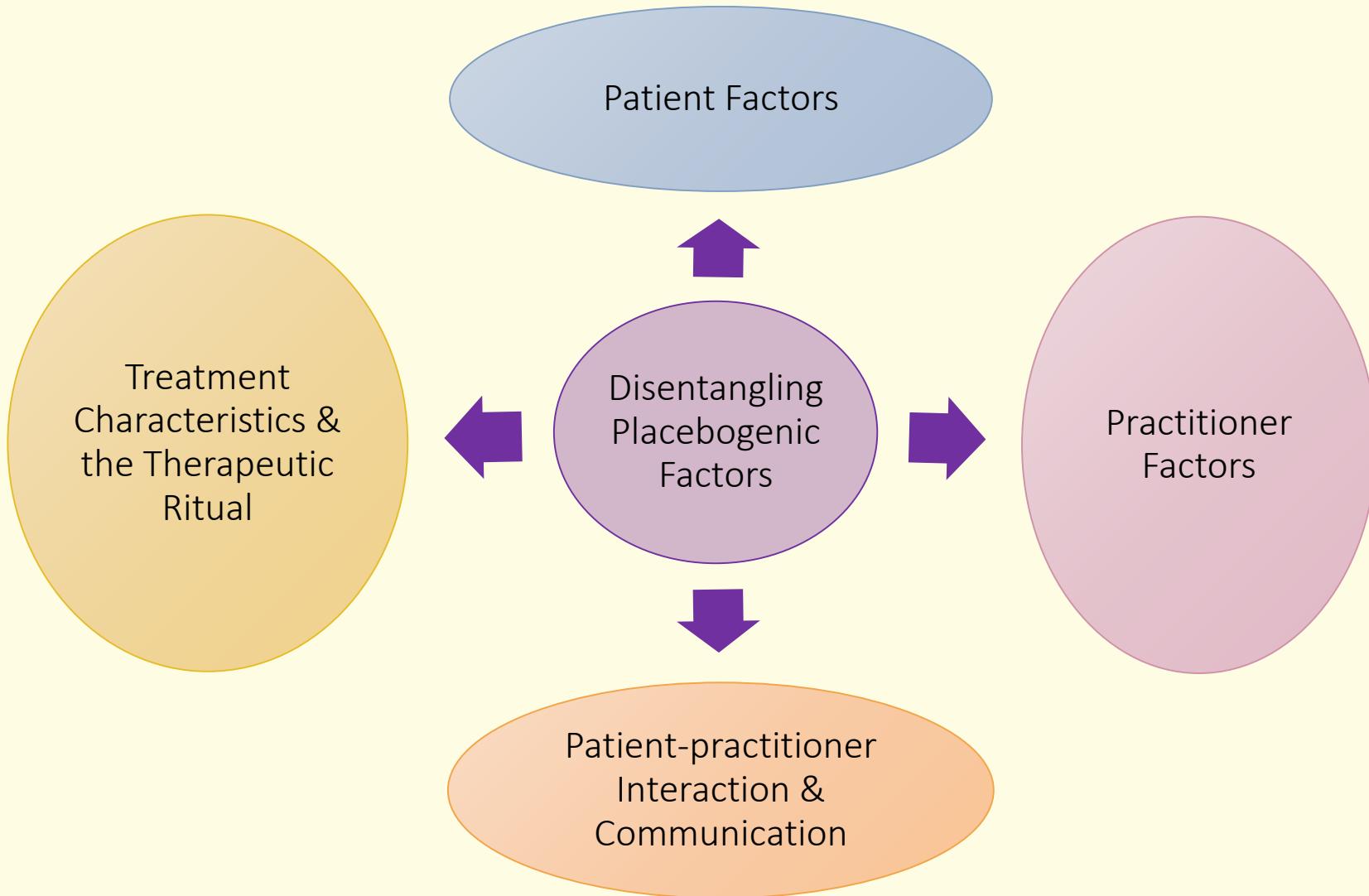
- Conditioned responses = ‘learned placebo responses’ (*Pacheco-Lopez, Engler, Niemi, & Schedlowski, 2006*)

Motivation

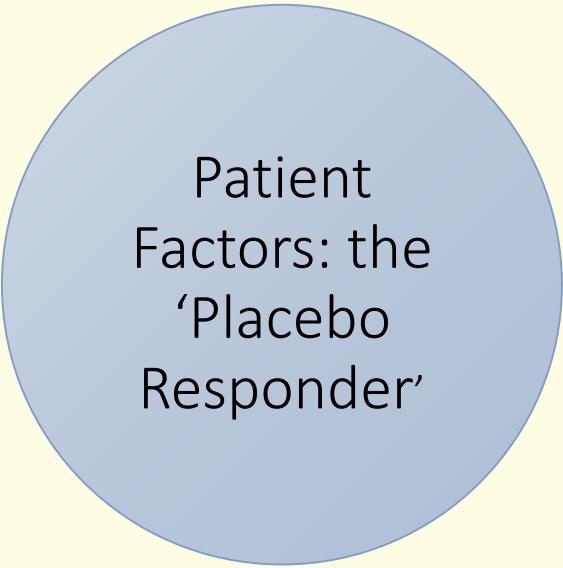
- Motivational concordance (*Hyland & Whalley, 2008*)

Perceptions and meaning

RQ2: Determinants



RQ2: Determinants



Patient
Factors: the
'Placebo
Responder'

- Interactionist hypothesis: Personality + situation → response (*Horing, Weimer, Muth, & Enck, 2014; Jaksic, Aukst-Margetic, & Jakovljevic, 2013*)
- Optimism/pessimism + certain expectations (*Geers, Helper, Kosbab, Weiland, & Landry, 2005; Geers, Kosbab, Helper, 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



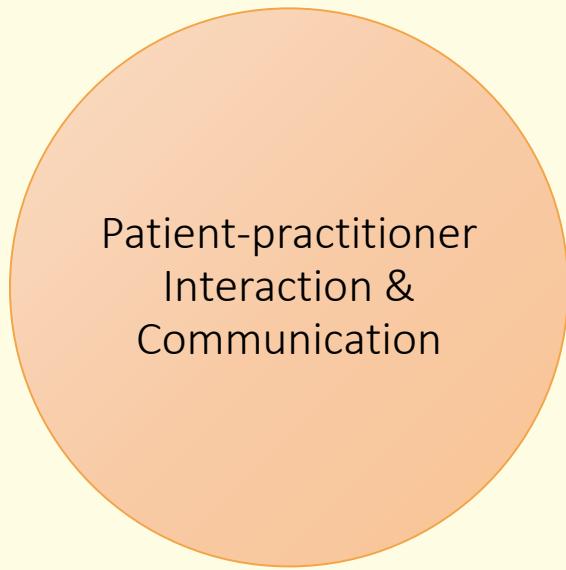
Practitioner
Factors

- 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

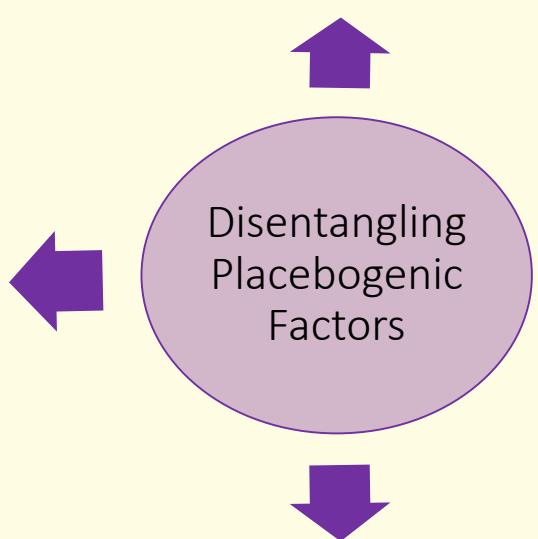
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- Colour/shape/brand/price of medication, route of administration, type of device, procedures, manual maneuvers
 - Multisensory therapeutic rituals (*Kaptchuk, 2002, 2011*)
 - Influence outcomes via symbolic meaning (*Moerman, 2000*)
- Placebo injections > 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



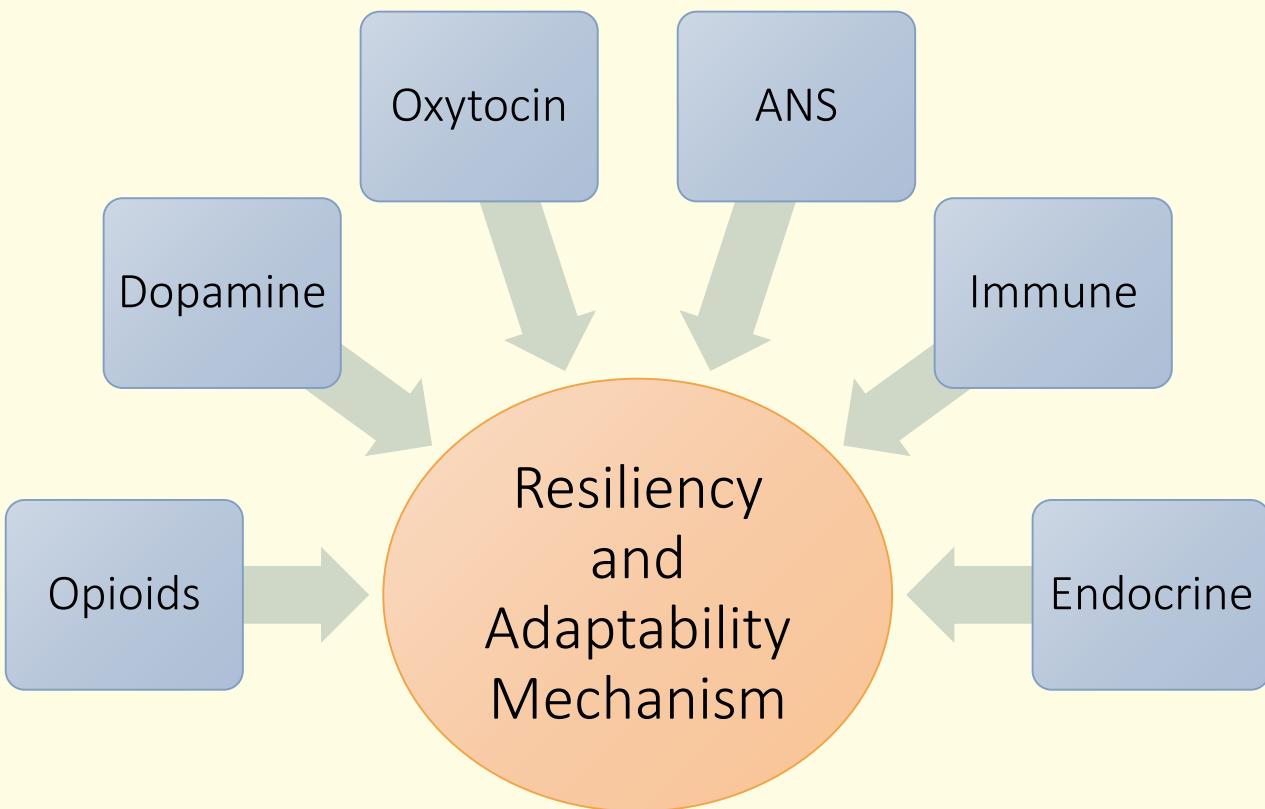
- Cognitive and emotional care
 - Pain, blood pressure, asthma (*Di Blasi, Harkness, Ernst, Georgiou, & Kleijnen, 2001*)
- Effective communication
 - Subjective and objective measures (*Griffin et al., 2004; Stewart, 1995*)
- Overt/covert paradigm of drug administration (*Colloca et al., 2004*)
- Empathy
 - HbA1C and LDL-C (*Hojat et al, 2011*)
 - Interleukin-8 and neutrophils (*Rakel et al., 2011*)

RQ2: Determinants

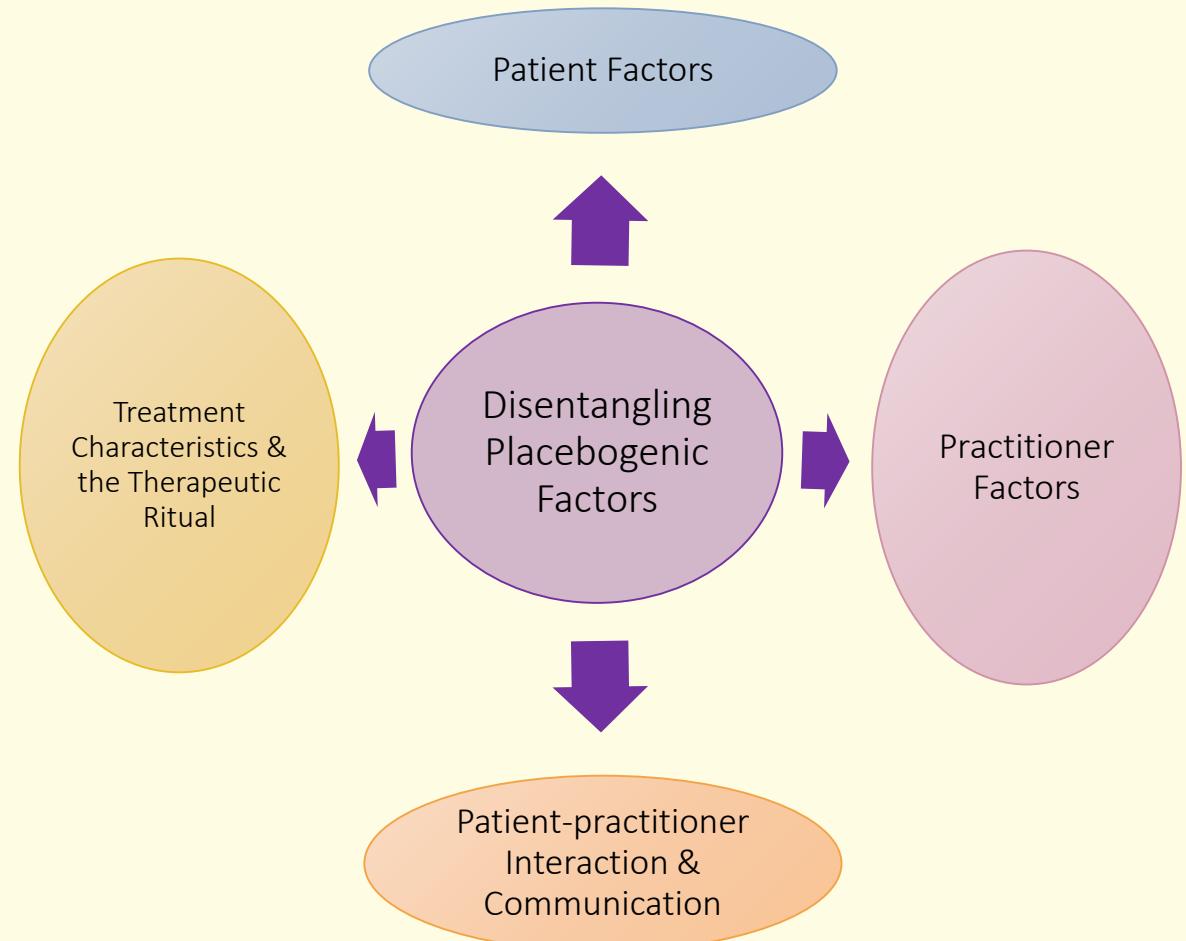


- Determinants can be separated and progressively re-combined to create graded clinical improvements in IBS (*Kaptchuk et al., 2008*)
- Open label placebo (*Kaptchuk et al., 2010*)
Positively framed persuasive rationale + supportive patient-practitioner relationship + engagement in therapeutic ritual

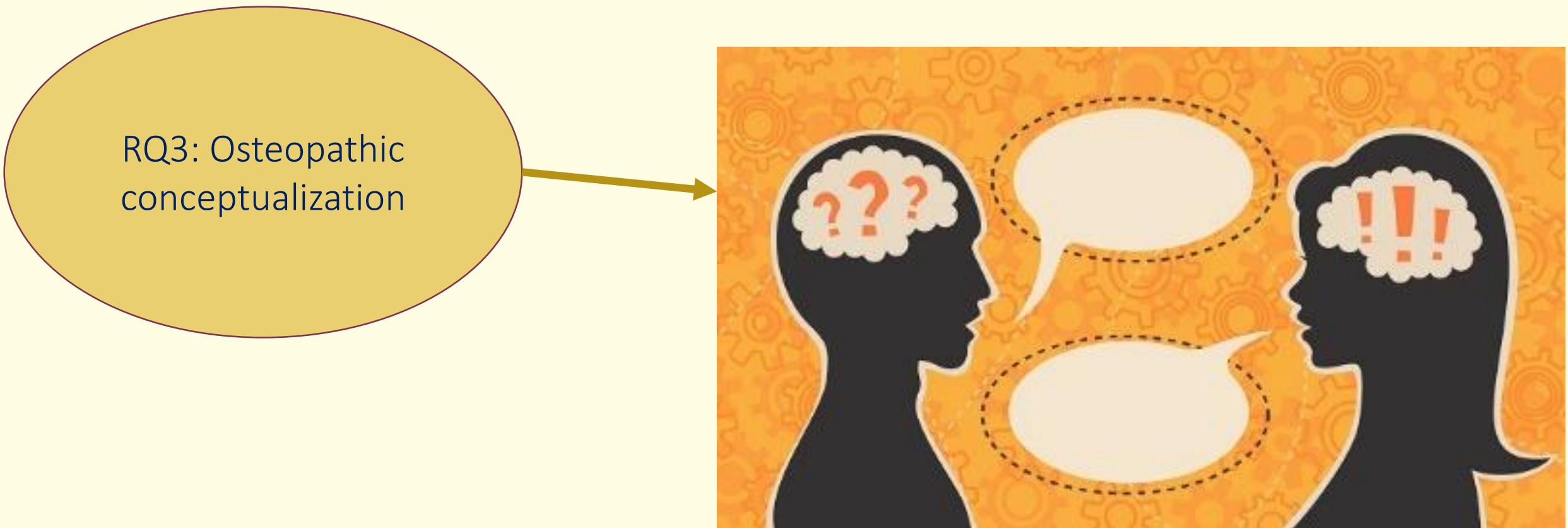
Mechanisms



Determinants



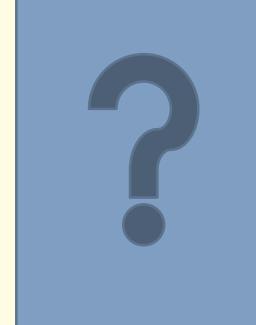
How do osteopaths conceptualize placebo effects as a phenomenon in clinical practice?



RQ3: Osteopathic conceptualization

"You can't call it a placebo if there is a measurable physiological effect." #10

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



"I don't think placebo – the way people want to define it – I don't think it exists." #18

"...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)

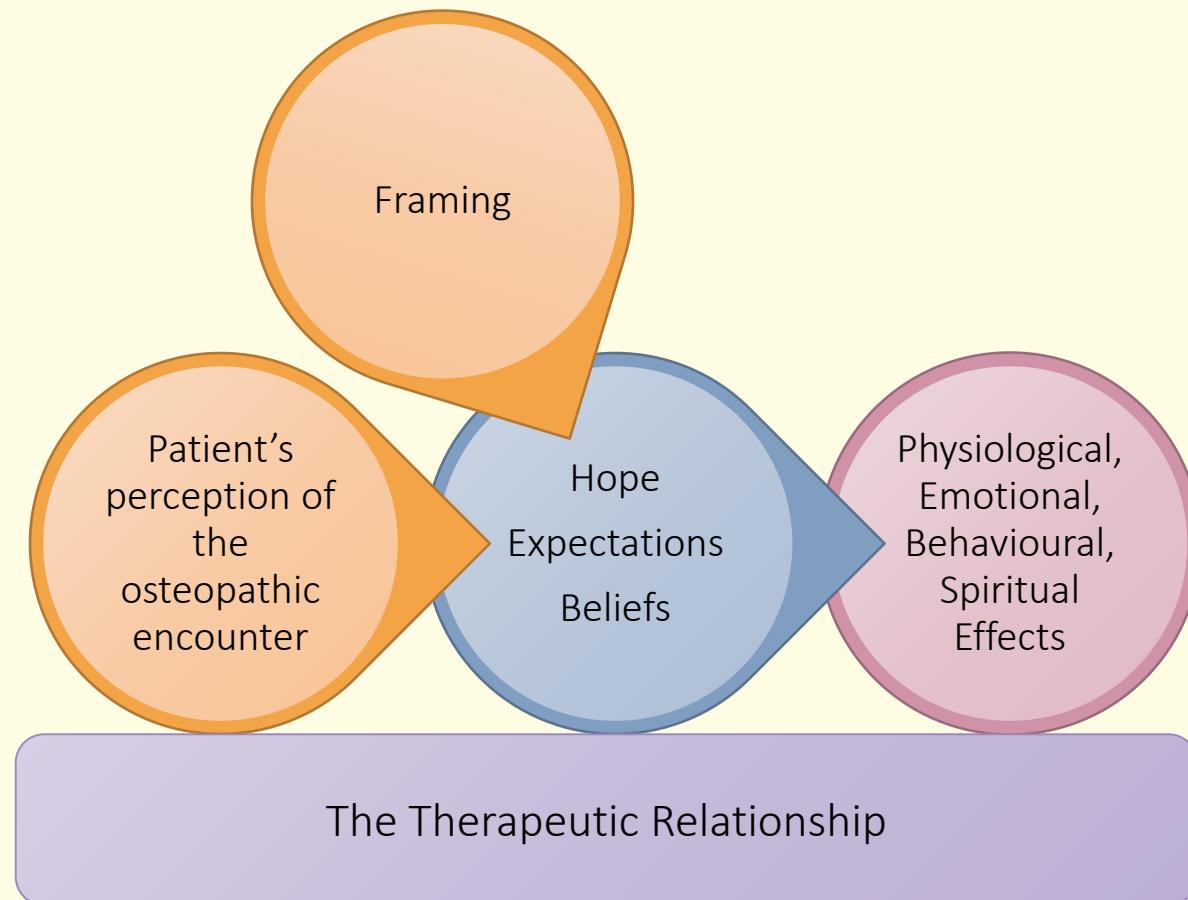
The whole clinical encounter
(consensus)

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

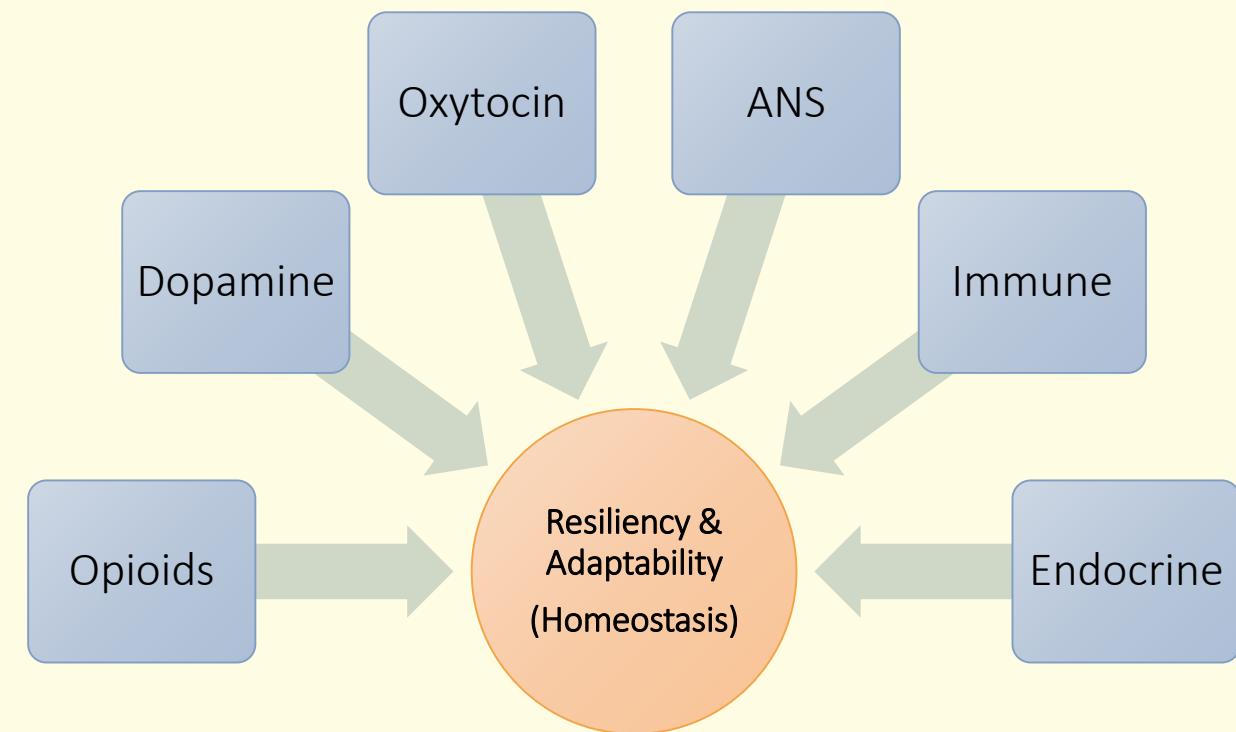
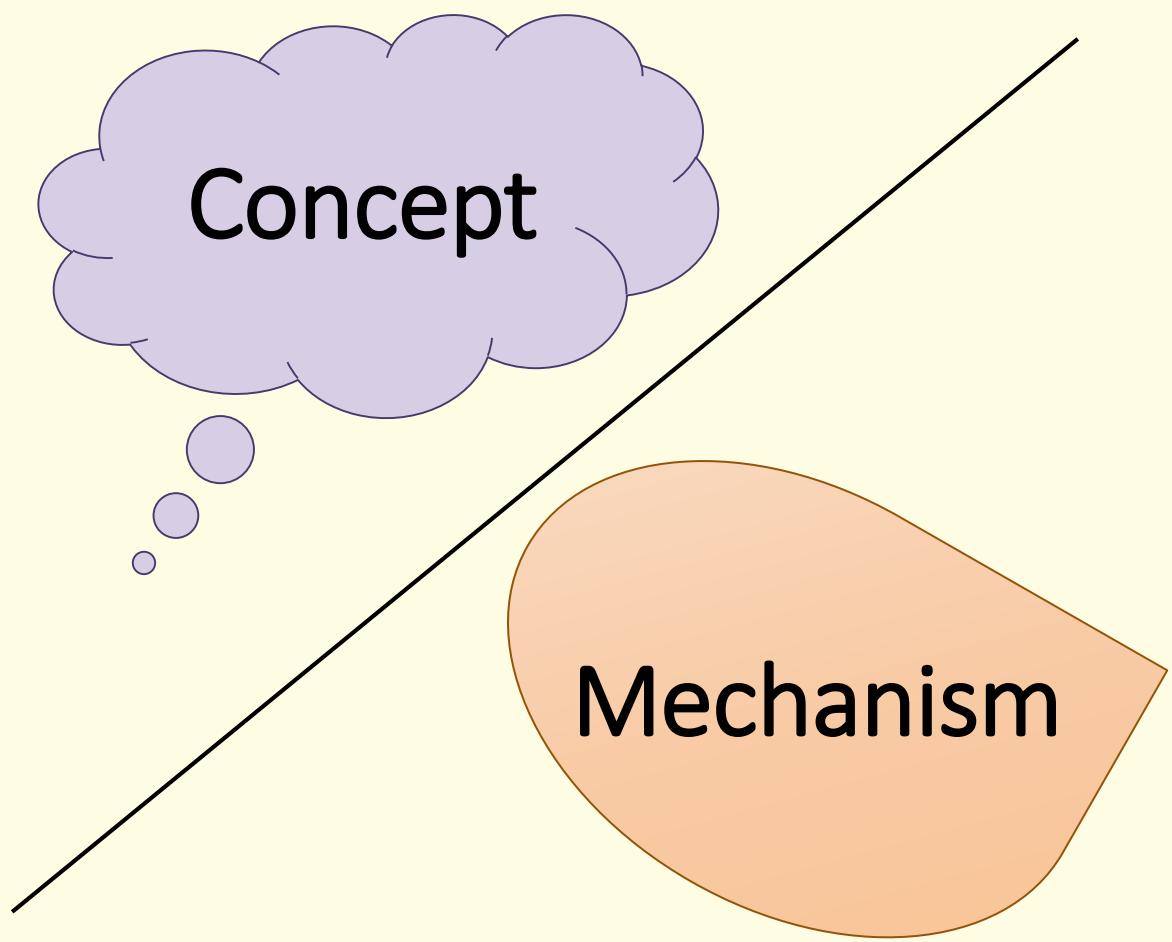
The therapeutic relationship
(all except #10, #14)

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





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

- *de la Fuente-Fernandez et al.*, 2001, 2002
- 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

Subjective

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

Objective measures:
Evaluation of 'disease'

Neurological

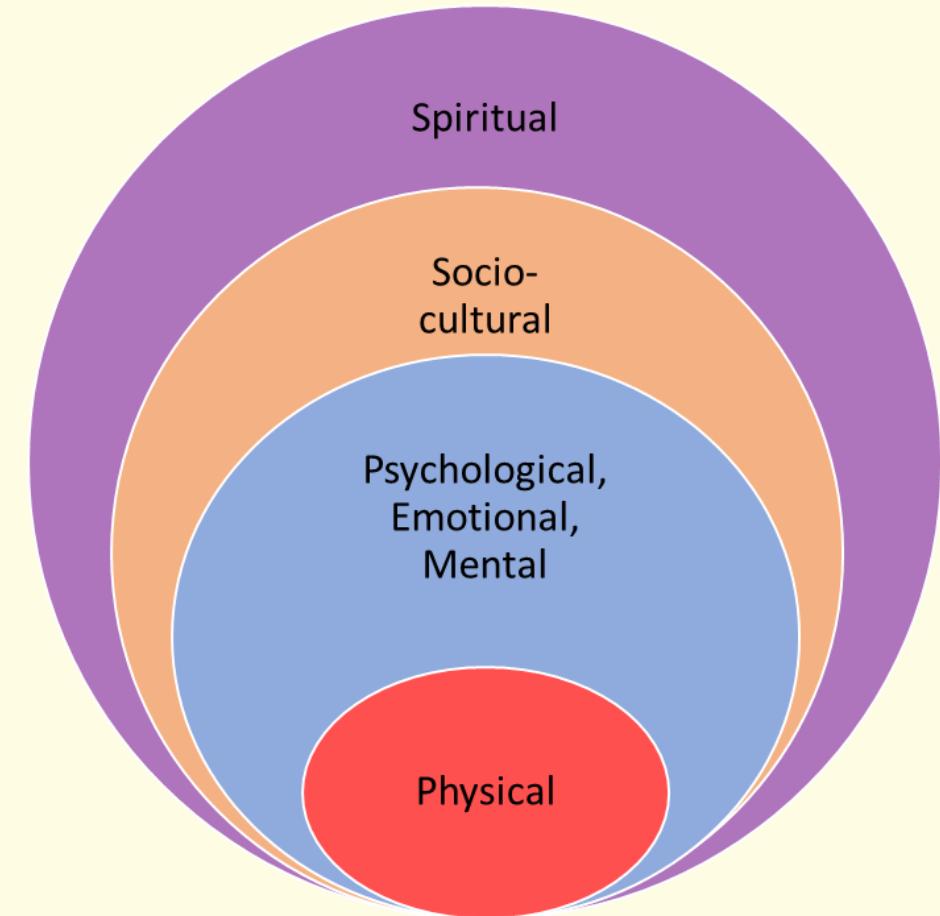
- fMRI
 - MRI
 - PET (+/- radiotracers)
-
- Blood serum markers
(Interleukin-8, Neutrophils,
Osteoprotegerin, Growth
Hormone)
-
- Accelerometers
 - Spirometry (FEV)
 - EGG
 - ECG, HR, BP

Biochemical

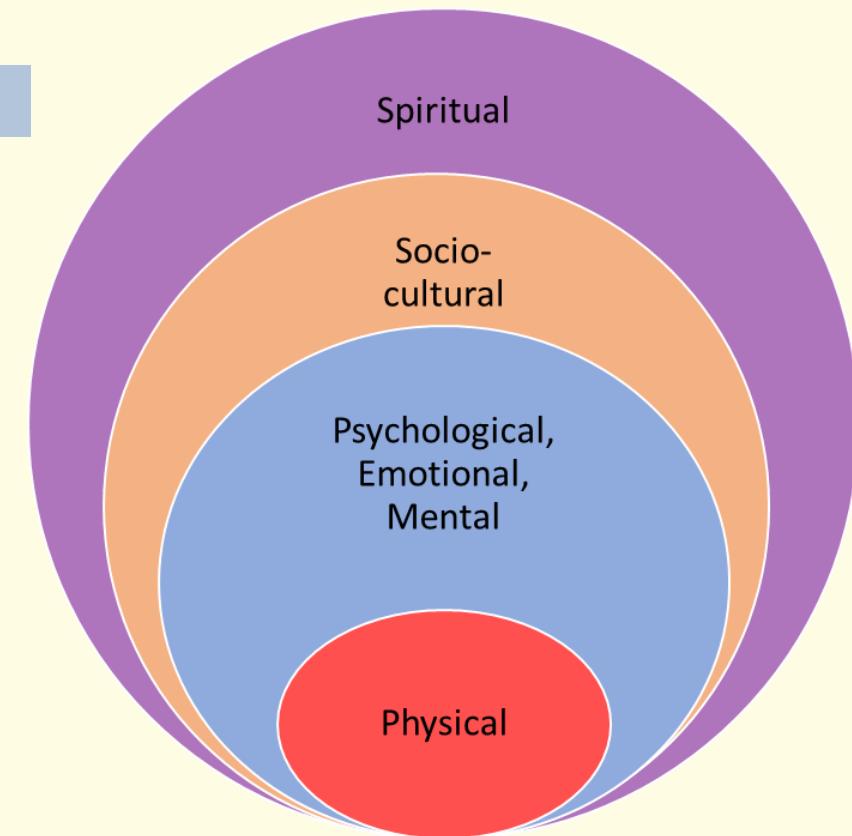
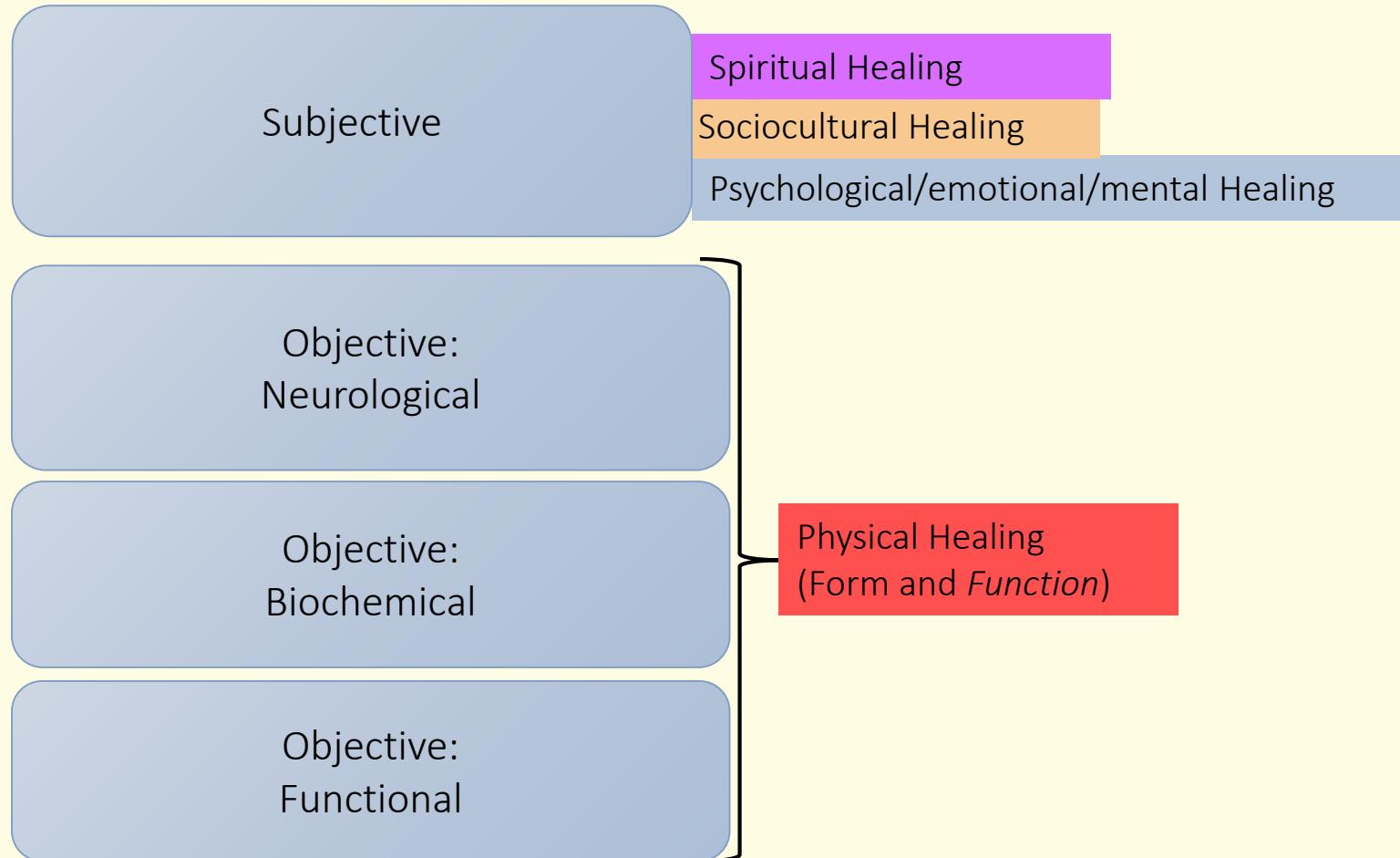
Functional

Towards an osteopathic understanding of healing

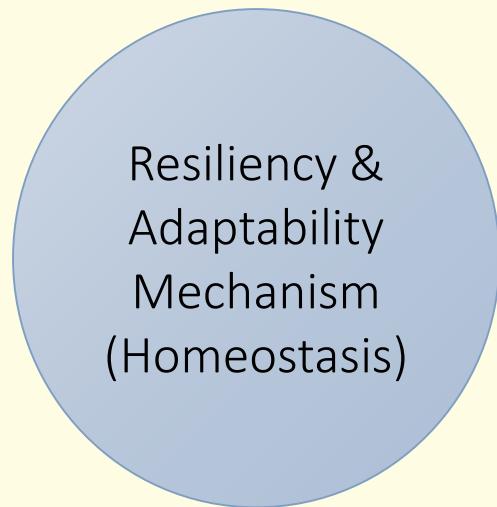
Healing is a natural inherent *restorative process* of finding balance, equilibrium and/or *homeostasis* within the body.



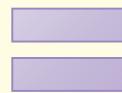
RQ4: Relating placebo effects to healing



RQ4: Relating placebo effects to healing



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

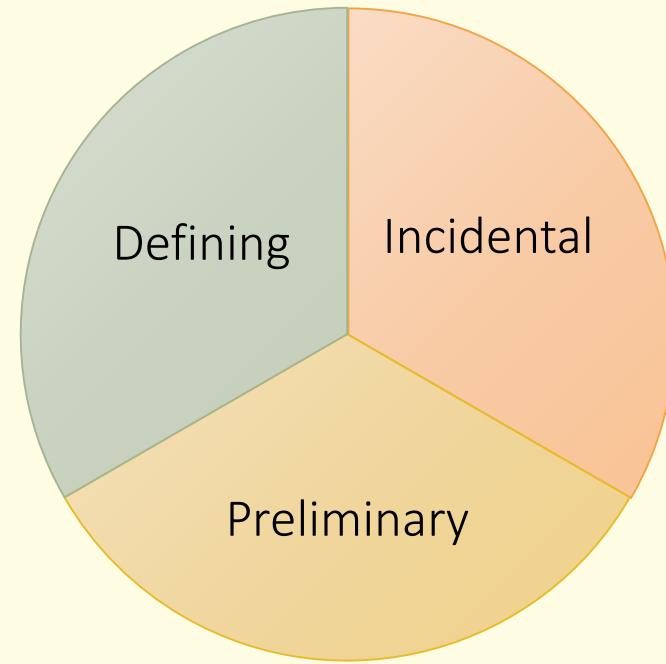
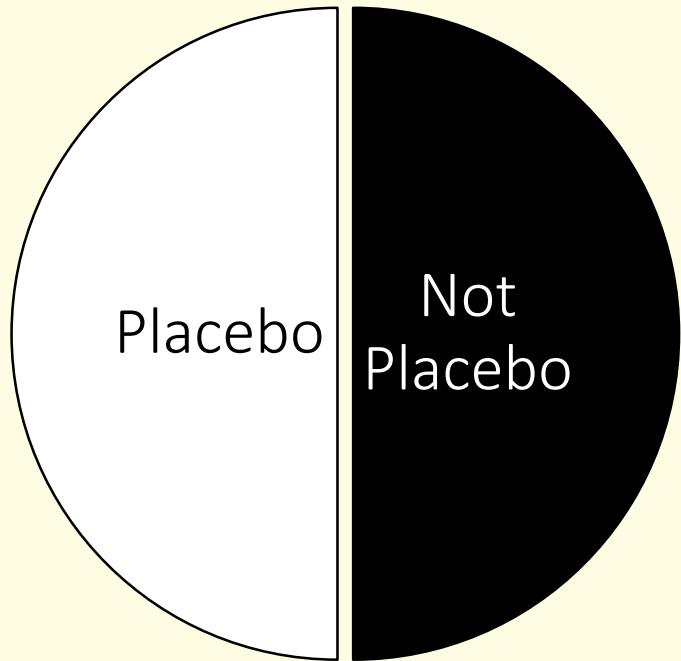
RQ5: Framework for Osteopathic Practice

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

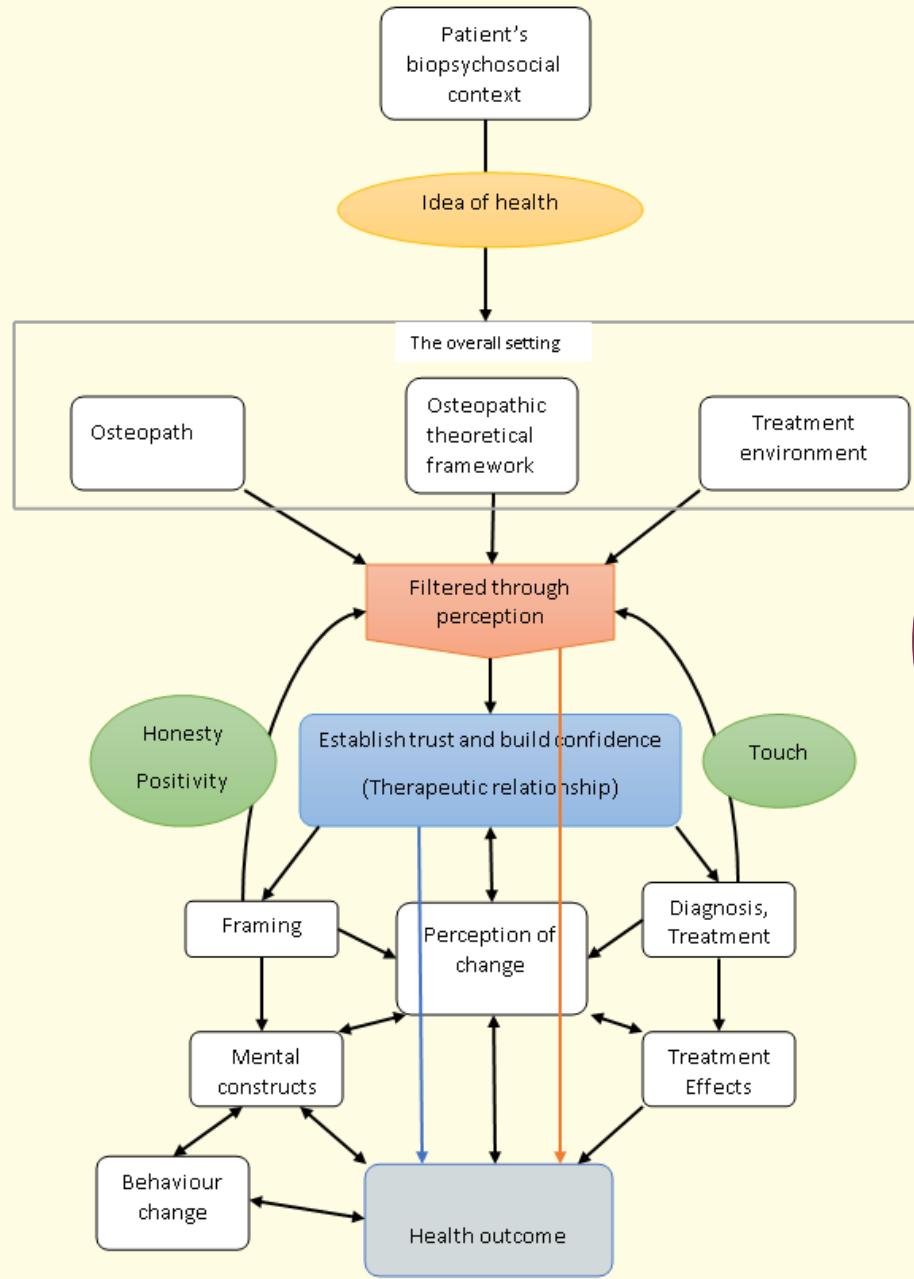
A new conceptual framework: Therapeutic Ingredients



Caspi, O., & Bootzin, R. R. (2002). Evaluating how placebos produce change. Logical and causal traps and understanding cognitive explanatory mechanisms. *Eval Health Prof*, 25(4), 436-464.

Process of health promotion in osteopathic practice

(generated by content from informant interviews)



Defining
vs.
Incidental?

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

What it is
What it does
How to do it

Build trusting partnerships

Utilize strategies of effective communication

Provide a framework

Recognize placebo-sensitive individuals and conditions

Create unique and comfortable environments

Engage in personal development and self-care

Recognize the role of ritual and meaning

Maintain honesty and ethics

Recognize the potential and know the limits

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.”

#17

Thank you for listening!



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Supplemental information

Strategies of effective communication

- See supplemental handout

Ask questions to gain an understanding of the whole person, addressing:

- primary complaint - allowing patient to discuss symptoms fully
- general health and other symptoms and concerns
- the patient's understanding of the cause/effect/meaning of their symptoms on their function and their health
- the patient's expectations of treatment

Actively listen and paraphrase by:

- pausing to give time for the patient to speak
- allowing the patient to 'tell their story'
- paraphrase to communicate understanding and check accuracy

Enable the patient and encourage active participation by:

- encouraging questions
- working towards a mutual agreement regarding cause and nature of the illness
- providing verbal and written information
- sharing in decision making about treatment options

Provide emotional support through:

- reassurance
- warmth
- empathy
- acceptance, non-judgement, validation
- demonstrating interest
- conveying care, compassion, and confidence
- appropriate use of humour

Utilize positive non-verbal communication through:

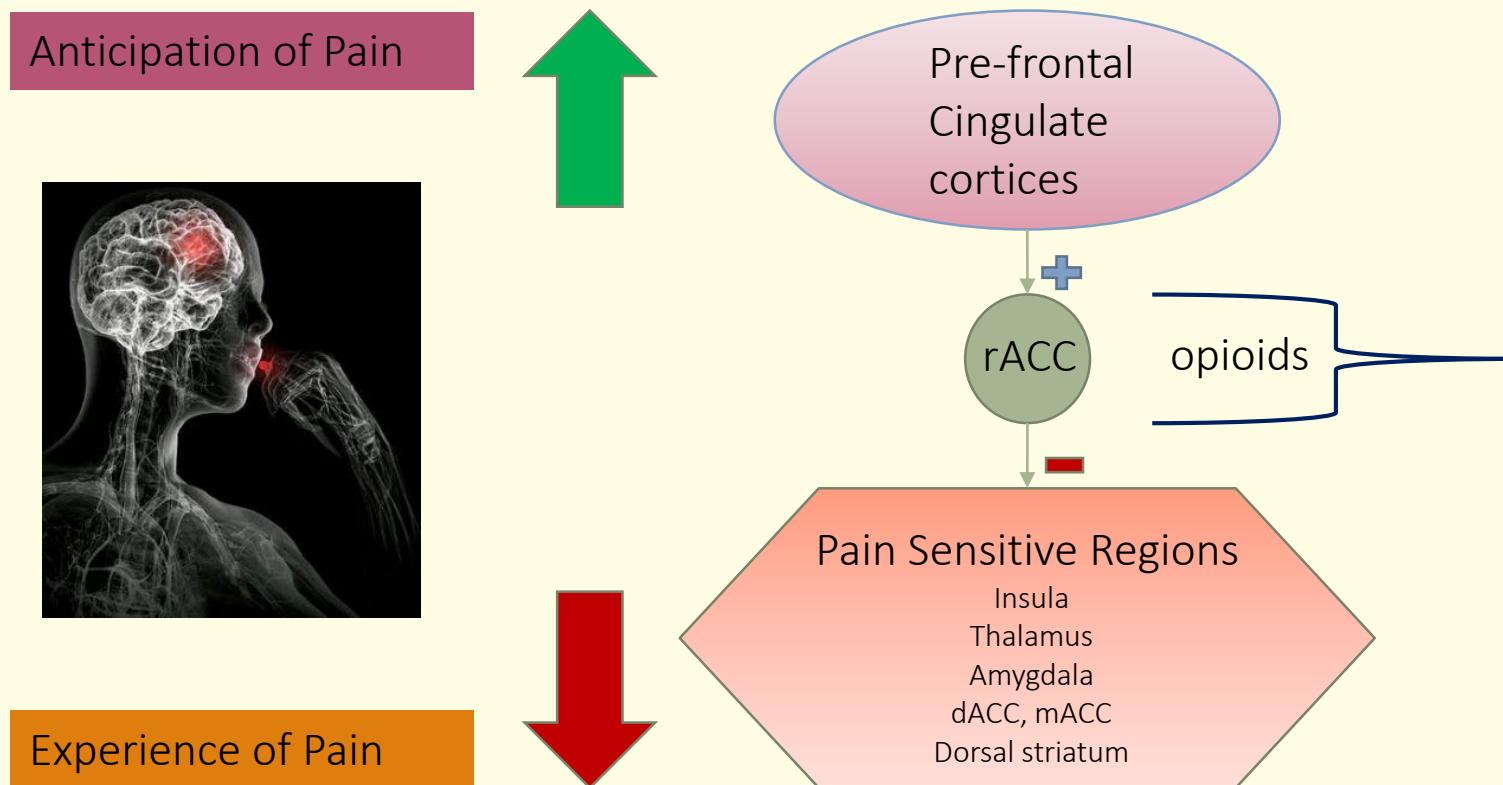
- eye contact
- orienting body to face the patient
- appropriate use of touch (conveyed confidently)
- maintaining presence
- interacting from a place of love, compassion, humility, and vulnerability

Provide information (a framework) about:

- the nature of osteopathic assessment and treatment
- the findings of the assessment and/or diagnosis and prognosis
- the rationale for the treatment plan
- the meaning of body signs and symptoms
- expectations of treatment outcomes

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)

Amanzio, Benedetti, Porro, Palermo, & Cauda, 2013;
Atlas & Wager, 2014

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

(Cicchetti, D. (2010). Resilience under conditions of extreme stress: a multilevel perspective. *World Psychiatry*, 9(3), 145-154.)