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Masterclass

Enhance placebo, avoid nocebo: How contextual factors affect physiotherapy outcomes

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ABSTRACT

Introduction: Placebo and nocebo represent complex and distinct psychoneurobiological phenomena in which behavioural and neurophysiological modifications occur together with the application of a treatment. Despite a better understanding of this topic in the medical field, little is known about their role in physiotherapy.
Purpose: The aim of this review is: a) to elucidate the neurobiology behind placebo and nocebo effects, b) to describe the role of the contextual factors as modulators of the clinical outcomes in rehabilitation and c) to provide clinical and research guidelines on their uses.
Implications: The physiotherapist's features, the patient's features, the patient–physiotherapist relationship, the characteristics of the treatment and the overall healthcare setting are all contextual factors influencing clinical outcomes. Since every physiotherapy treatment determines a specific and a contextual effect, physiotherapists should manage the contextual factors as a boosting element of any manual therapy to improve placebo effects and avoid detrimental nocebo effects.

1. Introduction

Every day physiotherapists (PTs) use different tools, such as manual techniques and exercises, to achieve their main professional goals: the improvement of pain, disability and patient's self-perceived health condition. The management of placebo and avoidance of nocebo responses have recently been suggested as promising additional clinical strategies (Gay and Bishop, 2014), generating a wide debate in manual therapy research (Benz and Flynn, 2013; Ingram et al., 2013; Kamper and Williams, 2013).

Placebo and nocebo represent complex and distinct psychoneurobiological phenomena in which behavioural and neurophysiological modifications occur following application of a treatment. The placebo (Latin "I shall please") is created by the positive psychosocial context that is capable of influencing the patient's brain (Benedetti, 2013). Instead, the nocebo (Latin "I shall harm") is the result of the negative ritual and therapeutic act on the patient's mind and body (Benedetti et al., 2007; Colloca and Benedetti, 2007; Colloca and Miller, 2011c).

From a psychobiological perspective (Fig. 1), conscious expectation and the unconscious classical conditioning, reward-learning, observational and social learning, modulation of anxiety, desire, motivation, memory and prior experience, somatic focus, personality traits and genetics work as facilitators of placebo or nocebo (Benedetti et al., 2011; Colloca and Miller, 2011b; Colloca, 2014) and modulate different responses across several diseases, illnesses, and treatment methods (Benedetti, 2008; Enck et al., 2013; Schedlowski et al., 2015). Although some attempts to identify (Michener et al., 2013) and to measure (Michener et al., 2015) the placebo response induced by sham techniques have been reported, to date the role of placebo response seems to be poorly recognized and applied by PTs in the clinical setting (Bialosky et al., 2011) and nocebo is still scarcely considered as a possible variable negatively influencing rehabilitation outcome. Agreeing that the conscious reinforcement of placebo strategies could represent an additional opportunity for every PT to improve their clinical outcomes, this masterclass aims to:

a) Synthesize the neurobiological mechanisms underlying the placebo and nocebo responses;
b) Describe the contextual factors as modulators of clinical outcomes in musculoskeletal rehabilitation;

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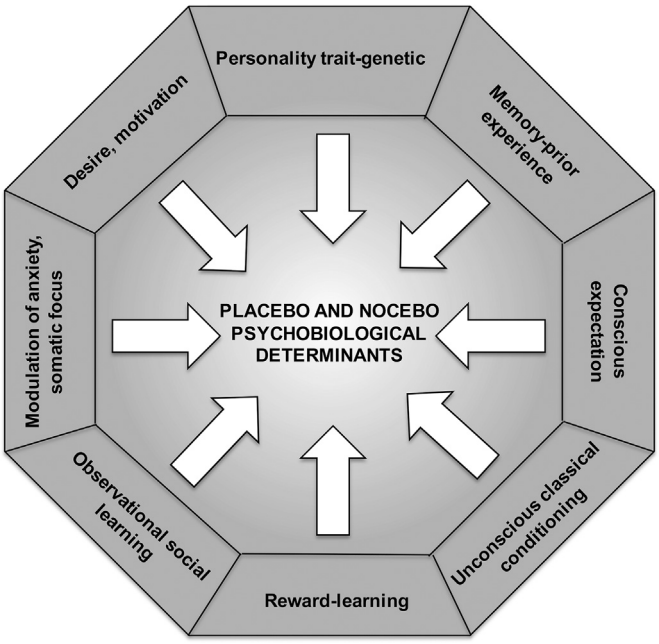

Fig. 1. Placebo and nocebo psychobiological determinants.

c) Provide guidance for the clinical implementation of placebo enhancement and/or nocebo avoidance;
d) Identify possible new lines of investigation in manual therapy research.

2. The neurobiological mechanisms behind placebo and nocebo responses

Pain and motor performance are the most frequently used models to describe the neural network involved during the placebo and nocebo responses (Tracey, 2010; Carlino et al., 2011; Colloca et al., 2013; Colagiuri et al., 2015).

2.1. Pain

Placebo and nocebo engage distinct top-down modulatory systems using different key neurotransmitters. Endogenous opioids, dopamine, cannabinoids, oxytocin and vasopressin are involved in placebo while cholecystokinin, dopamine, opioid deactivation and cyclooxygenase-prostaglandins activation interact with nocebo (Finniss and Benedetti, 2005; Benedetti and Amanzio, 2013; Carlino and Benedetti, 2016). Placebo analgesia and nocebo hyperalgesia largely involve, with opposite activation, numerous brain areas (Table 1).

Among them, placebo analgesia is mostly associated with an increased functional coupling of the dorsolateral prefrontal cortex, the anterior cingulate cortex, the hypothalamus, the amygdala, the periaqueductal grey and decreased activity in pain processing areas such as the thalamus, insula and the somatosensory cortex (Benedetti et al., 2005; Benedetti et al., 2011; Amanzio et al., 2013; Benedetti, 2014). On the contrary, negative expectations of pain increase the activation of affective-cognitive pain regions like the anterior cingulate cortex, the prefrontal cortex, the insula and the hippocampus. Furthermore, placebo and nocebo are capable of modulating pain processing at the spinal level (Benedetti et al., 2007; Colloca and Benedetti, 2007; Schedlowski et al., 2015). For a graphical representation see Fig. 2A and B.

2.2. Motor performance

Placebo and nocebo influence the activity of the motor system and the consequent motor performance (Beedie and Foad, 2009; Beedie, 2010; Pollo et al., 2011; Carlino et al., 2014b). It has been shown that placebo induces an increase of dopamine in the striatum and a change of neural activity in the basal ganglia and in limbic areas of the brain in patients affected by Parkinson disease (Frisaldi et al., 2014; Benedetti et al., 2016). Enhanced corticospinal system excitability (Fiorio et al., 2014) and reduced fatigue by modulating readiness potential during the anticipatory phase of movement (Piedimonte et al., 2015) were displayed in healthy subjects. Similarly, a nocebo procedure in which the induced expectation decreases force production modulated the corticospinal circuits influencing motor performance (Emadi Andani et al., 2015).

3. The contextual factors optimize the rehabilitation outcomes

The psychosocial context and the therapeutic ritual around the patient can also influence the patient's brain activity and the therapeutic outcome such as satisfaction and perceived effect (Colloca and Benedetti, 2005; Benedetti, 2013; Carlino et al., 2014a). As reported in Fig. 3, the physiotherapist's and patient's features, the patient–physiotherapist relationship, the characteristics of the treatment and the overall healthcare setting are the most relevant categories of contextual factors involved in placebo or nocebo effects (Blasi et al., 2001).

3.1. Physiotherapist's features

A “physiotherapist's effect” is present and influences the outcome of treatment in patients with musculoskeletal disorders (Lewis et al., 2010).

3.1.1. Professional reputation and appearance

The perception of expertise, professionalism, qualification, reputation and the level of training of PTs are important elements for the patient and can contribute to modifying the clinical outcome in musculoskeletal disorders (Hush et al., 2011; Bishop et al., 2013a; O'Keeffe et al., 2015). Moreover the way a therapist dresses is able to influence the patient's perception of care (Petrilli et al., 2015). Recently the results of a study by Mercer et al. (2008) reported that a laboratory coat and tailored clothing were ranked respectively most professional and preferred, by patients with low back pain (LBP). By contrast, patients were less satisfied if the professional appearance was poor and if PTs wore jeans during clinical practice (Mercer et al., 2008; Hush et al., 2011).

3.1.2. Beliefs and behaviours

Enthusiastic practitioners and their optimism or pessimism regarding the nature of a treatment can have an active effect on the outcome (Autret et al., 2012; Witt et al., 2012; Vaughn, 2014). This is a self-fulfilling prophecy whereby the convincement of a practitioner about the patient's outcome leads to an improvement (“Pygmalion effect” – “Rosenthal effect”) or a worsening (“Golem effect”) of the outcome itself (Sternberg et al., 2011). Recent evidence linked the attitudes and beliefs of patients with LBP with the attitudes and beliefs of the health care professional (including PTs) they had consulted (Darlow et al., 2012). Patients appreciated the PT's aptitude to encourage questions and to answer the patient's queries, to explore disease and illness experience and to trust their opinion. The PT's ability to deliver positive feedback, to give clear prognostic information and explanation about the patient's