



Review article

Pain in the body. Altered interoception in chronic pain conditions: A systematic review

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ABSTRACT

Interoception is the sense of the physiological condition of the body. Modern definitions differentiated three separated sub-constructs: accuracy (IAc), i.e., the ability to detect physiological states, sensibility (IAs), i.e., a self-evaluated measure of interoception, and awareness (IAw) i.e., a metacognitive awareness of the accuracy. Preliminary researches correlated pain with alterations in the interoceptive matrix albeit, to the best of our knowledge, interoceptive alterations in chronic pain conditions have never been studied systematically. We searched for studies that assessed interoception in subjects with chronic pain and compared it to healthy population. Eleven studies were included among different chronic pain conditions. Results suggested that chronic pain subjects might present low IAc and, allegedly, that IAc negatively correlates with symptoms severity in specific disorders. Data were inconclusive for IAs and IAw. The high risk of bias across multiple dimensions suggests to consider these conclusions with cautions. Nonetheless, deficits in interoceptive processes indicate a promising path for new form of therapies, and they require further attention and a more defined line of research.

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1. Background

Bodily sensations represent core elements in the conceptualization of the human self. Evidence from recent anatomical studies explored the neural pathways that create the consciousness of the body in the mind and defined the concept of interoception as the sense of the physiological condition of the entire body (Craig, 2002, 2003).

Interoception is a long-standing construct that can be resembled and traced back to Bernard's *milieu interieur*, over one and half century ago. Directed influences can be also identified in Cannon's idea of an internal set of parameters underlying the physiological state of the body (Cannon, 1963). Moreover, in the same period as Cannon, the James-Lange theory revisited the entire concept of emotion, considering bodily changes elicited by an event as precursors of the emotion itself, thus redefining interoceptive information as fundamental elements in emotions appraisal (James, 1955). Recent neuroanatomical studies indicate that the right anterior insula cortex (AIC) collects a meta-representation of the interoceptive activity in humans (Craig, 2002, 2003). This representation is shaped upon subsequent cinematic images of the status of the entire body and provides the subjective substrate for the perception of the material self as a physical and separate entity, through a process that directly leads to subjective feelings and self-awareness (Craig, 2003). Evidence identified small-diameter (Aδ and C) primary afferent fibres that fundamentally innervate the entire organism (Craig, 2002). These fibres converge in a specific neural region, on the most superficial layer of the spinal dorsal horn, called the lamina I (Sandkühler et al., 2000) that projects to a relay nucleus in the posterolateral thalamus (Craig, 2002). Although, lamina I neural region was usually considered linked to pain and temperature specific afferent labelled lines, evidence proved that the Aδ and C small-diameter fibres convey homeostatic inputs from all the tissues. This complex neurological system is selectively activated by temperature, pain, cardiorespiratory function, hunger, thirst (Cervero and Janig, 1992; Iggo, 1960; Mense and Meyer, 1985) local metabolism information, immune and hormonal activity, and mechanical stress (Craig, 2002). Moreover, lamina I spinobulbar neurons respond selectively to muscles contraction, providing additional evidence that the interoceptive system incorporates a wide range of bodily information, also from the muscle Aδ and C fibres (Wilson et al., 2002). Lamina I neurons likewise integrates many cutaneous C fibres that are sensitive to slow and weak mechanical activation, suggesting that interoceptive cortex incorporates sensual (limbic) touch (Vallbo et al., 1999) among other afferent inputs. AIC also connects with the anterior cingulate cortex (ACC) that showed a consistent co-activation in all imaging studies of emotions (Bartels and Zeki, 2000; Blood and Zatorre, 2001; Damasio et al., 2000; Reiman, 1997), supporting the hypothesis that this specific cortical region underlies the motivational behavioural agent that co-participates to the emotion itself. Thus, the activation of both the anterior insula cortex, which represents the interoceptive system, and the anterior cingulate cortex, which represents the integration with the motivational agent, generates an emergent emotional feature composed of both sensation and motivation.

An important implication of Craig's hypothesis regarding the interconnection between the AIC and the ACC, is that the interoceptive cortical matrix can incorporate motivational and behavioural urges, shaped upon memory, learning, and expectations through activation of the ACC. Moreover, since each "global emotional moment" (Craig, 2009) comprises both emotion and motivation contributions from respectively AIC and ACC, it is possible that activation of the behavioural agent in the ACC can actively shape the response in the interoceptive cortical matrix (Sarinopoulos et al., 2006). This consideration supports directly Damasio concept of as-if body loop, and at the same time resolve the issues present both

in the somatic marker hypothesis and in James-Lange theory. Furthermore, according to Craig's interconnected model, a selective pattern that sees activity in the ACC without integration in the AIC can lead to an emotional behaviour without awareness (Craig, 2009). In fact, most of the inputs from the interoceptive system do not usually reach consciousness. Microneurographic data provided evidence that only C nociceptors inputs are able to reach the active awareness (Craig, 2002) creating the perception of pain in humans (Gybel et al., 1979) while C fibres usually provide input related to current metabolic status, through a slow on-going discharge that is not perceived (Adreani and Kaufman, 1998; Schaible and Schmidt, 1983; Vallbo et al., 1999).

Craig's work provided a deep understanding of the lamina I spinothalamocortical system; nevertheless, interoception remains a quite complex concept in current psychophysiological literature. In the interoceptive system, composed by the anterior insular cortex (AIC), the anterior cingulate cortex (ACC), the prefrontal cortices and the somatomotor and somatosensory cortices, the AIC represents the core of the meta-representation that integrates all the active physiological processes inside the organism. AIC size and activity have been correlated to individuals' accuracy in sensing their own heartbeats (Critchley et al., 2004). Nevertheless, interoceptive awareness (IA) can be conceptualize both as a trait-like sensitivity and both as a state-like condition because it can be manipulated through processes that alter the autonomic activity (Schandry et al., 1993).

In recent years, several theoretical proposal suggested complementary approaches to coherently integrate different aspects of interoception (Fig. 1). These proposals are born from the necessity to understand equivocal results in the generalized assessment of interoception through different instruments. In detail, evidence showed that interoceptive awareness measured through self-reported questionnaires seems to refer to different constructs than interoception measured through behavioural related tasks (Cali et al., 2015; Ceunen et al., 2013; Garfinkel et al., 2015). Moreover, the two main behavioural tasks used for interoception assessment, i.e. heartbeat perception task (Schandry, 1981) and heartbeat discrimination task (Brener and Kluvitse, 1988; Whitehead et al., 1977), seem to measure two different – albeit connected and related – constructs too (Garfinkel et al., 2015; Schulz et al., 2013). Among other evidence, an interesting study showed that cold pressor stress induced opposite effects in interoceptive performances measured through the two heart-related tasks (Schulz et al., 2013).

This implies different modalities and pathways in the integration of interoceptive information, even though both tasks seem involved in the cortical areas connected to the interoceptive matrix as heartbeat detection correlates with the dimension and the activity of the AIC (Critchley et al., 2004).

In an attempt to clarify the field, Farb et al. (2015) proposed a detailed taxonomy identifying four principal interoceptive dimensions: accuracy represents the ability to detect interoceptive signals, i.e. heartbeat, and it is connected to a threshold dimension called sensitivity that represents the lower limit to detect an interoceptive signal (Holzl et al., 1996). Interoceptive sensibility defines "the individual's personal account of how they experience internal sensations" measured through self-reported scales, i.e. MAIA (Mehling et al., 2012), and coherence represents the correspondence "between physiological and subjective states" and "measures the degree to which objectively observable interoceptive signals manifest in reportable experience" (Farb et al., 2015).

Contrary, Cali et al. (2015) explored the interoceptive framework identifying a bi-dimensional construct composed by an accuracy aspect that, similarly to other authors, identifies the ability to perceive interoceptive information such as the heartbeat, and an interoceptive awareness dimension that refers to subjective feelings measured through self-reported scales and questionnaires

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