



A computationally informed distinction of interoception and exteroception

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ARTICLE INFO

Keywords:

Thermoception
Brain-body interactions
Sensor-effector loops
Homeostatic control
Allostatic control
Bayesian inference
Generative model
Mental health

ABSTRACT

While interoception is of major neuroscientific interest, its precise definition and delineation from exteroception continue to be debated. Here, we propose a functional distinction between interoception and exteroception based on computational concepts of sensor-effector loops. Under this view, the classification of sensory inputs as serving interoception or exteroception depends on the sensor-effector loop they feed into, for the control of either bodily (physiological and biochemical) or environmental states. We explain the utility of this perspective by examining the perception of skin temperature, one of the most challenging cases for distinguishing between interoception and exteroception. Specifically, we propose conceptualising thermoception as inference about the thermal state of the body (including the skin), which is directly coupled to thermoregulatory processes. This functional view emphasises the coupling to regulation (control) as a defining property of perception (inference) and connects the definition of interoception to contemporary computational theories of brain-body interactions.

1. Introduction

Over the last decades there has been a continuously growing interest in interoception (Khalsa et al., 2018). This interest appears to derive from its function: interoception plays a key role in homeostatic (reactive) and allostatic (anticipatory) control of physiological states and is thus integral to preserving bodily integrity. As such, it arguably comprises the most important form of sensory processing for an organism's direct survival and plays a critical part in self-awareness (Babo-Rebelo et al., 2016; Palmer and Tsakiris, 2018; Seth and Tsakiris, 2018), emotional experience (Critchley and Garfinkel, 2017; Wiens, 2005), and mental health (Bonaz et al., 2021; Khalsa et al., 2018).

Along with an increasing number of empirical studies and theoretical frameworks on interoception, there is an ongoing effort to fine-tune the definition of interoception to be inclusive enough to encompass numerous heterogeneous subsystems, while also pinpointing those aspects that qualify it as a distinct subcategory of perception (e.g. (Ceunen et al., 2016; Chen et al., 2021; Khalsa et al., 2018)). A clear definition of interoception is important to ensure reference to a consistent concept that allows the connection of insights across disciplines (Tsakiris and Critchley, 2016).

However, the distinction between interoception and exteroception ("perceptual inference on environmental states" (Petzschner et al.,

2017)) continues to be debated. A key reason for this is the fact that modern concepts of interoception represent a considerable expansion from the historical meaning of the word (Ceunen et al., 2016). The historical definition of interoception by Sherrington (Sherrington, 1906) related specifically to internal organs (viscera), while contemporary concepts of interoception – often inspired by Bayesian theories of perception – emphasise the perception of internal states, i.e., neural representations of the (inferred) physiological condition of the body (Khalsa et al., 2018; Craig, 2002; Ceunen et al., 2016; Tsakiris and Critchley, 2016; Seth, 2013; Gu et al., 2013; Barrett and Simmons, 2015; Stephan et al., 2016; Petzschner et al., 2017, 2021; Tallon-Baudry, 2023). While some modalities, e.g. cardiac perception, are considered interoceptive under both concepts of interoception, others have been reclassified in line with the redefinition of interoception. For example, the perception of skin temperature was traditionally regarded as an aspect of exteroception, but later redefined as an interoceptive function (Ceunen et al., 2016; Craig, 2002; Critchley et al., 2023; Crucianelli et al., 2022; Crucianelli and Ehrsson, 2023, 2022; Khalsa et al., 2018; Vabba et al., 2023). Diverging opinions about the delineation between interoception and exteroception typically concern these reclassified cases (see Figure 1 in (Nord and Garfinkel, 2022)).

Here, we propose a functional definition of interoception that is grounded in contemporary computational concepts of inference-control

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<https://doi.org/10.1016/j.neubiorev.2024.105608>

Received 6 December 2023; Received in revised form 23 February 2024; Accepted 26 February 2024

Available online 2 March 2024

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loops, which highlight the close coupling between perception and control (Gu et al., 2013; Petzschner et al., 2017; Pezzulo et al., 2015; Seth et al., 2012). Specifically, we suggest that perceptual processes are instances of interoception if they contain inferences about bodily (physiological and biochemical) states that are coupled to regulatory processes which serve to control these states. This definition emphasises the coupling to regulation (control) as a core property of perceptual processes, and implies that the origin of a sensory stimulus and the location of its receptors do not matter. Instead, the crucial question is what type of inference and associated control process the sensory stimulus elicits.

In order to motivate this definition, we will focus on the concrete example of temperature perception – a historically challenging case for achieving a clear delineation between interoception and exteroception. We propose that this computationally informed definition is a necessary extension of the contemporary concept of interoception as internal state perception that resolves the classification of skin temperature and other disputed modalities (see e.g. (Nord and Garfinkel, 2022)).

We begin by revisiting terminology and concepts in relation to interoception, noting how its meaning has evolved over time. Next, we review some of the key motivations behind the shift in the meaning of interoception by explaining why thermoception – and specifically the perception of skin temperature – is reasonably regarded as an interoceptive process. After pointing out the shortcomings of classical (location-oriented) criteria in establishing a meaningful distinction between interoception and exteroception, we introduce a functional definition based on contemporary computational theories of perception and control. To make this theoretical perspective more tangible, we describe how it may be physically understood in the context of the thermosensory-thermoregulatory system. Having motivated that thermoception is an interoceptive process, we consider if temperature perception can be exteroceptive – and if so, what distinguishes interoceptive and exteroceptive processing of thermal signals from each other. We conclude with a discussion of the practical impact of the proposed definition of interoception, and touch on open questions.

2. Terminology and concepts

In this section, we introduce terms that designate specific and distinct concepts throughout this article, such as the distinction between intersensation and interoception, thermosensation and thermoception, as well as homeostatic and allostatic control, which will play important roles in subsequent sections.

2.1. Interoception, intersensation

In his landmark 1906 publication *The Integrative Action of the Nervous System*, Sherrington described “three fields of reception, extero-ceptive, intero-ceptive and proprio-ceptive” (Sherrington, 1906). This distinction was based on the location of the respective sensory receptors: cutaneous (“extero-ceptive”), deep (“proprio-ceptive”), or visceral (“intero-ceptive”). Following from this classification, Sherrington considered temperature perception an aspect of exteroception (Sherrington, 1906). In 2002, Craig proposed that the term interoception should be redefined as “the sense of the physiological condition of the entire body, not just the viscera” (Craig, 2002), and that this sense might represent “the material me” (Craig, 2002). Craig based his suggestion on considerations of cutaneous sensations, such as temperature, and the lamina I spinothalamic pathway in which they are relayed. While Craig’s seminal paper triggered a widespread surge of interest in interoception research (Khalsa et al., 2018), the inclusion of signals from the skin in interoceptive processes remains a topic of debate. Many contemporary definitions of interoception are guided by functional considerations of interoception as the perception of the overall bodily state (Barrett and Simmons, 2015; Ceunen et al., 2016; Crucianelli and Ehrsson, 2023; Gu et al., 2013; Khalsa et al., 2018; Pezzulo et al., 2015; Seth et al., 2012; Seth and Friston, 2016; Tsakiris and Critchley, 2016)

and implicitly or explicitly (Khalsa et al., 2018; Ceunen et al., 2016; Schoeller et al., 2022; Crucianelli and Ehrsson, 2023) include the skin. It is worth highlighting that previous definitions of interoception have not only increasingly considered thermal signals from the skin, but also other skin-based signals such as pain and affective touch (Björnsdotter et al., 2010; Crucianelli et al., 2022; Crucianelli and Morrison, 2023; Fotopoulou et al., 2022; von Mohr and Fotopoulou, 2018). However, recent reviews (Ceunen et al., 2016; Chen et al., 2021; Nord and Garfinkel, 2022) highlight that the boundary between interoception and exteroception is not always clear and remains a matter of debate.

In recent years, computational theories of perception have had a major impact on concepts of interoception. These theories of perception are typically based on Bayesian principles and derive from the long-standing insight that the brain does not have direct access to the true state of the world (including the state of the body and the state of the external environment) (Knill and Richards, 1996; von Helmholtz, 1867). The brain only has access to sensations, i.e., inputs that originate from the activation of sensory receptors and reach the brain via its afferent channels. These sensations are not only affected by channel noise, but are also often ambiguous because the hidden (latent) states of the world that lead to activation of sensory receptors can interact nonlinearly or hierarchically (Friston, 2003). As a consequence, there can be many (sometimes infinite) possible interpretations of a given sensation (Kersten and Yuille, 2003). Bayesian theories of perception assume that the brain solves this problem by inverting a generative model of its sensory inputs (Friston, 2005; Petzschner et al., 2015). Simply speaking, a generative model is a probabilistic model that describes the prior probabilities of states of the world (priors) as well as the probability that any given state would lead to a particular sensation or input. By inverting this generative model, the brain can, in principle, identify which state of the world is most likely to have caused a particular sensation. From this Bayesian perspective, perception therefore corresponds to inference, i.e., an interpretation of sensations according to the brain’s probabilistic model of the world (Friston, 2005; Knill and Pouget, 2004). More specifically, this view conceptualises interoception as an act of inference that operates on intersensations (i.e., sensory inputs that signal information about the state of the body) (Barrett and Simmons, 2015; Owens et al., 2018; Petzschner et al., 2017; Seth et al., 2012; Seth and Friston, 2016).

2.2. Homeostatic/allostatic control

Theories of adaptive behaviour highlight that inference about states of the world (perception) is intertwined with eliciting actions to change these states (control) (Friston et al., 2010, 2009; Imhohsen et al., 2020; Millidge et al., 2020; Pezzulo et al., 2015; Soltani and Koehlin, 2022). In the context of bodily regulation, two modes of control can be distinguished:

First, homeostatic control refers to regulatory actions that are driven by the mismatch between a target value or setpoint (the anticipated signal from a sensory receptor) and the actual sensory input (Waterhouse, 2013). Homeostatic control is thus a reactive reflex-like form of control that is triggered by intersensations and aims to keep physiological variables within certain ranges that are compatible with life. It is worth pointing out that while the term “setpoint” is widely used in physiology, in thermoregulation research the term “balance point” is often used instead (Romanovsky, 2007). Use of the latter is intended to avoid semantic associations with the outdated notion of a single central thermoregulatory controller (which has been replaced by a concept of multiple independent thermoeffector loops for controlling body temperature, as described below).

Second, allostatic control is anticipatory, triggering prospective actions before sensory inputs deviate from expectations; it thus requires a model capable of making predictions or forecasts (Sterling, 2012). While initial concepts of allostatic control did not specify the nature of this model (Sterling and Eyer, 1988), Bayesian (active inference) theories assume that these predictions arise from the brain’s generative model (e.g., (Tschantz et al., 2022)). In other words, the forecasting required for

allostatic control is assumed to depend on inference, e.g., using “planning by inference” (Penny and Stephan, 2014; Toussaint et al., 2010) or predictive coding with generalised coordinates (Millidge et al., 2022) to infer on trajectories of bodily states. For both homeostatic and allostatic control, Bayesian models have been proposed to link these control modes to interoception and interoception, respectively (see (Petzschner et al., 2021) for review).

Physiologically, homeostatic and allostatic control are organised as sensor-effector loops (Ramsay and Woods, 2014): sensory inputs are coupled to effectors whose actions affect (directly or indirectly) the latent states that give rise to the sensory inputs. This organisation is particularly obvious in homeostatic control, which is implemented by reflex arcs. Here, sensory inputs that deviate from setpoints in spinal autonomic centres and subcortical nuclei (e.g. hypothalamus, periaqueductal grey) activate endocrine mechanisms and descending neuronal connections that modulate autonomic nervous system activity (for examples of tract tracing findings from different species, see (Pal-kovits, 1999; Saper et al., 1976)). For allostatic control, a superordinate step of inference or prediction is required that is likely implemented by cortical (particularly insular and cingulate) areas (Barrett and Simmons, 2015) and thought to both elicit behavioural changes and alter autonomic reflex arcs (Stephan et al., 2016). In terms of terminology, sensor-effector loops can therefore be classified into sensation-control loops (for reactive, homeostatic control) and inference-control loops. The latter can, in principle, serve both homeostatic control (if inference concerns only current physiological states) and allostatic control (if inference extends to future physiological states, i.e., prediction and forecasting) (Petzschner et al., 2017).

In this article, we build on the computational concepts of perception and control described above. Specifically, we propose a definition of interoception that is based on the notion of sensor-effector loops and underscores its functional role in the regulation of bodily states (homeostatic/allostatic control) (Petzschner et al., 2017; Stephan et al., 2016). In brief (see below for more details), we suggest that sensory and perceptual (inferential) processes should be understood as instances of interoception and interoception, respectively, if they are coupled to regulatory processes that serve to control physiological and biochemical states of the body. Conversely, perceptual processes should be considered instances of exteroception if they are linked to actions that serve to control states of the external environment. We emphasise that this distinction is not entirely novel, in the sense that it is an implicit corollary to previous computational concepts of brain-body interactions (Petzschner et al., 2017). Here, we explicitly spell out this (previously only implied) principle for distinguishing perceptual processes and illustrate the conceptual utility of this framework by examining the specific case of thermoception.

2.3. Thermoception

Like the word “interoceptive”, the word “thermoceptive” dates back to Sherrington, who referred to the “thermo-ceptive system” as a functional property of the “exteroceptive field” (Sherrington, 1906). Today, the term thermoception is often used as a synonym for (or contraction of) thermoreception, a term introduced by Hensel in 1952 (Hensel, 1952) to define “a process in which different levels of heat energy (temperature) are detected by living things” (Hensel, 1974). By this definition, thermoception refers to temperature *sensation* (Prescott and Ratté, 2017). The terminology used to refer to temperature sensation and perception varies considerably in recent publications. For example, the terms thermosensation (Crucianelli et al., 2024, 2022), thermosensory integration (Filingeri, 2016), thermosensory representation (Craig, 2018), temperature perception (Mano et al., 2017), perception of temperature (Vriens et al., 2014), thermal perception (Ma, 2010; Olausson et al., 2005), thermoception (King and Carnahan, 2019; Peltz et al., 2011; Strube et al., 2021), thermoperception (Ezquerro-Romano and Ezquerro, 2017) and thermoreception (ten Donkelaar et al., 2020)

are all used to refer to the cortical representation of afferent temperature information.

In line with the distinction between sensation and perception described above, and for conceptual clarity, throughout this article we use the term *thermosensation* to refer to the central nervous system’s detection of thermal sensory inputs that originate from thermoreceptors in the skin, mucosae and viscera, and are transmitted via afferent thermosensory pathways. On the other hand, we define *thermoception* as inference about the thermal state of the body (including its largest organ, the skin) that is directly connected to thermoregulatory processes (we will motivate and expand on this definition below). It is worth highlighting that this definition renders the term “thermoception” a subcategory of interoception (in analogy to terms like cardiac interoception or respiratory interoception). By contrast, we use the term “temperature perception” to refer to all aspects of temperature perception, i.e., as an umbrella term that covers interoceptive and exteroceptive types of temperature-related inference.

3. Interoceptive role of the skin

In this section we examine the shift in the meaning of interoception through the lens of thermoception – specifically, the perception of skin temperature –, which can arise due to sensory stimuli of natural origin or be induced experimentally through stimulation with a contact thermode or whole-body suit (Muzik et al., 2022, 2020), for example. We reiterate that considering skin temperature perception as part of interoception is not a novel proposal, but has a long history in interoception research (see Section 2.1 and, in particular, (Craig, 2018, 2002; Crucianelli and Ehrsson, 2023)). Here, we review some of the key insights that led to the departure from Sherrington’s definition and that continue to shape current concepts of interoception as the perception of bodily states. This section will thus serve as a basis for understanding why descriptive criteria (such as stimulus origin or receptor location) are not well suited for achieving a coherent and meaningful classification of sensory processes. We review (i) anatomical, (ii) physiological, and (iii) conceptual factors that motivate the view that temperature signals from the skin contribute to thermoeffector loops in which information about bodily states is directly coupled to homeostatic/allostatic (in this case, thermoregulatory) functions – a property which we propose as the central criterion for classifying a perceptual process as interoceptive. We conclude this section by addressing common points of confusion that are typically used to support arguments that skin temperature is inherently an exteroceptive sense.

3.1. Anatomical considerations

Sherrington’s classification of the senses was based on the anatomical understanding of his time; in particular, it was derived from contemporary knowledge about sensory receptors. For example, Sherrington suggested that the receptors he called “intero-ceptive” are activated by chemical stimuli (only) and form a homogeneous system; he highlighted this property as a key difference to “extero-ceptive” receptors, which were known to sense a variety of stimuli (such as pressure, light and heat) and were thus thought to belong to separate (e.g., “tango-ceptive”, “thermo-ceptive”, “noci-ceptive” or “musculo-ceptive”) systems (Sherrington, 1906). We now know that there are many types of sensory receptors inside the body (Berntson and Khalsa, 2021), which transmit signals from diverse sensory modalities (e.g., mechanoreceptors that sense the stretch of gastrointestinal organs, or chemoreceptors that sense the concentration of various molecules in the blood). Therefore, while Sherrington’s distinction between internal and external receptors seemed instructive in the early twentieth century, it is outdated based on our current understanding of the nervous system.

Like Sherrington, Craig motivated his (re)definition of interoception on the basis of his neuroanatomical understanding. However, Craig benefitted from nearly a century of subsequent scientific progress, which

included the development of sophisticated anatomical tract tracing and brain imaging techniques. Studies involving these methodological advances laid the foundation for Craig's proposal that primates evolved two parallel pathways that signal modality-specific information about the physiological condition of all tissues of the body, and that these pathways together constitute the afferent counterpart of the efferent autonomic nervous system (Craig, 2002). The first of these pathways passes through the nucleus of the solitary tract (NTS), a key structure in the transmission of parasympathetic (vagal and glossopharyngeal) afferent activity (Beckstead et al., 1980). The NTS pathway had long been considered the anatomical basis for interoception. Craig recognised that a second anatomical pathway via lamina I in the dorsal horn of the spinal cord signals sympathetic afferent activity. This pathway relays information from small-diameter afferent fibres, which innervate (almost) all tissues and organs in the body. The NTS and lamina I pathways project via neighbouring thalamic regions (i.e., the posterior and basal parts of the ventral medial nucleus) (Craig, 2002) to an area in the dorsal posterior insular cortex, which is thought to encode "a complete, unified, coherent topographic representation of homeostatic sensory activity from the entire body" (Craig, 2015) (see also (Allen et al., 1991; Cechetto and Saper, 1987)). This prompted Craig to suggest expanding the meaning of interoception to include homeostatically relevant afferent signals from the entire body – in other words, to cover the sensory pathways ascending through both the NTS and lamina I.

The lamina I pathway signals information about the physical, chemical and metabolic condition of all tissues and organs in the body, including pain and temperature information from the skin (Craig, 2015; Dum et al., 2009). In line with the historical classification of pain and temperature as aspects of touch, the lamina I spinothalamic pathway was originally considered a somatosensory pathway, along with the dorsal column-medial lemniscus pathway (Craig, 2015). However, although both of these pathways receive inputs from sensory receptors in the skin, they differ significantly from each other in function and morphology. While the lamina I pathway relays sensory information that is important for homeostatic regulation, the dorsal column pathway signals discriminative touch sensations (which represent aspects of external objects, rather than the body) via the medial lemniscus to primary somatosensory cortex (S1). The ventral medial thalamic nucleus within the lamina I pathway sends ancillary projections to S1, but its primary cortical target is the posterior insula (Craig, 2018, 2002; Craig et al., 2000). This finding from primate tract tracing studies (which was recently also shown in mice (Vestergaard et al., 2023)) is corroborated by clinical observations that damage to S1 produces no changes in thermal sensations, and stimulation of S1 produces no warm or cool sensations on the skin (discussed in (Craig, 2015)). Furthermore, the afferent fibres within these two pathways belong to different morphological/genetic families (Prechtl and Powley, 1990). In particular, afferent fibres in the lamina I pathway (known as small-diameter fibres) are genetically programmed to connect with lamina I neurons at a precisely defined stage of neural development (Chen et al., 2001). The latter originate from the progenitor cells of spinal autonomic nervous system neurons (i.e., homeostatic effectors), supporting the view that small-diameter fibres are homeostatic afferents (Craig, 2002; Prechtl and Powley, 1990). (For a more extensive discussion, the interested reader is referred to (Craig, 2015).)

In summary, Sherrington's original classification of interoception and exteroception was based on an anatomical understanding that is now outdated. More recent anatomical insights, notably including those by Craig regarding skin temperature, indicate that a definition of interoception based on the location or type of sensory receptors, or the anatomical pathways they are connected to, is not sufficient for a concept of interoception that has a compelling functional interpretation.

3.2. Physiological considerations

Throughout its history, the concept of interoception has been tied to the fundamental biological principle of homeostasis (Cameron, 2001).

Without accurate estimates of the numerous physiological and biochemical variables that are critical for bodily function and survival, the brain cannot assume its role as the highest homeostatic controller (e.g., by influencing local/organ-level homeostatic mechanisms via descending neuronal and hormonal pathways or by triggering motor behaviours that change external perturbations of bodily states). Consequently, afferent signals that contribute to the maintenance of homeostasis are conclusively considered to serve interoception (Khalsa et al., 2018).

Temperature perception represents an interesting case in this regard. Visceral thermoreceptors were long known to be important for the control of body temperature and therefore considered to serve an interoceptive function (for earlier reviews on interoception, see (György and Ádám, 1998; Thompson and Pickens, 1971; Vaitl, 1996)). By contrast, the role of skin temperature in homeostatic control was initially not recognised, and its inclusion in concepts of interoception has been a topic of debate (Ceunen et al., 2016; Nord and Garfinkel, 2022). However, from a physiological perspective there is now strong evidence that temperature information from the skin is crucial for homeostatic and allostatic processes. In the following, we review observations from thermosensory and thermoregulatory neuroscience research that establish a clear function of skin temperature in thermoregulation.

Borrowing from engineering control theory, early models of thermoregulatory function described a unified system in which a single central controller compares an integrated body temperature signal to an internal setpoint (Romanovsky, 2007; Werner, 1980). The central controller was thought to reside in the hypothalamus, specifically the hypothalamic preoptic area (POA). However, animal studies found that hypothalamic lesions affect some thermoregulatory responses (both autonomic and behavioural), while leaving others intact (reviewed in (Satinoff, 1978)). Even after decerebration below the hypothalamus (i.e., at the level of the lower pons or medulla), animals respond to cooling via shivering, vasoconstriction and piloerection (Chambers et al., 1974), indicating that body temperature is defended in the absence of a hypothalamic regulator. Thermoregulatory neuroscientists thus rejected the central thermostat-theory in the 1970s (Satinoff, 1978; Werner, 1980). In its place emerged an understanding of thermoregulation via independent thermoeffector loops, each triggered by a unique combination of core and skin temperatures, at different levels of the nervous system (Romanovsky, 2007). For example, in newborn guinea pigs non-shivering thermogenesis is driven by cutaneous thermal signals and hypothalamic thermoreceptor activation, while shivering responses are triggered by temperature signals from the skin and cervical spinal cord, but are independent of hypothalamic thermoreceptor activation (reviewed in (Brück and Wünnenberg, 1970)). Numerous further examples of this sort have led to the now widely accepted view that the regulated variable in the thermoregulatory system is not a single (either locally detected or computed mean) temperature, and that there is no central reference signal or setpoint (Romanovsky, 2007; Werner, 2010, 1980). Instead, "the regulated variable in the thermoregulation system is an integrative, spatially distributed temperature signal, which incorporates deep (core) body temperatures (those of the brain and viscera) and shell (peripheral) temperatures (those of the skin and subcutaneous tissues)" (Romanovsky, 2014). Put simply, cutaneous temperature signals provide the thermoregulatory system with feedback information that is critical for the efficient control of body temperature (discussed in detail in (Romanovsky, 2014; Werner, 2010)).

In particular, skin temperatures are relatively more important than deep temperatures for initiating most (but not all (Roberts, 1988)) behavioural thermoregulatory responses (Romanovsky, 2014). In humans and other homeothermic organisms, thermoregulation relies on behavioural responses as a first line of defence, while metabolic mechanisms, which are energetically costly, are recruited secondarily when behavioural responses and cutaneous vasoreaction are insufficient in the face of a thermal challenge (Flouris, 2011; Romanovsky, 2014, 2007). Several studies have demonstrated conclusively that TRPM8 channels (thermoreceptors that are activated by cold temperatures; see Box 1) in

Box 1**Thermosensory afferents** (see Fig. 1).*Primary afferents*

Warm-sensitive afferents are unmyelinated, small-diameter C-fibres. They exhibit ongoing activity at steady-state temperatures above 30°C (Darian-Smith et al., 1979; LaMotte and Campbell, 1978), reaching a maximum around 40–43°C (Duclaux and Kenshalo, 1980; Hensel and Iggo, 1971). This activity is silenced at temperatures above 50°C (Darian-Smith et al., 1979) and upon cooling (Darian-Smith et al., 1979; Duclaux and Kenshalo, 1980). Like warm fibres, cold fibres continuously fire action potentials at normal skin temperatures. Their activity is highest at steady-state temperatures around 20–30°C (Darian-Smith et al., 1973; Dubner et al., 1975) and typically very low or absent outside the range of 17–40°C (Scheppers and Ringkamp, 2010). Cool-sensitive afferents comprise fast-conducting, thinly myelinated A δ -fibres (Fowler et al., 1988; Yarnitsky and Ochoa, 1991) and slow-conducting, unmyelinated C-fibres (Campero et al., 2001; Konietzny, 1984). The overlapping steady-state activities of warm and cold fibres at normal skin temperatures (about 30–34°C) result in a thermoneutral sensation (Kenshalo, 1990).

Secondary afferents

Warm and cool primary afferents synapse onto secondary thermosensory neurons in lamina I of the superficial dorsal horn in the spinal cord. The receptive fields of secondary afferents are larger than those of primary afferents, indicating that they integrate information from multiple thermoreceptors (Craig, 2018). There are many more cold-sensitive than warm-sensitive secondary afferents (Craig, 2018). Secondary afferents are inhibited by opposite thermal stimulation (cool temperatures suppress activity in warm-sensitive neurons, and vice versa) (Andrew and Craig, 2001; Craig et al., 2001) and are generally insensitive to other sensory inputs (e.g., painful and tactile stimuli) (Craig, 2018). Secondary afferents project from lamina I to thalamic nuclei (VMpo (Blomqvist et al., 2000; Craig et al., 1994; Dostrovsky and Craig, 1996) and MDvc (Craig et al., 1994)) and the LPB (Nakamura and Morrison, 2010, 2008).

Tertiary afferents

Thermosensitive VMpo neurons are predominantly cold-sensitive, with similar response profiles to those of cold-sensitive secondary neurons (Craig, 2018; Craig et al., 1994). Their activity increases monotonically with decreasing temperature, plateaus at noxious cold temperatures, and is inhibited by warm temperatures (Craig, 2018; Craig et al., 1994). Neighbouring VMpo neurons have similar and overlapping receptive fields (Craig, 2018), and are organised somatotopically along an anteroposterior gradient (Craig et al., 1994) that is orthogonal to and independent of the somatotopy in ventral caudal nucleus, the main somatosensory thalamic nucleus (Craig, 2018). Thalamic afferents in VMpo relay thermal signals to the dorsal posterior insula, central sulcus, and cingulate sulcus (Craig, 2018). MDvc neurons only project to the cingulate sulcus (Craig, 2018; Dum et al., 2009). Tertiary LPB neurons target the hypothalamus (Nakamura and Morrison, 2010, 2008).

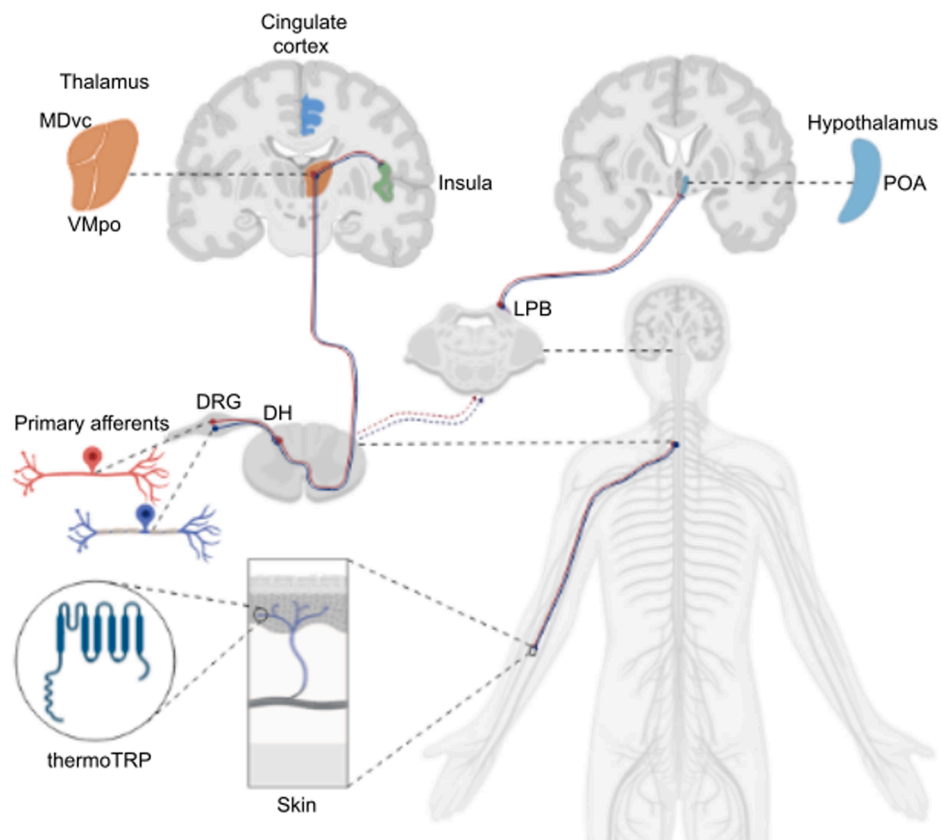


Fig. 1. Simplified schematic of the main human thermosensory pathways from the skin. The lamina I spinothalmo-cortical pathway (left) and the spino-parabrachial pathway (right). There are other thermosensory pathways (not shown here); in particular, several homeostatic centres in the brainstem receive inputs from lamina I thermosensory neurons (see main text). DRG: dorsal root ganglia; DH: dorsal horn of the spinal cord; MDvc: medial dorsal nucleus, ventral caudal part; VMpo: ventral medial nucleus, posterior part; LPB: lateral parabrachial nucleus; POA: preoptic area. Created with BioRender.com.

Box 2 Peripheral thermosensation.

Thermosensation begins with the activation of temperature-sensitive receptors. Several highly thermosensitive ion channels have been identified, most notably a group of temperature-activated transient receptor potential ion channels (“thermoTRPs” (Patapoutian et al., 2003)). For example, TRPM8 is activated by innocuous cool (temperatures below 26 °C), as well as the chemical agonists menthol, eucalyptol and icilin (McKemy et al., 2002; Peier et al., 2002a), which mimic cool temperatures. By contrast, TRPV3 (Peier et al., 2002b) and TRPV4 (Güler et al., 2002; Watanabe et al., 2002) are activated by temperatures above approximately 30–35 °C (Chung et al., 2004). While early mouse studies (Lee et al., 2005; Moqrich et al., 2005) implicated these two receptors in innocuous warmth sensation, more recent work (Huang et al., 2011) cast doubt on these initial conclusions. TRPM2, which is also activated by innocuous warm temperatures (above 35 °C) (Togashi et al., 2006), and the noxious heat-activated TRPV1 channel (Caterina et al., 1997), were subsequently proposed to underlie warm thermosensation (Tan and McNaughton, 2016; Yarmolinsky et al., 2016). More recently, however, it was reported that neither TRPM2 nor TRPV1 is essential for sensing innocuous warm temperatures, but the cool-activated TRPM8 receptor is (Paricio-Montesinos et al., 2020). Knockout-mouse studies (reviewed in (Filingeri, 2016; Schepers and Ringkamp, 2010; Vriens et al., 2014)) indicate that additional mechanisms likely contribute to thermosensation. In particular, it has been suggested that thermosensitive potassium channels of the TREK/TRAAK family modulate the excitability of thermosensory neurons (Kang et al., 2005; Noël et al., 2009).

Thermoreceptors are expressed in the free nerve endings of primary thermosensory afferents. These pseudo-unipolar neurons project one axon segment to target tissues in the periphery, such as the skin and visceral membranes, and a second axon segment to secondary afferents in the dorsal horn of the spinal cord (see Box 1). The cell bodies of primary thermosensory neurons innervating the head and the rest of the body are located in trigeminal ganglia and dorsal root ganglia, respectively. Primary afferents have either single or multiple (between 2 and 5) spot-like receptive fields, referred to as warm and cold spots (Duclaux and Kenshalo, 1980; Kenshalo and Duclaux, 1977). Overall, the human skin has more cold spots than warm spots (Hensel, 1981), consistent with the finding that we are more sensitive to cold than warm temperatures everywhere on the body (Stevens and Choo, 1998).

the skin are required for innocuous cold thermosensation and cold avoidance behaviour in mice (Bautista et al., 2007; Colburn et al., 2007; Dhaka et al., 2007). (Since cutaneous thermoreceptors are mostly cold-sensitive, skin temperature is relatively more important for activating cold-defence mechanisms than heat-defence responses; reviewed in (Romanovsky, 2014).) In humans, it has been shown that skin temperature drives behavioural thermoregulation (and autonomic responses) before core temperature changes can be detected (Schlader et al., 2013). As discussed elsewhere (Muzik et al., 2021; Terrien et al., 2011), more phylogenetically evolved species (such as humans) appear to rely on more extensive behavioural repertoires to reduce the workload on autonomic systems, suggesting that behavioural thermoregulation (and its guidance by skin temperature (Flouris, 2011)) may play an even more prominent role in humans than in rodents.

Evidence from rodent models also points to an essential role of cutaneous TRPM8 channels in the initiation of autonomic cold-defence responses (non-shivering thermogenesis and vasoconstriction) (Camila Almeida et al., 2012). While pharmacological blockade of TRPM8 in a constantly warm or cool environment did not affect core body temperature, transferring animals from a warm to a cool environment immediately after the manipulation led to the inactivation of autonomic thermoregulatory mechanisms and a subsequent decrease in core temperature (Camila Almeida et al., 2012). These results indicate that the activation of cutaneous TRPM8 channels is directly involved in – and essential for – the regulation of core temperature in rodents. Thus, even without considering behavioural thermoregulation and cutaneous vasoreaction, the skin is a fundamental component of the body’s thermoregulatory control circuit. Notably, the skin is both a thermosensory organ and a thermoregulatory effector organ. The thermoeffector function of the skin can be clearly observed in victims of major burn injuries, who display elevated core temperatures (and accompanying heat intolerance) due to their reduced ability to dissipate heat through the skin (Ben-Simchon et al., 1981).

The direct role of cutaneous thermal signals in the control of core temperature (via behavioural and autonomic thermoregulatory mechanisms) qualifies skin temperature as an interoceptive modality. Importantly, this does not require global changes in skin temperature: even locally restricted skin temperature changes trigger thermoregulatory processes. For example, exposure to cool air engages a thermoregulatory reflex to conserve heat that manifests as a decrease in respiratory

frequency (Diesel et al., 1990). It has been shown (in calves) that this reflex is primarily driven by cool stimulation of the face (rather than cooling of the airways) (Diesel et al., 1990). It is worth highlighting that local skin warming/cooling anywhere on the body can elicit thermoregulatory responses. For example, it has been shown that brief cool stimuli (25°C with a duration of 15–20 s) applied intermittently to the wrist over a prolonged time period lead to a decrease in distal skin temperature (bilaterally) over that time period (Xu et al., 2021). Thus, activation of cold receptors in the wrist alone drives widespread peripheral vasoconstriction (Xu et al., 2021).

Cutaneous thermal signals also contribute to a variety of homeostatic/allostatic processes beyond the control of body temperature. Here too, the skin temperature changes that drive homeostatic/allostatic control may be local and brief. The diving reflex, a cardiorespiratory response triggered by the activity of cutaneous thermoreceptors upon cold stimulation of the face (Panneton et al., 2012), represents just one well-known example. Similarly, immersing the body in cold water has immediate and dramatic effects on respiration that occur long before there is any change in core temperature, and are mediated by cutaneous cold receptors (for review, see (Datta and Tipton, 2006)).

In short, evidence from physiological studies in animals and humans shows that skin temperature plays a fundamental and direct role in the maintenance of homeostasis. Functionally, thermal signals from the skin thus satisfy the core requirement for being considered to serve interoception.

3.3. Conceptual considerations

The role of interoception extends beyond homeostatic and allostatic regulation: its importance in affective feelings and emotion has been proposed for over a century (reviewed in (Barrett and Bliss-Moreau, 2009)), and more recently it has been linked to subjective consciousness, body awareness, and many other aspects of cognition (reviewed in (Tsakiris and Critchley, 2016)). Moreover, interoceptive disturbances are increasingly recognised as important components of psychiatric and neurological diseases, including affective disorders (e.g. depression), eating disorders (e.g. anorexia nervosa) and addiction (Khalsa et al., 2018; Nord and Garfinkel, 2022; Paulus and Stewart, 2014; Tsakiris and Critchley, 2016). Experimental evidence indicates that, similarly to visceral (e.g. cardiac) signals, cutaneous thermal sensations contribute

Box 3 Thermoception and mental health.

Empirical observations point to an association between the processing of thermal signals and affective disorders, such as major depressive disorder (MDD). For example, MDD patients sweat less than healthy people, suggesting a dysfunction of thermoregulatory cooling mechanisms (Raison et al., 2015). In the 1980s resting skin conductance, an indirect index of sweating, was proposed as a potentially sensitive and specific diagnostic test for depression (Ward et al., 1983; Ward and Doerr, 1986). It is unclear if low skin conductance is a stable trait that increases vulnerability to MDD, or a reflection of the depressive state (reviewed in (Raison et al., 2015)). The latter is in line with clinical studies that report excessive sweating as a common side effect of many antidepressants (Mago et al., 2013; Marcy and Britton, 2005). A further indication of aberrant cooling responses in affective disorders is provided by reports of elevated core temperature as a common clinical symptom (Avery et al., 1999, 1982; Rausch et al., 2003; Schwartz et al., 1997; Souetre et al., 1988; Szuba et al., 1997), which appears to normalise following successful MDD treatment (Avery et al., 1982; Szuba et al., 1997). However, the cause of abnormal thermoregulatory cooling in MDD remains unknown. It has been proposed that, in some instances of depression, elevated body temperature results from reduced signalling in the warm-sensitive thermosensory pathway through the LPB (see Box 1) and serotonergic neurons in the dorsal raphe nucleus, which are also implicated in mood regulation (Hale et al., 2013; Raison et al., 2015). Activity in this pathway triggers thermoregulatory cooling mechanisms to maintain homeostasis; hence its dysfunction would lead to increased core temperature (Raison et al., 2015). Based on the idea that activating this pathway may reduce depressive symptoms in a targeted fashion, a randomised, double-blind, placebo-controlled study investigated the effect of a single session of whole-body hyperthermia in MDD patients (Janssen et al., 2016) and found that it was associated with a significant reduction in depression scores that persisted for 6 weeks post treatment. Other investigators have recently suggested hyperthermic baths for treating depression (Naumann et al., 2020, 2017). Interestingly, yet other studies have suggested the opposite thermal intervention – whole-body cryotherapy (Rymaszewska et al., 2008) and cold water immersion (reviewed in (Tipton et al., 2017)) – as possible treatments for depression

to a variety of cognitive processes, including affective and social functions, and are dysregulated in mental disorders (Raison et al., 2015) (see Box 3). Every temperature that humans can discriminate (i.e., any temperature that is not thermoneutral) is accompanied by a feeling of pleasantness or unpleasantness (Craig, 2018; Rolls et al., 2008). Notably, in contrast to thermal intensity, the degree of (un)pleasantness of thermal sensations depends on the body's thermal state (Cabanac et al., 1972; Mower, 1976). For example, as has been pointed out before (Craig, 2018), the same hot shower can feel highly aversive when you are overheated, or comfortably warming when your body is cold. Conversely, the same cold shower can feel pleasantly invigorating when you are overheated, or unpleasantly chilly when your body is cold. The body's thermal state influences affect and thermal comfort in response to local skin temperature changes differently for different body parts. For example, cooling/warming of the face is a stronger driver of thermal comfort/discomfort when you are warm (than stimulation of the chest and abdomen) (Nakamura et al., 2008). When you are cold, local thermal stimulation of the chest and abdomen has a stronger effect on thermal comfort/discomfort (than stimulation of the face) (Nakamura et al., 2008). Importantly, these differences cannot be explained by differing physiological properties (e.g., warm/cool receptor densities across the body) alone. (See also (Wang et al., 2019a) for the impact of cooling/warming different body parts on thermal comfort in warm/cool environments).

Moreover, these affective experiences manifest themselves long before any changes in core temperature occur, illustrating the skin's role in allostatic (i.e., anticipatory) regulation of body temperature. The affective feeling and behavioural drive that inherently arise with each thermal sensation support the notion that thermoregulation – and not the discrimination of object temperatures – is the primary biological purpose of cutaneous thermal sensitivity (Craig, 2018). An organism's survival (i.e., the structural integrity of biological tissues, the function of vitally important biochemical processes, and efficient energy regulation) critically depends on temperature, and the thermoregulatory networks responsible for maintaining body temperature rely on feedback about temperatures both inside and outside the body.

In summary, from a conceptual point of view there are important similarities between cutaneous and more classical (i.e., visceral) sensory signals with respect to their influence on affective, cognitive, and clinical phenomena.

3.4. Typical points of confusion

Confusion about the interoceptive function of skin temperature is often linked to the association of interoception/exteroception with words such as interior/exterior and the original location-oriented distinction between interoception and exteroception proposed by Sherrington. However, more modern definitions of interoception as the perception of (inference on) bodily states (Barrett and Simmons, 2015; Gu et al., 2013; Khalsa et al., 2018; Pezzulo et al., 2015; Seth et al., 2012; Seth and Friston, 2016; Tsakiris and Critchley, 2016) recognise that the human body is not a closed system that is isolated from its surroundings, and that many naturally occurring bodily states are evoked by external stimuli (perturbations). This resonates with longstanding approaches for investigating interoception experimentally: external stimuli have long been employed in 'classical' interoception studies, for example, inflatable balloons (Ladabaum et al., 2001; Mayer et al., 2005; Van Oudenhove et al., 2009; Wilder-Smith et al., 2004) or ingested water (Herbert et al., 2012; Van Dyck et al., 2016) to change the stretch of gastrointestinal organs, or vagus nerve stimulation (Richter et al., 2020; Villani et al., 2019). These stimulation methods are generally accepted as valid approaches for investigating interoception. In principle, there is no conceptual difference between using inflatable balloons (to briefly manipulate the stretch of the rectum or oesophagus) and using cutaneous thermal stimuli (to temporarily alter skin temperature) to study interoception. In both cases external stimuli are employed to alter the state of an organ that is perceived by the brain and informs homeostasis-oriented actions.

A further point of confusion is the assumption – which derives again from a location-oriented classification of interoception/exteroception – that sensory receptors and pathways must either belong to the interoceptive or exteroceptive domain (discussed in (Ceunen et al., 2016)). This assumed exclusivity leaves skin temperature perception in a state of limbo: cutaneous thermoreceptor temperature results from the interaction of internal and external thermal influences (Hensel, 1952). This is obvious when considering basic principles of heat exchange: the skin is in contact with subcutaneous tissues and the ambient environment; since it is not a perfect insulator, temperature gradients are established across it (Romanovsky, 2018). Therefore, if exteroception were defined strictly as the perception of external stimuli, the perception of skin temperature could not be called exteroceptive, because all sensory signals relayed by thermoreceptors contain information from internal thermal stimuli. Conversely, skin temperature perception could not be

called interoceptive if interoception were defined as pertaining only to stimuli of internal origin.

Thus, when considering the thermosensory system, it becomes clear that a categorisation of perceptual processes based on Sherrington's original (or similar) criteria does not allow a coherent distinction between interoception and exteroception. In other words, interoception and exteroception can receive sensory information from the same receptors and "need not be mutually exclusive on any of the levels preceding the higher order processing" (Ceunen et al., 2016) of afferent signals by the brain. Instead, the above considerations suggest that the functional consequences of a sensory stimulus – i.e., whether it serves to regulate bodily or environmental states – may be more important for the distinction between interoception and exteroception than the origin of the stimulus (i.e., whether it originates from within or outside the body).

4. A computationally informed view

The previous section described the importance of skin temperature for homeostatic and allostatic regulation, even beyond the control of core temperature. It also indicated the inadequacy of classical (Sherringtonian) criteria, such as stimulus origin or receptor location, for deciding whether thermoception is an interoceptive or exteroceptive process.

In the following, we revisit the computational concepts of interoception and homeostatic/allostatic regulation that we briefly introduced above to motivate functional definitions of thermosensation and thermoception. To make this physiologically concrete, we discuss sensor-effector loops involved in thermoregulation.

Generally, it is worth noting that we use the term "computational" in accordance with the levels of analyses proposed by (Marr and Poggio, 1976): what is the purpose of an information processing system, or put differently, what problem is it trying to solve? This teleological perspective is distinct from the more specific "algorithmic" level of analysis which details the exact operations by which the problem is solved. For this article, focusing on the computational (as opposed to the algorithmic) level is more appropriate for two reasons. First, we propose to distinguish interoception from exteroception by asking what purpose a given perceptual process serves. Second, there is a relatively broad consensus about the general architecture and objective function of the loops implementing sensation-control (homeostatic) and inference-control (allostatic); this is summarised in the section on sensor-effector loops below. By contrast, the algorithmic nature of these loops remains to be clarified. While some detailed concepts have been put forward (e.g. (Penny and Stephan, 2014; Sennesh et al., 2022; Stephan et al., 2016; Tschantz et al., 2022)), these are presently purely theoretical considerations, i.e. there are as yet no empirical data that would allow to disambiguate these proposals.

4.1. Interoception as inference

A major challenge for adaptive control of bodily homeostasis is that the brain does not have direct access to physiological and biochemical states of the body, but must infer them from the signals it receives via its sensory channels. This separation of the brain from the true state of the world is less critical for simple reflex-like homeostatic control actions, but poses a fundamental problem for more complex allostatic behaviours. It is therefore useful to distinguish between sensations (inputs from sensory channels) and perception (inference about the hidden states that give rise to sensations) (Petzschner et al., 2017). This distinction is not only important for understanding interoception (Khalsa et al., 2018), but represents a general challenge for perception: the noisy (due to the stochasticity inherent to any sensory channel) and ambiguous nature of sensory information can render it challenging to differentiate states of the world (including the body) precisely. For example, in visual neuroscience it has been noted that, in principle, an infinite set of objects could give rise to the same retinal image (Kersten

and Yuille, 2003).

As a solution to this challenge, contemporary theories of perception propose that the brain uses Bayesian inference to infer on hidden states of both the external and internal environment (i.e., exteroception and interoception) (Friston, 2005; Petzschner et al., 2017; Seth, 2013). For this, the brain is assumed to construct and continuously update a so-called "generative model", i.e., a probabilistic model that combines prior "beliefs" (i.e., *a priori* probability distributions of states of the world) with a probabilistic forward mapping from hidden states to sensory inputs (likelihood). By inverting such a generative model, the brain could compute the posterior probability of a state of the world, given the sensory inputs it receives. Notably, for a large set of statistical distributions (i.e., all distributions from the exponential family (Mathys, 2017, 2016)), computing the posterior probability can be understood as a belief update that depends only on the prediction error (the difference between the actual and the predicted sensory input) and a precision weight (which reflects the relative uncertainty of sensory inputs and predictions) (Mathys et al., 2014).

One popular theory of how Bayesian inference could be implemented algorithmically in the brain is predictive coding (Friston, 2005; Rao and Ballard, 1999). Predictive coding assumes that the brain's generative model has a hierarchical structure, where probabilistic representations (beliefs) about states of the world become increasingly more abstract at higher levels, and the belief at each level serves to predict the state of the level below. Belief updating is assumed to rely on the communication of predictions and prediction errors along descending and ascending connections in the hierarchy, respectively. This motif of a functional hierarchy fits well with anatomical hierarchies in cortex that have been described with respect to connectivity patterns and cytoarchitecture (Felleman and Van Essen, 1991; Hilgetag et al., 2000). Moving from perception to control, the action-oriented counterpart of predictive coding is active inference (Parr et al., 2022). Put simply, active inference postulates that the brain selects actions such that the ensuing changes of the world lead to sensory inputs that better match the brain's beliefs or predictions and thus reduce prediction errors. This is thought to be implemented by predictions (about the expected sensory consequences of actions) sent to "comparator" units of reflex arcs, e.g. visceromotor nuclei in the brainstem or motor neurons in the ventral horn of the spinal cord (Friston et al., 2010). Furthermore, the same prediction signals might be sent along a second anatomical pathway, i.e. along descending connections in cortical hierarchies, where they serve as priors (or "collateral discharge" signals) for perception (for a simple schematic, see Figure 3 in (Manjaly et al., 2019)).

As described below, Bayesian theories of interoception and bodily regulation frequently (but not unanimously, e.g. (Sennesh et al., 2022)) refer to predictive coding and active inference (PC/AI). While there are different proposals of how Bayesian processes akin to PC/AI could be implemented algorithmically (e.g. (Penny and Stephan, 2014; Smith et al., 2021b; Stephan et al., 2016; Tschantz et al., 2022)), they share the same objective function (the mathematically defined goal of an optimisation process), i.e. they assume that both perception and action serve to minimise (an approximation to) the brain's surprise about its sensory inputs (where "surprise" refers to information-theoretic [Shannon] surprise) and, over time, entropy of bodily states. Put differently, this perspective on brain-body interactions provides a mathematically precise notion of the problem that interoception and physiological regulation serve to address.

4.2. Sensor-effector loops

Current concepts of interoception increasingly recognise the importance of jointly considering afferent pathways and efferent regulatory pathways as functionally integrated circuits (Bertson and Khalsa, 2021; Chen et al., 2021) which mediate reciprocal interactions between the brain and body (Petzschner et al., 2021, 2017). These sensor-effector loops are a central infrastructural motif of brain-body interactions and

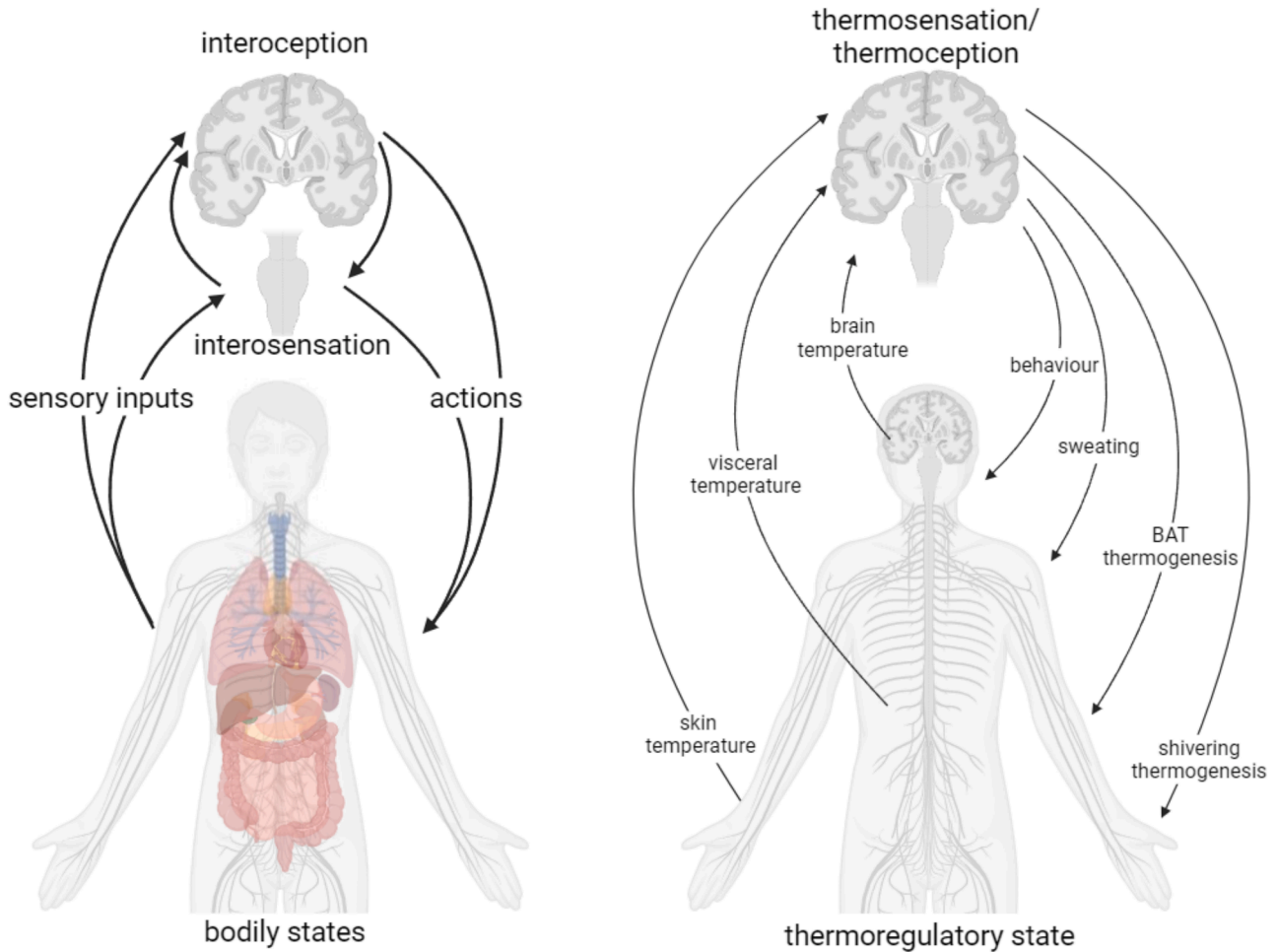


Fig. 2. Illustration of sensor-effector loops. Left: Simple schematic of sensor-effector loops for bodily regulation. Signals from sensory receptors reach homeostatic effector regions in the brainstem, triggering reflex-like homeostatic actions. Interoception-control loops can be modulated by higher-level interoception-control loops to initiate prospective actions for bodily regulation (i.e., allostatic control). Interoception is conceptualised as inference (in cortical areas) on the underlying bodily states that caused sensory inputs. Actions lead to changes in bodily states, which lead to changes in sensory inputs, forming closed loops. Right: The thermosensory-thermoregulatory system consists of multiple sensor-effector loops. Sensory inputs (including skin and visceral temperature signals) engage thermoregulatory reflexes and contribute to thermoception, i.e., inference on the body's thermal state. A wide array of thermoregulatory actions (including behaviours, such as putting on a jacket, and reflexes, such as shivering) enable flexible and effective control of body temperatures within their homeostatic ranges. BAT: brown adipose tissue. (Note that this figure is intended as a conceptual illustration only.) Created with BioRender.com.

underlie adaptive behaviour for survival: the afferent branch provides information about physiological states of the body, while the efferent branch mediates homeostatic reflexes and allostatic actions based on this information in order to control physiological states and keep them within ranges that are compatible with life.

Since reflexes or behavioural actions triggered by the (experienced or anticipated) deviation of a physiological state from its expected value effect a change in that state (directly or indirectly), sensor-effector loops are typically closed feedback loops (see Fig. 2). For example, shivering in response to a drop in body temperature raises body temperature. Continuing with this example, the brain can also counteract an anticipated drop in body temperature by initiating allostatic processes that raise body temperature (e.g., putting on warm clothes before leaving the house in winter). Due to the closed-loop nature of sensor-effector loops, the sensation or perception of bodily states must be considered jointly with the regulatory processes that control these states. Therefore, many recent concepts of interoception and homeostatic/allostatic control emphasise the functional unity of sensor-effector loops (Petzschner et al., 2021, 2017; Pezzulo et al., 2015; Seth and Friston, 2016; Stephan et al., 2016).

With the distinction between sensation and perception in mind, two kinds of sensor-effector loops can be distinguished: sensation-control loops and inference-control loops. Spinal and medullary reflexes constitute examples of sensation-control loops (commonly referred to as homeostatic reflex arcs). In these loops, homeostatic reflexes are triggered automatically, without the need for inference at higher levels of the neural processing hierarchy. By contrast, inference-control loops involve processes of inference at the level of cortical circuits and support allostatic control. Here it is worth keeping in mind that, from the perspective of Bayesian models of perception, inference may not only concern current physiological and biochemical states of the body, but also their evolution, e.g. a trajectory of states (Penny and Stephan, 2014). In other words, depending on context, the term "inference" can refer either to detecting current bodily states or forecasting (predicting) future bodily states.

Inference about bodily states is thought to rest on a hierarchical generative model (i.e., predictive coding) implemented in a network of insular-cingulate areas (Barrett and Simmons, 2015; Fermin et al., 2022). Specifically, neuroanatomical, neurophysiological, and neuroimaging results suggest that there is a posterior-anterior functional

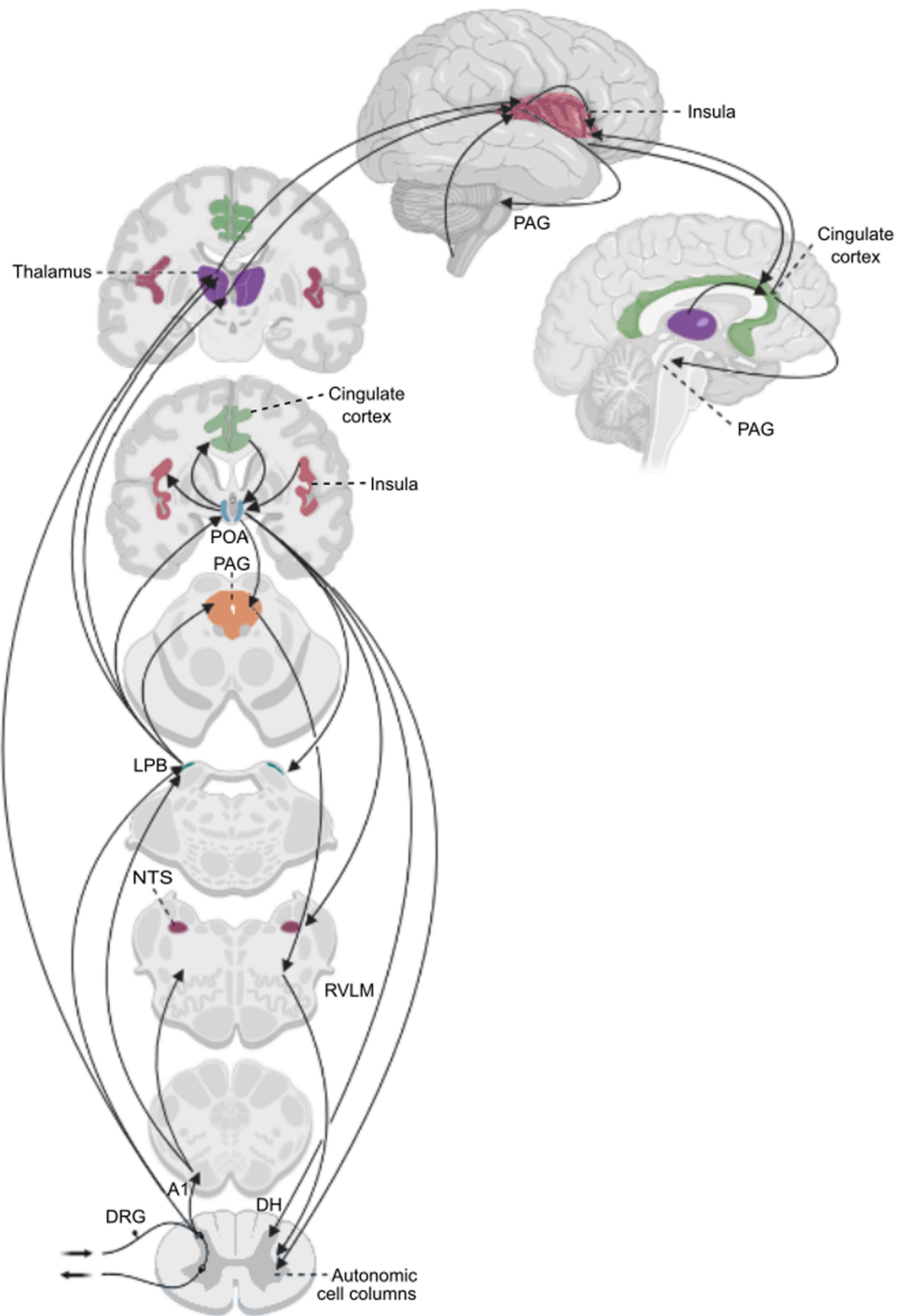


Fig. 3. Sensation- and inference-control loops for control of body temperature. Thermoregulation is achieved via a hierarchy of multiple interacting sensation-control and inference-control loops. Skin temperature signals enter the hierarchy at the level of the dorsal root ganglia (DRG). Based on Figure 1 in (Craig, 2003) and additional descriptions in (Craig, 2018). Generally, unless otherwise mentioned, anatomical connections described in this paper apply to the thermosensory-thermoregulatory system in humans and non-human primates. Please note that this figure is a simplification and not all known anatomical connections are represented. Ascending connections are shown on the left and descending connections are shown on the right; this is not meant to imply lateralisation of processes. Some brain structures are shown in multiple slices and/or views and can be identified by their colours. DH: dorsal horn of the spinal cord; A1: noradrenergic medullary A1 cells; RVLM: rostral ventrolateral medulla; NTS: nucleus of the solitary tract; LPB: lateral parabrachial nucleus; PAG: periaqueductal grey; POA: preoptic area of the hypothalamus. Created with BioRender.com.

gradient across the insula, from granular (posterior) to agranular (anterior) regions, that may relate to different hierarchical levels of a generative model (Barrett and Simmons, 2015; Fermin et al., 2022; Gu et al., 2013). In this hierarchy, more posterior insular regions are thought to contain topographic representations of sensory inputs from the body (Cechetto and Saper, 1987), including inputs from cutaneous thermoreceptors (Vestergaard et al., 2023). By contrast, anterior insula cortex (as well as cingulate and subgenual areas (Barrett and Simmons, 2015; Stephan et al., 2016)) may compute predictions about future physiological states (Livneh and Andermann, 2021).

The two types of sensor-effector loops show a hierarchical relation: inference processes at cortical levels are assumed to modulate lower-level homeostatic reflex arcs (Smith et al., 2017; Stephan et al., 2016). This putative mechanism is a well-known principle from other functional domains (e.g., modulation of spinal motor reflex arcs by descending projections from motor cortex; for reviews, see (Adams et al., 2013; Lemon, 2008)) and represents a mechanistic basis for allostatic control, i.e., descending projections from insular and cingulate areas are thought to dynamically change setpoints in homeostatic effector regions like the hypothalamus or PAG (Stephan et al., 2016). Notably, several loops can operate in parallel, each with its own setpoint that can change independently over time. This general computational view on allostasis resonates with conceptual changes in thermoregulation research of multiple independent thermoeffector loops and "balance points" (Romanovsky, 2007).

In the following sections, we describe concrete examples of sensation-control and inference-control loops that rely on afferent signals from the skin to regulate body temperature (see Fig. 3).

4.3. Sensation-control loops

Thermosensory neurons project from lamina I in the spinal cord (see Box 2) to multiple homeostatic effector regions in the spinal cord and brainstem (Craig, 2018). At the spinal level, they are reciprocally interconnected with autonomic cell columns that send efferent projections to muscles and skin (Craig, 2018). These homeostatic loops drive low-level responses for thermoregulatory control (Craig, 2018), such as the inhibition of cutaneous vasoconstrictor neurons in response to skin warming (Jänig, 2006), and their excitation in response to cooling (Wilson et al., 2007). Furthermore, dense lamina I projections target the lateral parabrachial nucleus (LPB) in the brainstem (Cechetto et al., 1985; Nakamura and Morrison, 2008) which contains neurons that are activated by either skin warming or cooling (Bratincsák and Palkovits, 2004; Nakamura and Morrison, 2010, 2008). These neurons provide inputs to the hypothalamic POA (Morrison and Nakamura, 2011; Nakamura and Morrison, 2010, 2008) and support thermoregulatory responses, such as cutaneous vasodilation (Morrison and Nakamura, 2011) and -constriction (Rathner et al., 2008). The POA is also the origin of efferent pathways for thermoregulatory control via shivering thermogenesis, non-shivering/brown adipose tissue (BAT) thermogenesis, sweating, and corrective (but not proactive) behavioural responses (reviewed in (Romanovsky, 2018)). These different thermoregulatory responses are the outputs of independent sensation-control loops involving distinct neuronal groups within the POA. For example, the POA sends efferents to lamina I neurons and spinal autonomic cell columns (Holstege, 1988). As mentioned above, however, the POA does not act as a single central temperature controller (see (Romanovsky, 2018, 2007)): many other subcortical sites – including the NTS, the rostral and caudal ventrolateral medulla (in the latter, specifically noradrenergic A1 cells), the locus coeruleus, and the periaqueductal grey (Craig and Dostrovsky, 2001) – form part of distinct thermoregulatory reflex loops with inputs from thermosensory-specific lamina I cells (reviewed in (Craig, 2018)). Lamina I neurons also extend projections to multiple homeostatic effector regions in the brainstem that form part of spino-bulbo-spinal reflex loops for regulating blood flow, heart rate, and respiration (Sato and Schmidt, 1973) – processes that interact with

thermoregulation.

4.4. Inference-control loops

Inferences about bodily states and their future evolution (i.e., prediction of thermal state trajectories in a particular environmental context) can inform two complementary types of allostatic regulation: voluntary control by means of changes in overt behaviour, and involuntary control through the autonomic nervous system. Both types of control are important for thermoregulation.

Beginning with involuntary allostatic control, several instances of anticipatory changes in autonomic function have been described. For example, mice that have learned to associate hypothermia with a specific olfactory stimulus are less hypothermic during cold water immersion following presentation of that stimulus than following presentation of a second stimulus associated with no immersion (Siegel, 2008). This is proposedly due to an anticipatory hyperthermic response that is triggered when the stimulus associated with hypothermia is presented (Siegel, 2008). In the wild, muskrats elevate their body temperature before entering water at near-freezing temperatures when foraging under ice in winter (MacArthur, 1979). This anticipatory thermoregulatory process allows them to develop only mild hypothermia. Remarkably, this "predictive elevation" (MacArthur, 1989) of core body temperature is not present in summer, nor does it occur when muskrats are forcibly immersed in cold water during experiments (MacArthur, 1979). Similar anticipatory temperature changes prior to thermal challenges have been observed in other aquatic mammals, e.g. beavers (Dyck and MacArthur, 1992), and in rodents (Pauls, 1979; Randall and Thiessen, 1980). In all of these examples, thermoregulation relies either on explicit forecasting (simulations of physiological state trajectories) or learned associations, and occurs *before* thermoreceptors detect the changes that these thermoregulatory mechanisms control.

The most powerful control of core body temperature is achieved through thermoregulatory behaviours (Romanovsky, 2018). Behavioural thermoregulation is often proactive (anticipatory). An example of this is putting on warm clothes *before* leaving the house in winter, i.e., before cutaneous thermoreceptors are activated and before any change in body temperature. Behavioural thermoregulation ranges from instinctual responses to complex action programs, all of which can be voluntarily recruited (Romanovsky, 2018). It is well established that behavioural thermoregulation is driven by feelings of thermal comfort or discomfort that depend on the body's homeostatic needs (which differ with other physiological states, as well as environmental conditions) (Cabanac et al., 1972; Mower, 1976). Put differently, motivated thermoregulatory behaviours rely on inference of the body's thermal state and its future development in the context of the surrounding environment. For example, if your body temperature is cold after swimming in the Atlantic Ocean on a hot summer's day in Cape Town, you will not put on a jacket on the beach (because you know that you will be sweating again soon). At exactly the same body temperature as in the case above, after taking a dip in a Swiss lake in winter, you will put on warm clothes as soon as you leave the water (to prevent hypothermia). As mentioned above, we refer to inferences that serve thermoregulatory control as *thermoception* (see Fig. 2).

The neural infrastructure for thermoception is located in cortical circuits. The dorsal posterior insula is the primary cortical area for processing warm and cool thermal stimuli, as demonstrated by studies in both humans (reviewed in (Craig, 2018)) and mice (Vestergaard et al., 2023). It encodes a somatotopic map with an anterior-posterior gradient (Hua et al., 2005; Vestergaard et al., 2023). Neural activity in this region is linearly correlated with the intensity of thermal stimuli (Craig et al., 2000). This representation of temperature intensity provides inputs to more anterior cortical areas implicated in the prediction of physiological states of the body, including the anterior insula, anterior cingulate cortex (ACC), subgenual cortex, and orbitofrontal cortex (Barrett and Simmons, 2015). These areas play a central role in Bayesian theories of

interoception and bodily regulation (Barrett and Simmons, 2015; Livneh and Andermann, 2021; Seth et al., 2012; Stephan et al., 2016). More concretely, they are thought to compute predictions and prediction errors that fulfil a dual role: on the one hand, prediction errors serve to update predictions (predictive coding); on the other hand, predictions trigger anticipatory actions which reduce prediction error in the longer run (active inference). Neurophysiologically, such prospective actions could be mediated in two ways: (i) overt behavioural actions could be elicited via connections to supplementary and primary motor areas, whereas (ii) involuntary changes in bodily regulation could be mediated by descending projections to the autonomic nervous system via brainstem nuclei and the spinal cord.

Taking the anterior insula as a concrete example, its potential role in interoceptive inference (predictive coding) is supported by neuroimaging findings that its activity reflects both prediction and prediction error signals when bodily states are manipulated (Harrison et al., 2021; Toussaint, 2023). Concerning anatomical connectivity, to our knowledge there are as yet no lamina-wise data from primate tract tracing studies to unequivocally confirm "backward"/"descending" connections from anterior to mid-/posterior insular regions, as assumed by predictive coding theories of interoceptive inference. However, the cytoarchitectonic differences between anterior (agranular) and more posterior (dysgranular, granular) areas imply the existence of these connections (Barrett and Simmons, 2015). Furthermore, the anterior insula features the required brain connectivity pattern for eliciting regulatory actions: its connections with supplementary and primary motor cortex, as well as prefrontal and parietal areas (Dionisio et al., 2019; Ghaziri et al., 2017), could mediate anticipatory adjustments of overt behaviour, while its projections to homeostatic effector regions in the brainstem, such as hypothalamus or PAG (for tract tracing studies of the agranular insula in rat and monkey, see (Allen et al., 1991; Öngür et al., 1998; Yasui et al., 1991)), are thought to modulate homeostatic reflex arcs and thus to elicit anticipatory changes in homeostatic control (Stephan et al., 2016).

As described above, inference-control loops are thought to modulate homeostatic reflex arcs by descending connections from cortical networks that perform inference and prediction for allostatic control. While the functional principle and general anatomical layout of these loops have been described (Manjaly et al., 2019; Smith et al., 2017; Stephan et al., 2016), comprehensive assessments of the hypothesised role of these circuits for allostatic control in humans are still lacking. As has been pointed out before (e.g. (Khalsa et al., 2018; Petzschner et al., 2017)), this is largely due to methodological difficulties, including the challenge of combining perturbations of bodily states (safe, temporally controlled and repeatable over a short period) with effective (directed) connectivity analyses and computational models of inference and prediction applied to neuroimaging data. Recent studies have begun to address individual components of the above challenges (e.g., (Harrison et al., 2021; Muzik et al., 2022, 2020; X. Wang et al., 2019b)) but a comprehensive approach for characterising interoceptive inference-control loops in humans is yet to be developed.

4.5. Interoception or exteroception?

Above, we considered inference-control loops that serve allostatic control of bodily states. Analogous feedback loops exist for controlling states of the external environment. Various proposals regarding the underlying computational principles and objective functions of exteroceptive inference-control loops have been put forward (for discussion, see (Petzschner et al., 2017)). However, they share the common notion of a predictive model to describe the interplay between the evolution of hidden states of the external environment, sensory inputs, and actions (e.g. see (Friston et al., 2010) for a juxtaposition of alternative models). The key difference to the inference-control loops for bodily regulation discussed above is that, in this case, both the process of perception (inference) and the act of control concern an external state of the world, e.g., the physical properties of external objects.

We propose that the concept of inference-control loops enables a functional distinction between interoception and exteroception: perceptual processes should be understood as instances of interoception if they contain inferences about physiological and biochemical states of the body that are coupled to regulatory processes which serve to control these states. Conversely, perceptual processes should be considered as instances of exteroception if they contain inferences about states of the external environment that are linked to actions which serve to control these states. This distinction based on the type of inference-control loop that a sensory signal feeds into resolves confusion resulting from Sherrington's original location-oriented classification (see above). Moreover, it aligns the concept of interoception with contemporary physiological and computational theories that emphasise the intertwined nature of perception and action (Adams et al., 2013; Friston et al., 2013).

4.6. Can temperature perception be exteroceptive?

We now return to the specific case of skin temperature perception. Given the functional definition introduced above, whether a particular sensory process is an example of interoception or exteroception depends on the inference-control loop it forms a part of. Above, we discussed numerous examples of how inferences concerning the thermal state of an organism serve the control of its thermal state. Importantly, these inferences are informed by sensory information from a variety of sources, including information from cutaneous thermoreceptors, which reflect temperature influences from the external environment (as well as the body's internal environment). This information is key for selecting appropriate thermoregulatory defences from a range of possible control actions: ambient temperature signals are an essential factor for inference about the likely trajectory of thermal states of the body within its surrounding environment (as in the above example of swimming in cold water in two very different environmental contexts).

This does not imply that temperature signals cannot inform exteroception. It is clear that thermoreceptors in the skin signal information that is also used in exteroceptive processes, for example, when a parent checks the temperature of milk before feeding their baby. In this case, the brain infers upon the thermal state of an external object (milk), and the elicited action serves to control the thermal state of the same external object (e.g., cooling or warming the milk bottle). Cutaneous thermoreceptors also contribute to the identification of object properties such as wetness (Bentley, 1900; Sullivan, 1923) and material composition (Ho and Jones, 2006). External temperature stimuli (and cutaneous thermoreceptors) thus play a role in both interoceptive and exteroceptive inference processes (Ho, 2019). Moreover, everyday experience demonstrates that interoceptive and exteroceptive processes can co-occur. When submerging your hand in a tub of bath water, you can determine that the water has reached the perfect temperature for a bath, while simultaneously noticing that your hand begins to feel pleasantly warm. This example demonstrates that it is even possible for interoceptive and exteroceptive inferences to enter conscious awareness together. Based on initial neuroimaging results, it has been suggested that interoceptive and exteroceptive processes involving thermal stimuli recruit distinct cortical regions (Craig, 2018; Mano et al., 2017; Rolls, 2019; Rolls et al., 2008). However, detailed functional principles of the cortical networks underlying the interoceptive and exteroceptive processing of temperature signals in humans, such as proposed implementations for perceptual inference, remain to be elucidated.

5. Implications for experimental approaches

Given the need of mental health research for assays of interoception (Khalsa et al., 2018; Schoeller et al., 2022), it is important not to miss the opportunities that the skin – the body's most accessible organ – offers for assessing interoceptive functions (see also (Crucianelli and Ehrsson, 2023)). The need for new empirical tests is widely acknowledged in interoception research (Garfinkel et al., 2022). Traditional approaches

for studying interoception have focused mostly on cardiac perception, using heartbeat counting (Dale and Anderson, 1978; Schandry, 1981), heartbeat tapping or tracking (Flynn & Clemens, 1988), and heartbeat detection or discrimination (Katkin et al., 1983; Whitehead et al., 1977) tasks. The validity of these methods for assessing interoception has been criticised (Corneille et al., 2020; Desmedt et al., 2018; Ring et al., 2015; Zamariola et al., 2018) (see (Legrand et al., 2022) for a concise summary of issues related to these tasks). While methodological developments (e.g., (Legrand et al., 2022)) might improve the validity of these tasks, it has been argued that tasks that rely on the subjective report of heartbeats are too difficult to complete at rest because the afferent signal is too weak (Desmedt et al., 2020). This can be cast within the framework of sensor-effector loops for homeostatic/allostatic control: during resting conditions, cardiac signals do not deviate much from their set-points and any prediction errors caused by random fluctuations are likely suppressed efficiently by reactive (homeostatic) control mechanisms, without significant activation of inferential/predictive processes in cortical hierarchies. In other words, experimental assessments of interoception that involve self-report (i.e., conscious perception) are likely to be more successful if bodily states are actively perturbed. For example, existing heartbeat tasks might be improved under conditions of physiological activation (see (Smith et al., 2021a, 2020)).

Skin temperature-based assessments offer the possibility of non-invasive and safe perturbations with precise temporal control. To this extent, initial tasks involving brief, local changes in skin temperature to study interoception have been developed (Crucianelli et al., 2022; Vabba et al., 2023) and correlated with self-reported depression, anxiety and stress scores (Crucianelli et al., 2024). A further opportunity entails direct tests of contemporary computational theories of interoception, such as theories based on predictive coding. For example, probabilistic manipulations of skin temperature could be used to elicit interoceptive prediction errors under controlled conditions. The safe and tolerable nature of cutaneous thermal stimuli makes it possible to perform experiments with a large number of trials – a typical prerequisite for testing computational models. Such an approach could also involve predictions about skin temperature changes, as in a recently developed task involving breathing resistances to assess respiratory interoception (Harrison et al., 2021). Validated skin temperature-based assays might thus help inform the development of computational biomarkers for psychiatry (Petzschner et al., 2021).

6. Limitations and (open) questions

In presenting our work to colleagues and reviewers, we encountered a number of questions that were both challenging and useful. We share our responses to these questions because they illustrate both the strengths and limitations of our definition, and they outline open questions for the future.

First, one may rightfully ask (as did one of our reviewers) why computational concepts are at all important for our proposed definition of interoception. Indeed, the definition we propose for interoception could also be motivated purely on the basis of anatomical and physiological arguments (compare the sections on anatomical and physiological considerations). However, adding a computational concept of the purpose of sensor-effector loops enables a more precise definition of interoception. For example, without a computational foundation, the notion of inference – which is important to our proposal and those of many previous papers on interoception (Gu et al., 2019; Khalsa et al., 2018; Petzschner et al., 2017; Pezzulo et al., 2015; Seth et al., 2012; Seth and Friston, 2016; Stephan et al., 2016) – would remain handwaving, as would the distinction between intersensation and interoception. Furthermore, even without specifying details of the algorithmic implementation, the Bayesian (PC/AD) perspective on brain-body interactions we refer to allows one to state the objective function of interoception, i.e. a minimisation of (an approximation to) information-theoretic surprise about bodily states (Friston et al., 2010). In other words, a

computational view on sensor-effector loops enables one to specify, in mathematical terms, what interoception and physiological regulation are thought to achieve.

Another fundamental question from one of our reviewers was whether a visual stimulus could lead to a perceptual process that qualifies as interoception according to our proposed definition. The answer to this question is yes: in general, visual stimuli (or more generally, stimuli from any exteroceptive modality) can trigger perceptual processes that involve inferences about physiological and biochemical states of the body and that are coupled to regulatory processes for controlling these states. In this case, the criteria of our proposed definition are fulfilled, and the perceptual process triggered by the visual stimulus would be called "interoceptive". (Notably, our definition does not require that the stimulus may not also simultaneously trigger a perceptual process that involves inferences about the external environment.)

To see why this makes sense in practice, let us consider an example mentioned by the reviewer: "For example, if I am having trouble moving my hand, and then I look at it and see evidence of impending frostbite (blue, stiff), this visual input informs me about the state of my body and suggests ways to regulate it (go inside and sit by a fire)." In this particular case (which assumes a person with light skin colour), the visual input allows for hierarchically structured inferences: about the colour of the skin (blueish) and about the underlying thermal state (cold) that gives rise to this skin colour. Put differently, the visual input would allow the brain to make inferences about hand tissue temperature because, in people with light skin, blueish skin colour is a plausible consequence of low tissue temperature. (Additionally, this inference about hand tissue temperature might be supported by simultaneous perceptual [inferential] processes triggered by proprioceptive input [stiffness of hand muscles] and thermal input [potentially from the hand itself, but also from other areas of the skin]. This additional information would help to rule out the alternative inference that the blueish skin colour is caused by low blood oxygen levels.) This inference about current hand tissue temperature can then be combined with inference about the (evolution of) the thermal state of the external environment to generate the prediction that regulatory action (moving to a warmer environment) is needed to prevent tissue damage (frostbite). In turn, this action will alter the thermal state of the hand, and thus the resulting visual, proprioceptive, and thermal inputs which trigger inferential processes that inform further regulatory actions (stay in the warm environment for longer or return to the cold environment) – thus closing the loop.

In the above example, it is important to distinguish between the visual stimulus per se and the resulting perceptual process (inference). According to our proposed definition, it is the latter that would qualify as interoception because it constitutes inference about a physiological state of the body (thermal state of hand tissue) which is coupled to regulatory action. By contrast, the visual stimulus per se is not interoceptive but corresponds to a sensation that represents one input amongst others to a perceptual (inferential) process about the state of the body.

A third question, which is related to the previous one, concerns the distinction between proprioception and interoception. In this article, we have focused specifically on the delineation between interoception and exteroception, and have not explored the concept of proprioception, the perception of the body's position and movement (temporal derivatives of location) in space. Hence, the type of inference is fundamentally different: when it comes to proprioception, inference is relative to the environment and is not coupled to homeostatic/allostatic regulation. Instead, it informs a different kind of sensor-effector loop in which perception (of the body's position and movement in space) controls the body's position and movement in space through motor actions. Based on these considerations, one could extend our previous categorisation of interoception and exteroception by a definition of proprioception: perceptual processes should be understood as instances of proprioception if they involve inferences about the body's location in space and its temporal derivatives that are coupled to motor actions which serve to

control these states.

Fourth, while experimental approaches involving cutaneous thermostimulation (such as the ones described above) are promising for testing these computational theories of interoception, an important open question is whether insights from thermoception studies apply to interoception more generally. Empirical findings point to at least some degree of domain specificity in interoceptive processing (Crucianelli et al., 2022; Ferentzi et al., 2018; Garfinkel et al., 2016; Vabba et al., 2023). It is not clear either whether, and to what degree, computational architectures (e.g. the nature of inference hierarchies) differ across interoceptive modalities, and how they interact across interoceptive modalities. The framework presented in this paper makes no specific proposals about where these networks overlap or how information from different organ systems is combined in sensor-effector loops.

This leads us to a further question by one of our reviewers, which does not directly concern our proposed definition of interoception but touches on a topic of high clinical importance: how does the brain distinguish whether unexpected sensory inputs from the body are attributable to a primary source inside the body (e.g. a pathology that causes accelerated heart rate) or are the downstream consequence of a cause in the social environment (e.g. allostatic activation of the sympathetic nervous system in response to unconscious predictions of social threats)? Furthermore, in such an ambiguous situation, how does the brain decide which sensor-effector loop to activate in response to prediction errors – or put differently, whether to attempt controlling bodily states or environmental (social) states?

While a comprehensive answer to this complex question is outside the scope of the current paper, we briefly comment on two things that would likely constitute central components of such an answer. First, the question raised by the reviewer essentially amounts to a question about meta-control, i.e. exerting control over control processes (e.g. switching between different control strategies). While meta-control is a fundamentally important aspect of adaptive behaviour, the computational and physiological foundations are only beginning to be investigated (for an overview, see (Eppinger et al., 2021)). Second, when decisions about control strategies depend on inference about the causes of sensory inputs, as in the above example, one likely determinant is the relative uncertainty associated with the different inferences (compare (Daw et al., 2005)). Simply speaking, the choice of control strategy should depend on which cause of the sensory inputs is most plausible. Here, "plausibility" could be operationalised in different ways: as the posterior precision of beliefs (about bodily or environmental states) within a single overarching generative model, or as the outcome of a (Bayesian) comparison between competing generative models. We emphasise that these are speculative thoughts at the present time, but anticipate that meta-control will become an important topic for future research on brain-body interactions.

A final challenging question by reviewers and colleagues concerns the relation of our proposal to consciousness. We would like to point out that our framework does not rely on a distinction between conscious and unconscious perception, and is generally agnostic about consciousness. Having said this, in the context of our distinction between sensation-control and inference-control loops, it seems plausible that sensory processes that occur entirely within sensation-control loops are not consciously experienced, as these loops represent reflex arcs that are restricted to spinal, brainstem, and subcortical structures in which the sensory signal itself triggers control actions automatically, without any need for inference or metacognition (e.g. self-monitoring). By contrast, sensory inputs feeding into inference-control loops may be associated with conscious experience. This is because these loops include cortical hierarchies (e.g. insular areas in the case of interoception) for perceptual inference on current and future states of the world, as a basis for more complex control actions which may require cognitive processes associated with consciousness, e.g. metacognitive monitoring or working memory. However, this speculation is not original (see e.g. (Smith et al., 2017)), and our proposal is not designed to make new predictions that

extend previous proposals linking interoception and consciousness (for example, (Seth et al., 2012)).

7. Conclusion

Historically, the word interoception referred to visceral sensory processes, but its meaning has evolved to designate the perception of physiological and biochemical states of the body. As a result of this substantial shift in meaning, the definition of the contemporary concept of interoception, and particularly its delineation from exteroception, is still a matter of debate. In this perspective, we proposed functional definitions of interoception and exteroception based on the notion of sensor-effector (and specifically inference-control) loops. These definitions directly reflect the different roles of interoceptive and exteroceptive processes of providing information either about the organism that the brain must regulate, or about the world beyond that organism. This functional distinction is independent of stimulus origin or location of sensory receptors, and categorises interoceptive and exteroceptive processes in a consistent manner. That is, the nature of a given perceptual process is determined by the type of inferences it involves and the control process it is coupled to. We demonstrated the utility of this computational perspective by means of the example of skin temperature, which can inform both interoception and exteroception. When temperature signals inform inferences about the body's thermal state that activate control loops for thermoregulation, they serve an interoceptive function. This is a fundamentally different role to exteroceptive functions that temperature signals may serve, such as the perception of external object properties (e.g., temperature, wetness).

In summary, the proposed classification of interoceptive and exteroceptive processes based on their association with different sensor-effector loops achieves a functionally meaningful grouping of perceptual processes in a manner that reflects contemporary computational concepts of brain function. The utility of such a revised classification goes beyond mere terminology but provides a basis for incorporating skin temperature interventions into the growing toolkit of experimental approaches for studying interoceptive processes.

Declarations of Competing Interest

none

Acknowledgements

This work was supported by the René and Susanne Braginsky Foundation (KES) and the Swiss National Science Foundation (grant no. 320030_179377 to KES).

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