Interoceptive stimulation in clinical neuroscience

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Abstract
Bodily signals play a crucial role in cognition and emotion, which may lead to catastrophic outcomes when interoception becomes dysfunctional. To characterize these mechanisms and intervene on interoception for either diagnostic or treatment purposes, a mounting body of research is concerned with interventions on interoceptive channels such as respiration, cardioception, or thermoception. However, we are still lacking a mechanistic understanding of their underlying psychophysiology. For example, interoceptive signals are often both the cause and consequences of some distress in various mental disorders, and the binding of interoceptive signals with exteroceptive cues is still unclear. In this article, we present existing technologies and their respective potential in light of the predictive processing framework describing interoception as a process of minimization of prediction errors. We distinguish between three kinds of stimuli: artificial sensations that concern the direct manipulation of interoceptive signals, interoceptive illusions that manipulate contextual cues to induce a predictable drift in bodily perception, and emotional augmentation technologies that blend artificial sensations with contextual cues of personal significance to the subject to generate specific moods or emotions. We discuss how each of these protocols can assess and intervene on the precision-weighting of prediction errors along the cortical hierarchy and conclude by discussing the clinical relevance of interoceptive technologies in terms of diagnostic stress test for evaluating interoceptive abilities across clinical conditions and as intervention protocols for conditions such as generalized anxiety disorders, post-traumatic stress disorders, and autism spectrum disorders.

Keywords
interoception, emotion, inference, artificial sensation, sensory substitution, misattribution of arousal, somatosensory, false feedback, calibration, stress test, aberrant emotional processing, psychopathology

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1. Introduction

The role of body perception (i.e., interoception) in driving emotion and decision processes has been well documented (Petzschner et al., 2021; Khalsa et al., 2018), including its dysfunction in psychopathology (Murphy et al., 2017; Khalsa, 2018; Paulus, 2019). Physiological variables are often manipulated in psychiatric settings to assess the susceptibility of patients to specific disorders marked by interoceptive dysfunctions (e.g., Sardina et al., 2009; Nardi, et al., 2002). Still, to this day, few experimental designs allow the controlled and standardized manipulation of interoception in the laboratory. Hence, interpreting data (concerning e.g., brain-body interaction, or intero-exteroceptive information integration) is rarely unequivocal. This can be partly explained by the historical emphasis on the brain as a physical site for cognition and emotion, as the corresponding instrumentation (in terms of e.g., single-person brain scanners) has led to a downplay of studies concerning the role of bodily signals in shaping human behavior.

To address this gap and facilitate the use of interoceptive technologies in clinical contexts, we propose a framework that provides crucial distinctions for various interventions, which can function at different clinical stages as either diagnostic, stress test or augmentation. We set aside pharmacological interventions with placebo conditions which are reviewed elsewhere (Arandia & DiPaolo, 2021). Various attempts have been made to make sense of interoceptive technologies systematically. For example, in the 1960s Vallins introduced the notion of misattribution of arousal (1960), later Cacciopo introduced the concept of somatovisceral illusions (Cacciopo et al., 1992), and within psychotherapy, the field of interoceptive conditioning or exposure (Furer & Walker, 2005; Schmidt & Trakowsky, 2004). While such interoceptive interventions and technologies provide an exciting opportunity for neuroscience and psychiatry, we still lack a precise understanding of the underlying psychophysiology to model evoked responses and thereby quantify or phenotype the central and peripheral correlates of interoceptive inference.

We can frame the special relevance of interoceptive technologies for psychiatry as follows: if psychology can be equated with inference about the state of the world (and our bodies), it follows that psychopathology can be characterized as false inference. For example, inferring things are there when they are not (e.g., hallucinations and delusions) or inferring things are not there when they are (e.g., agnosia and spatial neglect). Most of the available evidence suggests that such false inference in many psychiatric syndromes can be accounted for by aberrant precision control or, from a psychological perspective, aberrant attention or salience (Kapur, 2003; Lawson et al., 2014; Parr et al., 2018b; Powers et al., 2015). A mounting body of evidence suggests that bodily signals play an essential role in driving precision control, hinting towards the relevance of reliable body-based interventions for mental health and specific interventions depending on the patient's life history, conditions and symptoms. Bodily signals play an essential role in driving attention and tuning precision control. Their dysregulation in psychopathology may therefore offer an important way forward in terms of phenotyping in psychiatry. In the first section of the article, we review some basic terminology and the role of precision-weighting in (interoceptive and exteroceptive) hierarchical information processing, while briefly summarizing the physiology of each interoceptive system (temperature, respiration, cardiac, rectogenital, etc.). Readers already familiar with these notions can readily skip this introductory section.

Crucially, the controlled generation of artificial sensations afford a prescient stress test for disorders of emotional and interoceptive inference, leading to novel diagnostic or treatment options for patients. In order to make sense of how such stress tests should be designed, we review in the second section the current state-of-the art in interoceptive technologies and how they can help overcome some of the actual limitations in interoceptive neuroscience. Following the insight from vision science that illusion can teach a great deal about perception, we pay special attention to the case of interoceptive illusions, and offer a tentative model in terms of Bayesian predictive processing. The rationale is simple: an illusion is a sensory stimulation misleading perceptual inference, thereby providing an excellent opportunity to learn about the prior expectations underwriting pattern recognition (and in the context of interoception, about the exteroceptive/environmental influences on bodily perception). We also pay special attention to devices that can activate the so-called somatic markers for some specific emotions such as chills, tears, or disgust, shedding light on the essential role of bodily signals in emotional appraisal and decision-making. Finally, in the last section of this article, we consider the clinical applications for the devices described throughout the article, in the light of the theoretical considerations introduced in the first section.

2. A primer on interoception and its role in emotion

2.1. What is interoception?

Interoception refers to the neural processing of signals originating within the body, providing a moment by moment mapping of the body's physiological state (Khalsa, 2018). The definition of interoception is an old debate that dates back to the very origins of physiology (Ceunen et al., 2016). Following Chen et al. (2021), interoception can be broadly referred to as the adaptive monitoring of bodily signals emerging from within a living organism — i.e., 1) the sensing of internal signals through ascending pathways from the peripheral nervous system to the central nervous system, and 2) the regulation of these signals through descending neural pathways. These bidirectional processes allow the organism to represent its internal (metabolic) state and maintain vital parameters stable under changing environmental conditions (i.e., homeostasis — see Sterling, 2012). Hence interoceptive processes play an important role in shaping one's overall perception of some context and emotional grip on reality (e.g., so-called gut feelings).

Physiologically, interoception comprises various streams or channels (thermoception, respiratory, cardiovascular, chemosensory, gastrointestinal, circadian, rectogenital) transducing bodily signals (e.g., thermal, biochemical, mechanical changes) into electrical or chemical (hormonal) information, integrated within the brain (see table 1). One can classify interoceptive systems according to either (1) the classes and channels of information (e.g., respiratory, cardiovascular, gastrointestinal, genitourinary, endocrine, etc). (2) the receptor cells and generation of signals (e.g., mechanoreceptors, chemoreceptors, thermoreceptors, osmoreceptors, humoral receptors, etc.), or (3) the various afferent pathways (autonomic/neural vs. humoral [immune or endocrine]) — see Quadt et al. (2018). For instance, one may present the interoceptive systems in terms of organ systems (e.g., cardiovascular) and within each system we can evoke the type of receptors (e.g., baroreceptors, chemoreceptors present in blood vessels [e.g., carotid body/sinus] and heart chambers) and the afferent pathways (i.e., involved afferent fibers, etc.). For the sake of simplicity and with an eye for engineering, we highlighted in table 1 the specific channels of information, their respective setpoints, sensors, fibers, and their role in psychopathology.

2.2. Interoception as hierarchical predictive processing.

In recent decades, the classic Helmholtzian idea about the brain behaving as a prediction engine has resurfaced under the umbrella term of predictive processing. Within a hierarchical model of multisensory integration, the brain entails a predictive model in which ascending prediction errors are conveyed to higher levels to update expectations about states of the world. These expectations in turn provide descending predictions to lower hierarchical levels. At any level, signals are compared with top-down predictions to form a prediction error—informing expectations at the higher level (Ainley et al., 2016; Bastos et al., 2012; Parr et al., 2018b; Rao and Ballard, 1999; Shipp, 2016). This process of Bayesian belief updating continues until prediction error is minimized throughout the hierarchy; thereby furnishing posterior expectations at higher levels of abstraction that provide the best account of sensory input at the lowest level.

This formulation of perceptual synthesis in the brain is arguably one of the most influential accounts in cognitive neuroscience. However, it does not say much about action. Active inference extends the predictive processing account of brain function by noting that the same imperatives underlie perception and action; namely, resolving uncertainty or minimization of prediction errors (see figure 1). The predictions of motor and autonomic sensations can be regarded as providing set points for motor and autonomic reflexes (Friston et al., 2011; Parr and Friston, 2018; Seth and Friston, 2016). In this way, deeply informed predictions drive our (motor and autonomic) behavior; such that top-down predictions are fulfilled. For further reading, we refer the reader to the rich literature on the role of forward and inverse inference models in the motor system (e.g., see research by Wolpert (1996), Bhushan & Shadmehr, 1998, 1999).

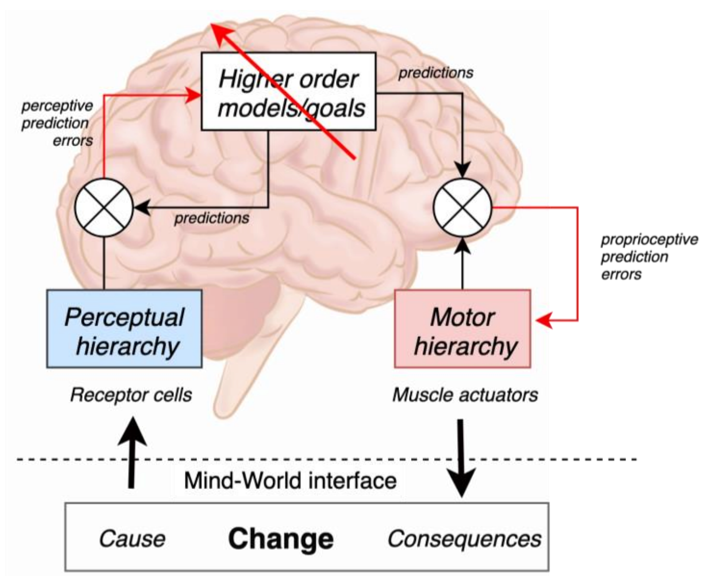

Figure N: Perception models afferent changes in states of the world detected by receptor cells (e.g., in the retina) all along the perceptual hierarchy. In this control diagram, ⊗ denotes a comparator. The red arrows denote inference and learning (i.e., driven by prediction errors) that compare (descending) predictions with (ascending) sensations. Cognition and higher order processing attempt to predict sensory input and futures states of the world based on available (generative) models; minimizing prediction error. Action organizes the motor hierarchy in an attempt to actively control the efferent consequences of ongoing events; namely, by modifying causes anticipated through perceptual means, thereby altering the system' dynamics to make them more predictable *(i.e., less surprising). Though not specified on this diagram, perception can be further subdivided into interoception and exteroception; respectively, modelling changes in the internal and external world. Emotion—and related notions of selfhood—usually arise via predictive processing of interoceptive sensations, often known as interoceptive inference (Seth, 2013, 2014; Seth & Friston, 2016). Adapted from (Schoeller et al., 2022).*

2.3. Interoception and emotion.

While interoception mostly occurs below the level of conscious awareness (e.g., cardiac, thermal, or respiratory regulation is below conscious control), we find that conscious bodily signals are crucial in the emergence of emotions (this is sometimes referred to as the James-Lange hypothesis). This has led to a model of emotional processes as explanation for interoceptive variation (Barrett, 2016). In this view, emotions are inferred as a high-level construct or hypothesis that provides a simple explanation for concurrent sensations (Barrett, 2016; Seth and Friston, 2016; Barrett and Simmons, 2015). Historically, hypotheses about emotion construction date back to William James and Wilhelm Wundt, but in modern times, the hypothesis can be traced to work by Mandler in the 1980s (2003), Schachter & Singer (1962), and Russell (2021).

Interoception figures in an important way in this kind of emotional inference; in the sense that being in an emotional state; e.g., 'I am anxious' will predict the consequences of being 'anxious' (i.e., why I may feel such or such changes). These consequences will, almost inevitably, include interoceptive sensations (e.g., gut feelings, some thermal changes, accelerated heart rate) that accompany the reallocation of attention towards bodily sensations or changes in the external world (Barrett, 2016; Barrett and Simmons, 2015; Craig, 2002, 2013; Seth and Friston, 2016). In turn, interoceptive sensations will usually feed back into the associated emotional state — e.g., throat sensation or dyspnea as both correlation and cause of fear and anxiety in somatic forms of obsessive-compulsive disorder. To make sense of this bidirectionality, Barrett's (2017) introduced the distinction of interoceptive feeling (continuous) vs. emotional concepts (discretized). Hence, interoceptive inference is an essential link between emotional state and their attached bodily sensations (i.e., the somatic markers), as both the cause and the correlate of the emotional states. Here, we begin to understand the relevance of technologies manipulating interoceptive signals in a systematic and controlled fashion for the diagnosis of and intervention on psychopathology, and their relevance for making sense of empirical data.

2.4. Interoception and second-order predictions.

The relationship between interoception and emotion can be taken a step further. Besides interoception tracking changes relative to homeostatic set-points, as was the focus of early predictive accounts of interoception (see Seth 2013), recent models of interoception suggest that body perception may also play a role in tracking the overall rate of change in error management over time (Joffily & Coricelli 2013; Hesp et al. 2019; Schoeller et al., 2018; Kiverstein et al. 2017), resonating with the original idea of allostasis (see Seth & Tsakiris, 2018). Allen and colleagues have introduced the model of self-interoceptive inference to account for how interoceptive cues may bind to exteroceptive signals and suggest the insula as a potential hub where these signals are integrated (Allen et al., 2022; Nikolova et al., 2021).

The most recent literature on the topic emphasizes the role of interoception and the conscious monitoring of the organism's action upon its environment (Marshall et al., 2018). Organisms track the 'fitness' of their model, in part, through a sensitivity to the rate at which overall prediction errors are reduced relative to expectations. In addition to tracking simple increases and decreases in prediction errors. This kind of modelling has very concrete consequences in terms of how we conceptualize emotions. For example, Schoeller (2015a) suggested a model of emotional chills as a null learning rate (denoting a local peak value: where the subject cannot learn more nor less). This model of emotional chills in terms of precision accounts both for their emergence in a context where predictions are fulfilled (say while listening to music or engaging with a film) and during traumatic event where no control can be exerted on the situation (in case of social phobia or during a car accident for example). What is common to both occurrences is the precision-weighting associated to prediction errors (Schoeller & Perlovsky 2016; Schoeller, 2015b) and the crucial role of some interoceptive (here, thermal) anomaly as a somatic marker for the emotion suggests novel avenues for interventions as we detail in the following section. This focus on precision-weighting has also some important consequences for driving experimental results. For example, extending on this line of research Sarasso and colleagues showed that chills were systematically related to improvements in memory, cognition and attention (Sarasso et al., 2021; Sarasso et al., 2019; Sarasso et al., 2020b; Sarasso et al., 2020a).

2.5. The manipulation of interoception under Bayesian formulation.

To better understand how interoception relates to a process of expectations and its ultimate role in driving behavior, it is useful to make a brief *détour* and consider the special case of interoceptive illusions. While we detail some concrete examples of interoceptive illusions in the next section, this subsection introduces some basic problems and definitions.

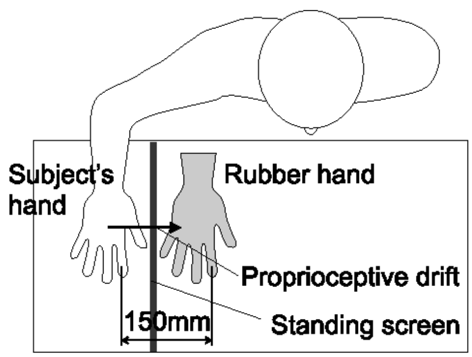

Figure 6. The rubber hand illusion. Interoceptive illusions generate some discrepancy between the "inferred" value of H and the "real" value of H, through false feedback.

Interoceptive illusions can be tentatively defined in analogy to proprioceptive illusions (e.g., the rubber hand illusion illustrated in Figure 5). In a standard Bayesian perceptual inference setup, the human subject must infer some hidden variable *H* (e.g., the position of the arm), based on prior information (e.g., my arm is connected to the rest of my body) and some sensory observations *O* (e.g., some incoming visual and proprioceptive signals related to my arm). Here, *H* is the inferred cause of *O*, i.e., a generative model of *O*. An illusion implies a situation where *H*, the "inferred" (subjective) position of the arm differs significantly from the "actual" (objective) position of the arm — whether that inference is reported explicitly (by conscious self-report) or implicitly (by unconscious behavior). In the rubber hand illusion, this can be induced (for example) by providing some false (visual) feedback, as a direct consequence of the above Bayesian formulation (Allen & Tsakiris, 2018). The inference implies a generative model, a body model or schema, whose two key components are the priors $P(H)$ and a likelihood function $P(O|H)$. Such Bayesian causal inference models of multisensory perception (visual, proprioceptive, and tactile) reproduce the rubber hand illusion accurately and predict the empirical observation that the illusion can occur without tactile simulation and be enhanced by synchronous stroking (see Samad et al., 2015).

We propose that a similar mechanism may be at play in the interoceptive domain. This implies some sort of "interoceptive schema" that is updated in the same Bayesian fashion as described above (i.e., testing hypothesis about hidden cause *H* against observed sensory outcome *O*). Imagine that the hidden state *H* concerns some homeostatic parameters such as hunger, thirst, effort, or fatigue level (i.e., a deviation from homeostatic setpoint). One can infer *H* by considering priors and observations—most of which are interoceptive observations (e.g., heart rate), but some of the evidence for *H* may also come from exteroceptive observations.

We saw previously that the weighting of prediction errors at various levels in the cortical hierarchy occurs in proportion to their precision, that is their reliability or predictability — understood in statistical terms as the inverse of variance (Ainley et al., 2016; Palmer et al., 2019; Parr et al., 2018a; Seth and Friston, 2016). At the lowest hierarchical level, precision scores the confidence placed in sensory information, whereas at higher levels, it indicates the reliability of prediction errors. This precision itself has to be estimated—a process often associated with attention (as a psychological function) and synaptic gain or efficacy (as a physiological structure) (Ainley et al., 2016; Auksztulewicz and Friston, 2015; Brown et al., 2013; Limanowski and Friston, 2018; Vossel et al., 2014).

This model offers a mechanistic overview of how non-interoceptive cues may play a role in interoceptive processing, as nothing prevents the estimation of effort or hunger levels to depend on a combination (or integration) of interoceptive, exteroceptive, and proprioceptive signals. We can think of this integration hierarchically, whereby lower levels comprise fairly modular homeostatic predictive coding loops (e.g., in the spine and brainstem), which maintain tightly controlled homeostatic setpoints on temperature, respiration, cardiac pulsation, etc. At higher hierarchical levels, interoceptive information will be primarily relevant for a multi-modal self-model. One model of "interoceptive self-inference" (Allen & Tsakiris, 2018) argues that at the most domain-general level (i.e., metacognition), interoceptive states are mostly used to estimate expected precision for both interoception and exteroception (Allen et al., 2018, 2019, 2022). Estimates of future expected precision are a condition on joint interoceptive and exteroceptive prediction errors.

Table 1. Classification of interoceptive systems based on human physiology (i.e., setpoints, receptor fields, fibers), technology (e.g., sensors and effectors), and psychopathology (signs or symptoms). Note that each system is susceptible to the influence of cycles: e.g., Infradian (e.g., deep sleep, REM sleep) Circadian (e.g. sleep-wake, temperature, hunger control via ghrelin/leptin, diurnal cortisol), and Ultradian (e.g., menstrual cycles in women). We extracted the data from Khalsa et al., 2018; Felten et al., 2016; Bernston & Khalsa, 2021; Chen et al., 2021)

System	Human physiology	Technology	Psychopathology
Thermoception	Receptor fields & fibers: Free nerve endings (Aδ and C fibers) projecting to spinal lamina I. Setpoint: 37° Celsius	Sensors: thermometer, CASE IV system; Whole-room calorimeter Peripheral actuator: peltier elements, room temperature	Panic disorder, Mood and affective disorders, Anxiety disorders, Substance use disorder (chills, high or low respiratory rate)
Respiratory	Receptor fields: Chemoreceptors sense and respond to partial pressures of arterial oxygen and carbon dioxide as well as blood pH. Setpoint: during normal unlabored breathing (i.e., eupnea), PaCO2 is maintained within a few mmHg of ~35 mmHg	Sensor: motion sensors (IMU), microphone, thermal camera at the nose, oxygen sensors, bio-impedance based respiration sensors. Center actuator: Many substances can impact respiratory and heart rates. In the laboratory, the most used systems to affect cardiovascular changes are the CO2, and caffeine challenge.	Anxiety, panic disorder (dyspnea, choking) , Somatic OCD, Substance use disorder (high or low respiratory rate)
Cardiovascular	Receptor fields: Baroreceptors involving PIEZO1 and PIEZO2 ion channels (i.e.,in the aorta and carotid arteries). Fibers: Information from baroreceptors (i.e., in the carotid sinus) about increased arterial pressure travel the afferent axons of CN IX which project to the caudal nucleus solitarius leading to decreased blood pressure and reflex bradycardia (Felten et al., 2016). Information from chemoreceptors in the carotid body about CO2 (i.e., hypoxic state) and low pH to a lesser extent travel afferent axons of CN IX which project to the medullary caudal nucleus solitarius leading to increased respiration (Felten et al., 2016). Setpoint: The normal resting adult human heart rate is 60–100 beats per minute. Normal systolic blood pressure is thought to be about 130 mmHg.	Sensors: heartbeat evoked potentials captured by EEG/MEG, stethoscope, electrodes (EEG, MEG), ultrasound, microphones, motion sensors, etc.	Panic disorder elevated HR/BP, palpitation, flushing), Substance use disorder (high or low HR/BP), Post-traumatic stress disorder (high HR/BP), Major depressive disorder (reduced baroreflex sensitivity, heart rate variability, heartbeat evoked potentials amplitude, heartbeat perception accuracy), ASD (impaired interoceptive accuracy based on the heartbeat tracking tasks in some studies; that might be associated with alexithymia) Eating disorders (mixed findings about interoceptive accuracy using heartbeat perception tasks in anorexia nervosa and bulimia nervosa)
Chemosensory	Receptor fields: Carotid body chemoreceptor sensitive to pCO2, pH, and pO2 (to a lesser extent); specific ion channels involved at the receptors level: e.g., Twik-related acid-sensitive K+ channels sensitive to pO2 and acidosis. Osmoreceptors sensitive to local osmotic pressure (involved in metabolic adjustment and thirst aiming to regulate body water imbalance). Setpoint: various	Sensor: Peripheral actuator: Center Actuator: Exteroceptive stimuli: audiovisual stimulation	?
Gastrointestinal	gastrointestinal humoral receptors, involving leptin/ghrelin/cholecystokinin. Hunger contractions regulate food intake. Secretion of the saliva at the salivary glands: basal - 800 – 1500 ml/day. Vomiting, gastric motility, EGG phase and frequency.	Sensor: Electrogastrography, Sallivaomics	Chronic stress, Panic disorder (nausea), Eating disorders, GAD (nausea and other gastrointestinal complaints), ASD
Rectogenital	Sexual stimulation: In men, the initial component of sexual response to erotic stimulation is engorgement of erectile tissue culminating in penile tumescence and erection. After erection but prior to ejaculation, lubricating fluid is secreted from Cowper's glands. In contrast, in the female the initial response to sexual stimulation consists of vaginal lubrication, with tumescence of the genital (erectile) tissue (glans clitoris) occurring afterwards but prior to orgasm.	Stimulus: Audiovisual Sexual Stimulation (AVSS) Sensor: RigiScan® by GoTop medical Actuator: vibrotactile stimulation, vacuum constriction device, penile prosthesis implants Medical therapies such as phosphodiesterase type 5 inhibitors (PDE5-Is), invasive methods such as	generalized anxiety disorder (GAD), social anxiety disorder, obsessive-compulsive disorder (OCD), and post-traumatic stress disorder (PTSD). Anxiety is associated with deficits in all phases of the sexual response cycle. In male, they take the form of erectile dysfunction and premature ejaculation. Low sexual arousal in depression.

		intracavernosal injection therapy of vaso-active substances	

3. Interoceptive technologies: Intervening on bodily signals

In the previous section, we presented the notion of body perception as a process of inference, aiming to maintain vital parameters stable. We discussed briefly the relation between interoception and emotion and the role of second order interoceptive predictions in emotional processes (predictions about interoceptive predictions). We introduced a table reviewing the various interoceptive systems (thermoception, respiroception, cardioception, chemosensations, gastric and rectogenital perception), and detailed for each the various sensor and effector technologies, and the dysfunctionality of these systems in various psychopathologies. We will now review existing technologies for manipulating interoception in clinical settings. Our aim is to understand their modalities of functioning, in order to assess in the next section their practical relevance in clinical settings.

Many kinds of interoceptive technologies exist whether in the laboratory or in various markets (health, entertainment, education). In order to make sense of the tools readily available to scientists and clinicians, a tentative typology is in order. Following the model introduced in the previous section, we can categorize interoceptive technologies depending on the hierarchical level where the error is subsumed under a more general (explanatory) model of the situation:

1. **Artificial sensations**: low-level bottom-up interoceptive stimulation at the level of the receptor cells, which result from controlled stimulation of the autonomic network (e.g., Di Lernia et al., 2018a, 2018b; Riva et al., 2017, 2019);
2. **Interoceptive illusions**: high-level interoceptive modulation, provided by (indirect) exteroceptive contextual cues altering the top-down predictions concerning the current state of the body and the most likely causes of interoceptive signals (e.g., Iodice et al., 2019; Pezzulo et al., 2018).

We will see later that the combination of these two types of technology may lead to interesting outcomes in terms of what we call emotional augmentation. Indeed, we are not aiming for an exhaustive review of all interoceptive technologies currently available, but an introduction to their modes of functioning and the specificities of various streams of technologies attempting to intervene on bodily signals to induce affective, cognitive, or behavioral changes.

3.1. Artificial sensations: Direct bottom-up interoceptive modulation.

The first, most basic, level of interoceptive engineering is that of bottom-up interoceptive modulation, which we refer to here as artificial sensations — i.e., an interoceptive or exteroceptive stimulus influencing directly the activity of the interoceptive system. There are few techniques to induce low-level modulations and their effects on brain and behavior are manifold. To show the range of possibility, we restrain our discussion to two known techniques with opposite effects: 1) C-tactile induced safety by affective touch and 2) CO2-induced fear by respiration-based illusions. What we aim to emphasize here is that the notion of artificial sensation is valence-independent.

a. *C-Tactile Stimulation (Affective Touch)*

An approach that is gaining in popularity is affective touch: the stimulation of C-Tactile small unmyelinated fibers. Specifically, slow (at 1–10 cm/s velocities), light-pressure (< 2.5 mN), dynamic (moving along the skin) touch has been shown to change the interoceptive experience. Importantly, there may be a dedicated neurophysiological system, the C-tactile (CT) system, coding this type of stimulation (Croy et al., 2016). At the peripheral level, the interoceptive system is composed of Aδ and C polymodal afferent fibers able to collect and convey a wide range of inputs. These fibers report to the Lamina I spinothalamocortical pathway (Craig, 2003) and, through this, to the insula and the interoceptive matrix. The interoceptive polymodal afferents collect and report well-studied information—such as afferents from temperature and noxious stimuli—but they can also report subtle changes in muscle contraction (Wilson, Andrew, & Craig, 2002), hormonal, endocrine, and immunological response, along with metabolic activity (Craig, 2002). Interestingly, this afferent system differentiates in free tactile arborization on the skin, creating a secondary touch system with deep involvement in different psychophysiological pathways (Olausson, Wessberg, & McGlone, 2016).

Though unusual in psychophysiology, we consider dermal C-Tactile sensations as interoceptive to the extent that they are connected to the same unmyelinated C-fibers network that conveys cutaneous temperature and pain sensations (Craig, 2015) and are primarily processed by the left insula rather than the somatosensory cortex (Gordon et al., 2013). The C-Tactile system provides non-invasive access to the interoceptive system, and stimulation of these afferents resulted in interesting effects such as modulation of body ownership (Crucianelli, Metcalf, Fotopoulou, & Jenkinson, 2013), a social buffering function in pain perception (M. von Mohr, Krahe, Beck, & Fotopoulou, 2018), and the ability to reduce feelings of social exclusion (Mariana von Mohr, Kirsch, & Fotopoulou, 2017).

This line of research suggests the C-Tactile system could be a potential target for interoceptive modulation with diverse applications. Crucially, interoceptive technologies capable of stimulating the CT interoceptive network have been developed (Fig 3) and several authors have used these technologies to modulate the autonomic parasympathetic response (Di Lernia et al., 2018a, b; Triscoli, Croy, Steudte-Schmiedgen, Olausson, & Sailer, 2017) and chronic pain (DiLernia et al., 2020). Refer to (DiLernia et al., 2020) for a full description of the protocol. In this context, low-level pre-conscious interoceptive modulation could rewrite dysfunctional responses to external or internal stimuli whereby, for example, CT stimulation could provide parasympathetic activation in a sympathetic context (e.g., phobic response to a non-threatening stimulus), effectively rewriting the interoceptive status and ultimately updating the prior beliefs that underwrite affective inference.

a. *Panicogenic hypercapnia*

It is well known that the cardiorespiratory changes associated with CO2 intake can affect affective and cognitive processes. Several protocols exist to induce fear, worry, and panic by perturbing cardiorespiratory mechanisms such as the acute hyperventilation challenge test (Sardina et al., 2009), the breath-holding test (Nardi et al., 2002), or the caffeine challenge (Charney et al., 1985). Both healthy and panic patients experience behavioral, physiologic, and biochemical reactions to carbon dioxide (Nardi et al., 2004; Woods, 1988). The acute hyperventilation challenge (~30 breaths/min for 4 min) is another technique to provoke CO2-induced ‘artificial’ panic attacks (also known as panicogenic hypercapnia) in both healthy and anxious patients (Tural, 2020; Van der Hout & Griez, 1984).

Panic attacks begin with a surprising onset of intense fear or terror, associated with many autonomic, especially cardiorespiratory symptoms (Roy-Byrne et al., 2006). Evidence suggests that, in contrast with healthy controls, subjects with panic disorder develop a panic-like reaction within minutes after breathing a gas containing 5% CO2 (Drury, 1919). These reactions are similar to those induced by another stimulation with similar anxiomimetic effects, namely caffeine. Similarly, oral administration of caffeine (10 mg/kg) produces significantly greater increases in anxiety, nervousness, fear, nausea, palpitations, restlessness, and tremors in panic patients compared with healthy subjects, noting that the behavioral effects of caffeine were similar to those experienced during panic attacks (Charney et al., 1985).

Interestingly, interindividual differences in susceptibility to the CO2 tests lead to different autonomic responses. Nardi and colleagues (2004) described the clinical features of hyperventilation-induced panic attacks in panic disorder patients and compared them with their spontaneous panic attacks. In the sample that did experience panic attacks, they found that artificially induced panic attacks were similar to organic, spontaneous panic episodes. However, in those that did not develop panic after hyperventilating, the spontaneous panic attacks were accompanied by thermal changes (e.g., chills and hot flashes) and less often accompanied by respiratory symptoms such as shortness of breath, choking sensation, chest pain/discomfort, paresthesia and fear of dying. Patients who panicked during the test more often had a family history of mental disorder, were older at the disorder onset and more often had a history of depressive episodes (Nardi et al., 2004). Hence, beyond mere interoceptive exposure, we see that such interoceptive intervention hold potential for discriminating patients, pathologies, and perhaps treatment response.

3.2. Modulating the context: exteroceptive influence on interoception.

We saw that direct interoceptive stimulation of interoception by CO2 intake or C-tactile stimulation can induce respectively general feelings of fear or safety. We can combine such direct interoceptive stimulation with exteroceptive cues to further discriminate the emotion and lead to a predictable outcome. As we detail in this section, sometimes mere exteroceptive stimulation is sufficient as with interoceptive illusions or false feedback (Makkar et al., 2012). The second form of interoceptive engineering consists in delivering a false, illusory, feedback signal in a particular context to generate predictable outcomes.

Though historically, the study of illusions chiefly concerned the domain of exteroception, an increasing number of studies concern the controlled manipulation of physiological variables by false interoceptive feedback (e.g., real-time visual or auditory cues on breathing or cardiac patterns) or sensory substitution (i.e., changing information from one sensory modality like audition into stimuli of another sensory modality like touch). Crucially, the effects of these interoceptive illusions can be increased with coordinated exteroceptive stimulation. Some examples would be the thermal grill illusion, whereby subjects pressing a hand against a fake grill experience an illusion of burning heat (Craig & Bushnell, 1994), false auditory heart rate during physical exercise inducing an illusion of effort (Iodice et al., 2019), or false cardiac feedback modulating romantic attraction (Valins, 1966).

a. *Proprioceptive illusions*

Even though not strictly interoceptive, several bodily illusions have been discovered in the domain of proprioception (the perception of the body in space, which according to Sherrington should not be counted as interoceptive), as in the rubber hand illusion, the Pinocchio illusion, body distortions illusion, the out-of-body illusion, and the phantom nose illusion. Crucially, these illusions produce actual effects on physiology and behavior. Experimentally induced out-of-body experiences have profound consequences on episodic remembering for events while under the illusion (Bergouignan et al., 2014). The rubber hand illusion has been shown to decrease the subject’s body temperature and to slow down the processing of tactile input (Moseley et al., 2008; Hohwy and Paton, 2010; Van Stralen et al., 2014; Aspell et al., 2013) and to trigger the participants' autonomic responses when perceiving a threat to the rubber hand (Armel and Ramachandran, 2003). Some cardio-visual analogues of multisensory illusions have also been developed (see Suzuki & Seth et al; Sel, Azevedo, Tsakiris).

a. *Interoceptive illusions proper*

Beyond mere proprioceptive illusions, a wide range of physiological variables have been manipulated such as oxygen consumption (Van Diest et al., 2007), thermoregulation (Jain et al., 2020, see also Janssen et al., 2002; Poguntke et al., 2019), cardiorespiratory pathways (Hassanpour et al., 2016) and a variety of other physiological parameters (e.g., Suzuki et al., 2013; Aspell et al., 2013; Solca et al., 2018, 2020; Heydrich et al., 2018; Haar et al., 2020; Schoeller et al., 2019; Costa et al., 2017, de Rooj et al., 2017; Windlin et al., 2019). Some researchers have also manipulated interoception by indirect means (by providing additional exteroceptive, say, somesthetic, information about interoception). For example, acoustic feedback about heart-rate during effort (Valins, 1966; Iodice et al., 2019), haptic feedback about heart-rate during public speech (Azevedo et al., 2017), time estimation of interoceptive stimuli (Di Lernia et al., 2018b), Other examples of interoceptive manipulations include visceral illusions during placebo conditions and other contextual manipulations, context-related pharmacologically induced visceral illusions (Khalsa et al., 2018), direct brain-stimulation induced vestibular illusions (Mazzola et al., 2017), auricular vagal nerve stimulation (Verma et al., 2021), and even corporeal illusions following spinal cord damage (Scandola et al., 2017).

a. *Scientific and clinical relevance*

What current scientific limitations can interoceptive illusions help overcome? Indeed, illusions afford an excellent opportunity to study the celebrated James-Lange hypothesis, that physiological changes may cause (rather than being the consequences of) specific emotions (James, 1890). These classical questions in psychophysiology have seen a regain of interest in recent years with the work of Antonio Damasio and colleagues on so-called somatic markers, leading to the working hypothesis that "changes in body state cause automatic physiological reactions and mental experiences — feelings — such as hunger, thirst, pain or fear" (Damasio & Carvalho, 2013; see also Craig, 2015; Seth and Friston, 2016). Interoceptive illusions may provide an experimental paradigm to examine these century-old questions and test computational models of the underlying physiological dynamics (Schoeller et al., 2018).

Relative to the model introduced in the first section, interoceptive illusions may help overcome several limitations in our understanding of the prediction mechanism of interoception. First, the hypothesis that we have something like an interoceptive model (or schema) is still to this day speculative. If there is indeed such a thing as an interoceptive schema, it is still not straightforward to define what are the relevant hypotheses that compose the putative interoceptive model (are these the setpoints introduced in table 1 or something different? Can we distinguish hierarchies amongst them and points of contact?). It is not obvious to define what are the prior and likelihood function of a putative interoceptive model, e.g., what observations (interoceptive or otherwise) are used to update H; and what is the precision of specific interoceptive channels (see Allen et al., 2019 for a tentative model).

Second, it is not straightforward ever to assess when one's "inferred" H differs from the "real" H (e.g., while for the rubber hand it is quite easy to measure the "real" position of the arm, the "real" value of H in your interoceptive system may not be trivial to measure). Finally, it is impractical to provide false interoceptive feedback (for various reasons). One subtle point is that if false feedback is delivered about (for example) heart rate frequency, one's "real" heart rate aligns or synchronizes to the false feedback. This would not count as an illusion according to our definition (and the false feedback would not be false anymore). In the rubber hand domain, this would be like moving your arm where the rubber hand is (a marvellous example of active inference)—so that there would be no more discrepancy between "inferred" and "real" hand position and hence no illusion.

a. *Motivation for further research in interoceptive illusion*

One primary motivation for designing novel interoceptive illusions is to address some of the above limitations. For example, if a subject is provided with false feedback about heart rate frequency and we observe that this manipulation influences their estimate of effort level (with the real heart rate unchanged), we can tentatively conclude that her internal generative model of effort level considers (the false) heart rate (in the likelihood model). Engineering cognitive illusions from interoceptive modulation is a first step toward manipulating the precision of various signals (to assess whether the update is Bayesian / precision-weighted or not). Many more illusions can be engineered using similar logic, in order to study 1) what hidden variables the brain monitors, 2) what interoceptive channels are relevant for their estimate, and ultimately 3) whether the idea of an interoceptive schema makes sense or not. Interoceptive illusions present a "window" into the interoceptive domain and its mechanisms (i.e., its generative models), that would otherwise be difficult to study experimentally. Importantly, one can then consider whether different clinical populations are more or less susceptible to interoceptive illusions, whereby poor susceptibility to interoceptive illusions may indicate poor interoceptive precision. In the last section of the article, we explore the relevance of interoceptive illusions to various clinical conditions and psychopathologies such as anhedonia and alexithymia.

4. Emotional augmentation

A third category of interoceptive intervention can be distinguished when the stimulation is delivered with temporal and spatial accuracy targeting the so-called somatic markers of emotions, with contextual cues of personal significance (or contextual cues that may therefore gain personal significance) to the participant in the experiment (e.g., some audiovisual stimulation or virtual reality environment). For example, Haar et al. (2020), could enhance cognitive and affective processing associated with the feeling of chills through timely thermal stimulation with salient audiovisual stimuli. Their thermoelectric device, called the Frisson, adheres to the back of a user and imitates the sensation of an aesthetic chill traversing down the spine at a particular time in a film or musical piece where aesthetic chills are experienced on average. Note that in this context the Peltier motors that comprises the device stimulate the thermoreceptors that give rise to the feeling of cold during psychogenic shivers (and that lead to the thermogenic shivering). Hence, the bodily response is not augmented *per se* (as that would amount to increasing temperature, not decreasing it), but rather stimulated. The chills response, that is ordinarily psychogenic (though most likely unconscious), is increased by means of additional (physical) evidence for the belief “I am cold”. Evidence suggests that this process may increase the propensity for chills and their intensity, but also augment the emotional responses in terms of pro-social behavior for example (Schoeller et al., 2019a, 2019b; Haar et al., 2020).

A second example is the MoveU device (figure 4), which is worn on the neck and uses galvanic vestibular stimulation to modulate nausea in virtual reality (VR), opening up pathways to modulate or influence disgust via vestibular stimulation (Sra and Jain, 2019). Other devices are built to generate the illusion of effort in VR using electronic muscle stimulation (Lopes, 2015): There is no shortage of devices that can alter our interoceptive sensations, and many can be mined from the field of human computer interaction, which builds wearable electronic devices to modulate sensation for alignment with visual virtual reality experience (Carr & Horowitz, 2020). These devices couple physiological sensors with electronic actuators, sensing the body even as they modulate it. Any technology built to induce interoceptive illusions must contend with the complexity of this loop between device actuation, bodily sensation, cognitive effect, and a consequent change in appraisal regarding device-driven sensations.

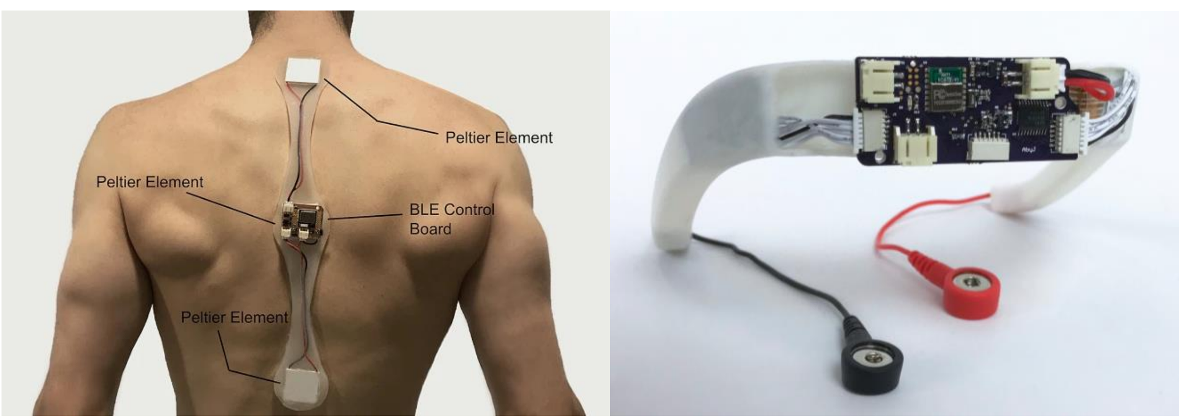

Figure 5. The Frisson and MoveU devices, designed respectively to enhance aesthetic chills (or psychogenic shivers) and to reduce motion sickness in VR.

Crucially, the downstream effects of these emotions can be manipulated experimentally. For example, the Frisson device enhances ratings of pleasures (associated with dopaminergic discharge during the chills), and pro-social tendencies known to derive from chills (Fukui & Toyoshima, 2014). Pezzulo and colleagues have shown that cardioacceleration after exercise facilitates the processing of fearful but not disgusted faces (Pezzulo et al., 2018). One core difficulty here is the distinction between an illusory sensation and an organic one: A device-driven chill or nausea experience can transition from one which is mistakenly perceived as internally generated into one which is in fact organic, as illusory nausea begets real nausea (if this distinction remains meaningful). This subtle change is hard to detect with wearable sensors and requires teasing apart, which should be a key focus for future work before tools for interoceptive illusion can enter clinical settings.

5. Interoceptive entrainment

When an incoming “error” sensory signal is sustained, the stimulation may cause the system to adjust its expectations, which may ultimately lead to temporal coordination (i.e., synchronization) between false feedback and actual interoceptive activity (Ferrer & Helm, 2013). In complex systems theory, entrainment is broadly defined in psychophysiology as the synchronization of nervous systems to their environment. Entrainment is most evident in music and dance, where the physical tempo of a song can directly influence breathing and heart rate, and the heart rates of singers in unison can speed up and slow down synchronously (Vickhoff et al., 2013). Perhaps the overarching case of human physiological entrainment is the spontaneous temporal coordination of mother-infant heart rhythms through episodes of interaction synchrony (Feldman et al., 2011). The term “neural entrainment” describes the synchronization of neural activity with the constant properties (frequency) of repetitive external stimuli (Thut et al., 2011). This synchronization can be elicited by many stimuli: from rhythmic auditory, visual, and tactile sensory stimulation, to controlled respiration, to magnetic and electrical fields generated by transcranial stimulations (Zmeykina et al., 2020; Vosskuhl et al., 2018). Clayton et al. (2005), suggested that two or more autonomous oscillating systems must be present in order to distinguish entrainment from other concepts. For example, in the human body, the periodic firing of neurons and different interoceptive processes including cardiac activity and respiration can be conceptualized as oscillating systems (Trost et al., 2017). This has been described as “autonomic physiological entrainment”, the tendency for biological rhythms, which are under the control of the sympathetic and para- sympathetic branches of the autonomic nervous system, to entrain to externally perceived rhythms (Trost et al., 2017).

Evidence suggests that interoceptive signals and their interpretation can be modulated using rhythmic auditory, tactile and visual stimuli, suggesting what is referred to as an entrainment pattern. For example, Kim and colleagues (2018) used a biofeedback device to enable real-time synchronization of relaxing music to the listener’s pulse. Compared to controls, the entrained-tempo condition led to a significantly stronger increase in peripheral blood flow and subjective well-being, suggesting its ability to generate a psychophysiological relaxation response. In a later study, Czub & Cowal (2019) used exposure to a breathing avatar in virtual reality to change the respiration rate of the observer. Specifically, the avatar was first breathing for 60 seconds in accordance with the observer's respiration rate. Then, it was either slowing down or speeding up, each condition lasting for 180 seconds. Their results suggest the efficacy of the provided visual cue in entraining participants’ respiration rate, with a clinically significant outcome. Another study by Azvedo and colleagues (2017) used a device able to deliver a slow heartbeat-like vibration to the wrist. Their results suggest the entrainment generated by the device had a calming effect in both physiological measures of arousal and subjective reports of anxiety.

Note that these studies do not provide direct evidence for entrainment effects, but a general trend in interoceptive research. Perhaps this research trend has the most to benefit from studies of real-world interactions and physiologic synchronization, demonstrating that collective ritual may evoke synchronized arousal over time between active participants and bystanders (Konvalinka et al., 2011). In a comprehensive article, Dumas & Fairhurst have reviewed the multiple type of reciprocity and alignment process during human interactions, from unconscious physiological coupling to intentional motor coordination and semantic alignment (Dumas & Fairhurst, 2021). In clinical settings, physiological synchronisation and behavioral mirroring has been suggested as a mechanism of the patient-clinician interaction, which remains yet to be enhanced by technological means (Ellingsen et al., 2020).

Table 2: A review of interoceptive interventions at various levels of the cortical hierarchy

Intervention	Definition	Studies

Artificial sensation	Low-level direct stimulation of interoceptive signals. Also known as interoceptive modulation or interoceptive exposure.	Crucianelli et al. 2013; von Mohr et al., 2018, 2017, Di Lernia et al., 2018a, b; Triscoli et al., 2017
Interoceptive illusion	Manipulation of contextual influences on interoception, altering the precision weighting of some interoceptive expectations at intermediate levels by means of exteroceptive cues.	Moseley et al., 2008; Hohwy and Paton, 2010; Van Stralen et al., 2014; Aspell et al., 2013; Armel and Ramachandran, 2003; Craig & Bushnell, 1994; Iodice et al., 2019; Valins, 1966; Van Diest et al., 2007; Jain et al., 2020, see also Janssen et al., 2002; Poguntke et al., 2019; Azevedo et al., 2017; Di Lernia et al., 2018b; Schoeller et al., 2019; Costa et al., 2017, de Rooj et al., 2017; Windlin et al., 2019); Hassanpour et al., 2016
Calibration or entrainment	Synchronization of perception with stimulation	Azevedo et al., 2017; Ferrer & Helm, 2013; Vickhoff et al., 2013; Feldman et al., 2011
Emotional augmentation	Temporally precise stimulation of interoceptive signals based on contextual cues. Mixed artificial sensation, interoceptive illusion, and contextual cues.	Schoeller et al., 2019a, b; Jain et al., 2020; Pezzulo et al., 2018; Sra and Jain, 2019

6. Clinical applications of interoceptive technologies

In the previous section, we reviewed some interoceptive technologies and classified them into 3 broad categories: direct (bottom-up stimulation), indirect (exteroceptive influence), and emotional or mixed (combination of interoceptive and exteroceptive stimulation). We organized the various studies and known interoceptive interventions to date in table 2. In this section, we address the crucial question driving this article, the clinical potential of these technologies in terms of diagnosis and treatment. Here again, the article is not meant to be exhaustive but to define potential interventions, and some key elements we can learn from the empirical and theoretical literature, and to be examined in future research.

6.1. Better diagnosis: Using artificial sensations as probes

In the clinical domain and despite the limitations mentioned, interoceptive technologies provide an excellent starting point for tailored intervention in symptom processing and interoceptive training for mental health broadly. A well-known example, which we already discussed in section 3 is interoceptive exposure to treat anxiety, panic, and fear (e.g., Schmidt, 2022). Another clue is provided by studies in the interoceptive basis of craving and addiction, in interoceptive conditioning (Paulus, 2015). Dysfunctional interoception is increasingly recognized as a crucial factor for mental health, and the lack of proper technology to train interoception has been repeatedly emphasized (Khalsa et al. 2018). If deployed at scale and broadly disseminated, interoceptive technologies may offer crucial intervention techniques.

Mounting evidence suggests that interoceptive deficits in the realm of psychopathology manifest most prominently during states of homeostatic perturbation (Smith et al., 2020). The literature on predictive coding hierarchies in interoception and visceral signals is quite abundant (e.g. Smith et al., 2017), particularly as related to psychopathological conditions (e.g. Petzschner et al., 2017), such as depression (Stephan et al., 2016) or post-traumatic stress disorder (Linson et al., 2020). Within the conceptual framework of active inference, it becomes possible to understand disorders of affect in terms of aberrant precision control, mediated by high-level representations of being in one emotional state or another (Clark et al., 2018; Friston, 2017; Parr et al., 2018a; Parr et al., 2018b). Obvious examples here include abnormal mood, stress, anxiety, obsessive-compulsive disorder and possibly other conditions such as autism and post-traumatic stress disorder (Badcock et al., 2017;

Kiverstein et al., 2019; Lawson et al., 2017; Palmer et al., 2017; Peters et al., 2017; Rae et al., 2019). In short, emotional inference and related psychopathology will, on an active inference reading, be accompanied by characteristic changes in the deployment of precision or attention (Adams et al., 2013; Edwards et al., 2012) that is accompanied by changes in the descending predictions of autonomic states. Because interoceptive predictions enslave autonomic reflexes, one would expect to see the correlates of emotional inference in both the central and peripheral (autonomic) nervous systems. For example, changes in the sensory precision afforded auditory or visual stimuli that are accompanied by sympathetic arousal would manifest in terms of changes in the amplitude of evoked potentials; e.g., Modulation of the mismatch negativity by emotional set [1]. Similarly, psychopathology should be associated with aberrant responses to interoceptive stimuli; e.g., nociception in autism [2]

It would be useful to quantify affective stimuli in terms of changes in precision or post-synaptic gain in the central nervous system—and peripheral measures (e.g., pupillary dilatation, galvanic skin response, heart rate variability, etc.). Artificial sensations provide an ideal opportunity to elicit the emotional inference and quantify the central and peripheral responses, for example by using non-invasive EEG and the peripheral measures described above. This protocol is sometimes referred to as aberrant emotional processing (Sadeh et al., 2014). This kind of phenotyping may find a powerful application in psychiatric conditions, both in diagnosis and measuring responses to therapeutic interventions. The idea here is not new. Perhaps one of the earliest examples of using responses to experimental perturbations was the dexamethasone suppression test that showed early promise in terms of phenotyping depression (Naughton et al., 2014). This test can be thought of as a form of 'stress test' used routinely in cardiology measuring cardiac ability to respond to external stress in a controlled clinical environment. The search for valid 'stress tests' for psychiatric syndromes continues—and speaks to a potential role for artificial sensations and interoceptive illusions.

One can imagine several paradigms in which artificial sensations are used to induce emotional processing that would contextualize the attention paid to interoceptive and exteroceptive sensations. For example, maybe for children with autism, artificial sensations that do and do not produce psychogenic shivers could be used to assess interoceptive sensitivity (Ainley et al., 2012; Fealey, 2013); with the prediction that individuals with alexithymia (e.g., Parkinson's disease (Poletti et al., 2012)) would not recognize or infer the difference—and fail to show differential event-related responses as measured with EEG.

More sophisticated designs could address key questions about the ability of individual subjects to modulate or attenuate interoceptive precision; e.g., children with autism (Gu et al., 2015; Lawson et al., 2014; Quattrocki and Friston, 2014; Van de Cruys et al., 2014). For example, using a mood induction paradigm in conjunction with artificial sensations might reveal the interaction between inferred or recognized emotional states and interoceptive responses to artificial sensations. In this example, artificial sensations would play the role of an experimentally well-controlled delivery of interoceptive stimulation, much like affiliative touch or noxious stimulation (Gomez et al., 2014; Gu et al., 2015; Krahe et al., 2013). However, the advantage of artificial sensations is that they do not cause pain and can be administered with very precise timing and somatosensory precision.

To practically realize the potential of artificial sensations—as an interoceptive probe of emotional processing—one would need to quantify the precision afforded by sensory signals. Happily, this can be achieved with the dynamic causal modelling of non-invasive data. To empirically measure precision, it is necessary to estimate the excitability or synaptic efficacy of neuronal representations at different levels in the interoceptive hierarchy. There is an established literature on this sort of estimation using dynamic causal modelling of exteroceptive hierarchies (Adams et al., 2016; Bhatt et al., 2016; Brown and Friston, 2012; FitzGerald et al., 2015; Pinotsis et al., 2014). In this setting, precision is usually associated with the disinhibition of neuronal populations, as measured by changes in intrinsic connectivity or self-inhibition.

5.2. Body-based interventions: Interfacing with the precision system.

We discussed in the first section how emotional valence (positive or negative emotions) tracks and assigns precision estimates relative to selected action policies (how likely some actions are to succeed given empirical priors). This pre-reflective, second-order information provides the agent with a feeling of what is possible given their current skills and the present context. As such, it plays an important role in the development and persistence of various psychiatric conditions (in the form for example of learned helplessness in depression), suggesting avenues for digital interventions. Here we consider the case of generalized anxiety disorder.

a. *Perduring precision in anxiety*

Pathological anxiety is considered to result from a persistent prior belief about one's own inability to manage error (Stephan, Manjaly et al. 2016, Peters, McEwen et al. 2017). A prior exists in this case about the volatility of the environment increasing error. In healthy adaptive systems this expectation about increasing error is corrected for either by updating priors to better fit the actual state of affairs, or by engaging regulatory actions that move the agent towards better opportunities for error resolution. In pathological cases this belief persists even when conditions offer opportunities for the agent to maintain a good predictive fit with the environment. Beliefs about volatility produce negative affective reactions, as we have outlined in the first section of the article, which entrain attention towards anxiety-related stimuli in the world, and drive internal anxiety-related thought patterns and rumination—both of which reinforce the anxiety-related prior (Wild et al. 2018). As the priors become increasingly precise, they also become resistant to updating (Paulus et al. 2019; Paulus & Stein 2006), and the strength of this prior means that there is a loss of top-down inhibitory control over those expectations (see Clark et al. 2018).

a. *Manipulating precision using interoceptive stimulation*

Interoceptive augmentation technology capable of imitating core affective systems related to valence may help to address such disorders by altering part of the bodily feedback process that adjusts precision on negative expectations. In effect, these technologies interface with the biofeedback loop that entrenches the pathological expectations underlying various forms of psychopathologies, including chronic anxiety. From an active inference perspective we can interpret this as augmenting emotional feedback disrupting the attribution of precision that characterizes pathological anxiety. By disrupting the pathological valenced reaction to a social situation, the agent is less likely to be drawn to anxiety-laden stimuli and so be in a better position to succeed in the situation. Success in an otherwise anxiety-provoking situation would increase confidence in managing such situations, and so contribute to a reduction in the pathological belief about their inability to succeed, which is the root condition. A review for some research this direction including VR/AR systems can be found in the fields of regenerative virtual therapy (Riva et al. 2021) and transformative experience design (Chirico & Gaggioli, 2021; Chirico et al., 2016; Schoeller et al., 2019; Quesnel & Riecke, 2018).

7. Conclusion and future research

We examined the literature on interoception as a mechanism of prediction and considered the clinical potential of various interoceptive interventions in light of various computational models. We emphasized the role of precision-weighting and distinguished between three types of interoceptive interventions: artificial sensations that directly influence interoceptive signals, interoceptive illusions that influence precision-weighting at a higher level usually by providing additional exteroceptive data to manipulate the interoceptive hypothesis, and emotional augmentation that makes up a mix of both artificial sensations and top-down exteroceptive cues, where the interoceptive signals manipulated correspond to those that can be expected under a particular emotional process (cf. the constructed theory of emotions). We concluded by suggesting two strains of applications for interoceptive technologies: one concern with diagnostic where artificial sensations can serve as a probe to test the susceptibility of some patients to interoceptive illusions, and one where emotional augmentation could serve for populations with mental disorders modulating the precision of some prediction, and accelerate desirable changes in maladaptive beliefs or behavior.

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