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RESEARCH ARTICLE



Interoception, blood pressure, and pain: unraveling their interaction under stressful and resting conditions

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ABSTRACT

Elevated blood pressure is commonly linked to diminished pain perception, a phenomenon known as *blood pressure-related hypoalgesia*. Interoception, the ability to perceive and interpret internal bodily signals, has been previously linked to both blood pressure and pain perception, although findings in the literature remain mixed. We investigated the relationship between blood pressure, pain perception, and interoception under both non-stressful (Pilot Study) and stressful (Main Study) conditions. In the Pilot Study, resting measures of blood pressure, pain thresholds and interoception were assessed in 26 healthy participants. Regression analysis revealed that higher systolic blood pressure was associated with increased pain thresholds, in line with previous findings. In the Main Study, the same variables were assessed in 46 healthy participants at rest and when a stress condition was induced by a validated virtual reality stress paradigm (i.e. the IMVEST). The effectiveness of the stress induction was confirmed through physiological measures (heart rate, heart rate variability, cortisol) and psychological assessments (perceived stress). No significant changes in blood pressure or pain threshold were observed following stress exposure. However, moderation analyses revealed that systolic blood pressure moderated the relationship between interoceptive beliefs (measured via the MAIA questionnaire) and pain perception: a positive association between the tendency to notice internal bodily sensations and pain threshold emerged only in individuals with high systolic blood pressure. This relationship was not observed in individuals with average or low systolic blood pressure. Taken together, these findings suggest that individual differences in cardiovascular physiology and interoceptive processes may shape pain perception.

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Blood pressure; cortisol; heart rate variability; interoception; pain perception; stress

Introduction

High blood pressure is a major risk for several clinical conditions and it can be influenced by both internal and external factors. In healthy individuals, the cardiovascular system is functionally interconnected with pain regulatory mechanisms (Olsen et al., 2013; Saccò et al., 2013).

For example, a meta-analysis by Makovac and colleagues recently quantified the association between pain perception and blood pressure (Makovac et al., 2020). Specifically, this relationship refers to a phenomenon known as blood pressure-related hypoalgesia, where people characterised by high blood pressure also show higher pain detection thresholds. In line with this pattern, reduced pain perception has been observed in individuals with borderline hypertension (Saccò et al., 2013), as well as in normotensive individuals during spontaneous (Olsen et al., 2013) or experimentally induced increases in blood pressure (Duschek et al., 2009).

To better elucidate the underlying mechanisms, several lines of evidence suggest that baroreceptor activation may contribute to blood pressure-related hypoalgesia, however additional evidence should be

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collected. In particular, literature shows that acute activation of baroreceptors has been associated with transient reductions in pain sensitivity (del Paso et al., 2014; Edwards et al., 2008; Ottaviani et al., 2018; Wilkinson et al., 2013). Arterial baroreceptors, located in the aortic arch and carotid sinus, are mechanoreceptors that play an important role in blood pressure regulation, by detecting stretch within arterial walls and transmitting afferent signals to the Nucleus of Tractus Solitarius (Burke et al., 2019). Specifically, phasic increases in systolic blood pressure transiently activate baroreceptors and have been shown to temporarily reduce pain perception (e.g. Edwards et al., 2002; Ottaviani et al., 2018; Wilkinson et al., 2013). Of note, the regulation of baroreceptor activity and pain appears to involve overlapping brain regions encompassing the brainstem and the insular cortex, suggesting that increases in blood pressure and pain modulation may be governed by a shared central neural mechanism (e.g. Bruehl & Chung, 2004; Zhang et al., 1999). Interestingly, the insular cortex also represents a key hub for interoceptive processing (e.g. Craig, 2009; Critchley et al., 2004; Pollatos et al., 2007).

Interoception is a multidimensional construct (Suksasilp & Garfinkel, 2022) that is essential for maintaining the homeostasis, and for a range of higher-order cognitive and emotional processes, such as self-awareness and social decision making (Cantoni et al., 2024; Feruglio et al., 2023; Iodice et al., 2019; Monti et al., 2020; Monti et al., 2021; Singh Solorzano et al., 2022; Vabba et al., 2022; Vabba et al., 2023). It comprises distinct domains: accuracy (i.e. performance measured on objective tasks), beliefs (i.e. self-reported interoceptive beliefs assessed via questionnaires), and insight (i.e. metacognitive awareness of one's interoceptive accuracy).

Interoception has been closely linked to pain perception, although findings remain inconsistent. Pollatos et al., (2012) reported that greater interoceptive accuracy is associated with heightened pain sensitivity, reduced pain tolerance and threshold, and increased sympathetic activity. In contrast, other studies have found no significant relationship between interoceptive accuracy and pain experience (Werner et al., 2009). More recent evidence suggests that these discrepancies may be partly explained by sex differences, with higher interoceptive accuracy being associated with higher pain thresholds in men but lower pain thresholds in women (Ferentzi et al., 2021).

With respect to the link between elevated blood pressure and interoception, the existing literature shows mixed results. Some studies describe reduced interoceptive ability in individuals with elevated blood pressure (Kollenbaum et al., 1996; Yoris et al., 2018), linking this impairment to the blunted pain perception commonly observed in hypertensives compared to normotensives (Elbert et al., 1988). Other investigations suggest enhanced cardiac awareness in presence of elevated blood pressure (Greenstadt et al., 1986; Koroboki et al., 2010; O'Brien and Reid, 1998; Yoris et al., 2020).

Considering the multidimensional nature of interoception, both interoceptive accuracy and interoceptive beliefs have been independently associated with variability in pain perception (Horsburgh et al., 2024). Interoceptive accuracy is thought to primarily influence the sensory–discriminative component of pain by modulating the precision of incoming bodily signals, whereas interoceptive beliefs are more closely related to affective–cognitive appraisal and attentional focus on internal sensations.

Analysing these constructs within the same theoretical framework allows the capture of complementary pathways through which interoception may contribute to pain processing and its modulation by blood pressure, while maintaining their conceptual distinction. Accordingly, we hypothesise that both interoceptive dimensions may play a role in blood pressure–related hypoalgesia, albeit via partially distinct mechanisms. Specifically, interoceptive accuracy is proposed to reflect bottom-up sensitivity to bodily signals potentially enhancing physiological inhibitory mechanisms, whereas interoceptive beliefs reflect interpretive processes that may amplify, attenuate, or even counteract these physiological effects depending on cognitive appraisal and expectations.

Changes in both blood pressure, interoceptive awareness and pain perception are also induced by acute stress. The physiological stress response is characterised by the activation of the sympathoadrenal medullary system and the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of adrenaline and cortisol, respectively (McEwen et al., 2015; McEwen, 2007). Cardiovascular and autonomic indices such as heart rate (HR; Nater et al., 2005), heart rate variability (HRV; Gordan et al., 2015; Hauschildt et al., 2011; Michels et al., 2013), and blood pressure (Bali & Jaggi, 2015; Pickering, 2007) are commonly used and reliable markers of stress reactivity. Stress responses typically manifest as increased HR and blood pressure alongside reduced HRV; however, atypical patterns have also been documented. In addition to exaggerated

reactivity, blunted cardiovascular responses to stress can occur and have been associated with behavioural, motivational, and physiological dysregulation and adverse health outcomes, indicating that attenuated reactivity should not be assumed to be without adverse consequences (Ginty et al., 2013; O’Riordan et al., 2023).

Acute stress also impacts both pain and interoception. Stress-induced analgesia is a well-documented adaptive mechanism that reduces pain sensitivity during fight or flight responses (Butler & Finn, 2009; Kazlou et al., 2024). According to a review by Schulz and Vögele (2015), acute stress activates physiological responses that stimulate peripheral interoceptive signals and central stress mediators (e.g. cortisol, sympathetic nervous system), thereby affecting the perception of bodily sensations such as a racing heart. In a more recent study, Lai and collaborators (2025) suggest that stress does not increase interoceptive accuracy per se, but rather shifts attentional resources toward interoceptive cues (as indicated by increased heartbeat-evoked potentials, HEPs), potentially compromising the processing of exteroceptive inputs (Lai and Bergmann, 2025). Nevertheless, the relationship between interoception and stress remains inconclusive with studies reporting mixed and often contradictory findings (Schlinkert et al., 2020; Schultchen et al., 2019; Schulz et al., 2013).

Given these converging effects, stress represents a particularly relevant context in which to examine how interoceptive processes and blood pressure jointly contribute to pain perception. On this basis, we investigated whether the relationships observed at rest changed under conditions of acute stress.

In a Pilot Study, we aimed to preliminarily investigate the relationship between interoceptive abilities (accuracy and beliefs), pain perception, and resting measures of blood pressure in a sample of healthy participants. The Main Study aimed to further investigate this relationship under stressful conditions induced by a virtual reality paradigm (i.e., the Italian version of IMVEST paradigm, Rodrigues et al., 2021).

In the Pilot Study, we hypothesised that both interoceptive abilities and blood pressure would be associated with pain threshold. Specifically, we expected a positive association between blood pressure and pain threshold (i.e. higher blood pressure corresponding to a higher pain threshold) and a negative association, despite mixed evidence in the literature (see above), between interoception and pain threshold (i.e. higher interoception corresponding to a lower pain threshold).

In the Main Study, we expected that stress induction would lead to increased levels of perceived stress and anxiety, elevated HR, blood pressure, and cortisol, and decreased HRV. As a consequence of increased blood pressure, we expected a decrease in pain perception (i.e. higher pain threshold). We also expected that, particularly under conditions of stress, blood pressure would moderate the relationship between participants’ interoceptive abilities (measured in terms of both interoceptive beliefs and accuracy) and pain perception. Finally, considering that being male or female might play a role with respect to stress reaction, pain perception, or interoception, we aimed to explore sex differences.

Materials and methods

Pilot study

Participants

To validate key measures (interoception, pain perception, and blood pressure), refine the procedure, and explore potential associations among these variables, we conducted a pilot study. A total of twenty-seven (18 females; age: $M \pm SD = 25.76 \pm 3.75$ years) healthy participants were recruited through advertisements at University classes and word-of-mouth. Exclusion criteria were the presence of neurological or psychiatric conditions, cardiovascular or respiratory diseases, or self-reported history of hypertension. In addition, pharmacological treatments that could potentially interfere with study variables, including but not limited to anti-hypertensives, beta-blockers, opioids, diuretics and psychiatric medications were considered exclusion criteria. One participant was excluded from the statistical analysis due to outlier values (>2.5 SD) at one of our main dependent variables (i.e. pain threshold). Hence, the final sample for the statistical analyses was of 26 participants (17 F; age: $M \pm SD = 25.71 \pm 3.81$ years). The study was approved by the Institutional Review Board at the Scientific Institute for Research Hospitalisation and Health Care - Santa Lucia Foundation in Rome (protocol nr. CE/PROG.751) and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Procedure

Participants were asked to avoid the intake of analgesic drugs and cannabidiol (CBD) products 24 hours before the experiment and the ingestion of caffeine or nicotine 2 hours before the experiment. Once arrived in the laboratory, participants read and signed informed consent. The experimental procedure started with a first measure of blood pressure (systolic and diastolic) at rest. Blood pressure was taken from the non-dominant arm by means of MyPress device (A&D 767 NFC, A&D Medical, U.S.A.). To have the most accurate measure possible, we followed the practices recommended by the European Society of Cardiology-ESC (Williams et al., 2018) such as as refraining from talking or moving during the measurement and keeping participants' palms facing upward. After skin preparation to reduce impedance, electrocardiogram (ECG) data were recorded using three electrodes placed according to a bipolar lead II configuration, in order to assess interoceptive accuracy through the Heartbeat Counting Task (Schandry, 1981). Subsequently, participants' pain threshold was measured (see Pain Threshold measurement paragraph). Following a brief rest period, a second blood pressure measurement was taken. At the end of the experimental procedure, participants completed a battery of self-report questionnaires measuring interoceptive beliefs, state and trait anxiety, depressive symptoms and pain catastrophizing.

The experimental procedure (illustrated in Figure 1) lasted about an hour.

Heartbeat counting task

In order to measure individual ability to perceive one's own cardiac signals, known as cardiac interoceptive accuracy (Garfinkel et al., 2015; Suksasilp & Garfinkel, 2022), participants underwent the Heartbeat Counting Task (Schandry, 1981). In this task, participants are asked to mentally count the number of heartbeats they perceive without relying on external cues (e.g. taking their own pulse), during four blocks having different time durations (25 s, 35 s, 45 s, 100 s). The four blocks were presented in a randomised order using E-Prime Software (Schneider et al. 2002, Psychology Software Tools, Inc.), and each counting period was signalled via two auditory cues (1000 Hz, 500 ms) delivered through a headset. Participants were asked to keep their

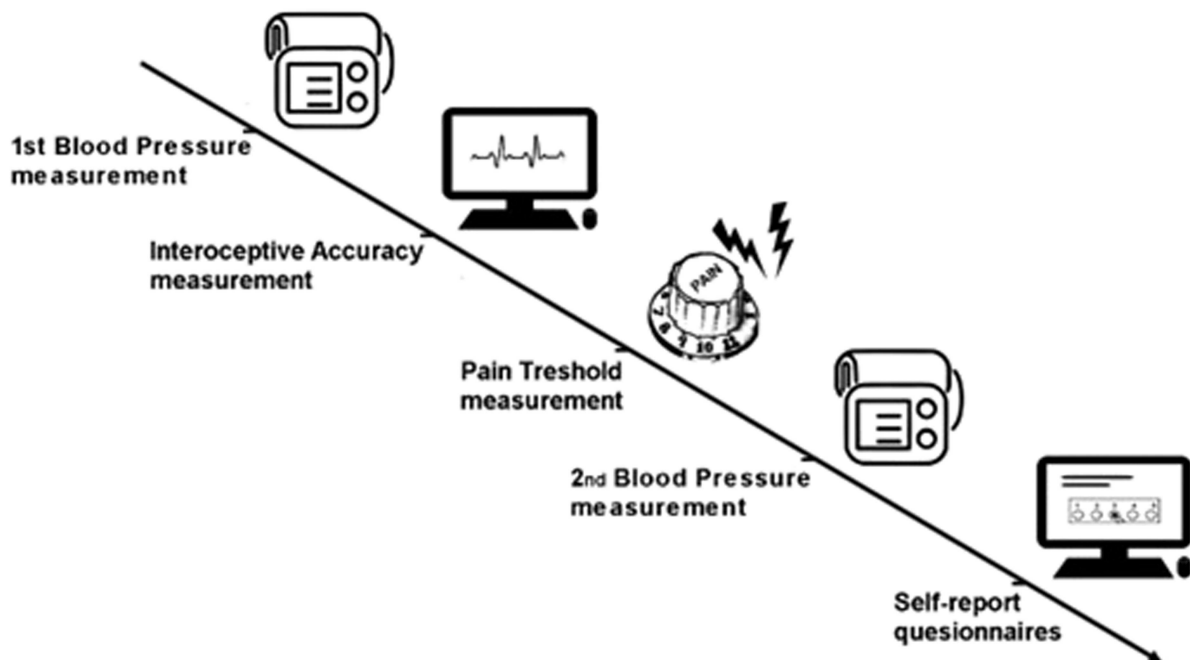


Figure 1. Experimental procedure of the Pilot Study. After reading and signing informed consent, a first blood pressure measurement was taken, followed by the cardiac interoceptive accuracy task (Heartbeat Counting Task). After that, pain threshold measurement was taken by means of an electrocutaneous stimulation over the left medial antebrachial cutaneous nerve. Finally, a second blood pressure measurement was taken and participants completed self-report questionnaires assessing pain catastrophizing (PCS), interoceptive beliefs (MAIA-II), severity and interference of pain (BPI), state and trait anxiety (STAI), and depressive symptomatology (CES-D).

eyes closed and their arms resting on the armrests of the chair during the counting periods. At the end of each counting period, participants entered the number of perceived heartbeats with a computer keyboard. In the present study, participants were explicitly asked not to estimate the number of heartbeats they believed occurred during the trial but to only consider heartbeats they truly perceived. During the task, participants' real heartbeats were recorded through a Biopac System MP150 (BIOPAC Systems, Inc.). The task lasted approximately 5 minutes.

Pain threshold measurement

To determine individual pain threshold, following a procedure similar to Ottaviani and collaborators (2018), ten electrocutaneous pulses were delivered to the left medial antebrachial cutaneous nerve using two Ag-AgCl electrodes connected to the Biopac MP150 acquisition system (BIOPAC Systems & Inc, 2005). Pain thresholds were assessed using the ascending method of limits (Fruhstorfer et al., 1976; Zaman et al., 2016). Participants rated the intensity of each stimulation on a 9-point scale, where 1 = "don't feel anything" and 9 = "painful stimulation". Each pulse lasted 5ms, and intensity was increased at a constant rate until the participant rated a stimulus as 9. If a participant did not rate any stimulation as painful (i.e. score of 9), we estimated the pain threshold using the relationship between actual and perceived stimulation intensity due to a safety-imposed maximum amplitude limit of the device. Specifically, using Origin software (May & Stevenson, 2009; Origin, 2020), we fitted each participant's data (i.e. actual amplitudes and corresponding perceived intensity ratings) into linear functions, and extracted the predicted amplitude corresponding to a rating of 9 ("painful stimulation"). The fit of each linear model was verified and found to be statistically significant in all cases (all $ps < 0.05$). Five participants (4 females, 1 male) in the Pilot study reached a painful stimulation (i.e. scored 9).

Self-report questionnaires

At the end of the experimental procedure, participants completed a series of self-report questionnaires measuring depressive symptoms (CES-D; Radloff, 1977; Fava, 1983), anxiety (STAI trait and state, Pedrabissi & Santinello, 1989), the way of approaching pain (PCS; Monticone et al., 2012; Sullivan et al., 1995), and interoceptive beliefs (MAIA-2; Mehling et al., 2018; Sagliano & Mehling, 2021). We used E-prime software (Psychology Software Tools, Inc.) to present the self-report questionnaires and collect participants' responses. Wellbeing measures were included to characterise the sample and control for lifestyle, psychological, and pain-related factors potentially influencing cardiovascular and interoceptive processes. Self-report questionnaires are described in the Supplementary Materials.

Data handling and statistical analysis

All statistical analyses were run via SPSS (IBM Corp, 2018) and RStudio (Allaire, 2012), with car (Fox et al., 2012), rockchalk (Johnson & Johnson, 2022), and gvlma (Peña & Slate, 2006) as packages.

Blood pressure measurement

To obtain two global measures of individual blood pressure, we calculated the average of two systolic and two diastolic measurements. However, in line with existing literature on blood pressure-related hypoalgesia, statistical analyses focused primarily on the systolic blood pressure (see below for details).

Interoceptive accuracy

For each participant, an interoceptive accuracy score (I_{Acc}) was calculated as the ratio of perceived to actual heartbeats, averaged across all blocks, using the following formula: $I_{Acc} = \frac{1}{4} \sum (1 - \frac{|\text{recorded heartbeats} - \text{counted heartbeats}|}{\text{recorded heartbeats}})$. Thus, the interoceptive accuracy index ranged from 0 to 1, with higher scores indicating greater interoceptive accuracy.

Regression analysis

We conducted a linear regression analysis to examine the effects of cardiac interoceptive accuracy and average systolic blood pressure (independent variables) on pain threshold (dependent variable). Prior to the analysis, assumptions of linearity, normality of residuals, and the absence of influential outliers were verified using Cook's distance and Mahalanobis distance. Multicollinearity was assessed using the variance inflation

factor (VIF), which was below 2 for all predictors, indicating no issues with multicollinearity. Overall, the data met the assumptions required for linear regression analysis.

Correlation analysis

To assess the validity of our pain threshold measure, we performed a correlation analysis between total scores on the PCS questionnaire and individual pain threshold.

Main study

Participants

An a priori power analysis was conducted using *MorePower* (Campbell & Thompson, 2012) to determine the minimum sample size required for detecting a medium-to-large effect in a repeated measures ANOVA design. The analysis was based on effect sizes reported in previous studies examining physiological responses to the IMVEST protocol (Rodrigues et al., 2021) and on stress-induced hypoalgesia (Timmers et al., 2018; Yilmaz et al., 2010). Assuming a medium-to-large effect size, an alpha level of 0.05, and a desired statistical power of 0.80, the analysis indicated that a minimum of 44 participants would be required.

Forty-six healthy individuals (27 females; age: $M \pm SD = 24 \pm 2.33$ years) were recruited via advertisements at University classes and word-of-mouth. Exclusion criteria included hypertension, prior cardiovascular or neurological events (e.g. stroke, myocardial infarction), and any psychiatric conditions. We also excluded individuals under pharmacological treatments that could potentially interfere with study variables, including but not limited to anti-hypertensives, beta-blockers, opioids, diuretics and psychiatric medications. In addition, participants were excluded if they reported recent use of analgesic medication or CBD products in the days preceding the experiment.

Participants were instructed to abstain from alcohol for 24 hours prior to the session, and to avoid caffeine and nicotine for at least 2 hour before the experiment. To minimise the impact of diurnal cortisol fluctuations, all experimental sessions were conducted in the afternoon, between 2 p.m. and 7 p.m. Written informed consent was provided by all participants. The study was approved by the Santa Lucia Foundation's ethical review board (Prot. Nr. CE/2023_036) and conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

General experimental procedure

The experimental session was divided into three consecutive blocks (T0, T1, T2) for a total duration of 2 hours and 30 minutes. An overview of the experimental blocks and associated measurements is provided in Figure 2, panel a.

Block 1- T(0) Baseline

Block 1 began with participants completing a series of baseline questionnaires aimed at assessing their current psychological state and perceived stress levels at rest.

Following the completion of the self-report questionnaires, a 10 minutes resting state ECG recording was conducted using a single-lead, wireless ECG system (MyHeart, Cardionica Italy) to measure HR and HRV.

Next, participants completed the Heartbeat Counting Task (Schandry, 1981; see the Pilot Study for methodological details). This was followed by a blood pressure measurement using a standard digital cuff. A saliva sample was then collected via sublingual swab for cortisol level assessment and stored at -20°C .

Lastly, pain threshold was assessed using an algometer (Algomed - Medoc Advanced Medical System CE 1282, compliant with 93/42/EEC MDD; see "Pain Threshold" section below for details).

Block 2—T(1) stress induction and self-reported questionnaires

The second block involved stress induction using a validated virtual reality (VR) scenario, namely the Italian version of the IMVEST protocol (Immersive Multimodal Virtual Environment Stress Test; Rodrigues et al.,

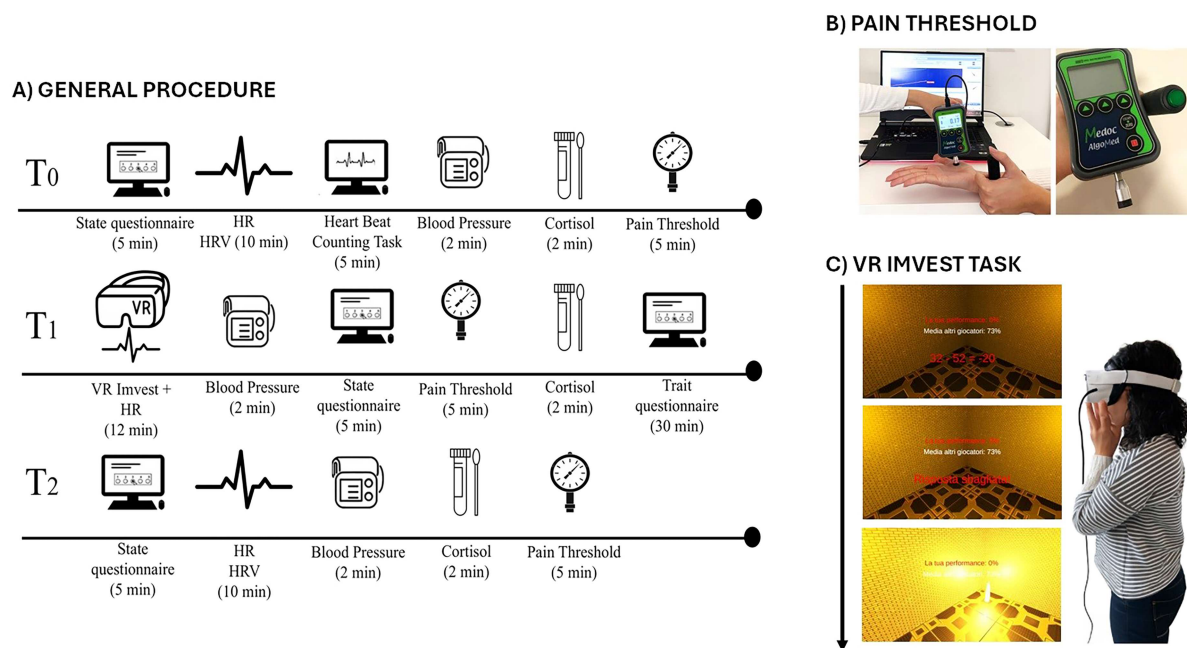


Figure 2. Experimental session- Panel A) illustrates the study design, durations of the measurements, and the variables measured over the three experimental blocks. During Block 1 (T0), we assessed psychological and physiological activation (heart rate, HR and heart rate variability, HRV for 10 minutes), we measured blood pressure, and took the first sample of cortisol and the first measure of pain threshold by means of an algometer. During Block 2 (T1), we asked participants to undergo a stressful induction (by means of a Virtual reality scenario: IMVEST, see Panel C for a more detailed illustration). Following the stressful scenario, we collected psychophysiological measures, namely blood pressure, visual analogue scales (VAS), pain threshold, and cortisol. Between the 20 minutes break necessary for recovery, participants filled a battery of self-report trait questionnaires measuring beliefs in stress (PSS), interoceptive beliefs (MAIA-II), depressive symptomatology (CES-D) and anxiety trait (STAI-T trait). Finally, Block 3 (T2) mimicked Block 1, therefore we collected a series of state questionnaires, 10-minutes HR and HRV recording, blood pressure, cortisol, and pain threshold; Panel B) shows the Algomed algometer, the instrument we used to assess pressure pain threshold; Panel C) shows a participant and three screenshots of the IMVEST paradigm.

2021). The ECG was continuously recorded throughout the stress induction procedure, which lasted approximately 12 minutes.

Immediately after the stress induction, the following psychophysiological and subjective measures were reassessed: blood pressure, perceived stress (via a 0–100 VAS), pain threshold (via algometry), and salivary cortisol collected 20 minutes after the end of stress induction.

Next, to allow participants to recover from the stress induction, a break of 20 minutes was introduced. During the break, participants were asked to complete a battery of questionnaires aimed at evaluating trait levels of anxiety (STAI for trait anxiety), stress (PSS; Cohen et al., 1983; Fossati et al., 2010), subclinical depression (CES-D), and interoceptive beliefs (MAIA-II). Detailed explanations of these measures and questionnaires are provided in the Supplementary Materials.

Block 3—T(2) baseline recovery

In the third block, participants underwent a final round of the same assessments conducted in Block 1, allowing us to evaluate recovery from the stress induction.

Pain threshold

Considering the challenges encountered in the Pilot Study using electrical stimulation to assess pain threshold, we adopted an alternative, validated method based on mechanical pressure. Pain was induced

using a pressure algometer (Algomed, Medoc Advanced Medical Systems Ltd, Israel - See [Figure 2b](#)), a non-invasive device that applies controlled pressure and quantifies it in kilopascals (1 KPa equals 101 Kg/m²).

The experimenter applied increasing pressure at a rate of 30 KPa/s to the thenar eminence of the participant's right hand. The specific anatomical location was selected due to its consistent adipose tissue content across individuals, which enhances measurement standardisation (Tashani et al., 2017). During the procedure, participants held a remote control with a button in their left hand and were instructed to press it as soon as they perceived the sensation as painful. Once the button was pressed, the applied pressure was immediately stopped, and the corresponding KPa value was recorded using Algomed software in order to determine pain threshold. The procedure comprised three consecutive trials (the first one was always discarded, and the mean of the second and third trials was used as the pain threshold), in line with the recommendations of Lacourt et al. (2012). In accordance with the manufacturer' safety guidelines, the maximum applicable pressure was set at 1000 KPa.

Pain threshold was measured at three time points: baseline (T0), at the very end of stress induction (T1), and in the recovery phase (T2).

Salivary cortisol samples

To collect saliva samples, participants were instructed to place a cotton swab under their tongue for a duration of two minutes. Saliva samples were collected, following the common practice, at baseline (T0), 20 minutes after stress induction (T1) and 40 minutes after stress induction (T2). After collection, each saliva sample was immediately sealed in a sterile tube and at a temperature of -20°C . During the analysis, the samples were thawed, brought to room temperature, and then subjected to centrifugation ($1500\text{g} \times 10\text{ min}$), resulting in a clear, low-viscosity supernatant. Salivary cortisol levels were assessed using an enzyme-linked immunosorbent assay (High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit: Salimetrics LLC, State College, PA). Duplicate samples were processed according to kit instructions on a 96-well plate, using the BioTek 800 TS absorbance reader and Gen5 software (BioTek Instruments Inc., Vermont, U.S.A.). To minimise inter-assay variability, all samples from the same participant were assayed in the same batch.

IMVEST protocol

The "IMVEST" (Immersive Multimodal Virtual Environment Stress Test) protocol is a widely validated paradigm that induces a controlled state of acute stress in an immersive virtual reality environment that can affect an individual's cortisol levels, cardiac activity (HR and HRV) and psychological state, i.e. perception of stress and anxiety (Rodrigues et al., 2021). Participants underwent this paradigm through an Oculus Quest 2 headset, which features a field of view of approximately 100° , a resolution of 1832×1920 (LCD) per eye, a 9:5 aspect ratio, and a vertical refresh rate of 90 Hz. [Figure 2c](#) illustrates the hardware setup, the virtual environment, and a sample arithmetic task from the IMVEST protocol.

Participants were immersed in a 15 m^2 virtual room with square floor tiles, where they were presented with a series of arithmetic calculations (additions or subtractions), each already solved. Participants were asked to indicate the correctness of the solution within 2.5 seconds using a handheld controller. Prior to this, a training session was conducted to allow participants to become familiar with the virtual environment, the arithmetic task, and the controller interface.

"Sonata for 2 Pianos and Percussion (Assai lento)" by Béla Bartók was played during the stress induction condition to create a restless atmosphere due to its high arousal and negative valence properties (Russo et al., 2013). In addition, incorrect answers or failure to respond in time resulted in the "explosion" of a floor tile beneath the participant, accompanied by a variety of alarming auditory and visual cues. This simulated a sense of danger, as the participant would fall down through the floor into another room accompanied by a screaming sound effect. Moreover, a performance score was displayed above the participant's current score, alongside the message "Average participants' score: 78%", to elicit social-evaluative threat. The difficulty of the arithmetic task was continuously and dynamically adjusted to maintain an artificially elevated average compared to the participant's actual performance. To introduce an element of unpredictability, there was a 5% chance that a correct answer would be incorrectly marked. The stress-

inducing scenario was divided into four 2.5-minute segments. Following each segment, an information message was displayed stating that participants' performance was below the mean and encouraged them to enhance their efforts. All these different elements of the IMVEST procedure are designed to induce cognitive, social, sensory and physical stress, as multimodal stressors have more efficacy compared to unimodal ones (Maras et al., 2014).

Data handling and statistical analyses

Statistical analyses were conducted using Jamovi (Open Source Software - Version 2.4.7) and the PROCESS macro for SPSS (Hays, 2018).

LabChart software (ADInstruments Pty Ltd.) was used to quantify the number of heartbeats for the interoceptive accuracy task. The ECG signal, recorded by the MyHeart device, was processed using a custom MATLAB script (The MathWorks, Inc.) that filtered out artifacts and adjusted the R-peak markers in case of detection errors. The resulting RR interval series was then imported into KUBIOS HRV software (Kubios Oy Ltd.) for HRV analysis. Specifically, HRV was assessed in terms of temporal variability between R peaks, using the Root Mean Square of Successive Differences (RMSSD).

In line with the Pilot Study, only Systolic Blood Pressure was included in the statistical models.

Separate mixed-design repeated measure analyses of variance (ANOVAs) were run on perceived anxiety, perceived stress, pain threshold, systolic blood pressure, HR, HRV, and salivary cortisol levels. The within-subject factor was Condition with three levels (Baseline (T0) vs. Stress (T1) vs. Recovery (T2) and the between-subject factor was biological sex (Male vs. Female). Tukey post-hoc tests were used in case of significant main or interaction effects.

Finally, two moderation analyses were performed to explore the role of blood pressure in the relationship between interoception and pain perception under stress. Both moderation models used pain threshold after stress as the outcome variable and systolic blood pressure immediately after stress as the moderator. However, the two models differed in their predictors: the first model included interoceptive accuracy, while the second model used interoceptive beliefs, i. e., the Noticing subscale of the MAIA-II.

Results

Pilot study

Descriptive statistics

Means and standard deviations of well-being variables (meditation behaviour, sport activity, smoking behaviour, anxiety and depressive symptomatology), blood pressure measurement, interoceptive ability (accuracy and belief) and pain-related measures (pain threshold, tendency to catastrophize painful stimulation and presence of interfering pain events) are presented in Table 1 of the Supplementary Materials.

Regression analysis

A linear regression analysis was conducted to examine the relationship between pain threshold (dependent variable), systolic blood pressure and interoceptive accuracy (independent variables). The overall model was statistically significant ($F_{2,23} = 3.93$; $p = 0.03$; $R^2 = .25$). Among the predictors, systolic blood pressure significantly predicted pain threshold ($\beta = 0.402$; $t = 2.24$; $p = 0.03$), indicating that higher blood pressure was associated with higher pain threshold, i.e. reduced pain perception. In contrast, interoceptive accuracy showed no significant association with pain threshold ($\beta = -0.33$; $t = 1.79$; $p = 0.08$). A second linear regression model was conducted using interoceptive beliefs measured by the Noticing subscale of MAIA-II, selected as it specifically assesses awareness of uncomfortable, comfortable, and neutral bodily sensations making it the most interesting with respect to our hypothesis, instead of interoceptive accuracy. In this case, the model was not statistically significant ($F_{2,23} = 2.49$; $p = 0.11$; $R^2 = .18$), suggesting that systolic blood pressure and interoceptive beliefs did not jointly predict pain threshold in a meaningful way.

Correlational analysis

A statistically significant negative correlation was found between pain threshold and the total score of the PCS questionnaire ($r = -0.39$; $p = 0.02$). This finding suggests that individuals with a greater tendency to catastrophize pain, reported lower pain threshold, and vice versa. This supports the notion that the objective and subjective measures capture different but related aspects of the same underlying construct, i.e. pain perception.

General considerations from pilot study

Since the electrical stimulation used to induce pain had to comply with safety guidelines, which prevented us from reaching intensities sufficient to elicit sensations classifiable as painful in all participants, and given its only marginal association with interoception, we decided to change the pain induction method in the Main Study and adopt a well-controlled pressure-based procedure.

Main study

Descriptive statistics

Mean and standard deviation of age, well-being measures (stress sensibility, anxiety, and depressive symptoms), physiological measures (blood pressure, cortisol levels, HR, and HRV), interoceptive abilities (accuracy and beliefs), and pain perception (pain threshold), can be found in Table 2 of the Supplementary Materials.

Effects of stress induction

Heart rate

The 2×3 ANOVA showed a significant main effect of the Condition ($F_{2,88} = 143.58$; $p < 0.001$), but no significant effect of Sex ($F_{1,44} = 1.28$, $p = 0.264$), or interaction between Sex and Condition ($F_{2,88} = 0.907$, $p = 0.407$). As expected, Tukey post hoc comparisons showed differences in the three Conditions, with higher HR measured during Stress compared to Baseline ($p < 0.001$) and Recovery ($p < .001$), see [Figure 3](#), panel A.

Heart rate variability

When we considered RMSSD as the dependent variable, the 2×3 ANOVA showed a significant main effect of Condition ($F_{2,88} = 36.21$, $p < 0.001$), while no effects of Sex ($F_{1,44} = 0.431$, $p = 0.515$) or Sex x Condition interaction ($F_{2,88} = 0.842$, $p = 0.434$) were found. Similarly to HR, RMSSD decreased during Stress compared to Baseline ($p < 0.001$) and Recovery ($p < 0.001$). In addition, Baseline HRV values were significantly lower than those recorded during Recovery ($p = .004$), see [Figure 3](#), panel B.

Systolic blood pressure

The 2×3 ANOVA showed a significant main effect of Condition ($F_{2,88} = 6.0541$, $p < 0.005$) and Sex ($F_{1,44} = 9.17$, $p < 0.005$) when we took into consideration systolic blood pressure as the dependent variable. Tukey post hoc comparisons following the main effect of Condition revealed a significant difference between Baseline and Stress ($p = 0.04$) and between Baseline and Recovery ($p = .009$), but not between Stress and Recovery ($p = 0.343$). In this case participants presented higher blood pressure values at Baseline (see [Figure 3](#) panel C). We also found that males had higher systolic blood pressure ($M_{\text{male}} \pm SD = 128 \pm 12.5$) compared to females ($M_{\text{female}} \pm SD = 118.6 \pm 11.6$). The interaction Condition x Sex was not significant.

Analyses were also conducted on diastolic blood pressure parameters; the results are reported in the Supplementary Materials.

Self-report perceived stress

The 2×3 ANOVA performed on perceived stress, measured on the 0-100 VAS, showed main effects of Condition ($F_{2,88} = 33.05$, $p < 0.001$) and Sex ($F_{1,44} = 6.16$, $p = 0.01$), while no interaction effects emerged

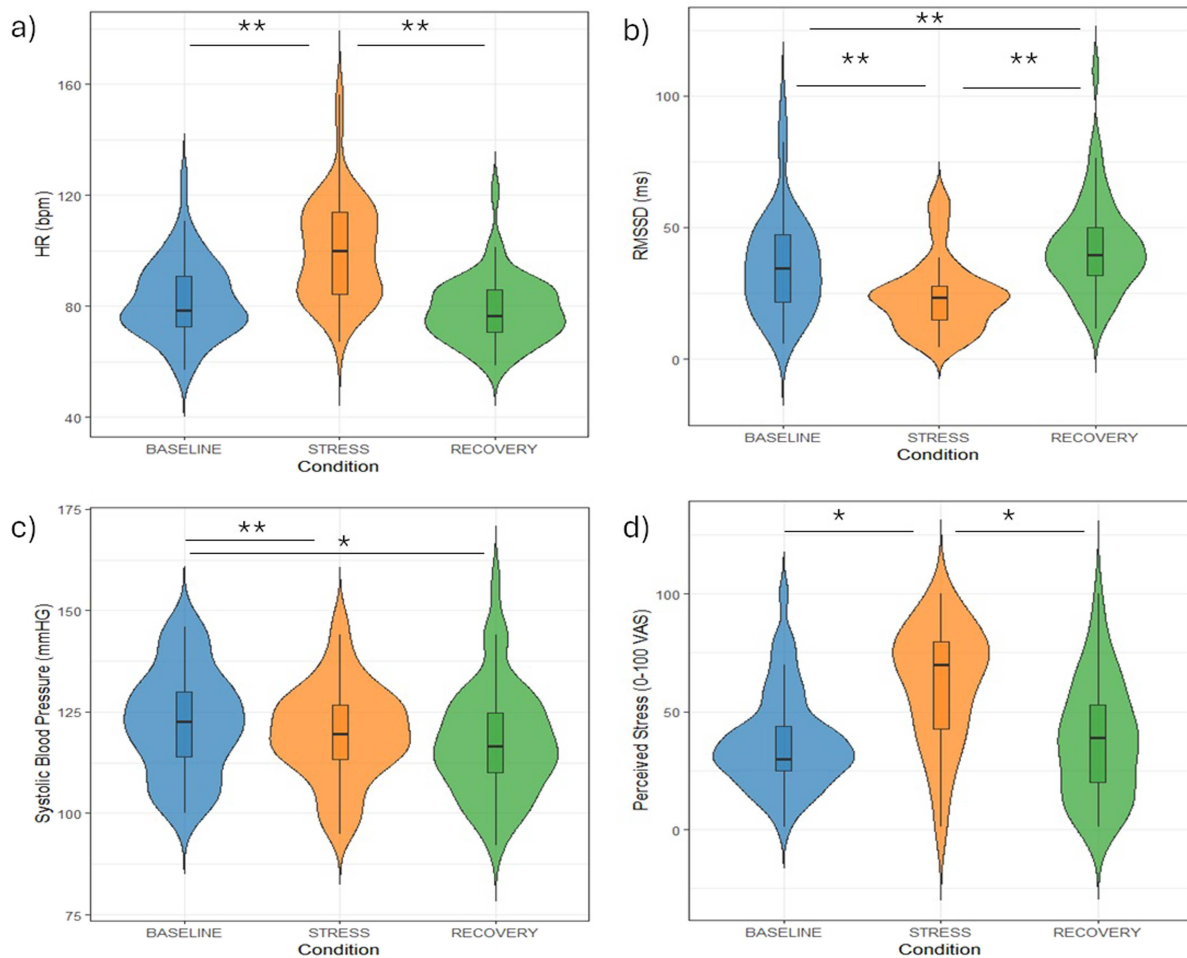


Figure 3. Illustration of the psychophysiological correlates of stress. A) Main effect of condition on heart rate: Increased HR during Stress compared to baseline and recovery; B) Main effect of condition on RMSSD: decreased HRV during stress compared to baseline and recovery. C) Main effect of condition on systolic blood pressure: increased blood pressure in Baseline compared to Stress and Recovery. d) Main effect of condition on perceived stress (0–100 VAS): Increased perceived stress during Stress compared to baseline and recovery. * = $p < .05$; ** = $p < .005$. HR = Heart rate; RMSSD = Root mean squared of standard deviation.

($F_{2,88} = 0.40$, $p = .67$). Tukey post hoc comparisons following the main effect of Condition highlighted a significant difference between Baseline ($p < 0.01$) and Recovery ($p < 0.01$) compared to Stress induction as shown in Figure 3, panel d. Baseline and Recovery did not differ ($p = 1.00$). In line with our hypotheses, higher values of perceived stress were found in the stressful compared to the non-stressful conditions. Finally, females reported higher levels of perceived stress ($M \pm SD = 68.4 \pm 21.7$) compared to males ($M \pm SD = 51.3 \pm 26.2$) independently of the Condition.

Pain threshold

The 2×3 ANOVA performed on pain thresholds showed no significant effects of Condition ($F_{2,88} = 1.639$, $p = 0.20$), Sex ($F_{1,44} = 0.03$, $p = 0.866$) or their interaction ($F_{2,88} = 0.188$, $p = 0.83$), suggesting that participants' pain perception did not change following a stress induction in males and females.

Salivary cortisol levels

The 2×3 ANOVA on salivary cortisol levels showed a significant main effect of Condition ($F_{2,84} = 9.95$, $p < 0.001$) and a Sex $\times$ Condition interaction ($F_{2,84} = 4.83$, $p = 0.01$). No significant main effect of Sex ($F_{1,42} = 1.17$, $p = 0.286$) was found. As to the main effect of Condition, Tukey post hoc revealed a statistically significant difference between Stress and Recovery ($p < 0.001$) and between Baseline and Recovery

($p = 0.036$), indicating higher levels of salivary cortisol at Baseline and during Stress compared to Recovery. No significant difference was found between Baseline and the Stress induction ($p = 0.17$). Tukey post hoc contrasts performed to explore the Sex $\times$ Condition interaction show that males presented higher levels of salivary cortisol 20 minutes after Stress induction compared to Recovery ($p = 0.004$) and marginally also compared to Baseline ($p = 0.052$). This difference between Stress and the other conditions was not found in females (all $ps > 0.05$), who only presented a significant difference between Baseline and Recovery ($p = 0.01$), with higher values of cortisol recorded at Baseline compared to Recovery. Sex differences in salivary cortisol are illustrated in Figure 4.

Moderation analysis

Preliminary analyses were performed to assess the assumptions underlying the moderation analyses aimed at testing the role of blood pressure in moderating the relationship between interoception (both beliefs and accuracy) and pain perception. In the first moderation model, the Noticing subscale of the MAIA questionnaire was used as the predictor variable. The assumptions of linearity and independence of errors were met, as indicated by a Durbin-Watson statistic of 1.88. Initial multicollinearity diagnostics revealed inflated variance inflation factors (VIFs), particularly for the interaction term, with all VIFs exceeding 30. To address this issue, the predictor and moderator variables were mean-centred prior to computing the interaction term. This preprocessing step successfully reduced all VIFs to approximately 1, indicating that multicollinearity was no longer a concern. Importantly, centering the variables did not alter the model structure but improved the stability and interpretability of the parameter estimates.

Due to violations of normality and homoscedasticity of residuals, a nonparametric bootstrap procedure with 1000 resamples was employed to obtain robust estimates. The use of bootstrap-derived standard errors ensured the validity of statistical inferences under conditions of non-normal and heteroscedastic residuals.

The moderation model was statistically significant ($R^2 = 0.19$, $F_{3, 42} = 3.27$, $p = 0.03$). Specifically, interoceptive beliefs (Noticing subscale of MAIA-II) marginally predicted individual pain threshold following the stress induction ($b = 40.45$, $SE = 20.63$, $t = 1.96$, $p = 0.05$, 95% CI $[-1.18, 82.08]$), suggesting that higher interoceptive beliefs could be associated with higher pain threshold, although the 95% confidence interval indicates uncertainty in the estimate and warrants cautious interpretation.

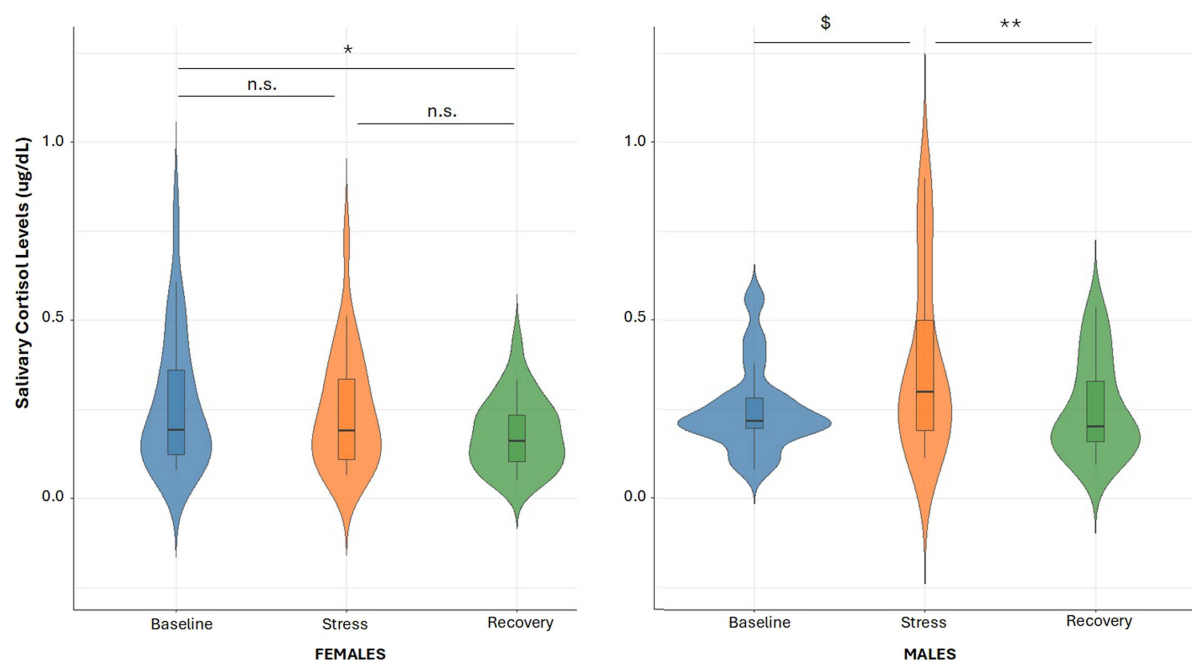


Figure 4. Illustration of the different effects of stress on cortisol levels in females and males. n.s. = non significant; \$ = marginally significant; * = $p < .05$; ** = $p < .005$.

Contrary to our hypothesis, systolic blood pressure did not predict pain threshold measured under Stress ($b = 1.579$, $SE = 1.42$, $t = 1.11$, $p = 0.27$, 95% CI $[-1.28, 4.44]$). Interestingly for the aim of the study, the interaction between systolic blood pressure and the Noticing subscale significantly predicted individual pain threshold ($b = 5.21$, $SE = 2.28$, $t = 2.28$, $p = 0.02$, 95% CI $[.61, 9.81]$). The interaction contributed to explain a significant and an additional $R^2 = 0.10$ ($F_{1,42} = 5.23$, $p = 0.02$). Simple slopes analysis showed that among individuals with high systolic blood pressure, interoceptive beliefs significantly and positively predicted higher pain threshold ($b = 101.83$, $SE = 39.69$, $t = 2.56$, $p = 0.01$, 95% CI $[21.73, 181.92]$). This suggests that under stressful conditions, individuals with higher blood pressure who are more attuned to their internal bodily signals tend to report higher pain thresholds. In contrast, no such relationship was observed in individuals with low ($b = -20.92$, $SE = 26.78$, $t = -0.78$, $p = 0.44$, 95% CI $[-74.98, 33.13]$) and medium ($b = 40.45$, $SE = 20.63$, $t = 1.96$, $p = 0.06$, 95% CI $[-1.18, 82.08]$) systolic blood pressure (see Figure 5).

When interoceptive accuracy (i.e. participants' performance at the Heartbeat Counting Task) was considered as a predictor, the moderation model was not significant ($R^2 = 0.09$, $F_3, 42 = 1.51$, $p = 0.23$).

Discussion

In this two-study experiment, we investigated the relationship between interoception, blood pressure and pain perception in a sample of young healthy volunteers both at resting and during stressful conditions. In a Pilot Study, we estimated individual pain thresholds using electrical stimulation, and employed a regression model to assess whether, and to what extent, interoception and blood pressure were significantly associated with pain perception under resting conditions. In the Main Study, we tested this three-way relationship under stressful conditions using moderation analysis, employing a more precise pain assessment method via pressure pain induced by an algometer.

The results of the Pilot Study revealed a relationship between pain perception and blood pressure: higher blood pressure was associated with higher pain threshold, reflecting the well-documented phenomenon of *blood pressure-related hypoalgesia*. This finding aligns with prior experimental evidence (Olsen et al., 2013; Saccò et al., 2013) and a recent meta-analysis quantifying the strength of this association (Makovac et al., 2020). Complementing these findings, two constructs of interoception were taken into consideration in the Pilot Study, namely interoceptive accuracy and interoceptive beliefs. The former refers

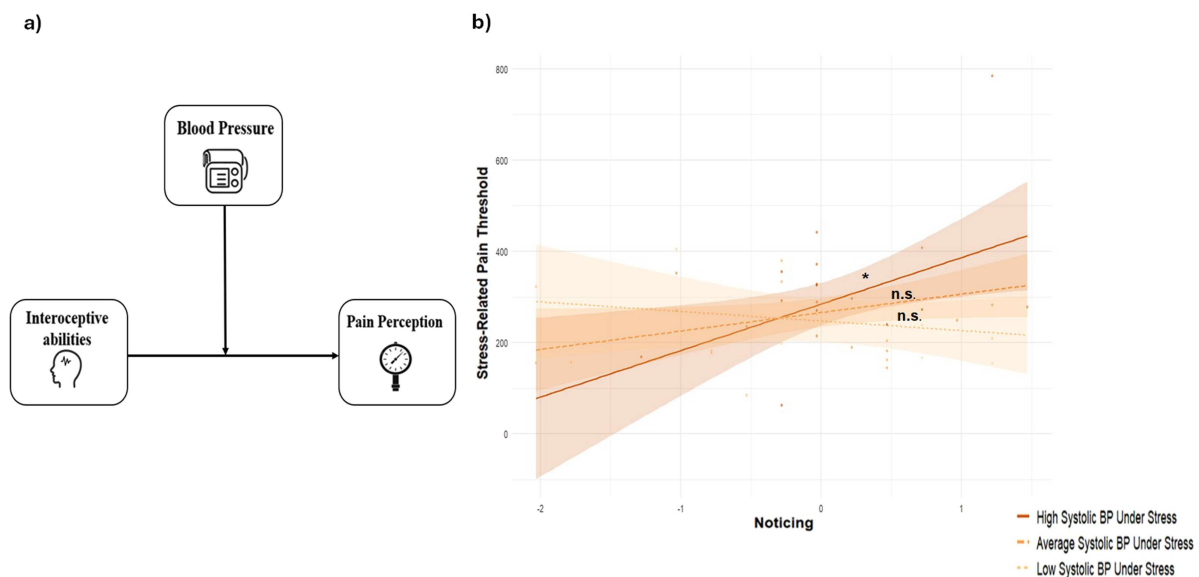


Figure 5. a) Theoretical diagram explaining the moderator role of blood pressure in the relationship between interoception and pain perception. b) Plot of the significant interaction term of the moderation analysis: after stress induction, people with high blood pressure at stress (Mean + 1 SD) show a positive relationship between interoceptive beliefs and pain threshold, namely the higher was their ability to notice internal signals, the higher was the pain threshold. This was not the case for people with low (Mean - 1 SD) or average (Mean) blood pressure. * = $p < .05$.

to the objective ability to count one's own heartbeats, while the latter represents subjective self-assessments of this ability (Garfinkel et al., 2015; Khalsa et al., 2018; Suksasilp & Garfinkel, 2022).

In the Pilot study, no significant association was found between interoceptive accuracy and pain threshold ($\beta = -0.33$; $p = .08$). This contrasts with previous research suggesting that individuals who are more accurate in perceiving their own cardiac signals tend to be more sensitive and responsive to painful stimuli. Specifically, greater pain sensitivity has been observed in people with higher cardiac interoceptive accuracy, and a general association between the two variables has been documented (Pollatos et al., 2012; Scholz et al., 2001). Neuroimaging studies further support the link, highlighting shared neural substrates between interoception and pain perception, particularly within the insula, anterior cingulate cortex, and somatosensory cortex (Critchley et al., 2004; Pollatos et al., 2007). However, the literature is not unanimous: for example, Werner et al. (2009) found no significant relationship between interoceptive awareness and pain sensitivity, and a study by Duschek et al. (2017) reported lower interoceptive ability in chronic pain patients compared to healthy controls.

When interpreting the preliminary results of the Pilot Study regarding the association between pain perception and cardiac interoception, it is important to acknowledge that a single measure of cardiac interoceptive accuracy may not generalise to other internal sensory modalities (Ferentzi et al., 2017). Consequently, the association between pain perception and interoception may depend both on the specific interoceptive domain and the assessment method. In addition, inconsistencies in the literature may also stem from the different methods used to evoke pain sensations, as different modalities elicit partially distinct psychophysiological mechanisms. For example, Goodin and colleagues (Goodin et al., 2012) demonstrated that pain administered through the cold pressor task (CPT), hot water task (HWT) and ischaemic pain task (IPT) resulted in comparable ratings of pain intensity and unpleasantness. However, the CPT elicited a significantly greater salivary cortisol response compared to the IPT, which mirrors the pronounced sympathetic and cardiovascular activation typically associated with cold-induced pain. These modality-specific physiological responses may be particularly relevant when considering outcomes such as blood pressure and cardiac interoception, which are closely linked to autonomic regulation. In line with this idea, previous studies have reported no significant associations between interoceptive accuracy and heat pain threshold (Werner et al., 2009) or ischaemic pain (Ferentzi et al., 2018), suggesting that the link between pain and interoception may differ across pain modalities. Taken together, these findings highlight the need for future research directly comparing different pain induction methods to clarify their differential effects on interoceptive processing.

Both experimental evidence and theoretical models suggest that stress may play a key role in the relationship between pain perception, interoception, and blood pressure. Experimental studies show that stress enhances interoceptive processes (Lai and Bergmann, 2025; Schulz & Vögele, 2015), reduces pain perception (Kazlou et al., 2024; Quelhas Martins et al., 2015; Tramullas et al., 2012) and generally increases blood pressure (Sparrenberger et al., 2009). In the Main Study, we tested this tripartite relationship under a stressful experimental manipulation, using the IMVEST protocol, a validated immersive virtual reality-based procedure that induces physical, cognitive, and social stress (Rodrigues et al., 2021).

To confirm the effectiveness of the IMVEST protocol, several physiological and psychological variables were assessed. Notably, stress induction led to an increase in salivary cortisol levels 20 minutes post-exposure, aligning with previous findings (Henze et al., 2017). This was evident in males but not females, supporting meta-analytic evidence of stronger salivary cortisol responses to a standardised stress induction protocol (i.e. Trier Social Stress Test) in males compared to females (Gu et al., 2022). Indeed, while males seem to be more susceptible to performance-related stress (Kirschbaum et al., 1992), women tend to exhibit stronger physiological stress responses in socially relevant contexts, particularly those involving interpersonal evaluation or peer rejection (Stroud et al., 2002; Stroud et al., 2017). On the other hand, females reported higher levels of perceived stress compared to males. This apparent divergence and non-linear relationship between subjective and objective indicators of stress is supported by previous findings showing that cortisol reactivity can occur independently of one's subjective response to stress, particularly when considering sex differences (Gillies & McArthur, 2010). While males are more likely to respond to stress through a "fright, fight or flight" pattern, females tend to engage in a "tend and befriend" response, which appears to be less directly associated with cortisol reactivity (Gillies & McArthur, 2010).

Moreover, sex differences in subjective and objective ratings of stress responses observed in the present study may also reflect differences in temporal dynamics of salivary cortisol secretion (Liu et al., 2017). Specifically, evidence suggests that the time trajectory of cortisol reactivity differs between males and females, with females often exhibiting a more gradual or delayed cortisol response compared to males. These differences are particularly evident in paradigms involving short recovery periods, suggesting that the length of the recovery window may be critical for detecting cortisol increases in females.

It is important to note that the IMVEST protocol also led to increased HR and reduced HRV (i.e. RMSSD) in both sexes, which is consistent with previous evidence showing heightened sympathetic activity and parasympathetic withdrawal under stressful conditions (Endukuru & Tripathi, 2016; Kim et al., 2018; Meyerhoff et al., 1988; Pieper et al., 2007; Vrijkotte et al., 2000).

However, contrary to our initial expectations, systolic blood pressure did not increase following stress induction with the IMVEST protocol; instead, a decrease was observed relative to baseline. It is important to note that blood pressure was not originally examined in the validation of the IMVEST paradigm (Rodrigues et al., 2021) and therefore its temporal dynamics in response to this stressor were unknown. Plausible explanations for these null findings could also be due to the fact that in the present study blood pressure was measured immediately after stress exposure rather than continuously during the task. As a result, transient stress-related elevations in blood pressure may have occurred during the stressor but normalised rapidly afterward, thereby escaping detection. In addition, anticipatory stress responses may have contributed to elevated baseline blood pressure, a phenomenon commonly referred to as the “white coat effect” (Pickering et al., 2002), potentially leading to an apparent decrease during the recovery phase.

Also, it can be argued that stress induction using virtual reality may differ from traditional laboratory paradigms in terms of perceived controllability or escapability, as participants are aware that removing the headset would terminate the exposure. In contrast, tasks such as the Trier Social Stress Test (TSST) may be experienced as more inescapable due to direct social evaluation and constrained disengagement options. Despite this potential difference, converging evidence indicates that virtual reality-based paradigms reliably elicit stress responses. Both the IMVEST and virtual reality-adapted TSST have been shown to induce significant activation of stress-related physiological systems, including increases in salivary cortisol, salivary alpha-amylase, and heart rate (Pieper et al., 2007; Rodrigues et al., 2021; Zimmer et al., 2019). Therefore, these findings suggest that immersive and socially evaluative features of virtual environments are sufficient to engage core stress mechanisms, even when an objective escape option exists.

Moreover, contrary to our initial hypothesis, stress induction did not significantly modulate pain perception. Although we expected increased pain threshold following stress (i.e. stress-related hypoalgesia; Aghajani et al., 2012; Timmers et al., 2018), this outcome may reflect the specific nature of the stressor. IMVEST incorporates multiple elements of social stress (e.g. negative performance feedback, score comparisons etc.) and the literature is mixed regarding social stressors and pain modulation (Gaab et al., 2017). From an evolutionary perspective, different stressors elicit distinct pain responses: physiological stressors would typically induce hypoalgesia, while social stressors may lead to hyperalgesia (Jennings et al., 2014; Piardi et al., 2020; Schneider et al., 2023). Thus, modulations of pain perception may depend on the specific characteristics of stressors.

Regarding the relationship between pain perception and blood pressure, no significant association was found between systolic blood pressure and pain threshold before and after stress exposure. Given our argument above about the lack of effects of stress exposure on both pain perception and blood pressure, future studies should include continuous blood pressure monitoring during stress exposure to clarify the relationship between pain perception and blood pressure under stressful conditions.

Nevertheless, we found that blood pressure moderated the relationship between interoceptive beliefs and pain perception. While the link between interoceptive accuracy and pain perception has been widely investigated and most studies suggest that higher interoception is associated with increased pain sensitivity (Pollatos et al., 2012; Scheuren et al., 2014; Weiss et al., 2014), particularly in chronic pain populations, our findings partly diverged. Specifically, after the stress induction, higher self-reported interoception (measured via the Noticing subscale of the MAIA-II questionnaire) was positively associated with pain threshold, but only in individuals with higher systolic blood pressure. This result echoes previous findings suggesting a positive relationship between cardiac interoceptive and pain threshold, especially in males (Ferentzi et al., 2021), a group naturally predisposed to higher blood pressure levels (Joyner et al., 2016).

Limitations

Both studies present some limitations. First, the sample size in the Pilot Study was small, which is particularly relevant given the correlational nature of the findings. Second, only cardiac interoception was assessed. While this focus is justified by our primary focus on blood pressure (strictly linked to the cardiac channel), future research should consider other interoceptive channels such as gastric and respiratory signals. Another limitation concerns the use of different pain assessment methods between the two studies: the Pilot Study employed electrical stimulation, whereas the Main Study relied on pressure pain. The observed inconsistencies may therefore be partly attributable to methodological differences in pain induction, as distinct nociceptive modalities are known to elicit different psychophysiological response profiles (Goodin et al., 2012). A multimodal pain assessment would enhance the robustness of the findings (Neddermeyer et al., 2008).

Also, the lack of continuous blood pressure monitoring during stress induction limits the interpretation of those results.

The present study included only young adults; therefore, the generalisability of the findings to older populations is limited. Given that age is known to influence stress reactivity, interoception, blood pressure, and pain perception (Khalsa et al., 2009; Lautenbacher et al., 2017; Pinto, 2007), future studies should include age-diverse samples to examine the role of aging in these relationships.

Finally, future studies should take into account the menstrual cycle phase and the use of hormonal contraceptives when studying the relationship between pain perception, interoception and stress in female samples, given the known effects of these factors on both subjective and physiological stress responses (Duchesne & Pruessner, 2013; Mengelkoch et al., 2024).

Conclusions and future perspectives

Taken together, the preliminary results from these studies suggest a complex relationship between interoception, blood pressure, and pain perception. While these results are based on healthy participants and should be interpreted with caution, they may inform future research in clinical contexts. Given the known reduction in pain sensitivity in individuals with borderline hypertension (Saccò et al., 2013), future studies could examine whether interoceptive processes contribute to blood pressure-related hypoalgesia in populations with clinical or subclinical hypertension. Such investigations may help clarify whether alterations in interoceptive processing characterise these populations.

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Author contributions

CRedit: **A. Salaris:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing – original draft, Writing – review & editing; **S. Ravenda:** Data curation, Formal analysis, Investigation, Writing – review & editing; **H. Al-Naqshbandi:** Data curation, Investigation, Visualization, Writing – review & editing; **L. Provenzano:** Methodology, Resources, Software, Writing – review & editing; **M. C. Gerra:** Resources, Writing – review & editing; **E. Mattei:** Resources, Software, Writing – review & editing; **G. Calcagnini:** Resources, Software, Writing – review & editing; **C. Ottaviani:** Conceptualization, Resources, Software, Writing – review & editing; **L. Carnevali:** Conceptualization, Resources, Software, Writing – review & editing; **G. Porciello:** Conceptualization, Funding acquisition, Project administration, Resources, Software, Visualization, Writing – original draft, Writing – review & editing.

Disclosure statement

The authors declare no competing interests.

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Data availability statement

Data and codes are available under request to corresponding authors.

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