



Interoception visualization relieves acute pain

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ARTICLE INFO

Keywords:

Bodily self-consciousness
Interoception
Rubber hand illusion
Pain
Somatosensory evoked potential

ABSTRACT

Interoception is the sensation of the physiological state inside one's body. Growing evidence suggests that visual feedback of interoception improves body self-consciousness (BSC) and reduces pain perception among patients with chronic pain. However, whether the integration of exteroception and interoception influences pain processing in healthy individuals remains largely unknown. To examine this question, we combined the rubber hand illusion (RHI) paradigm with visualized interoception –flashing of an LED light on the rubber hand synchronously or asynchronously with participants' real-time heartbeats. Under these conditions, we tested pain thresholds and corresponding event-related potentials. The interoceptive visual feedback inhibited the P2 component of pain, and the RHI inhibited pre-stimulus alpha-band brain activity. BSC had no significant effect on the processing of pain. These findings demonstrate that interoceptive signals with visual feedback inhibit pain processing, and that this psychophysiological process is largely independent of reported self-consciousness, in healthy individuals.

1. Introduction

Pain has a critical alert function that helps organisms to protect themselves from potential danger. The fast and accurate spatial identification of pain on the skin or inside the body helps us to identify which body part is being or has been damaged. Pain perception thus requires normal bodily self-consciousness (BSC) – the conscious experience of identifying with one's body, based on the integration of multiple bodily (i.e., somatic, visual, auditory, and motor) signals (Blanke, 2012; Olive, Tempelmann, Berthoz, & Heinze, 2015).

A prominent experimental paradigm used to investigate the mechanisms of BSC by testing participants' susceptibility to ownership illusion is the rubber hand illusion (RHI). For this paradigm, a human participant observes an artificial hand being stroked in synchrony with strokes applied to their own hidden hand, which leads to the subjective incorporation of the rubber hand as part of their own body (Botvinick & Cohen, 1998). The integration of visual and tactile feedback induces the participant to feel that the rubber hand is theirs. This illusory feeling decreases when the rubber hand and the participant's real hand are stroked asynchronously. The multisensory aspects of the RHI, including the synchronous presentation of visual and tactile stimulations, are referred to as "exteroception." The feeling that one's body belongs to oneself is a sense of ownership (SoO), a fundamental aspect of BSC

(Gallagher, 2000). The SoO enables distinction of the self from external objects and differentiation of one's body from those of other people (Tsakiris, Hesse, Boy, Haggard, & Fink, 2007). It can be induced in humans not only directly, but also through a virtual body connected to the "self" via the manipulation of spatiotemporal relationships between visual and tactile stimulations, as in the RHI. Although the RHI is a robust multisensory illusion, its relationship to pain perception remains elusive. Several studies have shown that the RHI increases pain tolerance compared with that under illusion-free conditions (Fang, Zhang, Zhao, Wang, & Zhou, 2019; Giummarra, Georgiou-Karistianis, Verdejo-Garcia, & Gibson, 2015; Hegedues et al., 2014; Siedlecka, Klimza, Lukowska, & Wierzchon, 2014), whereas participants in other studies experienced noxious stimuli as more painful under the RHI (Siedlecka, Spychala, Lukowska, Wiercioch, & Wierzchon, 2018) or reported that the RHI had no influence on pain perception (Mohan et al., 2012).

The multisensory aspects of the RHI, including the synchronous presentation of visual and tactile stimulations, constitute exteroception. Interoceptive information has been shown to play an important role in BSC (Tsakiris, Tajadura-Jimenez, & Costantini, 2011). Interoception is the perception of internal physiological body states, including hunger, temperature, and heart rate (Craig, 2003; Tsakiris et al., 2011). It is typically measured using mental tracking and heartbeat discrimination tasks to assess the perception of cardiac signals (Garfinkel, Seth, Barrett,

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<https://doi.org/10.1016/j.biopsycho.2022.108276>

Received 8 June 2021; Received in revised form 20 January 2022; Accepted 20 January 2022

Available online 22 January 2022

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Suzuki, & Critchley, 2015; Murphy, Geary, Millgate, Catmur, & Bird, 2018). Previous research suggests that interoception interacts with pain perception (Weiss, Sack, Henningsen, & Pollatos, 2014). For example, patients with chronic pain exhibited reduced interoceptive accuracy and interoceptive confidence relative to their healthy peers (Case, Solca, Blanke, & Faivre, 2020). Interoceptive visualization also reduced the pain ratings of patients with complex regional pain syndrome (Solca et al., 2018).

The brain's representation of the body is based on the integration of multisensory extero- and interoceptive signals. Under a combined RHI and cardiac-related visual feedback (cardiac-RHI) paradigm, the integration of extero- and interoception enhanced individuals' BSC (Aspell et al., 2013; Suzuki, Garfinkel, Critchley, & Seth, 2013), suggesting the importance of such integration for self-consciousness. Damage to the insula, a primary cortical region for interoception, has been associated with abnormal BSC states (Ronchi et al., 2015). BSC is critical for the construction of a coherent self, a strong individual form of psychological and physiological identification (Matamala-Gomez et al., 2019). It has also been shown to affect the processing of painful stimuli (Romano, Llobera, & Blanke, 2016), and greater BSC ("ownership" in Martini, Kiltner, Maselli, & Sanchez-Vives, 2015) of a virtual body has been shown to reduce pain perception.

Somatosensory evoked potentials (SEPs) have been used as an effective index of the neurological signature underlying pain-related processing (Hird, Jones, Talmi, & El-Dereby, 2017). They are induced most often by transcutaneous electrical stimulation, which activates myelinated A β somatosensory fibers and A δ nociceptive fibers (Hird et al., 2017; Kunde & Treede, 1993). Electrocutaneous stimuli have been shown to evoke an early deflection, peaking between 100 and 140 ms, and maximal primarily in the contralateral primary and secondary somatosensory cortices (SI and SII) (Eimer & Forster, 2003; van den Broeke et al., 2013). This component is thought to represent an early stage of somatosensory processing. At about 200 ms after stimulus presentation, a positive deflection that is maximal at the scalp vertex is usually observed (Christmann, Koeppel, Braus, Ruf, & Flor, 2007; Jung et al., 2012; Legrain, Guérin, Bruyer, & Plaghki, 2002). This component appears to originate in the anterior cingulate cortex and is thought to reflect a subjective (attentional and affective) response to the stimulus (Fiorio et al., 2012), although it has been argued to reflect pain-specific activation (Dowman, 2010). Thus, SEPs are useful for the study of the brain processes involved in nociception, allowing a better understanding of pain perception. Moreover, a growing body of electroencephalographic (EEG) oscillation studies has shown that the phase of ongoing alpha-frequency oscillations prior to stimulus onset can predict subsequent stimulus perception (Busch, Dubois, & VanRullen, 2009; Lu, Thompson, Zhang, & Hu, 2019; Mathewson, Gratton, Fabiani, Beck, & Ro, 2009). For example, Tu et al. (2016) found that alpha oscillations at bilateral central brain regions predicted brain responses to subsequent painful laser stimulation. In this vein, pre-stimulus alpha oscillations could be used as a measure of altered excitability of neuronal ensembles in the somatosensory cortices.

In this study, we used the cardiac-RHI paradigm to investigate whether the integration of vision and interoception modulated pain processes and, if so, whether this modulation was affected by BSC. We recorded participants' pain thresholds and SEPs in response to pain under the experimental conditions. Based on the effects of the integration of extero- and interoceptive bodily signals on BSC and modulation of pain perception by BSC (Nierula, Martini, Matamala-Gomez, Slater, & Sanchez-Vives, 2017), we hypothesized that (a) the pain perception in asynchronous condition of vision and interoception onsets would be more intense than the one in synchronous condition; (b) the reduction of pain in RHI condition would be larger relative to object (OBJ) condition. The amplitudes of SEPs would be the electrophysiological index of pain processing, and the power of pre-stimulus alpha band would be a predictor of pain. Confirmation of this hypothesis would mean that the provision of pain patients with feedback about their interoceptive

streams, along with exteroceptive cues, could markedly reduce acute pain, which would provide a new avenue for clinical analgesic practice.

2. Method

2.1. Design and stimuli

This study had a 2 (BSC: RHI, OBJ) \times 2 (interoception: synchronous, asynchronous) within-group design. For interoceptive visualization, we provided participants with visual cardiac feedback that was synchronous or asynchronous (i.e., faster or slower) with their real-time heartbeats. We used the RHI to modulate participants' BSC. To avoid visual feedback analgesia (i.e., the inhibition of pain perception by seeing one's own body, a mirror illusion or video of the body, or a virtual body; Diers et al., 2013; Longo, Betti, Aglioti, & Haggard, 2009; Martini, Perez-Marcos, & Sanchez-Vives, 2014) regarding the rubber hand (Boesch, Bellan, Moseley, & Stanton, 2016), we used cardboard as the object in the control condition. The experiment had four conditions: (a) RHI-synchronous (the edge of the rubber hand flashed synchronously with the heartbeat), (b) RHI-asynchronous (the edge of the rubber hand flashed asynchronously with the heartbeat), (c) OBJ-synchronous [the edge of the cardboard (the object) flashed synchronously with the heartbeat], and (d) OBJ-asynchronous (the edge of the cardboard flashed asynchronously with the heartbeat).

2.2. Participants

Twenty-six right-handed participants (15 female and 11 male) were recruited at Peking University. No participant reported a history of a neurological or mental disorder. All participants were free from pain and medication use at the time of the study, and had normal or corrected-to-normal vision. Because many women experience menstrual pain (Payne et al., 2019), the female participants were instructed to participate when they were not menstruating. This study was approved by the Academic Affairs Committee of the School of Psychological and Cognitive Sciences of Peking University. The participants were naïve to the full purpose of the experiment; they were informed that it was related to pain. All participants provided written consent and were informed that they could withdraw from the study at any moment.

2.3. Procedure

We adopted a block design for the experiment (Fig. 1). Each participant signed an informed consent form after arriving at the laboratory, and was instructed to sit at a table and hide their left hand behind an acrylic board. Then, the RHI or OBJ condition was induced and a pulse oximeter was clipped to the participant's right index finger for cardiovascular feedback provision. The order of the four experimental conditions was counterbalanced among participants. During subsequent SEP recording, the participant was asked to do nothing but focus on the rubber hand and received 30 painful stimuli per block. The interstimulus interval was 8–10 s. At the end of each block, the body location drift was measured and an SoO questionnaire was administered. The duration of each block was 20 min, and the total duration of testing was about 90 min. Each participant was paid 90 CNY (about US\$14) after the completion of all experiments.

2.4. Induction session

2.4.1. RHI experimental setup

Each participant sat on a chair with both arms resting on a table. A standing acrylic board was positioned to hide the participant's left arm from their view. To induce the RHI, we used a rubber hand located 10 cm in front of the acrylic board (Fig. 2). The space between the rubber arm and the individual's hidden arm, and the participant's right hand and shoulder, were covered with a black cloth. The experimenter

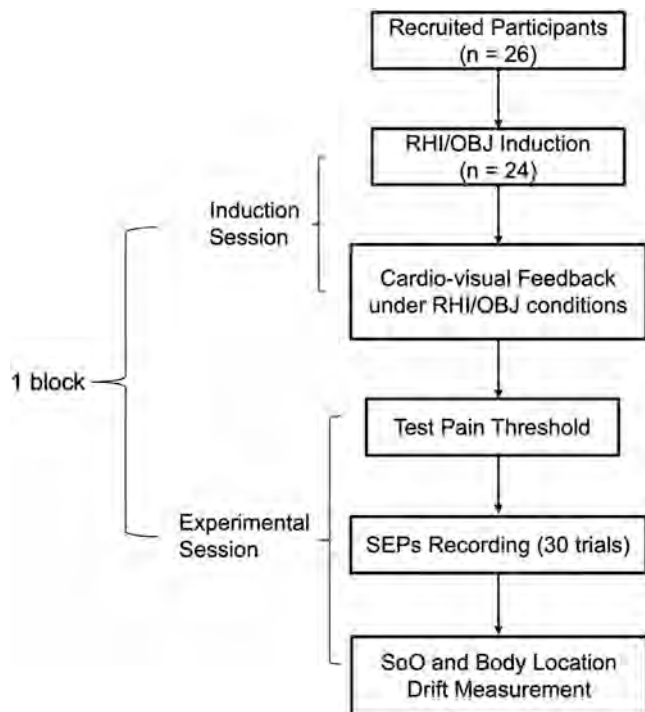


Fig. 1. The experimental procedure. RHI, rubber hand illusion; OBJ, object; SEP, somatosensory evoked potential; SoO, sense of ownership.

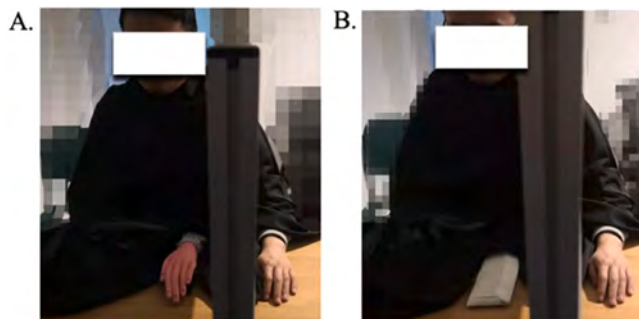


Fig. 2. The rubber hand illusion (A) and object (B) conditions.

stood opposite the participant.

To induce the RHI, the experimenter stroked the same anatomical locations on the participant's hidden left hand and the rubber hand with two identical brushes synchronously 30 times over a 2-min period (Fig. 3). The participant was then asked to rate whether they perceived the rubber hand as their own when it was stroked on a 7-point scale rating from 1 (totally not) to 7 (totally yes). Participants who provided ratings of 1 were excluded from the study. Under the OBJ condition, a piece of cardboard (22 × 10 × 2 cm) was used instead of the rubber hand, and the participant's hidden left hand was stroked 30 times as described above.

2.4.2. Cardio-visual feedback setup

We customized a cardio-visual feedback system consisting of a finger-clip photoplethysmographic (PPG) sensor (Beijing Reward Technology Development Co., Ltd., Beijing, China) and an LED light. The light was attached under the rubber hand or cardboard such that the edge of the rubber hand or cardboard would glow red when it was on. During synchronous feedback, the PPG sensor detected the participant's arterial pulse and output a signal to illuminate the light simultaneously for 160 ms. Asynchronous feedback was implemented by changing the

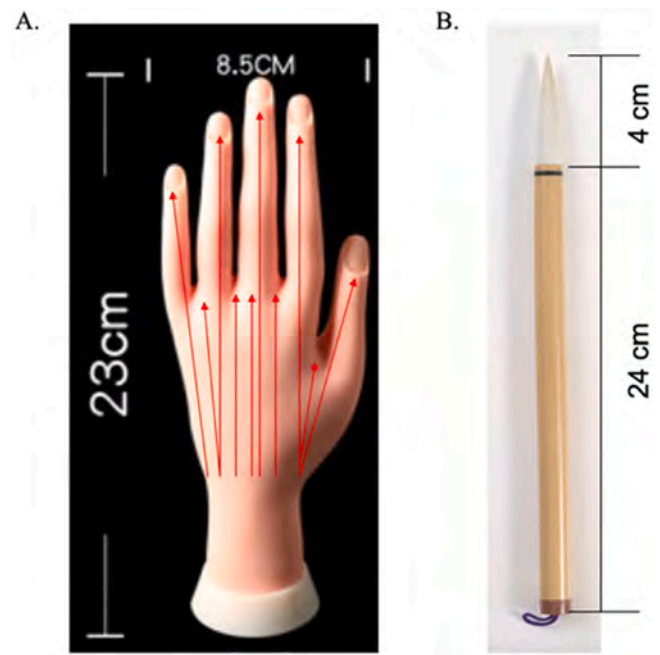


Fig. 3. (A) The rubber hand. The red lines represent the location and direction of stroking. (B) The bamboo and rabbit-hair brush used for stroking.

frequency of this illumination to be slower (70%) or faster (130%) than the participant's heartbeat. Slow and fast asynchronous trials occurred at equal frequencies for each participant, and their timing was fully counterbalanced. The participants were not informed of the purpose of the LED light and were not aware of the manipulation of congruency. Under all conditions, the participants were instructed to keep their own hands still and focus on the rubber hand or cardboard.

2.5. Experimental session

The participants were asked to observe the rubber hand/cardboard through the pain threshold testing and SEP recording stages under the four cardio-visual feedback conditions.

2.5.1. Pain threshold test

Two conventional Ag/AgCl electrodes were attached 1 cm apart about 2 cm above the participant's left wrist. Electrical skin stimuli consisting of single 2-ms square-wave pulses with a maximum voltage of 400 V were delivered by a constant-current stimulator (DS7A; Digitimer Ltd., Welwyn Garden City, UK). These stimulus form and duration parameters have been used in previous studies, and the credibility of the stimulus has been verified (de Tommaso et al., 2011; Schabrun, Jones, Kloster, & Hodges, 2013). From an initial amperage of 0 mA, we increased the stimulus intensity incrementally in 0.5-mA steps until the participant reported a score of 4 ("just beginning to feel pain") on a verbal rating scale ranging from 0 ("no feeling") to 10 ("the most intense pain imaginable"). This intensity was recorded in milliamps as the participant's pain threshold.

2.5.2. SEP recording

SEPs were recorded during blocks of 30 stimuli delivered at each participant's pain threshold intensity (Fig. 4). The participants were informed of the number and intensity of the stimuli. Continuous EEG data were collected using the Brain Products (Munich, Germany) 64-electrode actiCAP at a sampling rate of 1000 Hz. A vertical electrooculogram was recorded from electrodes placed below the participant's right eye. The reference electrode was placed at FCz and the ground electrode was placed at AFz. Electrode impedances were kept below 10

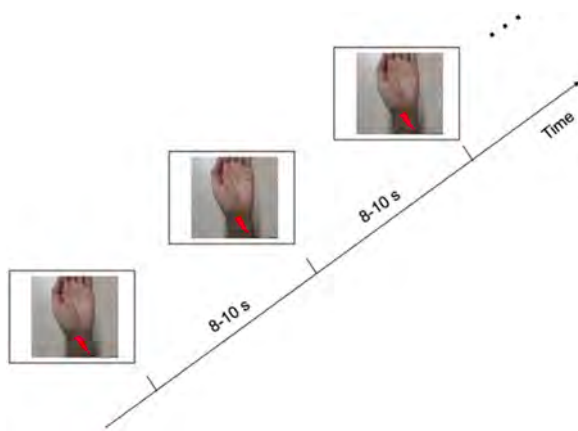


Fig. 4. The somatosensory evoked potential recording procedure.

KΩ.

2.5.3. BSC assessment

BSC was assessed by measuring the SoO and body location drift. To measure participants' SoO, we administered a 7-item questionnaire used previously by Filippetti and Tsakiris (2017), with responses structured by a 7-point Likert scale ranging from -3 (strongly disagree) to 3 (strongly agree; Table 1). Each participant's SoO questionnaire item responses were averaged to generate an SoO score. To measure whole-body location drift, we used the method reported by Lenggenhager, Tadi, Metzinger, and Blanke (2007). At the beginning of each test block, the experimenter positioned the participants' left arm 10 cm behind the acrylic board and asked the participant to retain this position, avoiding any movement of the hand or fingers. The experimenter then moved the participant's hidden left arm away from the table and asked the participant to return their arm to the initial position. The distance between the estimated and real initial positions was recorded as body location drift.

2.6. Data analysis

Offline EEG analysis was performed using the EEGLAB Toolbox for MATLAB (Delorme & Makeig, 2004) and custom-written MATLAB functions. First, the signals were re-referenced to the average of the right

Table 1
Mean (standard deviation) rubber hand illusion questionnaire scores.

Questionnaire item	RHI		OBJ	
	Asyn	Syn	Asyn	Syn
Q1: During the block it seemed like I was looking directly at my own hand, rather than at a rubber hand/cardboard	0.21 (1.98)	-0.13 (1.90)	-1.83 (1.34)	-2.21 (0.93)
Q2: During the block it seemed like the rubber hand/cardboard began to resemble my real hand	0.71 (1.78)	0.71 (1.60)	-1.58 (1.47)	-1.63 (1.61)
Q3: During the block it seemed like the rubber hand/cardboard belonged to me	0.67 (1.90)	0.67 (1.90)	-1.33 (1.93)	-1.67 (1.58)
Q4: During the block it seemed like the rubber hand/cardboard was my hand	0.04 (1.92)	0.08 (1.91)	-1.88 (1.30)	-1.63 (1.53)
Q5: During the block it seemed like the rubber hand was part of my body	0.13 (1.94)	0.13 (1.62)	-1.38 (1.64)	-2.08 (1.21)
Q6: During the block it seemed like my hand was in the location where the rubber hand/cardboard was	0.08 (2.17)	-0.29 (2.18)	-1.25 (1.48)	-1.71 (1.23)
Q7: During the block it seemed like the rubber hand/cardboard was in the location where my hand was	0.29 (2.27)	-0.25 (2.11)	-1.13 (1.60)	-1.08 (1.79)

RHI, rubber hand illusion; OBJ, object condition; asyn, asynchronous; syn, synchronous.

and left mastoids and down-sampled to 500 Hz. Then, a 1–30-Hz band-pass filter was applied. EEG epochs were extracted using a 3000-ms window (1000 ms before and 2000 ms after stimulus onset). The average signals were normalized to a baseline of the average amplitude of -200 to 0 ms. Next, using independent component analysis, we manually removed obvious artifacts such as saccades, blinks, cardiovascular signs, and tonic muscle noises. To identify relevant electrodes and peak latencies for statistical analysis of the SEP components, we averaged across BSC and interoception conditions within each stimulus category. Then, we calculated grand mean topographies of the respective components based on previous reports (Clauwaert, Torta, Danneels, & Van Damme, 2018; Ladouceur et al., 2018). By visual inspection, two components were identified: an earlier negative component near 140 ms (N140) with a topography contralateral to the stimulated hand and a later positive, centrally located component near 200 ms (P2). For each participant, the mean amplitudes between 130 and 150 ms at the contralateral primary sensory cortex (C4 electrode), and between 180 and 280 ms at the parietal cortex (Cz electrode), under each experimental condition were selected.

To assess modulation in the interoception of spontaneous EEG oscillations, we extracted EEG signals from a window ranging from -1000 to 1900 ms from stimulus onset (Michail, Dresel, Witkovsky, Stanke-witz, & Schulz, 2016). Time-frequency analysis of single epochs was carried out with a Morlet wavelet spanning 1450 linearly spaced frequencies from 2 to 40 Hz (five cycles) over a time course of 250 time-points (Zhao et al., 2020). The spectral amplitudes of alpha oscillations at 8–12 Hz were extracted from bilateral centroparietal regions (C3, CP3, C4, and CP4) (Lu, Yao, Thompson, & Hu, 2021) for statistical analysis. For each condition, we obtained a two-dimensional matrix (point frequency × timepoints). We averaged the four stimulus channels and calculated the mean alpha-band power (in decibels) as $10 \times \log_{10}$ change from baseline over the period of -1000 to 0 ms from stimulus onset.

We compared pain threshold, SoO, body location drift, SEP (N140 and P2) amplitude, and alpha-band power values obtained under the four experimental conditions using two-way repeated-measures analysis of variance, with BSC (RHI, OBJ) and interoceptive visualization (synchronous, asynchronous) serving as repeated measures. The statistical analyses were performed using SPSS 22.0 (IBM Corporation, Armonk, NY, USA), and GraphPad Prism 5.0 (GraphPad Software, La Jolla, CA, USA). The significance level was set at $p < 0.05$. When the assumption of sphericity was not met, Greenhouse–Geisser correction was used. Bonferroni correction was applied to post-hoc t tests.

3. Results

Two individuals were excluded because they reported that they did not at all perceive the rubber hand as their own during the RHI induction phase. Thus, 24 participants [13 female; mean age 22.17 years, standard deviation (SD) 2.36 years] took part in the experiment.

3.1. Pain processing

Participant's mean pain thresholds under the four conditions are presented in Fig. 5. No significant effect of BSC, interoception, or the interaction between them was observed (Table 2). These results indicate that BSC and interoception did not affect the perception of pain.

SEP amplitudes are shown in Fig. 6. For the N140 amplitude, no effect of BSC, interoception, or the interaction between them was observed (Table 3). For the P2 amplitude, a significant effect of interoception was observed ($F_{1,23} = 8.43$, $p = 0.008$, $\eta_p^2 = 0.268$; Table 3). Amplitudes were larger under asynchronous conditions (mean ± SD, $10.25 \pm 7.06 \mu\text{V}$) than under synchronous conditions (mean ± SD, $8.54 \pm 6.92 \mu\text{V}$), indicating that interoception visualization inhibited the processing of pain. No main effect of illusion or illusion × interoception was observed for this amplitude (Table 3).

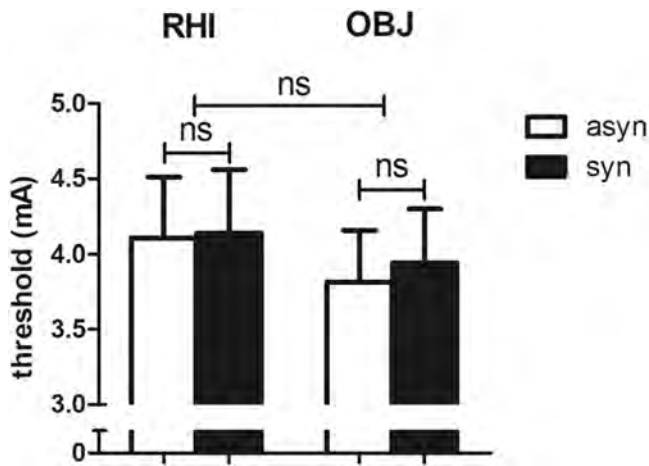


Fig. 5. Pain threshold results. The error bars represent standard errors of the mean. RHI, rubber hand illusion; OBJ, object condition; ns, not significant; asyn, asynchronous; syn, synchronous.

Time-frequency and alpha-band power data obtained under the four conditions are shown in Fig. 7. For the alpha-band power, the main effect of illusion was significant ($F_{1,23} = 7.45, p = 0.012, \eta^2_p = 0.245$). Values were lower under the RHI conditions (mean \pm SD, 13.75 ± 18.51) than under the OBJ conditions (mean \pm SD, 12.24 ± 19.29), indicating that the RHI inhibited the pre-stimulus alpha band. No effect of interoception or illusion \times interoception was observed (Table 3).

3.2. BSC

No effect of interoception or BSC \times interoception on SoO scores was observed (Table 2, Fig. 8). A significant main effect of BSC ($F_{1,23} = 32.90, p < 0.001, \eta^2_p = 0.589$) was observed: SoO scores were higher under the RHI conditions (mean \pm SD, 0.22 ± 1.66) than under the OBJ conditions (mean \pm SD, -1.60 ± 0.95 ; Table 2).

Body location drift values are presented in Fig. 9. No effect of interoception or illusion \times interoception was observed (Table 2). The main effect of interoception was significant ($F_{1,23} = 5.63, p = 0.026, \eta^2_p = 0.197$). Body location drift was greater under the synchronous conditions (mean \pm SD, 2.03 ± 2.34 cm) than under the asynchronous conditions (mean \pm SD, 1.19 ± 2.34 cm).

Table 2
Pain threshold, SoO, and body location drift results.

Variable	Pain threshold			SoO			Body location drift		
	F	p	η^2_p	F	p	η^2_p	F	p	η^2_p
BSC	1.41	0.247	0.058	32.90	<0.001	0.589	0.89	0.356	0.037
Interoception	0.23	0.635	0.010	0.60	0.446	0.025	5.63	0.026	0.197
BSC \times interoception	0.10	0.750	0.004	0.01	0.907	0.001	0.19	0.667	0.008

Results were obtained by 2 (BSC) \times 2 (interoception) two-way repeated-measures analysis of variance. BSC, bodily self-consciousness; SoO, sense of ownership.

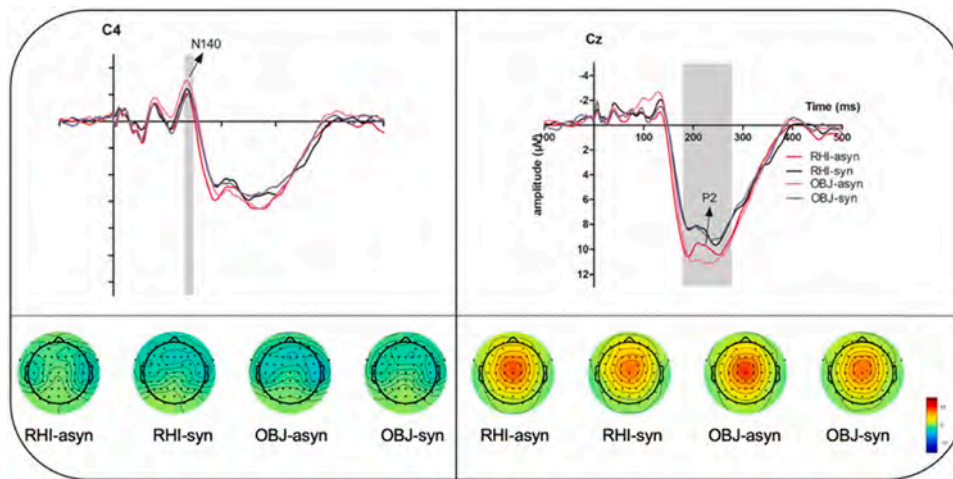


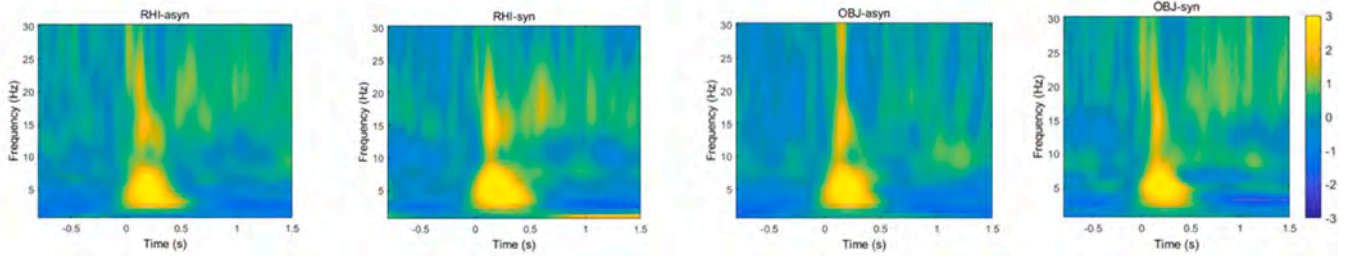
Fig. 6. Average amplitudes and topographic maps of somatosensory evoked potentials under each condition. RHI, rubber hand illusion; OBJ, object condition; asyn, asynchronous; syn, synchronous.

Table 3
N140 and P2 amplitude and alpha-band power results.

Variable	N140			P2			Alpha band		
	F	p	η^2_p	F	p	η^2_p	F	p	η^2_p
BSC	0.83	0.372	0.035	0.22	0.643	0.009	7.45	0.012	0.245
Interoception	0.19	0.663	0.008	8.43	0.008	0.268	0.29	0.596	0.012
BSC \times interoception	2.75	0.111	0.107	0.45	0.508	0.010	0.20	0.658	0.009

Results were obtained by 2 (BSC) \times 2 (interoception) two-way repeated-measures analysis of variance. BSC, bodily self-consciousness.

A.



B.

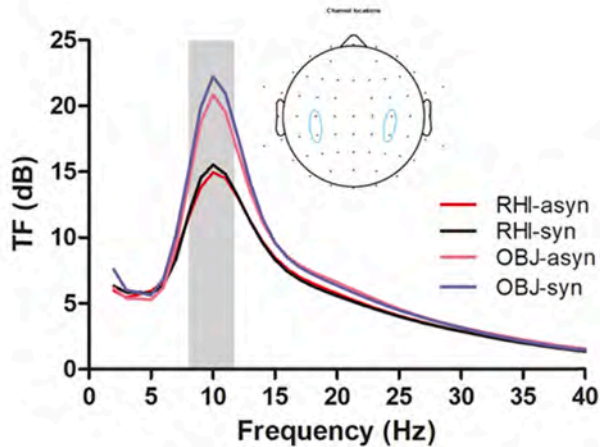


Fig. 7. (A) Average time frequencies. (B) Magnitudes of the pre-stimulus (-1000 to 0 ms) alpha bands within C3, CP3, C4, and CP4. RHI, rubber hand illusion; asyn, asynchronous; syn, synchronous; OBJ, object condition; TF, time frequency.

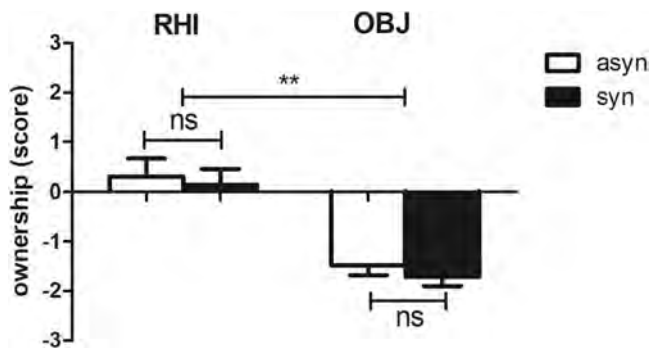


Fig. 8. Average sense of ownership questionnaire scores. Error bars represent standard errors of the mean. $** p < 0.01$. SoO: sense of ownership. RHI, rubber hand illusion; OBJ, object condition; asyn, asynchronous; syn, synchronous; ns, not significant.

4. Discussion

In this study, we tested the effect of interoceptive visualization on pain and its modulation by BSC by providing individuals with visual feedback on their real-time heartbeats under the RHI. Our results showed that visualized interoception inhibited acute pain potentials independently of BSC, but did not affect pain ratings, in healthy individuals.

4.1. The inhibiting effect of visualized interoception on pain processing

The observed inhibition of pain processing by interoceptive

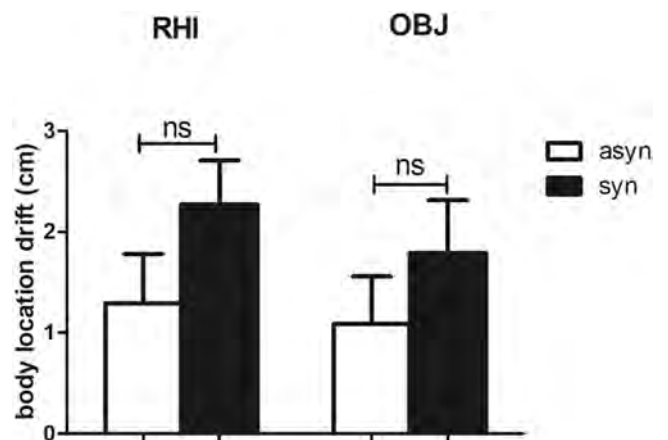


Fig. 9. Body location drift results. Mean values are represented and error bars represent standard errors of the mean. RHI, rubber hand illusion; OBJ, object condition; asyn, asynchronous; syn, synchronous; ns, not significant.

visualization supports our hypothesis. Previous studies reached no consistent conclusion on the relationship between interoception and pain. Werner, Duschek, Mattern, and Schandry (2009) found no difference in sensitivity to heat-induced pain between individuals with high and low cardiac interoception. Pollatos, Fuestoes, and Critchley (2012) found that interoceptive sensitivity correlated with the perception of cutaneous pressure-induced pain. In the present study, cardiac-visual feedback reduced P2 SEPs induced by pain but did not affect N140 amplitudes, likely reflecting sensory-discriminative processing of pain stimuli and imperviousness to cognitive modulation (Blom, Wiering, &

Van der Lubbe, 2012). We speculate that this analgesic effect is related to the influences of affective-cognition experiences of pain, given that P2 is known to correlate with the affective-motivational processing of pain (Fiorio et al., 2012; Legrain et al., 2012). For example, Gray, Minati, Paoletti, and Critchley (2010) found that baroreceptor activation abolished the painful expectancy reflected by P2 amplitudes. In addition, the processing of emotional stimuli is altered by the cardiac cycle; individuals perceive expressions of disgust and fear more intensely when they are presented at systole (Garfinkel et al., 2014; Gray et al., 2012). The N140 wave is thought to reflect the sensory-discriminative aspect of pain, which is processed mainly in the primary and secondary somatosensory cortices (Valentini et al., 2012). It is related predominantly to the ascending nociceptive input, regardless of the task demand (Colloca et al., 2008). These findings indicate that interoception is related closely to emotional processing, which may explain our results.

Under the synchronous conditions established in this study, the visual stimuli were presented simultaneously with finger pulses, about 260 ms after the electrocardiographic (ECG) R wave (Mozos et al., 2020). Systole occurs approximately 200–400 ms after the R wave, when baroreceptor firing is maximal (Gray, Rylander, Harrison, Wallin, & Critchley, 2009). Stimuli presented 300 ms after the ECG R wave are termed “baroreceptor active” (Gray et al., 2010). The onset of the visual (LED light) stimulus in this study was approximately consistent with that baroreceptor activation. Edwards, Inui, Ring, Wang, and Kakigi (2008) found that the cortical processing of laser-induced pain was attenuated during systole relative to that during diastole. The analgesia induced by interoception visualization may be a result of the coincidence of visual stimulation with systole. An alternative interpretation is that the visual stimulation rhythm is consistent with the cardiac cycle, but independent of its exact timing. This alternative needs to be explored further by recording individuals’ responses to painful stimulation at different timepoints during the cardiac cycle.

The lack of an effect of interoceptive visualization on participants’ pain thresholds in the current study is in line with the previous finding of no difference in pain ratings, but differences in SEPs (P2 component) in response to laser stimuli delivered at various intervals after the ECG R wave (Edwards et al., 2008). Both insignificant effects of cardiac cycle timing on pain perception in the current study and the study by Edwards et al. (2008), however, may be specific to natural variation of arterial baroreceptor stimulation in the cardiac cycle, which is due to the occurrence of the arterial pulse wave (Mancia & Mark, 1983). In contrast, the use of artificial forms of stimulation, such as neck suction (Al’Absi et al., 2005; Mini, Rau, Montoya, Palomba, & Birbaumer, 1995) and compression (Edwards et al., 2003; Rau et al., 1994), to manipulate carotid baroreceptor activity yields larger analgesic effects, with relatively coherent links between pain ratings and SEPs. These findings suggest that natural and artificial stimulation methods achieve different levels of baroreceptor activation or stimulate different populations of arterial baroreceptors, and thus achieve different effects on sensory perception.

4.2. The modulating effect of BSC

Although this study confirmed that visualized interoception affects pain, it revealed no influence of BSC. The integrated visual and tactile feedback under the RHI condition induced participants to perceive the rubber hand as their own and to have stronger SoOs than under the OBJ condition, reflecting a greater change in the SoO in the former case (Davies & White, 2013). However, we observed no difference in pain between the RHI and OBJ conditions, similar to the finding of Mohan et al. (2012). The pre-stimulus alpha band value was lower under the RHI condition than under the OBJ condition. Pre-stimulus alpha oscillation is associated with perceptual awareness (Davies & White, 2013) and pain-related emotion (Lu et al., 2019). We did not observe a direct relationship between pre-stimulus alpha oscillations and the subsequent processing of pain stimuli, which suggests that the results of oscillation

and self-reported pain are dissociated, typically when the affective component is not manipulated and measured directly in the current setting. In addition, we found that synchronous visual interoceptive feedback induced greater body location drift, but had no effect on SoO. These dissociation-related results suggest that the RHI and body location drift reflect different processes. Gallagher, Colzi, and Sedda (2021) suggested that proprioceptive drift reflects the multisensory integration of online sensory cues, whereas the SoO reflects cognitive aspects; their findings suggested that the effects of prolonged tactile cues on proprioceptive drift occurred in the absence of SoO effects. The whole-body location drift procedure used in our study (Lenggenhager et al., 2007) differs from that used previously (Hegedues et al., 2014; Xu et al., 2018), wherein participants were asked to report the perceived position of a hidden arm for evaluation of the illusion via the displacement of this position in the direction of the rubber hand. In this study, we explored BSC by examining drifts in the positions of participants’ hidden arms when they repositioned them with reference to their own center bodies under the RHI.

4.3. Implications

Pain, as an outer- and inner-body feeling that motivates behavior to maintain homeostasis, is inherently a type of interoception (Craig, 2003). It interacts with other interoceptive signals, such as the heartbeat. At the neural level, the insula, anterior cingulate cortex, and somatosensory cortex are the cortical regions thought to be most involved in cardiac signal awareness (Park et al., 2016, 2018; Salomon et al., 2016) and are central components of the “pain matrix” (Mouraux & Iannetti, 2018; Salomons, Iannetti, Liang, & Wood, 2016). Acute pain induces sympathetic system activation, which results in an increased heartbeat (Loggia, Juneau, & Bushnell, 2011; Tousignant-Laflamme, Rainville, & Marchand, 2005). The impairment of interoception in patients with chronic pain may be a risk factor for the aggravation of painful symptoms. Heartbeat perception training with visual feedback decreased symptom reporting among patients with somatoform disorders (Schaefer, Egloff, Gerlach, & Witthoft, 2014). The results of the present study suggest that interoceptive feedback, such as electro-cardiac visualization for heartbeat perception training, is useful for the alleviation of pain symptoms among patients with chronic pain, at least to a certain extent. A paradigm incorporating the modified RHI and interoception using virtual reality has been shown to enhance virtual whole-body BSC (Aspell et al., 2013). In the future, we may design corresponding paradigms for specific pain sites for the implementation of effective preventive programs to relieve pain syndromes.

4.4. Limitations

Our study has several limitations. First, we asked participants to reposition their hidden arms to measure body location drift, which might have caused motor noises or errors. Second, in the OBJ condition, we stroked only the hidden hand to balance the tactile experience under the RHI condition; we did not stroke the cardboard, resulting in a lack of visual stroking experience that may have affected the results. Third, the small sample may have affected the significance of the self-reported and behavioral performance findings; hence, the present results should be interpreted cautiously. Finally, the present study was conducted with healthy adults. Potential influences of age, health, and the affective state on interoception perception, which might also impact the analgesic effect, should be studied further.

4.5. Conclusion

In conclusion, visual interoceptive feedback suppressed healthy individuals’ processing of acute pain in this study. The analgesic effect of interoception was largely independent of BSC. These results emphasize the role of the integration of extero- and interoception on the

somatosensory experience and suggest that interoceptive visualization can be used for pain relief.

Disclosures

No conflict of interest was associated with this research. This work was supported by grants from the Natural Science Foundation of China (62061136001, 31861133012, and 11774379).

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