

Original Research Enhancing Interoceptive Abilities and Emotional Processing: Effects of HD-tDCS

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Abstract

Background: Interoception, the processing and integration of bodily signals, is crucial for emotional experiences and overall well-being. The interoceptive network, including the somatosensory cortices, has been recognized for its role in interoceptive and emotional processing. High-definition transcranial, direct-current stimulation (HD-tDCS) has been demonstrated to modulate brain activity in the primary somatosensory cortex (S1). Based on those findings, we hypothesized that anodal HD-tDCS over the right S1 would enhance interoceptive abilities and heighten emotional perception. **Methods**: Thirty-six healthy adults participated in two sessions separated by at least one week. A 20-min HD-tDCS stimulation (2 mA), and a sham stimulation, were applied in randomized order. Both conditions involved pre-tDCS physical activation by ergometer cycling. Interoceptive abilities were assessed before and after both sessions using a heartbeat-perception and respiratory-load task. Emotional proception was measured using four matched international affective picture system (IAPS) picture sets presented randomly. **Results**: Active HD-tDCS did not significantly improve interoceptive accuracy, interoceptive emotion evaluation, or interoceptive sensibility. However, a notable increase in cardiac interoceptive awareness was observed after active HD-tDCS. The expected enhancement of emotional processing was not observed. **Conclusions**: This study represents the first attempt to modulate interoceptive and emotional processing using HD-tDCS over S1. Although consistent enhancement was not observed, our findings provide insights into the modulation of interoceptive and emotional processes with HD-tDCS, suggesting avenues for further research. Further studies should consider the nuanced effects of stimulation techniques and the complex interplay between interoception and emotion.

Keywords: heartbeat perception; non-invasive neurostimulation; physical activation; primary somatosensory cortex; transcranial directcurrent stimulation

1. Introduction

We tend to describe our emotions through physical sensations, as illustrated by expressions such as "having a lump in your throat" when experiencing anxiety, or "butterflies in the stomach" when in love. This emphasizes the idea that interpretation of physical sensations is closely linked to emergence, detection, and processing of emotions. The idea that emotions depend on bodily changes has been around for well over a century. It was first proposed by William James [1], and has shaped emotion research significantly ever since. Of course, emotion theories have evolved since the controversial James-Lange theory of emotion [2]. Although more recent theories like Schachter and Singer's two-factor emotion-theory [3] or Damasio's somatic marker theory [4] integrate other factors such as cognition and appraisal into emotion processing, physical changes are still considered crucial.

The ability to process and integrate such bodily states, or interoception, has also been found to be essential to a wide range of other psychological and physiological processes [5,6]. Interoceptive processes are responsible for integrating afferent information about the body into conscious physical sensations through mental representation

[6,7]. Humans rely on interoception for the detection and understanding of physical sensations such as hunger or pain, most of the time without awareness of the process [5]. However, we are able to consciously perceive interoceptive processes, for instance by paying attention to the sensation of our heart beating. Three distinct interoceptive dimensions have been postulated and supported with empirical evidence [8,9]. As described by Garfinkel et al. [9], these dimensions are (1) *interoceptive accuracy:* the ability to accurately detect physical sensations, measurable with objective tests; (2) interoceptive awareness: a metacognitive ability for insight on one's interoceptive accuracy, measurable as confidence regarding accuracy; and (3) interoceptive sensibility: the subjectively perceived extent of being internally self-focused and detecting internal bodily signals, measurable through self-report. The most commonly researched interoceptive ability is heartbeat perception, usually measured with a heartbeat-perception task [10]. More recently interoceptive abilities in other modalities, such as respiratory or gastrointestinal sensations, have been investigated, suggesting a connection of interoceptive abilities across several physical systems [11–13].



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Interoceptive abilities have proven essential for maintaining mental health [7,14-16]. Interoceptive abilities differ individually, but alterations in interoceptive processes have been found to be associated with lower cognitive function, anxiety, depression, eating disorders, addictive disorders, and psychosomatic disorders [6,16–22]. Fortunately, interoceptive abilities have also been found to improve with training [23]. For instance, integrating mindfulness into depression treatments is a concept that is growing in popularity, and a connection between mindfulness treatment success and concurrent increasing interoceptive awareness has been observed [24]. In an overview evaluating interoceptive aspects for mental health interventions, the authors reported finding symptom reductions in anxiety disorders, eating disorders, as well as psychosomatic and addictive disorders [25]. Improvements in eating-disorder treatment [20] and a reduction of anxiety symptoms in autists [26] could also be observed after interoceptive training. Thus, strong evidence suggests that interoceptive abilities are amenable to improvement.

Empirical evidence also supports the commonly postulated role that physical changes, and therefore interoceptive processes, play in emotion, whether in perceiving an emotion or in emotional-language processing [14,27,28]. In individuals with alexithymia, a disorder affecting detection and expressing of emotions, there is often also a decrease in interoceptive abilities [29]. Furthermore, higher interoceptive abilities are strongly associated with a higher intensity of emotional experience, as well as higher neural activity, during emotional paradigms [14,30–32].

In line with this, recent research has attempted to identify and understand the neural substrates of interoception and emotion [6,33]. Evidence widely suggests that the insular cortex is part of a neural network involving both interoceptive and emotional processing [6,34-38]. The insula is a highly networked brain structure with connections to the prefrontal and orbitofrontal cortex, thalamus, amygdala, anterior cingulate cortex, and somatosensory cortex [6]. Cortical activity during interoceptive processing has already been documented in somatosensory cortex [34,35,39–42], so interoceptive pathways that include both insular and somatosensory activity have been postulated [33,43,44]. A growing body of work additionally supports the assumption that due to its role in physiological perception, the somatosensory cortex is also strongly involved in emotional processing [45]. Empirical evidence has shown somatosensory activation in visual emotion recognition, the actual experience of emotions, and emotion regulation [45-47]. The primary somatosensory cortex (S1), in particular, seems to be involved in interoceptive cardiac perception, as well as in the processing of aversive emotional stimuli [38,43]. The S1 comprises Brodman Areas 1, 2, and 3 and is located on the postcentral gyrus, representing the entire body and processing afferent information in somatotopically organized neurons [48,49]. The main function of the S1 is responding to somatosensory sensation [48].

In addition to cortical activity being found in the S1 during interoceptive and emotional processing, neurostimulation techniques targeting this brain region have been found to affect bodily perception [50-52]. Changes in cardiac-interoceptive accuracy could be produced using transcranial magnetic stimulation (TMS) over the right somatosensory cortex, [52], highlighting the role of the somatosensory cortex in interoception. Changes in pain perception, temperature detection, and tactile spatial perception have also been observed after transcranial directcurrent stimulation (tDCS) over the S1 [53-55]. TMS over interoceptive networks has also been found to alter emotional perception [56]. These findings illustrate both the interconnectivity of interoceptive and emotional processing, and their susceptibility to being changed by neurostimulation.

tDCS is a non-invasive neurostimulation method with growing popularity that can be used to modulate cortical excitability in humans [57–59]. Different effects can be observed with positive current (anodal tDCS) and negative current (cathodal tDCS). Anodal tDCS has been found to facilitate spontaneous and evoked cortical potentials, whereas cathodal tDCS robustly inhibits cortical excitability [51,57,60]. Conventionally, tDCS is accomplished by applying one target electrode and one reference electrode to the scalp of a participant [57]. Electrodes then emit a weak electrical direct current into the participant's brain, creating electric fields that modulate the somas and axon terminals of affected neurons [61]. Traditionally, sponge electrodes are used for tDCS application [51]. However, over the past 15 years, studies have been evaluating the use of ring electrodes, observing that they offer a higher degree of spatial focality than do traditional sponge or disc electrodes [62,63]. More specifically, so called High-Definition tDCS (HD-tDCS) using such ring electrodes has been the directcurrent-stimulation method of choice recently, with advantages over conventional tDCS including greater spatial precision and longer lasting after-effects [60,64-66]. HDtDCS provides a safe, effective, non-invasive neurostimulation method, and has proven to be effective in randomized controlled trials [66–68].

Interoceptive abilities and emotional perception are evidently modifiable and linked, as well as is specific, equally modifiable, cortical activity; because transcranial magnetic stimulation has been successfully used to modify both interoception and emotion perception [52,56], the question arises as to whether tDCS over the associated cortical regions can also achieve modulation of interoceptive abilities. Recently, effective modulation of hunger was achieved using cathodal tDCS over the tongue motor-cortex area [69]. Given the connection of the tongue motor cortex to the interoceptive neural network [33,70], and the importance of interoception in hunger [71], this is evidence for the potential of modulating interoception with tDCS. Although the insula is commonly considered the interoceptive center of the brain, the S1 is linked to both interoception and emotion processing. As the S1 is located closer to the scalp than is the insula [6], the S1 also provides a more easily accessible target for brain stimulation than the insular cortex. To date, no studies evaluating an attempt to affect interoceptive abilities and emotional perception using HD-tDCS over the somatosensory cortex are known to us.

In the present study, we attempted to enhance interoceptive abilities and emotional perception by applying anodal HD-tDCS over the right S1. We hypothesized that interoceptive accuracy, interoceptive awareness, and interoceptive sensibility would increase after *active tDCS*. We also applied a physical pre-activation task, consisting of ergometer cycling, in order to activate bodily signal processing from the bottom up. Based on the established connection between interoceptive and emotional processing, and the overlapping neural substrates, we further expected emotional experience to intensify after *active tDCS*, but not after *sham tDCS*.

2. Materials and Methods

2.1 Participants

G-Power analysis indicated an ideal sample size of 34 participants for our planned analysis of a two-factor, factorial, repeated-measures analysis of variance (ANOVA) for continuous dependent variables, at an expected effect of small to medium size (0.25), with a targeted power of 0.80. Sixty adults were recruited through local advertisements at Ulm University. After screening for tDCS contraindications and due to non-responsiveness, 24 participants were excluded and the remaining 36 healthy, native German speaking, adults (61.1% female), aged 18–30 yr (M = 23.5, SD = 2.903) participated in this study. Exclusion criteria and the inclusion process are depicted in Fig. 1. All participants gave written informed consent prior to participation. At the completion of the study, subjects were compensated with €45 or by course credit, according to their choice. The ethics commission of Ulm University approved the research protocol. The study was conducted in accordance with the Declaration of Helsinki.

2.2 Study Protocol

The experiment was conducted using a within-subject design with repeated measures, following the protocol depicted in Fig. 2.

Participants responded to an online survey from home in the first part of the study. We first assessed demographic information on each participant, and then measured handedness (Edinburgh Handedness Inventory, [72]), depressive symptom severity (Beck's Depression Inventory II; [73]), anxious symptom severity (State-Trait Anxiety Inventory, Trait-Scale; [74]), and physical activity levels (Freiburg Questionnaire on Physical Activity; [75]). We also mea-



Fig. 1. Participant selection.

sured baseline interoceptive sensibility using the Body Perception Questionnaire [76] and the Anxiety Sensitivity Index (ASI-3; [77]), and administered a questionnaire asking subjects to rate their general subjective perception of cardiac, respiratory, and gastrointestinal sensations, trembling, and temperature/sweating (Trait Interoceptive Awareness, TIA). After the online assessment, the second part of the study consisted of two laboratory sessions that each lasted around 2 h. The two sessions were conducted at least one week apart. The experimental protocol was identical in both sessions, except for variation of the tDCS condition. Each participant received the active tDCS condition once and received the sham tDCS condition once. Participants were blind to the type of condition, which was randomized using Research Randomizer software (version 4.0, web-based application, https://www.randomizer.org) [78]. Each laboratory pre- and post-assessment block began with a questionnaire on current anxiety severity (State-Trait Anxiety Inventory, State-Scale; [74]), and in the pre-assessment block, also pre-tDCS mood state (Profile of Mood States, POMS, German short-form; [79]).

A questionnaire on state interoceptive awareness (SIA) was used to assess interoceptive sensibility; subjects were asked to rate their current subjective perception of cardiac, respiratory, and gastrointestinal sensations, trembling, and temperature/sweating. Assessment of interoceptive accuracy was conducted using two paradigms. For cardiac interoceptive accuracy, participants completed the heartbeat



Fig. 2. Study protocol. SIA, state interoceptive awareness; POMS, Profile of Mood States; tDCS, transcranial direct current stimulation; STAI-S, State-Trait Anxiety Inventory, state scale.

perception task [10]. Four intervals (25, 35, 45, and 60 s) were presented in randomized order. During each interval, participants tracked their heartbeats mentally without actively feeling their pulse, and then indicated the number of heartbeats they counted in each interval, in accordance with a published protocol [80]. For respiratory interoceptive accuracy, subjects performed a respiratory-loadestimation task which was successfully used in the past [13,52]. Using a POWERbreathe® K5 respiratory training device (model K5, POWERbreathe®, Warwickshire, England, UK), we modified respiratory load, creating seven levels with varying inspiratory resistance (3, 5, 7, 10, 13, 19 and 25 cm H₂O). Participants first inhaled through each resistance level once, in increasing order, to become familiar with them. Then, seven trials were conducted, in which all resistance levels were presented in a randomized order, each occurring once. This randomized order was created using Random Allocation Software (version 1.0, Mahmood Saghaei, Isfahan, Iran) [81]. For each trial, participants were instructed to inhale once, and report the subjective respiratory load on a 7-point Likert scale. Scores for cardiac and respiratory interoceptive accuracy were calculated using the formulas described by Pollatos et al. [52], and range from 0 to 1, with higher values indicating higher interoceptive accuracy.

Interoceptive awareness was assessed as described by Pollatos *et al.* [52]. Participants rated confidence after each trial, cardiac and respiratory alike, on a nine-point Likert scale ranging from 'no confidence at all' to 'complete confidence'. Interoceptive evaluation measurement was also based on the protocol of Pollatos *et al.* [52]. For both the cardiac and respiratory tasks, participants were instructed, after each trial, to rate on 9-point Likert scales the valence (ranging from 'negative' to 'positive'), arousal (ranging from 'calm' to 'nervous'), and anxiety (ranging from 'not at all' to 'very'). The Self-Assessment Manikin [82] score was used to complement the valence and arousal Likert scales.

Using the International Affective Picture Set (IAPS [83]), we created four subsets of pictures, each containing 10 pictures of positive valence, 10 of neutral valence, and 10 of negative valence. We ensured that the average ratings of all four sets were identical for positive, neutral, and negative pictures, so as to make rating of the pictures comparable. In both assessment sessions, participants were presented with one set before and one set after tDCS stimulation. The order in which the four sets were presented to participants was also randomized. Each picture was presented for 2 s. Participants were asked to rate each picture as to their perceived valence and arousal, during picture presentation, on 9-point Self-Assessment Manikin (SAM) scales ranging from 'negative' to 'positive', and 'no arousal' to 'very high arousal'.

We used a paradigm to control for tDCS effectiveness of cortical modulation of the S1, in which we assessed whether our stimulation setup affected somatosensory perception of a tactile stimulation. The upper sternum was chosen as the location for this tactile stimulation due to



Fig. 3. HD-tDCS Setup. (A) Electrode configuration used for HD-tDCS. (B) HD-tDCS-induced electric fields in the brain. HD-tDCS, High-definition transcranial direct-current stimulation.

the overlap of the cortical representation of thoracic dermatomes and our tDCS target, both of which are located within Brodman Area 3 and thus the S1 [49,84,85]. We designed our control paradigm based on tactile-stimulation procedures that were previously linked to somatosensory cortical activity [86–89]. We used a soft, 1-cm-wide artist brush to make vertical strokes, 5-cm long, on the skin, moving the brush up and down along the T2-T3 dermatomes at a frequency of 2 Hz. This stimulation was applied manually for two intervals of 30 s, with a 10-s pause in between. Afterward, participants were presented with two 9-point Likert Scales and asked to rate subjectively sensed intensity (ranging from 'not at all intense' to 'very intense') and discomfort (ranging from 'very comfortable' to 'very uncomfortable').

In the active tDCS condition, we applied 20 min of anodal HD-tDCS over the right postcentral gyrus, where the S1 is located. Specifically, we targeted Brodman Area 3. HD-Targets[™] software (available at: https://soterixm edical.com/research/software/hd-targets) [90] was used to determine the most suitable electrode configuration for the target region. We used only anodal tDCS in our stimulation protocol, because we wanted to elicit heightened interoceptive and emotional processing. We were thus looking to facilitate cortical potentials, as is achieved by anodal tDCS, rather than inhibit cortical excitability, which is produced by cathodal tDCS. Fig. 3 presents the chosen configuration for electrode placement and the modeled electrical fields it elicits in the brain. We used ring electrodes with a diameter of 1 cm and applied conductive electrolyte gel around each electrode, after first moving participant's hair to the side and roughening the skin using cotton swabs. In the sham tDCS condition, HD-tDCS was prepared and initiated for the same stimulation configuration, set up in the same way as in the active tDCS condition, but was shut off 2 min after stimulation onset. This allowed scalp sensations to be identical to active tDCS, making the two conditions indistinguishable for participants, without reaching stimulation effects in the sham condition [91–95].

In both conditions, participants cycled on an ergometer immediately after stimulation onset. We instructed participants to adhere to a cycling frequency of 60/min and we increased cycling resistance once each minute, until participants reached a heart rate of 150 bpm. We tracked the participant's heart rate during the pre-activation phase using an Apple Watch Series 8 (Cupertino, San Francisco, CA, USA) around the wrist of the participant. Once the target heart rate was reached, we asked participants to continue cycling for one more minute, but now kept resistance steady. This preactivation was conducted to elevate stimulation effects; exercise with a heart rate over 150 bpm is associated with insular activation, and insular representation of bodily states is connected with somatosensory cortices [39,96].

Lower heart rates during exercise and faster heart rate recovery after exercise are both associated with cardiovascular fitness [97]. We therefore expected more physically fit participants to cycle longer until reaching the target heart rate and to recover from the physical strain faster than physically unfit participants. We began the post-assessment block 12 min after stimulation onset for every participant. This allowed enough time for highly trained participants to reach the target heart rate, and allowed for less-trained participants a longer heart rate recovery, while standardizing the duration of exposure to stimulation all participants received before post-assessment. Additionally, this enabled us to measure post-assessment during active stimulation, while allowing stimulation effects to be established prior to post-assessment [50,51,60].

2.3 Statistical Analysis

Data analysis was performed in SPSS (version 28.0, IBM Corp., Armonk, NY, USA) [98]. A decision was made against calculating a regression analysis due to autocorrelated residuals as a consequence of our repeated-measures design. We opted to analyze all outcomes measured for the within-subject factors Time (pre tDCS, post tDCS) and Condition (*sham, active tDCS*) with a 2-factor repeated-measures ANOVA. This includes cardiac and respiratory measures for interoceptive accuracy, interoceptive sensi-

bility, interoceptive evaluation, somatosensory perception, and state anxiety measures, as well as ratings of emotional pictures. Reported F-values are all uncorrected F-values, as we only compared two levels for each factor. The *t*-tests for paired samples were calculated to compare Condition (sham, active tDCS) in cycling time, average and maximum heart rate on the ergometer, and pre-tDCS mood state. Statistical significance levels reported correspond to p < 0.05. Due to technical malfunction, scores for the respiratoryload estimation task could not be computed for two participants, and data for emotional picture ratings had to be excluded for four participants. Analysis of interoceptive accuracy, interoceptive awareness, and interoceptive evaluation of the respiratory-load estimation task, was therefore conducted with n = 34, and analysis of emotional evaluation with n = 32.

3. Results

3.1 Baseline Characteristics

The baseline characteristics of the subjects are summarized in Table 1.

3.2 Comparison of Active and Sham tDCS Characteristics

Mean differences between *sham* and *active tDCS* condition are presented in Table 2. Baseline heart rate, average and maximum heart rate during cycling, and average cycling load and time did not differ between conditions. The interaction of Condition × Time was also not statistically significant ($F_{1,35} < 1.0$). We also found no statistically significant differences between *active tDCS* and *sham tDCS* measurement of mood states regarding POMS-Dejection, POMS-Vigor, POMS-Fatigue or POMS-Anger. Anxiety symptoms did not differ significantly between conditions ($F_{1,35} < 1.0$) or between before and after measurements ($F_{1,35} < 1.0$). We observed no significant mean differences in physical sensations during the stimulation protocol between the conditions.

3.3 Interoceptive Abilities

Mean interoceptive accuracy scores for heart beat perception and respiratory load estimation task are presented in Table 3.

Analysis of cardiac interoceptive accuracy revealed a significant main effect of Condition ($F_{1,35} = 7.675$, p < 0.01, partial $\eta^2 = 0.18$). Bonferroni-adjusted post-hoc analysis indicated significantly higher accuracy scores in the *sham tDCS* condition than in the *active tDCS* condition only in post-measurement [$M_{\text{Diff}} = 0.052$, 95% confidence interval (CI) (0.013; 0.092), p = 0.011. We found no significant interaction of Condition × Time ($F_{1,35} < 1.0$).

Exploratory data analysis on respiratory interoceptive accuracy revealed an outlier with a respiratory interoceptive accuracy of 0.4 (>3 SD below M) in the *active tDCS* condition for pre-measurement. We deemed this observation a genuine outlier. So as not to lower statistical power,

Variable	
Sociodemographic characteristics	
Age, mean (SD)	23.50 (2.903)
Female sex, n (%)	22 (61.1)
Educational level	
High, n (%)	35 (97.2)
Middle, n (%)	1 (2.8)
Occupation	
University student, n (%)	33 (91.7)
Psychology, n (%)	13 (36.1)
Medicine, n (%)	12 (33.3)
Employed, n (%)	3 (8.3)
Handedness	
Right-handed, n (%)	30 (83.3)
Ambidextrous, n (%)	1 (2.8)
Left-handed, n (%)	5 (13.9)
Health & fitness statistics	
BMI, mean (SD)	22.77 (3.05)
Weekly minutes of moderate physical activity,	171 36 (132 50)
mean (SD)	171.50 (152.50)
Weekly minutes of intense physical activity,	177 92 (157 50)
mean (SD)	177.92 (137.30)
Baseline heart rate	
Active tDCS session, mean (SD)	75.53 (13.71)
Sham tDCS session, mean (SD)	75.76 (12.36)
Depressive symptom severity (BDI-II)	
No depression (0–8), n (%)	34 (94.4)
Minimal depression (9–13), n (%)	1 (2.8)
Mild depression (14–19), n (%)	1 (2.8)
Anxious symptom severity	
STAI-T (range 20-80), mean (SD)	44.75 (4.91)
Anxiety Sensitivity (ASI-3)	
Cognitive concerns	
Normative AS, n (%)	25 (69.4)
Moderate AS, n (%)	9 (25.0)
High AS, n (%)	2 (5.6)
Physical concerns	
Normative AS, n (%)	35 (97.2)
Moderate AS, n (%)	1 (2.8)
Social concerns, mean (SD)	
Normative AS, n (%)	31 (86.1)
Moderate AS, n (%)	5 (13.9)
Interoceptive Sensibility	
TIA, mean (SD)	2.14 (0.51)
BPQ	
Body Awareness, mean (SD)	69.67 (16.87)
Supradiaphragmatic Symptoms, mean (SD)	21.39 (5.28)
Subdianhragmatic Symptoms, mean (SD)	9 86 (3 25)

ASI-3, Anxiety Sensitivity Index; SD, standard deviation; BMI, body mass index; BDI-II, Beck Depression Inventory; STAI-T, State-Trait Anxiety Inventory, trait scale; AS, anxiety sensitivity; TIA, trait interoceptive awareness; BPQ, Body Perception Questionnaire.

Table 2. Mean comparisons between active and sham tDCS.

	Active tDCS	Sham tDCS	t-test	<i>n</i> -value
	M (SD)	M (SD)	i test	<i>p</i> vulue
Baseline heart rate	75.17 (13.73)	75.76 (12.35)	$t_{(34)} = -0.327$	0.746
Average cycling heart rate	127.62 (7.67)	127.66 (7.84)	$t_{(28)} = 0.037$	0.971
Maximum cycling heart rate	156.91 (4.84)	157.78 (4.937)	$t_{(31)} = 1.059$	0.298
Cycling load	6.94 (2.00)	6.64 (2.24)	$t_{(35)} = -1.429$	0.162
Cycling time	5.5 (2.08)	5.17 (2.25)	$t_{(33)} = 1.580$	0.124
POMS-Dejection	10.72 (8.55)	12.39 (12.01)	$t_{(35)} = 0.949$	0.349
POMS-Vigor	21.67 (7.41)	21.39 (7.27)	$t_{(35)} = -0.255$	0.800
POMS-Fatigue	14.72 (7.33)	15.11 (6.63)	$t_{(35)} = 0.317$	0.753
POMS-Anger	6.03 (6.26)	6.00 (6.512)	$t_{(35)} = -0.025$	0.980
tDCS electrode sensation	1.94 (0.23)	1.89 (0.32)	$t_{(35)} = -1.00$	0.324
tDCS intensity	5.58 (1.67)	5.65 (1.91)	$t_{(30)} = 0.174$	0.863
tDCS (dis)comfort	4.78 (1.38)	5.19 (1.75)	$t_{(35)} = 1.324$	0.194
tDCS wellbeing	7.50 (1.42)	7.25 (1.87)	$t_{(35)} = 0.782$	0.439
tDCS pain	2.89 (1.80)	3.03 (1.80)	$t_{(35)} = 0.531$	0.599

POMS, Profile of Mood States.

Table 3. Interoceptive accuracy.

	Active	e tDCS	Sham tDCS		
	Pre	Post	Pre	Post	
	M (SD)	M (SD)	M (SD)	M (SD)	
Cardiac interoceptive accuracy	0.637 (0.17)	0.625 (0.20)	0.686 (0.18)	0.677 (0.19)	
Respiratory interoceptive accuracy	0.833 (0.10)	0.824 (0.05)	0.823 (0.08)	0.823 (0.06)	
		1		1.5.66	

Means and standard deviations for interoceptive accuracy by time of measurement and tDCS condition.

we decided to include it in data analysis. Analysis showed no significant interaction for Condition \times Time ($F_{1,33} = <1.0$).

Mean confidence ratings for heartbeat perception and respiratory-load estimation task are presented in Fig. 4.

Confidence ratings regarding the heart beat perception task did not differ significantly between conditions ($F_{1,35}$ <1.0), but we did find a significant main effect of Time ($F_{1,35} = 7.507$, p = 0.01, $\eta^2 = 0.177$). Bonferroni-adjusted post-hoc analysis revealed significantly higher (p < 0.01) confidence in post-measurement than in pre-measurement only in the *active tDCS* condition [$M_{\text{Diff}} = 0.799$, 95% CI (0.306; 1.291)]. The Condition × Time interaction was not statistically significant ($F_{1,35} < 1.0$). Analysis of respiratory confidence ratings revealed no significant interaction of Condition × Time ($F_{1,33} < 1.0$), but a significant main effect of Time ($F_{1,33} = 3.426$, p = 0.073).

Mean scores for the state interoceptive sensibility questionnaire are depicted in Fig. 5. We found no significant interaction of Condition × Time ($F_{1,35} < 1.0$), but the main effect of Time was statistically significant ($F_{1,35} =$ 25.271, p < 0.001, $\eta^2 = 0.419$). Bonferroni-adjusted *posthoc* tests revealed significantly higher interoceptive sensibility scores in post-measurement than in pre-measurement in the *active tDCS* condition $[M_{\text{Diff}} = 0.269, 95\% \text{ CI} (0.150; 0.388), p < 0.001]$ as well as in the *sham tDCS* condition $[M_{\text{Diff}} = 0.276, 95\% \text{ CI} (0.139; 0.413), p < 0.001]$.

Emotional evaluation ratings for the heartbeat perception and the respiratory-load estimation task are presented in Fig. 6. Results of statistical analysis are listed in Table 4. The only significant effect we observed was a main effect for Time regarding arousal in the heartbeat perception task. Exploratory data analysis revealed several outliers in cardiac and respiratory anxiety ratings. Violins in Fig. 6 represent sample distribution in emotion ratings, illustrating clearly the very low variance in anxiety ratings. Exclusion of the identified outliers would result in near-zero variance. We therefore decided to include all outliers regarding cardiac or respiratory interoceptive anxiety in our analysis.

Mean rating scores for emotional pictures are depicted in Fig. 7. As expected, ratings differed significantly between picture types, with higher ratings on the valence scale for positive pictures and lower ratings for negative pictures. Emotional pictures also elicited higher indicated arousal than did neutral pictures. For each picture type, we observed no significant interaction of Condition \times Time in valence ratings $F_{1,32} < 1.0$) or arousal ratings ($F_{1,32} < 1.0$).

Mean ratings for the tactile stimulation regarding perceived intensity and discomfort are depicted in Table 5.



Fig. 4. Interoceptive awareness. Sample distribution and mean \pm 95% confidence interval (CI) for pre and post tDCS confidence ratings regarding (A) heart beat perception task and (B) respiratory load task, compared for *active tDCS* and *sham tDCS*. ** p < 0.01.



Fig. 5. Interoceptive sensibility. Sample distribution and mean \pm 95% CI for state interoceptive awareness questionnaire scores, comparing pre and post tDCS measurements in the *active* and *sham tDCS* condition. *** p < 0.001.

Intensity-rating analysis determined that there were no significant main effects of Condition ($F_{1,35} < 1.0$) or Time ($F_{1,35} < 1.0$). The Condition \times Time interaction for perceived intensity also showed no statistical significance $(F_{1,35} < 1.0)$. Results of discomfort-rating analysis also indicate no significant main effects of Condition $(F_{1,35} < 1.0)$ or Time $(F_{1,35} < 1.0)$. The Condition \times Time interaction was not statistically significant either $(F_{1,35} < 1.0)$.

4. Discussion

The present study found diverse effects of HD-tDCS over the right S1 on various dimensions of interoceptive and emotional processing. Contrary to expectations, we did not observe improvement in either cardiac or respiratory interoceptive accuracy after active tDCS. For interoceptive sensibility, we observed an increase in both active and sham tDCS. This finding can be easily explained: participants completed the questionnaire shortly after undergoing ergometric pre-activation. The questionnaire assessed the participant's current awareness levels of various bodily sensations, including cardiac sensations, respiratory sensations, trembling, and temperature/sweating, all of which can be influenced by physical exercise. It is possible that the interval between ergometric activation and the response to the state interoceptive awareness questionnaire was too short to capture the effects elicited by tDCS. To address this, future studies may need to lengthen the interval between pre-activation and the completion of the questionnaire in order to observe potential tDCS effects more accurately. This adjustment could provide valuable insights into the impact of tDCS on interoceptive accuracy and sensibil-



Table 4. Interoceptive evaluation.						
	Valence Arou		usal An		kiety	
	Cardiac	Respiratory	Cardiac	Respiratory	Cardiac	Respiratory
ANOVA Condition	$F_{(1,35)} = 0.188$	$F_{(1,33)} = 0.023$	$F_{(1,35)} = 0.176$	$F_{(1,33)} = 0.050$	$F_{(1,35)} = 0.473$	$F_{(1,33)} = 0.069$
	p = 0.667	p = 0.880	p = 0.677	p = 0.825	p = 0.496	p = 0.795
ANOVA Time	$F_{(1,35)} = 2.532$	$F_{(1,33)} = 1.273$	$F_{(1,35)} = 14.957$	$F_{(1,33)} = 3.002$	$F_{(1,35)} = 0.572$	$F_{(1,33)} = 0.240$
	p = 0.121	p = 0.109	p < 0.001*	p = 0.092	p = 0.455	p = 0.628
ANOVA Condition × Time	$F_{(1,35)} = 0.486$	$F_{(1,33)} = 0.028$	$F_{(1,35)} = 0.552$	$F_{(1,33)} = 0.718$	$F_{(1,35)} = 1.205$	$F_{(1,33)} = 0.003$
	p = 0.490	p = 0.867	p = 0.463	p = 0.403	p = 0.280	p = 0.958

Table 4. Interoceptive evaluation.

Repeated-measures analysis of variance (ANOVA) results for emotional ratings regarding cardiac and respiratory interoceptive tasks. *p < 0.001.



Fig. 6. Interoceptive evaluation. Sample distribution and mean \pm 95% CI for ratings of (A) valence, (B) arousal and (C) anxiety for heartbeat perception task and ratings of (D) valence, (E) arousal and (F) anxiety for respiratory load task, comparing pre and post tDCS measurements in the *active* and *sham tDCS* conditions. * p < 0.05.



Fig. 7. Emotion processing. Sample distribution and mean \pm 95% CI for valence ratings of (A) positive, (B) neutral and (C) negative emotional pictures and arousal ratings of (D) positive, (E) neutral and (F) negative emotional pictures.

ity, and further our understanding of the potential benefits of tDCS in this context. Regarding *interoceptive awareness*, we noticed an improvement in the heartbeat perception task from before to after measurements for both tDCS conditions. However, we found statistical significance only for the increase after *active tDCS*. Unfortunately, the expected interaction of measurement time and condition was not statistically significant, and we did not observe a significant increase in *active tDCS* for respiratory awareness. The robust pre-to-post improvement in both the cardiac and respiratory tasks may be attributed to the participants' awareness that they had previously performed the interoceptive tasks in the pre-assessment. This knowledge could have increased their confidence in their performance during the post-measurement. Although this phenomenon could have influenced the results, it is essential to consider it as a potential confounding factor in the interpretation of the findings. To gain a comprehensive understanding of the impact of tDCS on interoceptive awareness, future studies may consider incorporating control measures to account for the effect of previous task experience. This way, we can further investigate the true effects of tDCS on interoceptive accuracy and ensure more robust and accurate conclusions. This is consistent with evidence of experienced meditators who rate confidence regarding cardiac interoceptive accuracy higher than do people with no experience in attending

Table 5. Rated somatosensory sensations.

	Active	tive tDCS Sham		tDCS	
	Pre	Pre Post Pre Post		ANOVA condition \times time	
	M (SD)	M (SD)	M (SD)	M (SD)	
Intensity	5.25 (1.61)	5.42 (1.92)	5.31 (1.72)	5.39 (1.87)	$F_{1,35} < 1.0$
Discomfort/comfort	0.833 (0.10)	0.824 (0.05)	0.823 (0.08)	0.823 (0.06)	$F_{1,35} < 1.0$

Mean, standard deviations, and ANOVA results for intensity and (dis)comfort ratings of somatosensory stimulation.

to body signals, even with no increase in actual cardiacperception accuracy [99]. Ergometric pre-activation may also contribute to pre-to-post improvements, affecting confidence ratings by increasing awareness of physical sensations [100] or through the expectation that heart rate must be elevated after physical exercise [101]. However, these influential factors should be present equally in both conditions and therefore do not sufficiently explain the significant increase of cardiac interoceptive awareness in the active tDCS condition only. This finding provides support, albeit limited, for our hypothesis that HD-tDCS over the right somatosensory cortex can improve interoceptive awareness for the heartbeat-perception task. Regarding emotional perception, again contradicting our initial hypothesis, we observed no changes after active tDCS in valence or arousal ratings for either perception of interoceptive tasks, or rating of emotional pictures. Overall, we were therefore unable to produce consistent enhancement of interoceptive abilities or emotional experience in this study.

Possible explanations for these findings range from methodological aspects referring to interoceptive-accuracy measurements both in the cardiac as well as respiratory domain, to the design of our tDCS protocol, and to HD-tDCS effectiveness itself.

Methodological aspects of the heartbeat-perception task mainly relate to factors affecting heartbeat perception other than interoceptive accuracy itself, thereby threatening the validity of the heartbeat-perception task. For instance, we did not account for participants' beliefs about their own heart rate, as well as cardiac processes such as blood pressure, which have both been found to be influential in heartbeat perception [101,102]. If differences between participants occurred in these factors, the factors potentially influenced cardiac interoceptive-accuracy and awareness scores and thereby, could have overpowered effects elicited by HD-tDCS. Taking heartbeat beliefs and cardiodynamics into account may strengthen further investigations on the effects of HD-tDCS over the S1 on cardiac interoception.

Compared to cardiac-interoception-measurement methods, there are few methods available for measuring respiratory interoception, and no standardized method has yet been established. We designed our paradigm based on previously used protocols, asking participants to rate which of several inspiratory loads at different levels they are presented with, and calculating accuracy

scores [13,52]. However, there are newly developed paradigms for evaluating respiratory interoception that might contribute to a higher reliability and standardization of respiratory-interoceptive measurements. For instance, variation of the length of inspiratory occlusion rather, than of the intensity of inspiratory load, has been proposed [103]. A respiratory-resistance-sensitivity task has also been presented in which subjects are presented with two inhales at different inspiratory loads in each trial, and asked to indicate which of the two inhales required more effort, using a two-interval forced-choice protocol [104]. A custom 3D-printed apparatus and adaptive algorithm for this task allows for automated and standardized measurement of the minimal stimulus an individual can reliably discriminate from a regular inhale [104]. Future studies assessing tDCS effects on interoception might implement such novel tasks to improve respiratory interoceptive assessment.

Regarding study design, future investigations may benefit from alterations to our ergometric pre-activation. With this paradigm, we aimed to add a bottom-up activation in interoceptive neural networks to the expected topdown activation from active HD-tDCS. The pre-to-post increase for both active and sham tDCS conditions that we observed for cardiac- and respiratory-interoceptive awareness supports the notion that this bottom-up activation was successful. We chose a target heart rate of 150 bpm for our pre-activation, as it has been found to elicit higher cortical activity in interoception related brain structures than did exercise with a lower intensity [96]. However, a moderate level of physical strain may be more effective for improvement in interoceptive perception than a high level of physical strain [100]. Additionally, a fixed target of 150 bpm does not necessarily result in equal levels of physical strain for every participant. Exercise intensity depends more on the relation of exercise heart rate to maximum heart rate, rather than absolute exercise heart rate itself [105]. As maximum heart rate differs individually depending on factors such age, sex, and body mass index, a fixed heart rate of 150 bpm likely results in a different exercise intensity for different people [105,106]. It might therefore be preferable to calculate maximum heart rate for each participant and set a fixed percentage of maximum heart rate as the target heart rate, to ensure that all participants reach a comparable level of exercise intensity. Taking these considerations

into account, adapted ergometric pre-activation may be better suited for supporting tDCS effects with a lower risk of overpowering them.

Future studies should also examine the suitability of different aspects of tDCS application itself. The high variability in methods of existing tDCS research creates a wide range of possible application conditions. Reviews and meta-analyses [50,60,107,108] show that there is great variability in many factors of tDCS application: for instance, there is great variety in stimulation duration, which can last from under 10 min to a full 30 min, and current intensity, which varies between 1 mA and 2 mA. In our study, we applied the maximum current intensity (2 mA) for the most commonly used duration (20 min) [50]. Our postassessment was designed to begin 12 min after stimulation onset. Previous studies began assessment of stimulation effects as early as stimulation onset, and many authors, like us, conducted post-assessment during active stimulation, with a varying amount of time passing between studies [50,107]. Although this procedure has led to significant tDCS effects in the past, several studies targeting the S1 opted to measure post-assessment offline instead, yet still observed effects [50]. Perhaps the most significant difference in tDCS methods lies in the number of administeredstimulation sessions. With more recent work, it seems that administering multiple, more precisely 5 to 10 sessions, is increasingly considered the appropriate approach [60,108]. Therefore, a wide range of possible stimulation designs is offered, and it might be beneficial to explore tDCS effects on interoceptive abilities and emotional experience with the application of multiple sessions and assessments conducted after the full duration of stimulation. It is important that meta-analyses show great variability not only in tDCS administration protocols, but also in effectiveness [60,107,109,110]. If future investigations continue to fail to observe consistent tDCS-induced changes in interoception and emotion, even with adjusted stimulation protocols as discussed, it may be necessary to discuss the utility and effectiveness of HD-tDCS in this area altogether. tDCS, as a neurostimulation method, delivers a weak electric current to the scalp, creating weak electric fields in the brain that can alter neuronal transmembrane potentials and thereby influence cortical excitability [111]. In contrast, TMS administers magnetic pulses that elicit focused currents in the brain, directly affecting and depolarizing neurons [111]. For altering interoceptive abilities and emotional processing, there is evidence emphasizing the utility of repetitive theta-burst TMS protocol [52,56]. Whether this approach is generally more suitable for stronger effects in neuromodulation will need to be evaluated continuously in the future.

The most critical point to be discussed is the possibility that our tDCS stimulation was ineffective. Since we observed no significant changes in somatosensory perception as a result of *active tDCS*, the question arises whether the stimulation protocol achieved the expected neuromod-

ulation of the S1. Explanations for a possibly unsuccessful neuromodulation of the S1 are several. For one, HD-Targets[™] electrode configurations [90], which are based on male head models, may only be inappropriate for our 60% female sample, as brain size differences in respect to sex are consistently found [112]. Beyond sex differences, neuroimaging research from past decades has found robust interindividual structural differences in size and location of structures in human brains [113,114]. Interindividual neuroanatomic variability at the stimulation target point is an even bigger risk using HD-tDCS, as it provides higher focality than traditional tDCS [115]. In future studies, using brain-imaging methods like an functional magnetic resonance imaging (fMRI) to determine the exact location of a target area may be useful to achieve higher precision in electrode placement and to ensure successful stimulation. Additionally, as the S1 comprises all of Brodman Area 1, 2, and 3 [48], and the HD-Targets[™] software offers multiple configurations for each area, a different configuration may prove more effective for observing the expected changes in interoceptive abilities.

The lack of changes in our somatosensory-perception measurement is not necessarily rooted in an unsuccessful neuromodulation. Although tactile stimulation has been found to elicit cortical activity [86], evidence for a causal relation between cortical activity and somatosensory perception is lacking. Animal studies on the relationship between neural activity and behavior illustrate that there is variability in behavior that cannot be conclusively explained solely through neural activity [116]. Furthermore, there is no established measuring instrument for somatosensory perception, and a self-report measure, as used by us, may be susceptible to numerous biases and response sets [117]. Tactile stimulation in this study was also applied manually, which may have caused slight differences in the application of the tactile stimuli, therefore possibly threatening the validity of our somatosensory measurement. All of these aspects lend credibility to the conclusion that despite not observing alterations in the somatosensory perception, the targeted neuromodulation in our study may very well have succeeded.

All aspects discussed are important when explaining why we did not observe a significant change in emotion processing. As many theories emphasize the role of interoception for emotional perception [1-4], a failure to improve interoceptive processing by neuromodulation may also account for the lack of effects on emotion processing. Empirically, reduced interoceptive accuracy, after TMS inhibition of interoceptive networks surrounding the frontotemporal anterior insula and somatosensory cortex, was found to be associated with a flattened emotional experience [56]. This indicates a causal relationship between interoceptive and emotion processing, which supports the idea that it is unlikely that changes in emotion processing can be observed, as long as there is no alteration in interoceptive processing, as we observed in this study. Furthermore, induction



of emotion may not have been entirely successful using the IAPS, as it consists of pictures that are several decades old, including violent and erotic pictures that may not produce the same effect on emotional arousal nowadays. The fact that the arousal measurements elicited by positive and negative pictures in our study were lower than reference values of the IAPS [118], supports this notion. Weaker emotional induction may limit the chance to observe tDCS-induced changes in emotional perception. Future studies may need to assess suitability of the IAPS for emotion induction 20 years after measurement of reference ratings.

For the first time, we attempted to enhance interoceptive abilities and emotional experience using HD-tDCS over the right S1, and our study design has several strengths. For instance, conducting a randomized trial with repeated measurements so that each participant would be exposed to both tDCS conditions eliminated any possible confounding of group-specific variables with the observed effects. We met criticism of varying sham protocols in previous tDCS studies [92] by assessing the physical sensations elicited by tDCS. This allowed us to conclude that participants experienced comparable physical sensations in both active tDCS and sham tDCS, and were unable to distinguish between the two. Even though investigators were not blind to the order in which participants received tDCS, risk of bias in stimulation effects in our study was very low, as our main outcome of interoceptive accuracy was assessed by objective measurement [119]. Another strength of our study lies in our meaningful group size, in comparison to many other tDCS studies in which sample sizes were seldom as large as 30 subjects [50,60].

Based on the insights our study provides, opportunities for improvement in future studies are created, as previously discussed. To extend these, we should mention that we did not include a subjective measure of interoceptive awareness such as the Multidimensional Assessment of Interoceptive Awareness (MAIA-2 [120]), which could have provided important insight into the awareness effect we observed. Furthermore, although the size of our sample is satisfactory, sample heterogeneity is not. We conducted this study with a very young, highly educated, physically active group of participants. Our results might therefore not be generalizable to populations with lower education levels or older age. Further studies with more diverse samples will be necessary to continue reliable examination of the potential for somatosensory tDCS stimulation on interoception and emotion.

5. Conclusions

The present study was the first to evaluate the effects of HD-tDCS over the right S1 on interoceptive abilities and emotional experience. Although we attempted to design and conduct the experiment with the utmost care and consideration of previous findings, we were unable to provide convincing evidence to support our initial hypothe-



ses. We observed no changes attributable to active HDtDCS in interoceptive accuracy, interoceptive sensibility, or emotional experience. Only cardiac interoceptive awareness increased significantly after active HD-tDCS. Despite the findings largely not supporting our assumptions, the present study contributes to the growing body of research on the association of interoception and emotion, and opens up new avenues for their potential modulation by non-invasive brain stimulation. Future studies may benefit by increasing the number of stimulation sessions, adjusting the electrode configuration, lowering the ergometric pre-activation intensity, and assessing additional variables with the potential to influence HD-tDCS effects. Overall, the present study provides an exciting novel approach to modulation of interoceptive and emotional processes, sheds light on potential areas of improvement, and thus creates meaningful grounds for future investigations.

Abbreviations

HD-tDCS, high-definition transcranial direct current stimulation; IAPS, International Affective Picture System; S1, primary somatosensory cortex; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

Availability of Data and Materials

The data analyzed in this article is available upon request to the corresponding author.

Author Contributions

JS, SAH, SML and OP designed the research study. JS and SAH performed the data assessment. SML provided help with participant recruitment and technical support during the experiment. JS, SAH, SML and OP analyzed and discussed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the ethics committee of Ulm University (study number 207/22). All participants were informed about the study and gave written consent.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] James W. What is an Emotion? Mind. 1884; 9: 188-205.
- [2] Lang PJ. The varieties of emotional experience: a meditation on James-Lange theory. Psychological Review. 1994; 101: 211– 221.
- [3] SCHACHTER S, SINGER JE. Cognitive, social, and physiological determinants of emotional state. Psychological Review. 1962; 69: 379–399.
- [4] Damasio AR. Descartes' Error: Emotion, Reason, and the Human Brain. G. P. Putnam's Sons: New York. 1994.
- [5] Craig AD. Interoception: the sense of the physiological condition of the body. Current Opinion in Neurobiology. 2003; 13: 500–505.
- [6] Quadt L, Critchley HD, Garfinkel SN. The neurobiology of interoception in health and disease. Annals of the New York Academy of Sciences. 2018; 1428: 112–128.
- [7] Critchley HD, Garfinkel SN. Interoception and emotion. Current Opinion in Psychology. 2017; 17: 7–14.
- [8] Garfinkel SN, Critchley HD. Interoception, emotion and brain: new insights link internal physiology to social behaviour. Commentary on: "Anterior insular cortex mediates bodily sensibility and social anxiety" by Terasawa *et al.* (2012). Social Cognitive and Affective Neuroscience. 2013; 8: 231–234.
- [9] Garfinkel SN, Seth AK, Barrett AB, Suzuki K, Critchley HD. Knowing your own heart: distinguishing interoceptive accuracy from interoceptive awareness. Biological Psychology. 2015; 104: 65–74.
- [10] Schandry R. Heart beat perception and emotional experience. Psychophysiology. 1981; 18: 483–488.
- [11] Herbert BM, Muth ER, Pollatos O, Herbert C. Interoception across modalities: on the relationship between cardiac awareness and the sensitivity for gastric functions. PloS One. 2012; 7: e36646.
- [12] Schroijen M, Fantoni S, Rivera C, Vervliet B, Schruers K, van den Bergh O, *et al*. Defensive activation to (un)predictable interoceptive threat: The NPU respiratory threat test (NPUr). Psychophysiology. 2016; 53: 905–913.
- [13] Petersen S, Schroijen M, Mölders C, Zenker S, Van den Bergh O. Categorical interoception: perceptual organization of sensations from inside. Psychological Science. 2014; 25: 1059–1066.
- [14] Pollatos O, Gramann K, Schandry R. Neural systems connecting interoceptive awareness and feelings. Human Brain Mapping. 2007; 28: 9–18.
- [15] Carvalho GB, Damasio A. Interoception and the origin of feelings: A new synthesis. BioEssays: News and Reviews in Molecular, Cellular and Developmental Biology. 2021; 43: e2000261.
- [16] Khalsa SS, Adolphs R, Cameron OG, Critchley HD, Davenport PW, Feinstein JS, *et al.* Interoception and Mental Health: A Roadmap. Biological Psychiatry. Cognitive Neuroscience and Neuroimaging. 2018; 3: 501–513.
- [17] Brewer R, Happé F, Cook R, Bird G. Commentary on "Autism, oxytocin and interoception": Alexithymia, not Autism Spectrum Disorders, is the consequence of interoceptive failure. Neuroscience and Biobehavioral Reviews. 2015; 56: 348–353.
- [18] Murphy J, Brewer R, Catmur C, Bird G. Interoception and psychopathology: A developmental neuroscience perspective. Developmental Cognitive Neuroscience. 2017; 23: 45–56.
- [19] Paulus MP, Stein MB. Interoception in anxiety and depression.

Brain Structure & Function. 2010; 214: 451-463.

- [20] Preyde M, Watson J, Remers S, Stuart R. Emotional dysregulation, interoceptive deficits, and treatment outcomes in patients with eating disorders. Social Work in Mental Health. 2016; 14: 227–244.
- [21] Smith R, Kuplicki R, Feinstein J, Forthman KL, Stewart JL, Paulus MP, et al. A Bayesian computational model reveals a failure to adapt interoceptive precision estimates across depression, anxiety, eating, and substance use disorders. PLoS Computational Biology. 2020; 16: e1008484.
- [22] Zamariola G, Vlemincx E, Corneille O, Luminet O. Relationship between interoceptive accuracy, interoceptive sensibility, and alexithymia. Personality and Individual Differences. 2018; 125: 14–20.
- [23] Nord CL, Garfinkel SN. Interoceptive pathways to understand and treat mental health conditions. Trends in Cognitive Sciences. 2022; 26: 499–513.
- [24] Fissler M, Winnebeck E, Schroeter T, Gummersbach M, Huntenburg JM, Gaertner M, et al. An Investigation of the Effects of Brief Mindfulness Training on Self-Reported Interoceptive Awareness, the Ability to Decenter, and Their Role in the Reduction of Depressive Symptoms. Mindfulness. 2016; 7: 1170–1181.
- [25] Khoury NM, Lutz J, Schuman-Olivier Z. Interoception in Psychiatric Disorders: A Review of Randomized, Controlled Trials with Interoception-Based Interventions. Harvard Review of Psychiatry. 2018; 26: 250–263.
- [26] Quadt L, Garfinkel SN, Mulcahy JS, Larsson DE, Silva M, Jones AM, *et al.* Interoceptive training to target anxiety in autistic adults (ADIE): A single-center, superiority randomized controlled trial. EClinicalMedicine. 2021; 39: 101042.
- [27] Weis PP, Herbert C. Bodily Reactions to Emotional Words Referring to Own versus Other People's Emotions. Frontiers in Psychology. 2017; 8: 1277.
- [28] Herbert C. Early, emotional and embodied? Processing of emotional words and body words in the native and a second language – evidence from early event-related brain potential modulation and rapid serial visual presentation. Language, Cognition and Neuroscience. 2022: 1–28.
- [29] Herbert BM, Herbert C, Pollatos O. On the relationship between interoceptive awareness and alexithymia: is interoceptive awareness related to emotional awareness? Journal of Personality. 2011; 79: 1149–1175.
- [30] Herbert BM, Pollatos O, Schandry R. Interoceptive sensitivity and emotion processing: an EEG study. International Journal of Psychophysiology. 2007; 65: 214–227.
- [31] Herbert BM, Pollatos O, Flor H, Enck P, Schandry R. Cardiac awareness and autonomic cardiac reactivity during emotional picture viewing and mental stress. Psychophysiology. 2010; 47: 342–354.
- [32] Pollatos O, Herbert BM, Matthias E, Schandry R. Heart rate response after emotional picture presentation is modulated by interoceptive awareness. International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology. 2007; 63: 117–124.
- [33] Berntson GG, Khalsa SS. Neural Circuits of Interoception. Trends in Neurosciences. 2021; 44: 17–28.
- [34] Pollatos O, Schandry R, Auer DP, Kaufmann C. Brain structures mediating cardiovascular arousal and interoceptive awareness. Brain Research. 2007; 1141: 178–187.
- [35] Critchley HD, Wiens S, Rotshtein P, Ohman A, Dolan RJ. Neural systems supporting interoceptive awareness. Nature Neuroscience. 2004; 7: 189–195.
- [36] Terasawa Y, Fukushima H, Umeda S. How does interoceptive awareness interact with the subjective experience of emotion? An fMRI study. Human Brain Mapping. 2013; 34: 598–612.

- [37] Smith R, Alkozei A, Bao J, Smith C, Lane RD, Killgore WDS. Resting state functional connectivity correlates of emotional awareness. NeuroImage. 2017; 159: 99–106.
- [38] Straube T, Miltner WHR. Attention to aversive emotion and specific activation of the right insula and right somatosensory cortex. NeuroImage. 2011; 54: 2534–2538.
- [39] Critchley HD, Mathias CJ, Dolan RJ. Neuroanatomical basis for first- and second-order representations of bodily states. Nature Neuroscience. 2001; 4: 207–212.
- [40] Park HD, Tallon-Baudry C. The neural subjective frame: from bodily signals to perceptual consciousness. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 2014; 369: 20130208.
- [41] Critchley HD, Harrison NA. Visceral influences on brain and behavior. Neuron. 2013; 77: 624–638.
- [42] Cameron OG, Minoshima S. Regional brain activation due to pharmacologically induced adrenergic interoceptive stimulation in humans. Psychosomatic Medicine. 2002; 64: 851–861.
- [43] Khalsa SS, Rudrauf D, Feinstein JS, Tranel D. The pathways of interoceptive awareness. Nature Neuroscience. 2009; 12: 1494– 1496.
- [44] Couto B, Salles A, Sedeño L, Peradejordi M, Barttfeld P, Canales-Johnson A, *et al.* The man who feels two hearts: the different pathways of interoception. Social Cognitive and Affective Neuroscience. 2014; 9: 1253–1260.
- [45] Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. The Journal of Neuroscience: the Official Journal of the Society for Neuroscience. 2000; 20: 2683–2690.
- [46] Kropf E, Syan SK, Minuzzi L, Frey BN. From anatomy to function: the role of the somatosensory cortex in emotional regulation. Revista Brasileira De Psiquiatria (Sao Paulo, Brazil: 1999). 2019; 41: 261–269.
- [47] Damasio AR, Grabowski TJ, Bechara A, Damasio H, Ponto LL, Parvizi J, *et al.* Subcortical and cortical brain activity during the feeling of self-generated emotions. Nature Neuroscience. 2000; 3: 1049–1056.
- [48] Strotzer M. One century of brain mapping using Brodmann areas. Klinische Neuroradiologie. 2009; 19: 179–186.
- [49] Donkelaar HJ ten, Broman J, van Domburg P. The Somatosensory System. In Stephen GW (ed.) Clinical Neuroanatomy. Springer: Cham. 2020.
- [50] Shin YI, Foerster Á, Nitsche MA. Reprint of: Transcranial direct current stimulation (tDCS) - Application in neuropsychology. Neuropsychologia. 2015; 74: 74–95.
- [51] Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, Antal A, *et al.* Transcranial direct current stimulation: State of the art 2008. Brain Stimulation. 2008; 1: 206–223.
- [52] Pollatos O, Herbert BM, Mai S, Kammer T. Changes in interoceptive processes following brain stimulation. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences. 2016; 371: 20160016.
- [53] Ragert P, Vandermeeren Y, Camus M, Cohen LG. Improvement of spatial tactile acuity by transcranial direct current stimulation. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology. 2008; 119: 805–811.
- [54] Grundmann L, Rolke R, Nitsche MA, Pavlakovic G, Happe S, Treede RD, *et al.* Effects of transcranial direct current stimulation of the primary sensory cortex on somatosensory perception. Brain Stimulation. 2011; 4: 253–260.
- [55] Antal A, Brepohl N, Poreisz C, Boros K, Csifcsak G, Paulus W. Transcranial direct current stimulation over somatosensory cortex decreases experimentally induced acute pain perception. The Clinical Journal of Pain. 2008; 24: 56–63.
- [56] Mai S, Braun J, Probst V, Kammer T, Pollatos O. Changes in

emotional processing following interoceptive network stimulation with rTMS. Neuroscience. 2019; 406: 405–419.

- [57] Thair H, Holloway AL, Newport R, Smith AD. Transcranial Direct Current Stimulation (tDCS): A Beginner's Guide for Design and Implementation. Frontiers in Neuroscience. 2017; 11: 641.
- [58] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. The Journal of Physiology. 2000; 527: 633–639.
- [59] Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W. Modulation of cortical excitability by weak direct current stimulation–technical, safety and functional aspects. Supplements to Clinical Neurophysiology. 2003; 56: 255–276.
- [60] Müller D, Habel U, Brodkin ES, Weidler C. High-definition transcranial direct current stimulation (HD-tDCS) for the enhancement of working memory - A systematic review and metaanalysis of healthy adults. Brain Stimulation. 2022; 15: 1475– 1485.
- [61] Rahman A, Reato D, Arlotti M, Gasca F, Datta A, Parra LC, et al. Cellular effects of acute direct current stimulation: somatic and synaptic terminal effects. The Journal of Physiology. 2013; 591: 2563–2578.
- [62] Datta A, Bansal V, Diaz J, Patel J, Reato D, Bikson M. Gyriprecise head model of transcranial direct current stimulation: improved spatial focality using a ring electrode versus conventional rectangular pad. Brain Stimulation. 2009; 2: 201–7, 207.e1.
- [63] Datta A, Elwassif M, Battaglia F, Bikson M. Transcranial current stimulation focality using disc and ring electrode configurations: FEM analysis. Journal of Neural Engineering. 2008; 5: 163– 174.
- [64] Kuo HI, Bikson M, Datta A, Minhas P, Paulus W, Kuo MF, et al. Comparing cortical plasticity induced by conventional and highdefinition 4 × 1 ring tDCS: a neurophysiological study. Brain Stimulation. 2013; 6: 644–648.
- [65] Dmochowski JP, Datta A, Bikson M, Su Y, Parra LC. Optimized multi-electrode stimulation increases focality and intensity at target. Journal of Neural Engineering. 2011; 8: 046011.
- [66] Borckardt JJ, Bikson M, Frohman H, Reeves ST, Datta A, Bansal V, *et al.* A pilot study of the tolerability and effects of high-definition transcranial direct current stimulation (HDtDCS) on pain perception. The Journal of Pain. 2012; 13: 112– 120.
- [67] Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. The International Journal of Neuropsychopharmacology. 2011; 14: 1133–1145.
- [68] Gandiga PC, Hummel FC, Cohen LG. Transcranial DC stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology. 2006; 117: 845–850.
- [69] Vicario CM, Salehinejad MA, Mosayebi-Samani M, Maezawa H, Avenanti A, Nitsche MA. Transcranial direct current stimulation over the tongue motor cortex reduces appetite in healthy humans. Brain Stimulation. 2020; 13: 1121–1123.
- [70] Alipour M, Chen Y, Jürgens U. Anterograde projections of the motorcortical tongue area in the saddle-back tamarin (Saguinus fuscicollis). Brain, Behavior and Evolution. 2002; 60: 101–116.
- [71] Stevenson RJ, Hill BJ, Hughes A, Wright M, Bartlett J, Saluja S, et al. Interoceptive hunger, eating attitudes and beliefs. Frontiers in Psychology. 2023; 14: 1148413.
- [72] Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971; 9: 97–113.
- [73] Beck AT, Steer RA, Brown G. Beck depression inventory–II. Psychological Assessment. 1996.

- [74] Spielberger CD. State-Trait Anxiety Inventory for Adults. APA PsycTests Database Records. 1983.
- [75] Frey I, Berg A, Grathwohl D, Keul J. Freiburg Questionnaire of physical activity-development, evaluation and application. Sozial- Und Praventivmedizin. 1999; 44: 55–64.
- [76] Cabrera A, Kolacz J, Pailhez G, Bulbena-Cabre A, Bulbena A, Porges SW. Assessing body awareness and autonomic reactivity: Factor structure and psychometric properties of the Body Perception Questionnaire-Short Form (BPQ-SF). International Journal of Methods in Psychiatric Research. 2018; 27: e1596.
- [77] Taylor S, Zvolensky MJ, Cox BJ, Deacon B, Heimberg RG, Ledley DR, *et al.* Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. Psychological Assessment. 2007; 19: 176–188.
- [78] Urbaniak GC, Plous S. Research Randomizer (Version 4.0) [Computer software]. 2013. Available at: http://www.randomiz er.org (Accessed: 11 January 2023).
- [79] Grulke N, Bailer H, Schmutzer G, Brähler E, Blaser G, Geyer M, et al. Standardization of the German short version of "profile of mood states" (POMS) in a representative sample–short communication. Psychotherapie, Psychosomatik, Medizinische Psychologie. 2006; 56: 403–405.
- [80] Pollatos O, Schandry R. Accuracy of heartbeat perception is reflected in the amplitude of the heartbeat-evoked brain potential. Psychophysiology. 2004; 41: 476–482.
- [81] Saghaei M. Random allocation software for parallel group randomized trials. BMC Medical Research Methodology. 2004; 4: 26.
- [82] Bradley MM, Lang PJ. Measuring emotion: the Self-Assessment Manikin and the Semantic Differential. Journal of Behavior Therapy and Experimental Psychiatry. 1994; 25: 49– 59.
- [83] Lang PJ, Bradley MM. International Affective Picture System (IAPS): Technical Manual and Affective Ratings. NIMH Center for the Study of Emotion and Attention. 1997; 1: 3.
- [84] Kaas JH, Collins CE. The organization of sensory cortex. Current Opinion in Neurobiology. 2001; 11: 498–504.
- [85] Trepel M, Mayer-Fally E. Neuroanatomie. Struktur und Funktion. 2017; 18: 30021–30027.
- [86] Olausson H, Ha B, Duncan GH, Morin C, Ptito A, Ptito M, et al. Cortical activation by tactile and painful stimuli in hemispherectomized patients. Brain: a Journal of Neurology. 2001; 124: 916–927.
- [87] Ghazni NF, Cahill CM, Stroman PW. Tactile sensory and pain networks in the human spinal cord and brain stem mapped by means of functional MR imaging. AJNR. American Journal of Neuroradiology. 2010; 31: 661–667.
- [88] Gaetz W, Cheyne D. Localization of sensorimotor cortical rhythms induced by tactile stimulation using spatially filtered MEG. NeuroImage. 2006; 30: 899–908.
- [89] Borsook D, Moulton EA, Tully S, Schmahmann JD, Becerra L. Human cerebellar responses to brush and heat stimuli in healthy and neuropathic pain subjects. Cerebellum (London, England). 2008; 7: 252–272.
- [90] Soterix Medical Inc. Neurophysiological stimulation software/medical HD-TargetsTM. Available at: https://soterixmedic al.com/research/software/hd-targets (Accessed: 10 July 2023).
- [91] Ambrus GG, Al-Moyed H, Chaieb L, Sarp L, Antal A, Paulus W. The fade-in-short stimulation-fade out approach to sham tDCSreliable at 1 mA for naïve and experienced subjects, but not investigators. Brain Stimulation. 2012; 5: 499–504.
- [92] Fonteneau C, Mondino M, Arns M, Baeken C, Bikson M, Brunoni AR, *et al.* Sham tDCS: A hidden source of variability? Reflections for further blinded, controlled trials. Brain Stimulation. 2019; 12: 668–673.
- [93] Richardson JD, Fillmore P, Datta A, Truong D, Bikson M,

Fridriksson J. Toward Development of Sham Protocols for High-Definition Transcranial Direct Current Stimulation (HD-tDCS). NeuroRegulation. 2014; 1: 62–72.

- [94] Garnett EO, den Ouden DB. Validating a Sham Condition for Use in High Definition Transcranial Direct Current Stimulation. Brain Stimulation. 2015; 8: 551–554.
- [95] Neri F, Mencarelli L, Menardi A, Giovannelli F, Rossi S, Sprugnoli G, et al. A novel tDCS sham approach based on modeldriven controlled shunting. Brain Stimulation. 2020; 13: 507– 516.
- [96] Williamson JW, McColl R, Mathews D, Ginsburg M, Mitchell JH. Activation of the insular cortex is affected by the intensity of exercise. Journal of Applied Physiology (Bethesda, Md.: 1985). 1999; 87: 1213–1219.
- [97] Dimkpa U. Post-exercise heart rate recovery: an index of cardiovascular fitness. Journal of Exercise Physiology. 2009; 12: 10–22.
- [98] IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.
- [99] Khalsa SS, Rudrauf D, Damasio AR, Davidson RJ, Lutz A, Tranel D. Interoceptive awareness in experienced meditators. Psychophysiology. 2008; 45: 671–677.
- [100] Schandry R, Bestler M, Montoya P. On the relation between cardiodynamics and heartbeat perception. Psychophysiology. 1993; 30: 467–474.
- [101] Phillips GC, Jones GE, Rieger EJ, Snell JB. Effects of the presentation of false heart-rate feedback on the performance of two common heartbeat-detection tasks. Psychophysiology. 1999; 36: 504–510.
- [102] Ring C, Brener J. Influence of beliefs about heart rate and actual heart rate on heartbeat counting. Psychophysiology. 1996; 33: 541–546.
- [103] Van Den Houte M, Vlemincx E, Franssen M, Van Diest I, Van Oudenhove L, Luminet O. The respiratory occlusion discrimination task: A new paradigm to measure respiratory interoceptive accuracy. Psychophysiology. 2021; 58: e13760.
- [104] Nikolova N, Harrison O, Toohey S, Brændholt M, Legrand N, Correa C, *et al.* The respiratory resistance sensitivity task: An automated method for quantifying respiratory interoception and metacognition. Biological Psychology. 2022; 170: 108325.
- [105] Mann T, Lamberts RP, Lambert MI. Methods of prescribing relative exercise intensity: physiological and practical considerations. Sports Medicine (Auckland, N.Z.). 2013; 43: 613–625.
- [106] She J, Nakamura H, Makino K, Ohyama Y, Hashimoto H. Selection of suitable maximum-heart-rate formulas for use with Karvonen formula to calculate exercise intensity. International Journal of Automation and Computing. 2015; 12: 62–69.
- [107] Ostrowski J, Svaldi J, Schroeder PA. More focal, less heterogeneous? Multi-level meta-analysis of cathodal high-definition transcranial direct current stimulation effects on language and cognition. Journal of Neural Transmission (Vienna, Austria: 1996). 2022; 129: 861–878.
- [108] Espert-Tortajada R, Rebull-Monje M, Gadea-Doménech M. Transcranial direct current stimulation (tDCS) as adjunctive treatment in tobacco use disorder: State of the art and future prospects. Revista Espanola de Drogodependencias. 2021; 46: 5–12.
- [109] Friehs MA, Frings C, Hartwigsen G. Effects of single-session transcranial direct current stimulation on reactive response inhibition. Neuroscience and Biobehavioral Reviews. 2021; 128: 749–765.
- [110] Dedoncker J, Brunoni AR, Baeken C, Vanderhasselt MA. A Systematic Review and Meta-Analysis of the Effects of Transcranial Direct Current Stimulation (tDCS) Over the Dorsolateral Prefrontal Cortex in Healthy and Neuropsychiatric Samples: Influence of Stimulation Parameters. Brain Stimulation. 2016; 9:

501-517.

- [111] Fregni F, Pascual-Leone A. Technology insight: noninvasive brain stimulation in neurology-perspectives on the therapeutic potential of rTMS and tDCS. Nature Clinical Practice. Neurology. 2007; 3: 383–393.
- [112] Eliot L, Ahmed A, Khan H, Patel J. Dump the "dimorphism": Comprehensive synthesis of human brain studies reveals few male-female differences beyond size. Neuroscience and Biobehavioral Reviews. 2021; 125: 667–697.
- [113] Uylings HBM, Rajkowska G, Sanz-Arigita E, Amunts K, Zilles K. Consequences of large interindividual variability for human brain atlases: converging macroscopical imaging and microscopical neuroanatomy. Anatomy and Embryology. 2005; 210: 423–431.
- [114] Llera A, Wolfers T, Mulders P, Beckmann CF. Inter-individual differences in human brain structure and morphology link to variation in demographics and behavior. eLife. 2019; 8: e44443.
- [115] Mikkonen M, Laakso I, Tanaka S, Hirata A. Cost of focality in

TDCS: Interindividual variability in electric fields. Brain Stimulation. 2020; 13: 117–124.

- [116] Renart A, Machens CK. Variability in neural activity and behavior. Current Opinion in Neurobiology. 2014; 25: 211–220.
- [117] Cronbach LJ. Response sets and test validity. Educational and Psychological Measurement. 1946; 6: 475–494.
- [118] Lang PJ, Bradley MM, Cuthbert BN. International affective picture system (IAPS): Technical manual and affective ratings. NIMH Center for the Study of Emotion and Attention. 1997; 1: 3.
- [119] Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ (Clinical Research Ed.). 2008; 336: 601–605.
- [120] Mehling WE, Acree M, Stewart A, Silas J, Jones A. The Multidimensional Assessment of Interoceptive Awareness, Version 2 (MAIA-2). PloS One. 2018; 13: e0208034.