Neural Dynamics of Interoceptive Attention and Awareness:

A Within-Participant fMRI Study

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Abstract

Interoception, the representation of the body's internal state, serves as a foundation for emotion, motivation, and wellbeing. Yet despite its centrality in human experience, the neural mechanisms of interoception are poorly understood. The Interoceptive/Exteroceptive Attention Task (IEAT) is a novel neuroimaging paradigm that compares behavioral tracking of the respiratory cycle (Active Interoception) to tracking of a visual stimulus (Active Exteroception). Twenty-two healthy participants attended two separate scanning sessions (N=44 scans) during a randomized control trial of Mindful Awareness in Body-oriented Therapy (MABT). Compared to Active Exteroception, Active Interoception led to widespread cortical deactivation. Greater self-reported interoceptive awareness (MAIA scale) predicted sparing from deactivation along the anterior cingulate cortex (ACC) and left lateral prefrontal cortex. The right insula- typically described as a primary interoceptive cortex- was only specifically implicated by its deactivation during a paced respiration condition (Active Matching), relative to both Active Exteroception and Interoception. Instead, psychophysiological interaction analysis characterized Active Interoception as promoting greater ACC connectivity with lateral frontal and parietal regions commonly referred to as the Dorsal Attention Network. By comparing attention between highly accessible interoceptive and exteroceptive stimuli, these findings recast interoceptive attention as broadly inhibitory, linking greater interoceptive awareness to spared cortical inhibition within well-characterized attentional networks. In contrast to a literature that relates detection of liminal signals such as the heartbeat to anterior insula activity, attention towards accessible body sensations such as the breath may lead to a context of cortical inhibition in which sensory signals from the body may be better discerned.

Introduction

Interoception is the sense of the body's internal state, enabled by a variety of cutaneous and subcutaneous sense-receptors (Craig, 2002; Khalsa et al., 2009). The brain's representation of the body is central to human experience, providing homeostatic cues (Strigo & Craig, 2016) that inform emotion (Barrett, 2017; Wiens, 2005), motivation (Craig, 2003; Critchley & Garfinkel, 2017), and our general sense of wellbeing (Farb et al., 2015; Ferentzi et al., 2019). Yet despite its centrality in human experience, interoception is not well-understood when compared to the five "canonical" human senses: vision, hearing, touch, taste and smell (Chen et al., 2021).

Improving our understanding of interoception's mechanisms is important given its centrality in contemporary theories of wellbeing. Embodied feelings are commonly argued to serve as the basis for human emotion (Barrett, 2017; Craig, 2002; Critchley & Garfinkel, 2017), and interceptive dysfunction is thought to underlie a variety of affective disorders (Chen et al., 2021; Paulus & Khalsa, 2021; Weng et al., 2021). Improving the capacity to skillfully attend to interoceptive cues remains a central target of contemplative interventions such as mindfulness training (Farb et al., 2015; Gibson, 2019; Price & Hooven, 2018), with established efficacy for a variety of clinical conditions, including depression (Kuyken et al., 2016), chronic pain (Hilton et al., 2017), and substance use (Li et al., 2017). Such interventions are thought to address intolerance for interoceptive signals, which leads vulnerable individuals into patterns of experiential avoidance (Anestis et al., 2007; Leyro et al., 2010; Price & Hooven, 2018).

Interoceptive sensitivity or intolerance is conceptualized in the clinical literature as *experiential avoidance* (Hayes et al., 1996); from an emotion regulation perspective, avoidance is a strategy that disengages attention from aversive stimulation (Gross, 2015). Avoidance provides short-term relief, but ultimately limits the ability to recognize distressing emotions and

engage in self-care (Price & Weng, 2021), or to notice improvements in symptom burden and savor positive experiences (Garland et al., 2017). As such, understanding the neural mechanisms supporting interoceptive attention appears to be an important aim for empirical research.

Interoceptive Attention vs. Accuracy

Despite its theorized importance for wellbeing, interoceptive attention is not generally the focus of interoception research. Instead, the literature has showcased an empirically tractable family of paradigms which investigate individual differences in interoceptive *accuracy*, tasks that scaffold interoceptive attention while leaving accuracy free to vary. For example, heartbeat detection paradigms focus on the ability to detect a liminal cardiac signal within an experimental context that presupposes the deployment of interoceptive attention (e.g., Garfinkel et al., 2015). This approach has been fruitful from a basic neuroscience perspective, with superior heartbeat detection accuracy linked to greater recruitment of the anterior cingulate (ACC) (Critchley et al., 2004) and anterior insula (Chong et al., 2015), hubs of the brain's "Salience Network" (SLN) (Chand & Dhamala, 2016; Seeley et al., 2007). However, tasks that hold interoceptive attention constant to probe variations in accuracy may not be optimal for understanding the mechanisms of engaging interoceptive attention itself.

Supporting this critique, empirical evidence suggests that clinical dysfunction is not related to compromised interoceptive accuracy. Patients with affective or anxiety disorders often fail to demonstrate compromised accuracy in detection tasks (Desmedt et al., 2020), and conversely, clinically-efficacious interoception-focused practices such as meditation do not appear to improve interoceptive accuracy (Khalsa et al., 2020; Parkin et al., 2014). Further, patients with anxiety or panic disorders have historically demonstrated *superior* interoceptive accuracy (Ehlers & Breuer, 1992; Zoellner & Craske, 1999), but do not respond adaptively to such signals,

tending instead to catastrophize interoceptive experience (Domschke et al., 2010). The ability to sustain attention to interoceptive signals remains a compelling if underexplored operationalization of interoception's role in mental health.

Compounding the issue, neuroimaging findings from interoceptive accuracy paradigms may not actually characterize an interoception-specific network, instead implicating more general neural correlates of sensory discrimination. The activation of the ACC and anterior insula is not unique to interoception, as these regions seem to respond more broadly to information salience across sensory modalities (Uddin, 2015), in keeping with these regions constituting the polymodal SLN (Seeley et al., 2007). Accordingly, recent empirical work directly investigating this issue has suggests that the precise regions engaged in heartbeat detection are not specific to interoception but are part of a broader error-monitoring system (Baltazar et al., 2021).

Emerging neuroimaging research supports the idea that the neural correlates of interoceptive attention may be distinct from correlates of interoceptive accuracy. A recent neuroimaging study that directly compared interoceptive attention and accuracy related interoceptive accuracy to SLN activity, but the dorsal middle insula supported the engagement of interoception attention itself (Haruki & Ogawa, 2021), consistent with its proposed role as a bridge between primary representation cortices in the posterior insula and somatosensory cortices, and sensory integration in the anterior insula (Craig, 2009; Farb et al., 2013a; Pollatos et al., 2007). Critically, clinical neuroimaging investigations of interoceptive attention link deficits in the dorsal mid-insula rather than the anterior insula or ACC to greater depression symptom burden (Avery et al., 2014; Farb et al., 2010). Similarly, hyper-activation of the dorsal mid-insula rather than the anterior insula or ACC is associated with levels of anxiety (Kerr et al., 2016; Tan

et al., 2018). Finally, a recent meta-analysis of psychopathology across a variety of disorders implicates the dorsal mid-insula a general candidate marker of psychopathology rather than the SLN (Nord et al., 2021). Together, these findings support the notion that the neural mechanisms supporting interoceptive representation may be distinct from those that leverage such representation to support accurate discrimination.

Beyond Attention to Skillful Engagement

The literature on anxiety and interoceptive catastrophization indicates that how interoceptive signals are appraised is also relevant for understanding interoception's contribution to wellbeing. Several additional lines of research point away from accuracy being the critical metric of healthy interoceptive processing. Instead, empirical studies favor the role of *interoceptive sensibility*: the quality of – or attitude towards- one's subjective engagement with interoceptive signals (Mehling, 2016). Within signal detection paradigms, interoceptive sensibility, not accuracy, is linked to well-being (Ferentzi et al., 2019; Schuette et al., 2021), and a growing qualitative literature relates trust and valuation of interoceptive signals as a positive indicator of wellbeing (Calì et al., 2015; Hanley et al., 2017; Trevisan et al., 2019).

Perhaps the most common and general (i.e., not task-specific) index of subjective interoceptive engagement is the Multidimensional Assessment of Interoceptive Awareness (MAIA), which in validation has demonstrated strong associations to subjective wellbeing (Mehling et al., 2012, 2018). The MAIA is a broad and general measure that examines multiple indicators of subjective interoceptive attention including awareness, comfort, skill at sustaining attention, and trust. The MAIA is sensitive to treatment effects from clinically efficacious interoceptive-focused interventions, with studies demonstrating a positive relationship between

improved interoceptive awareness on the MAIA and treatment health outcomes (Fissler et al., 2016; Price et al., 2019; Roberts et al., 2022).

Some prior attempts to explore the MAIA as a covariate of interoceptive engagement should be noted. One study examined MAIA moderation of interoceptive activation in a focal subregion of the insula (the dorsal dysgranular layer) but reported null results (Stewart et al., 2020). Another study related poorer subjective regulation of interoceptive signals to greater activity within interoceptive networks (Stern et al., 2017); however, this covariance focused on a problematic subfactor of MAIA items that was (i) found to have low consistency, prompting a revised version of the scale (Mehling et al., 2018), and (ii) focused on regulation difficulties rather than the presence of interoceptive awareness. Whether variation in subjective interoceptive awareness moderates neural engagement during interoceptive attention thus remains largely unknown.

Task Difficulty as a Confound

A final issue in interoception research has been a lack of experimental control between task conditions, such as presenting equivalent perceptual features and task difficulty. For example, our research group previously contrasted exteroceptive and interoceptive attention by comparing visual tasks against a passive breath monitoring condition (Farb et al., 2013). In this study, exteroceptive attention to a visual stimulus recruited visual cortices and aspects of the frontoparietal dorsal attention network (DAN) (Ptak, 2012; Szczepanski et al., 2013), while attention to internal sensations of the breath recruited the posterior cingulate cortex and posterior insula, which are respectively hubs of the default mode network (DMN) (Greicius et al., 2003) and primary interoceptive representation cortex (Craig, 2002, 2003). Yet in hindsight, the interoceptive task was less demanding than the exteroceptive task- interoception required passive

observation of the breath, with a static fixation cross on screen, while exteroception featured changing visual stimuli and occasional button responses. Thus, the DAN/DMN distinction between exteroception and interoception was confounded with effort and reporting demands. Supporting this concern, a recent paper contrasted interoceptive and exteroceptive attention to the breath, but this time the interoception condition was significantly more difficult than the exteroceptive condition (Wang et al., 2019). In accordance with a DAN-as-effort hypothesis, Wang et al. presented opposite findings to Farb et al. (2013): the more difficult interoceptive task recruited the DAN, whereas exteroception showed relatively greater DMN activity. Thus, our understanding of neural mechanisms supporting interoception has to date been obscured by difficulties in matching experimental task demands.

A Novel Paradigm

The present study aimed to better understand the neural mechanisms of interoceptive attention, improving upon limitations of past research. The Interoceptive/Exteroceptive Attention Task (IEAT) is a novel paradigm for exploring the neural dynamics of respiratory attention and awareness. The IEAT consisted of five conditions: Passive Exteroception, Passive Interoception, Active Interoception, Active Exteroception, and Active Matching (a paced breathing condition), as shown in Figure 1.

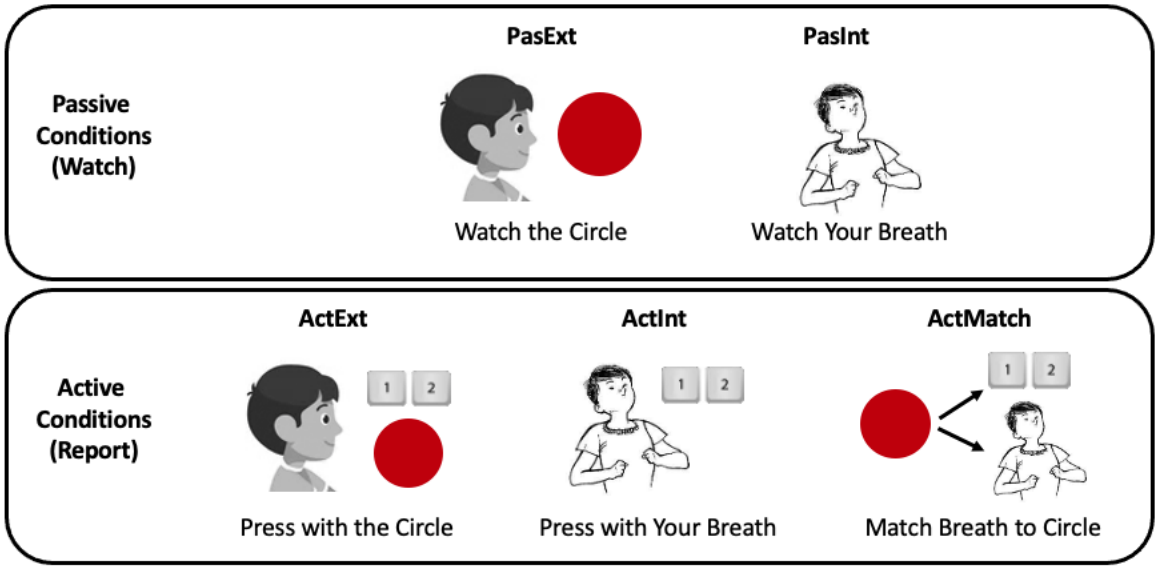

Figure 1. Schematics for the Interoceptive/Exteroceptive Attention Task (IEAT).

To promote a participant sample that varied in interoceptive awareness, the study was conducted in the context of a randomized control trial of Mindful Awareness in Body-oriented Therapy (MABT), a well-validated, clinical intervention the focuses on developing the interoceptive capacities of identifying, accessing, and appraising internal bodily signal to support adaptive emotion regulation (Price & Hooven, 2018). The trial was registered with ClinicalTrials.gov (NCT03583060) with the full study protocol pre-registered with the Open Science Framework (https://osf.io/y34ja). All study materials, including the code to run the experiment and subsequent fMRI analysis, statistics, and graphing scripts, are available on the Open Science Framework (https://osf.io/ctqrh/).

Hypotheses

The central task contrast within the IEAT involved having participants track the respiratory cycle (Active Interoception) compared to tracking a pulsing circle image (Active Exteroception). We hypothesized (H1) that compared to Active Exteroception, Active Interoception would

activate the right posterior and middle insula, without differentially engaging the DAN or the DMN.

Second, we were also interested in whether the subjective quality of interoceptive awareness might moderate neural representation. Our second hypothesis (H2) was that the contrast featured in H1 would be moderated by individual differences subjective interoceptive awareness. Specifically, we hypothesized that greater subjective interoceptive awareness (MAIA scores) would be linked to greater interoception-related activity in the SLN, such as the ACC and anterior insula.

Third, we explored the neural distinction between endogenous and exogenous control of the interoceptive signal by manipulating whether participants reported on spontaneous respiratory rhythm vs. matching respiration to an external stimulus. Endogenous and exogenous control of the visual system appears to be mediated by the same neural network (Peelen et al., 2004), but endogenous control leads in exteroceptive modalities leads to more sustained activation, indicative of enhanced sensory tracking of the sensory target over time (Serences & Yantis, 2007). It was therefore hypothesized (H3) that a right insula pathway would be more activated during reporting of endogenous breath sensation (Active Interoception) than when matching the breath to an exogenous stimulus (Active Matching), emphasizing the need for free sensory integration of the interoceptive signal to maximally engage interoceptive neural networks.

Finally, a conditional, exploratory hypothesis was made based on the expectation that a hub of interoceptive engagement would be identified that was sensitive to both (i) the interoception / exteroception distinction (H1), and (ii) individual differences in self-reported interoceptive awareness (H2). It was hypothesized (H4) that this hub would act as a seed region

embedded in a broader neural network. Specifically, we hypothesized that a psychophysiological interaction between [Active Interoception – Active Exteroception] and seed timecourse activity would implicate a broader attentional network supporting interoceptive awareness. Given a lack of consensus in prior research, we were agnostic as to whether this network would resemble the DAN associated with exteroceptive attention, or a posterior DMN associated with stimulus independent thought.

Results

Control Analyses / Manipulation Checks

Effects of Attention on Respiration Rate

Visual inspection suggested that respiration signal normalization (Figure 2A) was successful for all participant sessions. The study-wide average respiration frequency was .21 Hz. A main effect of IEAT task condition was observed, $F(4,850) = 9.33$, $p < .0001$, such that respiration was slower during Active Interoception than in any of the other conditions, with an average reduction of .02 Hz, 95% CI [.01, .03] (Table S1). No other conditions differed in average respiration rate (Figure 2B; Table S2).

Interoceptive and Exteroceptive Tracking Accuracy

Visual inspection suggested that keypress matching to respiration (Active Interoception) and visual circle waveforms (Active Exteroception and Active Matching) was successful for all participant sessions (Figure 2C). Participant tracking of the respiratory and circle cycles was analyzed to determine the maximum correlation between button-presses and change in respiration phase (inhalation/exhalation) or circle phase (growing/shrinking) during the three active response conditions. This technique estimated the correspondence between button-presses and both sensory targets for both Active Matching and Active Exteroception; for Active

Interoception, only the correspondence with the respiratory cycle was estimated, as the button-presses controlled the visual circle cycle in this condition, yielding a perfect button/stimulus correlation in all cases.

Figure 2D illustrates the excellent correspondence between respiration and button-presses in both the Active Interoception (spearman's r_s = .88) and Active Matching conditions (r_s = .90), and between the visual circle and button-presses in both the Active Exteroception (r_s = .89) and Active Matching conditions (r_s = .89). As a control condition, we also analyzed correspondence between respiration and button-presses in the Active Exteroception condition, where participants were attending to the visual circle rather than the respiratory cycle. A main effect of IEAT task condition was observed, $F(4,850) = 71.61$, $p < .0001$, such that button-press / target correspondence was lower for respiration during the Active Exteroception condition (r_s = .70) than in any of the other combination of targets and conditions, with an average spearman correlation reduction of .19 95% CI [.17, .21] (Table S3). No other conditions differed in target / button-press correspondence (Figure 2D; Table S4).

The results suggest that participants accurately and reliably tracked both their respiratory cycle and the visual circle when instructed to do so, with lower correspondence between button-presses and respiration observed during the Active Exteroception condition, where respiratory tracking was not required. Furthermore, no evidence of differences between the active tracking conditions was observed, suggesting equivalent accuracy between the Active Interoception and Exteroception conditions.

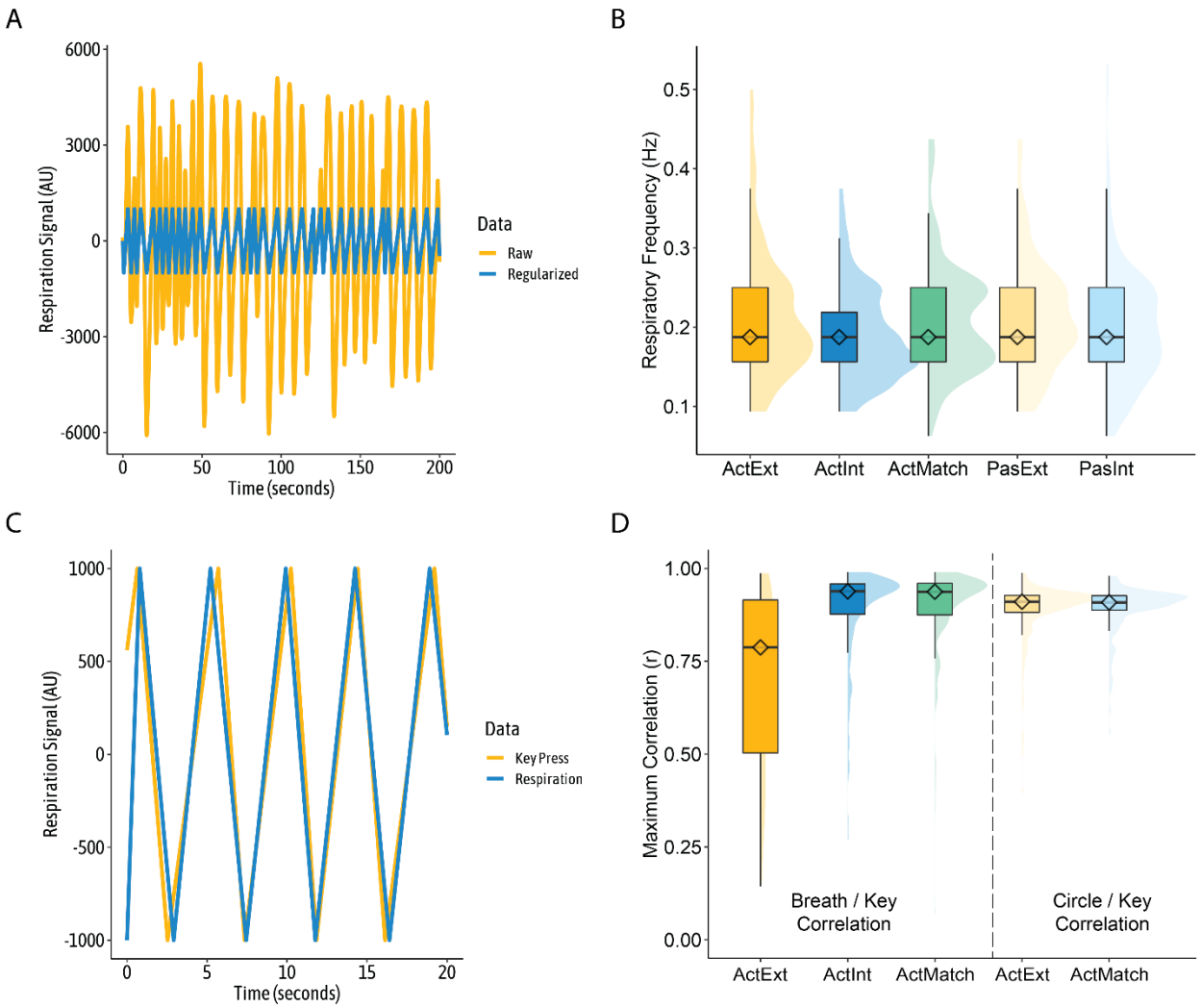

Figure 2. Respiration and Visual Tracking. **(A)** Respiration signal normalization was successful. **(B)** Respiration was slower during Active Interoception than in other conditions. **(C)** Matching participants' button-presses to respiration / visual stimulus cycle was reviewed through visual inspection. **(D)** Correlation analysis showed excellent correspondence between change in respiration phase (inhalation/exhalation) / button-presses and visual stimulus phase (expanding/contracting) / button-presses in all conditions relative to the control condition (respiration/button correspondence during ActExt, when respiration was not the target).

For the Active Exteroception and Match conditions, participant tracking of the circle stimulus cycle was additionally analyzed using behavioral log data that documented whether participants had pressed the correct button on the fMRI button box during each circle expansion and contraction phase, i.e., "1" for expansion, "2" for contraction. Participants performed well in circle tracking, with an error proportion of .094 [.058, .131] in the Match condition and .064

[.027, .101] in the Active Exteroception condition. The difference in tracking accuracy was not significant, $t(153) = -.03$ [-.07,-.01], p =.185, despite the additional requirement of matching the breath to the circle in the Active Matching condition.

Main Effects of Reporting Demand [Active vs. Passive]

As a manipulation check, we examined the main effect of Reporting Demand [Active > Passive], and as expected found elevated activity in left motor and somatosensory cortices and throughout the cerebellum, in keeping with the right-handed button-press requirements in the Active conditions (Table S5, Figure 3A). Unexpectedly, Active Reporting was also linked to deactivation throughout the cerebral cortex, and along the cortical midline and in DMN hubs such as the medial prefrontal cortex, posterior cingulate, and bilateral temporal parietal junction.

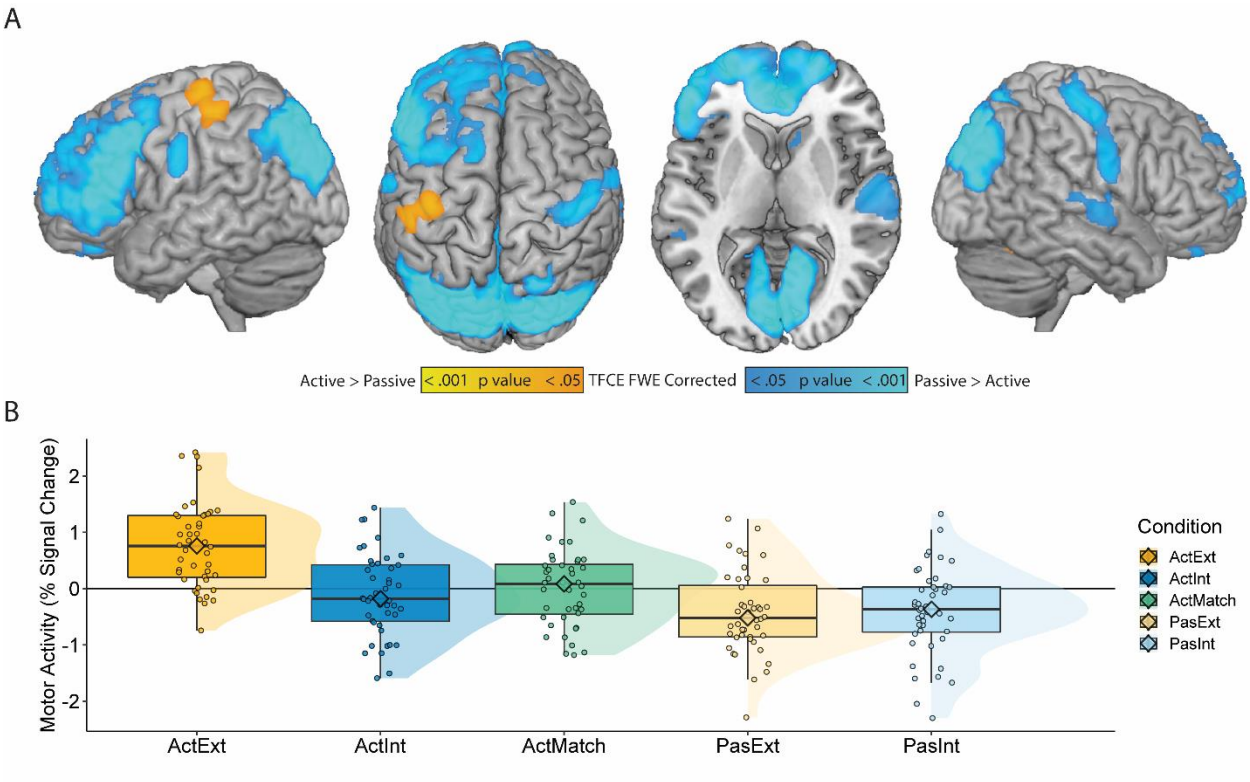

Figure 3. Main Effects of Interoceptive Reporting Demand [Active vs. Passive]. **(A)** [Active > Passive] revealed elevated activity in left motor and somatosensory cortices and throughout the cerebellum. [Passive > Active] revealed reduced activation along the cortical midline and in default mode network hubs, e.g., medial prefrontal cortex, posterior cingulate, and bilateral

temporal parietal junction. **(B)** Median % signal change across the regions revealed highest activation in the Active Exteroception condition and the lowest activation in the two Passive conditions.

Post-hoc signal extraction from the motor region (Figure 3B) revealed greater activity for Active Exteroception than for Active Interoception, β =.88, t(194) = .89, 95% CI [1.16, .61], and active matching, β = .75, t(194) = .75, 95% CI [1.02, .48], despite having nearly identical response requirements.

H1: Comparing Interoceptive and Exteroceptive Attention

Interaction between Reporting Demand and Attentional Target

The reasons for deactivation associated with active reporting, as well as the reduced activation in the motor area for the Active Matching and Active Interoception tasks, was clarified by a whole-brain interaction analysis between Reporting Demand [Active vs. Passive] and Attentional Target [Exteroception vs. Interoception]. The interaction implicated almost the entire cerebral cortex, with follow-up analysis revealing deactivation in the Active Interoceptive conditions (Active Interoception + Active Matching) relative to the other task conditions (Figure 4).

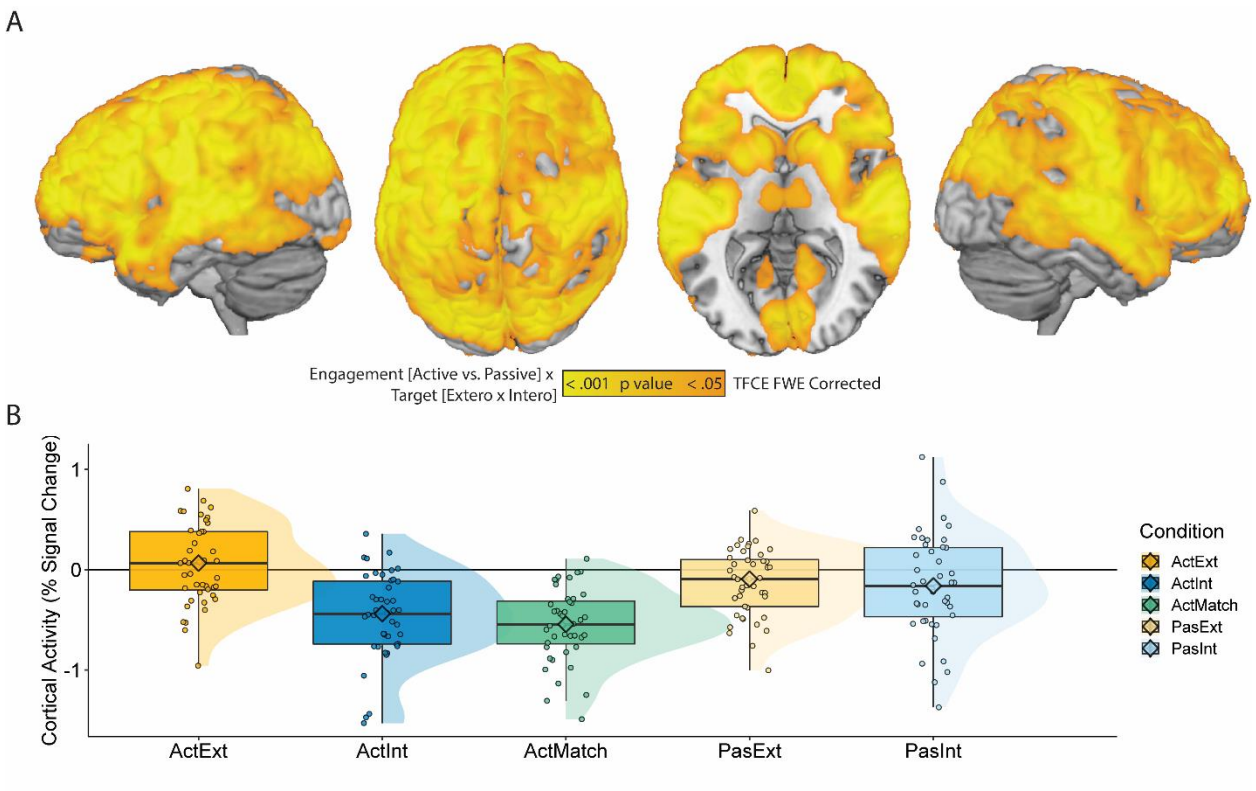

Figure 4. Interaction between Reporting Demand [Active vs. Passive] and Target [Exteroception vs. Interoception]. **(A)** The interaction implicated most of the cerebral cortex. **(B)** Median % signal change across the regions revealed deactivation in conditions involving Active Interoception, i.e., Active Interoception and Active Matching, relative to the other three tasks.

Follow-up simple effects analyses (Table S6) were conducted to explore the interaction effect more fully. Few differences were observed between the Passive conditions, except for greater activation in motion-related lateral occipital area V5 / MT during Passive Exteroception compared to Passive Interoception. The V5/MT finding is consistent with a post hoc realization that we had failed to fully match task features, as Passive Interoception was the only condition in which the circle stimulus remained stationary rather than pulsing.

When comparing the Active conditions, most of the cerebral cortex deactivated during Active Interoception and Active Matching compared to Active Exteroception, suggesting that the tracking the breath drove cortical deactivation. To confirm this interpretation, median percentage signal change was extracted from the interaction regions for all 5 experimental conditions. Post-

hoc pairwise comparisons suggested that all conditions deactivated relative to Active Exteroception except for Passive Exteroception, and that the Active Interoception conditions (Active Interoception + Active Matching) were also linked to deactivation relative to both Passive Exteroception and Passive Interoception (Table S7).

The unexpected, widespread deactivations during Active Interoception raised concerns among the research team that the effects might stem from using the Threshold Free Cluster Estimation (TFCE) method for multiple comparison correction. Post hoc analyses were run using conventional voxel height corrections at (i) $p < .001$ uncorrected, (ii) FWE corrected to $p < .05$, and FWE corrected to $p < .01$. However, as can be seen in Figure S1, the TFCE results were replicated at $p < .001$, with more focal deactivations remaining significant even at a conservative $p < .01$ FWE threshold within the sensorimotor cortex, temporal parietal junction, and in both medial and lateral aspects of the prefrontal cortex. The widespread pattern of deactivation therefore did not stem from using the TFCE technique.

H2: Covariates of Self-Reported Interoceptive Awareness

To better understand the nature of the deactivation observed during Active Interoception, a focal analysis was conducted on the first-level contrast of [Active Exteroception > Active Interoception] to investigate the potential moderating role of self-reported interoceptive awareness (MAIA scores) on this pattern of widespread cortical deactivation.

Interoceptive awareness was significantly related to the level of deactivation observed across a subset of the cortical regions implicated in interoception-related deactivation (Figure 5A/B). Specifically, activity in the anterior cingulate cortex (ACC), dorsomedial prefrontal cortex, and left lateralized frontoparietal regions all demonstrated significant associations with

interoceptive awareness, such that greater MAIA scores were associated with a *reduced deactivation* during Active Interoception relative to Active Exteroception (Figure 5C; Table S8).

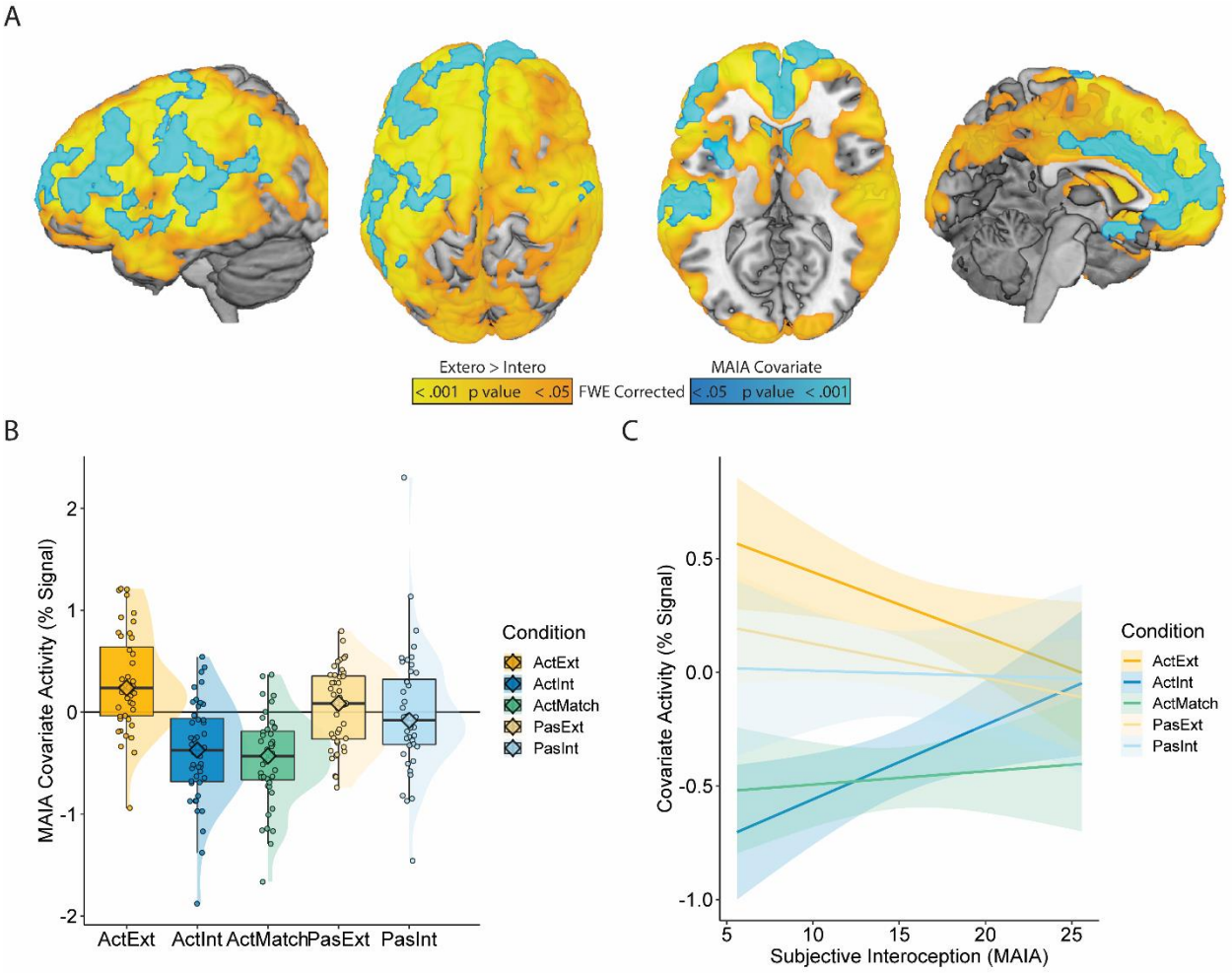

Figure 5. Covariates of Self-Reported Interoceptive Awareness. **(A)** Orange regions denote areas of deactivation during Active Interoception relative to Active Exteroception. Blue regions indicate MAIA covariates of this whole brain contrast. **(B)** Median signal extraction from the MAIA covariate regions for each of the 5 experimental conditions. **(C)** Relationship between MAIA score and neural activity during each of the 5 experimental conditions.

The formal conjunction of interoception-related deactivation [Active Exteroception > Active Interoception] and the MAIA covariate regressor implicated the ACC in particular, k = 465, peak Z = 3.92, x=0; y = 12; z=36. This region was retained as a seed region of interest (ROI) in the ensuing PPI analysis (H4) described below.

H3: Endogenous vs. Exogenous Sources of Interoceptive Control

The final planned analysis of task conditions involved comparisons between the two Active Interoception conditions (Active Interoception vs. active matching). Relative to the endogenously-paced Active Interoception condition, the exogenously-paced Active Matching condition led to deactivation along a right-lateralized insula/operculum pathway, and also within the ventral occipital cortex and cerebellum (Figure 6, Table S9). In other words, when participants were not allowed to report on their own natural respiratory rhythm, interoception-related deactivation extended into sensory cortices include a right-lateralized insula pathway, whereas endogenous interoception spared this pathway from deactivation.

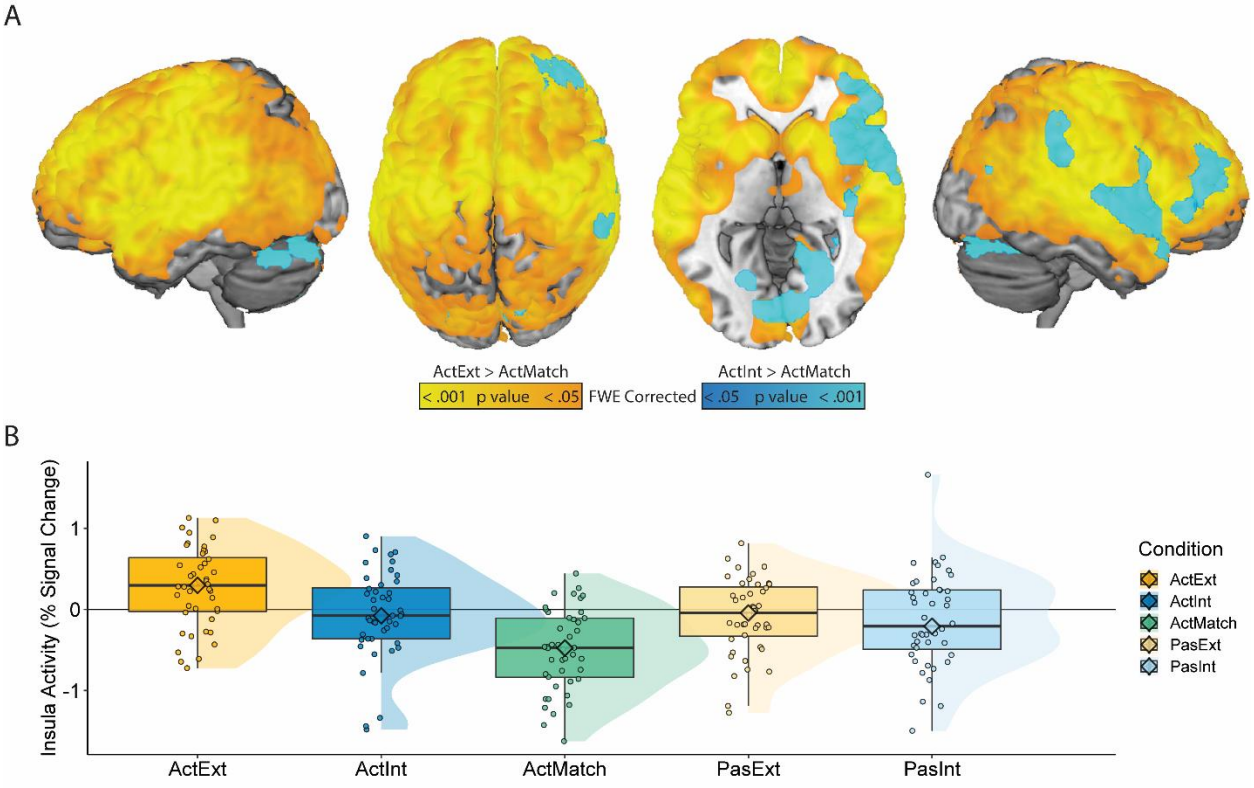

Figure 6. Endogenous vs. Exogenous Sources of Interoceptive Control. **(A)** Active matching was contrasted against both the Active Exteroception (Orange) and Active Interoception (Blue) conditions to reveal unique neural activity related to exogenous control of the respiratory rhythm. **(B)** The median % signal change across the regions identified via the [Active Interoception > Active Matching] contrast.

H4: Psychophysiological Interaction (PPI) Analysis

The anterior cingulate cortex (ACC) region of interest (Figure 7A/B) was entered as a seed region in a psychophysiological interaction (PPI) analysis. The PPI analysis explored changes in functional connectivity with the ACC (Figure 7C) as a function of the two experimental conditions (Active Interoception vs Active Exteroception). The analysis revealed a strong integration of the ACC into regions consistent with the DAN during Active Interoception (Figure 7D; Table S10).

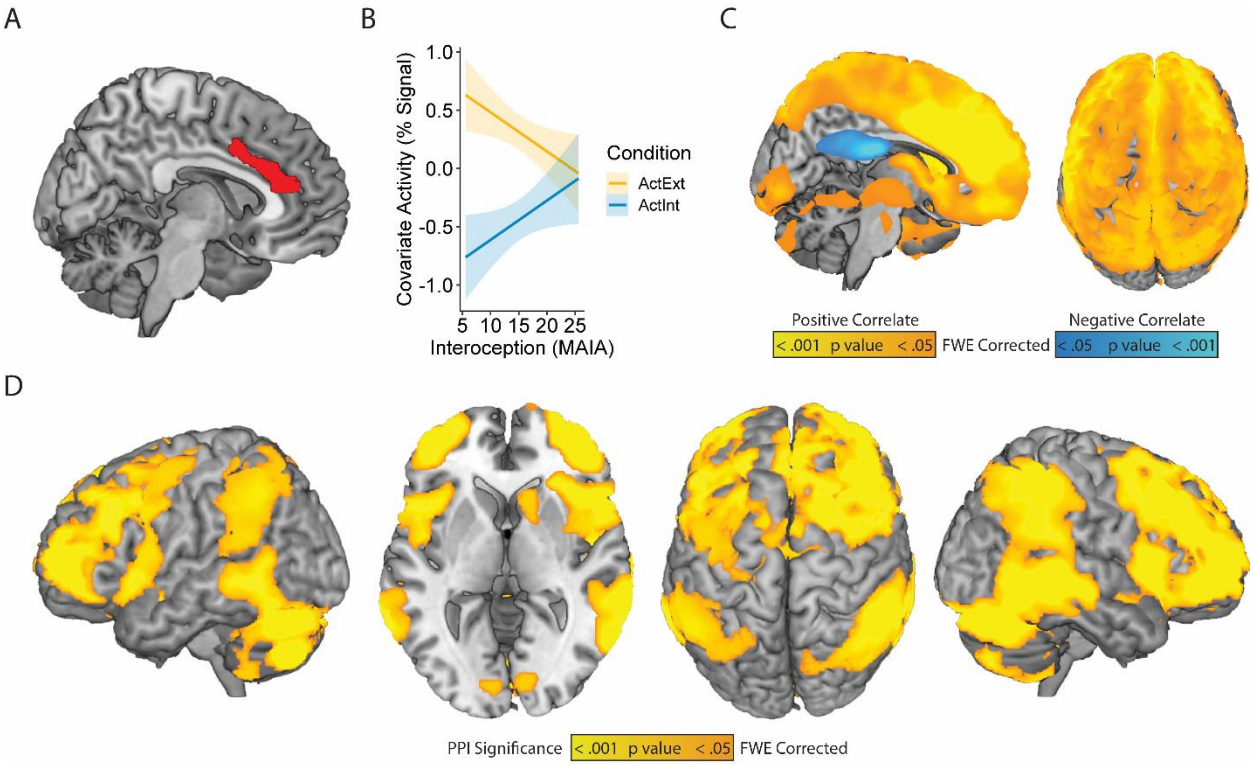

Figure 7. Psychophysiological Interaction (PPI) Analysis. **(A)** The ACC seed region obtained from the MAIA covariate analysis. **(B)** The relationship between MAIA scores and cortical activity displayed in Figure 4C, simplified to display only the Active Interoception and Active Exteroception conditions. **(C)** Functional connectivity with the ACC seed region, i.e., the main effects of ACC signal activity unmoderated by task condition. **(D)** PPI between ACC regional activity and task conditions, demonstrating enhanced ACC connectivity with a frontoparietal network during Active Interoception relative to Active Exteroception.

Discussion

The IEAT led to a different characterization of interoceptive attention than previously reported, possibly due to better control over several cofounding factors present in prior research. Most strikingly, actively reported interoception of the respiratory cycle resulted in widespread cortical deactivation relative to actively reported exteroception. This pattern of cortical inhibition was moderated by subjective interoceptive awareness, with greater awareness linked to attenuated deactivation of the ACC and left-lateralized frontoparietal regions.

The right anterior insula, commonly implicated in investigations of interoceptive accuracy (Critchley et al., 2004; Haruki & Ogawa, 2021; Wang et al., 2019), was comparably activated in actively-reported interoception and exteroception. This surprising finding is consistent with an account of continuous interoceptive representation in the brain, regardless of attentional target. Only when the respiratory cycle was yoked to an exogenous stimulus (the active matching condition) was the right insula specifically implicated, in the form of a *greater deactivation* along this pathway relative to endogenous, actively reported interoception. Finally, while there was a greater reduction in cortical *activity* during Active Interoception than during Active Exteroception, Active Interoception was linked to greater *connectivity* between the ACC and the frontoparietal dorsal attention network. Implications of these findings are discussed below.

The Interoceptive/Exteroceptive Attention Task (IEAT)

The IEAT was designed to address limitations of past research. First, the paradigm characterized interoceptive attention rather than interoceptive accuracy. This is in contrast to prior research that has focused on differences in discrimination performance once interoceptive attention was actively deployed (c.f., Critchley et al., 2004; Garfinkel et al., 2015). Few studies have investigated the process of directing attention to interoceptive targets compared to other

sensory modalities to isolate brain areas specific to the interoceptive process. Second, in investigating the respiratory signal, the paradigm more directly addresses the type of interoception most directly targeted in popular contemplative practices such as yoga and mindfulness meditation, addressing calls in the interoceptive research literature to move beyond a narrow focus on cardiac perception (Harrison, Köchli, et al., 2021; Khalsa et al., 2020). Third, the paradigm successfully matched task difficulty between interoceptive and exteroceptive conditions, which was not the case in the limited number of prior neuroimaging studies of respiratory attention (c.f., Farb et al., 2013; Wang et al., 2019). Fourth, the paradigm introduced two within-task manipulations that could serve as moderators of interoceptive representation: (i) the presence or absence of reporting demands (active reporting vs. passive monitoring) and (ii) the source of respiratory control within the active reporting condition (endogenous vs. exogenous). Task-demand moderators are important given recent controversy over whether 'canonical' interoceptive hubs such as the anterior insula respond generally to task demands rather than specifically to interoceptive content (Baltazar et al., 2021; Koeppel et al., 2020).

Unlike prior studies in respiratory interoception, the IEAT successfully matched the difficulty of interoceptive and exteroceptive task conditions, with equivalently high levels of accuracy for actively tracking interoceptive and exteroceptive stimuli. All participants were able to perform the task well above chance levels, with behavioral tracking routinely capturing more than 80% of the variance in the dynamic sensory targets. This consistently high level of performance stands in contrast to heartbeat detection paradigms (c.f., Ring & Brener, 2018), where many participants were not able to perform above chance levels. Matched accuracy is also unique relative to prior work on respiratory interoception, suggesting that some previous findings (including the first author's) may be spurious. After matching for task difficulty, past distinctions

between the default mode network (DMN) and dorsal attention network (DAN) were largely eliminated in the distinction between interoceptive and exteroceptive attention. Thus, neither DAN nor DMN activity appear to be differentially important for interoception compared to exteroception. This finding is particularly important given early conceptualizations of these networks as reflecting ‘inward’ vs. ‘outward’ processing (Fox et al., 2005), and is more compatible with recent work suggesting that active engagement of attention is associated with reduced DMN and greater DAN activity regardless of a person’s attentional focus (internal vs. external) (Scheibner et al., 2017), with the exception perhaps of attention towards automatic processes like mind-wandering (Christoff et al., 2009).

One additional advantage of the IEAT is that it requires no additional specialized equipment and can run on open-source software in a fully automated fashion, unlike other promising but more cumbersome paradigms such as respiratory occlusion (Van Den Houte et al., 2021) or filter detection tasks (Harrison, Garfinkel, et al., 2021), which require manual manipulation of filters that constrain airflow to a face mask. An additional issue with occlusion-based paradigms is that such occlusion also changes oxygen intake profiles for the breath, which can create significant changes to the hemodynamic response function on which fMRI research depends (Birn et al., 2006). For the purposes of manipulating respiratory attention in an fMRI context, the IEAT may offer some advantages over other paradigms.

The IEAT could be improved in one area in particular: the Passive Interoception condition featured a stationary circle stimulus, a design choice made to avoid involuntary attentional capture by a dynamic exteroceptive cue. However, this design led to a non-equivalent visual motion confound between passive interoception and the other four experimental conditions. Accordingly, Passive Interoception showed relative deactivation in the middle temporal (MT or

V5) region of the visual cortex, which is well-established for its sensitivity to motion (Albright & Stoner, 1995). Future iterations of the IEAT might introduce motion to the circle stimulus during Passive Interoception to equalize visual motion across all task conditions.

Hypothesis 1: Interoceptive Attention Activates the Insula and Posterior Cingulate

The first hypothesis (H1) predicted that comparing interoceptive and exteroceptive attention would replicate our prior findings (Farb et al., 2013), specifically that interoceptive attention would activate the posterior and middle insula relative to exteroceptive attention. This hypothesis was not supported. Beyond the motion confound noted above, there were no significant distinctions between the passive attention conditions, suggesting that prior findings employing passive breath interoception (e.g., Farb et al., 2013) may have been predicated primarily on failure to match task demands. Instead, unexpectedly large and diffuse deactivating effects were observed in the contrast between Active Interoception and Active Exteroception.

While prior research has related interoceptive accuracy to greater activity and connectivity within the SLN (Chong et al., 2017; Critchley et al., 2004; Tan et al., 2018), the current evidence suggests that actively attending to the respiratory cycle has a powerful inhibitory effect on the cortical BOLD response, including putative interoceptive regions within the SLN. Despite such deactivation, participants tracked their breaths with excellent accuracy, equivalent to performance in tracking an exteroceptive (visual) signal. These results suggest that interoceptive processing may be continuous and automatic, but largely obscured by additional cortical activity. Interoceptive awareness may require ‘addition by subtraction’, a reduction of competing neural representations rather than the activation of a dormant interoceptive pathway. The idea of an ‘always on’ interoceptive state is consistent with contemporary theories that place interoception as the background of consciousness, such as Damasio’s “Protoself” (Bosse et al., 2008) or “Core

Consciousness" (Parvizi, 2001), and the distinction between a subcortical "Core Self" and higher order representations in the cerebral cortex (Northoff & Panksepp, 2008).

Before characterizing interoceptive attention as a lower-energy monitoring state, several confounding explanations warrant discussion. First, respiratory cycles slowed by approximately .5 Hz in the Active Interoception condition relative to the other four experimental conditions. As such, neural deactivation could plausibly stem from a slower breathing rate, and less oxygen to drive the BOLD response observed by fMRI. However, variation in respiratory activity was controlled for at multiple levels of analysis: motion and cerebrospinal fluid activity were included in first (within-session) level models as physiological noise regressors, and variation in respiratory rate between conditions was modelled as a nuisance covariate in second (group) level models. In addition, the Active Matching condition also provoked cortical deactivation despite a lack of respiratory slowing (Figure 5), undermining the suggestion that respiratory slowing drove the deactivation effect.

Another confounding explanation for the deactivation might be that respiratory signals are amenable to conscious control; they may therefore be more predictable than the exogenous visual cue; and so greater predictability could lead to reduced prediction error and less cortical activity. However, the exteroceptive stimulus was periodic, consistent, and un-jittered, and tracking accuracy was no worse than for respiratory tracking, so there is little evidence of lower predictability. Furthermore, the Active Matching condition yoked respiration and key presses to the exogenous signal and still led to diffuse cortical deactivation, undermining appeals to differences in controllability as an explanation for cortical deactivation.

As changes in respiratory rhythm, task difficulty, predictability, or controllability of the interoceptive signal cannot explain the widespread cortical deactivation observed for

interoceptive relative to exteroceptive attention, it seems that interoceptive attention might indeed be characterized as a reduced-metabolic or low energy brain state. Exactly how the allocation of attention serves to reduce brain activity without impairing performance remains an intriguing question. Performance may be sustained because of noise inhibition along interoceptive pathways (c.f., Kuehn et al., 2016), which could offset the disadvantage seemingly implied by widespread cortical inhibition.

Hypothesis 2: Subjective Awareness is about Making Interoception Salient

A second aim was to explore the potential moderating effects of subjective interoceptive awareness (MAIA scores) on interoceptive network engagement, with the hypothesis that greater subjective interoceptive awareness would be supported by increased SLN activity in the ACC and anterior insula, commensurate with their established role in supporting interoceptive accuracy (Chong et al., 2017; Critchley et al., 2004; Harrison, Köchli, et al., 2021).

Despite an unexpected deactivation context, H2 was supported in showing greater activity within the SLN for participants reporting greater interoceptive awareness on the MAIA. Indeed, participants with the highest MAIA scores were almost totally spared from deactivation along the anterior cingulate and left anterior insula, hub regions of the SLN. These results serve to qualify the characterization of interoceptive attention as widespread cortical deactivation. Rather than simply reducing brain activity, greater interoceptive awareness is related to preserved activity in brain regions supporting attentional monitoring and reporting, counteracting the widespread inhibitory effects that otherwise characterize during interoceptive attention. This moderating effect is consistent with the ‘low-energy state’ theory proposed above, which

characterizes interoceptive attention as a state of preserved attentional monitoring in a less noisy neural environment.

Although not hypothesized, the MAIA moderation effect also included left-lateralized frontoparietal regions associated with language processing, such as Broca and Wernicke's areas (c.f., Blank, 2002 for a review). The inclusion of language areas in the areas related to greater subjective awareness is perhaps unsurprising given that *reportable* awareness requires both access to sensation and the ability to articulate that sensation through language or behavior; a similar activation of left-lateralized activation in and around Broca's area was also evident in participants naïve to mindfulness training when asked to reflect on the felt sense of the body in each moment (Farb et al., 2007).

While it is unknown whether participants higher in self-reported interoceptive awareness were labelling experiences to a greater degree than participants with lower awareness, the interoceptive awareness scale (MAIA) describes feeling comfort and familiarity with interoceptive signals that could reasonably indicate a greater affinity for labelling and describing interoceptive experience. The MAIA is positively correlated with the five-factor mindfulness questionnaire's 'describing' factor, which refers to the tendency to label internal experiences with words (Mehling et al., 2012; Shoji et al., 2018). Nevertheless, the relationship between self-reported interoceptive awareness and the tendency to label experience using subvocalized language (and therefore Broca's area) remains an area that would greatly benefit from further investigation, and may benefit from more focused phenomenological analysis (e.g., Petitmengin & Lachaux, 2013).

Clinical accounts support the characterization of interoceptive awareness as preserved attention within a less noisy field of awareness. For example, mindfulness-based training

programs first promote feelings of calm or relaxation, but then use this more stable attentional state to leverage greater awareness of subtle internal signals that would otherwise be masked by more salient signals. Indeed, a common metaphor in mindfulness-based trainings is to observe how when mental activity subsides (like ripples on a lake), it is easier to then explore the rich underwater environment (Kabat-Zinn, 2005) - indeed such metaphors have led to theoretical descriptions of mindful receptive states as “the brain on silent” (Vago & Zeidan, 2016). In clinical terms, this process may be tantamount to shifting from a state of active monitoring and reactive regulation to one of decentered and nonreactive exploration, which is thought to be a critical step in predicting response to therapeutic intervention (Bieling et al., 2012; van der Velden et al., 2015). Whether the degree of spared activation within the SLN and language processing regions during interoceptive attention *predicts* behavioral training effects or clinically meaningful symptom change has emerged as a tantalizing direction for future research.

Hypothesis 3: Endogenous Control of the Breath is Critical for Insula Activation

Our third hypothesis (H3) postulated that the right insula and cingulate pathway would be activated during exploration of endogenously driven respiration but suppressed when the task demands were focused on behavioral performance, i.e., matching an exogenous signal. In keeping with the mindfulness literature described above, we hypothesized that a state of open exploration of endogenous interoceptive signals was required for maximal engagement of interoceptive neural networks.

This third hypothesis was largely confirmed, specifically implicating the right insula as being responsive to the endogenous/exogenous distinction: right insula activity was inhibited when participants had to control rather than monitor the interoceptive signal. At first glance, two

equally compelling interpretations of this finding are apparent. One possible explanation is that any yoking of behavior to an exogenous sensory signal results in insula deactivation; this explanation however does not explain why the Active Exteroception engaged the right insula comparably to Active Interoception, despite requiring tracking of an exogenous (visual) stimulus. A second potential explanation is that any need to control the respiratory cycle reduces the integration of sensory information and thereby deactivates the insula pathway, which is putatively the *sensory* hub of the SLN (Chand & Dhamala, 2016; Uddin, 2015). From this perspective, any time that respiratory control is emphasized over awareness, a reduction in insula activity should be observed. This reduction in insula activity for respiration but not for a visual stimulus may be due precisely because of the unique characteristics of respiration; an internal 'clock' keeps respiration operating in service of homeostasis and provides an endogenous signal to be integrated along the insula pathway. A visual stimulus, by contrast, has no corresponding endogenous 'clock' driving its behavior; all reporting of exteroceptive signals integrates exogenous sensation, so there is no intrinsic integration process to be suppressed or manipulated.

The explanation that insula activity is suppressed when one ignores the body's endogenous rhythm could be tested in future research by including a condition in which participants perform 'box breathing', holding an internal (endogenous) count of the respiratory cycle that is nevertheless not the product of 'unadulterated'- and presumably homeostatic- signaling. If endogenously paced breathing yields reduced activity in the right insula pathway, it would support the explanation that any constraint on observing the body's intrinsic respiration cycle serves to reduce sensory salience. However, if paced breathing still results in comparable insula activity to Active Interoception, it would clarify attention to any endogenous signal, whether

spontaneous or controlled, is sufficient to engage insula activity, and that it is the presence of an exogenous control signal that suppresses insula activity.

H4: Characterizing the Network Supporting Interoceptive Awareness

The final and most exploratory of our hypotheses examined whether regions sensitive to both interoceptive attention and subjective awareness could implicate a broader interoceptive network. Based on prior research, it was thought that this network would consist primarily of the posterior insula and posterior cingulate cortex (Farb et al., 2013). To test this hypothesis, the ACC was identified as a region where interoception-related deactivation was spared as a function of greater subjective interoceptive awareness. The ACC region was entered into a psychophysiological interaction (PPI) analysis, convolving ACC signal with the Active Interoception vs. Active Exteroception contrast.

The posterior insula / cingulate connectivity hypothesis was not supported. Instead, the analysis revealed that activity within regions commonly characterized as the frontoparietal dorsal attention network (DAN; Spreng et al., 2013; Szczepanski et al., 2013) became more strongly correlated with the ACC during interoception than exteroception. Thus, contrary to a prior suggestion that interoception engages a distinct attentional network (Farb et al., 2013), the same attentional network implicated in exteroceptive neuroimaging paradigms was also implicated by the PPI analysis.

However, it should be noted that DAN activity was still broadly inhibited during interoception; the DAN was only indirectly spared from deactivation via its increased association to the ACC during Active Interoception. As only a subset of participants high in subjective interoceptive awareness showed preserved ACC activity, this yielded a study-wide profile of

DAN interoception-related deactivation at the group level. Hypothetically, a study that formally contrasted groups reporting high and low interoceptive awareness might relate higher interoception to reduced deactivation within the DAN as well as the SLN and left-lateralized language production areas. Regardless of future research's ability to show spared DAN activity during interoception, the present findings relate interoceptive attention to DAN connectivity in a context of broader cortical deactivation, with greater connectivity to the ACC potentially offsetting the reduced metabolic resources afforded to many DAN sub-regions.

Ideas and Speculation

A Question of Certainty?

The current findings stand in contrast to a neuroimaging literature that relates interoceptive accuracy to activation of the SLN, with a particular emphasis on the ACC and the anterior insula (Chong et al., 2017; Critchley et al., 2004; Harrison, Garfinkel, et al., 2021; Ueno et al., 2020). We suggest however that this effect may be more about the uncertainty and ambiguity in judgments required by accuracy paradigms than a unique characteristic of interoceptive attention.

Interoception paradigms optimized to measure accuracy motivate researchers to create high-uncertainty task environments. Modelling individual differences in accuracy requires that accuracy is limited to allow variability in accuracy scores. For example, heartbeat discrimination tasks require that participants perform a two-alternative forced choice as to whether an external signal is in phase with one's heartbeat, yielding a chance performance level of 50%. A recent report of this task described that 50 out of 80 participants had < 60% accuracy (Garfinkel et al., 2015), which parallels the accuracy rate of 62% described in one of the first neuroimaging investigations of this task over a decade earlier (Critchley et al., 2004). When most participants demonstrate ~60% accuracy, it is reasonable to describe a task as a liminal, or high-uncertainty

reporting situation. For respiratory interoception, filter detection paradigms likewise use a psychophysics staircase method to constrain accuracy to between 65%-80%, which again can be reasonably described as a high-uncertainty decision making paradigm. Although a recent respiration discrimination paradigm (Wang et al., 2019) produced better discrimination accuracy rates of 75-82%, this still indicates uncertainty in synchrony judgments. Thus, it is reasonable to categorize most interoceptive accuracy paradigms as requiring decision-making in contexts of *low certainty*.

In contrast to these paradigms, tracking accuracy of the breath via key press during the IEAT was nearly perfectly accurate for all participants. It is reasonable therefore to characterize the IEAT as a *high certainty* paradigm. This is not to disparage the value of the existing research, but rather to suggest that the IEAT has external validity for a different set of *in vivo* situations than may be characterized by low certainty paradigms. There are many situations where one is not sure whether they are detecting an interoceptive signal accurately, i.e., when one is unsure about what one is feeling, e.g., do I feel comfortable with the new person that I just met or not? Am I coming down with an illness, or am I just having a moment of heartburn? In attempting to report on low certainty interoceptive signals, an SLN model of interoception may be appropriate for distinguishing accurate detectors from those who are mostly guessing at their internal state.

On the other hand, many of life's most important interoceptive moments do *not* involve substantial uncertainty around interoceptive dynamics. We are rarely unsure about whether we have become aroused or fatigued – the extremity of these signals often captures our awareness despite our best efforts to focus elsewhere. Indeed, at high levels of emotion provocation, many people will report a need to distract themselves from the salience of their arousal, seeking to establish psychological distance from intense interoceptive feelings before engaging with the re-

interpretation or regulation of such feelings (Shafir et al., 2015; Sheppes et al., 2011). Thus, while there are many situations where interoceptive accuracy is variable and signals are subtle, our most salient emotional situations are arguably those where attention is drawn by a highly salient, low-uncertainty set of interoceptive signals where there is little or no ambiguity, e.g., whether one's breath is labored or racing, that one's heart is pounding, or when feeling hot or cold. In low certainty paradigms, SLN activation could signal participants' readiness to report, a sign that signals within the sensory milieu have met some detection threshold, rather than representation of the interoceptive signal itself. As the IEAT is one of the few behavioral tasks to model interoception in a high certainty situation, here SLN activity is more a function of whether one is required to report on sensory signals at all, irrespective of sensory modality, in keeping with recent research characterizing the SLN as polymodal with respect to its sensory afferents (e.g., Baltazar et al., 2021).

Clinical Implications

The present findings help to characterize the neural mechanisms of clinically efficacious contemplative interventions such as mindfulness training, which stresses the importance of learning to attend to interoceptive signals (Kabat-Zinn, 1990; Weng et al., 2021). Higher MAIA scores, which are associated with a history of contemplative training (Bornemann et al., 2015), were associated with preserved SLN activity within a more general pattern of cortical deactivation, consistent with a preserved capacity to monitor interoceptive experience while filtering out extraneous cognitive elaboration and exteroceptive signals.

The ability to maintain attention to sensation without reacting, elaborating, or evaluating is consistent with psychological definitions of mindfulness (Kabat-Zinn, 2003). The present

findings add nuance to neuroscience models of this dynamic of nonreactive attention. Rather than simply increasing interoceptive representation, or 'emptying' the mind, skillful attention to the breath appears to require a combination of inhibitory and activating mechanisms, as has been recently noted (Lippelt et al., 2014). Here, the neural characterization of interoceptive attention for participants scoring highly on the MAIA scale is consistent with consensus definitions of focused attention during meditation (Lutz et al., 2008), the capacity to increase concentrative awareness by limiting attention to non-targets, thereby improving the ability to observe and report on internal experience. It may therefore be important in clinical contexts to emphasize this 'middle path' between an empty and cluttered attentional field to new practitioners- an empirical question for future studies in mindfulness pedagogy.

A second finding relevant for clinical intervention or contemplative training is that evidence for interoception as a distinct brain state was only apparent during active monitoring, but not during the passive monitoring conditions. While contemplative training may produce states of phenomenologically 'effortless' attention (Bruya, 2010; Tang et al., 2022), the present results suggest that in novice practitioners, an active monitoring/reporting orientation may be optimal for promoting distinct brain states. Advanced practitioners, with tens of thousands of hours of practice, may enjoy reflective attention states with a seeming absence of even SLN activity (Brefczynski-Lewis et al., 2007), but the present findings emphasize a lesser cited finding in this same seminal paper- namely, that attentional networks show a u-shaped function with respect to neural activity during meditation. The present findings support the view that focal neural activation- and presumably commensurate effort to engage these attentional monitoring networks- must first be present before a sustainable effortless state can be reliably achieved, and it may require *years* of practice before such activation / effort is no longer required. From a

pedagogical perspective, it may again be important to emphasize a ‘middle way’ between striving and passivity in cultivating interoceptive awareness, requiring some effort to engage in active monitoring. Empirical research around particular emphasis and phrasing in delivering meditation instructions is needed to substantiate this hypothesis.

Moving from contemplative training to the clinical realm, an implication of the present study is that practicing *active reporting* of interoceptive states may be beneficial and serve as a candidate mechanism by which interoceptive-focused therapeutic interventions promote relief from distressing rumination while affording opportunities for insight and growth. As shown in a recent cross-sectional study, interoceptive attention (noticing and body listening MAIA subscales) predicts emotion regulation and adaptive coping (Schuette et al., 2021). Furthermore, active labelling of affective experience is linked to amygdala deactivation (Lieberman et al., 2007); an effect that is stronger with greater dispositional mindfulness (Creswell et al., 2007), which is also consistent with reduced depressive symptomatology (Way et al., 2010). To support active reporting of internal bodily experience, it may be fruitful to explore movement and self-touch during contemplative training, a technique used by interventions such as MABT, which has demonstrated clinical efficacy in vulnerable populations for who sustained attention to the body may be particularly challenging or triggering (Price & Hooven, 2018).

Interoception as a Low Energy State

The finding of widespread deactivation during both Active Interoception and Active Matching was unexpected and in need of further replication and exploration. Since no obvious confound can explain this finding, this deactivation could result from an increased efficiency in processing interoceptive information. Interoception may thus act as a ‘brake’ signal on cortical

activity while conserving motor and reporting ability. Convergingly, research on heartbeat-evoked potentials, a neural correlate of the cardiac rhythm, has recently shown that exteroceptive cues that match interoceptive signals enhance the subsequent suppression of processing of these signals, which is interpreted as evidence of more efficient interoceptive processing (Marshall et al., 2022).

It is possible that a lower energy state, where widespread cortical activity is inhibited, is necessary to observe interoceptive signal that have been ubiquitous since before birth and may therefore be commonly tagged as irrelevant relative to less common signals. This hypothesis is consistent with developmental cognitive theories which suggest that interoception is the first thing humans develop because of the critical roles homeostasis plays in ensuring survival (Filippetti, 2021; Fotopoulou & Tsakiris, 2017). In other words, interoceptive signals may be continuously represented for so long that they become habitually ignored, in keeping with neural repetition suppression effects for familiar and repeatedly represented sensory signals (Barron et al., 2016; Summerfield et al., 2008). The effect of this putative neural habituation to interoceptive signals may create a poor signal-to-noise ratio for detecting ongoing interoceptive activity. Widespread cortical inhibition might therefore be important for recovering interoceptive salience, supporting subjective awareness and reportability. Together, these results recast existing models of interoceptive attention to leverage the DAN in a lower activity state, where interoceptive processing is marked by selective sparing of the broad deactivation pattern.

Limitations and Constraints on Generalizability

Several constraints on generalizability are apparent. We present unexpected and exploratory findings from a relatively small sample, and so replication is needed given the paucity of studies in this area. The sample also does not include participants suffering from

major clinical conditions, who may show deficits in interoceptive processing, nor does it include advanced contemplative practitioners who hold expertise in engaging and sustaining interoceptive attention. Whether the neural dynamics described herein generalize to either clinical or expert populations therefore remains a question for future research. Similarly, respiration is only one of many possible interoceptive signals, which vary in their salience and controllability, and may be characterized by distinct neural dynamics. Multimodal interoceptive research is needed to determine the generalizability of the patterns discussed here, to clarify the impact of active reporting vs. passive engagement, the salience of the sensory signal, and the degree of certainty of sensory judgments made.

A further limitation to the present findings is that all practices were conducted during with eyes-open, which may be dissimilar to many meditation practices. Following repeated evidence that opening one's eyes decreases the functional connectivity between the SLN and the DMN, it was theorized that reducing the connectivity between these networks reflects an orientation to external rather than internal events (Han et al., 2020). However, the present analyses cast this interpretation into doubt; relative to exteroceptive attention, interoceptive attention with eyes open led to greater connectivity between the ACC seed region (an efferent hub of the SLN) and both the DAN and more posterior aspects of the insula rather than the DMN. It is possible that dynamics for interoceptive awareness may be altered in eyes-closed paradigms. It seems reasonable that DMN coupling may represent a distinct form of internal awareness that is not simply a matter of one's eyes being a closed, an elaborative, semantic level of processing distinct from interoceptive awareness, as has been previously proposed (Andrews-Hanna et al., 2014; Farb et al., 2007; Gusnard et al., 2001).

Concluding Remarks

The introduction of the IEAT represents a new method for characterizing interoceptive awareness of the breath. It appears to be well-tolerated by participants, allowing them to achieve equivalently high levels of accuracy in both interoceptive and exteroceptive tasks. While it may benefit from further modification, such as introducing visual motion to the Passive Interoception condition, the results affirm the importance of active reporting for maximizing neural distinctions between interoceptive and exteroceptive states. The paradigm also introduced the possibility that the interoceptive attention state is one of broadly reduced cortical activity, wherein awareness is reflected by selective sparing of the SLN and language processing regions amidst this deactivation pattern. Finally, the results suggest that the traditional DAN associated with exteroceptive attention is also relevant for interoception but requires maintaining anterior cingulate activity to preserve function within a broader profile of deactivation.

Future research might fruitfully explore whether the broad pattern of deactivation can be replicated within respiratory attention and whether such deactivation generalizes to other sensory modalities. The present findings represent an important clarification of several issues in interoception research, distinguishing the mechanisms of interoceptive attention from profiles of interoceptive accuracy, and introducing the pattern of cortical deactivation / SLN sparing as a candidate biomarker of interoceptive-focused, clinically efficacious training.

Materials and Methods

Design Overview

The study was conducted as an opportunity to validate a novel interoceptive attention task as part of an NIH-funded pilot study, a two-group randomized control trial to examine the neural correlates of interoceptive awareness in an MABT training context. The study procedures and

consent forms were reviewed and approved by the institutional review board at the University of Washington in accord with the World Medical Association Declaration of Helsinki.

Participants

Twenty-five healthy individuals with self-reported elevated stress were initially recruited through advertisements in a local newspaper and through the University of Washington (UW) research volunteer website and flyers posted on the UW campus. Inclusion criteria were: 1) being over 18 years of age; 2) Perceived Stress Scale (Taylor, 2015) scores indicating moderate stress levels; 3) naive to mindfulness-based approaches (no prior experience), 4) agrees to forgo (non-study) manual therapies (e.g., massage) and mind-body therapies (e.g., mindfulness meditation) for 12 weeks (baseline to post-test); 5) fluent in English; 6) can attend MABT and assessment sessions; and 7) right-handed (for uniformity of neuroimaging results). Exclusion criteria were: 1) lifetime diagnosis of mental health disorder; 2) unable to complete study participation (including planned relocation, pending inpatient treatment, planned extensive surgical procedures, etc.); 3) cognitive impairment, assessed by the Mini-Mental Status Exam (MMSE) (Folstein et al., 1975) if demonstrated difficulty comprehending the consent; 4) use of medications in the past 30 days that affect hemodynamic response; 5) lifetime head injuries or loss of consciousness longer than 5 minutes; 6) currently pregnant; or 7) contraindications for MRI, e.g., claustrophobia, metal objects in body, etc.

Twenty-two study participants (11 male and 11 female), of adult age (mean: 36.1 years, range: 18-62) were enrolled and completed both baseline and post-test assessments. 20 participants self-identified as Caucasian, 1 as African American, and 2 as Hispanic. Their highest education levels were high school (n = 5), 2 years of college (n = 2), Bachelor’s degree (n = 8), and Master’s degree or higher (n = 7).

Eleven participants (50% of the sample) were randomly allocated to receive eight 1.25-hour MABT sessions, delivered individually once/week for eight weeks. While the parent trial explored training-related change, the focus of the present study was to characterize and distinguish the neural processing differences in exteroceptive and interoceptive attention in response to a novel neuroimaging task. Because the methodological research question could be addressed regardless of group assignment, and benefitted from variation in interoceptive attention skills, the data from the study's two assessment timepoints were combined across the full sample, with group and time included in all statistical models as nuisance covariates.

Procedures

Participants completed an interoceptive/exteroceptive attention task within the fMRI at two timepoints, baseline and 3-month follow-up. A self-report questionnaire to assess interoceptive awareness was administered at baseline. Additional tasks and training effects were examined and will be the subject of separate reports.

Interoceptive/Exteroceptive Attention Task (IEAT)

To expand upon the task description featured at the end of the Introduction section: in the exteroceptive conditions, participants watched a circle expand and contract; in the interoceptive conditions, participants paid attention to their inhalation and exhalation. In the passive conditions, participants simply observed the circle or their breath; in the active conditions, participants pressed buttons when the circle expanded or contracted and when they inhaled or exhaled. In the matching condition, participants reported on the circle's movements while intentionally matching their breathing to the circle's movements.

During Passive Exteroception, participants were asked to visually monitor a circle as it 'pulsed', i.e., expanded and contracted rhythmically on the MRI-compatible visual display. The

circle pulse frequency was set to the participant's in-scanner estimated breathing frequency (~12 Hz), and no behavioral response was required. During the Passive Interoception, participants were asked to view a stationary circle on the screen while attending to the sensations of the breath from moment to moment. No behavioral response was required. During Active Interoception, participants were asked to report on their inhalations and exhalations by making button-presses with their right-hand index and middle fingers, respectively. The circle on the screen also responded to these button-presses, approximating the frequency of circle movement apparent in the Passive Exteroception condition. During Active Exteroception participants were asked to report on the expansion and contraction of the circle on the screen, which again was set to pulse at the participants' in-scanner respiratory frequency. Finally, in Active Matching, participants were asked both to report on the expansion and contraction of the circle as in the Active Exteroception condition, but also to match their breathing to the circle's expansion and contraction with inhalation and exhalation, respectively.

Each condition was order-counterbalanced and repeated twice in each functional run, including a 10 second instruction screen and a 30 second task period, for a total of 13.4 minutes over two 6.7 minute runs.

Self-Reported Interoceptive Awareness

The Multidimensional Assessment of Interoceptive Awareness (MAIA) (Mehling et al., 2012) was used to assess subjective interoception. The MAIA was a 32-item scale designed to measure multidimensional facets of self-reported interoceptive awareness relevant for wellbeing. The eight subscales canvas experiential domains such as Noticing, Listening, and Emotional Awareness, as well as regulatory domains such as Attention Regulation, Self-Regulation, and Trusting. As noted above, the MAIA has an updated version to improve the reliability of the two

reverse-coded subscales (Mehling et al., 2018), but as the new version was not available at study outset, the total score from the original version was employed, which yielded very good reliability (Cronbach's $\alpha = .85$) in the present sample.

Data Analysis

Respiration Frequency. Respiration data was acquired using a MR-compatible respiration belt sampling at 500 Hz. Respiration data was first smoothed using a 1-sec zero phase low-pass filter window and then mean-corrected. Breath frequency was then estimated using a Fast Fourier Transform (FFT) of the respiration period. The FFT was used to produce imaging covariates because it is robust against variations in the phase of the respiration signal over each relatively short 30s trial period. Then, using the onsets and offsets of each of the task conditions, additional FFTs were applied to the respiratory data for each task period, and the peak frequency was taken as the respiratory frequency for that task period.

Interoceptive and Exteroceptive Tracking Accuracy. Tracking accuracy was analyzed using a novel methodology developed for the present study. Three of the localizer conditions, Active Exteroception, Active Interoception, and Active Matching required button-presses to track the sensory target, i.e. inhalation/exhalation during the respiratory cycle, or expansion/contraction during the visual circle cycle. The button-presses were extracted from participant behavioral log files, with button-presses serving as 'peak' and 'trough' inflection points that were then used to create idealized waveforms scaled to 1000 and -1000 arbitrary units [AU] respectively. As the waveforms were intended to be compared to the respiratory signal, the waveforms were generated at a sampling rate of 500 Hz to match the data acquired by the respiration belt.

For the respiration data, the 'pracma' library (Borchers, 2021) in the R statistical programming environment (R Core Team, 2017) was used to find peaks and troughs within the

timeseries. The minimum peak difference was set to the sampling rate, as individual breaths were unlikely to have a period of less than 1 second. The time indexes of peaks and troughs were combined in temporal order, and the idealized signal was set to 1000 at peaks and -1000 at trough locations in the timeseries. The idealized respiratory signal was then linearly interpolated between peaks and troughs, as illustrated in Figure 2A. Visual inspection was performed on each timeseries to ensure the algorithm was functioning correctly. The idealized time series could then be partitioned by task onsets and offsets for the accuracy analysis described below.

For the visual circle timeseries, the code used to generate the circle stimulus during the experiment was adapted to generate the timeseries. The circle expanded and contracted at participant-specific breathing frequencies that were assessed during structural MRI acquisition and then input into the experiment software. To convert this animation into an idealized timeseries, for each exteroception trial the timeseries began at an arbitrary unit of 0. The expansion/contraction period was symmetrical and defined as half the participant respiratory period. The circle value was then extrapolated as increasing from -1 for the expansion period to reach exactly 1 by the end of the period; the circle timecourse then ‘paused’ at 1 for 0.2 * the expansion period; the circle then decreased at the same rate for the contraction period to reach exactly -1 by the end of the period, and then ‘paused’ again for .2 * the contraction period before repeating the cycle. This timecourse simulation continued until the end of each task block.

To calculate trial-specific tracking accuracy, idealized respiration time courses and behavioral button-press data were extracted from their respective timeseries using the onsets and offsets from the behavioral logs. For exteroceptive target tracking, the trial-specific visual circle timecourse was simulated as described above. For both interoception and exteroception conditions, the idealized waveforms were then entered into a normalized cross-correlation (NCC)

analysis using the 'dtwclust' library in R to estimate the maximum correlation between behavior and respiration/circle timecourse signals (Sardá-Espinosa, 2019). The NCC was used instead of a standard correlation coefficient to account for differences in phase between the transduction of button-presses and stimulus perception. The correlation between the idealized button-press signal and the idealized sensory signal was then calculated using spearman's correlation coefficient.

The complete algorithm for generating idealized waveforms and their comparison is available on the Open Science Framework (https://osf.io/ctqrh/); the analyses are conducted separately for the respiration and visual targets in the "RespirationTracking.R" and the "CircleTracking.R" files, respectively.

Task-Embedded Accuracy Quality Control. Two of the localizer conditions, Active Exteroception and Active Matching, required participants to align their button presses with the expansion and contraction of the visual circle stimulus, which did not require integration of data from the respiration belt, and afforded real-time coding of tracking accuracy. For each expansion and contraction, participant button presses were automatically coded for whether they accurately reported on the phase of the circle, with absent button presses also coded as errors. For each condition, error rates were aggregated as a mean error rate across the scanning session. This data was immediately available in log files and could be used to quickly assess participant compliance with task instructions, as well as to later compare difficulty between the Active Exteroception and Active Matching conditions.

Neuroimaging Data Acquisition. Neuroimaging was performed using a 3T Philips Achieva scanner (Philips Inc., Amsterdam, Netherlands) at the Diagnostic Imaging Sciences Center, University of Washington. Imaging began with the acquisition of a T1-weighted anatomical scan (MPRAGE) to guide normalization of functional images (~ 6 minutes) with TR = 7.60 ms,

TE = 3.52 ms, TI = 1100 ms, acquisition matrix = 256 × 256, flip angle = 7°, shot interval = 2530 ms, and 1mm isotropic voxel size. Functional data were acquired using a T2∗-weighted echo-planar-imaging (EPI) sequence with TR = 2000, TE = 25 ms, flip angle α = 79°, field of view = 240 × 240 × 129 mm, 33 slices, and a voxel size of 3 × 3 × 3.3 mm with 3.3 mm gap. Button presses were registered using a 2-button MR-compatible response pad.

Preprocessing. A set of preprocessing steps was performed using the consortium-developed fMRIprep robust preprocessing pipeline for fMRI data (https://fmriprep.readthedocs.io/en/stable/). Briefly, preprocessing consisted of realignment and unwarping of functional images, slice timing correction, and motion correction. The functional images were resliced using a voxel size of 2 × 2 × 2 mm and smoothed using a 6-mm FWHM isotropic Gaussian kernel.

First Level Analysis. Within subject statistical models were used to characterize the interoceptive networks at the participant level. Participant time series from the interoceptive tasks were submitted to separate first-level general linear statistical models using Statistical Parametric Mapping software (v12). Task-specific boxcar stimulus functions were convolved with the canonical hemodynamic response function, separately modeling the onsets of the interoceptive and visual control conditions for each participant.

A component-based noise correction method (CompCor; Behzadi et al., 2007) was used to address the confounding effects of participant movement and physiological noise. Structural (MPRAGE) images acquired at the beginning of each fMRI session were segmented into cerebrospinal fluid (CSF), white matter, and grey matter. The first principal component related to the segmented CSF signal was extracted and included as confound regressor in first-level analyses along with six standard movement parameters and respiration rate.

Second Level Analysis. Participant first-level maps for each experimental condition [Passive Interoception, Passive Exteroception, Active Interoception, Active Exteroception, Active Matching] were analyzed at the second level using a full-factorial mixed-model ANOVA in SPM12 (Friston, 2007). The second level contrasts first subdivided the tasks in two main effects and their interaction term: Reporting Demand [Active vs. Passive] x Target [Interoception vs. Exteroception]. Follow up comparisons within Active [Active Interoception vs. Active Exteroception vs. Active Matching] and within Passive [Passive Interoception vs. Passive Exteroception] were also modelled.

Familywise control for multiple comparisons (corrected $p < 0.05$) in whole-brain analyses was achieved through threshold-free cluster enhancement (TFCE) TFCE controls familywise error rate based on a permutation testing approach and determines optimal voxel-wise cluster-forming thresholds using an automated algorithmic method (Smith & Nichols, 2009). It therefore eliminates to choose arbitrary thresholds to correct for multiple comparisons.

Respiration Confounds. To control for the confounding influences of changing respiration rates between these conditions, several efforts were made. First, images corrected for physiological artifacts used the 6 'aCompCor' parameters during first level analysis, derived from the fmriprep preprocessing pipeline. Second, trial-specific respiration frequency was modelled at the second level for inclusion as a nuisance covariate.

Trial-level Confounds. The current study comes from an exploratory clinical trial, the results of which are the subject of a separate report. We combined data across the trial to power the comparison of IEAT task conditions and modelled any effects of trial Group (MABT vs. Control), Time (Baseline vs. Post-Intervention) and their interactions as nuisance covariates. All models also contained condition-averaged respiration rate as a covariate, to further control for

variation in respiration between experimental conditions. Post hoc analyses that did not include the nuisance covariates of Group and Time did not meaningfully change the reported results.

Region of Interest (ROI) Analysis. For region of interest (ROI) analysis, all signal extractions were taken from models containing the nuisance covariates. Using the built-in SPM12 function, the median value of the raw, unwhitened signal was extracted from all voxels within the ROI, yielding one value per participant at each time point. These values were entered into a linear mixed-effects model with restricted likelihood estimation was applied using the 'lme4' library (Bates et al., 2015) in the R statistical programming environment.

Task-Demand Moderators. As preliminary manipulation check, we first evaluated the impact of reporting demands by comparing active conditions (Active Exteroception, Active Interoception, and active matching) to the passive task conditions (passive exteroception, passive interoception). We were particularly interested in confirming the presence of greater motor activity as a quality-control check on the dataset, as well as evaluating whole brain data for evidence of other unforeseen differences related to task demands.

Hypothesis Testing. Hypothesis 1 aimed to compare interoceptive and exteroceptive attention. To this end we first evaluated a whole-brain interaction between reporting demand [active vs. passive] and attentional target [interoception vs. exteroception] to evaluate whether the effects of attentional target should be evaluated separately for the active and passive reporting conditions. Subsequent analyses compared the simple effects of attentional target within each reporting demand condition, i.e. [passive interoception vs. passive exteroception] and [Active Exteroception vs. Active Interoception]. To perform these contrasts, all 5 task conditions were estimated separately at the first (individual session) level of analysis and entered into a full factorial design in SPM12.

Hypothesis 2 aimed to investigate whether the differences between exteroception and interoception were moderated by individual differences subjective interoceptive awareness (MAIA scores). Focusing on the contrast of [Active Interoception vs. Active Exteroception], we first created contrast maps at the first (within session) level of analysis. These first level maps were then entered into a second (group) level analysis that included normalized (z-scored) MAIA scale total scores as a covariate of interest. The MAIA covariate was subjected to TFCE correction in the same fashion as other whole brain analyses, and respiration rate change between the two conditions was also included in the factorial model as a nuisance covariate to control for variation associated with changes in respiratory rate.

Hypothesis 3 tested the potential moderating factor of endogenous vs. exogenous control of the respiratory cycle by comparing the contrast of [Active Interoception vs. active matching] conditions from the full 5 condition + respiration rate model used in testing Hypothesis 1.

Hypothesis 4 aimed to understand how engaging in Active Interoception changes brain connectivity relative to Active Exteroception. To accomplish this aim, a psychophysiological interaction analysis (PPI) was conducted in SPM12 using the Generalized PPI Toolbox (v. 13.1), which improves upon standard PPI analyses by estimating the effect each task condition has upon connectivity independently (McLaren et al., 2012). Here, we used the model employed in Hypotheses 2, a second (group) level full factorial model that contained first level contrasts of [Active Interoception – Active Exteroception] and the MAIA covariate term. The conjunction of the [Active Exteroception - Active Interoception] contrast and the positive MAIA contrast was evaluated, using an exploratory threshold of $p < .001$ for each contrast, resulting in a conjoint probability comparable to conservative FWE correction of $p < 1x10^{-6}$. The largest cluster observed was used as a seed region, K= 794 voxels, peak Z = 4.06, x = -4, y = 58, z = 14,

consistent with dorsal anterior cingulate cortex (Brodmann area 24). At the first level of analysis, mean timecourse activity extracted from this seed region was convolved with separate boxcar regressors indicating the onsets and durations of the Active Exteroception and active inteorception conditions, and the ensuing whole brain maps were then contrasted to model the PPI effect for each participant session. These first level PPI maps were then collected and analyzed using the same full factorial modelling approach described above.

Acknowledgements

This work was supported by a RIFP award from the School of Nursing at the University of Washington and a grant from the National Center for Advancing Translational Sciences of the National Institutes of Health [UL1 TR002319. Data analysis infrastructure and trainee expenses were supported by a Canadian Natural Sciences and Engineering Council Discovery grant [RGPIN-2015-05901]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. We extend our gratitude to Natalie Koh and Sophie Xie for their coordination and data collection efforts, and to Dr. Thomas Grabowski, Dr. Chris Gatenby, and Ms. Liza Young at the Integrated Brain Research Center at the University of Washington for their collaboration.

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Table S1. Estimated Marginal Means for Respiration Frequency

Condition	Estimated Marginal Mean	SE	df	95% CI Lower	95% CI Upper
ActExt	0.22	0.011	25	0.19	0.24
ActInt	0.19	0.011	25	0.17	0.21
ActMatch	0.21	0.011	25	0.19	0.23
PasExt	0.21	0.011	25	0.19	0.24
PasInt	0.21	0.011	25	0.18	0.23

ActExt = Active Exteroception; ActInt = Active Interoception; ActMatch = Active Matching; PasExt = Passive Exteroception; PasInt = Passive Interoception

Table S2. Tukey-Adjusted Pairwise Comparisons of Respiration Frequency

Contrast			Estimate	SE	df	*t* value	*p* value	
ActExt	vs.	ActInt	0.027	0.005	854	5.226	<.0001	*
ActExt	vs.	ActMatch	0.006	0.005	854	1.241	0.727	
ActExt	vs.	PasExt	0.005	0.005	854	1.015	0.849	
ActExt	vs.	PasInt	0.011	0.005	854	2.074	0.232	
ActInt	vs.	ActMatch	-0.021	0.005	854	-3.984	0.001	*
ActInt	vs.	PasExt	-0.022	0.005	854	-4.211	0.000	*
ActInt	vs.	PasInt	-0.016	0.005	854	-3.152	0.015	*
ActMatch	vs.	PasExt	-0.001	0.005	854	-0.226	0.999	
ActMatch	vs.	PasInt	0.004	0.005	854	0.833	0.920	
PasExt	vs.	PasInt	0.005	0.005	854	1.059	0.827	

ActExt = Active Exteroception; ActInt = Active Interoception; ActMatch = Active Matching; PasExt = Passive Exteroception; PasInt = Passive Interoception
* highlights p < 05 (Tukey adjusted for multiple comparisons)

Table S3. Estimated Marginal Means for Target / Keypress Correlations

Target	Condition	Estimated Marginal Mean	SE	df	95% CI Lower	95% CI Upper
Breath	ActExt	0.70	0.014	54.1	0.67	0.73
	ActInt	0.88	0.014	54.4	0.85	0.91
	ActMatch	0.90	0.014	53.8	0.87	0.92
Circle	ActExt	0.89	0.014	54.1	0.86	0.91
	ActMatch	0.89	0.014	53.8	0.86	0.92

ActExt = Active Exteroception; ActInt = Active Interoception; ActMatch = Active Matching

Table S4. Tukey-Adjusted Pairwise Comparisons of Target / Keypress Correlations

Contrast			Estimate	SE	df	*t* value	*p* value	
Breath_ActExt	vs.	Breath_ActInt	-0.182	0.0141	850	-12.97	<.0001	*
Breath_ActExt	vs.	Breath_ActMatch	-0.193	0.014	850	-13.81	<.0001	*
Breath_ActExt	vs.	Circle_ActExt	-0.183	0.014	850	-13.08	<.0001	*
Breath_ActExt	vs.	Circle_ActMatch	-0.190	0.014	850	-13.59	<.0001	*
Breath_ActInt	vs.	Breath_ActMatch	-0.011	0.014	850	-0.81	0.929	
Breath_ActInt	vs.	Circle_ActExt	-0.001	0.0141	850	-0.09	1.000	
Breath_ActInt	vs.	Circle_ActMatch	-0.008	0.014	850	-0.59	0.977	
Breath_ActMatch	vs.	Circle_ActExt	0.010	0.014	850	0.71	0.953	
Breath_ActMatch	vs.	Circle_ActMatch	0.003	0.014	850	0.22	1.000	
Circle_ActExt	vs.	Circle_ActMatch	-0.007	0.014	850	-0.50	0.988	

ActExt = Active Exteroception; ActInt = Active Interoception; ActMatch = Active Matching
The contrasts are labelled using the format Target_Condition
e.g., Breath_ActInt means the correlation between the respiratory target and keypresses during the Active Interoception condition
* highlights p < 05 (Tukey adjusted for multiple comparisons)

Table S5. Whole Brain Effects of Reporting Demand and Target

Contrast	Brain Region(s)	Brodmann Areas	Side	Cluster Size	Peak TFCE	Peak Z	Coordinates (mm)		
							x	y	z
Active > Passive	Cerebellum	-	R	963	4458.46	3.54	24	-54	-24
	Primary Motor / Somatosensory	2 / 3 / 4	L	985	2564.66	3.54	-40	-24	56
	Cerebellum	-	R	247	1736.84	3.24	18	-68	-50
	Cerebellum	-	L	129	1433.75	2.99	-36	-52	-28
Passive > Active	Lateral occipital / Angular gyrus / Cuneus / Precuneus / Cingulate / Intra-calcarine / Lingual gyrus	7 / 17 / 18 / 19 / 23 / 39	L / R	22012	6350.58	3.54	-12	-86	50
	Frontal pole / Middle frontal / inferior frontal / Superior frontal / Frontal orbital / Cingulate / Paracingulate	6 / 8 / 9 / 10 / 11 / 24 / 32 / 44 / 45 / 46 / 47	L / R	20963	3507.67	3.35	8	42	-6
	Precentral gyrus / Postcentral gyrus	3 / 4 / 6	R	3185	2458.89	3.54	52	-16	58
	Superior temporal gyrus	21 / 22	L	70	1306.62	2.95	-54	-38	4
Internal > Exteral			*No significant clusters*						
External > Internal	Cerebral cortex	-	L / R	92240	6402.11	3.54	-4	-54	24
Active / Passive x Internal / External	Cerebral cortex	-	L / R	81356	4247.24	3.54	-60	-18	14
	Occipital (V1)	17	L	49	1263.71	2.91	2	-88	8

Active vs. Passive: [ActInt + ActExt + ActMatch] – [PasInt + PasExt]
Internal vs External: [ActInt + PasInt] – [ActExt + PasExt]
Active/Passive x Internal/External: [ActExt + PasInt] – [ActInt + PasExt]; the reverse contrast resulted in no significant effects

Table S6. Simple Effects of Task

Contrast	Brain Region	Brodmann Areas	Side	Cluster Size	Peak TFCE	Peak Z	Coordinates (mm)		
Passive: Int > Ext			*No significant clusters*						
Passive: Ext > Int	Lateral occipital (V5/MT)	37	R	136	1325.77	3.24	46	-64	4
Active: Ext > Int	Cerebral cortex	-	L / R	128580	12047.74	3.54	-4	52	24
Active: Ext > Match	Cerebral cortex	-	L / R	144705	15807.48	3.54	-54	-24	14
Active: Int > Ext			*No significant clusters*						
Active: Match > Ext			*No significant clusters*						

Table S7. Estimated marginal mean comparisons between experimental conditions on cortical activation

Contrast	Estimate	SE	df	t.ratio	p.value
ActExt-ActInt	0.4771	0.0762	194	6.263	<.0001*
ActExt-ActMatch	0.5545	0.0762	194	7.278	<.0001*
ActExt-PasExt	0.1644	0.0762	194	2.157	0.2005
ActExt-PasInt	0.2348	0.0762	194	3.081	0.0198*
ActInt-ActMatch	0.0773	0.0762	194	1.015	0.8482
ActInt-PasExt	-0.3128	0.0762	194	-4.105	0.0006*
ActInt-PasInt	-0.2424	0.0762	194	-3.181	0.0146*
ActMatch-PasExt	-0.3901	0.0762	194	-5.12	<.0001*
ActMatch-PasInt	-0.3197	0.0762	194	-4.196	0.0004*
PasExt-PasInt	0.0704	0.0762	194	0.924	0.8873

* highlights p < 05 (Tukey adjusted for multiple comparisons)

Table S8. MAIA Covariates of ActExt > ActInt

Contrast	Brain Region	Brodmann Areas	Side	Cluster Size	Peak TFCE	Peak Z	Coordinates (mm)		
MAIA positive covariate	Anterior cingulate / Paracingulate / Frontal pole / Subcallosal cortex / Mid Frontal / Inferior Frontal / Anterior Insula	23 / 24 / 32 / 10 / 11 / 46 / 45 / 48	L / R	13145	1869.84	3.09	0	12	36
	Inferior Frontal	45	R	630	1475.35	2.82	54	34	30
	Superior Frontal	8 / 9	R	628	1417.54	2.95	20	46	54
	Superior Frontal	8	R	303	1414.87	2.85	-6	38	62
	Postcentral gyrus	43	R	404	1401.63	2.77	54	-22	30
	Orbitofrontal / Olfactory	11	R	253	1395.49	3.24	2	50	-32
	Supplementary Motor Area	6	R	43	1352.15	2.65	26	-14	78
	Post-Central Gyrus	4	R	101	1349.45	2.77	46	-10	66
	Frontopolar Gyrus	10	R	11	1347.03	2.71	16	62	26
	Superior Occipital	18	R	30	1336.94	3.24	10	-96	34
	Superior Occipital	18	L	33	1331.45	2.79	-8	-88	46
	Superior Frontal	9	L	21	1317.49	2.62	-24	50	46
	Postcentral gyrus	4	R	5	1262.8	2.75	52	-14	62
MAIA negative covariate	*No significant clusters*								

Table S9. Comparisons between Endogenous (ActInt) and Exogenous (ActMatch) Interoceptive Control Conditions

Contrast	Brain Region	Brodmann Areas	Side	Cluster Size	Peak TFCE	Peak Z	Coordinates (mm)		
ActInt > ActMatch	Temporal pole / Central operculum / Precentral gyrus	21 / 38 / 44 / 45 / 46	R	1856	2134.5	3.35	58	10	-6
	Frontal operculum / Insula	48	R	1137	1820.58	3.35	34	48	26
	Lateral occipital / Intracalcarine / Cuneus / Lingual gyrus / Fusiform	17 / 18 / 19 / 37	R	4487	1762.41	3.54	6	-82	2
	Supramarginal Gyrus	40	R	173	1269.45	3.24	62	-36	44
	Lateral occipital cortex (ventral)	19 / 39	R	86	1227.51	2.91	36	-86	-22
	Supramarginal gyrus	40	R	48	1206.91	2.62	42	-56	-26
	Lateral occipital cortex (dorsal)	19	R	18	1200.83	3.04	32	-76	22
	Cerebellum	-	R	9	1191.42	3.09	14	-82	40
ActMatch > ActInt	*No significant clusters*								

Table S10. PPI Results: Anterior Cingulate Connectivity x [ActInt vs. ActExt]

Contrast	Brain Region	Brodmann Areas	Side	Cluster Size	Peak TFCE	Peak Z	Coordinates (mm)		
ActInt > ActExt	Cerebellum	-	L / R	26284	3815.36	3.54	14	-78	-24
	Cerebral Cortex	-	L / R	28639	3584.63	3.54	44	24	42
ActExt > ActInt	*No significant clusters*								
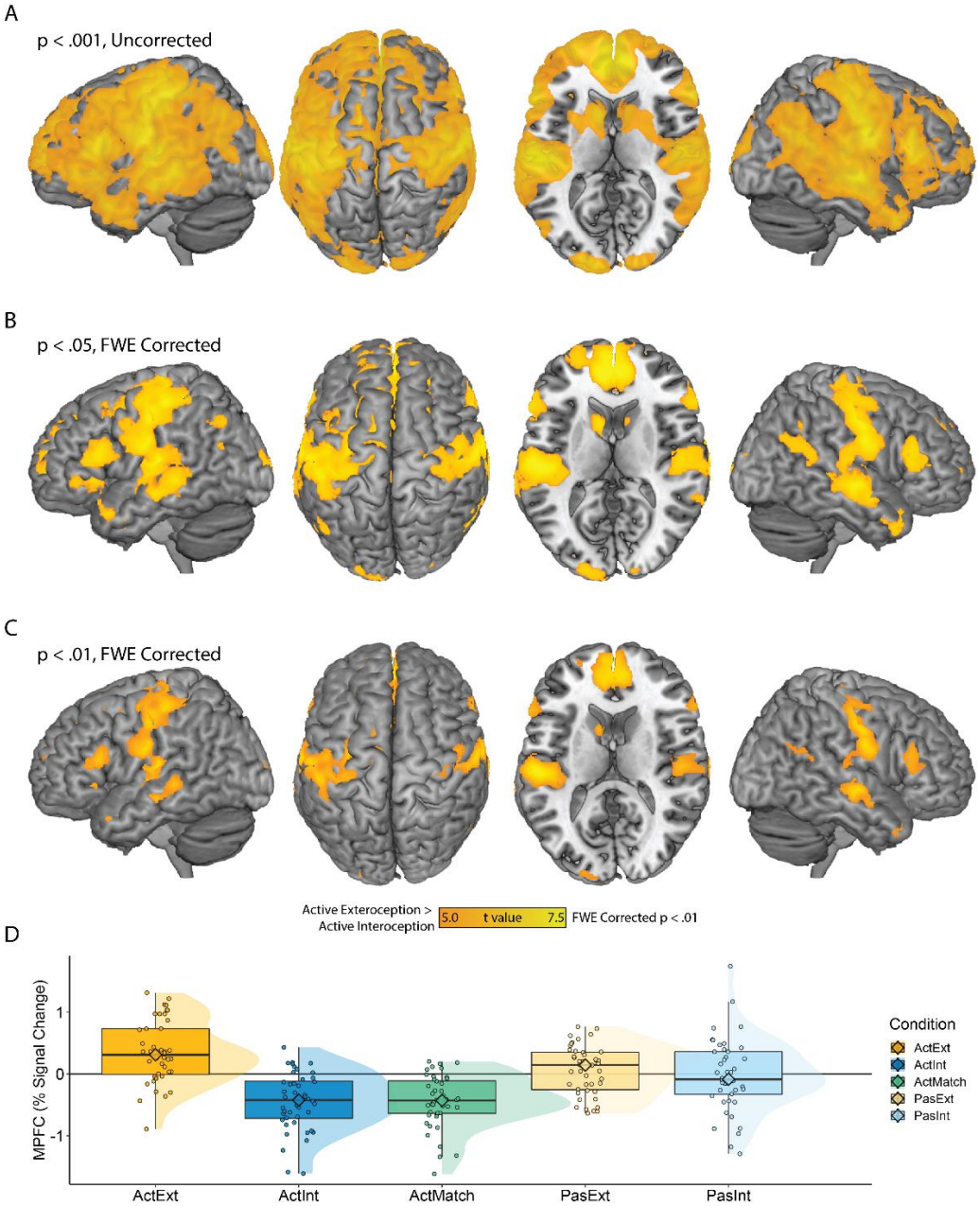
Figure S1. Active Exteroception – Active Interoception at Alternative Voxel Height Correction Thresholds