



Spatial-topographic nestedness of interoceptive regions within the networks of decision making and emotion regulation: Combining ALE meta-analysis and MACM analysis

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ABSTRACT

Prominent theories propose that interoception modulates our behavioral and emotional responses involving decision-making and emotion regulation. Are the regions implicated in interoception also spatially related to and possibly nested within the networks of decision making and emotion regulation? Addressing this question, we performed three meta-analyses of functional magnetic resonance imaging studies to identify the regions that are commonly activated by the three domains using activation likelihood estimation (ALE). Additionally, we assessed the coactivation pattern of identified common regions using meta-analytic connectivity modeling (MACM). The results showed major overlaps of interoception with both decision making and emotion regulation in specifically the right dorsal anterior insula. The pairwise contrast analyses confirmed this finding and revealed conjunction-based activities in decision making and emotion regulation in the dorsal anterior cingulate cortex (dACC). MACM based on the identified insula revealed a widespread convergent coactivation pattern with the left anterior insula, dACC, and bilateral thalamus which, together, constitute the salience network. Among these co-activated regions, bilateral insula and the dACC were shared among all three domains. These results suggest that the regions mediating interoception including intero-exteroceptive integration and salience attribution are contained and thus spatially nested within the more extensive networks recruited during decision making and emotion regulation.

1. Introduction

Interoception refers to the processing and perception of inner bodily signals by the nervous system (Cameron, 2001; Craig, 2002). The impact of interoceptive processing is not limited to our perception of inner bodily signals though. A growing number of research indicates that interoception also modulates both decision making (Dunn et al., 2010; Furman et al., 2013; Herman et al., 2021; Salvato et al., 2019; Werner et al., 2009; Wölk et al., 2014) and emotion regulation (Füstös et al., 2013; Jakubczyk et al., 2019; Kever et al., 2015; Pollatos et al., 2015; Zamariola et al., 2019). However, the exact spatial-topographic neural features underlying and mediating such modulations

of decision making and emotion regulation by interoception remain limited.

The integration of internal bodily signals with external environmental stimuli is essential for homeostasis and self-regulation, which is important for attaining higher-level or long-term goals (Chen et al., 2021; Pezzulo et al., 2015; Quigley et al., 2021; Stephan et al., 2016). Many influential theories link interoception with feelings and further regulation of emotions and behaviors. For example, the James-Lange theory of emotion states that the perception of activity in the body constitutes feelings of emotions (James, 1884; Lange, 1887), which is a prerequisite of successful emotion regulation (Barrett et al., 2004). Further, the Somatic Marker Hypothesis extends the role of interoception into the domain of cognition mainly including decision making (Damasio, 1994).

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Specifically, this hypothesis argues that a ‘maker’ of emotional state, constituting a collection of bodily and neural activity, can anticipate future outcomes and guide decision-making toward advantageous choices.

Converging evidence indicates that the insular cortex, especially the anterior portion is an essential neural substrate for interoception, which involves integrating information from internal body and external environment (Berntson and Khalsa, 2021; Craig, 2003, 2010; Critchley et al., 2004; Kurth et al., 2010; Pollatos et al., 2015; Pollatos, Gramann and Schandry, 2007; Qin et al., 2020; Seth, 2013; Simmons et al., 2013; Wang et al., 2019). The anterior insula receives bodily signals from the mid- and posterior insula and issues predictions to the hypothalamus and brainstem (Barrett and Simmons, 2015; Craig, 2002; Paulus and Stein, 2006; Seth and Critchley, 2013). In addition, together with the anterior cingulate cortex (ACC), the anterior insula is a core region of the Salience Network (SN) which is assumed to detect emotional saliency (Menon and Uddin, 2010; Seeley et al., 2007; Uddin, 2015). Therefore, the attribution of salience as mediated by the anterior insula may be shared among interoception, decision making and emotion regulation (Bar-On et al., 2003; Critchley, 2005; Garfinkel and Critchley, 2013; Gu et al., 2013; Gu et al., 2012; Ibañez et al., 2010; Mohr et al., 2010; Paulus and Frank, 2006; Pollatos, et al., 2007; Singer et al., 2009; Uddin et al., 2014; Uddin et al., 2017; Weller et al., 2009; Zhang et al., 2020). This is supported by for instance the insula’s involvement in interoceptive awareness (Critchley et al., 2004), representing emotional feelings (Damasio et al., 2000) and coding risk prediction error (Mohr et al., 2010). Furthermore, integrated in the anterior insula, bodily and emotional signals shapes decision making and emotion regulation (Berntson et al., 2011; Brass and Haggard, 2010; Critchley and Garfinkel, 2017; Critchley and Harrison, 2013; Damasio and Carvalho, 2013; Garfinkel et al., 2015; Gogolla, 2017; Naqvi and Bechara, 2009; Schultchen et al., 2019; Seth and Tsakiris, 2018; Tajadura-Jiménez and Tsakiris, 2014; Tsakiris and Critchley, 2016; Tsakiris et al., 2011; von Mohr et al., 2021). Despite initial support on psychological levels (e.g., Füstös et al., 2013; Werner et al., 2009) and indirect neural evidence from multiple sources (e.g., Canessa et al., 2013; Zhang et al., 2020), direct neuro-anatomical evidence for the overlap of these different functional domains is yet missing.

Are the regions and their spatial topography recruited during interoception also implicated during decision making and emotion regulation? Addressing this question is the main goal of our investigation. A recent meta-analysis on self showed that interoceptive regions of SN are also implicated and thus spatially nested within the more extensive networks recruited during higher layers of self (mental and extero-proprioceptive; Qin et al., 2020). Given the above stated observation of interoceptive modulation, we hypothesize that regions recruited during interoception are also implicated and thus spatial-topographically nested within the more extensive networks of decision making and emotion regulation.

To this end, we conducted a quantitative meta-analysis of the available functional magnetic resonance imaging (fMRI) studies concerning interoception, decision making and emotion regulation. First, using activation likelihood estimation (ALE), we performed three meta-analyses of fMRI studies to identify the regions that are activated in the three domains respectively (Eickhoff et al., 2009; Laird et al., 2005; Turkeltaub et al., 2002). We also compared the three domains with each other using contrast and conjunction analyses. We next calculated the overlapping brain regions commonly activated by the three domains. In addition, we assessed the coactivation patterns of identified common regions using meta-analytic connectivity modeling (MACM). Conducting these analyses, we first assumed that the regions of interoception like the anterior insula are contained and thus spatially nested within those recruited during decision making and emotion regulation. We second hypothesized that the SN that includes the anterior insula as a key region, is involved in all three domains, interoception, emotion regulation and decision making.

2. Methods

2.1. Study selection

For the articles of interoception, we used keywords as follows: "interoception" AND "fMRI" OR "functional magnetic resonance imaging", OR "interoceptive" AND "fMRI" OR "functional magnetic resonance imaging", OR "visceral perception" AND "fMRI" OR "functional magnetic resonance imaging". We searched the literature using PubMed (www.pubmed.com) and Google Scholar before 10th August 2020. Additional articles were identified by previous meta-analyses (Adolfi et al., 2017; Qin et al., 2020; Salvato et al., 2020; Schulz, 2016) and by tracing references from acquired papers.

Moreover, to select the literature related to decision making, we searched the PubMed (www.pubmed.com) and Google Scholar before 10th August 2020 using the following keywords: "decision making" AND "fMRI" OR "functional magnetic resonance imaging", OR "risk decision" AND "fMRI" OR "functional magnetic resonance imaging". Additional relevant papers were identified by tracing references from acquired papers and previous meta-analyses (Defoe et al., 2015; Keuken et al., 2014).

Furthermore, for emotion regulation, we searched the PubMed (www.pubmed.com) and Google Scholar before 10th August 2020 based on the keywords "Emotion regulation" AND "fMRI" OR "functional magnetic resonance imaging", OR "cognitive reappraisal" AND "fMRI" OR "functional magnetic resonance imaging", OR "suppression" AND "fMRI" OR "functional magnetic resonance imaging". Also, we identified additional studies by tracing references from retrieved articles and by previous meta-analyses (Kohn et al., 2014; Morawetz et al., 2017).

Inclusion criteria for the three categories of literature were as follows: a) written in English; b) subjects including unmedicated and healthy adults without training experience related to interoception, decision making or emotion regulation; c) measurement of blood oxygenation through fMRI; d) whole brain analysis rather than ROI analysis, and ROI-based studies without whole brain data were excluded; e) standard coordinates (Talairach or Montreal Neurological Institute); f) tasks which involved core processes of interoception, decision making or emotion regulation without involving high-level processes or aiming at more specific goals; g) employment of image contrast of respective tasks > control tasks or baseline, rather than the contrast between the different respective tasks levels; e) activations rather than deactivations were included, because deactivations have not been often reported and the interpretations of reported deactivations are unclear (Gusnard and Raichle, 2001; Hutchinson et al., 1999; Lindquist et al., 2015). According to the above criteria, peer-reviewed neuroimaging articles related to interoception (29 articles), decision making (43 articles), and emotion regulation (58 articles) by August 10th, 2020 were selected for meta-analysis (see supplementary material Table S1, Table S2, and Table S3 for lists of included studies). We conducted these comprehensive literature search according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement (Moher et al., 2015). The specific screening processes of the article are shown in the supplementary materials (Figure S1, Figure S2, and Figure S3). In the following the term “study” means a scientific publication, reporting several contrasts. The term “experiment” refers to a contrast analysis in one study (Laird et al., 2011).

2.2. Brief introduction of ALE

The Ginger ALE 3.0.2 software (<http://www.brainmap.org/>) was used to perform coordinate-based meta-analyses of neuroimaging results (Eickhoff et al., 2009; Laird et al., 2005; Turkeltaub et al., 2002). The core principle of ALE is to use the reported activation foci from studies as centers of three-dimensional Gaussian probability distribution to capture the spatial uncertainty associated with each focus (Caspers et al., 2010). In a particular experiment, the probability distributions of all ac-

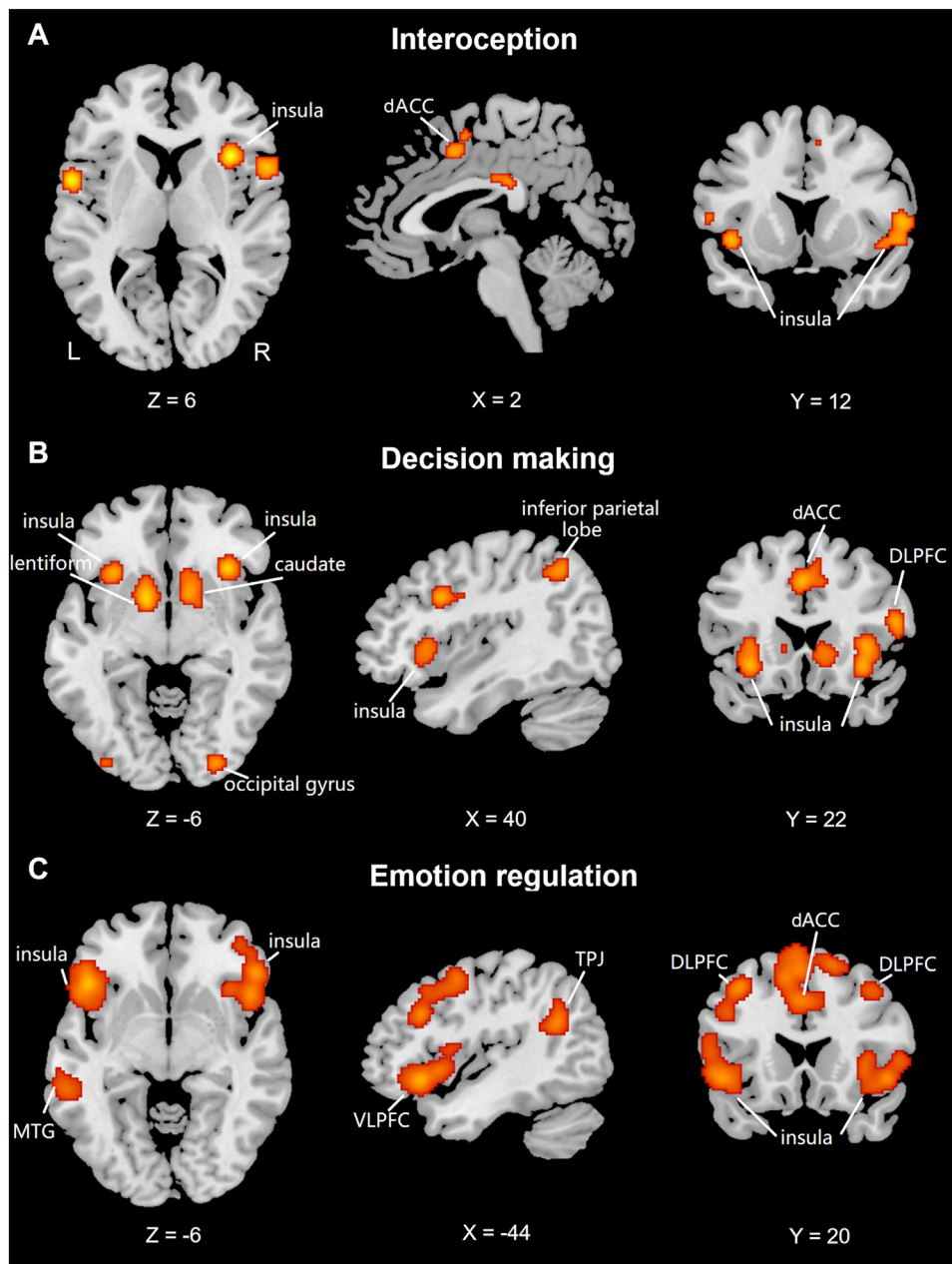


Figure 1. Single analysis results of the three domains. A: Interoception; B: Decision making; C: Emotion regulation. Colored regions are FEW corrected at $p < .05$ with primary alpha level of .001 and a minimum cluster size of 200 mm³. Abbreviations - L: left; R: right; dACC: dorsal anterior cingulate cortex; DLPFC: dorsal lateral prefrontal cortex; MTG: middle temporal gyrus; VLPFC: ventral lateral prefrontal gyrus; TPJ: temporal parietal junction.

tivation foci were combined to produce a modeled activation map (MA Map). In the single analysis, taking the union across these MA maps yields voxel-wise ALE scores describing the convergence between experiments at each particular location (Evans et al., 1994). Each this ALE score is then compared to the activation likelihood of standard space voxel calculated under an analytically derived null distribution of random spatial correlation between experiments (Fitzgerald et al., 2008; Sabatinelli et al., 2011). In this way, ALE algorithm allows to determine whether the convergence between experiments across different studies reflects meaningful operations rather than random clustering in the brain (Eickhoff et al., 2009; Turkeltaub et al., 2002).

2.3. Meta-analysis algorithm

In this research, we were interested not only in which brain regions are involved in the three mental processes, but also in how their activities differ among the three mental processes. To this end, we combined different methods, that are, single analysis, contrast analysis, overlap

analysis, and meta-analytic connectivity mapping (MACM) analysis. Single analysis of ALE was used to identify brain regions involved in three domains respectively. Contrast analysis of ALE was used to reveal the differential brain regions between two domains, thus indicating domain-specific systems, and to reveal the shared brain regions between the two behavioral domains. Overlap analysis was adopted to reveal the common regions across the three domains. Furthermore, we used MACM analysis to explore the potential common networks underlying the processes involved identified overlapping regions among all three domains.

2.4. Statistical analyses

2.4.1. Single analyses

First, studies reported in Talairach coordinates were transformed to Montreal Neurological Institute (MNI) space using the implemented algorithm in GingerALE 3.0.2 (Laird et al., 2011). Based on the collected papers and the transformed MNI three-dimensional coordinates, ALE analyses were conducted for the three datasets of interoception, decision

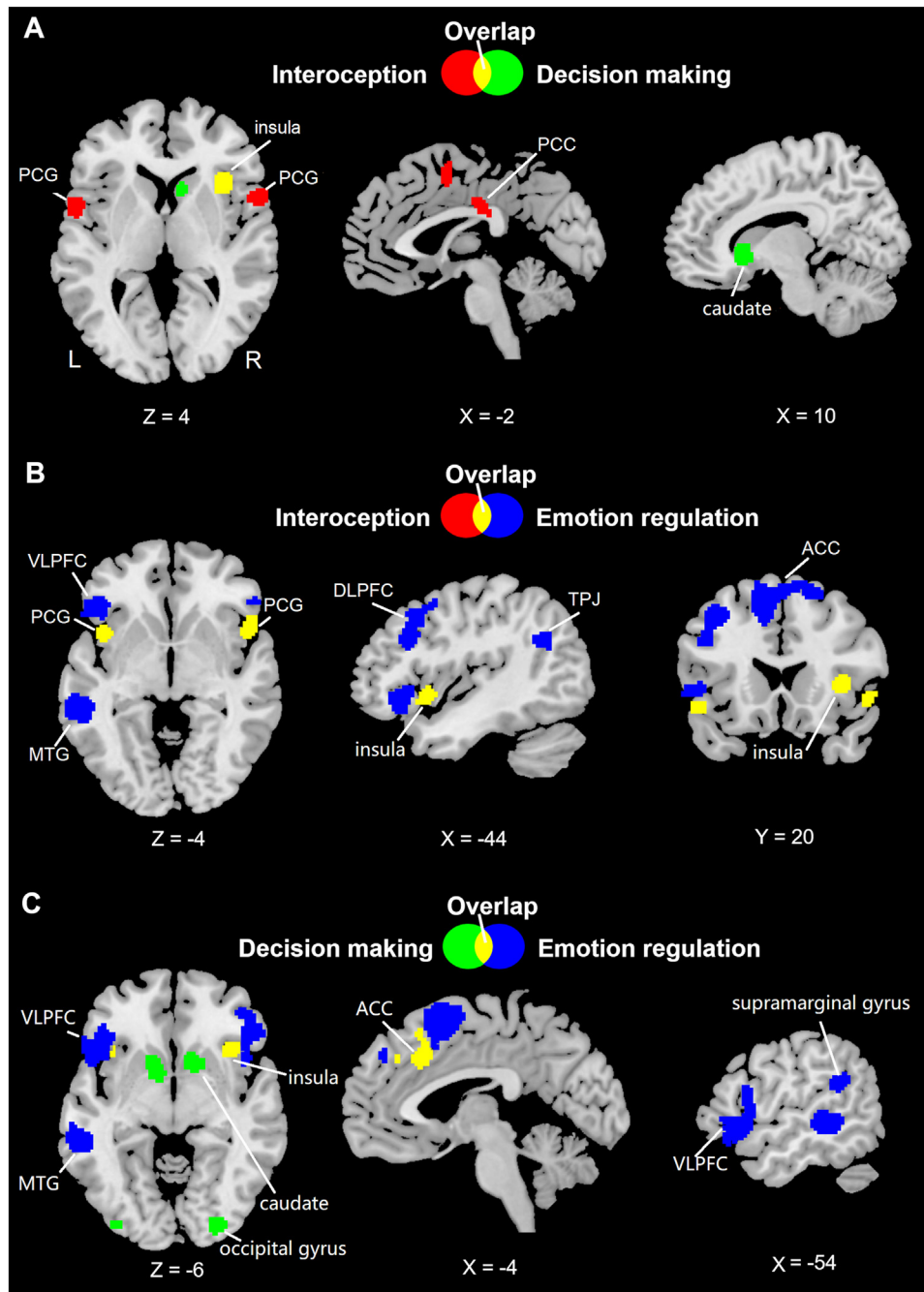


Figure 2. Pairwise conjunction and contrast analysis results of the three domains. A: Interoception and / versus Emotion regulation; B: Interoception and / versus Decision making; C: Emotion regulation and / versus Decision making. Clusters are thresholded at $p < .01$, with a minimum cluster size of 200 mm³. Abbreviations - L: left; R: right; PCG: precentral gyrus; PCC: posterior cingulate cortex; MTG: middle temporal gyrus; VLPFC: ventral lateral prefrontal gyrus; DLPFC: dorsal lateral prefrontal cortex; TPJ: temporal parietal junction; ACC: anterior cingulate cortex.

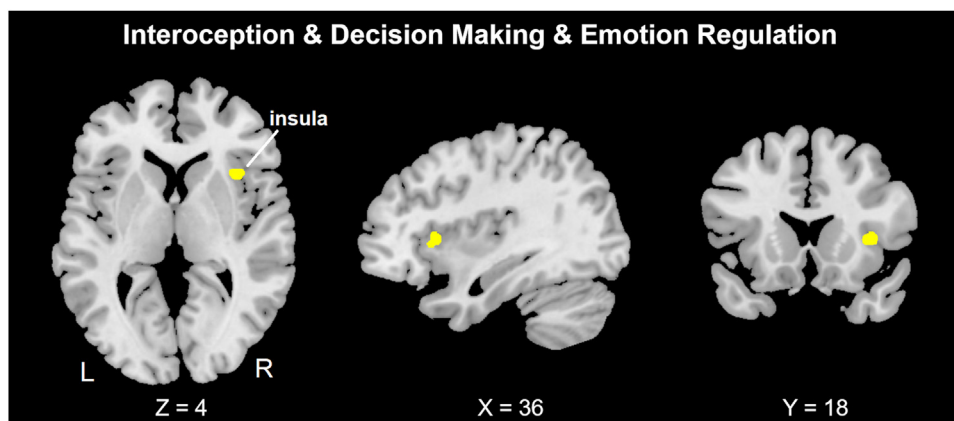


Figure 3. Overlap of interoception, decision making, and emotion regulation. FEW corrected at $p < .05$ with primary alpha level of .001 and a minimum cluster size of 200 mm³. Abbreviations - L: left; R: right.

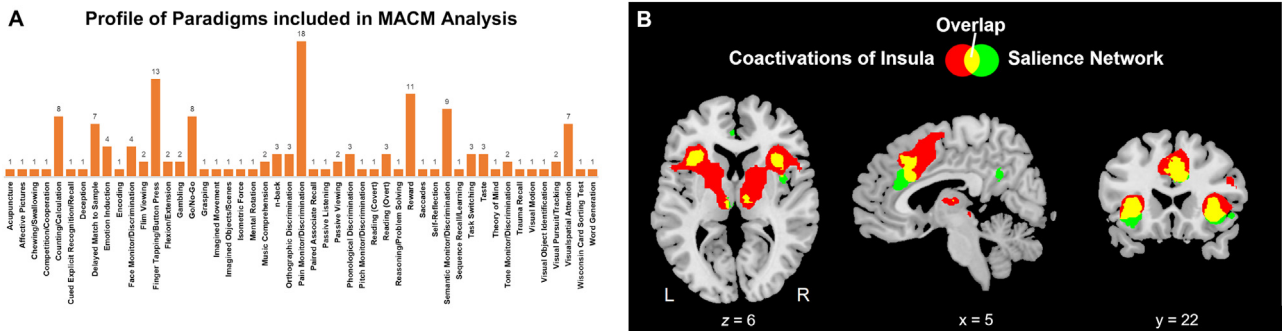


Figure 4. Results from meta-analytic connectivity mapping (MACM) for the right anterior insula. A: Profile of paradigm class included in the MACM; B: Coactivation patterns with the right anterior insula and overlap between MACM results with Saliency network. Clusters are thresholded at $p < 0.05$, FWE corrected in the MACM analysis. Abbreviations - L: left; R: right.

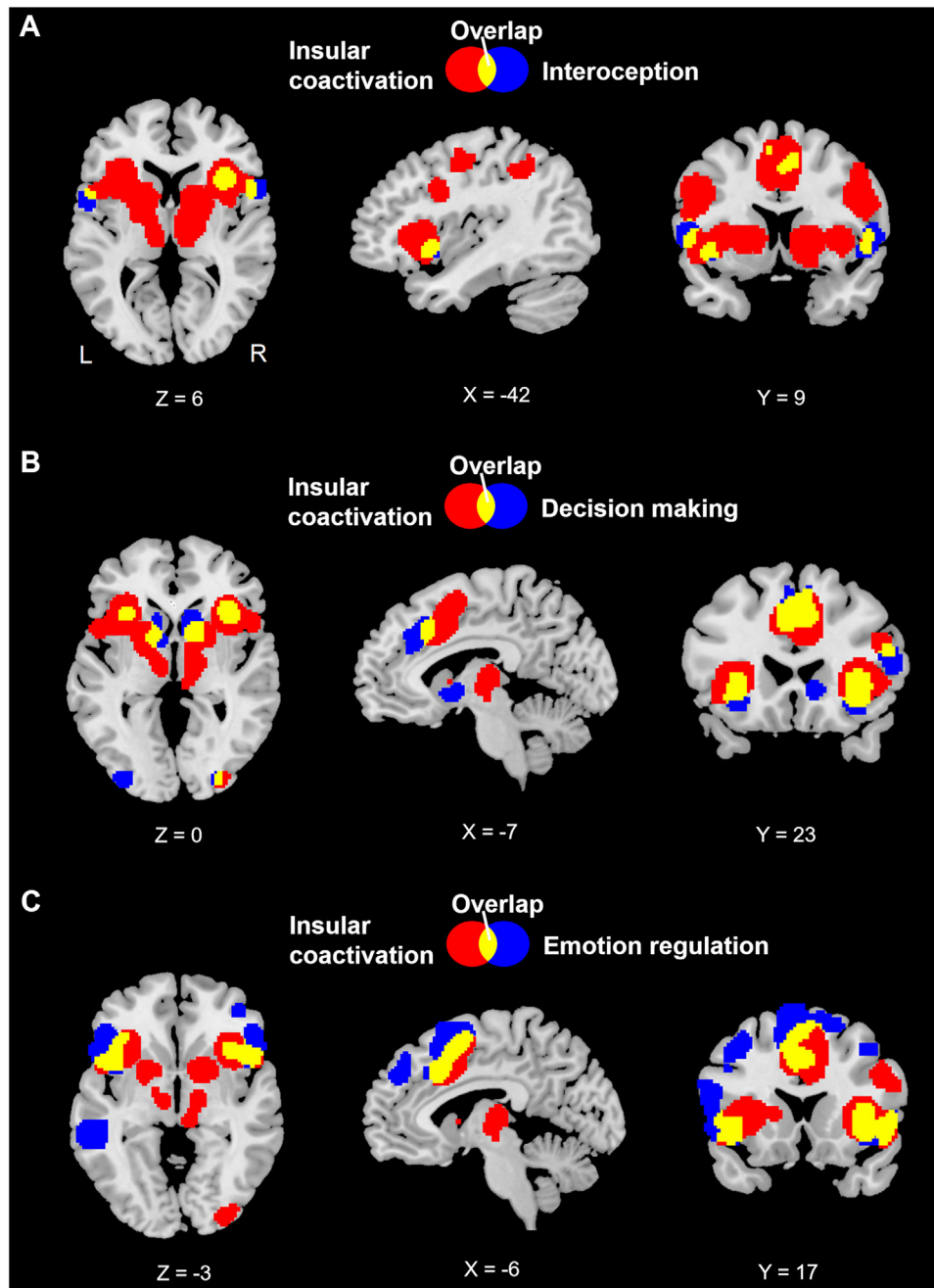


Figure 5. Overlap between MACM results with single analysis results of the three domains. A: Overlap between MACM results with single analysis results of interoception; B: Overlap between MACM results with single analysis results of decision making; C: Overlap between MACM results with single analysis results of emotion regulation. Abbreviations - L: left; R: right.

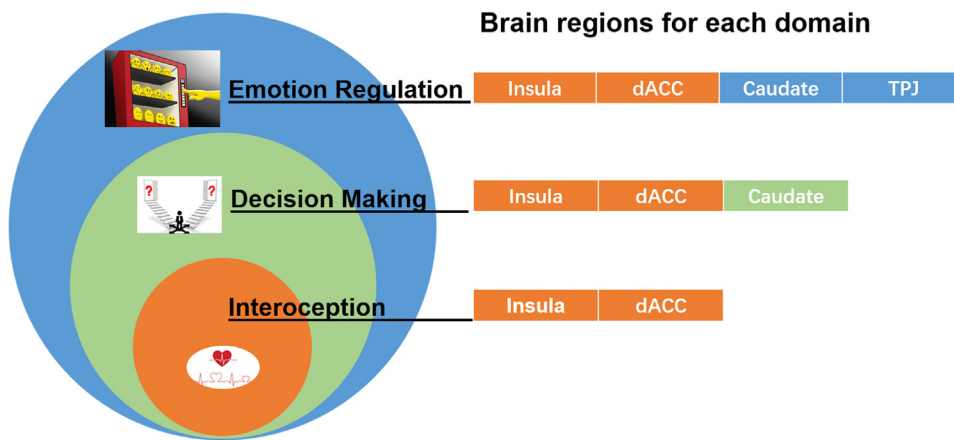


Figure 6. Neural model of interoception, decision making, and emotion regulation. Abbreviations - dACC: dorsal anterior cingulate cortex; TPJ: temporal parietal junction.

making and emotion regulation, respectively. ALE maps were created by modeling each focus as a 3D Gaussian function. Cluster inclusion thresholded at voxel-level $p < .001$ (1000 permutations, minimum volume 200 mm³). Clustering level family-wise error (FWE) correction was used to threshold the significance of the results at $p < .05$. (Eickhoff et al. 2012; Eklund et al., 2016). The p -value map was converted to z -scores for display.

2.4.2. Conjunction and contrast analyses

Contrast analysis compares and contrasts two datasets. GingerALE 3.0.2 was further used for contrast analyses between decision making and interoception, between emotion regulation and interoception, and between decision making and emotion regulation. We first combined two datasets files obtained from the original study selections into one pooled file, and then a single analysis was performed for the pooled dataset. Cluster inclusion thresholded at voxel-level $p < .001$ (1000 permutations, minimum volume 200 mm³). Clustering level family-wise error (FWE) correction was used to threshold the significance of the results at $p < .05$. A conjunction image was created using the voxel-wise minimum value between the two thresholded ALE images. It contains the shared regions that exist in both ALE images (Eickhoff et al., 2011). Next, we computed the voxel-wise difference between the two ALE maps of the two behavioral domains. Permutation tests were performed to assess the significance of the observed difference of ALE scores between each pair of voxels in the two images. Finally, inferences of contrast analysis were made based on the significance of the true difference scores according to the following threshold: $p < .01$, with 1,000 permutations and an additional cluster volume threshold of 200 mm³ (Eickhoff et al., 2012). The p -value map obtained after the permutation tests was converted to z -scores for display.

2.4.3. Overlap analysis among interoception, decision making and emotion regulation

To distinguish the common brain regions across the three domains, we used the “image calculator” in SPM8 to determine the intersection between the thresholded statistical parametric maps of three single analyses on interoception, decision making and emotion regulation.

2.4.4. MACM analysis

Then we defined the intersection of the brain regions obtained from the above overlap analysis as our regions of interest (ROIs). In particular, we used Dpabi (Yan et al., 2016) to extract the brain intersections of the three behavioral domains generated by the overlay analysis, and further re-sampled them to generate ROIs. In order to explore the coactivation patterns of the ROIs, we carried out a meta-analytic connectivity mapping (MACM) analysis by using the BrainMap Database (<http://www.brainmap.org/>) (Laird et al. 2009). MACM used the neuroimaging database to describe the coactivation patterns in different

tasks, and generated data-driven coactivation maps based on the predefined ROIs (Langner et al., 2014). In this analysis, we limited our analysis to fMRI experiments in normal whole-brain neuroimaging studies in healthy people, which reported activation in standard space. Other studies that looked at differences in age, sex, interventions or clinical populations were excluded. This analysis consisted of the following steps. First, we downloaded all the whole-brain peak coordinates in the Brain-Map Database (<http://www.brainmap.org/>) if the results of a particular study include at least one activation foci in the ROIs. Second, ALE meta-analysis was performed on all coordinates of the retrieved experiments to quantify their convergence and coactivation with the ROIs. Finally, ALE map was corrected using family-wise error (FWE) at $p < 0.05$ at the clustering level.

In addition, to assess to what extent this coactivation pattern of the right insula overlapped with the SN, we obtained a SN mask by online meta-analysis (A total of 126 studies with 4237 foci were included) using neurosynth (<https://www.neurosynth.org/>).

Furthermore, we used Mango to extract the size and voxel number of the brain networks of interoception, decision making, emotion regulation, SN, insular coactivation, overlap of the insular coactivation and the interoception, overlap of the insular coactivation and the decision making, overlap of the insular coactivation and the emotion regulation, overlap of the insular coactivation and the SN. Additionally, the percentages of overlap between the insular coactivation and the interoception, decision making, emotion regulation, SN were calculated respectively (See Table S5 and Table S6 in the supplementary material).

For visualization purposes, all the results were registered onto a standard brain in an MNI template (Ch2better.nii, a template from the Dpabi; Yan et al., 2016) using Mango (<http://www.brainmap.org/>). Anatomical location was labelled with reference to the Nearest Grey Matter MIN labels through Mango.

3. Results

3.1. Single analyses

A total of 54 experiments examining interoception with a total of 399 foci, a total of 91 experiments examining decision making with a total of 712 foci, and a total of 82 experiments examining emotion regulation with a total of 1199 foci were respectively identified to perform the single meta-analysis. Particularly, two experiments in the emotion regulation category involved interoceptive processing (e.g. attention to breath), implying a close relationship between interoception and emotion regulation (Doll et al., 2016; Murakami et al., 2015). We did not find any experiments in the decision-making domain involved interoception-related processing in our dataset.

Table 1a

Results of the meta-analysis of contrast analysis between decision making and interoception task.

Cluster	Brain regions	Volume (mm ³)	Brodmann area	Z scores	MNI coordinates		
					x	y	z
Interoception task > Decision making task							
1	R Precentral Gyrus	1528	44	3.89	58	7.7	6.5
2	L Superior Temporal Gyrus	1192	22	3.89	-57.8	6.7	1.8
	L Precentral Gyrus		44	3.72	-56.4	8.4	6.8
3	L Medial Frontal Gyrus	560	6	3.29	-5.2	2	54
	L Medial Frontal Gyrus		6	3.16	0	2	58
4	L Cingulate Gyrus	512	23	3.89	-4	-22	30
Decision making task > Interoception task							
1	R Caudate Head	1016		2.88	8.7	16.7	-3.3
	R Caudate Body			2.83	8	18	4
	R Caudate Head			2.79	8	22	0
2	R Fusiform Gyrus	872	19	2.99	26	-86	-8
	R Inferior Occipital Gyrus		18	2.91	26	-91	-4
	R Inferior Occipital Gyrus		18	2.89	26	-92	-8
Conjunction brain activations under interoception task and decision making task							
1	R Insula	688	13		36	20	4

Note: L. left hemisphere; R. Right hemisphere; MNI: Montreal Neurological Institute.

3.1.1. Interoception

The single meta-analysis of interoceptive tasks revealed increased activation in bilateral anterior insula, bilateral precentral gyrus, the supplementary motor area (SMA) and pre-SMA, the dorsal ACC (dACC), and the posterior cingulate gyrus (see Table S1 and Figure 1A).

3.1.2. Decision making

The decision-making meta-analysis results included the dACC, bilateral dorsal prefrontal cortex, and bilateral anterior insula. Other brain areas such as bilateral inferior parietal lobe, the right angular gyrus, the right caudate head, the left lentiform nucleus, the SMA and pre-SMA, and bilateral occipital gyri were also involved (see Table S1 and Figure 1B).

3.1.3. Emotion regulation

The meta-analysis of emotion regulation studies indicated enhanced activity in bilateral ventral lateral prefrontal cortex (VLPFC), bilateral dorsal lateral prefrontal cortex (DLPFC), the dACC, bilateral anterior insula and bilateral temporo-parietal junction (TPJ). Other brain areas such as bilateral angular gyri, the left middle temporal gyrus (MTG), the SMA and pre-SMA, and the left caudate body were also found more activated during emotion regulation (see Table S1 and Figure 1C).

3.2. Conjunction and contrast analyses

The pairwise conjunction and contrast results are presented in Figure 2. For cluster information, please see Table 1.

3.2.1. Comparison between interoception and decision making

As seen in Figure 2A, a conjunction-based activation in the right anterior insula is seen in interoception and decision making. In addition, the interoceptive process involved increased activation in bilateral precentral gyrus and the posterior cingulate gyrus compared to the decision making. While decision-making task involved more activations in the right caudate body and head, the right fusiform gyrus and the right occipital gyrus compared to interoceptive task (see Table 1a and Figure 2A).

3.2.2. Comparison between interoception and emotion regulation

The conjunction-based brain activations in interoceptive task and emotion regulation task included bilateral precentral gyrus and bilateral anterior insula. In addition, the interoceptive task involved increased activation in the SMA and pre-SMA compared to the emotion regulation task. While the emotion regulation task involved more activations in the DLPFC, the ACC, the left MTG, bilateral angular gyri and the left TPJ compared to interoceptive task (see Table 1b and Figure 2B).

3.2.3. Comparison between decision making and emotion regulation

The conjunction-based brain activations in decision making task and emotion regulation tasks included the right anterior insula and the ACC. In addition, decision-making involved more activations in the occipital gyrus, the left lentiform nucleus, and the right caudate head compared to emotion regulation. While the emotion regulation tasks involved increased activation in bilateral VLPFC, the left MTG, bilateral supra-marginal gyrus and the left caudate body compared to the decision-making task (see Table 1c and Figure 2C).

3.3. Overlap among the three domains

The overlap analysis among three domains revealed a cluster in the right insula as the common area underlying interoception, decision making and emotion regulation. As shown in Figure 3, the overlap is at the right dorsal anterior insula (peak coordinate: $x = 36, y = 18, z = 4$). The cluster volume is 400 mm³. When lowering the statistical threshold for single analyses of each domain (primary alpha level: $p < .01$; FWE corrected at $p < .05$, with a minimum cluster size of 200 mm³), besides the right anterior insula, the left anterior insula and the dACC are also shown in the overlap among all the three domains.

3.4. MACM analysis

The MACM analysis was run to identify the data-driven coactivation maps based on the right dorsal anterior insula as a common brain region (data are based on all studies prior to May of 2021). For the insula ROI, 86 papers, 102 experiments, 1,989 foci from 1,435 participants were identified to investigate the meta-analytic coactivation pattern. The profile of the included paradigms is shown in Figure 4A. The right anterior insula ROI showed convergent coactivation with the left anterior insula, bilateral DLPFC, the dorsal ACC, bilateral thalamus, right claustrum, right lentiform nucleus, left putamen and inferior parietal lobule (see Table 2 and Figure 4B). This coactivation network included the key nodes of the SN. Then we overlaid the resultant MACM map with the SN mask. As presented in Figure 4B, the coactivation pattern of the right insula are largely overlapped with the SN.

Finally, we raised the question whether the regions of the SN identified in MACM also are recruited in all three domains. We therefore visualized the overlapping regions between MACM coactivation map of the right insula with the networks of interoception, decision making, and emotion regulation obtained from the single analysis, respectively. As shown in Figure 5, the SN with especially the insula and the dACC of the MACM overlap with the regions recruited during all the three domains. This strongly suggests that the two core regions of the SN are

Table 1b

Results of the meta-analysis of contrast analysis between interoception task and emotion regulation.

Cluster	Brain regions	Volume (mm ³)	Brodmann area	Z scores	MNI coordinates		
					x	y	z
Interoception task > Emotion regulation task							
1	L Superior Temporal Gyrus	680	22	3.72	-58.3	2	0.7
	L Precentral Gyrus		6	3.09	-60	4	8
Emotion regulation task > Interoception task							
1	L Superior Frontal Gyrus	6520	6	3.89	-9.5	19.4	54.3
	R Superior Frontal Gyrus		6	3.24	22	16	62
	R Superior Frontal Gyrus		6	3.12	18	14	64
	R Middle Frontal Gyrus		6	3.06	22	20	60
	R Superior Frontal Gyrus		6	2.85	14	20	64
2	L Middle Frontal Gyrus	2952	6	3.89	-36.2	15.8	42.5
	L Middle Frontal Gyrus		6	3.72	-37.4	14.9	45.1
	L Precentral Gyrus		9	3.54	-42	20	38
3	L Middle Frontal Gyrus	2344	9	3.16	-42	20	29
	L Inferior Frontal Gyrus		47	3.72	-52	32	-8
4	L Inferior Frontal Gyrus	2144	47	3.54	-48	32	-8
	L Inferior Frontal Gyrus		47	3.43	-44	30	-6
	L Inferior Frontal Gyrus		45	3.29	-54	20	0
	L Inferior Frontal Gyrus		45	3.12	-48	22	0
5	L Middle Temporal Gyrus	2144	21	3.89	-60.6	-34.4	-6
6	L Middle Frontal Gyrus	984	9	3.19	-30	46	22
	L Middle Frontal Gyrus		10	3.04	-28	46	17
7	L Medial Frontal Gyrus	888	9	2.85	-26	44	12
	R Middle Frontal Gyrus		8	3.43	38	34	40
8	R Inferior Frontal Gyrus	704	47	3.04	46	34	-12
	R Inferior Frontal Gyrus		47	2.68	46	28	-12
	R Inferior Frontal Gyrus		45	2.54	54	32	-4
9	L Putamen	672		2.86	-20	10	5
	L Putamen			2.83	-20	6	8
10	L Middle Temporal Gyrus	576	39	3.29	-48	-58	28
	L Superior Temporal Gyrus		39	3.12	-50	-56	24
11	L Superior Frontal Gyrus	488	8	2.88	-6	48	38
	L Medial Frontal Gyrus		8	2.77	-6	52	34
12	L Supramarginal Gyrus	224	40	2.74	-60	-53	26
Conjunction brain activations under interoception task and Emotion regulation task							
1	R Inferior Frontal Gyrus	944	47		54	16	-6
	R Precentral Gyrus		44		54	16	4
2	L Insula	760	13		-42	12	-4
	L Inferior Frontal Gyrus		47		-50	18	-10
3	R Insula	544	13		36	20	4
4	L Precentral Gyrus	216	44		-54	10	10

Note: L. left hemisphere; R. Right hemisphere; MNI: Montreal Neurological Institute.

implicated in all three interoception, decision making, and emotion regulation.

4. Discussion

We here conducted meta-analyses in order to demonstrate how regions of interoception are related to and thus spatial-topographically nested within those recruited during decision making and emotion regulation. Our main findings are: (i) overlap of the right dorsal anterior insula among all three interoception, decision making and emotion regulation; (ii) connection of the right anterior insula with regions of the Salience Network like dACC which are recruited during interoception, decision making and emotion regulation. Together, our findings suggest that regions of interoception like right anterior insula and its connection to regions of the SN like dACC are also recruited during decision making and emotion regulation.

Albeit tentatively, this suggests that interoception as featured by intero-exteroceptive integration (Craig, 2009; Critchley and Harrison, 2013) and salience attribution (Seth, 2013; Uddin, 2015) is topographically contained and thus spatially nested within the networks of decision making and emotion regulation. Such spatial-topographic nestedness may well account for the various observation that interoception of our bodily signals modulates decision making (Dunn et al., 2010; Furman et al., 2013; Herman et al., 2021; Salvato et al., 2019; Werner et al., 2009; Wölk et al., 2014) and emotion regula-

tion (Füstös et al., 2013; Jakubczyk et al., 2019; Kever et al., 2015; Pollatos et al., 2015; Zamariola et al., 2019).

The single meta-analysis of interoceptive tasks revealed brain regions that are typically highlighted in previous research on interoception (Craig, 2002; Critchley et al., 2004; Wang et al., 2019). These include bilateral insula and the dACC as well as others like precentral gyrus and medial frontal gyrus, which is consistent with recent meta-analyses involving interoception (Adolfi et al., 2017; Salvato et al., 2020; Schulz, 2016; Qin et al., 2020). Interestingly, especially insula and dorsal ACC are also recruited during decision making and emotion regulation. This is further confirmed by our pairwise conjunction and overlap of all three that highlighted especially the right anterior insula as commonly shared region. It has been suggested that the dorsal anterior insula is involved in attention and executive functions, while the ventral region is implicated in emotional and affective processes (Touroutoglou et al., 2012). Recently, Korn and Bach (2019) combined a risk task with behavioral modeling and fMRI. The results indicate that the insula (extending to the IFG) and the dACC are part of a brain network supporting optimal decision making and specifically refers to minimizing threats and maximizing rewards in approach-avoidance situations. Furthermore, a recent neuroimaging meta-analysis of emotion regulation revealed the dACC and the bilateral anterior insular cortex, as a domain-general functional network of emotion regulation, has been consistently involved in a variety of different emotion regulation strategies (Pico-Perez et al., 2019).

Table 1c
Results of the meta-analysis of contrast analysis between decision making and emotion regulation.

Cluster	Brain regions	Volume (mm ³)	Brodmann area	Z scores	MNI coordinates		
					x	y	z
Emotion regulation task > Decision making task							
1	L Medial Frontal Gyrus	7872	6	3.89	-4.8	10.1	62
	R Superior Frontal Gyrus		6	3.72	11.3	18.7	65.3
2	L Medial Frontal Gyrus	5864	32	2.99	-11	17	44
	L Inferior Frontal Gyrus		47	3.89	-49.2	20.3	-5.2
	L Inferior Frontal Gyrus		44	3.54	-58	12	18
	L Inferior Frontal Gyrus		44	3.43	-52	12	8
	L Inferior Frontal Gyrus		45	2.81	-52	32	0
3	L Precentral Gyrus	3256	6	3.89	-47.1	2.6	51.3
	L Middle Frontal Gyrus		6	3.54	-36	20	52
	L Middle Frontal Gyrus		6	3.35	-32	20	50
4	L Middle Temporal Gyrus	3072	21	3.89	-59.5	-35.8	-2
5	R Inferior Frontal Gyrus	2728	46	3.89	48.3	38.4	-7.5
	R Inferior Frontal Gyrus		47	3.43	46	30	-12
	R Inferior Frontal Gyrus		47	3.29	44	18	-10
6	L Inferior Parietal Lobule	2424	40	3.89	-55.5	-43.5	27.5
	L Inferior Parietal Lobule		40	3.72	-50	-44	27.3
	L Supramarginal Gyrus		40	3.43	-64.4	-47.2	24.8
	L Superior Temporal Gyrus		13	3.29	-44	-48.7	24
7	L Middle Frontal Gyrus	1344	10	3.43	-28	45	16
	L Superior Frontal Gyrus		9	3.54	-30	48	23
	L Middle Frontal Gyrus		10	2.97	-30	48	6
8	R Tuber	1024		3.89	36.8	-62.6	-29.2
9	L Superior Frontal Gyrus	832	8	3.72	-12	52	38
	L Superior Frontal Gyrus		8	3.35	-16	51	34
10	L Caudate	760		3.72	-20	8	14
	L Caudate			3.43	-18	10	10
11	R Inferior Parietal Lobule	688	40	3.89	56.7	-49.3	43.3
	R Inferior Parietal Lobule		40	3.54	56	-55	42
12	L Middle Frontal Gyrus	560	9	3.16	-42	28	28
13	R Middle Frontal Gyrus	496	6	2.83	38	18	42
	R Middle Frontal Gyrus		8	2.74	35	31	37
14	R Superior Temporal Gyrus	456	39	3.12	59	-59	24
	R Supramarginal Gyrus		40	2.72	60	-46	28
	R Supramarginal Gyrus		40	2.62	60	-50	26
15	R Superior Frontal Gyrus	320	10	3.89	31.3	50.7	16
16	R Precentral Gyrus	296	44	2.76	59	20	2
Decision making task > Emotion regulation task							
1	L Inferior Occipital Gyrus	1232	18	3.89	-34.3	-90.1	-1.3
	L Middle Occipital Gyrus		18	3.35	-36	-92	4
2	R Middle Occipital Gyrus	1024	18	3.89	27.9	-89.7	-7.6
	R Fusiform Gyrus		18	3.35	25	-90.5	-9.5
3	L Lenticular Nucleus	872		3.35	-10.7	7.3	-4.7
4	R Caudate Head	648		3.09	8	12	-4
5	R Superior Parietal Lobule	336	7	3.35	32	-50	46
	R Inferior Parietal Lobule		7	3.29	36	-54	48
6	R Precentral Gyrus	328	6	3.43	42	4	30
Conjunction brain activations under emotion regulation task and decision making task							
1	L Cingulate Gyrus	2120	32		-2	22	38
2	R Insula	1336	13		36	20	2
	R Insula				34	22	-4

Note: L. left hemisphere; R. Right hemisphere; MNI: Montreal Neurological Institute.

Our finding of the dorsal anterior insula as shared region of the three domains corroborates its role in regulation of attention and behaviors. When lowering the statistical threshold, we also obtained the dorsal ACC and the left anterior insula as regions overlapping between all three domains; this further supports the important role of insula and dACC in integrating disparate functional systems (Cauda et al., 2012; Chang et al., 2013; Torta & Cauda, 2011). Together, these regions constitute the Salience Network (Menon and Uddin, 2010; Seeley et al., 2007; Uddin, 2015). The Salience Network is assumed to detect emotional saliency, which is crucial for guiding emotion control and decision making (Carvalho and Damasio, 2021).

Our meta-analytic findings are complemented by the results on co-activated regions of the identified right anterior insula. The right anterior insula is connected to dACC and bilateral thalamus and other regions typical of the SN, which is confirmed by the overlap between the resultant MACM map and the Salience Network mask. The result is con-

sistent with previous research in both non-human primates and humans revealing heavy anatomical and functional connectivity between the insula and extensive networks underlying autonomic, emotional and cognitive processing (Gogolla, 2017; Augustine, 1996). The obtained profile of MACM analysis suggests that insula as a key node of Salience Network plays an important role in various psychological processes such as pain monitor and reward. Furthermore, those co-activated regions, in turn, were overlapped with the single analysis results of interoception, decision making and emotion regulation. That strongly suggests that the right anterior insula and connected SN are implicated not only in interoception but also in decision making and emotion regulation.

Together our findings show that the regions recruited during interoception are spatial-topographically nested within the networks involved in decision making and emotion regulation. Interoception requires intero-exteroceptive integration (Ceunen et al., 2016; Craig, 2009; Critchley and Harrison, 2013; Frewen et al., 2020) which, in turn, al-

Table 2
Results of the meta-analysis of functional connectivity with the identified right insula as a seed.

Cluster	Brain Regions	Volume (mm ³)	Brodmann area	Z scores	MNI coordinates		
					x	y	z
1	R Insula	21288	13	27.64	36	18	4
	R Thalamus			7.43	16	-8	8
	R Lentiform Nucleus			7.18	16	6	0
	R Insula			5.41	52	16	-2
2	R Brainstem.Midbrain. Red Nucleus	17952	32	4.56	8	-26	-6
	R Cingulate Gyrus			9.87	6	18	40
	L Medial Frontal Gyrus			9.43	0	10	48
3	L Insula	17192	13	15.64	-34	18	4
	L Putamen			6.86	-22	8	2
	L Thalamus			5.39	-10	-20	8
4	R Inferior Frontal Gyrus	14944	9	8.11	48	8	28
	R Superior Frontal Gyrus			7.02	42	40	26
	R Middle Frontal Gyrus			6.50	32	0	50
	R Middle Frontal Gyrus			5.75	34	42	26
	R Precentral Gyrus			5.01	48	4	44
	R Middle Frontal Gyrus			4.47	46	28	22
5	L Inferior Frontal Gyrus	8056	6	7.38	-48	6	30
	L Precentral Gyrus			6.25	-28	-2	50
	L Precentral Gyrus			4.92	-44	-6	50
	L Middle Frontal Gyrus			3.87	-24	-8	62
6	L Superior Parietal Lobule	6536	7	5.94	-26	-62	50
	L Precuneus			5.73	-20	-70	44
	L Inferior Parietal Lobule			4.67	-34	-52	52
	L Inferior Parietal Lobule			4.59	-40	-42	42
7	R Precuneus	5680	7	5.63	34	-44	44
	R Superior Parietal Lobule			5.26	32	-54	52
	R Superior Parietal Lobule			4.05	28	-64	54
	R Precuneus			3.94	20	-68	48
	R Inferior Parietal Lobule			3.68	50	-36	46
8	R Inferior Occipital Gyrus	1160	18	5.12	32	-92	-4

Note: L. left hemisphere; R. Right hemisphere; MNI: Montreal Neurological Institute.

lows for salience attribution (Seth, 2013; Uddin, 2015). Our result of spatial-topographic nestedness of interoceptive regions within the networks of decision making and emotion regulation suggests that intero-exteroceptive integration and salience attribution are also involved in the latter two domains (see Figure 6). This is also well compatible with the observation that interoception of our bodily signals modulates decision making (Dunn et al., 2010; Furman et al., 2013; Herman et al., 2021; Salvato et al., 2019; Werner et al., 2009; Wölk et al., 2014) and emotion regulation (Füstös et al., 2013; Jakubczyk et al., 2019; Kever et al., 2015; Pollatos et al., 2015; Zamariola et al., 2019).

There are several limitations to this research. First, there is lack of direct behavioral data to support the role of interoception in both decision making and emotion regulation. Future research needs to combine behavioral and neuroimaging methods to investigate the relationships between interoception, decision making and emotion regulation together. Second, it has been suggested that different interoceptive modalities such as heart, stomach, bladder and respiration involve diverse neural networks. The present meta-analysis included a variety of interoceptive functions, which need further investigation on diversity of interoceptive networks. Third, some of the included studies on interoception in this meta-analysis used the heartbeat counting/detection tasks, which have been criticized for low validity. Therefore, conclusions from these studies should be considered with caution.

5. Conclusions

We here show that the regions mediating interoception, namely dorsal anterior insula and dACC are also recruited during decision making and emotion regulation. Topographically, this suggests spatial nestedness of the interoceptive regions within the networks of the latter. Albeit tentatively, these findings suggest that intero-exteroceptive integration and salience attribution as key features of interoception are also implicated and thus functionally nested in emotion, i.e., emotion

regulation, and cognition, i.e., decision making processes. Such spatial nestedness may explain well the observation that interoception modulates both decision making and emotion regulation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Credit authorship contribution statement

Yafei Tan: Conceptualization, Investigation, Data curation, Writing – original draft, Funding acquisition. **Ranran Yan:** Data curation, Methodology, Formal analysis, Writing – review & editing. **Yuan Gao:** Data curation, Methodology, Formal analysis, Writing – review & editing. **Meng Zhang:** Methodology, Investigation, Project administration, Funding acquisition, Writing – original draft. **Georg Northoff:** Conceptualization, Supervision, Writing – original draft.

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Data and code availability statement

This manuscript entitled “Spatial-topographic nestedness of interoceptive regions within the networks of decision making and emotion regulation: Combining ALE meta-analysis and MACM analysis” is a meta-analysis paper that does not include any primary research involving data and code. Data and code would have to be requested from the primary sources that are cited in the current manuscript and supplementary material.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.neuroimage.2022.119500](https://doi.org/10.1016/j.neuroimage.2022.119500).

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