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The Nature of the Task Influences Intrinsic Connectivity Networks: An Exploratory fMRI Study in Healthy Subjects

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Abstract

Task-induced variations in neural activity and their effects on the topological architecture of intrinsic connectivity networks (ICNs) of the brain are still a matter of ongoing research. In this exploratory study, we used spatial independent component analysis (ICA) as a data-driven technique to characterize ICNs related to two different tasks in healthy subjects who underwent 3T blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI). The fMRI tasks consisted of (a) a viscerosensory stimulation of an internal organ (interoceptive task), and (b) passive viewing of emotionally expressive faces and pictures from the International Affective Picture System (exteroceptive emotion task). Comparison of the network volumes and peak activations during each task condition demonstrated that changes in ICN volume and corresponding peak activation differed between the interoceptive and exteroceptive emotion tasks when compared to the baseline rest. Further, salience network was the most task-activated ICN for both fMRI task conditions. However, different spatial characteristics were observed between the salience networks derived from the interoceptive task and the one derived from the exteroceptive emotion task. This study is a step in the direction of better understanding the influence of task condition on ICN topology. Future research with a larger sample size and task variations should delve deeper into what aspects of network topology really matter, with further investigations regarding the observed differences due to gender and age.

I. INTRODUCTION

The human brain is intrinsically organized into largescale intrinsic connectivity networks (ICNs) [1]. Several ICNs have been consistently identified in multivariate decompositions of both resting-state and task functional magnetic resonance imaging (fMRI) data using blind source separation methods – most notably, independent components analysis (ICA) [2]–[4]. Spatial ICA is a datadriven technique that identifies temporally coherent patterns of blood oxygen-level dependent (BOLD) signal that are maximally independent from each other [4]. In contrast to general linear modeling (GLM) of the BOLD fMRI time series, which requires the assumption of brain's hemodynamic responses and the use of a design matrix (i.e., set of regressors), ICA requires no prior information about the neuronal activity. However, the

ontology of ICN topology and their hierarchy are not well understood. For example, previous studies demonstrated that ICA is sensitive to the number of components one asks the algorithm to produce [5]. But the underlying reason for observed differences in ICN hierarchical subdivision based on model dimensionality is not clear yet. More recent studies showed that experimental variables such as stimulus and design paradigms of the fMRI task can be used to delineate functional differences between networks [2]. Still, the extent to which the nature of the fMRI task can impact ICN features in particular their functional topologies (i.e., ICA-derived spatial maps) has not been thoroughly investigated.

Therefore, the objective of the present study was to investigate the effects of different brain activation schemes (different task conditions) on the topological architecture of the ICNs. Two types of tasks were chosen to be compared in a group of healthy subjects: (a) an interoceptive (bodily sensation) and (b) an exteroceptive negative emotion task. This allowed the quantitative determination of how strongly each ICN features is related to a given task. We expected both tasks activate the salience [6], and subcortical networks such as amygdalohippocampal regions. But we hypothesized that due to differences in task stimuli (i.e., homeostatically significant stimuli vs external visual stimuli with emotional salience), ICN spatial maps and variations in network topology would be different between the two task conditions.

II. MATERIALS AND METHODS

A. Participants and Imaging Paradigm

Participants were 33 medication-free individuals with no current mental or urological disorders as assessed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), and urodynamic measurements, respectively. After providing IRB-approved informed consent, participants were divided into two groups. The interoceptive group ($n = 15$, mean age $\pm$ SD = 31.7 ± 8.4 years) underwent viscerosensory stimulation task that involved controlled infusion and drainage of the bladder with fluid in a block design [7] (Fig. 1A). The exteroceptive emotion group ($n = 18$, mean age $\pm$ SD = 29.7 ± 9.6 years) were scanned during the emotion processing task comprised of a block design presentation of emotionally salient visual stimuli (Fig. 1B). The visual stimuli consisted of negative human facial expressions taken from the NimStim face set, and pictures depicting objects, persons or scenes taken from the International Affective Picture System (IAPS). Imaging data were obtained with a 3T MRI scanner (Philips Medical Systems, Best, The Netherlands). T2*-weighted functional images with BOLD contrast were acquired with a gradient-echo, echo-planar imaging sequence for the interoceptive task: TR = 2000 ms, TE = 40 ms, field of view = 240 mm, image matrix size in plane = 96×96 , flip angle = 80° , and for the emotion task: TR = 2700 ms, TE = 30 ms, field of view = 240 mm, image matrix size in plane = 80×80 , flip angle = 80° . A baseline resting state and a high-resolution anatomical scan (using a three-dimensional magnetization-prepared rapid acquisition gradient-echo sequence with TR/TE = 8.2/3.8 ms, field of view = 250 mm, flip angle = 8° , and a 256×256 matrix) were also collected during the same scan session. Scans covered whole brain including cerebellum and brainstem.

B. Data Analysis

Data preprocessing was performed using the Statistical Parametric Mapping software package (SPM12, Wellcome Department of Imaging Neuroscience, UCL; www.fil.ion.ucl.ac.uk/spm/) and Conn-fMRI toolbox 18a (www.nitrc.org/projects/conn) implemented on MATLAB (Mathworks, Inc., MA, USA). Functional images were motion and slice time corrected, unwrapped, coregistered to each participant's T1-weighted high resolution structural image, spatially normalized into the standard Montreal Neurological Institute (MNI) space, resampled at 3 mm³, and smoothed with an 8-mm FWHM (full width half maximum) isotropic Gaussian kernel.

Preprocessed images were analyzed with the Group ICA of fMRI Toolbox (GIFT) software package (v4.0b; Medical Image Analysis Lab, University of New Mexico; <http://icatb.sourceforge.net/groupica.htm>). Spatial ICA was performed separately for each task condition in four stages. Stage 1: The optimum dimensionality of each fMRI data (i.e., the optimal number of components for each task condition) were estimated using the Minimum Description Length (MDL) criteria in GIFT software package. Stage 2: A twostep principal component analysis (PCA) was executed to lower the imaging data dimensionality in an attempt to avoid otherwise prohibitive memory requirements [4]. In the first reduction step dimensionality was reduced at the individual subject level by the PCA with a standard economy-size decomposition. Reduced data from all subjects were concatenated and put through a second (group data) reduction step using the expectation-maximization algorithm [4]. Stage 3: independent component estimation was performed using the infomax algorithm and repeated 20 times in ICASSO (<http://research.ics.tkk.fi/ica/icasso>) to assess the consistency of the components. For each IC the "centroid" (i.e. the most stable result) was determined following the agglomerative hierarchical clustering with average-linkage criterion, and its consistency was calculated with a cluster quality index (I_q) ranging from 0 to 1 [8]. Stage 4: Subject-specific spatial maps and associated time courses were back-reconstructed using GICA3 method provided in GIFT software package.

A systematic approach was used to identify non-artifactual ICs (i.e., ICNs) [4]. First, I_q index from ICASSO was assessed as the criterion to validate the IC decomposition stability. Components with the I_q value less than 0.8 from 20 ICASSO repetitions were excluded. Second, visual evaluation of IC spatial patterns (e.g., ringing) as well as frequency inspection of IC time course spectra (e.g., time courses vastly dominated by low-frequency fluctuations) allowed additional components related to artifacts to be excluded from analysis [7]. Identification of remaining components was accomplished by performing spatial correlation with publicly available GIFT network templates [4], as well as comparing the components to other established ICNs described in previous studies [2]. To define significant brain regions in each non-artifactual component, the spatial map of each component was normalized into z-scores, and the averaged maps of z-scores were entered into the second-level random effects analysis in SPM12 [4]. The significance threshold was set at family-wise error (FEW)-corrected threshold of $p < 0.05$ for multiple comparisons of voxel-wise whole-brain analysis. To evaluate ICN volumetric changes, the number of voxels in ICN that survived FEW-corrected $p < 0.05$ were counted in SPM12 for each subject and task condition. ICN volumes were then compared to the baseline resting state data by means of

paired t -test at Bonferroni corrected p -value of 0.05. A voxel-wise one sample t -test were performed for each IC, and separately for each task using SPM12 [7]. The highest t -value and the locus of the peak activation (x, y, z) in the real world as well as the MNI coordinates were saved and labeled using the AAL (anatomical automatic labeling) toolbox (www.gin.cnrs.fr/AAL). ICNs with time courses related to each of the experimental design were identified with multiple regression using the temporal sorting feature of the GIFT software package. The anatomical localization of significant clusters of common task-related ICNs between the task conditions were investigated with SPM Anatomy toolbox.

III. RESULTS

The ICA model dimensionality for both task conditions was determined to be about 40 using MDL criteria (mean $\pm$ SD = 39.4 ± 6.15 for the interoceptive task, and mean $\pm$ SD = 39.7 ± 2.4 for the exteroceptive emotion task). Figure 2 shows ICASSO results. For each task condition, cluster plots of 2D curvilinear component analysis projections of the component estimates is shown on the left. The black dots are the single-run estimates of the components from each ICASSO run. I_q values for all 40 ICs are displayed on the right. Components with I_q less than 0.8 were excluded from further analysis. Out of 40 ICA components, 24 and 20 ICs were eventually identified as non-artifactual ICs for the interoceptive, and exteroceptive emotion tasks, respectively (Fig. 4A and 4B). ICNs were grouped into 7 categories including the visual (VN), sensorimotor (SMN), cerebellar (CN), cognitive and attention (CAN), default-mode (DMN), subcortical (SCN) and brainstem (BSN) networks. Volume of each network during the corresponding task condition compared to the baseline resting state and their peak activation (t -value and the locus of the peak activation) are shown in Fig. 3. Generally, task-related ICNs expanded during the task compared to baseline rest, and these volumetric changes were different between the interoceptive and exteroceptive emotion tasks (e.g., expansion of the CN, CANs, and SCNs during the interoceptive task vs. expansion of the VNs during the exteroceptive emotion task). Task-relatedness of ICNs were determined by regressing the corresponding time courses against task paradigms. Overall, interoceptive task activated four CANs (ICs 16, 26, 11, and 2), two SCNs (ICs 3 and 24) and CNs. The exteroceptive emotion activated three CANs (ICs 18, 28, 14), a VN (IC 25), and a CN (IC 6). As hypothesized, salience networks (ICs 16, 26, and 11 for the interoceptive task and IC 18 for the exteroceptive emotion task) were the most task-related component (higher beta values). However, different spatial characteristics was observed between the salience networks from the Interoceptive task and the salience network from the exteroceptive emotion task (Fig. 5). Detailed information of the salience network differences in spatial features such as significant clusters of activation, ICN volume and peak activation t -value, and coordinates are provided in Table 1.

IV. Discussion and Conclusion

We compared ICN spatial features derived from the interoceptive and exteroceptive negative emotion tasks in healthy subjects. Statistical analysis showed several network spatial features differed significantly between the two task conditions. The stability of ICA decomposition (Fig. 2) and network parcellation (Fig. 4) were different between the two tasks. Furthermore, the quantification of the network spatial maps showed that the network

volumes and activation loci differed between the two tasks compared to the baseline rest (Fig. 3). Specifically, the SMN (IC 38), CN (IC 14), 2 CANs (IC 2: self-referential network, and IC 16: salience network), and 2 SCNs (ICs 3 and 17) showed significant volumetric expansion during the interoceptive task. In comparison, 2 VNs (ICs 22, and 35) and a CAN (IC 37: central executive network) significantly changed in volume during the exteroceptive emotion task. In accordance with our hypothesis, we found both tasks activated the salience network. Three salience networks (ICs 16, 26, and 11) were identified for the interoceptive task. IC16 is an anterior salience network comprised of the bilateral anterior insula/frontal opercula (BA 13/16) extending to the inferior frontal gyrus (BA 47). IC 26 is a posterior salience network which encompasses the bilateral posterior and mid insula (BA 13) as well as the anterior cingulate cortex (BA 9/32). IC11 is a striatal salience network, which includes bilateral striatum, insula (BA 13), and limbic association areas. Because of the fundamental role that the striatum plays in salience processing, this network was assigned to SN category despite the lack of striatal structures in the original description of this network [6]. In contrast to interoceptive task, only one ICN was identified as a mixed salience network for the exteroceptive emotion task. This ICN (IC 18) encompasses the key areas of ventral emotional system including the bilateral insula, anterior cingulate and ventromedial cortices, amygdala, parahippocampal gyri, and thalamus. Future research with a larger sample size and additional task conditions are needed to replicate and extend the findings to shed more light on the emergence of task-related spatial differences in ICNs.

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Fig. 1. The sequence and timing of stimuli presentation for (A) interoceptive, and (B) exteroceptive emotion paradigms are displayed.

Fig. 2. ICASSO results for (A) interoceptive, and (B) exteroceptive emotion task conditions. For each condition, 2D curvilinear component analysis projections of the component estimates (left) and I_q values of all ICs (right) are shown.

Fig. 3.

Network volumes and peak activations for (A) interoceptive, and (B) exteroceptive emotion task conditions. For each task condition, the top panel illustrates the network volumes averaged over all subjects at FEW-corrected p -value of 0.05 as compared to baseline rest. The bottom panel lists the t -value and xyz coordinates of the maximum activation for each ICN in real world and MNI space and their corresponding brain regions. Stars depict ICNs surviving paired t -test at Bonferroni-corrected 0.05 level.

Fig. 4. ICNs identified for (A) interoceptive, and (B) exteroceptive emotion task conditions. For display purposes, ICN spatial maps are superimposed on the MNI template in neurological convention (right is right). The significance threshold is set at family-wise error-corrected threshold of p -value of 0.05 for multiple comparisons of voxel-wise whole-brain analysis.

Fig. 5.
Comparison of the salience networks derived from (A) interoceptive task (ICs 16, 26, 11),
and (B) exteroceptive emotion task (IC 18).

TABLE 1

Spatial characteristics of the interoceptive versus exteroceptive emotion task-derived salience networks

IC	Brain region	Cluster Size (voxels)	Tmax	MNI Coordinates
16	L Insula Lobe	1549	26.19	(-39, -5, 5)
	L Rolandic Operculum	same cluster	20.98	(-54, 5, 6)
	R Insula Lobe	1026	31.90	(45, -1, 0)
	R Inferior Frontal Gyrus	same cluster	18.43	(48, 20, -6)
26	R Insula Lobe	2568	44.03	(39, -19, 12)
	L Insula Lobe	2052	22.91	(-36, -13, 6)
	R Anterior Cingulate Cortex	216	8.83	(15, 38, 21)
11	R Insula Lobe	3979	50.75	(39, -7, -6)
	L Putamen	same cluster	31.22	(-30, -1, 9)
18	R Insula Lobe	2412	15.87	(42, 16, -8)
	R Inferior Frontal Gyrus	same cluster	15.38	(42, 15, 9)
	L Insula Lobe	1810	17.66	(-33, 21, -2)
	L Thalamus	740	15.48	(-6, -10, 6)
	R Hippocampus	646	15.29	(18, -4, -11)
	R Putamen	same cluster	13.34	(18, 8, -9)
	R Amygdala	same cluster	10.80	(22, 0, -18)
	R Mid Orbital Gyrus	210	12.10	(4, 44, -6)