

THE ACTIVITY IN THE ANTERIOR INSULAE IS MODULATED BY PERCEPTUAL DECISION-MAKING DIFFICULTY

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Abstract—Previous neuroimaging studies provide evidence for the involvement of the anterior insulae (INs) in perceptual decision-making processes. However, how the insular cortex is involved in integration of degraded sensory information to create a conscious percept of environment and to drive our behaviors still remains a mystery. In this study, using functional magnetic resonance imaging (fMRI) and four different perceptual categorization tasks in visual and audio-visual domains, we measured blood oxygen level dependent (BOLD) signals and examined the roles of INs in easy and difficult perceptual decision-making. We created a varying degree of degraded stimuli by manipulating the task-specific stimuli in these four experiments to examine the effects of task difficulty on insular cortex response. We hypothesized that significantly higher BOLD response would be associated with the ambiguity of the sensory information and decision-making difficulty. In all of our experimental tasks, we found the INS activity consistently increased with task difficulty and participants' behavioral performance changed with the ambiguity of the presented sensory information. These findings support the hypothesis that the anterior insulae are involved in sensory-guided, goal-directed behaviors and their activities can predict perceptual load and task difficulty. © 2016 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: functional magnetic resonance imaging, task difficulty, response time, salience network.

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Abbreviations: BOLD, blood oxygen level dependent; C, color coherence; dACC, dorsal anterior cingulate cortex; fMRI, functional magnetic resonance imaging; GLM, general linear model; IC, color incoherence; INs, anterior insulae; MNI, Montreal Neurological Institute; PDM, perceptual decision-making; RDM, random dots motion; RT, response time; TR, repetition time.

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INTRODUCTION

The anterior insulae (INs) have widespread efferent and afferent projections and functional connection with a large-scale network of sensorimotor, affective, and cognitive regions (Mesulam and Mufson, 1982a,b; Deen et al., 2011; Cauda et al., 2012; Touroutoglou et al., 2012; Chang et al., 2013; Uddin et al., 2014). The INs, along with other brain areas, have been shown to be involved in various cognitive processes (Heekeren et al., 2004; Rushworth et al., 2004; Ho et al., 2009; Venkatraman et al., 2009; Menon and Uddin, 2010; Wiech et al., 2010; Woolgar et al., 2011; Krebs et al., 2012; Srinivasan et al., 2013), yet, their role in perceptual decision-making (PDM) still remains to be understood. Insular cortex has been traditionally considered as a limbic structure (Mesulam and Mufson, 1982b; Augustine, 1996) and was found active across a wide variety of paradigms involving the subjective awareness of feelings, including studies of anger, disgust, judgments of trustworthiness, sexual arousal, subjective feelings of empathy (Craig, 2003, 2009). However, this area may not be restricted to these roles. In our current work, we challenge this notion by examining the role of INs in PDM using an experimental paradigm that uses decision-making on two facial expressions with clear and noisy images. We hypothesize that if the insular activation is the function of perceived emotional expression, clear picture types should activate it more as the affective salience is clearly visible in clear pictures compared to noisy pictures.

Furthermore, INS activities were reported while facing uncertainty and risk in various perceptual and reward based experimental tasks (Ernst and Paulus, 2005; Preuschoff et al., 2008; Singer et al., 2009; Gu et al., 2010; Lamm and Singer, 2010). Insular cortices have been suggested to participate in attentional control in such tasks because more activation was observed on cognitively demanding tasks compared to easy tasks (Philiastides and Sajda, 2007; Heekeren et al., 2008; Tosoni et al., 2008) as harder task required more attentional resources. However, the other studies suggested that higher insular activity during ambiguous sensory information (i.e. harder task) might be due to the uncertainty in perceptual decision which might reflect the uncertainty in choosing an appropriate action (Ho et al., 2009; Woolgar et al., 2011; Shenhav et al., 2013).

The effort in a cognitive process of integrating sensory information should be reflected in the brain activity underlying a difficult task compared to the one with an easier task, which would further support its integrative

role in PDM (Kurth et al., 2010; Sterzer and Kleinschmidt, 2010; Chang et al., 2013; Langner and Eickhoff, 2013). In recent years, there has been increasing evidence from functional neuroimaging studies that the insular cortex is involved in a more diverse set of perceptual paradigm; for example, visual (Rebola et al., 2012), auditory discrimination (Binder et al., 2004), audiovisual asynchrony–synchrony discrimination (Lamichhane and Dhamala, 2015b), language and music perception (Platel et al., 1997; Mutschler et al., 2007; Ackermann and Riecker, 2010). Similar to the previous studies with PDM paradigm (Thielscher and Pessoa, 2007; Venkatraman et al., 2009; Gu et al., 2010; Deen et al., 2011; Chang et al., 2013; Shenhav et al., 2013; Lamichhane and Dhamala, 2015b), we aimed to expand our understanding of insular function by running the same perceptual-tasks used in the previous studies over the past decade.

We measured the BOLD activity in four PDM experiments: (1) face-house discrimination task, (2) happy-angry face discrimination task, (3) audio-visual asynchrony and synchrony perception task, and (4) random dots motion direction discrimination (RDM) task. These tasks were different from each other in terms of stimulus modality [single or multiple sensory modality (task 3), between-category discrimination (task 1) or within-category discrimination (task 2), static-moving stimuli (task 4)], but all were perceptual in nature. The experiments 1 and 4 were the most popular tasks to investigate PDM in the visual domain (for details, see Experimental procedures section). Similarly, experiment 3 provided us the opportunity for such study with multiple sensory approaches. Here, we looked at the INS activities associated with PDM, with a prediction of higher insular activation for the increased in the ambiguity in the sensory information. We examined how they were correlated with behaviors. We investigated whether the insular cortex activity was associated with perceptual decision-making and, if so, how the availability of sensory information and difficulty of decision-making modulate the activity. In all experimental tasks, we first established that the ambiguity of the presented sensory information changed the participants' behavioral performance and affected the decision response times. Finally, looking at the brain response of tasks on insular cortex, we investigated whether INSs serve as centers for integration of sensory information, which would be necessary for a perceptual decision leading to a behavioral action including a motor response.

EXPERIMENTAL PROCEDURES

Participants

This study included four experiments with these tasks: (1) face-house categorization, (2) happy-angry face categorization, (3) audio-visual asynchrony and synchrony perception, and (4) random dots motion direction discrimination. These tasks, perceptual in nature, allow us the opportunity to examine and explore the PDM in multi (bi-) sensory domain (in task 3) and in visual domain (remaining other three tasks). In

experiments 1 and 3, there were thirty-three human participants (17 females, 16 males; mean age \pm standard deviation = 27.5 ± 4.7 years) whereas in experiments 2 and 4, there were thirty-two participants (16 males, 16 females; mean age \pm standard deviation = 27.6 ± 4.7 years). Thirty two participants were common and completed all four tasks. They completed tasks in two visits, two tasks in each visit; experiments 1 and 3 in the first visit (3 functional scanning sessions of experiment 1 in sequence first and then a functional scanning session of experiment 3), and remaining experiments 2 and 4 in the second visit (4 functional scanning sessions). Behavioral experiments were performed outside the scanner and then the corresponding functional scanning sessions were carried out inside the scanner. They all had normal or corrected to normal vision and reported normal neurological history. Out of 33 participants, 4 reported that they were left handed, 2 reported that they used both hands equally but preferred left hand for writing, and remaining 27 reported that they were right handed. They provided written signed informed consent forms and were compensated for their participation in the experiments. Institutional Review Board for Joint Georgia State University and Georgia Institute of Technology Center for Advanced Brain Imaging, Atlanta, Georgia, USA approved this study.

Stimuli and experimental task paradigms

The stimulus software presentation (<http://www.neurobs.com>) was used to display stimuli (detail is given below, and shown in Fig. 1) and to randomize task trial sequences (Fig. 1) in all tasks. Each experimental task was divided into two separate sessions: the first session involved acquiring behavioral data outside the MRI scanner and the second session was inside the scanner where we acquired both fMRI and behavioral data. Outside the MRI scanner, participants were asked to indicate their decisions as quickly and as accurately as possible by the left and right mouse clicks for the given two stimuli. They were instructed to press the space bar in the computer keyboard to proceed to the next trial. Inside the MRI scanner, participants were instructed to focus on the central crossbar on the screen during experimental run. They were asked to perceive the presented stimuli, to wait for the display of a question mark on the screen and then to indicate their choice by pressing a response key on a button-box by using either right index or the middle finger. In both sessions, the stimulus types with their times of presentation and the response times to that stimuli were recorded. Prior to the experimental tasks, they were briefly explained about the study and the tasks. In addition, they took part in a practice session, which helped them to be familiar with the sample stimuli and the experimental tasks.

Experiment 1: face-house categorization task. We used a total of 14 images of faces and 14 images of houses as stimuli. All pictures were downloaded from F.A.C.E. Training – an interactive training by Paul

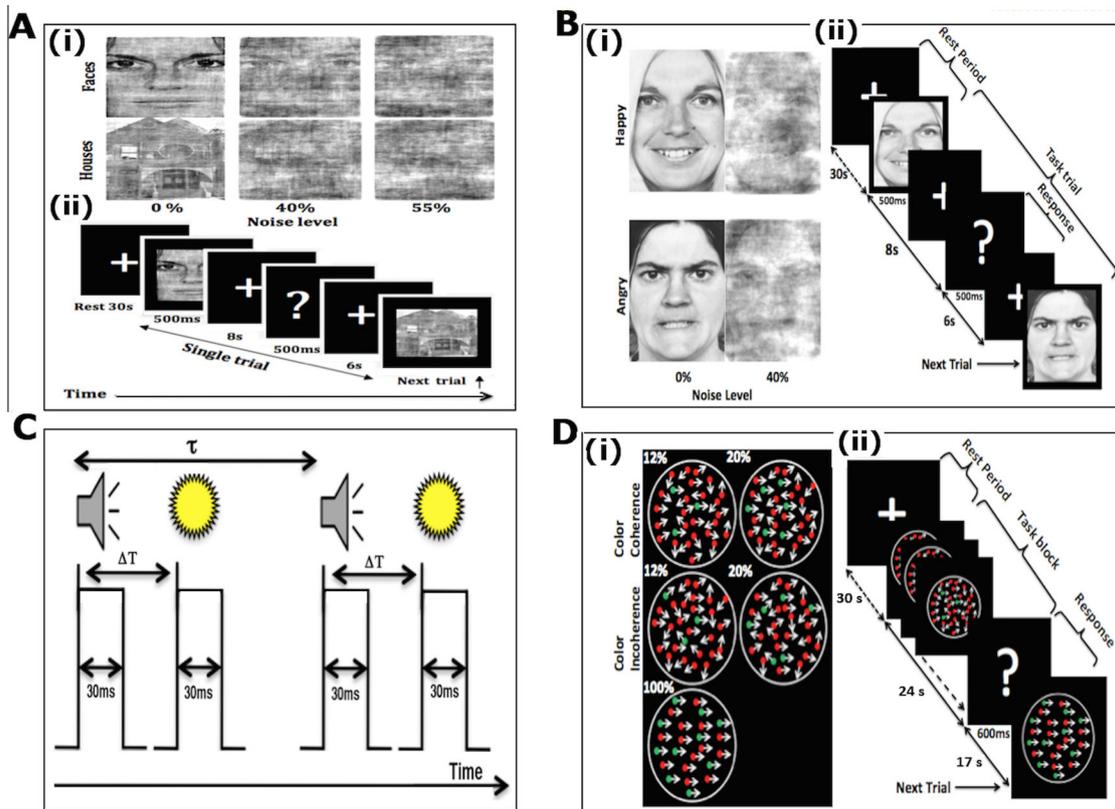


Fig. 1. Experimental paradigms. (A) *Face-house categorization task*: Participants were instructed to press the left or right mouse clicks (outside the scanner) and a left or right response key on a button-box (inside the scanner) if the presented stimulus picture was a face or a house. (i) Sample images at three noise levels for face and house stimuli set. (ii) Task paradigm during a functional run, starting from the initial 30 s rest followed by a task trial that included 500-ms stimulus presentation, 8 s of decision time, and 500-ms display of a question mark, requiring participants to indicate their decision within the next 6 s (Lamichhane and Dhamala, 2015a). (B) *Happy-angry face categorization task*: In this task, participants were instructed to press the left or right mouse clicks (outside the scanner) and a left or right response key on a button-box (inside the scanner) if the presented stimulus picture was a happy face or an angry face. (i) Sample images at two noise levels of both happy and angry stimuli set. (ii) Task paradigm during the functional experiment starting from initial 30-s rest followed by task trial with a brief stimulus presentation for 500-ms duration, 8 s of decision time, followed by a briefly presented question mark for 500 ms referring participants to indicate their decision within the next 6 s (for details, see Bajaj et al., 2013). (C) *Audio-visual synchrony and asynchrony perception task*: In this task, participants were instructed to press the left or right mouse clicks (outside the scanner) and a left or right response key on a button-box (inside the scanner) if they perceived the presented stimulus (beep-flash pair) asynchronous or synchronous. Task paradigm during the functional experiment started with initial 30 s of rest followed by task blocks and 35 s of rest at the end of the run. There were two types of block: multisensory blocks (beep-flash pair were presented for 30 ms, as shown in figure) and unisensory blocks (flash only or beep only were presented, not shown in figure). The time intervals between a flash and a beep sound (ΔT) were varied participants to participants. Stimuli within the block were presented with the random pause (τ) of 1666 to 1926 ms followed by the cue of 600 ms at the end of each block; totaling about 24 s of one block. Participants were asked to respond after the cue was presented. In unisensory blocks, no question was asked about asynchrony and synchrony perception at end of block (for details, see Lamichhane and Dhamala, 2015b). (D) *Random dots motion direction discrimination task*: In this task, participants were instructed to press the left or right mouse clicks (outside the scanner) and a left or right response key on a button-box (inside the scanner) when the net direction of motion constituted by randomly moving dots was either to the left or to the right. (i) Symbolic representation of random dots motion (RDM) stimuli: color coherence 12% and 20% (top), color incoherence 12% and 20% (middle) and 100% (bottom). (ii) Task paradigm during the functional experiment started with initial 30 s rest followed by the block of RDM presented for 15 consecutive times for the total of 24 s. A question mark presented for 600 ms asking participants to indicate their decision, which is followed by 17 s of pause. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Ekman (<https://www.paulekman.com/product/pictures-of-facial-affect-pofa/>). All the images were equalized for luminance and contrast by converting them to gray scale and were cropped to make equal size. Furthermore, both face and house images were degraded by manipulating images and adding noise (Rainer and Miller, 2000). Image pixel phase randomization and addition of Gaussian noise enabled us to make visual image stimuli noisy. Stimuli consisted of three different noise levels: 0%, 40% and 55%, for both sets of images. These three noise levels would allow us the

opportunity to compare how behavioral measures and brain responses varied with increased task difficulty level, keeping the performance accuracy at least 70%.

The behavioral study, outside the scanner, consisted of a single run. Three noise level conditions were repeated 60 times each (30 times each for faces and houses) in a random order, generating 180 trials in total. Inside the fMRI scanner, participants performed this face-house categorization task in three functional runs, each 614 s long. The number of trials for each noise level was 36 (18 faces and 18 houses), and the total

trials were 108 for all 3 conditions in each run. Stimuli were presented in a random order as in an event-related design. There were rest periods of 30 s at the beginning and of 35 s at the end of each run. Each picture was presented for 500 ms, followed by 8-s-long displays of fixation cross, and a briefly presented question mark for 500 ms at the end of this 8 s' interval. The next 6-s time was allowed for participants to report their decisions. Trials in which participants failed to respond were discarded from the final analysis. Fig. 1[A(i)] shows the sample images at three noise levels for both sets, face and house stimuli whereas Fig. 1[A(ii)] shows a schematic representation of the behavioral paradigm used in this experiment.

Experiment 2: happy-angry face categorization task.

Two sets of human face images, a happy set and an angry set, were used as the stimuli. Each set consisted of eight images (4 males and 4 females). Both happy and angry sets of images were degraded (as in experiment 1). The particular noise levels were decided to make the task more difficult at or above 70% behavioral accuracy. It was based on the estimates of behavioral performance from some behavioral trial runs before the actual experiments. Based on the percent of noise level, we had two image categories: clear images (0% noise) and noisy images (40% noise), as shown in Fig. 1[B(i)]. Here, we categorized the task stimuli based on noise level instead of happy or angry faces. In both behavioral and fMRI runs, the pictures were presented in a random order at the center of the computer screen for 500 ms. Outside the fMRI scanner, we have a single run where each condition (clear and noisy images) was presented 60 times randomly, totaling 120 trials. However, inside the fMRI scanner, participants performed two functional runs, each run of 674 s long and the total number of trials was 80, that is, 40 trials for each condition (clear and noisy). There were rest periods of 30 s at the beginning and of 35 s at the end of each run. A trial sequence consisted of 500-ms stimulus picture presentation, followed by 8-s-long displays of fixation cross, a briefly presented question mark for 500 ms at the end of this 8-s interval, and the next 6 s for participants to report their decisions [Fig. 1(B(ii))]. Previously reported data where analysis was based on emotional facial expressions (happy and angry faces) (Bajaj et al., 2013), were reanalyzed here, based on different noise levels present on these stimuli.

Experiment 3: audio-visual asynchrony and synchrony perception task. We used a pair of auditory (a tone) and visual (a flash of light) stimuli. The auditory stimulus consisted of a 440-Hz–30-ms tone, while the visual stimulus consisted of a 30-ms yellow–red disk flash (0.7 cm radius). The auditory stimulus was delivered through a pair of earphones, one on each ear, and visual stimulus was flashed at the central position on the computer screen.

The experimental task outside the scanner was divided into two separate sessions, consisting of a single run each. The first session was aimed to identify

a “point of subjective simultaneity”, i.e. how far apart in time the asynchronously presented audio and visual pair could be perceived as synchronous. This behavioral run started with 5 s of initial rest followed by the presentation of audio and visual stimuli with a systematically varying asynchrony lag of 66.6, 83.3, 100, 116.6, 133.3, 150, and 166.6 ms, based on previous literature that humans can correctly detect audiovisual asynchrony within these limits (Zampini et al., 2003, 2005; van Wassenhove et al., 2007; van Eijk et al., 2008; Pons and Lewkowicz, 2014). Each condition was presented 20 times, totaling 140 trials. The time between each pair (the pause, τ) was chosen randomly between 1000 and 1160 ms. Looking at the fraction of the trials from this run, we chose the time lag (ΔT), as a threshold value, where the performance accuracy was 50:50 or close to it for the trials that were perceived as synchronous or asynchronous. For behavioral recordings outside the scanner, the time lags (Δ) were varied beyond the individual's threshold value for audio-visual simultaneity with an increment between -16.6 ms and $+16.6$ ms. The pair of stimuli was presented 60 times, 20 times at each Δ . These time lags were used for fMRI data acquisition and behavioral recordings inside the scanner. This run started with 30 s of initial rest followed by 24 multisensory task blocks and 8 unisensory task blocks. Blocks were presented in a random order and consisted of 8 pairs of stimuli in the multisensory block where both the tone and flash were presented. In the unisensory block, either 8 flashes or 8 beeps were presented. Stimuli within a block were presented with the random pause of 1666 to 1926 ms followed by the cue of 600 ms at the end of each block, totaling about 24 s for one block. There were about 10 s of pause in-between blocks and the run ended with 35 s of a final rest period. The schematic of experimental task paradigm was as shown in Fig. 1(C). Here, we reanalyzed the same data that were previously used to look at the interactions within the salience network including insular cortices (Lamichhane and Dhamala, 2015b).

Experiment 4: random dots motion direction discrimination task. The RDM stimuli were displayed within a circular aperture at the center of screen. RDM direction discrimination task consists of randomly moving noisy field of dots where coherence level was determined by the fraction of dots moving in the left or right direction while the rest of the dots were moving in the random direction. Dots were drawn on black background within in a circular aperture of 7.5 cm (also called degree) diameter for 34 ms. Dots were redrawn after 50 ms at either a random location or a neighboring spatial location to induce apparent motion. The resultant motion effect appeared to move between 3° and $7^\circ/s$, and dots were drawn at a density of 16.7 dots per degree/s.

In order to further modulate the task difficulty level, we manipulated the mixture of red and green dots in our RDM task. This was done by (i) varying the proportion of the dots that are either moving left or right independent of color (color incoherence, IC) and (ii) by giving the green color for the dots that are moving in particular direction either left or right (color coherence, C) and red to the

randomly moving dots. We have included three coherence levels in RDM task (12%, 20% and 100%) in both C and IC conditions. In C, for example 12% C, 12% of dots were green and all moved in one direction (left or right) and while remaining (red) dots were moving in random directions. In IC, for example in 12%, RDM still consisted of 12% of green and 88% red. However only 12% of dots independent of color were moving in particular direction while the remaining 88 % were moving in random directions. There were no difference in 100% C and IC (50% of red dots and 50% green) and all moved in one direction, as shown in Fig. 1[D(i)]. Outside the scanner recordings, RDM was presented for 1 s as a single event and consisted of a single run. Each condition was presented for 30 times, totaling 180 trials.

Inside the scanner, RDM task with identical parameters (either 12%, 20% and 100% C or IC) were presented for 15 consecutive times, for the total of 24 s. These sets of identical stimuli are called blocks. At the end of each block, participants were shown a “?” for 600 ms as the cue to respond and next trial starts after 17 s [Fig. 1(D(ii))]. There were twelve trials each condition (in block), all together 72 trials (block) inside the scanner in two functional runs. Each run started with 30 s of initial rest and ended with 35 s of final rest.

Data acquisition and analysis

Behavioral data analysis. A participant's response time (RT), the time between the onset of a stimulus and the button press in each trial, was recorded for the experimental tasks performed outside the scanner. Participants were required to press buttons on response-box only to indicate their decisions inside the scanner. Participants' behavioral performance, both outside and inside the scanner, was analyzed using Matlab. Trial by trial RTs of each participant from outside-scanner button presses were separated and averaged across noise conditions. No RT calculation was done for the recorded behavioral data inside the scanner as participants were instructed to wait until the question mark was displayed to indicate their decisions. *T*-tests were used to assess the significance levels of performance accuracy and RT across noise levels for different tasks stimuli. In RDM task, recordings were done separately for two stimulus types 12% and 20% for both C and IC. But, we neither found the statistically significant difference on behavioral response nor found the significant difference in RT between these two stimulus conditions. The data from these two conditions (12% and 20%) were combined separately for coherence and incoherence. Finally, we had 3 stimulus conditions: 12% and 20% C, 12% and 20% IC and 100% for further analysis.

Functional magnetic resonance imaging data. The whole-brain MR imaging was done on a 3-Tesla Siemens scanner available at Georgia State University and Georgia Institute of Technology Center for Advanced Brain Imaging, Atlanta, Georgia. High-

resolution anatomical images were acquired (parallel to anterior-posterior commissural line) for anatomical references using a magnetization-prepared rapid gradient-echo sequence (with repetition time (TR) = 2250 ms, echo time (TE) = 4.18 ms, flip angle = 9°, inversion time = 900 ms, voxel size = $1 \times 1 \times 1 \text{ mm}^3$). Functional scans were acquired with T2*-weighted gradient echo-planar imaging protocol with the following parameters: TE = 30 ms, TR = 2000 ms, flip angle = 90°, voxel size = $3 \times 3 \times 3 \text{ mm}^3$, field of view = 204 mm \times 204 mm, matrix size = 68 \times 68 and 37 axial slices each of 3 mm thickness. Experiment 1 had 3 functional runs having 307 volumes each, experiment 2 had 2 functional runs consisting of 337 volumes each, experiment 3 had a functional run with 449 volumes and experiment 4 had two functional runs having 409 volumes each. MRI data were analyzed using Statistical Parametric Mapping (SPM8, Wellcome Trust Center, London, <http://www.fil.ion.ucl.ac.uk/spm>) which included slice timing correction, motion correction, co-registration to individual anatomical image, normalization to Montreal Neurological Institute (MNI) template (Friston et al., 1995). Spatial smoothing of the normalized image was done with an 8 mm isotropic Gaussian kernel. A random-effects model-based univariate statistical analysis was performed in two level procedures. At the first level, a separate general linear model (GLM) was specified according to the task sequences and behavioral responses for each participant. Only correct trials for each stimulus type with different noise-levels/ conditions, rest and six motion parameters were included in GLM analysis. We restricted our analysis to correct trials only because there were very few incorrect trials, especially in easier task conditions, which were not enough for reliable estimates of differences across conditions. Six motion parameters, here, were entered as nuisance covariates and were regressed out of the data. Individual contrast images of all participants from the first level analysis were then entered into a second level analysis for a separate one-sample *t*-test, which gives the brain activations for that noise-level/condition versus baseline comparison condition. Another possibility of defining contrast is *F*-contrast, which is a two-tailed version of *t*-contrast, testing for both brain activations and deactivations for the particular noise-level/condition versus baseline comparison condition. The resulting summary statistical maps, activation maps, were then thresholded and overlaid on high-resolution structural images in MNI orientation. The activation clusters were identified under the statistical significance $p < 0.05$, family-wise error (FWE) correction with multiple comparisons correction and cluster extent $k \geq 10$; except in moving dots task where statistical significance was $p < 0.01$, FWE correction. Considering the activated brain areas, we extracted the contrast values (the beta parameters) by defining a sphere of 6-mm radius centered at the local peak activity voxel in MarsBaR (Brett et al., 2002). These above-mentioned parameters and MRI data analysis procedures were common in all four experimental tasks.

In the face-house categorization task, only correct trials for each of the three noise-levels of face-house

stimuli (0%, 40% and 55%), rest and six motion parameters were included in GLM analysis. In the happy-angry face categorization task, a GLM was specified according to correct behavioral responses on clear and noisy images. We also included rest and six motion parameters as nuisance covariates in GLM analysis. Behavioral responses for asynchrony and synchrony perception, rest, and six motion parameters were included in GLM analysis in audio-visual asynchrony and synchrony perception task. In RDM task, a GLM was specified for three behavioral responses (12% and 20% C, 12% and 20% IC and 100%), rest and six motion parameters.

Brain-behavior relation. Participants were asked to indicate their decisions as quickly and as accurately as possible by the left and right mouse clicks for the given two stimuli for outside the scanner recordings. They were instructed to focus on the central crossbar on the screen, to perceive the presented stimuli, to wait for the display of a question mark on the screen and then to indicate their choice by pressing a response key on a button-box using either right index or the middle finger for the inside the MRI scanner recordings. For each stimulus type and each participant, we calculated mean RT and performance accuracy for outside the scanner recordings and performance accuracy inside the scanner recordings. From brain data, we extracted beta contrast values (brain activity) for left and right insulae. We then correlated RTs (outside the scanner) with insular activity (inside the scanner) for brain-behavior relation. The relationship in the scatterplot was assessed by both Spearman's rank correlation and Pearson's correlation. A correlation was considered significant if the significance threshold was $p < 0.05$ for both results. The results are reported here in terms of Spearman's rank correlation.

RESULTS

We here, presented both behavioral results [Table 2a] and brain results [Tables 1 and 2b] from all the experimental tasks.

Experiment 1: face-house categorization task

Behavioral results. The mean performance (i.e. the group level accuracy) for images with 0% noise-level was very high. The accuracy rate for 0% noise was 99.3% for outside scanner and that of inside the scanner was 97.9%. The performance levels were found decreased for 40% noise-level and the rates were 89.5% and 87.0% for outside and inside the scanner respectively. The rates were further decreased to 68.5% and 65.1% for outside and inside the scanner respectively when the noise level increased to 55%. A repeated analysis of variance was performed to see the significant effect of task difficulty (or, noise-level) on behavioral accuracy. The behavioral accuracy rates decreased with noise level [Fig. 2(A)]. Outside the scanner recordings, performance accuracy rates were

reliably different across 0%, 40% and 55% noise-levels on picture stimuli ($F(2, 64) = 265.0, p < 0.001$) with clear picture (0% noise-level) yielding higher performance accuracy rate relative to 40% noise-level ($F(1, 32) = 57.9, p < 0.001$) and 55% noise-level ($F(1, 32) = 486.8, p < 0.001$). Inside the scanner, performance accuracy rates differed reliably across 0%, 40% and 55% noise-levels on picture stimuli ($F(2, 64) = 186.3, p < 0.001$) with clear picture yielding higher performance accuracy rate relative to 40% noise-level ($F(1, 32) = 72.0, p < 0.001$) and 55% noise-level ($F(1, 32) = 350.2, p < 0.001$).

RTs, measured outside the scanner, increased with noise-level on picture stimuli. The mean RT for clear pictures was 0.79 s and that for 40% noisy-pictures was 0.94 s and it further increased to 1.13 s for 55% noisy pictures [Fig. 2(A)]. Outside the scanner recordings, RTs differed reliably different across 0%, 40% and 55% noise-levels on picture stimuli ($F(2, 64) = 76.2, p < 0.001$) with clear picture yielding lesser RT relative to 40% noise-level ($F(1, 32) = 46.5, p < 0.001$) and 55% noise-level ($F(1, 32) = 97.5, p < 0.001$).

Brain results. Brain activations were computed by contrasting the difficult picture (40% and 55% noisy pictures combined, independent of faces and houses) presented conditions versus clear pictures. We observed significant brain activations in prefrontal cortices, left and right insulae (INs), left supplementary motor area extending to dorsal anterior cingulate cortex (dACC) [Fig. 2(B) and Table 1].

The group average contrast values were plotted for both INs in each noise level [Fig. 2(C)]. For the left INs, brain activities were reliably different across 0%, 40% and 55% noise-levels on picture stimuli ($F(2, 64) = 16.0, p < 0.001$) with clear picture yielding lesser activity relative to 40% noise-level ($F(1, 32) = 32.7, p < 0.001$) and 55% noise-level ($F(1, 32) = 25.0, p < 0.001$). Regarding the right INs, brain activities differed reliably across these three noise-levels on picture stimuli ($F(2, 64) = 21.8, p < 0.001$) with clear picture yielding lesser activity relative to 40% noise-level ($F(1, 32) = 23.3, p < 0.001$) and 55% noise-level ($F(1, 32) = 33.3, p < 0.001$).

Experiment 2: happy-angry face categorization task

Behavioral results. Behavioral performances were computed from the behavioral experiments done outside the scanner and inside the scanner. Participants correctly responded with an average rate of 98.9% for clear images and with 86.4% for noisy images outside the scanner and that of inside the scanner were of 97.7% and 76.3% respectively for clear and noisy images [Fig. 3(A)]. Further, more time was taken to respond to noisy images ($RT = 1.07 \pm 0.04$ s) compared to clear images ($RT = 0.89 \pm 0.03$ s). Behavioral accuracy rate decreased significantly with increase in noise level (40% noise) compared to clear images both inside the scanner ($F(1, 31) = 107.3, p < 0.001$) and outside the scanner ($F(1, 31) = 86.6,$

Table 1. Brain activations for various contrasts. The table includes the information about the anatomical locations, cluster sizes, *t*-value (z-score) and MNI coordinates for the peak activations under statistical significance $p < 0.05$ (family-wise error, FWE) correction for multiple comparisons correction and cluster extent $k \geq 10$. The abbreviations used here are: L = left, R = right, INS = Insula, dACC = dorsal anterior cingulate cortex, dlPFC = dorsolateral prefrontal cortex, IFG = inferior frontal gyrus, IPL = inferior parietal lobule, VC = visual cortex (occipital lobe), MFG = middle frontal gyrus, MOG = middle occipital gyrus, MT = middle temporal cortex, SEF = supplementary eye fields, C = color coherence, IC = color incoherence

| Contrast | Brain regions | Cluster size | Voxel <i>t</i> (z-equivalent) | MNI coordinates x, y, z |
|---|---------------|--------------|-------------------------------|-------------------------|
| Noisy (faces + houses) versus clear (faces + houses) | R INS | 54 | 8.75 (6.21) | 33, 20, 4 |
| | dACC | 109 | 7.96 (5.87) | −6, 17, 52 |
| | L INS | 40 | 7.85 (5.82) | −30, 23, 1 |
| | L IFG | 25 | 6.70 (5.26) | −39, 5, 34 |
| Noisy versus clear (happy + angry faces) | R IFG | 27 | 6.67 (5.24) | 45, 8, 25 |
| | R INS | 64 | 8.94 (6.24) | 33, 20, 4 |
| | L INS | 65 | 8.12 (5.90) | −30, 23, 4 |
| Audio-visual versus (beep + flash) | dACC | 34 | 6.42 (5.08) | 0, 17, 52 |
| | dACC | 122 | 9.78 (6.61) | −6, 11, 52 |
| | R MOG | 71 | 8.84 (6.24) | 27, −97, −5 |
| | L IFG | 47 | 8.42 (6.07) | −60, 8, 28 |
| | R Thalamus | 101 | 8.41 (6.07) | 3, −3, 1 |
| | L INS | 84 | 7.76 (5.78) | −30, 20, 4 |
| | R INS | 117 | 7.69 (5.75) | 33, 23, 4 |
| | L MOG | 37 | 6.80 (5.31) | −27, −94, −5 |
| | L IPL | 42 | 6.67 (5.24) | −33, −49, 46 |
| Moving dots (12% + 20%) C + (12% + 20%) IC versus 100% (C + IC) | R VC | 1026 | 13.17 (7.59) | 24, −88, −11 |
| | L VC | 774 | 12.66 (7.46) | −21, −97, 7 |
| | R MT | 103 | 9.86 (6.59) | 48, −67, 4 |
| | R INS | 108 | 9.71 (6.53) | 30, 20, 4 |
| | L INS | 50 | 9.19 (6.34) | −30, 20, 4 |
| | R dlPFC | 356 | 8.74 (6.16) | 42, 11, 22 |
| | R SEF | 146 | 8.42 (6.03) | 36, −1, 49 |
| | L IPL | 75 | 7.92 (5.81) | −30, −49, 46 |
| | R IPL | 144 | 7.69 (5.71) | 39, −40, 43 |
| | L MT | 28 | 7.60 (5.66) | −42, −64, 4 |
| | dACC | 14 | 7.58 (5.66) | −6, 11, 52 |
| | L dlPFC | 59 | 7.35 (5.55) | −51, 2, 34 |
| | R MOG | 11 | 6.87 (5.31) | 30, −67, 25 |
| L SEF | 12 | 6.69 (5.22) | −33, −7, 52 | |

$p < 0.001$). In addition to the decrease in performance accuracy rate, the addition of noise on images also increased RT ($F(1, 31) = 65.4$, $p < 0.001$). These results clearly show that the task became more difficult with the addition of noise on images [Fig. 3(A), third column].

Brain results. INs were found activated more by the addition of 40% noise on pictures compared to clear pictures [Fig. 3(B) and Table 1]. The group average contrast values were plotted for INs separately for noisy and clear picture conditions. We found significantly higher brain activity ($F(1, 31) = 27.2$, $p < 0.001$ for the left INS and $F(1, 31) = 60.7$, $p < 0.001$ for the right INS) in noisy pictures compared to the clear pictures [Fig. 3(C)].

Experiment 3: audio-visual asynchrony and synchrony perception task

Behavioral results. We categorized the behavioral responses based on participants' perception of asynchrony and synchrony. The mean perceptual accuracy outside the scanner was 33.6% and 66.4% for

asynchrony and synchrony perception respectively [significantly different ($F(1, 32) = 21.5$, $p < 0.001$)]. Similarly, the mean perceptual accuracy inside the scanner was 41.4% for asynchrony and 58.6% for synchrony perception [statistically different ($F(1, 32) = 7.74$, $p < 0.01$)]. However, more time was taken to respond with the asynchrony perception (RT = 0.96 s) compared to synchrony perception (RT = 0.79 s). This was statistically significant ($F(1, 32) = 10.5$, $p \leq 0.01$). These behavioral results are shown in Fig. 4(A) and Table 2a.

Brain results. Audio-visual synchrony and asynchrony perception activated the bilateral insula along with frontal, parietal and occipital cortices [Fig. 4(B) and Table 1]. Here, we contrasted (asynchrony perception + synchrony perception) > [auditory (beep only) + visual (flash only)]. Finally, the group average contrast values for INs were plotted for both synchrony and asynchrony perceptions. We found significantly higher brain activity in asynchrony perception compared to synchrony perception ($F(1, 32) = 13.0$, $p < 0.001$ for the left INS and $F(1, 32) = 16.4$, $p < 0.001$ for the right INS) as shown in Fig. 4(C).

Table 2a. Results of behavioral data analysis. The notations used here are: s.e.m. = standard error of the mean, η^2 (eta squared) = effect size, Asyn = asynchrony perception, Syn = synchrony perception, C = color coherence, IC = color incoherence

| | Outside scanner % accuracy | Inside scanner % accuracy | Outside scanner Response time |
|--|--|--|---|
| <i>Face-house categorization task</i> | | | |
| Mean \pm s.e.m. | 0% noise: 99.3 \pm 0.2 40% noise: 89.5 \pm 1.3 55% noise: 68.5 \pm 1.4 | 0% noise: 97.9 \pm 0.6 40% noise: 87.0 \pm 1.4 55% noise: 65.1 \pm 1.7 | 0% noise: 0.79 \pm 0.03 s 40% noise: 0.95 \pm 0.04 s 55% noise: 1.13 \pm 0.05 s |
| <i>ANOVA test</i> | | | |
| Overall | $F(2,64) = 265.0$, $p < 10^{-9}$, $\eta^2 = 0.89$ | $F(2,64) = 186.3$, $p < 10^{-12}$, $\eta^2 = 0.85$ | $F(2,64) = 76.2$, $p < 10^{-9}$, $\eta^2 = 0.71$ |
| 0% and 40% noise | $F(1,32) = 57.9$, $p < 10^{-7}$, $\eta^2 = 0.65$ | $F(1,32) = 72.0$, $p < 10^{-8}$, $\eta^2 = 0.69$ | $F(1,32) = 46.5$, $p < 10^{-6}$, $\eta^2 = 0.60$ |
| 0% and 55% noise | $F(1,32) = 486.8$, $p < 10^{-12}$, $\eta^2 = 0.94$ | $F(1,32) = 350.2$, $p < 10^{-12}$, $\eta^2 = 0.92$ | $F(1,32) = 97.5$, $p < 10^{-10}$, $\eta^2 = 0.76$ |
| <i>Happy-angry face categorization task</i> | | | |
| Mean \pm s.e.m. | 0% noise: 98.9 \pm 0.4 40% noise: 86.4 \pm 1.5 | 0% noise: 97.7 \pm 0.6 40% noise: 76.3 \pm 2.1 | 0% noise: 0.89 \pm 0.03 s 40% noise: 1.07 \pm 0.04 s |
| ANOVA test: overall | $F(1,31) = 86.6$, $p < 10^{-9}$, $\eta^2 = 0.74$ | $F(1,31) = 107.3$, $p < 10^{-10}$, $\eta^2 = 0.78$ | $F(1,31) = 65.4$, $p < 10^{-8}$, $\eta^2 = 0.68$ |
| <i>Audio-visual asynchrony and synchrony perception task</i> | | | |
| Mean \pm s.e.m. | Asyn: 33.6 \pm 3.5 Syn: 66.4 \pm 3.5 | Asyn: 41.4 \pm 3.06 Syn: 58.6 \pm 3.06 | Asyn: 0.96 \pm 0.06 s Syn: 0.79 \pm 0.04 s |
| ANOVA test: overall | $F(1,32) = 21.5$, $p < 10^{-4}$, $\eta^2 = 0.41$ | $F(1,32) = 7.74$, $p < 10^{-2}$, $\eta^2 = 0.20$ | $F(1,32) = 10.5$, $p < 10^{-2}$, $\eta^2 = 0.26$ |
| <i>Random dots motion direction discrimination task</i> | | | |
| Mean \pm s.e.m. | 100% C-IC: 99.3 \pm 0.2 12%, 20% C: 89.5 \pm 1.3 12%, 20% IC: 68.5 \pm 1.4 | 100% C-IC: 97.5 \pm 0.9 12%, 20% C: 94.0 \pm 1.6 12%, 20% IC: 98.3 \pm 0.8 | 100% C-IC: 1.06 \pm 0.06 s 12%, 20% C: 1.23 \pm 0.06 s 12%, 20% IC: 1.25 \pm 0.05 s |
| <i>ANOVA test</i> | | | |
| Overall | $F(2,62) = 160.0$, $p < 10^{-12}$, $\eta^2 = 0.84$ | $F(2,62) = 4.89$, $p < 10^{-2}$, $\eta^2 = 0.14$ | $F(2,62) = 25.3$, $p < 10^{-7}$, $\eta^2 = 0.46$ |
| 100% C-IC and 12%, 20% C | $F(1,31) = 92.7$, $p < 10^{-9}$, $\eta^2 = 0.75$ | $F(1,31) = 3.84$, $p = 0.06$, $\eta^2 = 0.11$ | $F(1,31) = 30.3$, $p < 10^{-5}$, $\eta^2 = 0.50$ |
| 100% C-IC and 12%, 20% IC | $F(1,31) = 311.2$, $p < 10^{-12}$, $\eta^2 = 0.91$ | $F(1,31) = 8.44$, $p < 10^{-2}$, $\eta^2 = 0.21$ | $F(1,31) = 30.0$, $p < 10^{-5}$, $\eta^2 = 0.50$ |

Experiment 4: random dots motion direction discrimination task

Behavioral results. Participants correctly decided the direction of RMD with an average rate of 99.3% for 100% stimulus case, 89.5% for 12% and 20% C case and the performance accuracy rate was reduced to 68.5% for 12% and 20% IC case outside the scanner. The performance accuracy rate, inside the scanner, was 97.5%, 94.0% and 98.3% respectively for 100% stimulus case, 12% and 20% C case and 12% and 20% IC case. Further, less time was taken to report their decision (RT = 1.06 \pm 0.06 s) to 100% stimulus case and it increased to 1.23 s and 1.25 s for 12% and 20% C case and 12% and 20% IC case respectively. Behavioral accuracy decreased for both 12% and 20% C case and 12% and 20% IC case when compared with 100% stimulus case, however, RT increased outside the scanner. The behavioral results are shown in Fig. 5(A). Outside the scanner, performance accuracy rates were reliably different across 100% stimulus case, 12% and 20% C case, and 12% and 20% IC case ($F(2, 62) = 160.0$, $p < 0.001$) with 100% stimulus case yielding

higher performance accuracy rate relative to 12% and 20% C case ($F(1, 31) = 92.7$, $p < 0.001$) and 12% and 20% IC case ($F(1, 31) = 311.2$, $p < 0.001$). Inside the scanner, performance accuracy rates differed reliably across 100% stimulus case, 12% and 20% C case, and 12% and 20% IC case ($F(2, 62) = 4.9$, $p < 0.01$) with 100% stimulus case equivalent performance accuracy rate relative to 12% and 20% C case ($F(1, 31) = 3.8$, $p = 0.06$) and yielding higher performance rate relative to 12% and 20% IC case ($F(1, 31) = 8.4$, $p < 0.01$). Outside the scanner, RTs differed reliably across 100% stimulus case, 12% and 20% C case, and 12% and 20% IC case ($F(2, 62) = 25.3$, $p < 0.001$) with 100% stimulus case yielding higher performance accuracy rate relative to 12% and 20% C case ($F(1, 31) = 30.3$, $p < 0.001$) and 12% and 20% IC case ($F(1, 31) = 30.0$, $p < 0.001$).

Brain results. We contrasted brain activity of 100% stimulus case with that of 12% and 20% C and 12% and 20% IC cases. Insular, frontal and parietal cortices were found activated by difficult task [Fig. 5(B) for insular activation, and Table 1]. Finally, the group average contrast values were plotted for both INSSs in all

Table 2b. Brain results. The notations used here are: L = left, R = right, INS = insula, s.e.m. = standard error of the mean, η^2 (eta squared) = effect size, Asyn = asynchrony perception, Syn = synchrony perception, C = color coherence, IC = color incoherence

| | L INS Brain activity (β value) | R INS Brain activity (β value) |
|--|---|--|
| <i>Face-house categorization task</i> | | |
| Mean \pm s.e.m. | 0% noise: 0.27 \pm 0.16 40% noise: 1.18 \pm 0.16 55% noise: 1.53 \pm 0.25 | 0% noise: 0.38 \pm 0.15 40% noise: 1.19 \pm 0.17 55% noise: 1.55 \pm 0.20 |
| <i>ANOVA test</i> | | |
| Overall | $F(2,64) = 16.0$, $p < 10^{-5}$, $\eta^2 = 0.34$ | $F(2,64) = 21.8$, $p < 10^{-7}$, $\eta^2 = 0.41$ |
| 0% and 40% noise | $F(1,32) = 32.7$, $p < 10^{-5}$, $\eta^2 = 0.51$ | $F(1,32) = 23.3$, $p < 10^{-5}$, $\eta^2 = 0.42$ |
| 0% and 55% noise | $F(1,32) = 25.0$, $p < 10^{-4}$, $\eta^2 = 0.44$ | $F(1,32) = 33.3$, $p < 10^{-5}$, $\eta^2 = 0.51$ |
| <i>Happy-angry face categorization task</i> | | |
| Mean \pm s.e.m. | 0% noise: 0.27 \pm 0.11 40% noise: 1.09 \pm 0.18 | 0% noise: 0.60 \pm 0.11 40% noise: 1.79 \pm 0.18 |
| ANOVA test: overall | $F(1,31) = 27.2$, $p < 10^{-4}$, $\eta^2 = 0.47$ | $F(1,31) = 60.7$, $p < 10^{-8}$, $\eta^2 = 0.66$ |
| <i>Audio-visual asynchrony and synchrony perception task</i> | | |
| Mean \pm s.e.m. | Asyn: 0.38 \pm 0.06 Syn: 0.18 \pm 0.05 | Asyn: 0.44 \pm 0.07 Syn: 0.21 \pm 0.06 |
| ANOVA test: overall | $F(1,32) = 13.0$, $p = 10^{-3}$, $\eta^2 = 0.29$ | $F(1,32) = 16.4$, $p < 10^{-3}$, $\eta^2 = 0.35$ |
| <i>Random dots motion direction discrimination task</i> | | |
| Mean \pm s.e.m. | 100% C-IC: -0.04 \pm 0.03 12%, 20% C: 0.10 \pm 0.04 12%, 20% IC: 0.28 \pm 0.04 | 100% C-IC: 0.01 \pm 0.03 12%, 20% C: 0.16 \pm 0.04 12%, 20% IC: 0.32 \pm 0.04 |
| <i>ANOVA test</i> | | |
| Overall | $F(2,62) = 29.2$, $p < 10^{-8}$, $\eta^2 = 0.49$ | $F(2,62) = 23.1$, $p < 10^{-7}$, $\eta^2 = 0.43$ |
| 100% C-IC and 12%, 20% C | $F(1,31) = 13.1$, $p = 10^{-3}$, $\eta^2 = 0.30$ | $F(1,31) = 13.0$, $p = 10^{-3}$, $\eta^2 = 0.30$ |
| 100% C-IC and 12%, 20% IC | $F(1,31) = 72.7$, $p < 10^{-8}$, $\eta^2 = 0.70$ | $F(1,31) = 60.6$, $p < 10^{-8}$, $\eta^2 = 0.66$ |

three categories of RMD [Fig. 5(C)]. For the left INS, brain activities were reliably different across 100% stimulus case, 12% and 20% C case, and 12% and 20% IC case ($F(2, 62) = 29.2, p < 0.001$) with 100% stimulus case yielding lesser activity relative to 12% and 20% C case ($F(1, 31) = 13.1, p = 0.001$) and 12% and 20% IC case ($F(1, 31) = 72.7, p < 0.001$). Regarding the right

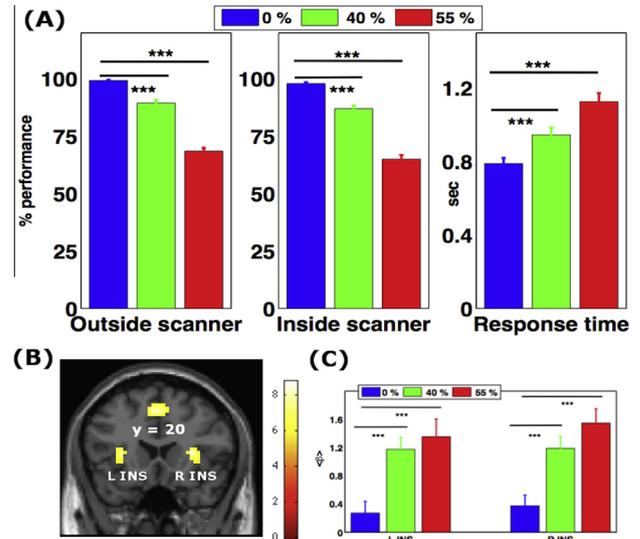


Fig. 2. Results of face-house categorization task. (A) *Behavioral results:* The bar plots show mean performance (%) outside the scanner (first column), inside the fMRI scanner (second column) for three noise-levels and response time outside the fMRI scanner (third column). (B, C) *Brain results:* Insular brain activations shown in (B) were associated with contrast noisy faces + houses (40% and 55% noise levels) versus clear faces + houses (0% noise level). Mean contrast values (β) are shown in (C) for three noise levels from the left insula (L INS) and the right insula (R INS). Error bars represent standard error of the mean throughout the manuscript unless it is stated and *** $p < 0.001$.

INS, brain activities differed reliably across 100% stimulus case, 12% and 20% C case, and 12% and 20% IC case ($F(2, 62) = 23.1, p < 0.001$) with 100% stimulus case yielding lesser activity relative to 12% and 20% C case ($F(1, 31) = 13.0, p = 0.001$) and 12% and 20% IC case ($F(1, 31) = 60.6, p < 0.001$).

Brain-behavior relation. In all tasks, RT was negatively correlated with performance accuracy (z-score) for recordings outside the scanner. For the recordings inside the scanner, we found the significant negative correlation between insular activity and performance accuracy (z-score) in all tasks except in task 4 where the insular activity was negatively correlated with performance accuracy but the results were not significant. The significant results (except correlation result between RT and performance accuracy in task 4) are shown in Fig. 6(A–C). A negative correlation indicated that lower performance accuracy related to longer RT or higher brain activity. This showed that the easier the tasks, better the performance accuracy and hence the lower the RT and the lower the insular activity, and vice-versa.

DISCUSSION

We used four sensory discrimination tasks in visual and audio-visual domains with the varying degree of degraded sensory input and found the involvement of bilateral insulae (INSs) in these tasks. INS activation increased as a function of the PDM difficulty, measured

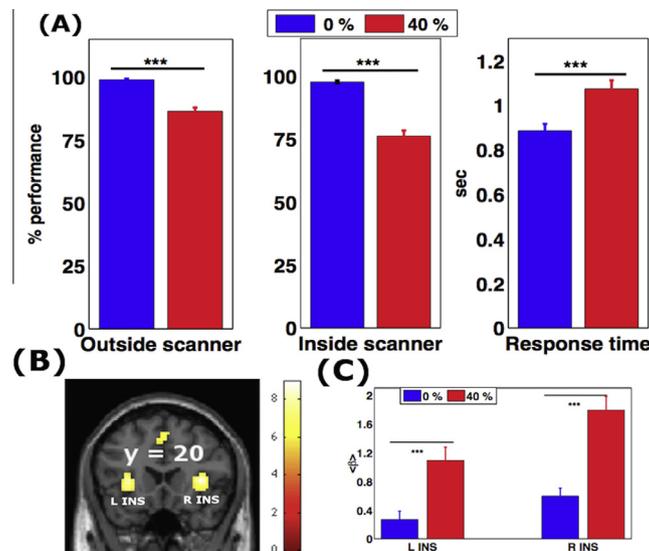


Fig. 3. Results of happy-angry face categorization task. (A) *Behavioral results*: The bar plots represent mean performance (%) outside the scanner (first column), inside the fMRI scanner (second column) and response time outside the fMRI scanner (third column) for two noise-levels. (B, C) *Brain results*: Insular brain activations shown in (B) were associated with contrast noisy (40% noise level) versus clear (0 % noise level) for happy and angry faces. Comparison of mean contrast values ($\langle \beta \rangle$) is shown in (C) for two noise levels from the left insula (L INS) and the right insula (R INS). Here, *** $p < 0.001$.

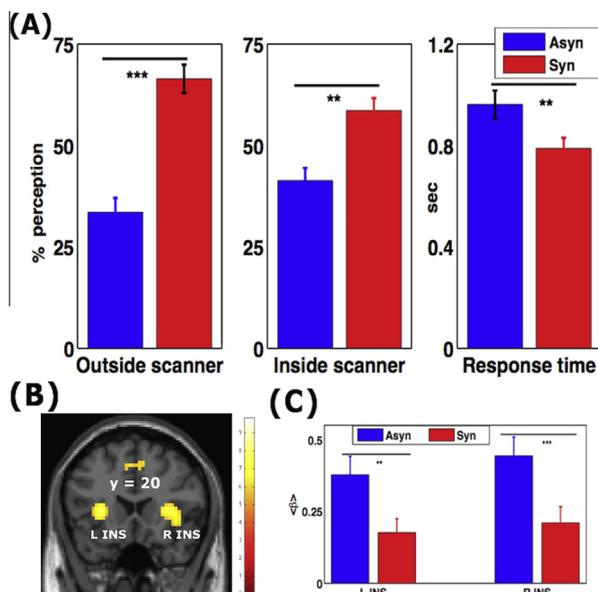


Fig. 4. Results of audio-visual asynchrony and synchrony perception task. (A) *Behavioral results*: Behavioral responses were categorized based on participants' perception of asynchrony and synchrony. The bar plots show mean asynchrony (Asyn) perception and synchrony (Syn) perception in percentage outside the scanner (first column), inside the fMRI scanner (second column) and response time outside the fMRI scanner (third column). (B, C) *Brain results*: Insular brain activations shown in (B) were associated with audio-visual asynchrony and synchrony perception versus beep + flash (multisensory stimuli versus unisensory stimuli). Mean contrast values ($\langle \beta \rangle$) are plotted in (C) for asynchrony perception and synchrony perception from the left insula (L INS) and the right insula (R INS). Here, ** $p < 0.01$, and *** $p < 0.001$.

by behavioral performance and response time, in all experiments. The observed load-dependent insular activity may reflect the degree of cognitive effort in

sensory processing and its role might not be limited to error, attentional control or processing of affective information as proposed by previous studies.

INSs are among the brain regions most commonly found activated in functional brain imaging studies on perceptual paradigm (Philiastides and Sajda, 2007; Heekeren et al., 2008; Tosoni et al., 2008). However, most of these studies do not explicitly address the functional role of this specific brain region in perception, but rather report its activation as a byproduct. The significantly higher insular response with fMRI when participant recognized an image while slowly being revealed suggested that insular activation is not simply recruited by general arousal or by the tonic maintenance of attention (Ploran et al., 2007). Previous studies have shown the involvement of INSs in the integration of perceptual information in different modalities (Binder et al., 2004; Pessoa and Padmala, 2007; Venkatraman et al., 2009; Deen et al., 2011; Chang et al., 2013). The role of INSs in decision-making is further supported by insular involvement in PDM that is independent of whether responses were made with eye movements or button presses (Grinband et al., 2006; Ho et al., 2009).

We have attempted to illustrate that INSs are involved in a multitude of PDM tasks. Focusing on correctly performed trials, we found higher insular activation when the ambiguity in the sensory information is increased. INSs might be involved in resolving the ambiguity by integrating the information that is salient to make a decision (Rushworth et al., 2004; Ho et al., 2009; Venkatraman et al., 2009; Wiech et al., 2010; Woolgar et al., 2011; Krebs et al., 2012; Srinivasan et al., 2013). We proposed that the higher INS activity in difficult task might reflect the effort in integrating sensory information when information salient to one versus other category is not obvious or ambiguous (Lewis et al., 2000; Bushara

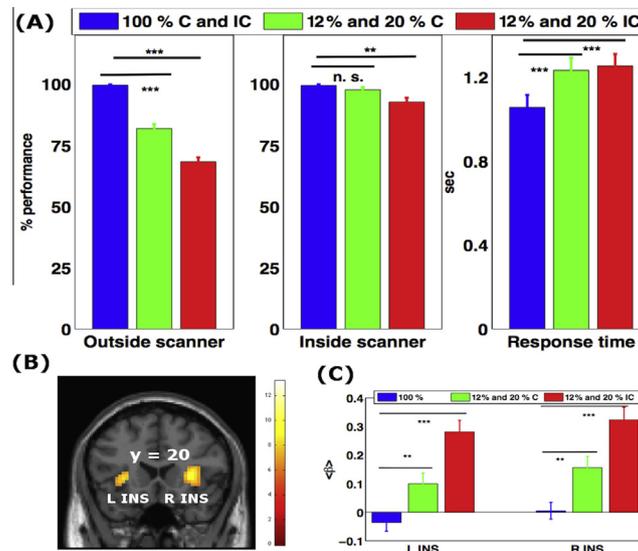


Fig. 5. Results of random dots motion direction discrimination task: (A) *Behavioral results:* The bar plots represent mean performance (%) outside the scanner (first column), inside the fMRI scanner (second column) and response time outside the fMRI scanner (third column) for three task levels (100% coherence and incoherence, 12% and 20% coherence, and 12% and 20% incoherence respectively). (B, C) *Brain results:* The insular brain activations shown in (B) were associated with 100% coherence and incoherence versus 12% and 20% coherence plus incoherence. Mean contrast values (β) for these three-task difficulty levels are plotted in (C) for both left insula (L INS) and right insula (R INS). Here, n.s. = not significant, ** $p < 0.01$, and *** $p < 0.001$.

et al., 2001; Sterzer and Kleinschmidt, 2010; Gu et al., 2012; Lamichhane and Dhamala, 2015b). These results do not support that the greater insular activity in difficult task is a byproduct of decision process as assumed by previous studies. A possible explanation in these cases could be that for one percept to occur, the ambiguous information has to be resolved before reaching to the perceptual decisions (Botvinick et al., 2001), more processing resources are required and these resources are made available through activation of a neural circuit that includes INSs. Our recent study showed the involvement of INSs in the processing of ambiguous sensory information and the integrative role of INSs in PDM (Lamichhane and Dhamala, 2015b). Further, for the correct performance, the uncertainty in response selection must be resolved, such as through INS integration of scant sensory information (Rushworth et al., 2004; Srinivasan et al., 2013). Some recent studies (Cai et al., 2014; Ghahremani et al., 2015) did not find any support for INS role in error processing.

INSs have also been shown involved in perceptual decisions about facial expressions, such as when determining whether a face is “positive” or “negative” (Calder et al., 2000; Phan et al., 2002; Critchley et al., 2004; Pessoa and Padmala, 2007; Thielscher and Pessoa, 2007). Most of previous work on the perception of emotional faces has focused on how the emotional content of the stimuli affect brain responses. Unlike many previous studies that focused on its role in affect processing, our principal focus was its role on PDM. This is consistent with the recent report (Damasio et al., 2013), which stated that a patient with bilateral insula damage was still able to feel emotion (including pain, pleasure, itch, tickle, happiness, sadness, apprehension, irritation, caring and compassion). We found significant differences in behavioral

accuracy and response time between the decisions of clear and noisy images. The striking finding for perception of facial expressions of noisy pictures was that it activated INSs significantly higher in noisy pictures compared to clear pictures. This raised the concerns whether the INS activities really represent emotional content of the stimuli in such decision or what role INSs play in perceptual tasks with minimum emotional content (i.e. in noisy information). We argued that the types of activation we found could closely reflect decision processes in agreement with previous study (Thielscher and Pessoa, 2007). Thus, the involvement of INSs during perceptual decision of facial expression may be due to higher demand for additional effort that is required in sensory processing in case of noisy stimuli than in clear stimuli for both happy and angry cases.

Number of neuroimaging studies have shown the role of INSs in auditory processing [for a review, see (Bamiou et al., 2003)] and also in cross-modal interactions (Calvert, 2001). Similar to our recent study (Lamichhane and Dhamala, 2015b), visual and auditory stimuli were presented either synchronously or asynchronously with varying delays in a PET study (Bushara et al., 2001). Comparing asynchronous and synchronous conditions, this study delineated a large-scale network comprising INSs as well as prefrontal and posterior parietal regions during asynchronous stimulation. Interestingly, increasing task demand (i.e., decreasing intermodal delay) correlated with activity in the right insula. In a study (Miller and D’Esposito, 2005), where cross-modal integration of speech was investigated, auditory and visual speech stimuli were presented synchronously or asynchronously. These regions showed greater responses during asynchronous stimulus presentation as in the study by Bushara and colleagues (Bushara et al., 2003). In another

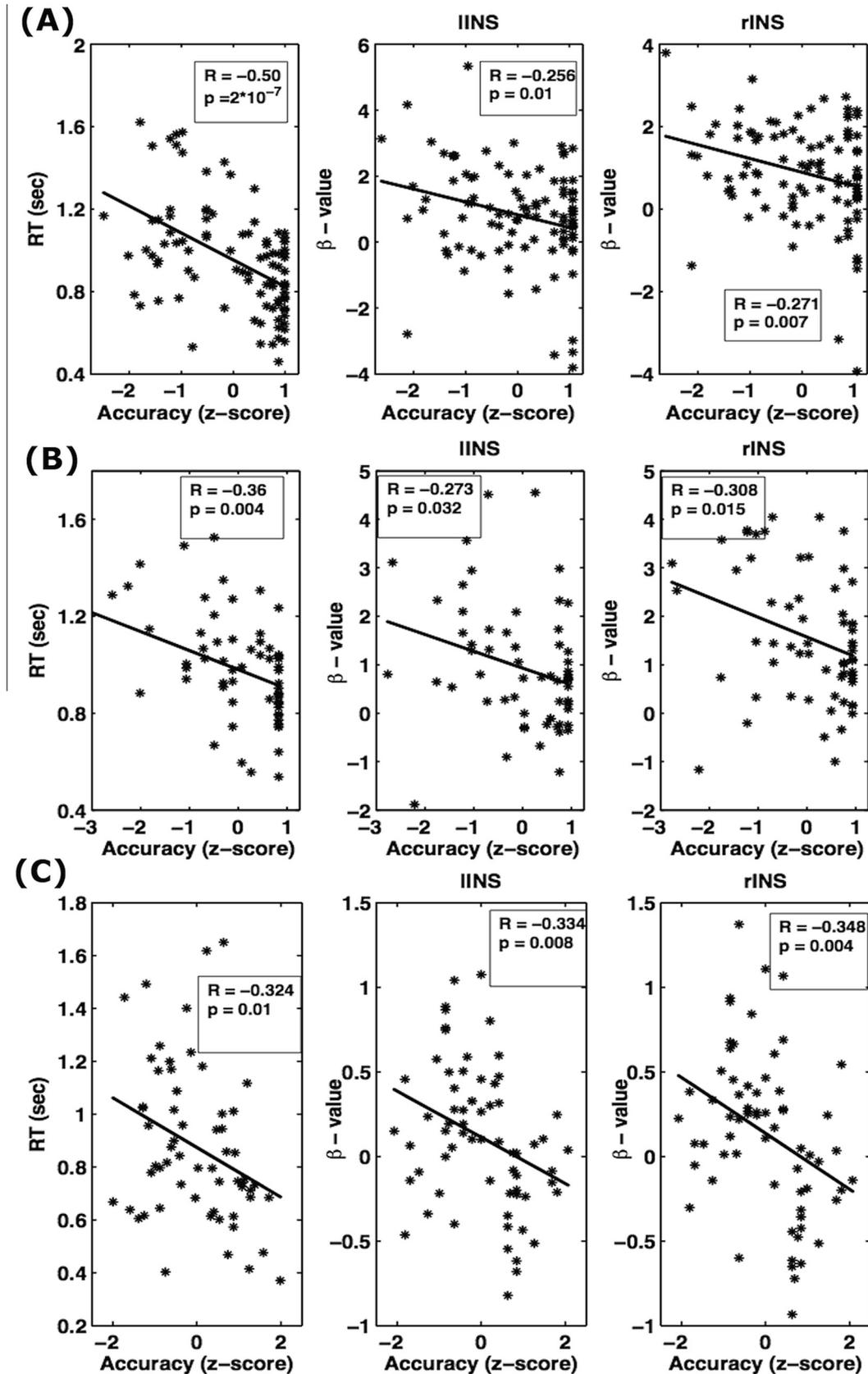


Fig. 6. Relation between response time (RT)/brain activity and performance accuracy: (A) *face-house categorization task*, (B) *happy-angry face categorization task*, and (C) *audio-visual asynchrony and synchrony perception task*. The first column of each row represents the relation between RT and performance accuracy for recordings outside the scanner, second and third columns represent the relation between brain activity and performance accuracy for the left insula (IINS) and the right insula (rINS) respectively for the recordings inside the scanner.

study, authors investigated the neural correlates of decision processes in auditory perception (Binder et al., 2004). Participants discriminated two synthesized speech syllables, /ba/ and /da/, which differed only in minor ways. To probe the neural correlates of decision processes, they used RT as an index of decision-making and searched for voxels whose time series exhibited significant correlations with RT. They found that the anterior insular and adjacent frontal opercular cortices were involved in decision processes.

Many neuroimaging studies have shown INs were involved in a wide variety of timing tasks, including attention to time (Coull et al., 2000, 2004), time perception (Craig, 2009; Kosillo and Smith, 2010), auditory and visual rhythm perception estimation (temporal sequencing) (Schubotz et al., 2000), interval sequence encoding (Schubotz et al., 2000), sensorimotor synchronization (Rubia and Smith, 2004). Harrington et al. (2004) found the insular cortex showed significant effect of discrimination difficulty during the decision phase in time perception of auditory stimuli (Harrington et al., 2004). Robust activation in bilateral anterior insula along with bilateral dorsolateral prefrontal cortex, and putamen were found to be associated with increased task difficulty on a temporal discrimination task (Tregellas et al., 2006). These results suggested that recruitment of INs during PDM tasks is load-dependent and further support our hypothesis that the recruitment of insula in sensory processing. The strong load dependent activation of INs observed in all of our experimental tasks further supports the specific involvement of these regions in information processing rather than a more general attention and emotion.

Furthermore, we sought more convincing evidence to support that INs were part of a functional network involved in PDM process. Recently, we provided novel insights into the input–output relations of the insula and the functions it served in decision-making processes (Lamichhane and Dhamala, 2015b). With the use of dynamic causal modeling, we demonstrated that input of external stimuli on brain regions, also called driving input, mostly entered through right insula in salience network. The existence of functional INs to dACC connectivity further supports that INs drive dACC to guide behavior in choosing the appropriate response in PDM tasks. This clearly supports the above-mentioned role of INs and our argument that INs are the part of a system involved in PDM processes. Even though all of these tasks are perceptual in nature, they differ from each other in terms of stimulus modality and level of task difficulties, which can be regarded as a potential limitation of this study. However, despite these differences, INs were consistently activated and modulated by the task difficulty in PDM.

Moreover, the laterality of the insular function has not been understood well. It remains argumentative (Craig, 2009) possibly because the left and right insulae are usually coactivated (Critchley et al., 2004; Singer et al., 2009; Ploner et al., 2010; Sterzer and Kleinschmidt, 2010). The right INS is activated generally by arousing to the body stimuli (for example, pain), whereas the left INS is activated mainly by positive and affiliative emotional feelings (Craig, 2009). For examples, the activation of the left INS

was reported in mothers viewing photos of their own child (Leibenluft et al., 2004), subjects either seeing or making a smile (Jabbi et al., 2007), attending to happy voices (Johnstone et al., 2006), hearing pleasant music (Koelsch et al., 2006), experiencing joy (Takahashi et al., 2008) etc. The left INS was found activated as verbal information about each person was retrieved and rehearsed (Tsukiura et al., 2002). Bilateral IC activation were reported during time perception (Coull, 2004), inspection time (Deary et al., 2004), moment of recognition (Ploran et al., 2007), PDM (Thielscher and Pessoa, 2007), feeling of knowing (Kikyo et al., 2002) etc. A fMRI study, (Pallaer et al., 2003), showed several brain regions including the left INS, left hippocampus, middle temporal gyrus, and bilateral cerebellum during blocks of learned faces whereas right-lateralized regions; right INS, right precuneus, and right dorsolateral prefrontal cortex were activated more during memory judgments than during gender judgments. In our study, we found bilateral insular activations in all four perceptual tasks. In our previous study (Lamichhane and Dhamala, 2015b), we found the sensory input to the right INS was much higher than to the left INS which is consistent with the earlier proposal that the right INS aids in the coordination and evaluation of task performance across behavioral tasks with varying perceptual and response demands (Sridharan et al., 2008; Eckert et al., 2009; Ham et al., 2013).

Here, we focused on functional role of INs in perceptual-paradigm, which points us to a unifying theory that the insular cortex supports various functions including emotion, empathy, uncertainty and error processing. Goal-directed motivation and behavioral control contingencies were found to activate frontal-parietal and insular cortices although our experiments did not involve direct monetary reward (Pessoa and Engelmann, 2010). The higher RT and increased BOLD response in INs in difficult task conditions might be effortful cognitive engagement for the desired outcome (or performance optimization) (for review, (Braver et al., 2014)).

In summary, we performed fMRI experiments with four PDM tasks of varying difficulty (noise) level. PDM processes in human brain recruited INs that are usually known to be involved in a wide range of tasks across sensory, affective and cognitive domains, and widespread brain regions including dACC, prefrontal and parietal cortices. We focused on differentiating the influence of task difficulty on insular activity in all of four PDM tasks and showed a strong positive correlation between perceptual difficulty and insular activity. The higher BOLD activity in a difficult task compared to easy one may support the involvement of the human insulae in sensory processing and load-dependent cognitive process as hypothesized. These results, along with our previously reported results (Lamichhane and Dhamala, 2015b), contribute to our understanding of the functional role of INs in PDM and provided insights into possible mechanisms for other sensory-guided goal-directed action those usually involved brain regions responsible for sensorimotor integration, response selection, and perception.

DISCLOSURE STATEMENT

There is no conflict of interest for any of the author.

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