At the Heart of the Ventral Attention System: The Right Anterior Insula

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Abstract: The anterior insula has been hypothesized to provide a link between attention-related problem solving and salience systems during the coordination and evaluation of task performance. Here, we test the hypothesis that the anterior insula/medial frontal operculum (aI/fO) provides linkage across systems supporting task demands and attention systems by examining the patterns of functional connectivity during word recognition and spatial attention functional imaging tasks. A shared set of frontal regions (right aI/fO, right dorsolateral prefrontal cortex, bilateral anterior cingulate) were engaged, regardless of perceptual domain (auditory or visual) or mode of response (word production or button press). We present novel evidence that: (1) the right aI/fO is functionally connected with other frontal regions implicated in executive function and not just brain regions responsive to stimulus salience; and (2) that the aI/fO, but not the ACC, exhibits significantly correlated activity with other brain regions specifically engaged by tasks with varying perceptual and behavioral demands. These results support the hypothesis that the right aI/fO aids in the coordination and evaluation of task performance across behavioral tasks with varying perceptual and response demands. *Hum Brain Mapp 30:2530–2541, 2009.* © 2008 Wiley-Liss, Inc.

Key words: ventral attention system; dorsal attention system; anterior cingulate cortex; dorsolateral prefrontal cortex; problem solving; salience; task performance; response selection

INTRODUCTION

Every waking moment we must allocate the appropriate attentional resources to plan activities, respond to novel or unexpected events, select appropriate behavioral responses among many alternatives, and evaluate the success or failure of our performance to guide future behavior. A large body of literature points to regions within frontal cortex, parietal cortex, thalamic, and brain stem regions that support attention-related behavior [Aston-Jones et al., 2000; Baddeley, 1998; Barch et al., 1997; Botvinick et al., 1999; Dosenbach et al., 2006; Fan et al., 2005; Fox et al., 2006; Kerns et al., 2004; Ridderinkhof et al., 2004; Seeley et al., 2007]. Based on evidence from functional imaging and lesion studies, attention has been fractionated into systems that support executive function (problem solving or goal-directed behavior), selection or direction of attention, and arousal [Fan et al., 2005; Posner, 2004]. Functional connectivity analyses involving resting state data demonstrate

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correlated patterns of activity between distinct brain regions that support goal-directed behavior (the dorsal attention system) and those that support responses to salient stimuli in the environment (ventral attention system) [Fox et al., 2006; Seeley et al., 2007]. Examination of frontal responses during task performance suggests that these two hypothetical systems interact during behavioral tasks and that this interaction occurs through the aI/fO [Dosenbach et al., 2006; Sridharan et al., 2008].

Central to the dorsal and ventral attention systems are the aI/fO, the anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC) [Dosenbach et al., 2006]. These frontal lobe regions are consistently engaged during challenging task conditions [Barch et al., 1997; Binder et al., 2004; Gehring and Knight, 2000; Giraud et al., 2004; Kerns et al., 2004; MacDonald et al., 2000; Ridderinkhof et al., 2004; Sharp et al., 2006] that involve conflict monitoring, error detection, response inhibition, problem solving, decision making, and performance monitoring [Casey et al., 2000; Huettel et al., 2005; Knutson et al., 2007; Liu et al., 2007; MacDonald et al., 2000; Thielscher and Pessoa, 2007; Ullsperger and von Cramon, 2001]. The ACC is engaged across a variety of auditory and visual behavioral tasks [Barch et al., 2001] and is hypothesized to provide DLPFC with information about conflicting or ambiguous perceptual information so that DLPFC can guide the selection of an appropriate response [Botvinick et al., 1999; Kerns et al., 2004; Ridderinkhof et al., 2004]. The right aI/fO has been linked to cortical control of autonomic function [Abboud et al., 2006; Hoffman and Rasmussen, 1953; Meyer et al., 2004; Penfield and Faulk, 1955] and is consistently reported to be activated during imaging experiments in which the task conditions are challenging [Binder et al., 2004]. Because the right aI/fO is activated across the duration of a task [Dosenbach et al., 2006], it has been described as central to the ventral attention system for coordinating task performance [Dosenbach et al., 2007; Sridharan et al., 2008].

The results from studies summarized above guide the hypothesis that the right aI/fO engages brain regions selectively responsive to task demands and attention systems critical for coordinating task performance. We tested this hypothesis by examining the patterns of functional connectivity during verbal and spatial tasks. Specifically, auditory (word recognition) and visual attention (Eriksen flanker) tasks were used to examine the pattern of connectivity from within right ACC, DLPFC, and aI/fO regions that were engaged in both tasks. Our event-related experiments were designed so that subjects could not anticipate the stimulus type or difficulty of a trial, thereby increasing the trial-by-trial engagement of the brain's attentional system [Corbetta and Shulman, 2002]. Moreover, there was no risk or specific reward associated with tasks nor were the tasks probabilistic in nature such that subjects were expected to make a judgment based on the probability of an event [Knutson and Bossaerts, 2007; Platt and Huettel, 2008]. Instead, the tasks used in this study required subjects to make a perceptual decision of varying difficulty [Altmann et al., 2008]. We predicted that increasing task demands would produce increased interaction between the right aI/fO and (1) attention-related brain regions that were generally engaged across different tasks and (2) brain regions that were specifically engaged by the different perceptual and behavioral demands of the tasks.

MATERIALS AND METHODS

Subjects

The 11 right-handed adults (mean age 32.8 ± 10.9 years; five females; mean Edinburgh handedness score = 95.0 ± 8.9; mean education in years = 18.8 ± 1.9) in this study were recruited from the Medical University of South Carolina (MUSC) community and Charleston, SC area through word of mouth. The aims of this study were explained to each participant; MUSC IRB-approved informed consent was obtained; and the experiments were conducted in accordance with the Declaration of Helsinki. All subjects in this study had audiometric thresholds below 25 dB HL [ANSI, 1996] at octave frequencies from 0.25 to 3.0 kHz. As described later, we also controlled for individual variability in hearing thresholds by presenting words in background noise. Subjects who did not have normal vision had contact lens corrected vision. The subjects in this study were also included in a larger study on age-related changes in brain structure and function [Eckert et al., 2008] using the attended word recognition study described later.

Event-Related Task Designs

To address the aims of this study, we used existing datasets that were collected for a study examining brain activity for attended word recognition and unattended listening tasks. Each experiment was designed to examine the responsiveness of temporal lobe cortex for varying levels of speech intelligibility. In the word recognition task, subjects attended to spoken words [Eckert et al., 2008]. In the unattended listening task, the Eriksen flanker task [Eriksen and Eriksen, 1974] was used to direct attention to visual stimuli and away from the speech. In both tasks, the engagement of frontal regions was dependent on the behavioral demands of the task, either word repetition for the word recognition task or button pressing in response to visual stimuli during the Eriksen flanker task. For this reason, the two experiments were used to examine the engagement and connectivity of the aI/fO across experiments with different behavioral demands. The tasks were performed during the same scanning session, with the word recognition task always following the Eriksen flanker task so that instructions for the word recognition task did not influence behavior during the Eriksen flanker task.

Word recognition task

Each subject performed a word recognition task in which they listened to 40 words that were presented across four low-pass frequency filtering conditions (upper cutoff frequencies = 400, 1,000, 1,600, 3,150 Hz; the lower cutoff frequency was fixed at 200 Hz) to degrade word intelligibility. The words selected for this study were nouns from a list of 400 monosyllabic consonant–vowel–consonant words used by Dirks et al. [2001]. The nouns represented a normal distribution of lexical difficulty based on the combination of lexical features that influence word recognition difficulty (word frequency, the number of similar sounding words, and the mean word frequency of those similar sounding words) [Luce and Pisoni, 1998]. The words were presented at 75 dB SPL. A broadband masker was always present to minimize individual differences in hearing thresholds. The broadband masker was digitally generated and then its spectrum adjusted at one-third-octave intervals to produce equivalent masked thresholds for all subjects. Band levels of the noise were set to achieve masked thresholds of 20–25 dB HL from 0.2 to 3.15 kHz, 30 dB HL at 4.0 and 5.0 kHz, and 40 dB HL at 6.3 kHz. The overall level of the masker was 62.5 dB SPL. Eprime software (Psychology Software Tools) and an IFIS-SA control system (Invivo Corp.) were used to present the word stimuli. The broadband noise was presented on a separate PC throughout the experiment. The words were mixed with the broadband noise at precisely 2.5 s into the 8 s TR using a standard audio mixer, and then delivered to the participant through custom-made piezoelectric insert earphones (Sensimetrics Corp.). The earphones were calibrated at the MRI scanner to deliver the words at 75 dB SPL and the spectrally shaped noise at 62.5 dB SPL using a sound-level meter (Bruel & Kjaer, Type 2231). The sparse sampling design used for this study limited the confounding influence of scanner noise on the stimuli and on neural responses to the stimuli, provided time to generate a verbal response, and provided time for subjects to stabilize their heads prior to the next TR.

Subjects were instructed to listen and respond with the word they heard or with "nope" if they could not recognize the word, ensuring that a motor response was produced on each trial. Each response was recorded as correct, incorrect, or "nope" by two raters (M.E. and A.W.). An overt oral response was chosen so that the results were directly relatable to audiologic assessment of word recognition and because speech production tasks have been used successfully in other language studies [Fridriksson et al., 2006; Gracco et al., 2005; Shuster and Lemieux, 2005]. In addition, the ecological validity of button pressing during language tasks has been questioned [Small and Nusbaum, 2004].

Eriksen flanker task

Each adult also participated in a visual attention experiment using a modified version of the Eriksen flanker task [Eriksen and Eriksen, 1974]. The Eriksen flanker task has been used to demonstrate frontal activation for response inhibition and, more specifically, conflict monitoring [Botvinick et al., 1999]. The task involves deciding on the direction in which a center stimulus is pointing. Low conflict or congruent flanking stimuli are oriented in the same direction as the center stimulus (>>**>**>>, <<**<**<<); bold font added for illustration). High conflict or incongruent flanking stimuli are oriented in the opposite direction as the center stimulus (>>**<**>>, <<**>**<<).

Each participant was instructed to button press as quickly as possible with their right thumb when the center stimulus pointed to the left and their right index finger when the center stimulus pointed to the right. The white arrow-head stimuli were presented on a black background for 200 ms to ensure engagement of systems that support conflict monitoring [Miller, 1991; Rueda et al., 2004]. Eprime software and an IFIS-SA control system were used to control stimulus presentation, as well as record the correct or incorrect button press and response latency from an MRI Devices Corp. button response key pad.

During the Eriksen flanker task, low-pass filtered words (400, 1,000, 1,600, 3,150 Hz) and broadband noise were presented to the subjects at the exact time that the visual flanker stimuli were presented. The subjects were instructed that words would be presented during the Eriksen flanker task, but they would not be asked to perform any tasks related to the words during or after the scanning session, and that they should focus on performing the Eriksen flanker task.

Image Acquisition and Processing

For both the word recognition and flanker tasks, T2*-weighted functional images were acquired using a single shot echo-planar image (EPI) sequence on a Phillips 3T scanner and SENSE head coil that covered the brain with the following parameters: 32 slices with a 64×64 matrix, TR = 8,000 ms, TE = 30 ms, slice thickness = 3.25 mm, and a TA = 1,647 ms. This protocol provided a 6,353-ms silent period for stimulus presentation and task execution.

Image preprocessing was performed using SPM5 algorithms (http://www.fil.ion.ucl.ac.uk/spm). Each participant's native space images were realigned to the first volume and unwarped to correct for head movement and susceptibility distortions. Image volumes, slices, and voxels with significant artifact were identified using the ArtRepair toolbox (http://cibsr.stanford.edu/tools/ArtRepair/ArtRepair.htm) based on scan-to-scan motion (1 sd change in head position) and outliers relative to the global mean signal (3 sd from the global mean). An average of three image volumes from the word recognition ($\pm$ 1.57) and Eriksen flanker ($\pm$ 1.25) EPI datasets were excluded for artifact. Slice timing was not performed because temporal interpolation can introduce distortion to images collected with a long TR. The images were then normalized to the ICBM EPI template and smoothed with an 8-mm Gaussian kernel to ensure that the data met the assumption of normal distribution for parametric testing. A first level fixed-effects statistical analysis was performed for each individual's images to generate parametric estimates of the change in brain activation across the filtered word conditions and to compare incongruent and congruent flanker task conditions. In addition to the two dummy scans that were omitted for each run, the first real scan from each run was omitted to limit longitudinal magnetization effects that occur at the beginning of each fMRI experiment. The data were convolved with the SPM5 canonical hemodynamic response function and high-pass filtered at 128 s.

Second-level random effects analyses were performed to examine regions that exhibited parametric responses in the word recognition experiment and incongruent versus congruent flanker task conditions across the adults. A joint statistical threshold of peak voxel $P < 0.01$ and cluster extent $P < 0.01$ was used for all of the second-level analyses to be sensitive to sharp peak and broadly distributed effects [Poline et al., 1997; Seeley et al., 2007]. Statistical analyses were also performed to determine the extent to which confounding factors may have influenced the results and whether individual variability predicted brain activation. In particular, word generation tasks elicit increased ACC activity [Crosson et al., 1999]. To ensure that the results, particularly the incorrect versus correct comparison described earlier, were not due to word generation in the low intelligibility conditions, we examined the percentage of incorrect responses relative to "nope" responses. Some subjects produced more incorrect responses than "nope" responses compared with other subjects, suggesting that they were more likely to generate an incorrect response even if the word was not intelligible. The percentage of incorrect responses minus "nope" responses was not significantly related to the degree of aI/fO, ACC, and DLPFC activation across subjects for the incorrect minus correct contrast. We also collected the reaction time and percent of correct incongruent responses to use as correlates in a second-level analysis for the Eriksen flanker task. The results of this analysis are presented in Figure 3.

Functional connectivity was performed from the right aI/fO, ACC, and right DLPFC regions that exhibited increased activity with increased task difficulty in the word recognition and Eriksen flanker task. Masks of these overlapping clusters were used with Marsbar [Brett et al., 2002] to collect the average time series from each frontal region of interest for each participant's word recognition and Eriksen flanker image data sets. Whole brain gray matter, white matter, and CSF regions of interest were also created to collect time series that reflected whole brain fluctuations in signal. These time series were used as covariates to identify brain regions exhibiting correlated activity with each frontal regions of interest that was independent of global changes in signal over the course of each experiment for each participant. These single subject analyses identified regions across the brain exhibiting correlated activity with the region of interest throughout each experiment. A second-level analysis identified patterns of correlated activity that were consistent across the subjects [Seeley et al., 2007]. Paired *t*-tests were performed, limiting the analyses to the regions that were significantly correlated during each task, to compare the patterns of correlated activity between tasks.

RESULTS

A Task-Independent Frontal Network

This section presents results confirming findings from metaanalysis studies [Nee et al., 2007] that the same frontal regions are engaged across tasks. We include this section to show that aI/fO, ACC, and DLPFC regions are engaged across tasks within the same subjects and to provide the empirical foundation for examining the functional connectivity of each frontal region below.

Supporting Information Figure 1a shows that word recognition varied linearly as a function of the four low-pass filter cutoff frequencies ($r_{(3)} = 0.99$). Consistent with previous observations [Davis and Johnsrude, 2003; Scott et al., 2006], Supporting Information Figure 1b shows that increasing word intelligibility was associated with increasing anterior superior temporal gyrus and sulcus activity. The group results in Figure 1a,b and Supporting Information Table I demonstrate that decreasing word intelligibility was associated with increasing activity in right aI/fO, bilateral ACC, and bilateral DLPFC.

The same subjects performed a modified version of the Eriksen flanker task [Eriksen and Eriksen, 1974]. The average reaction time for congruent and incongruent trial responses was 768.3 ms (± 147.9) and 927.7 ms (± 203.9), respectively. Comparison of the incongruent and congruent trials elicited increased right aI/fO, bilateral ACC, and right DLPFC activity. Figure 1a and Supporting Information Table II also demonstrate that additional frontal and intraparietal sulcus (IPS) regions exhibited increased activity in the incongruent compared with congruent condition, which is consistent with previous studies [Fan et al., 2007; Ullsperger and von Cramon, 2001]. The unattended word stimuli produced an increasing response in temporal lobe cortex with increasing word intelligibility (results not presented). Importantly, however, decreasing word intelligibility did not result in increased frontal activity as in the word recognition task or the flanker task. The frontal activity observed during this task appeared to be driven specifically by the response demands of the Eriksen flanker task.

Figure 1a shows the overlapping right aI/fO, ACC, and right DLPFC results between the Eriksen flanker and word recognition experiments. The overlapping results within individual subjects are presented in Supporting Information Figure 2. These results indicate that a shared set of frontal regions are used for response selection regardless of the perceptual domain (auditory or visual), response type (word production or button press), or experimental design. Importantly, this shared set of right hemisphere regions was activated across tasks within the same subjects.

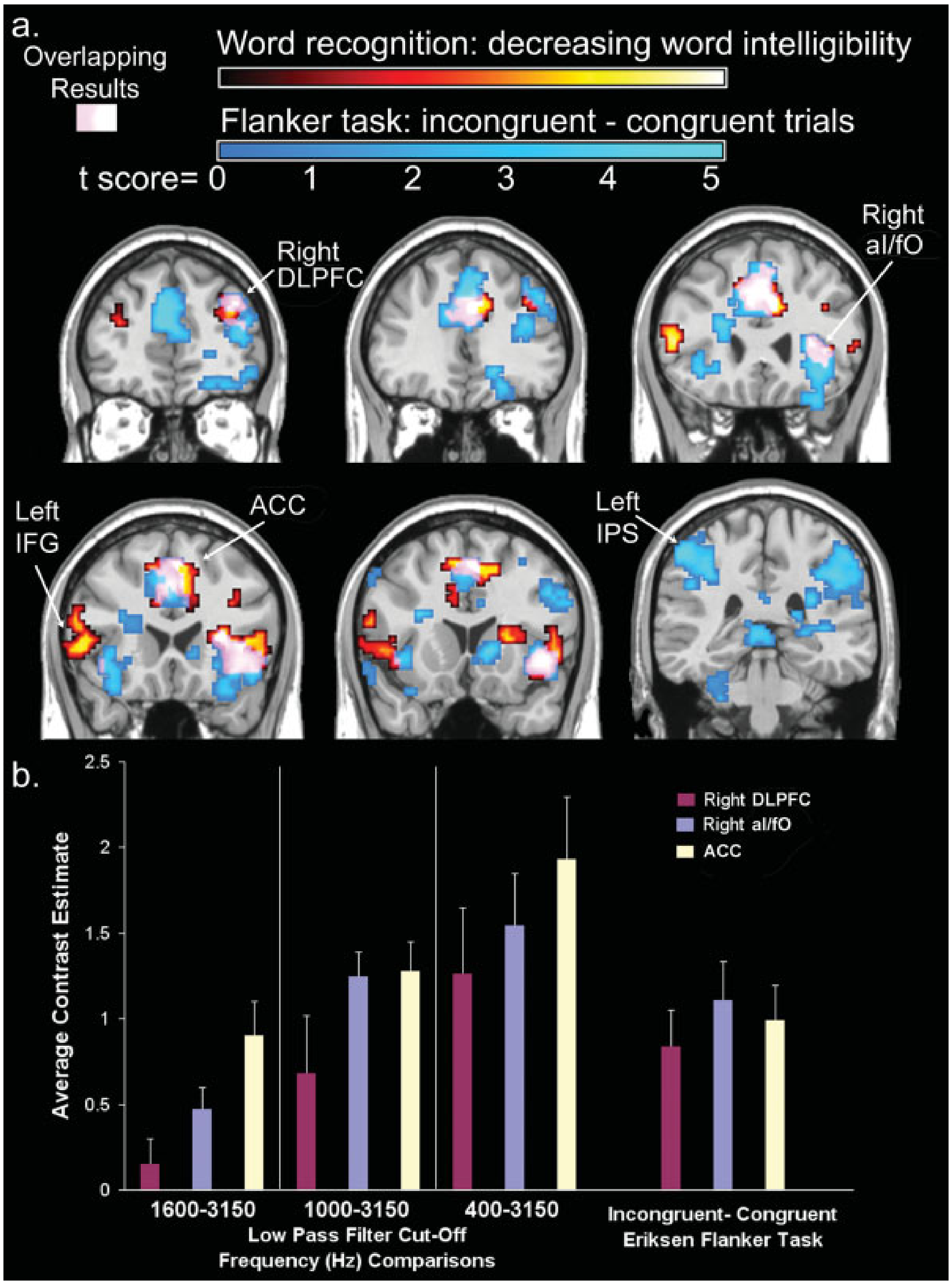

Figure 1.

(**a**) Right aI/fO, ACC, and right DLPFC regions exhibited increased activity with decreasing word intelligibility and increased activity for the incongruent compared with congruent Eriksen flanker task conditions (overlapping results: pink-white clusters). Also, note the increased left inferior frontal gyrus and left DLPFC activity with decreasing word intelligibility (orange), as well as the increased intraparietal sulcus (IPS) activity for the incongruent compared with congruent Eriksen flanker task trials. These regions demonstrate differences in functional connectivity with the aI/fO in the behavioral task comparison (shown in Fig. 4). (**b**) The average contrast estimates from within the overlapping right aI/fO, ACC, and right DLPFC regions are presented in the bar-graph. These contrast estimates are for low-pass filter cutoff comparisons of the lesser intelligible conditions (1,600, 1,000, 400 Hz) relative to the most intelligible condition (3,150 Hz). This graph shows that the increase in frontal activity with decreasing word intelligibility is linear rather than nonlinear. The contrast estimates for the flanker task also are presented for comparison across regions and to the word recognition experiment.

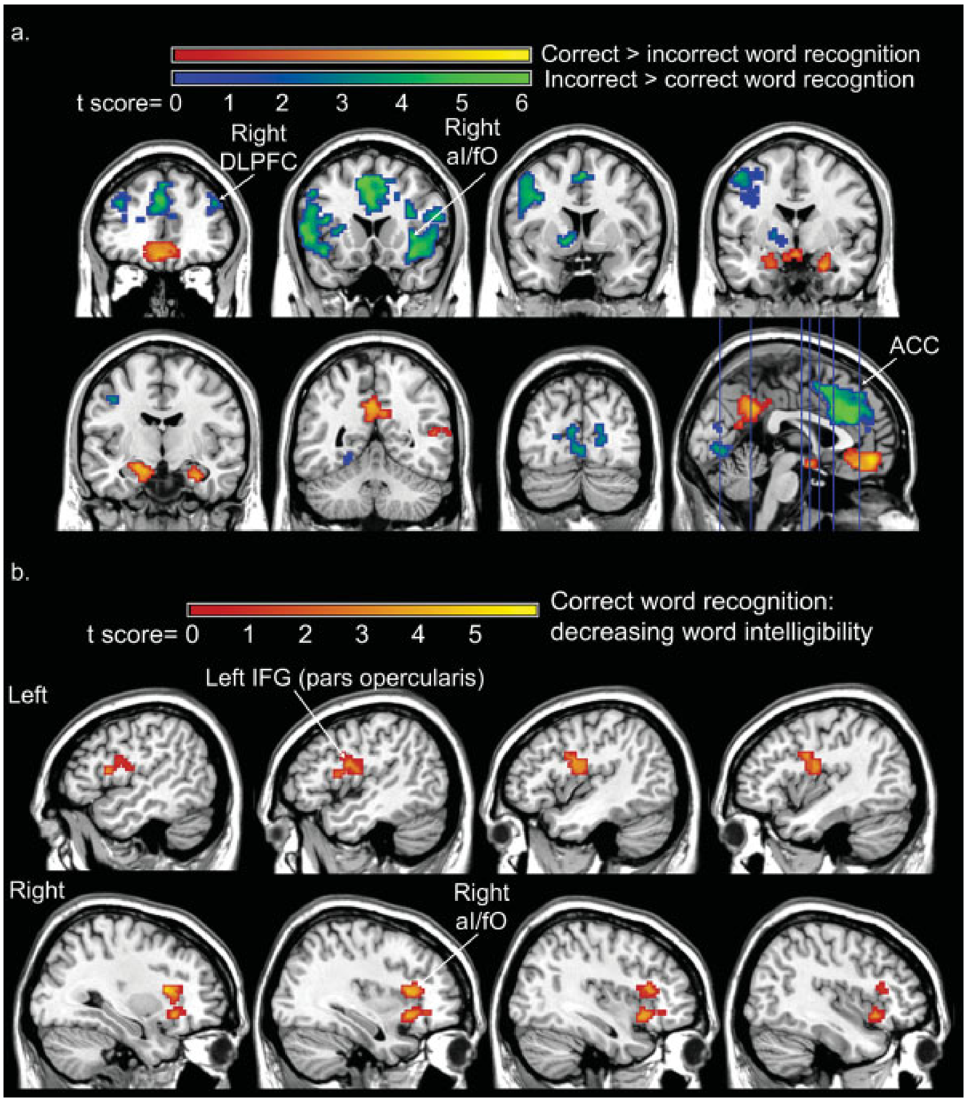

Figure 2.

(**a**) Incorrect compared with correct word recognition was associated with increased aI/fO, IFG, DLPFC, ACC, primary and secondary visual cortex bilaterally. Correct compared with incorrect word recognition was associated with increased medial prefrontal cortex, posterior cingulate, amygdala, and hippocampal activity bilaterally. (**b**) A parametric increase in right aI/fO was observed when the decreasing intelligibility analysis was restricted to correct word recognition response. Increased activity with decreasing word intelligibility was also observed in the left pars opercularis and left premotor cortex.

Relation to Task Performance

Task performance was examined to determine the extent to which increased frontal activity was associated with either superior or poor performance. Figure 2a shows that incorrect word recognition compared with correct word recognition resulted in significantly increased bilateral aI/fO, lateral inferior frontal gyrus, DLPFC, and ACC activity. Figure 2b shows, however, that a parametric increase in right aI/fO activity was observed for decreasing word intelligibility when the analysis was restricted to correct word recognition trials. Similar results were observed in the Eriksen flanker task data. Supporting Information Figure 3 shows that long reaction times and poor performance for the incongruent flanker trials, which were significantly correlated ($r_{(10)} = -0.95$), were associated with increased right aI/fO, IPS, and ACC activity.

Functional Connectivity of the Right aI/fO, ACC, and DLPFC

To determine the extent to which right aI/fO, ACC, and right DLPFC were part of the same functional network in

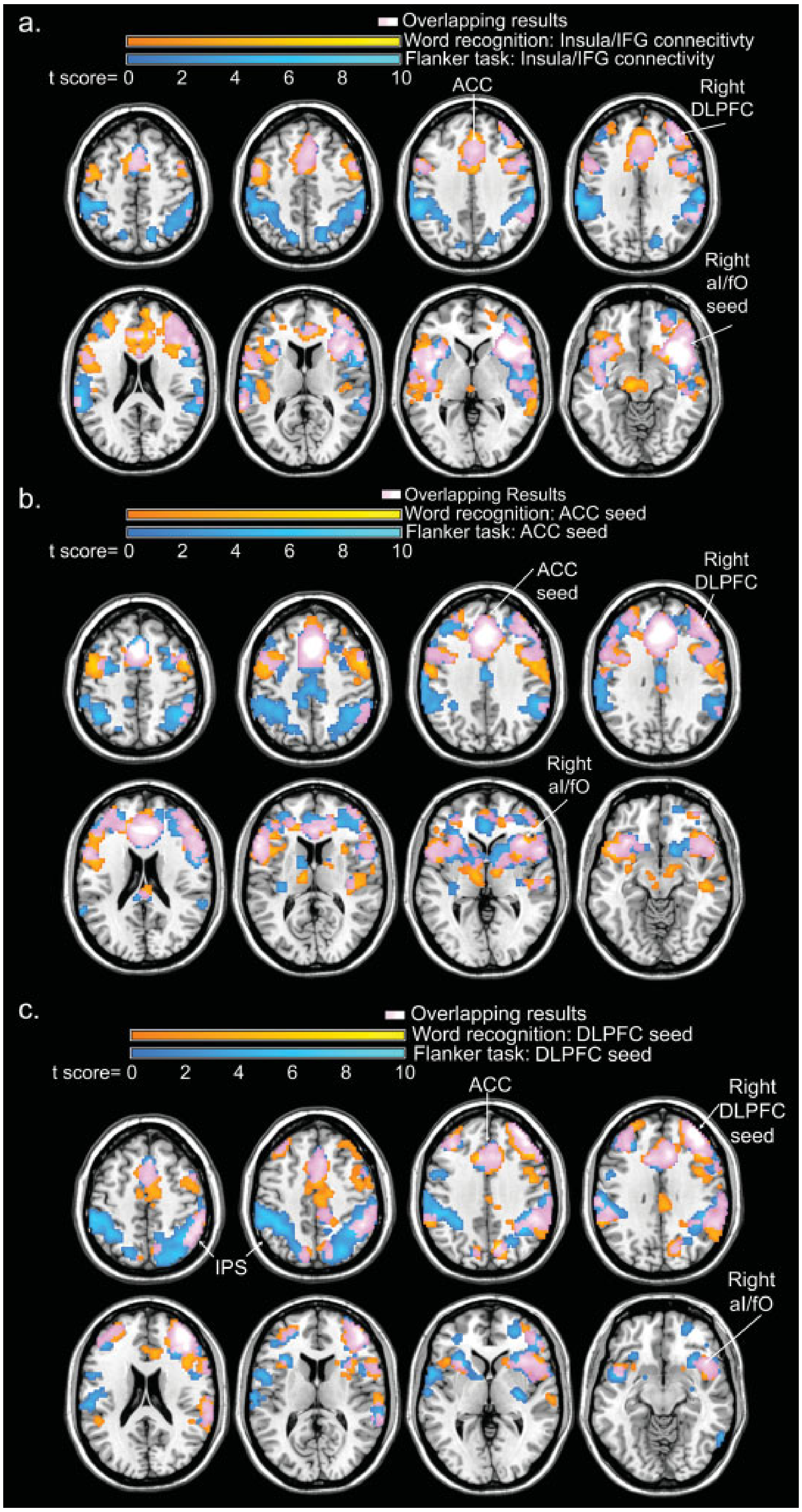

Figure 3.

Functional connectivity results for time series from the (**a**) right aI/fO, (**b**) ACC, and (**c**) right DLPFC clusters that were significantly activated in the word recognition (orange) and Eriksen flanker tasks (blue). The pink-white areas indicate areas that were significantly correlated with the aI/fO, ACC, or DLPFC in both tasks. The aI/fO, ACC, and DLPFC were significantly correlated across all three analyses.

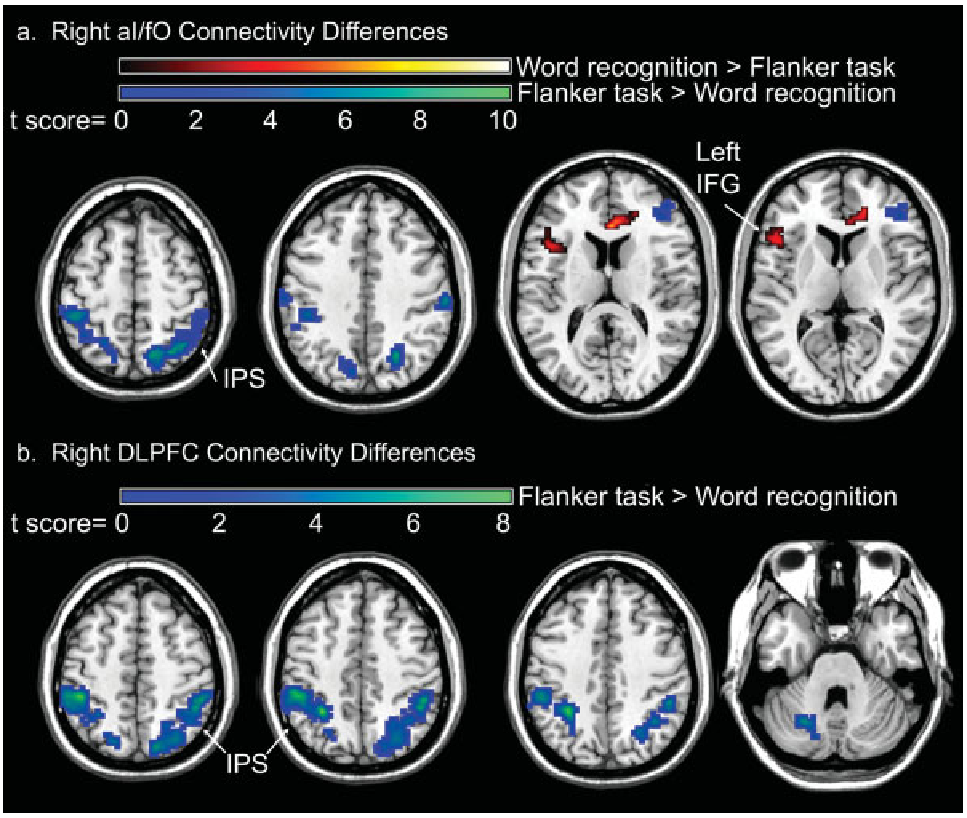

Figure 4.

Paired *t*-test results comparing differences in connectivity between the word recognition and flanker tasks for the right aI/fO and the right DLPFC. There were not significant differences in connectivity between the tasks for the ACC. (**a**) Right aI/fO: the increased left IFG connectivity during the word recognition task (orange-red) and bilateral intraparietal sulcus activity during the Eriksen flanker task (blue) are regions that were specifically activated by the word recognition and flanker tasks, respectively (shown in Fig. 1). (**b**) Right DLPFC: increased bilateral IPS connectivity during the Eriksen flanker task compared with the word recognition task.

the word recognition and Eriksen flanker tasks, functional connectivity was performed using the time series from these regions for each participant. Figure 3a and Supporting Information Table III demonstrate that the right aI/fO region exhibited significantly correlated activity with bilateral inferior frontal, bilateral DLPFC, and ACC regions in the word recognition and Eriksen flanker tasks. The functional connectivity results presented in Figure 3b,c, in which the functional connectivity analyses were initiated from the ACC and DLPFC, confirm that each of the three frontal regions exhibited significant correlated activity with each other over the course of the word recognition and Eriksen flanker tasks.

Figure 4a and Supporting Information Table III also demonstrate different patterns of correlated right aI/fO activity between the two experiments. A paired *t*-test comparing the functional connectivity patterns of correlated activity demonstrated that the right aI/fO region exhibited (1) significantly greater coupled activity with the left lateral inferior frontal gyrus during the word recognition task compared with the Eriksen flanker task and (2) significantly greater coupled activity with the parietal and visual cortex during the Eriksen flanker task compared with the word recognition task. These results are consistent with observations that the right aI/fO and the left inferior frontal cortex exhibit increased activity during language-related tasks [Bedny and Thompson-Schill, 2006; Binder et al., 2004; Giraud et al., 2004], whereas the right aI/fO and posterior parietal cortex exhibit increased activity during visual spatial tasks [Casey et al., 2000; Menon et al., 2001].

Task-related differences in connectivity were most pronounced when the right aI/fO was used as the seed point. There were no significant task-related differences for the ACC analysis. Figure 4b shows that the right DLPFC exhibited significantly increased correlated activity with bilateral IPS regions for the Eriksen flanker task compared with the word recognition task. No significant results were observed for the opposite contrast. These results demonstrate a trend for greater engagement of the right aI/fO with brain regions engaged by either visual or auditory tasks compared with the ACC or right DLPFC.

DISCUSSION

The results of this study are consistent with our predictions that (1) the right aI/fO (ventral attention system) exhibits significant functional connectivity with frontal lobe regions implicated in goal-directed behavior [dorsal attention system; [Fox et al., 2006; Seeley et al., 2007]] and (2) that the right aI/fO exhibits significant functional connectivity with brain regions specifically involved in task performance. These findings support hypotheses that the right aI/fO engages cognitive control systems by communicating the salience of a stimulus and represents task performance [Dosenbach et al., 2007; Sridharan et al., 2008]. The right aI/fO may be particularly critical for modulating cognitive control systems in challenging task conditions, in which cognitive control is necessary for optimal performance and for altering behavioral strategies in the face of declining performance.

Dorsal and Ventral Attention System Interactions

Resting state connectivity studies demonstrate dissociable patterns of correlated activity between brain regions (right aI/fO, right DLPFC, right ACC, amygdala, dorsomedial nucleus of the thalamus, ventral tegmental area, hypothalamus) that are hypothesized to support a salience or a ventral attention system and brain regions (bilateral dorsolateral prefrontal cortex, frontal eye fields, the supplementary motor area, caudate nucleus, and IPS) that are hypothesized to support executive function or a dorsal attention system [Fox et al., 2006; Seeley et al., 2007]. Studies involving perceptual and cognitive tasks, like this study, do not show such clear distinctions between these systems when there is a high attentional demand [Dosenbach et al., 2006]. For example, the right aI/fO (ventral attention system) exhibited robust correlated activity with regions in the IPS (dorsal attention system) during the Ericksen flanker task.

A retrospective study examining right aI/fO time course activity demonstrated that the right aI/fO is engaged throughout a task, from stimulus perception and response planning to the evaluation of task performance [Dosenbach et al., 2007]. Although we were not able to examine the time course of right aI/fO activity in this study because of our sparse sampling design, we did observe that the right aI/fO exhibits significant correlated activity with brain regions specifically involved with a task and regions generally engaged across tasks, as well as exhibiting significant associations with task performance. These results suggest that the right aI/fO modulates the activity of other brain regions during challenging tasks.

An alternative explanation for the correlated activity of the right aI/fO with brain regions specifically involved in the task and with regions consistently engaged across behavioral tasks is that the correlated activity simply reflects elevated autonomic response to challenging tasks and does not reflect a specific role in coordinating behavioral responses. However, recent evidence suggests that aI/fO activity drives the activity within other brain regions during task performance [Corbetta et al., 2008; Sridharan et al., 2007]. Indeed, the right aI/fO appears to have a causal role in the initiation of cognitive control systems based on Granger causality analysis results showing that right aI/fO activity precedes activity in DLPFC during auditory and visual attention tasks [Sridharan et al., 2008].

Task Demands

We observed a task-dependent dissociation in the correlated activity of the right aI/fO that supports the premise for selective right aI/fO engagement of brain regions specifically involved in a task. For example, the right aI/fO exhibited significantly greater correlated activity with bilateral intraparietal sulcus regions during the Eriksen flanker task compared with the word recognition task. Conversely, the right aI/fO exhibited significantly greater correlated activity with the left aI/fO and left inferior frontal gyrus regions during the word recognition task compared with the Eriksen flanker task.

Although there was a significant difference in right and left aI/fO correlated activity between the tasks, right aI/fO activity was significantly correlated with left aI/fO activity across tasks and this observation is consistent with functional connectivity findings that homologous regions in each hemisphere exhibit significantly correlated patterns of activation [Salvador et al., 2005]. However, the functional significance of this correlated activity across tasks is not clear. There is uncertainty in the extant literature regarding the degree to which the left aI/fO is specifically involved in speech articulation [Dronkers, 1996] versus nonspeech motor function [Bonilha et al., 2006]. The results of this study suggest that there is a greater interaction between left and right aI/fO during word recognition than when selecting a nonspeech motor response (flanker task button press). This study was not designed to characterize the role of the left aI/fO, but the results do suggest that task difficulty is a critical factor in the pattern of left aI/fO activity and the degree to which it exhibits correlated activity with the right aI/fO.

Increased right aI/fO activation was associated with poor performance during the word recognition and Ericksen flanker tasks. These results are consistent with evidence that activity in the right aI/fO is associated with increased responsiveness to challenging tasks in which subjects require long reaction times to perform a task [Binder et al., 2004] and when they make behavioral errors [Menon et al., 2001; Ramautar et al., 2006]. An examination of trials in which subjects made correct responses indicated, however, that the right aI/fO is engaged not only when people make an error but also when they make a correct response in challenging task conditions, thereby suggesting that right aI/fO activity reflects the difficulty of a task. More broadly, these results support the premise that right aI/fO is important for evaluating the saliency of the stimuli and task outcome [Dosenbach et al., 2007].

The engagement of right aI/fO during challenging tasks involving salient stimuli has implications for studies of clinical populations, particularly those with developmental or age-related speech and language impairments. Our results guide the prediction that speech and language disability is associated with increased right aI/fO activity during tasks that are relatively easy for control groups. In support of this prediction, increased right aI/fO activity has been observed in: (1) dyslexic adults compared with controls during a syllable perception task [Dufor et al., 2007]; (2) older dyslexic children compared with younger dyslexic children during a nonword rhyming task [Shaywitz et al., 2007]; and (3) older adults with poor word generation performance and reaction time compared with younger adults during a verb generation task [Persson et al., 2004]. In the context of aI/fO involvement in autonomic system function [Abboud et al., 2006; Hoffman and Rasmussen, 1953; Meyer et al., 2004; Penfield and Faulk, 1955], the engagement of aI/fO appears to reflect the control of arousal in the face of challenging task conditions.

The Right aI/fO and Saliency

Several lines of evidence from lesion, electrophysiological, and anatomical studies indicate that the right aI/fO aids in the evaluation of stimulus or task salience and allocates the appropriate arousal for successful task performance. In particular, the right anterior insula appears to support cortical control of sympathetic nervous system function. For example, right anterior insula lesions lead to elevated heart rate [Abboud et al., 2006] and peripheral noradrenergic transmitter levels [Meyer et al., 2004]. In addition, stimulation of the anterior insula influences gastrointestinal motility [Penfield and Faulk, 1955]. Recent functional imaging evidence demonstrates that galvanic skin response and heart rate measures of arousal are related to the level of right anterior insula activity [Critchley et al., 2002], and that individuals with anxiety disorders exhibit elevated right anterior insula activity [Etkin and Wager, 2007]. Consistent with these functional observations, anatomical studies of the right aI/fO demonstrate connections with ACC, principal sulcus (area 46), orbitofrontal cortex, hypothalamus, amygdala and throughout the medial temporal lobe [Mesulam and Mufson, 1982b; Mufson and Mesulam, 1982]. Based on this evidence, the right anterior insula has been hypothesized to integrate autonomic, visceral, and sensory information to provide an interoceptive representation of the body that guides decision making [Craig, 2003; Critchley et al., 2002; Mesulam and Mufson, 1982a]. For example, Mesulam and Muffson [1982b] wrote "...anterior insula may participate in a wide range of behavior ranging from the modulation of complex ingestive behavior to the expression of autonomic patterns in response to affective tone" (p51).

Based on the evidence reviewed earlier and the results of this study, a speculative hypothesis here is that excessive ventral attention system activity may limit optimal engagement of problem-solving systems and instead produce elevated autonomic arousal that may limit performance. In this context, the level of ventral system activity relative to dorsal attention system activity may form the basis for the Hebb/Yerkes-Dobson law, which states that optimal performance is associated with an optimal level of arousal, and that too little arousal or too much arousal is associated with declines in perception [Easterbrook, 1959; Hebb, 1955] and learning [Broadhurst, 1957; Yerkes and Dodson, 1908]. In support of this hypothesis, Seeley et al. [2007] demonstrated that elevated ventral attention system activity was associated with prescan anxiety levels but not dorsal-attention related systems, whereas superior task switching attention performance was related to increased dorsal attention system activity during a resting state task.

CONCLUSIONS

The results of this study indicate more significant interaction between dorsal and ventral attention systems than previously described based on resting state studies [Fox et al., 2006; Seeley et al., 2007], which is consistent with the premise that the right aI/fO is important for monitoring performance and selecting appropriate response strategies [Dosenbach et al., 2007]. An important issue that could not be addressed because of limitations of our sparse sampling experimental design is the extent to which activity within the right aI/fO modulates that activity within DLPFC regions that is important for planning behavior. A task design relying on a more rapid scanning acquisition than used in this study could examine the extent to which aI/fO activity precedes the onset of correlated DLPFC activity [Sridharan et al., 2008] and the extent to which the degree of right aI/fO activity throughout a task is related to performance. We suggest that the ventral attention system modulates the excitability of the dorsal attention system and task specific systems. Too little right aI/fO activity or too little autonomic arousal [attention deficit; [Dickstein et al., 2006]] may fail to entrain DLPFC, thereby resulting in careless mistakes, whereas too much right aI/fO activity limits DLPFC function and selection of optimal responses in people with elevated anxiety [Etkin and Wager, 2007].

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