

The role of the insula in speech and language processing



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ABSTRACT

Lesion and neuroimaging studies indicate that the insula mediates motor aspects of speech production, specifically, articulatory control. Although it has direct connections to Broca's area, the canonical speech production region, the insula is also broadly connected with other speech and language centres, and may play a role in coordinating higher-order cognitive aspects of speech and language production. The extent of the insula's involvement in speech and language processing was assessed using the Activation Likelihood Estimation (ALE) method. Meta-analyses of 42 fMRI studies with healthy adults were performed, comparing insula activation during performance of language (expressive and receptive) and speech (production and perception) tasks. Both tasks activated bilateral anterior insulae. However, speech perception tasks preferentially activated the left dorsal mid-insula, whereas expressive language tasks activated left ventral mid-insula. Results suggest distinct regions of the mid-insula play different roles in speech and language processing.

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1. Introduction

Speech and language production is a complex cognitive, motor and sensory process mediated by a host of interconnected cortical and subcortical regions including the left inferior frontal gyrus (IFG; BA 44/45), primary motor cortex (BA 4), premotor cortex (BA 6), superior temporal gyrus (BA22) and basal ganglia (Guenther, 2006). The classic neuropsychological models point to the left inferior frontal gyrus, or Broca's area, as the hub of speech and language production (Broca, 1861; Geschwind, 1970). However, based on lesion studies with patients with articulation difficulties, the insula has also been put forth as a brain region involved in the motor control of speech production (Cereda, Ghika, Maeder, & Bogousslavsky, 2002; Dronkers, 1996; Duffau, Bauchet, Lehericy, & Capelle, 2001; Starkstein, Berthier, & Leiguarda, 1988).

The insula shares reciprocal functional and structural connections with linguistic, motor, limbic and sensory brain areas (Augustine, 1996). Based on these findings, there has been speculation that the insula is involved in certain aspects of speech and language (Augustine, 1985). Additionally, the insula is involved in other perceptual-motor functions such as feeding behaviors,

interoception (i.e., internal monitoring of bodily states), and also autonomic processes (e.g., respiratory control). The coordination and control of these functions are essential for the smooth, coordinated production of speech (Craig, 2002, 2003).

The role of the insula in speech production arose from studies in patients who suffered from an apraxia of speech, usually as a consequence of stroke (Dronkers, 1996; Nagao, Takeda, Komori, Isozaki, & Hirai, 1999; Ogar et al., 2006; Ogar, Dronkers, Brambati, Miller, & Gorno-Tempini, 2007). Patients with articulatory dysfunction in the absence of a muscular problem (i.e., dysarthria), had lesions in the left superior tip of the precentral gyrus of the insula (Dronkers, 1996). Other studies with patients with progressive apraxia (Nestor et al., 2003), reduced fluency (Bates et al., 2003; Borovsky, Saygin, Bates, & Dronkers, 2007), or impairments with rapidly changing articulatory movements (Baldo, Wilkins, Ogar, Willock, & Dronkers, 2011) were also reported to have left anterior insular damage. Neuroimaging studies with healthy studies also suggested that the left precentral gyrus of the insula is involved in articulatory coordination (Murphy et al., 1997). Results indicate that the region may be preferentially involved in speech motor control, and may not be essential for language processing.

Contrary to these data is evidence from experimental neuroimaging studies with healthy adults indicating that the insula may be a core region for both speech and language processing. For example, Eickhoff, Heim, Zilles, and Amunts (2009) performed meta-analyses of fMRI and PET studies of expressive language tasks

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and demonstrated a core network of activation in BA 44, anterior insula, caudate nucleus, cerebellum, pre- and primary motor cortices. In this same paper, the authors examined the effective connectivity between these areas during speech production and concluded that the insular cortex may function as a relay between the cognitive aspects of language analyzed in BA 44 and the motor preparation for vocalization in basal ganglia and cerebellum. This finding was later supported by Activation Likelihood Estimation (ALE) meta-analyses of neuroimaging studies examining normal speech production and the comprehension of distorted speech (Adank, 2012). Left anterior insula was associated with speech production; however, bilateral anterior insulae activations were associated with distorted speech comprehension suggesting increased insular recruitment during difficult speech-language processing.

Based on these previous findings and the known anatomical connectivity of the insula, it is possible that the insula also mediates higher-order cognitive functions involved in speech and language processing. However, no single study has assessed whether the insula is primarily involved in speech motor control, or if it plays a supportive role in both speech and language processing. If the insula functions as a hub, connecting speech and language areas, it should be activated by both types of tasks; whereas, if the insula is solely involved in speech articulation, it should also be seen in cases of overt language production, but not with other types of language processing where articulation is controlled.

We tested this hypothesis using a meta-analysis of fMRI studies that reported insular activation during language (expressive and receptive) and speech (production and perception) tasks. We distinguished language and speech based on whole-word content. If whole words, or sequences of whole words were involved, this was classified in the 'language' category; however, if parts of words (e.g., syllables, syllable sequences or phonemes) were involved, this was classified in the 'speech' category. We implemented the ALE method (Eickhoff, Laird, Grefkes, Wang, Zilles, et al., 2009; Turkeltaub, Eden, Jones, & Zeffiro, 2002) to generate three-dimensional probability maps that described the spatial extent and localization of activation in the insula associated with language and speech processing.

2. Methods

2.1. Article selection and literature search

Studies reporting language or speech-evoked activation in the insula were obtained from an initial broad search of the literature using the Web of Science (<http://www.isiknowledge.com>) from January 1990 to September 2012. To identify all potential studies reporting insula activation in language and speech processing as measured by fMRI, the keywords used were: functional magnetic resonance imaging, insula, language and speech. A total of 59 studies were found.

Articles were screened for specific inclusion and exclusion criteria before analysis using the ALE method. Inclusion criteria consisted of studies that: (1) were written in English; (2) were performed as fMRI experiments; (3) reported stereotactic coordinates; (4) used healthy adult human participants; (5) used high-quality stimuli (i.e., non-degraded); and (6) applied a general linear model for analysis. Exclusion criteria were: (1) data from patients, case studies, or special populations, (2) functional connectivity (not localization) analyses, (3) pharmacological interventions, (4) deactivation coordinates, and (5) review articles or meta-analyses. As a result, 17 articles were excluded (tested clinical populations: 7; used reading paradigms: 3; assessed emotional tones of word stimuli: 2; assessed pitch processing: 2; completed laterality analysis: 1; presented speeded speech stimuli: 1; assessed working memory 1).

A total of 42 studies met our criteria and were included in the meta-analysis. For each article, the following information was recorded: author names, academic journal title, year of publication, number of participants, mean age of participants, gender of participants, handedness of participants, strength of MRI scanner in Tesla (T), task description, stimulus type, language of stimulation, and contrast(s) of interest.

The studies were further categorized into language and speech tasks. Studies that involved covert or overt linguistic processing (e.g., whole words, syntax, word morphology, pragmatics) were categorized as language studies; this resulted in a total of 28 articles (Table 1). These studies were divided into 'receptive' and 'expressive' language categories. The 'receptive' category included studies of language reception and comprehension, such as listening to words and making a semantic judgment. The 'expressive' category included studies of covert and overt language production. For example, this category would include studies asking participants to produce as many words possible beginning with a visually presented letter.

Fourteen studies used phonetic, syllabic, or non-word stimuli and were categorized as speech studies (Table 1). The studies were then divided into speech 'perception' and 'production' categories. The 'perception' category included studies that presented simple and complex speech stimuli. For example, this would include studies asking participants to passively listen to nonsense syllables, or studies requiring subjects to classify phonemes or speech sounds. The 'production' category included articles where subjects produced a speech sound or sounds. This would include studies involving the pronunciation of syllable sequences; however, full words were not produced.

2.2. Meta-analytic method

Activation foci reported for each study were entered into four separate meta-analyses (receptive language, expressive language, speech perception, and speech production). To account for spatial disparities between MNI and Talairach brain templates used across studies, coordinates reported in MNI space were converted to Talairach space using the Lancaster transform, icbm2tal, within the GingerALE software package (Laird et al., 2010; Lancaster et al., 2007; Talairach & Tournoux, 1988). All further analyses were conducted in Talairach space, and figures are presented in TAL space.

The ALE method (Eickhoff et al., 2009; Laird et al., 2005; Turkeltaub et al., 2002) was used to create probabilistic maps that describe the spatial location and extent of activation in response to each of the four categories of interest. Reported foci were treated as the center of probability distributions within a standard image space (GingerALE v 2.1.1 – <http://brainmap.org/ale/>). Data were smoothed using a Gaussian blurring kernel. The size of each kernel's full-width at half maximum (FWHM) was calculated based on the number of participants in each individual study. For each voxel in the brain, the probability of activation for all reported foci was computed, resulting in an ALE value. A permutation test was then utilized to distinguish real convergence across studies from random convergence or "noise". This process compared each study's ALE values to a null-distribution of randomly generated ALE values. The creation of the ALE null-distribution values involved the sampling of a random voxel from each study 2×10^{10} times. Data were corrected for multiple comparisons using the false discovery rate (FDR) with $q = 0.001$ (Laird et al., 2005). The resultant ALE maps contain voxels that have a significant probability of activation. To view these results, the ALE maps were overlaid on a template MRI (Colin1 in Talairach space) using the program mricron (<http://www.mccauslandcenter.sc.edu/mri-cro/mricron/>). Anatomical areas within the insular cortex were categorized according to Craig (2009).

Table 1
Summary of included studies.

Study (year)	Imaging	N	Task	Language	Stimulus type	Modality
<i>Receptive language</i>						
Anderson et al. (2010)	fMRI 3.0	15	Auditory-phase recognition	English	Phrase and sentence	Sound
Buchweitz, Keller, Meyler, and Just (2012)	fMRI 3.0	12	Dual-tasking	English	Sentence	Sound
Carreiras, Mechelli, and Price (2006)	fMRI 1.5	16	Lexical decision	Spanish	Word	Visual
Fiebach, Friederici, Muller, von Cramon, and Hernandez (2003)	fMRI 1.5	12	Lexical decision	German	Noun and pseudo word	Visual and sound
Gandour et al. (2007)	fMRI 1.5	10	Sentence comprehension	Chinese English	Sentence	Sound
Hernandez et al. (2004)	fMRI 3.0	9	Grammatical gender decision	Spanish	Noun	Visual
Hesling, Clement, Bordessoules, and Allard (2005)	fMRI 3.0	12	Passive listening	English	Sentence	Sound
Isel, Baumgaertner, Thran, Meisel, and Buchel (2010)	fMRI 3.0	20	Semantic categorization	French	Noun	Visual
				German		
Mason and Just (2007)	fMRI 1.5	12	Lexical ambiguity	English	Sentence	Visual
Noesselt, Shah, and Jancke (2003)	fMRI 1.5	10	Passive listening	German	Noun	Sound
			Semantic categorization			
Sass, Krach, Sachs, and Kircher (2009)	fMRI 1.5	15	Lexical decision	English	Word	Visual and sound
Schmidt and Seger (2009)	fMRI 3.0	10	Metaphor comprehension	English	Literal sentence metaphorical sentence non-word sentence	Visual
Thompson, den Ouden, Bonakdarpour, Garibaldi, and Parrish (2010)	fMRI 3.0	7	Sentence comprehension	English	Sentence and picture	Sound
						Visual
Zemleni, Haverkort, Renken, and Stowe (2007)	fMRI 3.0	17	Relatedness judgement task	Dutch	Figurative sentence Ambiguous sentence	Visual
<i>Expressive language</i>						
Abel, Dressel, Weiller, and Huber (2012)	fMRI 3.0	19	Picture-word interference	German	Drawing	Visual
Chee, Soon, Lee, and Pallier (2004)	fMRI 3.0	30	Phonological working memory	French	Word and pseudo word	Sound
Christoffels, Formisano, and Schiller (2007)	fMRI 3.0	14	Overt picture naming	Dutch	White-on-black drawing	Visual
Gauthier, Duyme, Zanca, and Capron (2009)	fMRI 1.5	44	Covert verbal fluency	French	Letter	Sound
Grande et al. (2012)	fMRI 3.0	18	Picture description	German	Line drawing	Visual
Haller, Radue, Erb, Grodd, and Kircher (2005)	fMRI 1.5	15	Sentence generation	German	Three word	Visual
Heim, Oritz, and Friederici (2002)	fMRI 3.0	12	Picture naming	German	Line drawing	Visual
Loevenbruck, Baci, Segebarth, and Abry (2005)	fMRI 3.0	16	Speech production	French	Sentence	Visual
Lurito, Kareken, Lowe, Chen, and Mathews (2000)	fMRI 1.5	5	Covert word generation	English	Letter	Visual
Mechelli, Josephs, Lambon Ralph, McClelland, and Price (2007)	fMRI 3.0	20	Reading and picture naming	English	Word pair	Visual
Richter, Miltner, and Straube (2008)	fMRI 1.5	8	Word stem completion	German	Word stem	Visual
Riecker, Ackermann, Wildgruber, Dogil, and Grodd (2000)	fMRI 1.5	18	Overt speech	German	Symbol	Visual
Shuster and Lemieux (2005)	fMRI 1.5	10	Overt word production	English	Noun	Sound
Voets et al. (2006)	fMRI 3.0	12	Covert phonemic fluency	English	Letter	Visual
			Covert semantic fluency		Category name	
<i>Speech perception</i>						
Aleman et al. (2005)	fMRI 1.5	6	Metrical stress evaluation	Dutch	Bisyllabic word	Sound
Benson et al. (2001)	fMRI 1.5	12	Passive listening	English	Nonsense syllable (V, CV, CVC)	Sound
Falkenberg, Specht, and Westerhausen (2011)	fMRI 3.0	40	Dichotic listening	English	CV syllable	Sound
Golestani and Zatorre (2004)	fMRI 1.5	10	Phonetic contrast identification	English	CV syllable	Sound
Marvel and Desmond (2012)	fMRI 3.0	16	Verbal working memory	English	Letter	Visual
Szenkovits, Peelle, Norris, and Davis (2012)	fMRI 3.0	21	Active listening	English	CVC pseudo word	Sound
<i>Speech production</i>						
Bohland and Guenther (2006)	fMRI 3.0	13	CV syllable production	English	Three syllable sequence	Visual
Brendel et al. (2010)	fMRI 1.5	18	Syllable (/ta/) production	German	Acoustic click	Sound
Dogil et al. (2002)	fMRI 1.5	18	Syllable production	German	Syllable	Visual
Golestani and Pallier (2007)	fMRI 3.0	21	Phoneme production	French	CV syllable	Sound
				Persian	Bisyllabic non-word	
Moser et al. (2009)	fMRI 3.0	30	Speech repetition	English	Multisyllabic non-word	Sound
Riecker, Brendel, Ziegler, Erb, and Ackermann (2008)	fMRI 3.0	9	Syllable production	German	Bisyllabic pseudo word	Visual
Riecker, Kassubek, Groschel, Grodd, and Ackermann (2006)	fMRI 1.5	8	Syllable (/pa/) production	English	Click series	Sound
Soros et al. (2006)	fMRI 3.0	9	Syllable (/pataka/) production	English	Verbal cue	Sound

3. Results

3.1. Demographic information

The 44 studies of speech and language tasks included 639 participants (58.5% male). The median age across studies was computed from the reported mean age in each study, and was 28.5 yrs ($SD = 3.2$). The majority (88.9%) of the studies assessed handedness. Most studies tested right-handed individuals with only a few including left-handed or ambidextrous individuals. Details of the studies included in the meta-analyses are listed in Table 1.

3.2. Receptive language stimuli

A total of 64 foci were extracted from 14 studies reporting activation in the insula associated with receptive language tasks. Activations occurred in the accessory gyrus of the anterior insula, bilaterally. A portion of the left-sided cluster was observed in the region of the dorsal dysgranular zone of the anterior short insular gyrus as seen in the bottom left corner of Fig. 1 (Table 2).

3.3. Expressive language stimuli

Expressive language functions were associated with 41 foci from 14 studies. These stimuli were most likely to activate the left

accessory gyrus in the territory of the dorsal dysgranular zone. Activation was observed in the region of the left anterior short insular gyrus that extended into the ventral mid-insula (Fig. 1; Table 2). A small non-significant peak was located in the right anterior insula.

3.4. Speech perception stimuli

Speech perception stimuli were associated with 18 foci from 6 studies. In response to these stimuli, left-sided activations occurred in the region of the granular zone of the dorsal middle short insular gyrus. Right-sided activations were more likely to occur in a slightly more anterior region, that is, in the ventral granular zone of the anterior short insular gyrus (Fig. 2; Table 2).

3.5. Speech production stimuli

The ALE maps for speech production were created from 38 foci from 8 studies. Activations were localized predominately on the left side, in the accessory gyrus and anterior short insular gyrus. A small right-sided cluster of activation was observed in the region of the dorsal dysgranular accessory gyrus (Fig. 2; Table 2).

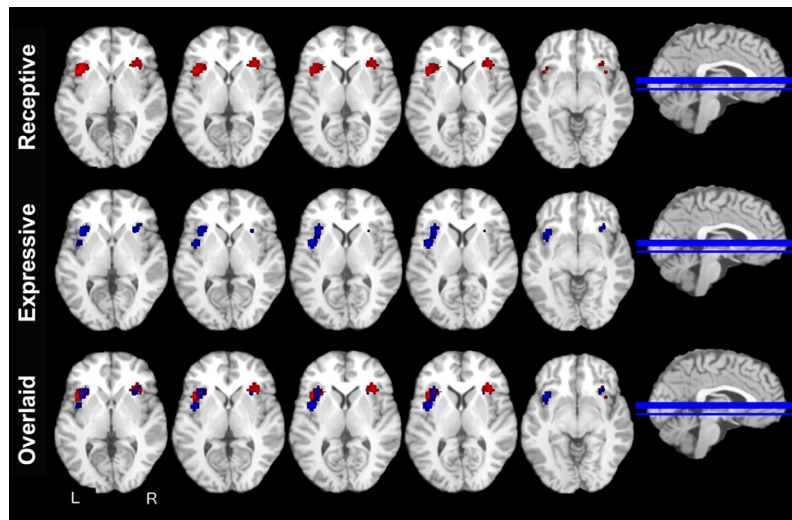


Fig. 1. ALE meta-analyses across language studies. Multi-slice ALE maps for receptive language stimuli displayed in red (top row), expressive language stimuli displayed in blue (middle row), and overlaid language stimuli (bottom row). ALE maps are overlaid on axial slices from a template in TAL space. These figures show that for receptive language, activations occurred in the accessory gyrus of the anterior insula bilaterally. For expressive language, activations were most likely to activate the left accessory gyrus in the territory of the dorsal dysgranular zone.

Table 2

Results from meta-analyses for all speech and language stimuli. Activation foci obtained from insula responses to language and speech stimuli. Activation Likelihood Estimation (ALE) values range from a minimum of 0 to a maximum of 1. Greater likelihood of activation in response to stimuli is indicated by higher ALE values. Significant clusters of voxels are listed in order from largest to smallest. Coordinates are in Talairach space (Talairach & Tournoux, 1988).

Stimuli	Side	Insula region	Cluster #	x	y	z	Volume (mm ³)	ALE value	P value
Receptive language	Left	Anterior	1	−36	16	5	4056	0.02	<0.000001
	Right	Anterior	2	33	21	3	2168	0.02	<0.000001
	Right	Mid	3	38	−3	16	408	0.01	<0.000001
	Left	Anterior	4	−38	−13	11	320	0.01	<0.000001
Expressive language	Left	Anterior	1	−35	11	3	3896	0.02	<0.000001
	Right	Anterior	2	31	20	−1	936	0.02	<0.000001
Speech perception	Left	Mid	1	−35	7	10	1896	0.03	<0.000001
	Right	Anterior	2	38	9	12	184	0.02	<0.000001
	Right	Anterior	3	48	27	21	48	0.01	<0.000001
Speech production	Left	Anterior	1	−35	14	5	3176	0.06	<0.000001
	Right	Anterior	2	35	20	8	440	0.03	<0.000001
	Left	Anterior	3	−36	6	10	8	0.02	<0.000001

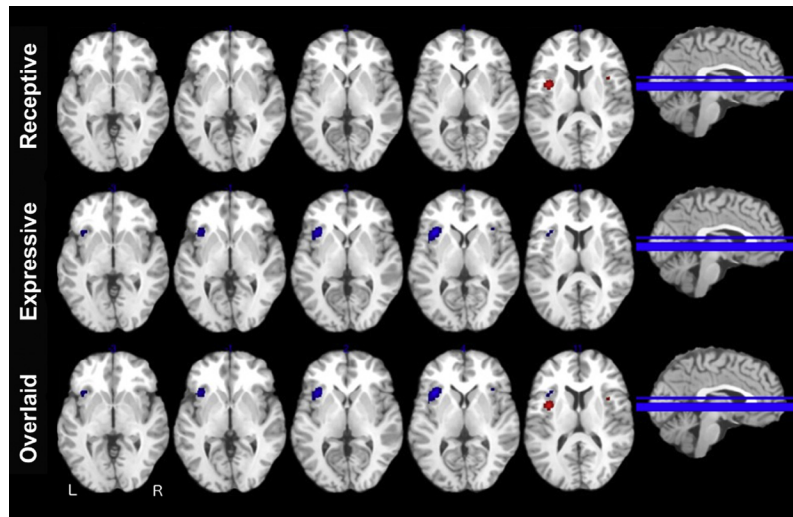


Fig. 2. ALE meta-analyses across speech studies. Multi-slice ALE maps for speech perception stimuli displayed in red (top row), speech production stimuli displayed in blue (middle row), and overlaid speech stimuli (bottom row). ALE maps are overlaid on axial slices from a template in TAL space. These figures show that for speech perception, activations occurred in the granular zone of the left dorsal middle short insular gyrus. For speech production, activations were predominately in the left accessory gyrus and left anterior short insular gyrus.

4. Discussion

Using an ALE-based meta-analysis of existing functional neuroimaging data, we provide information on the spatial location and extent of activation in the insula during various speech and language tasks. Our results are striking in that it is evident that receptive language, expressive language and speech production activate very similar regions of the anterior insula while activation in response to the perception of speech was processed separately in the left dorsal mid insula. As well, expressive language further showed activations in the left ventral mid-insula. Moreover, all tasks activated bilateral regions in the insula; the language tasks were more equally bilaterally represented while the speech tasks tended to show more left-hemisphere dominance.

4.1. Receptive and expressive language

For the language tasks, activations were similar for both receptive and expressive language stimuli. These tasks were most likely to activate bilateral anterior regions of the insula, specifically, the accessory insular gyrus; and in the left hemisphere, the spatial extent of the likelihood of activation spread to the anterior short insular gyrus. The only distinction between the receptive and expressive language tasks was a discrete ALE peak of activation in left mid-insula for the expressive language task.

Activation of the left anterior insula with these language tasks was not surprising as this area is known to have a direct anatomical connection to inferior frontal and lateral frontal regions (Kalab, Molnár, Bogner, Béres, & Berényi, 2012). Further, the left anterior insula has extensive and reciprocal functional connections with frontal areas involved in language processing, such as the prefrontal cortex and frontal operculum (Augustine, 1996). Specifically, IFG activation has been associated with semantic retrieval, lexical decisions, and the generation of semantic categories. Finally, neuroimaging studies have implicated the IFG in syntactic processing (e.g., Friederici, Bahlmann, Heim, Schubotz, & Anwander, 2006; Kaan & Swaab, 2002; Roder, Stock, Neville, Bien, & Rosler, 2002). These classic areas are known to be involved in language processing; and, the IFG has been long associated with the semantic, phonological and syntactic aspects of language (e.g., Bedny, Caramazza, Grossman, Pascual-Leone, & Saxe, 2008; Kemeny, Ye,

Birn, & Braun, 2005; Rodd, Johnsrude, & Davis, 2010). Studies reported that the frontal operculum is involved in sentence comprehension (Friederici & Kotz, 2003; Friederici et al., 2006) and syntactic speech (Friederici, Meyer, & von Cramon, 2000). This activation was observed predominantly in the left hemisphere and emphasizes that the left frontal cortex is associated with the processing of syntactic information.

Of note, while the classic Broca–Wernicke model of language separates expressive and receptive language into frontal and temporal foci, respectively, there is now substantial empirical evidence that the language system is much more complex. In a meta-analysis of 485 neuroimaging studies, Liakakis, Nickel, and Seitz (2011) showed that the IFG (canonical Broca's area) is involved in both the perceptive and productive aspects of language. In fact, studies have found that bilateral insular damage may produce total auditory agnosia (Bamiou, Musiek, & Luxon, 2003). A functional imaging study showed that the insula was involved in several key processes such as auditory attention allocation, auditory tuning to novel stimuli, temporal processing, phonological processing, and auditory-visual integration (Bamiou et al., 2003). Thus, it is possible that the anterior insulae serves as an integration hub for auditory stimuli and plays a role in auditory processing as well (Bamiou et al., 2003).

Another interesting finding is that the right anterior insula was activated by both language tasks. While language is considered to be left-hemisphere dominant, substantial evidence indicates that the right hemisphere is also important for language processing. Therefore, activity in the right anterior insula could be heightened during language tasks due to the existence of functional connections with frontal right-hemisphere regions that support language functioning. These were the conclusions of a PET study, which found bilateral activation in anterior insulae elicited by sentence stimuli (Wong et al., 2002). Right hemisphere frontal areas offer resources to maintain language function and this points to the high likelihood of a pre-existing language network in the right hemisphere that can be recruited when needed (Perani et al., 2003; Voets et al., 2006; Winhuisen et al., 2005). For example, a number of reports indicate that language dominance shifts to homologous right-hemisphere regions following a disabling left hemisphere brain injury (Lazar et al., 2000; Staudt et al., 2002; Tivarus, Starling, Newport, & Langfitt, 2012). However, the role of the right insula in language processing requires further study to determine

its specificity of function as the activation could be related to other cognitive processes subserving irrelevant task features.

Although syntactic and semantic processes are supported primarily by the left-hemisphere, the processing of prosody is primarily a function of the right-hemisphere (Gandour et al., 2004; Pell, 2006; Friederici, 2002). More specifically, frontal brain regions in the right hemisphere play a role in the comprehension and production of affective prosody. George et al. (1996) used PET to examine the brain regions involved in understanding emotional prosody versus content-based emotion. An increase in activity in the right prefrontal cortex was observed during the detection of emotional prosody of verbal sentences. On the other hand, left prefrontal activation was observed when participants were asked to concentrate on the content of sentences instead of the prosody. More recently, an fMRI study investigating neural responses to sentences varying in pitch information (normal intonation versus synthesized flattened speech) and syntactic information (normal speech versus synthesized, de-lexicalized speech) found right fronto-lateral activation in response to prosodic cues. The right-superior temporal region and fronto-opercular cortex were identified as being more involved in processing prosodic information (Meyer, Alter, & Friederici, 2003). These findings suggest that the right hemisphere frontal lobe support prosodic comprehension. Finally, in an experiment by Pell (1999), subjects with right hemisphere brain damage were found to employ fewer prosodic cues than healthy controls in a sentence elicitation task, resulting in a reduction of emotional inflection as perceived by the listeners. While we did not specifically assess prosody within the current study, potentially some tasks included in the meta-analyses used prosodic stimuli that evoked activity in the right hemisphere. The results of our meta-analysis provide support for the hypothesis that right-hemisphere areas, in particular the anterior insula, mediate the production and perception of prosodic elements of language. Future work in this area should examine activation in the insula in response to tasks with and without prosodic linguistic stimuli to clarify its contribution to these processes.

The left ventral mid-insula showed preferential activation in response to language production tasks. The role of the ventral mid-insula in language processing remains unclear although this region looks similar to the insular region implicated in patients with apraxia of speech (Dronkers, 1996; Nestor et al., 2003). These regions need to be directly compared for confirmation. The right mid-insula has been implicated in viscerosensory processing, that is, processing regarding the state of one's own body (Menon & Uddin, 2010), particularly linking representations of the outside world with the body's internal state (Farb, Segal, & Anderson, *in press*). Therefore the left mid-insula may serve the function of monitoring the body's internal state, but focuses particularly on language impact and relations. This is purely speculative, however, and requires empirical testing.

4.2. Speech perception and production

For the speech tasks, our meta-analysis revealed some distinct differences. While both speech perception and production involved strong left-hemisphere anterior insula activation, the ALE clusters were in separate anatomical locations. Speech production activated bilateral accessory gyri of the insula and the left anterior short gyrus of the insula. Speech perception activated only the short gyrus of the insula, in the superior middle portion in the left hemisphere, and the anterior portion in the right hemisphere. Although both speech perception and production activated both left and right insula, speech production was more left dominant, and speech perception is more equally bilateral.

The activation in the anterior short insula in response to both speech and language tasks provides important information on

the function of this region in linguistic processing. While previous evidence from clinical and neuroimaging studies would support the role of the anterior insula in solely motor speech production (see Ackermann & Riecker, 2010, for a review) our findings would indicate that this region serves a broader function beyond motor speech control, and is in fact a crucial region that mediates language function.

Finally, our results showed bilateral anterior insula involvement in speech perception, in locations distinct from those that have been involved in the language and speech production tasks. This finding was expected, as the perception of speech relies on slightly different cognitive and sensory processes than those implicated in language perception. However, in future studies, meta-analytic methods could be used to compare speech perception with tone and melody perception to ascertain whether they share common brain regions.

Activation in the insula in response to speech perception is likely due to this region's extensive connections with the auditory cortex, temporal pole, and superior temporal sulcus (Augustine, 1996). A number of neuroimaging studies have indicated the involvement of the insula in auditory processing (for a review, see Bamiou et al., 2003). A more recent clinical report has suggested that the insula may be involved in temporal processing, as insular damage was correlated with temporal resolution and sequencing impairments (Bamiou et al., 2006). Neuroimaging studies in control populations, using different stimuli and paradigms showed that increased task difficulty on a temporal discrimination task (Tregellas, Davalos, & Rojas, 2006) and increased frequency of click trains in a passive-listening task (Ackermann et al., 2001; Steinbrink, Ackermann, Lachmann, & Riecker, 2009) were associated with robust activation in bilateral anterior insula. Potentially, our finding of bilateral anterior insula activation in response to speech stimuli raises the possibility of insular recruitment in the encoding and processing of temporal information within the auditory system.

4.3. Summary and future research

Meta-analysis is a robust tool that permits the determination of contiguous brain regions showing reliable activation in response to particular tasks or cognitive functions. This technique summarizes findings across studies and can reduce the impact of confounds inherent in single fMRI studies such as image artifacts, head motion, few subjects, low signal-to-noise ratio, type I and II errors, and contamination of unassociated task features (Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012; Price, Devlin, Moore, Morton, & Laird, 2005; Raemaekers et al., 2007). Additionally it aids in overcoming assumptions that experimental and control tasks solely represent particular cognitive functions (Price et al., 2005).

In the current studies, we performed meta-analysis of neuroimaging data from a variety of speech and language experimental paradigms and did not take into account differences in tasks or stimuli. The resulting probability maps are indicative of reliable activation in the insula in response to different experimental paradigms and provide information on the spatial extent and localization of general speech and language processes.

Our finding of common left-sided activation in the anterior insula in response to speech production and language tasks may point to this region as being a functional hub for canonical and non-canonical language areas. Furthermore, our finding of bilateral activation, even with explicit language stimuli, points to the right hemisphere as an important mediator of speech and language function. Future research should examine the functional and structural organization of the insula relative to the entire speech and language processing connectome to better understand outcomes

seen after damage to this region as a result of neurological injury or disease.

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