Impaired Recognition of Emotional Faces after Stroke Involving Right Amygdala or Insula

Donna C. Tippett, M.P.H, M.A., CCC-SLP,[1,2,3] Brittany R. Godin, M.S., CCC-SLP,[4] Kumiko Oishi, Ph.D.,[5] Kenichi Oishi, M.D., Ph.D.,[6] Cameron Davis, M.S.,[1] Yessenia Gomez, B.S.,[1] Lydia A. Trupe, M.P.H.,[1] Eun Hye Kim, B.S., B.A.,[1] and Argye E. Hillis, M.D., M.A.[1,3,7]

ABSTRACT

Despite its basic and translational importance, the neural circuitry supporting the perception of emotional faces remains incompletely understood. Functional imaging studies and chronic lesion studies indicate distinct roles of the amygdala and insula in recognition of fear and disgust in facial expressions, whereas intracranial encephalography studies, which are not encumbered by variations in human anatomy, indicate a somewhat different role of these structures. In this article, we leveraged lesion-mapping techniques in individuals with *acute* right hemisphere stroke to investigate lesions associated with impaired recognition of prototypic emotional faces before significant neural reorganization can occur during recovery from stroke. Right hemisphere stroke patients were significantly less accurate than controls on a test of emotional facial recognition for both positive and negative emotions. Patients with right amygdala or anterior insula lesions had significantly lower scores than other right hemisphere stroke patients on recognition of angry and happy faces. Lesion volume within several regions, including the right amygdala and anterior insula, each independently contributed to the error rate in recognition of individual emotions. Results provide additional support for a necessary role of the

[1]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore Maryland; [2]Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore Maryland; [3]Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore Maryland; [4]Rehabilitation Services, University of Maryland Charles Regional Medical Center, La Plata, Maryland; [5]Center for Imaging Science, Whiting School of Engineering, Johns Hopkins University, Baltimore, Maryland; [6]Department of Radiology, Johns Hopkins University School of Medicine, Baltimore Maryland; [7]Department of Cognitive Science, Krieger School of Arts and Sciences, Johns Hopkins University, Baltimore, Maryland.

Address for correspondence: Donna C. Tippett, M.P.H., M.A., CCC-SLP, Department of Otolaryngology—Head and Neck Surgery, Johns Hopkins University, 601 N. Caroline Street, 6th floor, Baltimore, MD 21287-0910 (e-mail: dtippet1@jhmi.edu).

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right amygdala and anterior insula within a network of regions underlying recognition of facial expressions, particularly those that have biological importance or motivational relevance and have implications for clinical practice.

KEYWORDS: Emotion perception, facial recognition, stroke, magnetic resonance imaging, brain mapping

Learning Outcomes: As a result of this activity, the reader will be able to (1) describe the role of the amygdala and insula in recognition of facial expressions; (2) discuss the findings of functional imaging and intracranial electroencephalography regarding the roles of the amygdala and insula as well as inconsistencies in this literature and study limitations; and (3) explain functional implications of deficits in recognition of facial expression and potential application to clinical practice.

The ability to recognize another's emotion from their facial expression is crucial for effective human interactions in both social and professional realms. Visual recognition of facial expression is an important means to judge emotional tenor and thus evoke an appropriately empathic response.[1,2] An extensive literature addresses the neurologic basis of emotional facial recognition, using functional imaging studies and chronic lesion studies.[3–7] However, this literature does not yield entirely consistent conclusions. Several chronic lesion studies demonstrate right hemisphere (RH) dominance for emotional facial recognition, or at least processing of certain emotions[8,9] (but see Abbott et al[10]). Functional imaging studies reveal a bilateral network of neural regions that are engaged during emotional facial recognition tasks and show that distinct areas are specifically activated in response to certain emotions (e.g., anger or disgust).[11,12] However, functional imaging studies only show that blood oxygen dependent signal in an area (i.e., areas where blood flow exceeds oxygenation, corresponding to activation of neurons) is correlated with performance on a task, whereas lesion studies are needed to show which of those areas are essential for the task.

ROLE OF THE RIGHT HEMISPHERE

The concept of cortical asymmetry of emotion dates to the nineteenth century work of Hughlings-Jackson,[13] who proposed that emotion is lateralized to the RH. The "right hemisphere hypothesis" traditionally ascribes a greater role in emotion processing, regardless of valence, to the right, rather than the left, hemisphere.[9,14] The "valence hypothesis" invokes the RH for negative or unpleasant emotions, and the left hemisphere for positive or pleasant emotions.[3,15] A somewhat different hypothesis is that primary emotions (e.g., anger, fear, sadness) are preferentially modulated by the RH, whereas social emotions (e.g., affection, pride, embarrassment) are preferentially processed by the left hemisphere.[16,17] More recently, Abbott et al proposed that the RH processes emotional facial expressions from both configural information (global facial qualities) and featural information (constituent aspects of faces, that is, eyes and mouth, depicted in the partial faces), and the left hemisphere processes emotional facial expressions from primarily featural facial information.[18] Interestingly, using eye tracking, Thomas et al found participants fixated more on right side of the mouth when judging happiness and fixated more on the left eye when judging sadness.[19] A recent study combining behavioral categorization of whole and half faces displaying anger, sadness, or surprise, computational modeling and event-related potentials (ERP) revealed additional evidence that expression encoding and emotional assessment require holistic processing, mainly in the RH.[20] Together, these studies indicate a critical role of the RH in (1) global or configural processing of faces and (2) faces expressing negative emotions, like fear and anger.

FEAR AND THE AMYGDALA

Both the right and left amygdalae are implicated in fear conditioning in animals and are activated in humans when fearful faces are viewed.[11,21–23] A meta-analysis of neuroimaging studies in 1,600 healthy individuals revealed bilateral amygdala engagement during processing of fearful faces and to a lesser degree happy faces and sad faces (right amygdala only).[12] A recent functional magnetic resonance imaging (fMRI) study of 235 male and 235 female adolescents matched for age and handedness revealed significantly stronger right amygdala activation in male subjects compared with female subjects during emotional face perception.[24] One recent study found that the right amygdala was activated in response to threatening faces, but only in central vision, and the striatum (caudate and putamen) were preferentially activated by threatening faces in peripheral vision.[25] In single-subject case studies and small case series of individuals with bilateral amygdala damage, impaired recognition of the facial expression of fear was documented.[26–29] A follow-up study of one patient indicated that the impairment in fear processing can be attributed to inability to use information from the eye region in processing emotional faces.[30] A recent eye-tracking study of three patients with bilateral ventromedial prefrontal cortex damage showed that this damage disrupted attention to the eye region and interfered with recognition of emotional faces, particularly fear.[31] In individuals with frontotemporal dementia, atrophy of the right amygdala and anterior cingulate were associated with impaired fear recognition[32]; however, redirecting attention to the eyes did not improve recognition of emotion,[33] as it does in some patients with more selective amygdala dysfunction or those with Alzheimer disease who have early bilateral amygdala atrophy.[34]

Although the involvement of the amygdala in processing of fear is replicated in functional imaging studies and studies of neurodegenerative disease, the role of this structure in the processing of other emotions requires further clarification.[35,36] Studies that specifically investigate the role of the amygdala in other emotions, particularly intense emotions or those that might stimulate an autonomic response, confirm other roles, such as processing anger and joy.[37–40] Together, these studies indicate that although right and left amygdalae are likely to be components of a network normally engaged in processing fear (also including orbitofrontal, ventromedial prefrontal cortex) and other emotions in faces, the amygdalae are not sufficient for, nor specific to, fear recognition. Some of the inconsistent results between studies regarding the critical role of the right or left amygdala in recognizing fearful faces could be due to: (1) studying patients with lesions at variable times in the course of recovery or adaptation to the lesion or (2) studying controls with varying degrees of attention to the eyes or use of stimuli that draw varying attention to the eyes.[41,42]

DISGUST AND THE INSULA

Disgust recognition involves the insula and perhaps components of the basal ganglia. In normal volunteers, one study found significant activation of the *right* anterior insula was associated with processing facial expressions of disgust.[43] In contrast, other studies of normal volunteers have revealed activation in the *left* anterior insula, bilateral putamen, *right* globus pallidus and caudate nucleus, and superior, middle, and inferior posterior temporal gyri or bilateral insula, occipital, and fronto-orbital cortex in response to facial expressions of disgust.[44,45] A meta-analysis of healthy participants revealed bilateral insular activation during processing of disgusted faces.[12] An individual with a stroke involving left anterior insula, posterior insula, putamen, and globus pallidus was selectively impaired in recognizing facial expressions of disgust.[46] In individuals with Huntington disease, left insula volume positively correlated with accuracy in disgust recognition.[47] Similarly, in individuals with frontotemporal dementia, volume of the left insula and left temporal pole correlated with disgust recognition.[32] However, the insula is not only important for recognition of disgust. Accuracy in recognition of angry facial expressions was associated with bilateral posterior insular cortex volume in patients with frontotemporal lobar degeneration.[48] Furthermore, the insula is not the only area important for recognition of disgust. Impaired recognition of disgusted faces in patients with Huntington disease and Parkinson disease was attributed to disruption to impaired subcortical-cortical

circuits that include basal ganglia, thalamus, and right cortical regions.[49,50]

Consistent with the lesions studies, the insula is also activated in response to other emotions.[36] One meta-analysis indicated the left insula showed activation in response to fearful faces but was more sensitive to disgust than fear.[12] These studies indicate that both the left and right insula are likely to be involved in processing facial expression of disgust, but the relationship is neither specific to the insula (other lesions can cause impaired processing of disgust, as noted for Huntington disease and Parkinson disease), nor specific to disgust (the insula is involved in processing other emotions). Again, some of the inconsistencies across lesion studies could be due to studying patients at variable times after onset of the lesion, with variable opportunity for structure-function reorganization or accommodation to the lesion.

EVIDENCE AGAINST SPECIFICITY OF AMYGDALA AND INSULA FOR FEAR AND DISGUST

Additional evidence against specificity of these structures for fear as well as disgust comes from intracranial electroencephalography (iEEG), in which activity from individual neurons or groups of neurons is recorded, indicating that the amygdala activation observed in response to fearful faces may reflect the amygdala's role in encoding emotionally relevant stimuli.[51] Unlike imaging, iEEG is not encumbered by normal variations in human anatomy, a limitation of imaging studies. One iEEG study demonstrated that single neurons in the amygdala spiked in response to emotional faces but not exclusively fearful faces.[52] Likewise, Rutishauser et al did not find differential spiking to fearful faces versus other emotional faces in the amygdala.[53] An ERP study also showed late differential responses in the amygdala to both fearful and disgusted faces compared with neutral and happy faces.[54] Together, these results indicate that the amygdala may be critical to encoding the emotional relevance or biological importance of facial expressions (see also Breiter et al[11]), and the right amygdala may be particularly critical for aversive emotional faces, important in the recognition of imminent danger. The insula, which has many connections to the limbic system, including the amygdala, may similarly be part of a complex cortico-limbic-autonomic network underlying recognition of the emotional relevance of facial expression. However, there have been inconsistencies across studies regarding the necessary role of the insula and the amygdala in recognizing emotional faces other than disgust and fear, and less consistent areas of activation associated with processing of anger, sadness, and happiness in functional imaging studies (see Table 1 for summary).[11,36,55,56]

One problem in studying emotional facial recognition with iEEG or functional imaging is that these studies can only reveal areas that are engaged in the task, not areas that are critical for the task.[57] Small changes in task demands or control conditions can result in differences in the areas where activity is significantly associated with a particular task, which may account for conflicting results. Lesion studies are needed to determine if a particular area is essential for the function. However, *chronic* lesion studies may fail to reveal regions necessary for recognition of basic emotions such as happiness and sadness, because these functions may recover quickly after unilateral lesions.

In this article, data are presented to show brain lesions associated with impaired recognition of emotional facial expressions before significant neural reorganization can occur during recovery from *acute* RH stroke. Participants viewed faces of prototypic emotions and were asked to identify the emotional label in a seven-item forced-choice response format. Magnetic resonance images were analyzed to investigate lesions in the RH that contributed to impaired performance on recognition of particular emotions in facial expression. We hypothesized that acute lesions in right amygdala and right anterior insula are associated with impaired recognition of motivationally relevant (including aversive) emotional facial expressions and that other right cortical lesions differentially contribute to recognition of distinct emotions in facial expression.

Table 1 Summary of Associations between Amygdala and Insula and Emotional Facial Expressions

	Happy	Joy	Angry	Disgust	Fear	Sad
Right amygdala	Fusar-Poli et al, 2009[12]				Kumfor et al, 2013[32]	Fusar-Poli et al, 2009[12]
Bilateral amygdala		Milesi et al, 2014[39]	Milesi et al, 2014[39]	Krolak-Salmon et al, 2004[54]	Breiter et al, 1996[11]; Fusar-Poli et al, 2009[12]; Paré et al, 2004[22]; Lindquist et al, 2012[23]; Adolphs et al, 1994,[26] 1995[27]; Calder et al, 1996[28]; Sprengelmeyer et al, 1999[29]; Milesi et al, 2014[39]; Krolak-Salmon et al, 2004[54]	
Right insula				Philippi et al, 2009[43]		
Left insula				Kumfor et al, 2013[32]; Phillips et al, 1998[44]; Calder et al, 2000[46]; Kipps et al, 2007[47]	Fusar-Poli et al, 2009[12]	
Bilateral insula			Omar et al, 2011[48]	Fusar-Poli et al, 2009[12]; Jehna et al, 2011[45]		

MATERIALS AND METHODS

Participants

Thirty patients with RH stroke (mean age = 52.8 ± 12.1 years; 13 female subjects; mean education = 14.4 ± 2.5 years) and 30 healthy controls (mean age = 50.5 ± 14.6 years; 15 female subjects; mean education = 15.6 ± 2.6 years) were enrolled. Patients and controls were not significantly different in age ($t[60] = -0.7$, $p = 0.49$), education ($t[60] = +1.43$, $p = 0.16$), or gender (Fisher exact [FE]: $p = 0.80$). Patients and controls provided informed consent to participate in the study under a protocol approved by the Institutional Review Board of the Johns Hopkins University. Participants had none of the following exclusion criteria: (1) prior neurological disease; (2) reduced level of consciousness or ongoing sedation; (3) uncorrected hearing or vision impairment; (4) lack of premorbid competency in English; and (5) failure to follow task directions. Patients were also excluded if they were unable to have magnetic resonance imaging (MRI) due to claustrophobia, implanted ferrous metal, or weight > 300 pounds. Stroke patients were recruited from the inpatient service in the hospital. Controls were recruited from a convenience sample in the community.

Imaging and Image Processing

For each participant, we obtained an MRI within 24 hours of admission to the hospital for acute ischemic stroke. Images were processed according to procedures published previously.[58–61]

Facial Expression Task

Integrity of recognition of emotions was examined from static facial expressions in an emotion categorization task as described in an earlier study from our laboratory.[62] Faces expressing one of seven basic emotions (happy, surprise, angry, disgust, fear, sad, neutral) were presented centrally one at a time using color photographs. Participants viewed these faces of prototypic emotions and were asked to identify the emotional label in a seven-item forced-choice response format (alternatives: happy, surprise, angry, disgust, fear, sad, neutral). There were eight exemplars of each emotion (each emotion depicted by

each of eight actors or actresses), for a total of 56 trials. The stimuli for facial expressions were selected from a set of perceptually validated pictures including individuals of different genders and races.[63] Understanding of the emotional labels and ability to use the computerized response box were confirmed prior to testing. Response time was unlimited, but participants were encouraged to respond as quickly as possible.

Statistical Analysis

Patterns of performance on the emotional face recognition test by RH stroke patients and controls were compared quantitatively and qualitatively. We compared performance of RH stroke patients and controls using unpaired *t* tests (STATA version 12 [Stata Corp., College Station, TX]) and Fisher exact test (Social Science Statistics, http://www.socscistatistics.com). We compared recognition of specific emotions of patients with lesions including right amygdala and right anterior insula to RH stroke patients without lesions in the right amygdala or right anterior insula also using unpaired *t* tests and Fisher exact test. We identified cutoff scores for normal performance on the facial recognition task based on the performance of our 30 controls who were of comparable age, gender, and education as our stroke patients. The cutoff scores were >2 standard deviations (SD) below the mean for controls, which would be outside the range of normal for this population. Multiple regression analyses were performed to investigate whether additional gray or white matter lesions in the right hemisphere contribute to impaired performance on recognition of particular emotions in facial expression.

RESULTS

Controls versus Right Hemisphere Patients

RH stroke patients were significantly less accurate than controls in identifying all positive and negative emotional facial expressions and neutral expressions (i.e., happy, surprise) (mean 82.9% versus 92.9% correct; $t[58] = 3.1760$; $p = 0.0024$), negative or aversive emotions (i.e., angry, disgust, fear, sad) (mean 58.9% versus 77.5% correct; $t[58] = 4.5$; $p < 0.0001$), and neutral emotional faces (mean 82.1% versus 98.4% correct; $t[58] = 2.7$; $p = 0.0094$). Positive facial expressions were identified correctly more frequently than negative facial expressions for 28/30 (93%) patients and all controls (Table 2).

The mean score for healthy controls on positive faces was 92.9% ± 5.4% correct. All controls and 19/30 (63%) RH stroke patients scored within 2 SD of the mean for healthy controls (i.e., ≥82.1%) for positive emotions. The mean score for healthy controls on aversive faces was 77.5% ± 9.8% correct. All but one of the controls and 15/30 (50%) RH stroke patients scored within 2 SD of the mean for healthy controls (i.e., ≥57.9%). RH stroke was strongly associated with significant impairment in recognizing both positive and negative/aversive faces (FE = 0.0001 for both, $p < 0.05$).

Table 2 Mean Percent Correct for RH Stroke Patients and Controls on Facial Recognition

Facial Expressions	Mean (SD)		t Value	df	*p* Value
	RH Stroke ($n = 30$)	Controls ($n = 30$)			
Positive	0.83 (0.16)	0.93 (0.05)	3.1760	58	0.0024
Negative	0.59 (0.21)	0.78 (0.10)	4.478	58	0.0000
Happy	0.94 (0.14)	0.99 (0.03)	2.0371	58	0.046
Surprise	0.72 (0.27)	0.86 (0.11)	2.6589	58	0.010
Angry	0.63 (0.29)	0.83 (0.17)	3.2183	58	0.0021
Disgust	0.75 (0.28)	0.88 (0.18)	2.0655	58	0.043
Fear	0.34 (0.25)	0.54 (0.21)	3.3163	58	0.0016
Sad	0.63 (0.27)	0.85 (0.12)	4.1451	58	0.0001
Neutral	0.82 (0.31)	0.98 (0.07)	2.6856	58	0.0094

RH, right hemisphere; SD, standard deviation.

Effects of Right Amygdala Lesions

Patients with right amygdala lesions (Fig. 1) had significantly lower scores than RH stroke patients without lesions in the amygdala and insula on recognition of happiness (mean 82.1% versus 98.6% correct; $t[23] = 3.1$; $p = 0.0028$) and anger (mean 48.2% versus 73.6% correct; $t[23] = 2.1$; $p = 0.023$). Furthermore, more patients with right amygdala lesions compared with patients without right amygdala lesions were impaired in recognizing happy faces. The mean score for healthy control on happy faces was 98.6% ± 4.0%. In patients with right amygdala lesions, 4/7 (57%) scored more than 2 SD below the mean for healthy controls on happy faces (i.e., scored below 94.6%), whereas only 2/18 (11%) RH stroke patients without right amygdala or insula lesions scored more than 2 SD below the mean score for healthy controls on happy faces (FE = 0.03, $p < 0.05$).

Also, more patients with right amygdala lesions were significantly impaired in recognizing angry faces than patients without amygdala lesions. The mean score for healthy controls on angry faces was 83.2% ± 17.3%. Among patients with right amygdala lesions, 4/7 (57%) scored more than 2 SD below the mean for healthy controls on angry faces (i.e., <48.6%) (FE: = 0.03; $p < 0.05$), whereas 2/18 (11%) RH stroke patients without right amygdala or insula lesions scored more than 2 SD below the mean score for healthy controls on angry faces.

Effects of Right Anterior Insular Lesions

Patients with right anterior insula lesions (Fig. 2) had significantly lower scores than RH stroke patients without lesions in the amygdala and insula on recognition of happiness (mean 87.5% versus 98.6% correct; $t[27] = 2.2$; $p = 0.035$) and anger (mean 47.7% versus 73.6% correct; $t[27] = 2.6$; $p = 0.0083$). Furthermore, more patients with right anterior insula lesions were associated with significant impairment in angry faces, compared with patients without insular lesions. The mean score for healthy controls on angry faces was 83.2% ± 17.3%. Among patients with right anterior insula lesions, 6/11 (55%) scored more than 2 SD below the mean for healthy controls on angry faces (i.e., below 48.6%), whereas 2/18 (11%) RH stroke patients without right amygdala or insula lesions scored more than 2 SD below the mean score for healthy controls on angry faces (FE = 0.0281; $p < 0.05$).

Contribution of Specific Gray and White Matter Structures

We tested the hypothesis that acute lesions to distinct areas of the brain differentially affect recognition of facial expression of individual emotions by running multivariable regression analyses, with accuracy (percent correct) in recognition of facial expressions of individual

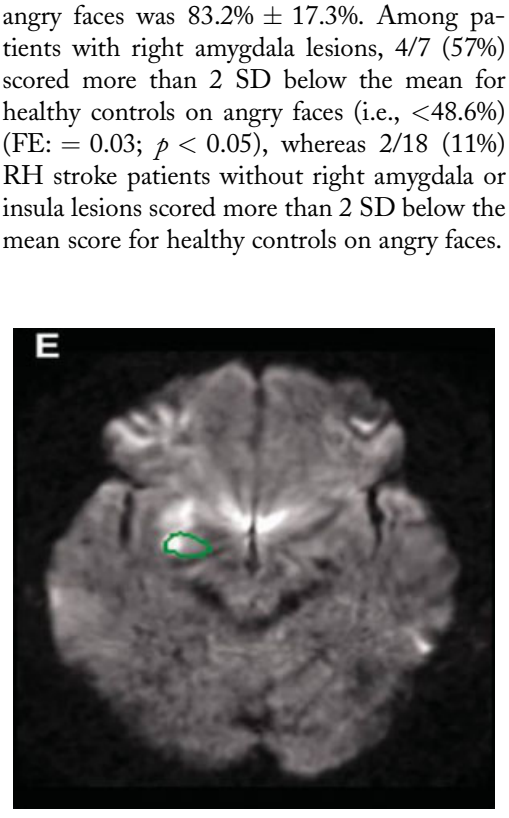

Figure 1 Infarction in the right amygdala.

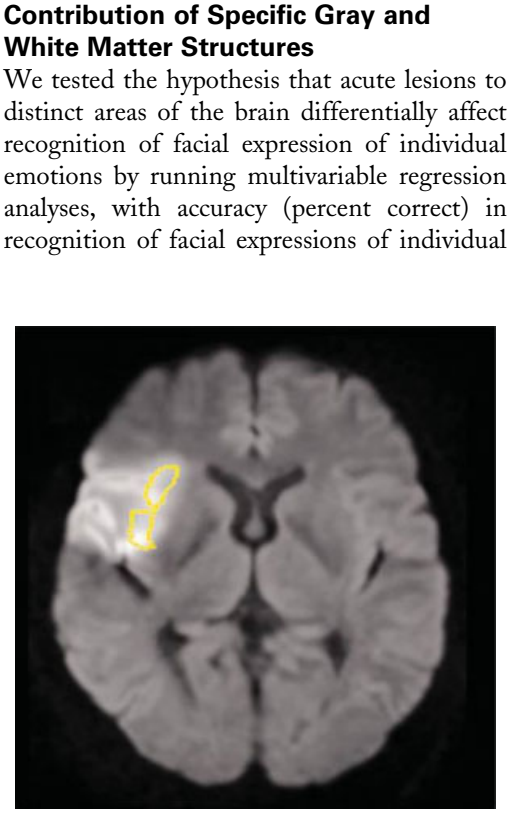

Figure 2 Infarction in the right anterior insula.

emotions (e.g., happiness) as the dependent variable and the percent damage to individual gray and white matter structures in the JHU-MNI atlas as the independent variables.

The model that best accounted for recognition of happy facial expressions included percent damage to thalamus, caudate, superior temporal gyrus (STG), orbitofrontal gyrus, STG pole, middle temporal gyrus, middle temporal gyrus pole, inferior temporal gyrus, anterior insula, amygdala, putamen, globus pallidus, genu of the corpus callosum, inferior fronto-occipital fasciculus, sagittal stratum, and uncinate ($r^2 = 0.93$; adjusted $r^2 = 0.90$; $p < 0.0001$). Medial orbitofrontal gyrus, anterior cingulate cortex, and fusiform gyrus were omitted because of collinearity. All variables *independently* contributed to accuracy rate in recognition of happy faces except thalamus, caudate, and STG. The percent of damage to the same areas accounted for recognition of surprised faces ($r^2 = 0.41$; adjusted $r^2 = 0.19$; $p = 0.049$), neutral faces ($r^2 = 0.66$; adjusted $r^2 = 0.53$; $p < 0.0001$), angry faces ($r^2 = 0.50$; adjusted $r^2 = 0.31$; $p = 0.0051$), and sad faces ($r^2 = 0.47$; adjusted $r^2 = 0.28$; $p = 0.01$), although the areas each carried a different "weight" in recognizing each emotion.

There were no models in which higher percent damage to individual areas in combination or alone accounted for lower accuracy in recognition of facial expressions of disgust or fear. However, a significant impairment (>2 SD below the mean for normal controls) in recognizing disgusted facial expressions was associated with lesion to the anterior insula (FE: $p = 0.049$) or inferior fronto-occipital fasciculus (FE: $p = 0.03$)

DISCUSSION

Overall, and as expected, RH stroke patients performed significantly worse than controls in recognizing emotional faces. This result is consistent with functional imaging studies and lesion data showing a dominant role of the RH in processing (at least some) emotional facial expressions.[64] Negative or aversive emotions were identified with lower accuracy than positive or neutral emotions by both RH stroke patients and controls (as shown in Table 1). Moreover, there was a greater difference between RH stroke patients and controls on aversive faces than positive and neutral faces, even though there was higher power for (more instances of) positive than negative emotions.

The finding that some facial expressions are more difficult to identify than others is consistent with previous behavioral research showing more accurate identification of happy expressions than negative expressions.[65,66] This phenomenon is attributed to happy facial expressions being promptly identified based on its unique feature, the smile; other nonhappy facial expressions have less distinctive or confusing features, complicating their identification,[67,68] or require more global or configural processing, which is particularly challenging after right hemisphere lesions.

Importantly, not all patients with RH lesions were impaired in recognition of emotional faces. Nine patients with RH lesions scored less than 2 SD below the mean for controls. Only the subset with focal lesions in critical areas, such as amygdala or anterior insula, had significantly impaired recognition of emotions from faces. Our results are consistent with iEEG results indicating that the amygdala and insula are especially important in recognition of aversive facial expressions or perhaps facial expressions that have behavioral relevance. In our study, patients with amygdala or anterior insula damage had significantly more difficulty than other RH stroke patients in recognition of anger. Multivariable regression analysis also confirmed that the degree of damage to the right amygdala and right anterior insula was independently associated with error rate in recognition of certain aversive faces. Our results are consistent with some fMRI, ERP, and lesion studies indicating a role of the amygdala (and anterior insula) in discriminating the emotional relevance of the stimuli, rather than recognizing only specific emotions.[36,51]

Patients with amygdala or anterior insular damage were also impaired in recognition of happy faces, and the degree of damage to these areas was independently associated with the severity of impairment. These findings are in line with lesion study showed that patients with anterior temporal lobectomy confused joyful

faces with neutral faces.[39] An fMRI study showed that execution of happy facial expressions led to significantly stronger right amygdala activation than execution of the nonemotional or neutral facial expressions.[69] However, most studies have found it difficult to identify lesions associated with impaired recognition of happy faces or areas activated specifically with recognition of happy faces. Our study may be novel because we studied patients acutely after stroke, before the opportunity for recovery, or before other areas of the brain assume the function of the right amygdala in this critical social function. We identified other gray and white matter areas where acute damage independently contributed to error rate in recognition of happy faces, including right superior and middle temporal pole, uncinate fasciculus, and inferior fronto-occipital fasciculus. It is possible that if some of these areas are spared, they may be able to rapidly assume the role of the right amygdala in recognition of happy faces (accounting for variability across chronic lesion studies).

We confirmed a role of the anterior insula in recognition of disgust but also found that anterior insula was critical in recognition of other emotional facial expressions, including anger. Similar results have been reported in preclinical Huntington disease, in which volume of insula was associated with accuracy in recognition of negative emotional faces but not limited to faces of disgust.[70] The anterior insula has widespread connections to orbitofrontal and other limbic areas, making it a plausible critical link in emotional processing. Again, its role may be duplicated by the left anterior insula, or other regions, such that other areas can quickly assume its function in recovery after unilateral stroke. The strong association we and others have identified between lesions in right anterior insula and emotional face processing could be at least partly responsible for its role in emotional empathy.[61]

We were not able to show a strong association between damage to the right amygdala and fear, likely because all RH stroke patients showed low accuracy in recognizing fear from photographs of faces. Other studies have shown that it is difficult to differentiate fear and surprise in facial expressions, particularly out of context.[71] Our negative results should not be taken as evidence against the role of right amygdala and fear recognition, but further evidence of the complexity of showing fear through facial expression alone.

We showed that the percent damage to the right temporal pole and orbitofrontal cortex independently contributed to predicting lower accuracy in recognizing happy, surprise, and neutral faces, consistent with a role of these areas in emotional recognition from faces reported in lesion studies and functional imaging studies.[32,55,72] Likewise, we confirmed a role of the right inferior fronto-occipital fasciculus and uncinate fasciculus in recognizing happy, surprised, sad, and neutral emotion from facial expressions.[43,73] We are not claiming these structures are important only for a subset of emotions. The significant results for a subset of emotions may reflect the range of performance across patients with and without damage to these structures. Greater power might reveal associations between damage to these structures and impairment in recognizing other emotions.

This study has several limitations. We studied acute stroke patients, allowing us the opportunity to investigate performance before recovery occurs. Although the study of individuals with chronic stroke is complicated by the influence of neural reorganization and compensations, the study of individuals with acute stroke may be complicated by the influence of diaschisis. Convergence of evidence is vital in clarifying controversial issues. As noted previously, the results of this study were consistent with prior functional imaging studies. Another limitation of this study was the fact that we did not evaluate performance by left hemisphere stroke patients (because patients with acute lesions involving left amygdala and anterior insula typically have impaired comprehension and cannot reliably perform the task). Future studies will evaluate emotional facial recognition using nonverbal tasks (e.g., skin conductance response and priming tasks) with right and left hemisphere stroke and controls, so that we do not have to exclude patients with verbal comprehension deficits (and the lesions of interest in the left hemisphere). An additional limitation is that we did not evaluate patients' assessments of the valence or emotional

relevance of the stimuli or assess our participants at later time points to investigate change over time. Future research will also address these limitations. We also included relatively small numbers of patients with specific lesions (8 with amygdala and 11 with anterior insular damage), which limited the types of analyses we could conduct. Finally, we measured accuracy in facial expression rather than reaction time. Reaction time is very variable in acute stroke, and measuring reaction time would not have allowed the clinician to help the patient find the button corresponding to the spoken name of the emotion (when patients named aloud the emotion spontaneously) to compensate for any hemispatial neglect.

CLINICAL IMPLICATIONS

Despite its limitations, the results of our study have implications for clinical practice and research. Deficits in recognition of facial expression caused by particular RH lesions have implications for interpersonal interactions. Individuals with lesions in the amygdala, insula, temporal pole, orbitofrontal cortex, fronto-occipital fasciculus, or uncinate may make incorrect assessments of another's affective state and respond inappropriately, resulting in social isolation, as demonstrated in a variety of disease states.[74–76] Blonder et al showed that after RH stroke, the inability to recognize facial expressions is associated with decreased marital satisfaction. Behavioral therapy to promote social cognition, such as facial expression recognition, has received little attention in the stroke population.[7] Therapy to improve facial expression recognition may be indicated in the RH stroke population, particularly those with amygdala and insula damage. Adolphs et al reported that simply instructing a patient with bilateral amygdala damage to attend to the eyes improved recognition of fear in faces.[30] Patients with other lesions may need other interventions; future studies must identify the specific roles of individual structures in the complex network underlying recognition of emotions from faces.[77] This study contributes some novel evidence regarding the critical structures within this network.

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