Differential Effects of Lesions of the Amygdala and Prefrontal Cortex on Recognizing Facial Expressions of Complex Emotions

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Abstract

■ Humans can detect facial expressions of both simple, basic emotions and expressions reflecting more complex states of mind. The latter includes emotional expressions that regulate social interactions ("social expressions" such as looking hostile or friendly) and expressions that reflect the inner thought state of others ("cognitive expressions" such as looking pensive). To explore the neural substrate of this skill, we examined performance on a test of detection of such complex expressions in patients with lesions of the temporal lobe ($n = 54$) or frontal lobe ($n = 31$). Of the temporal group, 18 had unilateral focal lesions of the amygdala and of the frontal group, 14 patients had unilateral lesions of the ventromedial prefrontal cortex—two regions held to be pivotal in mediating social cognitive skills. Damage to either the left or right amygdala was associated with impairment in the recognition of both social and cognitive expressions, despite an intact ability to extract information relating to invariant physical attributes. Lesions to all of the right prefrontal cortex—not just the ventromedial portions—led to a specific deficit in recognizing complex social expressions with a negative valence. The deficit in the group with right prefrontal cortical damage may contribute to the disturbances in social behavior associated with such lesions. The results also suggest that the amygdala has a role in processing a wide range of emotional expressions. ■

INTRODUCTION

Lesion studies have contributed greatly to the delineation of the neural substrate of components of social cognition, including the ability to recognize what another person might be feeling on the basis of their facial expression. Damage to the amygdala has been consistently linked with deficits in the recognition of emotional expressions (Stone, Baron-Cohen, Calder, Keane, & Young, 2003; Adolphs, Baron-Cohen, & Tranel, 2002; Adolphs, Tranel, Damasio, & Damasio, 1995). This complements amygdala activation observed through neuroimaging studies when healthy subjects are shown faces depicting a range of emotional expressions or social attributes (Zald, 2003; Winston, Strange, O'Doherty, & Dolan, 2002; Baron-Cohen, Ring, et al., 1999). Similarly, both lesion and functional neuroimaging studies implicate the prefrontal cortex (PFC) in the recognition of emotional expressions (Wager, Phan, Liberzon, & Taylor, 2003; Eslinger & Damasio, 1985).

There is no universally accepted typology of emotional expressions, but one widely used division separates the six basic emotions (fear, sadness, disgust, anger, surprise, and happiness) from more complex emotional expressions. The complex emotional expressions can be further divided into "social expressions," which intimately regulate social behaviors, and "cognitive expressions," which reflect the inner thought state of an individual. The social expressions can only be understood in a social context and typically have a clear valence, either positive (e.g., "friendly") or negative (e.g., "hostile" or "contemptuous"). Cognitive expressions, by contrast, provide a display of the inner thought state of an individual, and do not have such a clear valence (examples are looking "pensive," "thoughtful," or "contemplative"). Support for this division comes partly from studies of patients with amygdala lesions, who are impaired in the recognition of social, but not cognitive, expressions (Adolphs, Baron-Cohen, et al., 2002). The further division of the social expressions on the basis of valence receives support from studies suggesting that the right hemisphere processes stimuli with a negative valence which evoke avoidance behaviors, and the left hemisphere processes stimuli with a positive valence which evoke approach behaviors (Mandal et al., 1999; Davidson, 1992a, 1993). The question arises as to whether a similar interaction of valence with laterality may also be found in the detection of more complex social and cognitive expressions.

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Previous lesion studies into the recognition of complex emotional expressions have several limitations. Firstly, many of the patients with amygdala damage that have been reported had extensive damage to surrounding structures, which may themselves play a role in the recognition of facial expressions of emotions. To disentangle the contribution of the amygdala from its adjacent structures, we compare directly the performance of patients with focal lesions of the amygdala with patients with focal lesions that completely spare the amygdala.

Similarly, the relative contribution of different regions of the PFC in the recognition of complex emotional expressions is unclear. Many lesions studies implicate the ventromedial prefrontal cortex (VMPFC) in not only in the recognition of emotions, but also in subjective emotional experience, social behavior, and decision making (Hornak et al., 2003; Tranel, Bechara, & Denburg, 2002) Functional neuroimaging studies have demonstrated activation of regions of the VMPFC, specifically the orbito-frontal cortex (OFC), as healthy subjects make social judgments on the basis of external appearance (O'Doherty et al., 2003; Winston et al., 2002). However, other lesion studies suggest that the dorsolateral prefrontal cortex (DLPFC) may also be involved in recognition of complex social stimuli (Mah, Arnold, & Grafman, 2004; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003). In the present study, we thus aimed to characterize deficits in the recognition of facial expressions associated with unilateral lesions of different regions of the PFC.

The paradigm we used was the revised version of the "Reading the Mind in the Eyes" task (abbreviated to the "Eyes task"). (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001; Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997). This requires subjects to detect the mental states of another on the basis of expressions around the eye region. It includes items which depict cognitive and social expressions, both positive and negative in valence. The task benefits from a knowledge of the neural substrate supporting its performance in healthy subjects derived from both functional imaging and ERP studies and is complemented by the "Reading the Mind in the Voice" task (Sabbagh, Moulson, & Harkness, 2004; Rutherford, Baron-Cohen, & Wheelwright, 2002; Baron-Cohen, Wheelwright, Stone, & Rutherford, 1999).

In light of previous studies, we hypothesized that:

1. Patients with focal damage to the amygdala, but not the surrounding structures, would be impaired in the recognition of all complex facial expressions. We predicted a particularly severe deficit in the recognition of social, rather than cognitive expressions.
2. Damage to the PFC would also be associated with specific deficits in the recognition of social rather than cognitive expressions. Within the PFC, it was expected that damage to the VMPFC would be associated with more severe impairments than damage to the DLPFC.
3. Finally, we examined the effect of valence of the stimuli on recognition. We predicted that patients with right-sided damage would show poorer recognition of stimuli with a positive valence, and patients with left-sided damage would show poorer recognition of stimuli with a negative valence.

RESULTS

There were no significant group differences in sex balance ($\chi^2 = 1.6$, $p = .8$), verbal IQ [$F(4,166) = 2.0$, $p = .09$], or age of onset of epilepsy in the patient groups [$F(3,60) = 0.17$, $p = .91$]. There was a significant group difference in age at time of testing [$F(4,171) = 2.5$, $p = .05$], although post hoc analyses with Bonferroni correction did not show any significant pairwise group differences.

There was also no significant difference between groups who completed the control task of gender identification, with all groups performing near ceiling [$F(2,143) = 1.3$, $p = .27$]. For the lesion groups there was no difference between the subgroups and healthy controls in the Benton Facial Recognition test [$F(3,75) = 2.4$, $p = .08$].

Initial analyses examined the performance on the component parts of the "Eyes task" in the right temporal (RT), left temporal (LT), right frontal (RF), left frontal (LF), and healthy control groups. The category of Expression was entered as the within-subjects factor in a repeated-measures ANOVA, using the divisions discussed earlier: cognitive (e.g., contemplative, daydreaming), positive social (e.g., friendly, flirtatious), and negative social (e.g., hostile, accusing) emotional expressions.

There was a main effect of group [$F(4,171) = 10.4$, $p < .001$]. Post hoc comparisons with Bonferroni correction showed that the RT ($p < .001$), LT ($p = .001$), and RF ($p = .03$) groups all scored lower than the healthy controls. In addition, the RT group was impaired overall relative to the LF group ($p = .008$). There was a main effect of category of expression [$F(2,342) = 5.2$, $p = .006$]. Post hoc tests showed better performance for the positive social expressions compared with both the negative social expressions ($p = .03$) and cognitive expressions ($p = .03$). There was a near-significant interaction between expressions category and group [$F(8,342) = 1.85$, $p = .07$], which was further explored with one-way ANOVAs within each category of expressions (results are shown in Table 1).

There were significant group differences in all the component parts of the "Eyes task." In the recognition of cognitive expressions, the RT group was impaired relative to the healthy controls and LF group and the LT group was significantly impaired relative to healthy controls. There was a marked effect of valence in the

Table 1. The Mean Scores (Standard Deviations) for Each Group in the Recognition of Components of the "Eyes Task"

	RT	*LT*	*RF*	*LF*	*HC*	*One-Way ANOVA*	*Post Hoc Comparisons (Bonferroni Correction)*
Cognitive	57 (16)	66 (16)	68 (16)	74 (13)	77 (13)	$F = 12.8, p < .001$	RT, LT < HC ($p < .001$); RT < LF ($p = .002$)
Social—positive	61 (28)	69 (24)	78 (23)	83 (21)	81 (19)	$F = 5.1, p = .001$	RT < HC ($p = .001$); RT < LF ($p = .03$)
Social—negative	67 (28)	69 (26)	56 (25)	73 (20)	76 (19)	$F = 3.7, p = .006$	RF < HC ($p = .01$)

RT = right temporal damage group; LT = left temporal damage group; RF = right frontal damage group; LF = left frontal damage group; HC = healthy control group.

recognition of social expressions. The RT group was impaired in recognizing positive social expressions and the RF group was impaired in negative social expressions.

The Specific Contribution of the Amygdala

To define the specific contribution of the amygdala, patients with focal amygdala lesions ($n = 18$) were compared with patients with focal lesions of the temporal lobe that completely spared the amygdala ($n = 13$) and the healthy controls ($n = 91$). Nonparametric tests were used as the data for each group were not normally distributed and there were unequal group sizes. There were significant group effects in overall performance and in the recognition of cognitive expressions, but no significant group difference in the detection of social expressions—neither negative nor positive (see Table 2).

Pairwise Mann–Whitney *U* tests showed that the right focal amygdala group was significantly impaired relative to healthy controls in overall performance and in the detection of cognitive, but not social, expressions. There was a trend for impairment in the focal left amygdala group relative to the healthy controls in overall performance and a tendency to be poor at identifying cognitive expressions. There were no significant differences between the focal nonamygdala lesion group and healthy controls.

In summary, the deficits were only apparent in patients with focal amygdala damage. Lesions of the temporal lobe, which spared the amygdala, did not produce significant impairments relative to healthy controls. The deficits were present in overall performance, but were more pronounced for the cognitive expressions.

Frontal Lobes: The Specific Contribution of the Dorsolateral and Ventromedial Prefrontal Cortices

To assess the effect of side and exact site of damage patients were initially categorized according to the main site of damage as either right DLPFC ($n = 6$), left DLPFC ($n = 3$), right VMPFC ($n = 8$), left VMPFC ($n = 6$), and healthy controls. Patients with extensive damage to both areas ($n = 8$) were excluded from this analysis. A Kruskal–Wallis test showed an overall significant difference in total scores between groups ($\chi^2 = 11.9, p = .01$). Paired Mann–Whitney *U* tests with Bonferroni correction for multiple comparisons were made and showed a significant impairment in the right DLPFC relative to the healthy controls only ($p = .003$), with no other group differences surviving the adjustment for multiple compar-

Table 2. The Median Scores for Patients with Focal Amygdala Damage and Comparison Groups of Subjects with Focal Lesions which Spared the Amygdala and Healthy Controls

	R Amygdala	*L Amygdala*	*R Focal Lesion (Sparing Amygdala)*	*L Focal Lesion (Sparing Amygdala)*	*Healthy Controls*	*Kruskal Wallis—$\chi(4)^2$ (p value)*	*Pairwise Group Comparisons*
Overall score	69	61	72	71	78	16.4 ($p = .003$)	RA < HC ($Z = -2.8, p = .005$); LA < HC ($Z = -2.5, p = .013$)
Cognitive expressions	47	60	73	67	80	20.5 ($p < .001$)	RA < HC ($Z = -3.6, p < .001$); LA < HC ($Z = -2.4, p = .01$)
Social—positive valence	60	60	80	80	80	7.6 ($p = .11$)	N/A
Social—negative valence	83	67	83	67	83	2.3 ($p = .66$)	N/A

RA = right amygdala damage; LA = left amygdala damage; HC = healthy controls.

isons. There were no group differences in performance of each of the subdivisions (cognitive or social expressions).

To complement this analysis, overlay maps were created of the lesions in patients who were severely impaired on the ''Eyes task'' (see E-Figure 2 at the Web link www.em-online.org/JOCN). There were six patients with severe impairment (defined as two standard deviations less than the healthy controls): five with right-sided damage and one patient (f24) with left-sided damage. Among the patients with right-sided damage, there were areas of overlap in at least two patients in all of the regions of the PFC. Overlap between three patients occurred on the lateral aspect of the PFC.

A further three patients with right-sided damage (f1, f2, f14) had mild impairment—all with Z scores of −1.38. As can be seen from the reconstructions of the frontal lesions of each patient (see E-Figure 1 at the Web link www.em-online.org/JOCN), these three patients similarly had involvement of all three regions of the PFC.

As there are some similarities between the ''Eyes task'' and tasks of theory of mind (ToM) reasoning, patients whose lesions overlapped with the peak activations reported in fMRI studies were compared with the patients with damage to other regions of the PFC and healthy controls. Eighteen patients had lesions which involved at least one of the peak activations reported within the medial PFC (f3, f5, f6, f7, f8, f10, f13, f16, f18, f20, f21, f22, f25, f30, f31, f26, f27, f28, f29). The mean total score of those with no ''ToM'' area lesion was 71 (*SD* 12) and the mean score for the group with no involvement was 67 (*SD* 10). The difference between the groups was not significant [$t(29) = 1.1, p = .28$]. There were no significant differences in the recognition of the cognitive or social expressions (all $p > .1$).

Thus, for the frontal-damage patients, there was a clear effect of side, but not site, of damage. Contrary to predictions, damage to the VMPFC was not specifically associated with impairments in detecting complex cognitive or social expressions. Damage to each of the regions was found among the patients who were most severely impaired. Indeed, when grouped by the main site of damage, involvement of the right DLPFC was associated with an overall impairment in the detection of complex mental states relative to healthy controls.

Effects of Possible Moderating Variables

Correlations between the overall performance in the detection of complex cognitive and social expressions and age, estimated IQ, and age of onset of epilepsy where applicable are shown in Table 3.

The main analyses were conducted with estimated IQ entered as a covariate as it was significantly associated with performance in the temporal lobe group and other studies have reported a modest association between verbal IQ and performance in the task among healthy controls (not found in this study). There was little change in the overall pattern of results. For overall scores, the main effect of group remained [$F(4,161) = 9.1$, $p < .001$] with post hoc Bonferroni comparisons showing deficits relative to healthy controls in the RT ($p < .001$) and LT groups($p = .034$). The RF group remained impaired in the detection of negative valence stimuli relative to healthy controls [$F(4,161) = 2.6$, $p = .04$; RF < HC $p = .03$].

The age of onset of habitual epilepsy was also considered, and there was no overall correlation across all groups with performance (Pearson's rho = −.19, $p = .12$) or within each subgroup. To assess the possible impact of diverse etiology on performance, the frontal lesion patients were divided on the basis of the clinical indication for the frontal resection (intractable epilepsy, focal tumor, or arteriovenous malformation) as noted above. There was no significant difference between these groups in overall performance (Kruskal–Wallis $\chi^2 = 3.39$, $p = .18$). For the temporal lesion patients, the underlying cause of medically intractable epilepsy present in all cases was also considered comparing patients with underlying mesial temporal sclerosis with all other pathologies. Again, there was no significant effect on performance of underlying etiology (Mann-Whitney u; $z = -1.0$, $p = .30$).

Table 3. Spearman's Correlations between Overall Performance and Age at Testing, Age of Onset of Epilepsy, and Verbal IQ

	Age	*Age of Onset of Epilepsy*	*IQ*
Temporal lobe damage	−0.2 (p = .15)	−0.29 (p = .03)	0.37 (p = .007)
Frontal lobe damage	0.07 (p = .71)	0.007 (p = .99)	0.45 (p = .01)
Healthy controls	−0.22 (p = .08)	–	0.12 (p = .35)

DISCUSSION

We tested patients with either prefrontal cortical or temporal lobe damage on the ability to recognize social and cognitive expressions, using the ''Reading the Mind in the Eyes'' task (Baron-Cohen, Wheelwright, Hill, et al., 2001). The primary findings indicate that anterior temporal lobe damage is associated with impairments in the recognition of expressions of cognitive and social expressions. This occurs despite an intact ability to extract other forms of information relating to nonemotional attributes such as gender from the same stimuli. Within the anterior temporal lobe, the amygdala appears to mediate this affective processing. Focal damage to structures which spare the amygdala led to performance that did not differ significantly from healthy controls. Although there was a suggestion that focal right amygdala damage was associated with more profound impairments than focal left amygdala damage, the results did not support a clear lateralization of function at this subcortical level. Contrary to expectations, damage to the amygdala and anterior temporal lobe was more strongly associated with impaired recognition of cognitive, rather than social, expressions.

This is in marked contrast to effects of lesions of the PFC. Deficits were only present among those with right prefrontal cortical damage, and contrary to our expectations, were as marked in those with dorsolateral as orbito-frontal or medial damage. The deficits among the right prefrontal damage patients were confined to the recognition of negative social expressions.

The Effects of Damage to the Amygdala

This study provides evidence of a specific contribution of the amygdala, as opposed to closely associated structures, in the recognition of facial expressions of states other than the basic emotions. This is a significant finding as previous studies into the effects of unilateral amygdala damage have typically used patients with extensive surgical damage to the anterior and medial-temporal lobe and had varying degrees of damage to the amygdala itself (Brierley, Medford, Shaw, & David, 2004; Adolphs, Tranel, et al., 2001; Boucsein, Weniger, Mursch, Steinhoff, & Irle, 2001; Anderson, Spencer, Fulbright, & Phelps, 2000). Indeed, Adolphs, Tranel, et al. (2001) reported only a weak correlation between the extent of amygdala damage and the deficits in emotion perception. Another study of a small number of patients with focal lesions incorporating the amygdala did not find the patients to be severely impaired in the recognition of emotions, unlike patients who had more diffuse mesial temporal lobe sclerosis (Meletti et al., 2003). Our demonstration of clear impairments in the recognition of complex social and cognitive expressions benefits from the relatively large number of patients included and the relative uniformity of the underlying pathology of the amygdala lesion.

The current study replicates a previous report of deficits in the decoding of cognitive and social expressions among patients with damage to either amygdala (Adolphs, Baron-Cohen, et al., 2002), This study further found evidence of a selective deficit among patients with amygdala damage in the recognition of social, but not cognitive, expressions. Our results show the opposite pattern, with more severe impairment in the recognition of cognitive expressions. It is unlikely that the differences are due to factors in the design, as both studies used the same stimuli. Factors relating to the participants are more likely to account for the differences. For example, in the Adolphs et al. study, the patients had variable amounts of amygdala damage, unlike the uniform total excision in the anterior temporal lobectomy patients we studied.

The amygdala plays an important role in interpreting eye gaze, and deficits in recognition of facial expressions of basic emotions such as fear can be ameliorated when patients are guided in making eye contact within the face (Adolphs & Tranel, 2003). Thus, the patients with amygdala lesions in this study may simply not have been performing the task normally, perhaps scanning the stimuli in a highly aberrant manner. As we did not track the eye movements of patients during the task, we cannot exclude this possibility. However, two findings suggest that the patients were processing the stimuli to some degree. Firstly, the patients with amygdala damage were intact in the control condition and were thus able to extract information relating to a nonemotional, physical property. Secondly, the patients were not significantly impaired in the recognition of social expressions, relative to those with focal nonamygdala damage. However, future studies with patients who have lesions of the amygdala would benefit from detailed examination of how patients scan the stimuli.

The Effects of Prefrontal Damage

The results in patients with prefrontal damage have several notable features. Deficits were found almost exclusively in patients with right prefrontal cortical damage. There was a marked effect of valence with the impairment in the right frontal groups confined to social expressions with a negative valence. This loss of sensitivity to negative valence social signals can be placed in the context of other social cognitive sequelae of damage to the right PFC. Marked behavioral disinhibition and social insensitivity has been reported with right, but not left, PFC damage (Gomez-Beldarrain, Harries, Garcia-Monco, Ballus, & Grafman, 2004; Tranel et al., 2002; Kolb & Taylor, 1981). Our finding of a failure to recognize negative social expressions might partly explain the social insensitivity and behavioral disinhibition found after right prefrontal cortical damage.

It has been argued that the right hemisphere is dominant for positive emotions and the left hemisphere is dominant for negative emotion (Davidson, Jackson, & Kalin, 2000; Davidson, 1992b). We report that damage to the right PFC is associated with poorer recognition of negative social expressions, which might prompt withdrawal behavior. However, we did not find impairments in the recognition of positive social expressions (which might motivate approach behavior) in the patients with left prefrontal cortical damage. In part this may reflect the psychometric properties of the test as the positive emotional expressions were significantly easier to identify and a ceiling effect may have thus masked subtle deficits among the left prefrontal cortical damage group.

Table 4. Basic Demographic and Neuropsychological Details for Each Group

	Sex (M:F)	*Age, yrs*	*Onset of Epilepsy, age*	*IQ*	*Benton Facial Recognition Task*
Right temporal	11:16	37 (11)	16 (11)	102 (14)	43.2 (3.0)
Left temporal	10:17	32 (10)	14 (13)	103 (14)	43.3 (4.7)
Right frontal	8:8	41 (15)	16 (22)	105 (13)	45.9 (4.6)
Left frontal	8:7	39 (14)	15 (10)	112 (8)	46.0 (3.8)
Healthy controls	43:48	34 (12)	–	107 (10)	–

Mean and standard deviation are given for each continuous variable.

In its present format the valence of the distracter items in the "Eyes task" is not systematically manipulated (thus, some items had purely positively or negatively valenced distracters and some had a valence mix). Future versions might manipulate the valence of the distracters to test for the possibility of a general bias in choosing positively valenced descriptors in right and negatively valenced descriptors among left prefrontal cortical damage patients.

There are other possible interpretations of the finding of right-sided processing of complex social expressions that may relate to the nature of the stimuli. Facial expressions of the basic emotions, such as fear, disgust, and anger, are held to be cross-cultural signals, which do not depend upon social knowledge for their interpretation and which may be detected by dedicated innate neural circuits (Ekman, 1992; Ekman, Sorenson, & Friesen, 1969). By contrast, social expressions are defined with reference to social situations and understanding, and their detection will rely in part on social knowledge and prior experience (Baron-Cohen, Wheelwright, Hill, et al., 2001). The right PFC has been associated with both episodic and autobiographical memory processes, which may be recruited when retrieving social and personal knowledge necessary for decoding social expressions (Fink et al., 1996; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994). There is also some evidence of more extensive activation of the right PFC when scenes are viewed which evoke moral emotions such as outrage (Moll et al., 2002). Although the stimuli used to evoke moral emotions were of complex interpersonal scenes, they share with the stimuli we

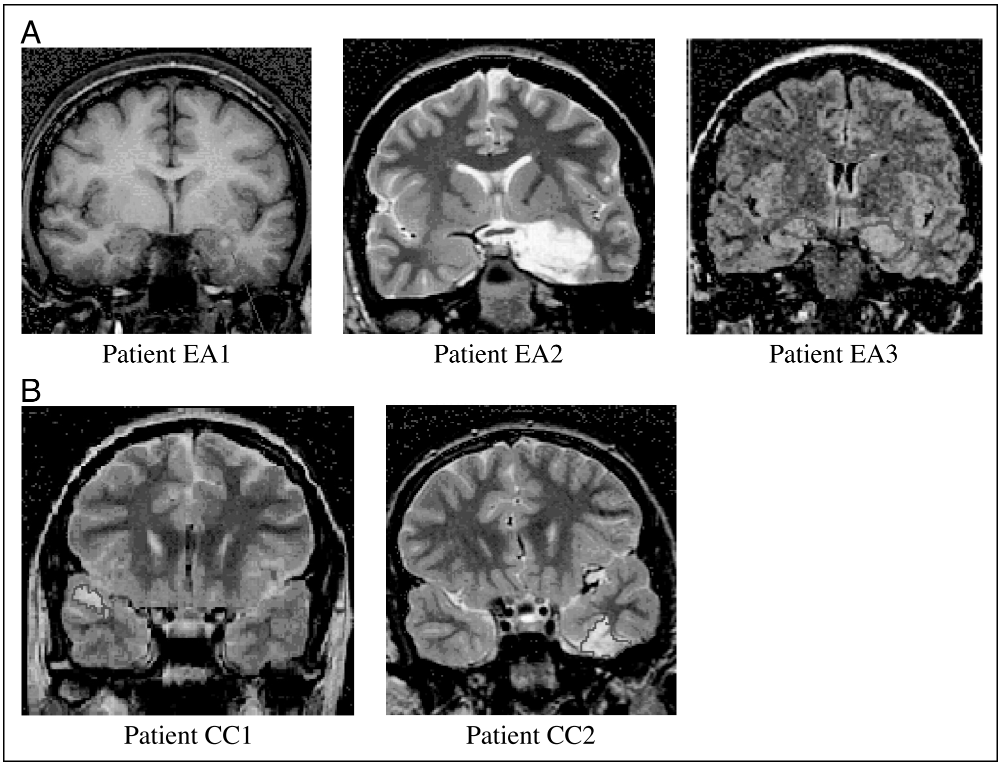

Figure 1. Selected MR images of patients in the early amygdala damage and clinical control groups. (A) Three patients in the early amygdala damage group are shown. Patient EA1 had the smallest lesion of this group seen as a hyperdense lesion on T1 sequence in the superolateral portion of the left amygdala (indicated by the red line). Patient EA2 had a large lesion centered on the amygdala extending toward the temporal pole and incorporating the anterior hippocampus. The presence of a DNET was confirmed when the patient proceeded with the operation. Patient EA3 has gross enlargement of the left amygdala, seen best on the FLAIR sequence. (B) Two patients in the clinical control group. Patient CC1 had a lesion in the right temporal operculum. Patient CC2 had a lesion lying in the antero-inferior aspect of the right anterior temporal lobe.

used the property of a reliance on social knowledge and experience for interpretation. This account has the advantage of placing the social perceptual deficits in the context of broader problems with social cognition. However, it does not account for the sensitivity to valence of the complex mental state we report.

Contrary to our prediction, we did not find more severe impairments on the ''Eyes task'' among patients with orbito-frontal or medial damage, relative to those with dorsolateral prefrontal cortical damage. Indeed, the group with most severe deficits had predominant damage to the right DLPFC, although the small number of patients in this group means this finding needs to be interpreted with caution. The findings are perhaps surprising given the wealth of lesion and neuroimaging evidence mentioned earlier, which implicates the VMPFC in the recognition of emotional expressions and other social cognitive processes. However, there have been other findings of a lack of correlation with selective damage to the VMPFC and deficits in tasks held to be mediated by this region—such as affective decision making as indexed by the Iowa gambling task. Indeed, one large study found that damage to the right DLPFC correlated more strongly with deficits on the task than damage to the VMPFC (Clark, Manes, Antoun, Sahakian, & Robbins, 2003), with the best overall predictor of faulty emotional decision making being the total amount of damage to the entire PFC. In a recent large lesion study, Mah et al. (2004) have reported that lesions of either the DLPFC or OFC were associated with impairments in social perception (Mah et al., 2004). A previous study which included nearly all the patients who participated in the ''Eyes task'' also failed to find any differential effects of lesion location on ToM reasoning (Rowe, Bullock, Polkey, & Morris, 2001).

The findings from our study may also seem to be at odds with functional neuroimaging in healthy subjects. Firstly, peak activations during performance of the ''Eyes task'' in healthy subjects have been reported as greater in the left rather than the right PFC (Baron-Cohen, Ring, et al., 1999). Secondly, there is substantial evidence suggesting that the medial PFC is activated when healthy subjects attribute mental states to others (Frith & Frith, 2003). However, damage in our patients to the medial PFC was not specifically associated with impaired performance on the ''Eyes task.'' This was true even when the lesion incorporated regions which are maximally activated in healthy subjects during ToM reasoning. Interestingly, others have reported intact ToM reasoning despite complete loss of regions of the medial PFC held to support such reasoning (Bird, Castelli, Malik, Frith, & Husain, 2004). Overall, the findings suggest that the right PFC acts as an integrated functional system in the detection of complex cognitive and social expressions. Thus, damage to any one of its components (orbito-frontal, dorsolateral, or medial) can lead to impairments.

Limitations of the Study

The ''Eyes task'' was originally described as an advanced test of ToM on the grounds that it involves the attribution of a relevant mental state (e.g., daydreaming). Clearly, it does not include the second stage of inferring the content of that mental state (e.g., daydreaming *about* an impending holiday) (Baron-Cohen, Wheelwright, Hill, et al., 2001). However, some reserve the term ''ToM'' for tasks which incorporate both stages. In this article, we therefore use different terminology, dividing the stimuli into cognitive and social expressions. The distinction we employ has proved useful in other neuropsychological studies, although we acknowledge that there are many other ways of classifying the stimuli (Adolphs, Baron-Cohen, et al., 2002).

The ''Eyes task'' has been analyzed as requiring subjects to have a lexicon which includes cognitive (thought-state), social, emotional, or mental state terms and to know the semantics of these terms. The task involves mapping these terms to the stimuli presented (the eye region of the human face) (Baron-Cohen, Wheelwright, Hill, et al., 2001). The mean score on the ''Eyes task'' for healthy controls in our study was similar to the normative scores given in the original report of the task (Baron-Cohen, Wheelwright, Hill, et al., 2001). The test has proved to have concurrent validity in that it correlates well with measures of personality traits of empathic understanding (Lawrence, Shaw, Baker, Baron-Cohen, & David, 2004). It is also sensitive to deficits among subjects with Asperger's syndrome who have core deficits in aspects of social cognition such as the accurate detection of mental states (Baron-Cohen, Ring, et al., 1999). However, the control condition used in the task of gender assignment differs in its level of difficulty as there are only two choices, and these choices are fixed throughout (male vs. female). This may have resulted in a partial ceiling effect obscuring group differences. The stimuli were of the human eye region only and static in nature, features which might be criticized for lacking ecological validity. However, previous studies have shown that the detection of complex mental states from the eye region does not differ greatly when the entire face region is used (Baron-Cohen, Jolliffe, et al., 1997) and the eye region is the natural focus of attention when decoding mental states of others.

Although this is one of the largest studies with unilateral focal lesions of the amygdala and PFC in social perception, there is still a risk of type 1 errors when the performance of subgroups are considered. There is also some variability in the extent of exact damage within each group, particularly among the patients with focal lesions of the temporal lobe. This possible confound is less marked in the frontal group, in which all lesions were surgical and defined on the basis of neurosurgical reconstructions of the excised areas, allowing precision in defining the boundaries of the lesion.

Conclusion

This study delineates the involvement of the amygdalae and the right PFC in the recognition of cognitive and social expressions. The amygdala appears to process facial expressions extending beyond the basic emotions into displays of more complex cognitive and social expressions. The study also demonstrates the effects of damage to the right PFC on the detection of negative social expressions. This provides a plausible neurocognitive substrate for the clinical presentation associated with damage to the region.

METHODS

Participants

All patients were recruited from the Department of Neurosurgery at the Regional Neurosciences Centre at King's College London. Demographic and clinical details are given in Tables 1 and 4. Ethical approval was given by the local ethics committees. All participants gave informed consent.

Ninety-one healthy control subjects, with no psychiatric or neurological disorders, were recruited in part from a database of healthy volunteers held at the Institute of Psychiatry.

Patient Groups

Fifty-four patients with temporal lobe damage were tested: 27 had RT damage and 27 had LT damage. Thirty-one patients with frontal lobe damage were included, 16 with RF and 15 with LF damage. The temporal lobe damage group was composed of the following patients (see Figure 1 for images of patients from each group).

The 54 temporal lobe-damaged patients were further divided as follows:

1. 23 anterior temporal lobectomy patients. All patients in this group had en bloc surgical resection of the anterior temporal lobe to treat medically intractable epilepsy. All operations were en bloc resections (8 left-sided and 15 right-sided) with complete excision of the amygdala in all cases.
2. 18 patients with focal amygdala lesions (7 right and 11 left). All patients in this group had focal amygdala lesions, 8 with extension beyond this structure. On the basis of neuroradiological features and clinical histories, these lesions were thought to be indolent nonprogressive tumors such as dysembryoblastic neuroepithelial tumors (DNETs) or gangliogliomas (16 patients) or arteriovenous malformations (2 patients).
3. 13 patients with focal nonamygdala lesions (5 right- and 8 left-sided). All patients in this group had focal lesions of the temporal lobes that completely spared the amygdala. The lesions were made up of indolent nonprogressive tumors (10 patients), and one subject each with an arteriovenous malformation, developmental anomaly, and epidermoid cyst.

Frontal Lobe Patients

The 31 frontal lobe patients all had surgical resections as treatment of medically intractable epilepsy (n = 11), vascular malformations (n = 3), or tumor excisions (n = 17). The groups were further classified according to side and the prefrontal sectors of functional significance into which the lesions predominately encroached. The areas were defined anatomically as DLPFC (Brodmann's areas 9 and 46, including medial portions) or VMPFC (which was taken as including either the orbital or medial PFC, correspomding to, Brodmann's areas 10, 11, 12, and 25). The characterization of this group has been described elsewhere (Hornak et al., 2003; Rowe et al., 2001). These four groups (R VMPFC, L VMPFC, R DLPFC, and L DLPFC) did not differ significantly in terms of estimated IQ (χ^2 = 3.3, p = .35) or sex (χ^2 = 1.2, p = .87). The extent of the lesions is illustrated in E-Figure 1 at the Web link www.em-online.org/JOCN. In 19 cases, the lesions were reconstructed on the basis of postoperative MR images. In three cases, postoperative MR imaging was not possible due to the presence of intracranial metal clips, and in nine cases, MR images from different neuroimaging centers could not be obtained. In these cases, the neurosurgeon's reconstructions of the resected areas were used.

In addition, overlay maps were created by superimposing the individual lesions of patients who showed impairment on the "Eyes task." Each patient's score was expressed as the number of standard deviations from the mean of the healthy controls (i.e., Z scores). Severe impairment was defined as a Z score < -2. The lesions of these impaired patients were superimposed manually onto a standard brain template. Given the relatively small number of patients who were impaired (n = 6) and the unavailability of some postoperative scans on these patients, a voxel-based method of defining lesion overlap was not used (these images of E-Figure 2 can be viewed at www.em-online.org/JOCN).

The "Eyes task" involves the attribution of an emotional or mental state to others. This is arguably a preliminary step to inferring and reasoning about the content of the mental states of others—an ability often referred to as "ToM reasoning." The peak activations reported during the performance in healthy participants of ToM tasks have fallen mainly with the medial PFC (Frith & Frith, 2003). We divided our frontal damage patients on the basis of involvement or sparing of the reported peak areas of activation. The performance of these groups was compared to determine whether lesions of the regions found to support on-line ToM reasoning in fMRI studies were associated with particularly severe impairment in the "Eyes task."

Tasks

All subjects completed the National Adult Reading Test to estimate intelligence (Nelson, 1982). All patients in the temporal lobe damage group and 25 in the frontal damage group also completed the Benton Facial Recognition test as damage to the anterior brain can be associated with facial processing deficits (Benton, Sivan, Hamsher, Varney, & Spreen, 1983).

Experimental Tasks

In the "Reading the Mind in the Eyes" task (revised version)—or "Eyes task"—subjects were presented with pictures of the eye region of actors. The pictures are flanked by four terms (the correct term and three foils) and the subjects were asked to choose which term best describes what the actor is thinking or feeling (Baron-Cohen, Wheelwright, Hill, et al., 2001). The terms do not include any basic emotional descriptors (happy, sad, angry, frightened, disgusted, or surprised). To ensure subjects understood the terms, a glossary of definitions was provided and subjects were encouraged to ask about the meaning of any unfamiliar words. As an additional non-emotional control task, the temporal lobe damage and healthy control groups were asked to judge the gender of the actor, as amygdala damage has been associated with specific impairments in decoding the eye region.

In this study, four independent assessors divided the stimuli into those which depicted cognitive expressions (e.g., "pensive," "daydreaming," "contemplative") or social expressions. The social expressions were then further divided into those with a positive valence (e.g., flirtatious, playful, friendly) and those with a negative valence (e.g., hostile, suspicious, defiant, accusing). Only items on which there was complete agreement on the categorization were included in further analyses. Examples of each of the type of stimuli can be seen on the Web link: www.em-online.org/JOCN, E-Figure 3.

A score of 1 point was given for a correct answer, and 0 for an incorrect answer. Scores were converted to percentages to allow comparisons in the performance across the cognitive and social expressions.

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