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Depression is associated with increased sensitivity to signals of disgust: A functional magnetic resonance imaging study

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ABSTRACT

Emotions of fear and disgust are related to core symptoms of depression. The neurobiological mechanisms of these associations are poorly understood. This functional magnetic resonance imaging study aimed at examining the Blood oxygenation level dependent (BOLD) response to facial expressions of fear and disgust in patients with major depressive disorder.

Nine patients in an episode of major depression and nine healthy controls underwent two functional magnetic resonance imaging experiments where they judged the gender of facial identities displaying different degrees (mild, strong) of fear or disgust, intermixed with non-emotional faces.

Compared with healthy controls, patients with depression demonstrated greater activation in left insula, left orbito-frontal gyrus, left middle/inferior temporal gyrus, and right middle/inferior temporal gyrus to expressions of strong disgust. Depressed patients also demonstrated reduced activation in left inferior parietal lobe to mildly fearful faces.

Enhanced activation to facial expressions of disgust may reflect an emotion processing bias that suggests high relevance of emotion of disgust to depression.

1. Introduction

Negative biases during facial affect processing in major depressive disorder (MDD) have been reported frequently in previous studies. In particular, findings indicate that depressed patients recognise significantly more sadness in facial expressions compared with healthy volunteers (Bouhuys et al., 1999; Gur et al., 1992) or perceive positive emotional faces as less positive (Surguladze et al., 2004). Depressed individuals may also have greater direction of attention towards negative facial expressions (Gotlib et al., 2004) or away from happy facial expressions (Suslow et al., 2001).

Functional neuroimaging studies examining negative, mood-congruent attentional biases in depression have demonstrated in depressed individuals patterns of abnormally increased activity in limbic-subcortical and extrastriate visual object processing regions in response to sad and abnormally decreased activity in these regions in response to happy facial expressions (Surguladze et al., 2005; Fu et al., 2007). There are discrepant findings, however, regarding the nature of subcortical limbic regional activation in response to fearful faces in depressed individuals. One study (Lawrence et al., 2004) demonstrated reduced activation in right amygdala/hippocampus and in right parahippocampal gyrus relative to healthy controls during implicit processing of mild and strong fearful expressions, respectively, while earlier findings (Sheline et al., 2001) had demonstrated increased amygdala activity in response to masked fearful facial expressions in depressed patients relative to healthy controls. A recent study showed no significant difference in amygdala activity to fearful faces in depressed individuals relative to healthy controls (Almeida et al., in press).

Although disgust is an important negative emotion (Ekman, 1992), its role in depression has been largely unrecognised. The experience of disgust may be associated not only with food but

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also with social interactions, and, in some cases could be directed to one's self. These social and self-related aspects of disgust are especially relevant to depression. In particular, since the facial expressions of disgust may convey social rejection (Rozin et al., 1994; Marzillier and Davey, 2004), increased sensitivity to disgust (expressed by others) may be characteristic to depression. Indeed, there have been reports demonstrating that the processing of facial expressions of disgust is enhanced in people with depression. Hayward et al. (2005) observed enhanced recognition of facial expressions of disgust in a recovered depressed sample compared with healthy control subjects. Acute tryptophan depletion (ATD) in remitted patients with a history of major depressive disorder (a procedure previously shown to induce transient depressed mood in such individuals) was associated with decreased recognition of expressions of fear, but faster recognition of disgust (Merens et al., 2008). There have also been findings of no difference between depressed individuals and controls with regard to labelling the facial expressions of disgust (Bediou et al., 2005).

Regarding self-directed disgust, some authors (Power and Dalgleish, 1997) argued that the commonly experienced secondary emotions of shame and guilt in depression are derived from the basic emotion of disgust, and that depression may in part depend on a coupling of sadness and self-disgust. This proposal was supported in a study (Power and Tarsia, 2007) found that the emotion of disgust was experienced significantly more by individuals with depression, anxiety or with comorbid anxiety and depression – compared with healthy controls. Another study (Overton et al., 2008) provided direct evidence that self-disgust (as measured by the newly developed Self-Disgust Scale) played an important role in depression by mediating the relationship between dysfunctional cognitions and depressive symptomatology. It should be noted however that the questionnaire-based study of disgust sensitivity (Schienle et al., 2003) did not find any elevation in disgust sensitivity in patients with depression – in contrast to those with schizophrenia and OCD. The authors suggested that whereas the questionnaire tapped on the disgust directed to external stimuli, the crucial feelings for depression would be self-disgust, shame and guilt which were not covered by the questionnaire.

The neurobiology of processing of facial expressions of disgust is well established and has been shown to involve the insula, striatum, inferior frontal cortex, in addition to visual object processing regions such as extrastriate and inferior temporal cortices (Calder et al., 2000; Phillips et al., 1997). There has been little research that has examined the extent to which abnormalities in neural systems implicated in disgust perception are associated with depression. The only study of this kind published so far (McCabe et al., 2009) showed that the unmedicated individuals recovered from depression had an increased activity in bilateral caudate in response to the disgust-eliciting pictures of mouldy food. We were interested in social dimensions of the emotion of disgust in people with depression. Therefore in the present study we examined patterns of neural activation to facial expressions of disgust and fear in currently depressed individuals with a history of MDD. The emotional expressions of fear were included in the study to provide additional emotionally negative stimuli which may help to differentiate the neural responses specific for the processing of disgust. Based on the close associations between disgust and depression, we hypothesized that depressed patients would show greater activity in visual object processing and limbic regions to facial expressions of disgust than healthy controls, but that activity in these regions to facial expressions of fear would be less likely to distinguish the two groups.

2. Materials and methods

2.1. Participants

Nine individuals with DSM-IV primary diagnosis of Major Depressive Disorder were recruited from the hospital and community services of the South London and Maudsley National Health Service Trust. None of them had diagnosable comorbidity in terms of other Axis I disorders.

Nine healthy individuals without a history of major depressive disorder or other psychiatric history, determined by interview, were recruited from the local community and ancillary staff of the Institute of Psychiatry.

Ethical approval was obtained from the Ethical Committee of the South London and Maudsley Trust and the Institute of Psychiatry. Written consent was obtained from all subjects prior to participation in the study. All participants were right-handed (Oldfield, 1971). Both groups were matched for age, sex ratio, and years of education. There was no significant difference between depressed group and controls in age of male ($t[9] = 1.7$; $p = .2$), or female subjects ($t[7] = .3$; $p = .8$).

Exclusion criteria included a history of head injury, illicit substance abuse, and a score of less than 24 on the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). Depression severity was measured using the Beck Depression Inventory (BDI, Beck et al., 1986) and the Hamilton Depression Rating Scale (HDRS, Hamilton, 1960). Depressed individuals had significantly higher BDI scores compared with healthy individuals ($U = 0$, $p < .001$), ranging from 15 to 50 with mean score 31.8 corresponding to moderate/severe depression (Table 1). There was no evidence for psychotic symptoms experienced by patients either at the time of assessment or in their past. All data on duration of illness in depressed individuals was collected from the medical records and interview with each depressed individual.

All patients were taking antidepressant medication. Four of them were taking the serotonin and noradrenaline re-uptake inhibitor venlafaxine; three, selective serotonin re-uptake inhibitors (sertraline and paroxetine); one patient was taking the MAO inhibitor phenelzine; and one, the tricyclic antidepressant dothiepine. Two patients were additionally treated with Lithium; one, with diazepam; and one, with promethazine. As in our previous study (Surguladze et al., 2005), for the purposes of further analysis medication dose was coded from 1 (low-dose) to 4 (high-dose), and the group of patients was divided into two subgroups depending on

Table 1
Socio-demographic and clinical characteristics and on-line performance data.

	MDD patients ($n = 9$)	Control subjects ($n = 9$)
Female/Male ratio	4/5	4/5
Age, years	42.8 ± 7.2	39.7 ± 14.6
Education, years	13.4 ± 2.4	13.6 ± 1.7
Duration of illness, years	8.0 ± 5.1	–
Mini-Mental State Examination	28.7 ± 1.7	30 ± 0
Beck Depression Inventory**	31.8 ± 11.8	2.8 ± 3.8
Hamilton Depression Rating Scale	17.7 ± 5.5	–
Correct responses for gender decision in disgust task	47.2 ± 9.5	48.6 ± 7.6
Reaction time to 50% disgust faces, sec.	1.17 ± .31	.97 ± .26
Reaction time to 100% disgust faces, sec.	1.17 ± .26	1.0 ± .26
Correct responses for gender decision in fear task	49.2 ± 7.4	49.5 ± 7.6
Reaction time to 50% fearful faces, sec.	1.1 ± .22	1.0 ± .24
Reaction time to 100% fearful faces, sec.	1.2 ± .33	1.0 ± .25

**$p < .01$.
Values shown are means ± SD.