Effects of Cognitive and Neural Negative Biases Present in Dysphoric Volunteers on an Emotional Test Battery and the Associated Modulation of fMRI BOLD Signals

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Abstract

Background: Depression is reported to be strongly associated with negative biases in processing emotional information. The current study aimed to evaluate whether a group of medication-free participants, meeting criteria for sub-threshold depression or major depression (dysphoric group) differed from a non-dysphoric group in neural processing of emotional information using an emotional test battery.

Methods: Males or females aged 18 to 45 years with BDI score of 0-5 or ≥10 at both screening and assessment visits and HAM-D score of <24 at both, were studied using a battery of emotional tasks sensitive to the affect of words or faces with behavioural or fMRI (BOLD at 3T) measures as outcomes.

Results: Dysphoric participants had increased amygdala activation to fearful faces and threatening words. In addition dysphorics had increased activation in the fusiform area to fearful faces. A reciprocal pattern of activation was observed between dorsal and ventral prefrontal cortex in non-dysphorics and this pattern of activity was reversed in dysphoric participants. Dysphorics were also impaired in recalling positive words from a word categorisation task when compared with controls.

Discussion: Dysphoric participants have negative biases in the neural processing of emotional information that are similar to those reported in studies of depressed patients (Harmer et al 2009). Recruitment of dysphoric participants was fast and efficient compared to recruiting drug free depressed patients from primary or secondary healthcare centres. The results indicate that this dysphoric group can be differentiated from non-dysphoric participants in terms of emotional processing and behaviour. Harmer, C.J., O'Sullivan, U., Favaron, E., Massey-Chase, R., Ayers, R., Goodwin, G.M., Cowen, P., 2009. Effect of Acute Antidepressant Administration on Negative Affective Bias in Depressed Patients. American Journal of Psychiatry, 166, 166:1178-1184.

Introduction

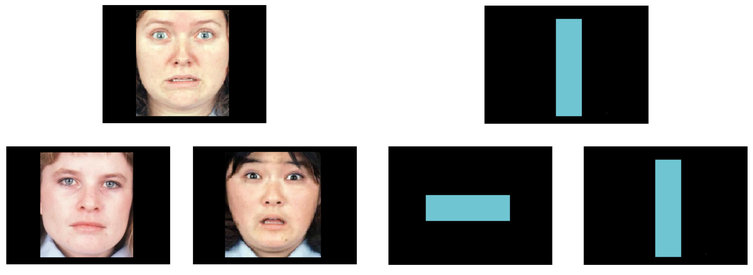
- Depression is associated with abnormal neural responses to emotional information processing.
- Neuroimaging studies of depressed patients have consistently reported amygdala hyperactivity in response to negative emotional stimuli[1].
- However, it is unclear whether this hyperactivity is also apparent as a function of dysphoria.

Hypotheses

- Dysphoric participants will have an overactive amygdala in response to fearful stimuli.
- Previous studies have reported a reciprocal pattern between the amygdala and orbitofrontal cortex when processing emotional information[2].
- Hence, we also hypothesised that there will be greater activation in the OFC in dysphoric participants to happy than fearful faces.

Methods

- 24 dysphoric participants (Beck Depression Inventory, BDI > 10) and 24 matched healthy controls (BDI < 5).
- Participated in a faces – shapes matching task.
- Alternate blocks of fear, happy and control faces were presented.



References

1. Siegle *et al* (2007). Biological Psychiatry, 61, 198 - 209.

2. Wright *et al* (2008). NeuroImage, 39, 894 - 902.

Imaging Analysis

- Block design with 3 explanatory variables modelled: fear, happy and control.
- *A priori* regions: rostral anterior cingulate (rAC), dorsal AC (dAC), anterior cingulate (ACC), ventral striatum (VS), amygdala, lateral orbitofrontal cortex, hippocampus, parietal cortex, visual cortex insula, midbrain and thalamus.
- Significance defined at p < 0.05 FDR small volume corrected (SVCs) using 10mm diameter sphere centred on the *a priori* regions.

Demographics

Variables	Dysphorics	Controls	Significance
Age	26 (5.6)	24 (4.4)	> 0.1
Gender	13F, 11M	13F, 11M	> 0.1
BDI	19 (10)	0.3 (1.0)	< 0.001
HAM-D	12.5 (6.4)	0.1 (0.9)	< 0.001
NART (IQ)	117.9 (3.8)	1117.8 (5.3)	> 0.1

Table 1: Demographics and baseline depression severity scores for both dysphorics and controls. Mean with standard deviation n parentheses.

Imaging Results

Dysphorics *vs* Controls

Brain Regions	Peak voxels	Z value	P value
Fear > Happy			
R Amygdala	24, -8, -18	3.75	0.020
R Fusiform Gyrus	24,-36, -16	3.70	0.023
Happy > Fear			
Lateral Orbitofrontal Cortex	-26, 46, -8	3.91	0.012

Table 2: Peak voxels of brain regions significantly increased in dysphorics vs controls with their corresponding z and p values

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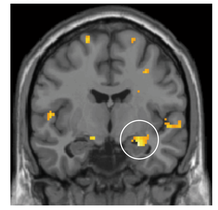
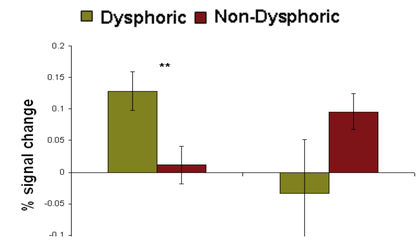
Imaging Results *(continued)*

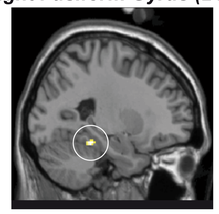
Dysphoric *vs* Controls : Fear > Happy

Amygdala (24, -8, -18)



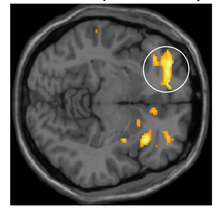


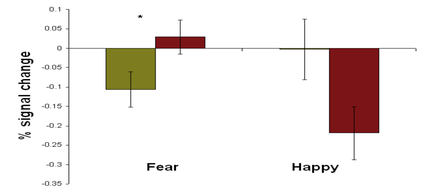
Right Fusiform Gyrus (24, -36, -16)



Dysphoric *vs* Controls : Happy > Fear

Lateral OFC (-26, 46, -8)





Summary

- Compared to controls, dysphoric participants had greater activation of the amygdala and fusiform gyrus when looking at fearful, but not happy, faces.
- In contrast, dysphoric participants had greater activation in the lateral OFC to happy than fearful faces when compared to controls.
- This pattern of neural activity is believed to contribute to biases in processing negative stimuli in depression.

Disclosures:

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