Assessing the Influence of Negative Mood on Brain Processing of Visceral Sensation

S. J. Coen[1], M. Mitterschiffthaler[1], L. J. Gregory[2], L. Yágüez[3], M. J. Brammer[1], S. C. Williams[1], and Q. Aziz[4]

[1]Neuroimaging Research Group, Centre for Neuroimaging Sciences, Institute of Psychiatry, Kings College, London, United Kingdom, [2]Translational Imaging Unit, University of Manchester, United Kingdom, [3]Department of Psychology, Institute of Psychiatry, Kings College, London, United Kingdom, [4]Section of GI Sciences, University of Manchester, United Kingdom

INTRODUCTION

A link between negative emotional state and abnormal visceral sensation, such as abdominal pain experienced in patients suffering from functional gastrointestinal disorders is continuously reported. In order to probe this relationship, functional brain imaging studies have examined the effect that emotion has on the visceral sensory neuromatrix in normal healthy volunteers [1]. However, the influence of negative emotion on the brain processing of painful visceral sensation has yet to be investigated. Aims: Using functional magnetic resonance imaging (fMRI), and emotionally salient music as a method by which to induce a negative mood [2], the purpose of this study was to investigate the effects of negative mood on the brain processing of painful and non-painful oesophageal sensation.

METHODS

12 healthy, male volunteers (mean age 25 years, 3 months) participated in the study. All subjects gave informed, written consent prior to intubation and scanning. The study was approved by the local ethics committee for research (Ethics ref.311/03). ***Oesophageal stimulation (OS):*** A standard manometry catheter with a silicone balloon attached was passed trans-nasally into the distal oesophagus. The catheter was attached to a pump that inflated the balloon with air at regular intervals throughout each experimental run. ***Mood induction:*** in order to manipulate mood the present study employed classical music previously validated in a study examining the neural correlates of neutral and sad mood [2]. Mood induction commenced prior to scanning in order to ensure volunteers were in the appropriate mood state before stimulation and image acquisition. fMRI images were acquired during two experimental runs throughout which volunteers received randomised phasic non-painful (20 stimuli/run) and painful (20 stimuli/run) distensions to the oesophagus under a) neutral mood induction and b) negative mood induction. Behavioural data measuring the subjective perception of the stimulus (0 = non-painful, 5 = discomfort, 10 = extreme pain) was acquired after each oesophageal stimulus, using visual analogue scales (VAS). Mood ratings were acquired following each scan. The order of mood induction was not randomised (neutral always first) due to the lingering effects of exposure to sad stimuli on subsequent processing of happy or neutral stimuli [3].

fMRI acquisition: Functional Magnetic Resonance Imaging was performed using a GE Neuro-optimised 1.5 Tesla system (General Electric, Milwaukee WI, USA), based at the Maudsley Hospital, London. A total of 360 T2* weighted images per slice (16x7mm slices, 0.7 interslice gap, TE 40ms, TR 3000ms, flip angle 90°, matrix 64^2, total no of images per scan 5760), depicting BOLD contrast [4] were collected over a 18 minute period of continuous acquisition, during which, subjects underwent mood induction and received painful and non-painful phasic distensions to the oesophagus. This procedure was performed on two occasions to collect data for brain processing of oesophageal sensation during both neutral and negative mood. ***Image Analysis:*** An event related analysis was employed. The data were first realigned [5] to minimize motion related artefacts and were smoothed by using a Gaussian filter (full width at half maximum, 7.2 mm). Responses to the experimental paradigms were then detected by time-series analysis with gamma variate functions (peak responses at 4 and 8 seconds) to model locally variable hemodynamic response functions. Spatially realigned BOLD responses were modelled as the weighted sum of the input function convolved with two Poisson functions. A goodness of fit statistic was computed and a voxel-wise inference was carried out non-parametrically. At the group level, individual statistic maps were transformed into standard stereotactic space and median activation images constructed. ***ANOVA*:** To estimate the difference between brain activations across all phases and conditions of the study, all corresponding sum of squares quotient (SSQ) ratios were combined and fitted to an analysis of variance model at each voxel generically activated by the activation condition in one or both of the phases and conditions (painful or non-painful stimulation and neutral vs negative mood induction). The null hypothesis of zero difference between conditions in mean SSQ was tested by a permutation test, as previously described in detail [5].

RESULTS

All subjects tolerated the study well. Mean moods ratings confirmed sadness increased significantly following negative mood induction ($P<0.01$). Painful stimulation was rated as significantly more painful than non-painful stimulation during both neutral ($P<0.001$) and negative mood ($P<0.01$). However, there was no significant effect of mood on VAS ratings of painful ($P>0.05$) and non-painful ($P>0.05$) stimulation, see figure 1. ***ANOVA:*** *Neutral v Negative mood during painful stimulation:* Brain activation following painful stimulation increased during negative mood induction in the anterior cingulate cortex (ACC, BA24 & BA32), anterior insula, inferior frontal gyrus and SMA. All significant increases were located in the right hemisphere of the brain, see figure 2 & 3. *Neutral v Negative mood during non-painful stimulation:* Following non-painful stimulation during negative mood, significant increases in brain activity were localised to the right anterior insula, ACC (BA24 & BA32), and bilateral posterior cingulate, see figure 4.

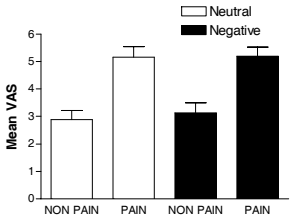

Figure 1: Mean group OS ratings during negative and neutral mood induction.

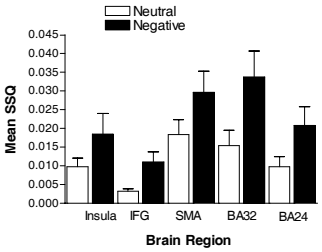

Figure 2: Shows results of ANOVA between neutral and negative mood following painful OS

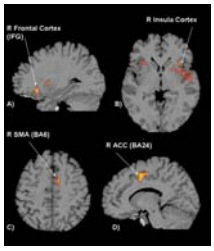

Figure 3: Summary of brain regions showing significant increase in activity when painful OS is delivered during negative mood

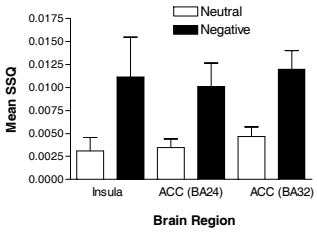

Figure 4: Shows results of ANOVA between neutral and negative mood following non-painful OS

DISCUSSION

This study provides novel information on the influence of negative affect on central processing of painful OS, and supports previous findings on non-painful OS [1]. Brain activity following both painful and non-painful stimulation suggests a possible right-hemispheric dominance in processing the affective motivational components of OS, which may be explained by the suggestion that sympathetic activity is represented in the right hemisphere [6]. Increased activation of the right anterior insula during negative emotion supports previous evidence suggesting this area is particularly important in evaluation of internal feelings with emotional significance, such as unpleasantness. Moreover, the data provides further evidence to suggest the right anterior insula is integral to the mental generation of knowledge of physical and emotional state through interoception [6, 7]. This study adds important knowledge concerning the brain processing of the affective component of oesophageal pain, information which may be valuable in evaluating central processing of visceral sensation in functional clinical disorders that have visceral pain as a primary symptom.

References

1. Phillips ML, et al. The effect of negative emotional context on neural and behavioural responses to oesophageal stimulation. Brain 2003;126:669-684.
2. Mitterschiffthaler MT, et al. Neural Correlates of Happy and Sad Mood Induction with Music. Neuroimage 2004;22:e329.
3. Ekman P, et al. Facial signs of emotional experience. [Article]. Journal of Personality & Social Psychology 1980;39:1125-1134.
4. Ogawa S, et al. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc Natl Acad Sci U S A 1990;87:9868-9872.
5. Bullmore ET, et al. Diagnosis and treatment of stimulus-correlated motion in generic brain activation studies using fMRI. Hum Brain Mapp 1999;7:38-48.
6. Craig AD. How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci 2002;3:655-666.
7. Craig AD. Forebrain emotional asymmetry: a neuroanatomical basis? Trends Cogn Sci 2005;9:566-571.