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Running Head: Emotional categorisation and depression

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ABSTRACT

Negative biases in emotional processing are a major characteristic of depression. Recent research has shown that such negative biases are evident in high risk individuals even in the absence of personal history of depression, suggesting that they may serve as key vulnerability markers of depression. However, the neural basis of these behavioural observations has not been fully explored. This study therefore aimed to (1) illustrate the neural processes involved in the categorisation of emotional personality-trait words; and (2) examine whether these neural mechanisms are biased towards negative information in high risk individuals. Risk for depression was defined by high neuroticism (N). We recruited a sample of high risk (high N) and low risk (low N) never-depressed young adults. Functional magnetic resonance imaging (fMRI) was acquired during the categorisation and memory for positive and negative self-referent personality-trait words (e.g. honest, rude). High risk volunteers showed greater responses in the right superior parietal cortex than low risk volunteers specifically during the categorisation of negative words. Moreover, neuroticism score was positively correlated with neural responses in the left anterior cingulate during the categorisation of negative words but negatively correlated within the same region during the retrieval of these words. These results highlight a role of the fronto-parietal circuitry in emotional processing and further suggest that negative biases in these neural processes may be involved in risk for depression.

INTRODUCTION

Neuroimaging studies of acute depression have revealed abnormalities within key areas of the brain involved in emotional processing and regulation. In particular, major depression is associated with enhanced activity levels of amygdala, orbital and ventrolateral prefrontal cortex and subgenual cingulate at rest (Drevets et al 2000, 2001, 2003) and exaggerated responses within this circuitry during emotional provocation, particularly to negative affective stimuli (Fu et al 2004, Sheline et al 2001, Drevets 2000, Gotlib et al 2005, Surgladze et al 2005). Such results are consistent with negative biases in information processing shown behaviourally in depression (Bradley et al 1997, Gur et al 1992, Bouhuys et al 1999, Surguladze et al 2004, Mogg et al 2006, Bradley et al 1996, Bradley and Mathews 1983), and with the cognitive theories hypothesizing the importance of such biases in the aetiology and maintenance of depression (Beck et al 1979). However, it remains unclear whether these neural and behavioural abnormalities represent long term vulnerability prior to illness onset, or whether they occur as a result of current or past depressive episodes.

One way to identify the neural and cognitive correlates of vulnerability to depression is to observe individuals who have a high risk for depression but have never been depressed. Robust evidence has suggested that neuroticism (N) is a key predictor for depression (Kendler et al 1993, 2002, 2004, 2006) and largely mediates the genetic risk for this disorder (Sen et al 2004). In a recent study we found significant negative biases in highly neurotic never-depressed volunteers across a battery of emotional processing tasks (Chan et al 2007). Specifically, high N volunteers showed increased speed to categorise negative vs. positive personality-trait words and reduced positive memory intrusion in their subsequent recall. The negative biases seen in the

categorisation of self-referent adjectives were found to be particularly important in predicting depressed mood 18 months later, explaining 87% of the variance in Hamilton depression score in interaction with recent stressful life events (Chan et al, in preparation). These behavioural findings suggested that emotional processing biases represent vulnerability markers for depression rather than occurring through prior experience or treatment of depression.

The current study aimed to explore the neural substrates of these emotional processing biases seen as a function of neuroticism. Previous studies have implicated the role of a fronto-parietal network in the processes involved in this categorisation and memory for positive and negative personality-trait words in healthy volunteers (e.g. Gusnard et al 2001, Keenan et al 2001, Stuss 1991, Moran et al 2006). Specifically, the medial prefrontal cortex has been suggested to play a key role in the categorisation and retrieval of self-referent words (Craik et al 1999, Kelley et al 2002, Fossati et al 2003, 2004). Multiple areas within the parietal cortex have also been implicated, with some studies implicating the superior regions (e.g. Kircher et al 2000) while others implicating the inferior areas (e.g. Fossati et al 2003, 2004). Recent studies have further revealed that neural responses within a similar fronto-parietal network are sensitive to drug treatments effective in depression (Norbury et al 2007, Miskowiak et al 2007), thus suggesting that dysfunctions of this neural system may contribute to the aetiology or maintenance of depression.

Based on these studies and our previous behavioural findings (Chan et al 2007), we hypothesised that high N individuals would display greater responses in this fronto-parietal network, especially the medial prefrontal cortex, during the categorisation of

negative vs. positive personality-trait words. We further hypothesised that such enhanced neural processes in the categorisation of negative words would facilitate the retrieval of these words, resulting in reduced responses in high N individuals during the recognition of these negative words.

METHODS

Subjects

Twenty-six right-handed healthy volunteers with high or low N scores (see below) gave written informed consent to the study, which was approved by the Oxford Research Ethics Committee. The Structured Clinical Interview for DSM-IV (Spitzer et al 1995) was used to verify that all subjects were free of current or past axis-1 disorders, and all of them were free of medication excluding contraceptive pills. These participants were a subset of those previously taking part in the behavioural assessment of emotional processing (Chan et al 2007), but the testing sessions were on average 11 months apart. Due to a technical problem with response collection, five volunteers were excluded prior to data analysis. Thus, the data presented here represented 21 participants (14 women, aged 18-21).

N scores for screening were derived from the 12-item neuroticism scale of the shortened Eysenck Personality Questionnaire (EPQ: Eysenck et al 1985). Eleven (8 women) were in the high N group (N range 8-12), and 10 (6 women) in low N group (N range 0-4). This range of N scores was consistent with our previous behavioural study (Chan et al 2007). The two groups were matched for age (mean 19.91, SD 0.54 vs. mean 19.90, SD 1.20), gender, verbal IQ (mean 119.42, SD 2.92 vs. mean 117.51, SD 3.54) and spatial IQ (in ms: mean 2578, SD 982 vs. mean 1842, SD 631) as assessed by NART (Nelson 1982) and WAIS-R (Wechsler 1981). One subject from the high N group had a first degree relative with depression.

Mood and personality variables

To obtain a wider range of N scores across the sample, the full version of EPQ (Eysenck and Eysenck 1975) was administered. In addition, Beck Depression Inventory (BDI: Beck et al 1961) and State-Trait Anxiety Inventory (STAI: Spielberger et al 1970) were used to measure self-rated mood.

Verbal stimuli

For the emotional categorisation task, a list of 90 personality adjectives was constructed, of which half were unambiguously positive and half negative (Anderson 1968). Positive and negative words were matched on length, frequency (Francis et al 1982) and meaningfulness. Ten presentations of each of 'left' and 'right' were included as a baseline control condition. The words 'left' and 'right' were selected in order to control for the sensorimotor aspects of the task without requiring subjective assessment of the positive or negative aspects of the word. Thus, 110 words were presented in total, with the order randomised across subjects. The same words were used for each subject.

For the surprise memory task, the previously categorised words (old words) were mixed with 45 positive and 45 negative distracters (new words) taken from Anderson's list (Anderson 1968). The new words were unambiguously positive or negative and matched to the old words on length, frequency and meaningfulness. Thus, 180 words were presented in total, with the order randomised across subjects.

Task design

Functional MRI scans were acquired while subjects performed both the self-referent categorisation and memory tasks. Stimuli were presented on a personal computer

using E-Prime (version 1.0; Psychology Software Tools Inc., Pittsburgh, PA) and projected onto an opaque screen at the foot of the scanner bore, which subjects viewed using angled mirrors.

During the categorisation task subjects were instructed to characterise the words as 'like' or 'dislike' in a self-referential fashion as quickly and accurately as possible. Specifically, subjects were asked to imagine whether they would like or dislike it if they overheard someone referring to them as possessing each of these personality traits. This instruction was previously used in our behavioural study (Chan et al 2007) and other behavioural and neuroimaging studies (Harmer et al 2004, Norbury et al 2007, Miskowiak et al 2007). Subjects indicated their decision as 'like' or 'dislike' by pressing a button with the right index or middle finger, respectively. For the control words 'left' and 'right', subjects responded with their right index or middle finger respectively. Subject responses were recorded using an MRI-compatible keypad. Accuracy and reaction times were recorded by E-Prime. Each trial consisted of a fixation cross (500ms) immediately followed by a personality or control word (500ms). The duration of the intertrial interval (ITI) varied between 4000 and 8000ms according to a Poission distribution, with a mean ITI of 5000ms. Total duration of the catergorisation experiment was 550s.

Self-referent categorisation was immediately followed by an unexpected memory task. Subjects were asked to discriminate between studied (old) words and unstudied (new) words. Subjects indicated their decision of "yes" (old) or "no" (new) by pressing a button with the right index or middle finger, respectively. Trial presentation

was identical to that during the categorisation task. The total duration of this memory experiment was 900s.

fMRI data acquisition

Imaging data were acquired at 1.5 Tesla on a Siemens Sonata scanner located at the Oxford Centre for Clinical Magnetic Resonance Research (OCMR). Functional imaging consisted of 30 contiguous T_2*-weighted echo-planar image (EPI) slices [TR/TE; 3000ms/50ms, matrix size/field of view; 64 x 64/192 x 192, slice thickness = 4 mm]. A Turbo FLASH sequence (TR = 12ms, TE = 5.65, voxel size = 1mm^3) was also acquired to facilitate later coregistration of the fMRI data into standard space. The first two EPI volumes in each run were discarded to ensure T_1 equilibration.

Data Analyses

Functional MRI data was preprocessed using FSL version 3.2β (Smith et al 2004), which included slice acquisition time correction, within-subject image realignment (Jenkinson et al 2002), non-brain removal (Smith 2002), spatial normalisation (to Montreal Neurological Institute [MNI] 152 stereotactic template), and spatial smoothing (5mm FWHM). The time series were high pass-filtered (to a maximum of 0.025Hz).

Analyses of data from individual subjects were computed using a general linear model with local autocorrelation correction (Woolrich et al 2001). For the categorisation task three explanatory variables were modelled: 'negative', 'positive' and 'control' words. For the memory task two explanatory variables were modelled: 'positive remembered' and 'negative remembered'. In addition, temporal derivatives were

included in the model as covariates of no interest to increase statistical sensitivity. All variables were modelled by convolving the onset of each word with a heamodynamic response function, using a variant of a gamma function (i.e. a normalisation of the probability density function of the gamma function) with a standard deviation of 3 s and a mean lag of 6 s.

Individual data were combined at the group level using a mixed effects analyses (Woolrich et al 2004). This mixed effects approach accounts for intra-subject variability and allows population inferences to be drawn. Significant activations were identified using cluster-based threshold of statistical images with a height threshold of $Z = 2.0$ and a (corrected) spatial extent threshold of $P < 0.05$ (Friston et al 1994). Corresponding Brodmann Areas (BA) were identified by transforming MNI coordinates into Talairach space (Talairach and Tournoux 1988).

The main contrasts of interest were the main effects of task and group x valence interactions. For the categorisation task we contrasted activation during the categorisation of emotional words (positive or negative) versus control words, as well as between positive and negative words. For the recognition task we contrasted correctly remembered positive words versus correctly remembered negative words. All the above contrasts were examined across the whole brain, corrected for multiple comparisons as described above. Significant interactions were further explored by extracting percent Blood Oxygen Level Dependent (BOLD) signal change within the areas that showed significant difference in the above contrasts. While the primary interest of the study was to examine the neural differences between high N and low N volunteers, the effect of N could also be explored as a continuous personality trait.

Therefore, in a secondary analysis, N score was correlated with neural responses for the categorisation and correct recognition of positive and negative words across the entire sample.

Behavioural data (accuracy and mean reaction time) were analysed using repeated measures analysis of variance (ANOVA, SPSS v.14.0) with group as the between-subject variable and valence as the within-subjects variable (positive, negative and control words for categorisation task; positive and negative words for memory task). Here, accuracy is defined as percent of 'correct' responses. In the categorisation task, 'correct' refers to the trials where participants categorise positive words as 'like' or negative words as 'dislike'. In the memory task, 'correct' refers to the trials where participants recognize an old word and reject a new word correctly. Due to technical difficulties, accuracy data were not available for two subjects (one from each group). Independent samples t tests were performed to clarify any significant interactions, as well as to examine group differences in mood ratings.

RESULTS

Behavioural Results

As expected, high N subjects had significantly higher scores on neuroticism (N), depressed mood (BDI), and trait / state anxiety (STAI) (all p's <0.05). The two groups did not differ in terms of accuracy or response time in categorising positive and negative self-referent words (all p's >0.05). For the memory task there was no group difference for accuracy (p>0.05), although high N subjects showed reduced latency in recognising both positive and negative words than did low N subjects (group effect: p<0.01). See Table 1.

Functional Imaging Results

Main effects of task (across groups)

Emotional categorisation

Relative to control words, categorisation of negative and positive words was associated with greater activation in right lingual and left inferior frontal gyrus. In addition, categorisation of negative vs. control words elicited greater activation in left precentral gyrus and anterior cingulate. For positive vs. negative and negative vs. positive words, increased activation was seen in the right postcentral and left superior frontal gyri respectively (see table 2).

Emotional recognition

There were no significant differences in the neural responses during the recognition of positive and negative words, suggesting that a similar neural network is engaged in the recognition of both types of words.

Between-group differences (high N vs. low N)

Emotional categorisation

Across the whole brain we observed a significant group x word type (i.e. negative vs. positive words) interaction in right superior parietal cortex (BA7, MNI: 20, -64, 64, z=2.94; F(1,19)=16.722, p=0.001; volume = 3544 mm^3; see Figures 1A & B). *Post hoc* analyses showed that in right superior parietal cortex BOLD response (as percentage signal change) to negative words was significantly greater in the high N subjects (t(19)=3.180, p=0.005). By contrast, the two groups had similar activation for positive words (t(19)=0.417, p=0.681). This group-by-valence interaction remained significant even after including BDI or STAI scores as covariates (all p<0.01).

Emotional recognition

We did not observe any significant between-group differences during recognition of positive vs. negative words.

Correlation between N score and neural activity

Emotional categorisation

Across the entire sample, N was positively correlated with BOLD responses in the left anterior cingulate (BA24, MNI: -8,-8,52, Z=3.43; volume = 5888 mm^3; see Figure 2A) and left parietal cortex (BA4, MNI: -20,-28,66, Z=3.28; volume = 4296 mm^3; Figure 2A) during categorisation of negative words. A positive correlation was also observed between trait neuroticism and BOLD response in the left inferior frontal

gyrus (BA47, MNI:-46, 26,-6, z=3.28; volume = 5712 mm^3; see Figure 2B) during categorisation of positive words.

Emotional recognition

N score was found to be negatively correlated with activity in the right precentral gyrus during recognition of positive words (BA6, MNI: 48, 0, 12, Z=3.45; volume = 3840mm^3). Moreover, N score was negatively correlated with activity in the left anterior cingulate (BA6/32, MNI: -10, 8, 54, Z-3.31; volume = 3608mm^3; see Figure 3A) during the correct recognition of negative words. Notably, this area overlapped with the cingulate activation reported above, although the correlation was in the opposite direction. To further explore these findings, we constructed a binary mask including only those voxels that were significantly correlated with both categorisation and recognition of negative words (BA6, MNI:-10, 26, 46, z=5.37, volume=312mm^3; see Figure 3A). ANOVA analyses of the percent BOLD signal change of this overlap area found a significant group-by-task interaction (F(1,19)=16.431, p=0.001; see Figure 3B). *Post hoc* simple main effects analysis revealed that this interaction was driven by high N subjects having greater activation during the categorisation of negative words (t(19)=3.181,p=0.005) but reduced activation during the recognition of these words (t(19)=-3.909, p=0.001). This group-by-task interaction remained significant even after including BDI or STAI scores as covariates (all p<0.05).

DISCUSSION

The current study illustrates that high risk for depression is associated with neural biases in the processing of positive and negative personality-trait words. Our high N never-depressed volunteers exhibited greater activity in the right superior parietal cortex than low risk volunteers specifically during the categorisation of negative words. Neuroticism was also found to be correlated with increased activation in the left anterior cingulate during the categorisation of negative words and reduced activation within the same area during the memory retrieval of these words. In addition, neuroticism was associated with increased responses in the left parietal and left inferior frontal cortex during emotional categorisation, and reduced responses in the right pre-central gyrus during emotional memory. These findings build upon and extend our previous findings of behavioural biases in high N volunteers (Chan et al 2007) and suggest the involvement of fronto-parietal systems in this effect. These neural areas overlap, in part, with those implicated in previous studies using a similar task and those found to be modulated by antidepressant drug administration (Norbury et al 2007, Miskowiak et al 2007).

Whilst this study primarily aimed to determine the neural basis of emotional processing biases related to risk for depression, it also illustrated the neural network involved in the processing of emotional stimuli. Specifically, analyses of all volunteers revealed that the categorisation of emotional personality-trait words engaged a distributed neural network including the lingual, precentral, inferior frontal, anterior cingulate, superior frontal and postcentral gyrus. These results are consistent with previous neuroimaging studies that have reported increased activation in multiple regions of the frontal cortex during the processing of personality descriptors (Norbury

et al 2007, Gusnard et al 2001, Keenan et al 2001, Stuss 1991). By contrast, the medial prefrontal cortex, an area proposed to be specifically linked to self-referential processing tasks (Craik et al 1999, Kelley et al 2002, Fossati et al 2003, 2004), was not implicated in the present study. This may be because the current task provides a relatively indirect measure of self-referential processing compared to previous studies (e.g. Craik et al 1999, Kelley et al 2002, Fossati et al 2003, 2004, Kircher et al 2000). In particular, previous tasks have required the participant to judge whether a particular personality descriptive word describes them, whereas in the current study volunteers were asked whether they would like or dislike to be described as that descriptor. The current task was chosen to ensure similar response patterns across the two groups (i.e. to prevent differences in the number or type of trials included in the fMRI analysis between high and low N groups). However, we acknowledge that the use of this design may have reduced the level of self-referential processing required and hence the need for medial PFC involvement.

In support of our hypothesis, this study revealed significant neural differences between high N and low N individuals independent of any effects of current or past depressive illness. Specifically, aberrant responses in the same area within the anterior cingulate are evident in our high risk volunteers in both tasks of emotional categorisation and memory, thus suggesting that dysfunctions in this area may be an important marker for vulnerability to depression. In particular, activity of the anterior cingulate increased with N during the categorisation of negative words but reduced with N within the same area during the later retrieval of these words. This implies that better categorisation of negative words led to a reduced retrieval effort at recognition. Indeed, if high N individuals devoted higher attention or effortful processing to the

negative personality-trait words, it would be predicted that these words would be retrieved more readily at recognition.

The anterior cingulate is believed to play a key role in the regulation of emotional and cognitive processing through appropriate allocation of attentional resources (Bush et al 2000, Kerns et al 2004). Our results are therefore consistent with the hypothesis that high risk for depression is associated with negative biases in cognitive processing through increased allocation of attention to negative information (Joormann & Gotlib, 2007, JAP). This finding is noteworthy given the well documented role of the anterior cingulate in acute depression. For example, depression has been associated with increased cingulate activity in PET studies (Drevets 1999) and especially during the processing of negative emotional stimuli (Gotlib et al 2005, Fu et al 2004, Elliott et al 2002), although other studies have also reported hypoactivity or no effects in this area using a different task battery (Davidson et al 2002 Elliott et al 1997, Okada et al 2003, Wagner et al 2006, George et al 1997). A recent study has reported dysregulation in the anterior cingulate, during an emotional Stroop task, in high risk volunteers with family history of depression (Mannie, in press). Taken together, these results suggest that dysfunction in this area are important for both vulnerability to and experience of depression. This hypothesis is also supported by the finding that successful treatment is able to normalise metabolism in this area (Drevets et al 2002, Mayberg et at 1997).

The present study also highlighted a particular role for the superior parietal cortex in the emotional categorisation biases seen in high risk participants. First, compared to our low risk group, high N subjects showed significantly increased activation in the right superior parietal cortex during the categorisation of negative words. Second,

neural responses in the left parietal cortex were found to increase with neuroticism score during the categorisation of negative words. In support of our hypotheses, these results suggested that bilateral hyperactivity in parietal cortex is a feature of high neuroticism whether explored as a categorical risk factor or continuous personality variable.

The role of superior parietal cortex in the self-referent processing has been implicated in studies using self-descriptive words (e.g. Kircher et al 2000). It has also been associated with self-face recognition, concept of self, and perception of social relationship (Uddin et al 2005, Feinburg 2001, Decety and Sommerville 2003, Carr et al 2003, Farrer and Frith 2002, Iacoboni et al 2004). Consistent with this, our results suggested that high neuroticism is linked to an increased self-awareness of negative personality traits, which could in part contribute to the excessive self criticism observed in high N individuals and depressed patients.

The current observation of increased responses in the parietal cortex and anterior cingulate seems to reflect the neural basis of vulnerability to depression *per se*, not simply dysphoric mood. Symptoms of low mood are often observed in neuroticism, and it is sometimes proposed that N is simply a measure of usual mood. Although the high N volunteers displayed higher scores on current depression and anxiety scales, the range of these mood scores was well below that in syndromal states and was low compared with other high N samples we have studied. Analyses with BDI and STAI as covariates further suggested that current mood scores are unlikely to explain the current imaging findings.

Apart from the anterior cingulate and superior parietal cortex, high N was also related to greater activation in a left inferior frontal area during the categorisation of positive words. Inferior prefrontal cortex has previously been implicated in emotional control and inhibitory processes during inhibition of distracting information (Dolcos et al 2006, Dolcos and McCarthy 2006, Ochsner and Gross 2005, Aron et al 2004, Jha et al 2004, Jonides et al 1998). Thus, high neuroticism may imply greater inhibitory processes over positive information, and thus reduced positive emotional processing in high N individuals. These effects are hypothesis generating and must be regarded with caution until replicated.

The current study did not observe behavioural differences between high N and low N subjects, which was expected due to the demanding environment under fMRI scanning. This lack of behavioural difference was advantageous in that it allowed the neural differences to be attributed to group differences unconfounded by behavioural differences.

As noted earlier, risk factors for depression such as neuroticism have long been identified as clinical phenomena, yet very little is known about their underlying cognitive and neurobiological mechanisms. Some studies have investigated the neural basis of neuroticism in unselected samples (Canli 2001, 2004) and neuroticism is especially linked with increased neural activation in the left middle temporal and frontal gyri in response to the simple presentation of negative or frightening pictures (Canli et al 2001). Our study further suggests a systematic effect of N on emotional categorisation and memory in a neural network known to be related to depression, including the anterior cingulate and other frontal-parietal areas.

Finally, although high neuroticism is a robust risk factor for depression, the relatively low prevalence rates of depression imply that only a small proportion of the high N population will go on to develop depression, thereby potentially diluting any effects that we may have seen. Longitudinal studies are required to assess the predictive power of negative biases for subsequent depression in a sample adequately powered for the detection of infrequent events.

In conclusion, this study established a clear association between high neuroticism and negative biases in emotional categorisation and memory implicated by aberrant activation in the superior parietal, anterior cingulate and prefrontal areas. The current findings suggest that aberrant brain reactivity towards negative stimuli is apparent in high N never-depressed individuals in a similar way as depressed patients. Thus, these aberrant neural responses appear to be important in both aetiology and maintenance of depression. We believe that this finding has important theoretical and clinical implications for the prevention and treatment of depression.

ACKNOWLEDGEMENTS

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TABLE 1 Mood ratings and behavioural data of high N and low N volunteers. Values represent group mean ± standard deviations.

Measures	High N	Low N	Statistics
Mood and Personality Ratings			
N as full EPQ	16.45 (2.54)	5.50 (3.21)	$t(19)=8.72$; $p=0.000$
BDI	2.55 (2.02)	0.90 (1.45)	$t(19)=2.13$; $p=0.047$
State Anxiety	32.73 (7.06)	24.70 (3.47)	$t(19)=3.35$; $p=0.004$
Trait Anxiety	39.55 (8.31)	26.30 (3.47)	$t(19)=4.84$; $p=0.000$
Categorisation Task			
Accuracy %			Group effect:
Control	99.00 (2.11)	100.00 (0.00)	$F(1,17)=0.498$; $p=0.490$
Positive	98.45 (2.80)	97.25 (2.42)	Group x valence:
Negative	97.55 (1.28)	96.23 (3.87)	$F(2,34)=1.653$; $p=0.207$
Reaction time			Group effect:
Control	756.31 (146.92)	748.01 (88.16)	$F(1,19)=0.047$; $p=0.831$
Positive	865.85 (198.61)	902.24 (89.73)	Group x valence
Negative	929.71 (173.04)	939.56 (116.21)	$F(2,38)=0.641$; $p=0.532$
Memory Task			
Accuracy %			Group effect:
Positive	82.52 (6.93)	80.51 (9.66)	$F(1,17)=0.143$; $p=0.710$
Negative	73.89 (14.17)	72.24 (16.19)	Group x valence:
			$F(1,17)=0.004$; $p=0.951$
Reaction time			Group effect:
Positive	954.84 (185.27)	1189.72 (181.57)	$F(1,19)=9.114$; $p=0.007$
Negative	999.75 (194.14)	1210.85 (153.04)	Group x valence:
			$F(1,19)=0.199$; $p=0.661$

TABLE 2 Main effects of task. Presented below are the brain regions that show differential activations for categorised positive, negative and control words across the entire sample.

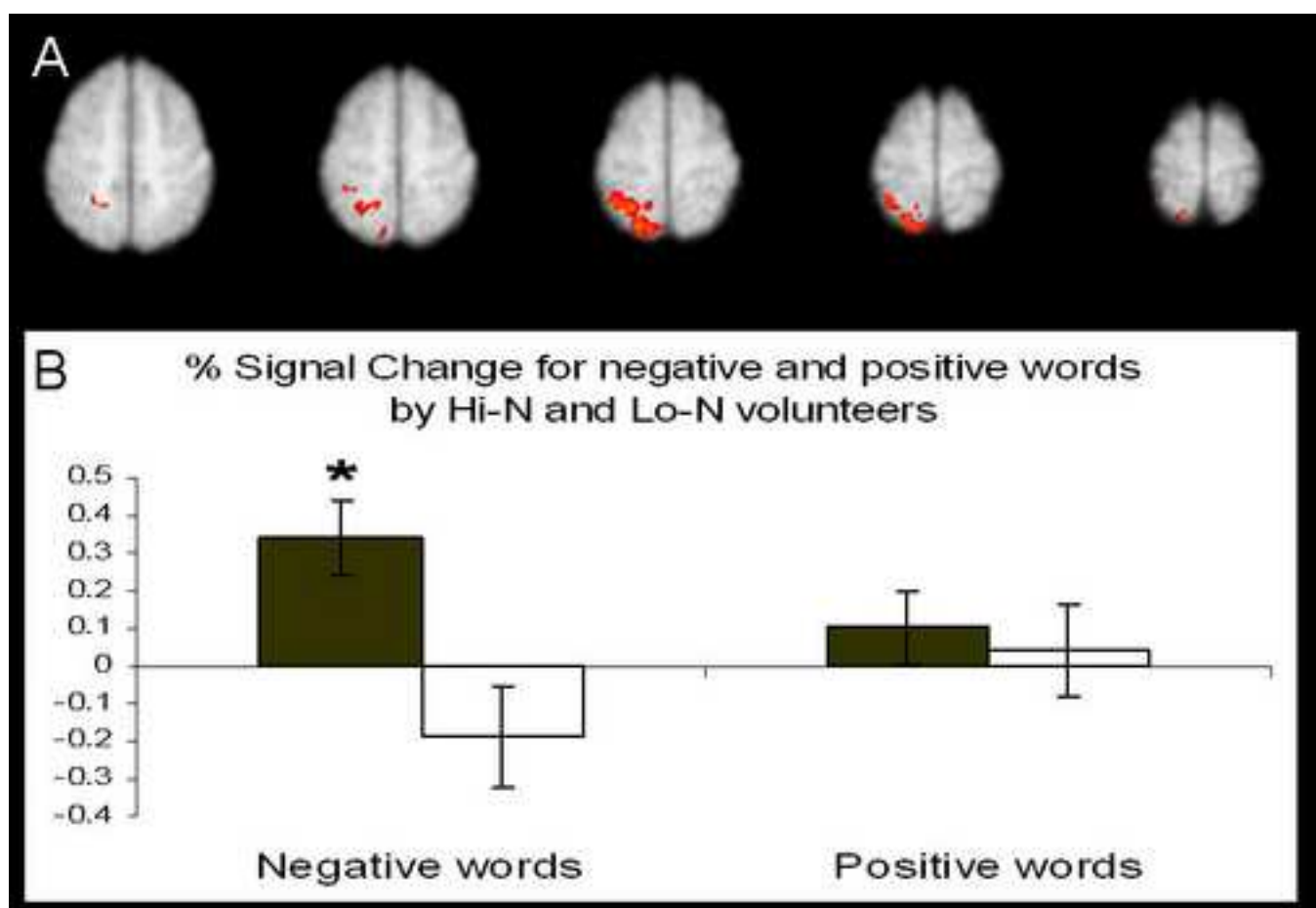| Brain Regions	Left/ Right	Brodmann Area	MNI	Volume (mm^3)	Z
Negative vs. control					
Lingual gyrus	R	17	14 -84 6	38264	4.3
Precentral gyrus	L	6	-4 56 24	5840	4.03
Inferior frontal gyrus	L	47	-44 28 -10	14968	4.27
Anterior cingulate	L	32	-2 18 42	7104	3.72
Positive vs. control					
Lingual gyrus	R	18	14 -82 4	48448	4.48
Inferior frontal gyrus	L	47	-56 28 -2	10144	3.75
Positive vs. negative					
Postcentral gyrus	R	43	66 -18 30	5016	3.04
Negative vs. positive					
Superior frontal gyrus	L	6	-24 14 66	3992	3.17

FIGURE LEGENDS

FIGURE 1 The image (A) and percent BOLD signal change (B) of the right superior parietal cortex (BA7, MNI: 20, -64, 64, 3544mm^3) which shows increased activation for the categorised negative vs. positive words in high N (black) vs. low N (white) subjects. Values represent group mean ± SEM. Asterisk (*) indicates significant group difference p<0.05.

FIGURE 2 (A) Activations in left anterior cingulate (5888mm^3) and parietal cortex (4296mm^3) were positively correlated with N during categorisation of negative words. (B) Activations in inferior frontal gyrus were positively correlated with N during categorisation of positive words (5712mm^3).

FIGURE 3 (A) The anterior cingulate cortical area which was (1) positively correlated with N during categorisation of negative words (5888mm^3); (2) negatively correlated with N during recognition of negative words (3608mm^3); (3) overlapped between the two clusters above (312mm^3). (B) Percent BOLD signal change within the overlapped cluster of high N (black) and low N (white) subjects. Values represent group mean ± SEM. Asterisk (*) indicates significant group difference p<0.05.

Figure 1
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A

B % Signal Change for negative and positive words
by Hi-N and Lo-N volunteers

Figure 2

Figure 2A

Left Cingulate Gyrus
BA24; MNI:-8,-8,52

Left Parietal Cortex
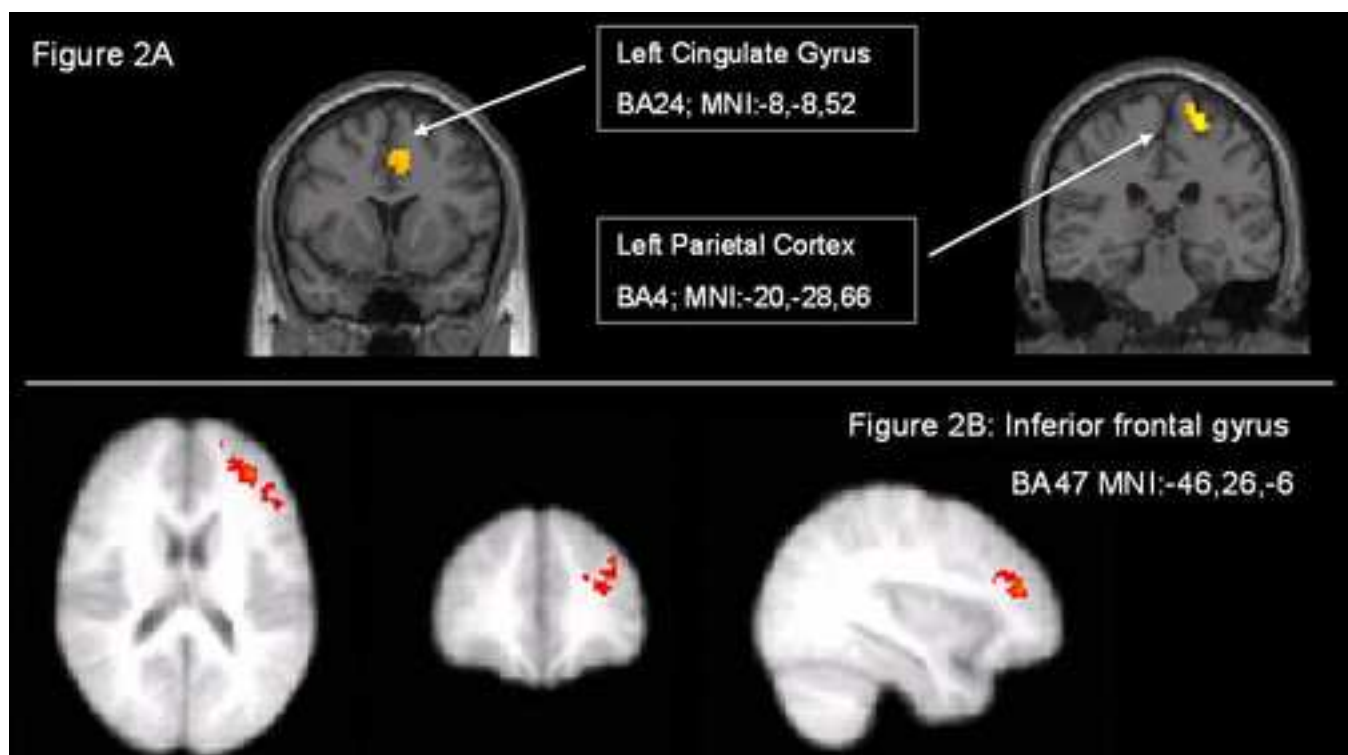BA4; MNI:-20,-28,66

Figure 2B: Inferior frontal gyrus
BA47 MNI:-46,26,-6

Figure 3
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A 1. encoding of negative words   2. recognition of negative words   3. Overlap area

B Percent BOLD signal change of the overlapped cluster

Encoding of negative words   Recognition of negative words