

Neural Antecedents of Emotional Disorders:

An fMRI Study of Subsyndromal Emotional Symptoms in Adolescent Girls

Supplemental Information

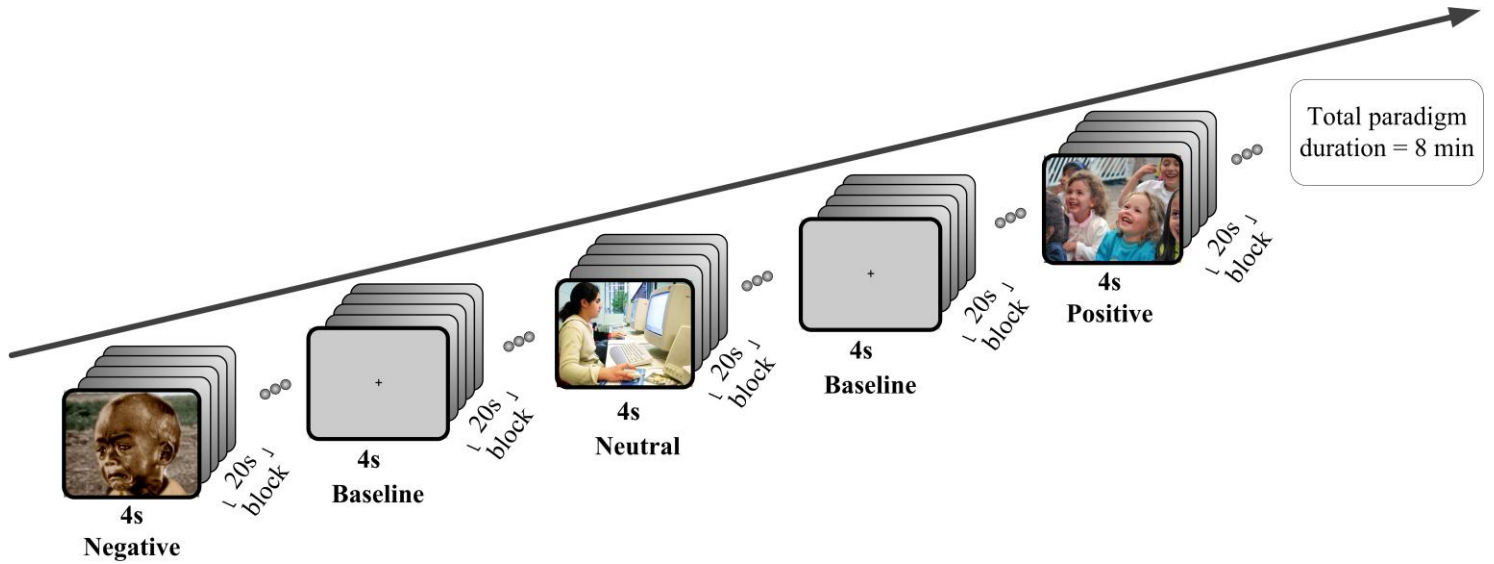


Figure S1. Images were displayed in 20-second blocks (5 images per block, and 2 blocks of each valence per run), alternating with 20-second baseline blocks of blank, greyscale images (6 blocks per run), over two functional runs of four minutes each.

Data Analysis

Approaches undertaken in the analysis:

Step 1. Based on clinical ratings it was determined which clinical measure most strongly discriminated the two groups (this analysis was conducted by CC).

Step 2. Based on fMRI data the brain regions were identified that displayed significant differences between groups during emotion-processing (this analysis was conducted by PD).

Step 3. To examine the putative neural correlates of the clinical measures that discriminated groups, a correlation analysis was performed between the percent BOLD signal changes in the regions showing significant differences between groups (from Step 2) and clinical measures that differentiated groups (from Step 1).

Step 4. A post-hoc functional connectivity analysis was carried out with the region showing the strongest correlation in Step 3 as the seed region to investigate whether impaired connectivity among the FLN nodes contributes to the clinical symptoms that differentiate groups.

fMRI Data Analysis

Pre-processing

Data analyses were carried out using SPM5 software (<http://www.fil.ion.ucl.ac.uk/spm/software/spm5>). Each subject's functional and structural images were first inspected visually for scanner artifacts and gross anatomical abnormalities, and then re-oriented so that the origin of the image lay within 3cm of the anterior commissure (AC). Functional images were realigned, corrected for slice time variation, and were spatially normalised to a common stereotactic space using the Montreal Neurological Institute (MNI) EPI template. The MNI template employed is that of an adult brain, however, it has been shown that spatial normalisation to an adult-derived template is feasible in children greater than age seven (1). Finally, the functional images were spatially smoothed with a Gaussian kernel of 8mm³ full width at half maximum.

Table S2. Brain regions where BOLD activity differed between adolescents with (ES+) and without (ES-) subsyndromal emotional symptoms during processing of negative and positive (compared to neutral) images.

Regions	Cluster Size	MNI co-ords x,y,z {mm}	voxel T	voxel equivZ	voxel p(unc)
Negative - Neutral					
<u>ES+ < ES-</u>					
Frontal regions					
Inferior Frontal Gyrus	151	54 36 3	3.8	3.57	0.000
Anterior Cingulate Gyrus	14	0 9 30	2.67	2.58	0.005
Limbic regions					
Hippocampus	10	-21 -36 9	3.52	3.33	0.000
Hippocampus ventral	23	-15 -33 -3	3.08	2.94	0.002
<u>ES+ > ES-</u>					
<i>None</i>					
Positive - Neutral					
<u>ES+ < ES-</u>					
<i>None</i>					
<u>ES+ > ES-</u>					
Frontal regions					
InferiorFrontal Gyrus	19	-48 33 18	3.27	3.11	0.001
Anterior Cingulate Gyrus	10	-3 48 -3	2.14	2.19	0.014

Table S3. Regions in the fronto-limbic network that displayed significant neural activity during processing of emotional images as compared to neutral images in all subjects.

Regions	Cluster	MNI co-ords	voxel	voxel	p-value
	Size	x,y,z {mm}	F	equivZ (FDR-corr)	
Negative - Neutral					
Frontal regions					
Inferior frontal gyrus	429	42 18 24	84.6	7.08	0.000
	59	-42 45 9	14.12	3.35	0.002
Anterior Cingulate	204	6 51 24	46.68	5.7	0.000
Limbic regions					
Amygdala	74	-21 -3 -24	80.12	6.95	0.000
	86	24 -3 -21	47.86	5.75	0.000
Hippocampus	217	-18 -3 -21	71.65	6.68	0.000
	188	21 -6 -21	70.81	6.66	0.000
Insula	110	-30 15 -21	30.19	4.76	0.001
	89	30 12 -21	23.95	4.30	0.001
Positive - Neutral					
Frontal regions					
Inferior frontal gyrus	30	-45 36 21	16.71	3.64	0.012
Anterior Cingulate	222	0 48 0	23.26	4.24	0.012

References

1. Kang HC, Burgund ED, Lugar HM, Petersen SE, Schlaggar BL (2003): Comparison of functional activation foci in children and adults using a common stereotactic space. *Neuroimage*. 19:16-28.

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In this issue statement

Das et al. investigates the emotional networks of the adolescent brain, using fMRI so as to identify the neural antecedents of common mental disorders such as anxiety and depression. They found that adolescents with subsyndromal emotional symptoms had increased frontal activity when processing positive emotions and decreased frontal and limbic activity when processing negative emotions and that trait anxiety correlated negatively with hippocampal neural activity when processing negative emotions. These findings of differential activity in the emotional fronto-limbic network are potential precursors to the development of emotional disorders and should be targeted in future studies.

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