Emotional Brain Processes in Adolescent Depression

Nazia Jassim[1,2], Luca Villa[1], Rosemary Holt[1], Kirstie Whitaker[1], John Suckling[1]

1. Department of Psychiatry, University of Cambridge, 2. Department of Education and Psychology, Free University of Berlin

Background

Adolescence is a period of heightened vulnerability to mental health issues.

A major contributor to the onset of depression during adolescence is the developmental imbalance between "hot" emotional and "cold" cognitive systems in the brain[1]. Hot systems refer to bottom-up emotional processes arising from limbic and subcortical regions, while cold systems engage the prefrontal and frontal areas for top-down cognitive processing.

In this fMRI study, we use an emotional face processing task to study brain function in adolescent depression in context of the dual process model of depression. We hypothesize that depressed adolescents show hyper-active corticolimbic regions during the processing of sad expressions; hypoactivity during happy processing; and an overall hypoactivity of frontal and prefrontal regions.

Relevance

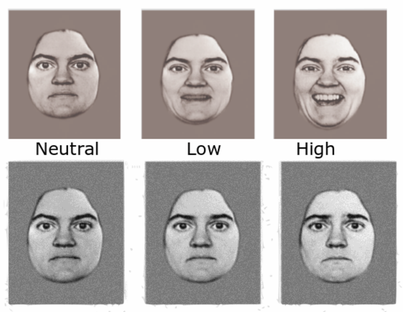
While brain function has been widely studied in adult depression, it has been less explored in the adolescent population. The crucial need for targeted early interventions makes brain function in adolescent depression a major research priority.

This study addresses the following questions:
- Which brain regions are engaged during the processing of positive and negative emotions in adolescent depression?
- Are depressed adolescents sensitive to varying intensities of emotional stimuli?

Methods

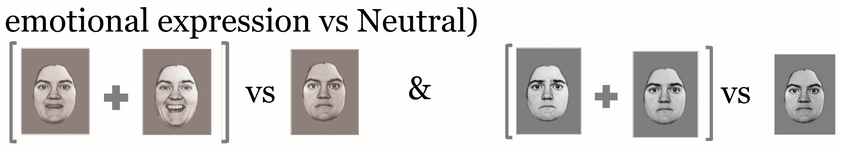
Participants:
A total of 128 participants, aged 12- 17 years, consisting of 94 depressed adolescents (71 females, 23 males) and 34 control subjects (25 females, 9 males) were studied. They were recruited through the MR-IMPACT study .[2]

Task:
An emotional face-processing task with happy and sad conditions was used. Each condition consisted of faces of varying emotional intensities- neutral, low and medium. Participants were asked to indicate the gender of the face by means of a button press.



Analysis Models:

Capacity : Measures the overall processing capacity of happy and sad emotions. (Overall emotional expression vs Neutral)



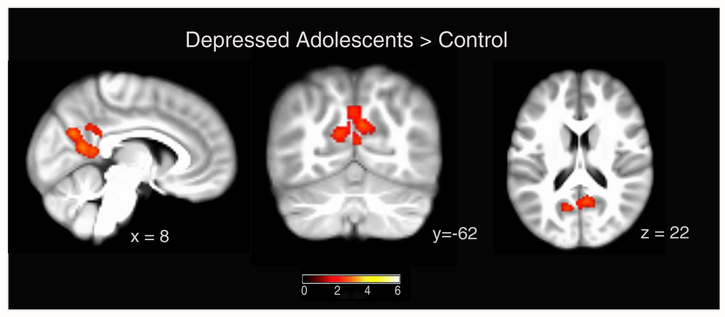
Dynamic Range : Measures the response to a varying range of intensities. (Low vs High intensity)

Imaging analyses were done using FSL FLAME1, or FMRIB'S Local Analyses of Mixed Effects. Age and gender were included as covariates.

Results

fMRI results revealed group differences in **processing capacity**.

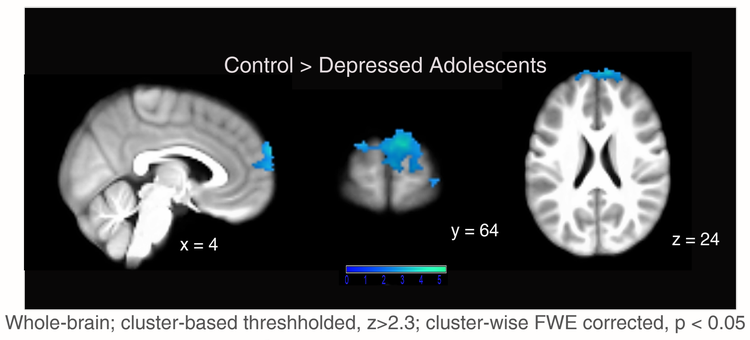
I. Happy processing capacity was marked by greater precuneus activity in depressed adolescents.



Whole-brain; cluster-based threshholded, z>2.3; cluster-wise FWE corrected, p < 0.05

Overall Happy > Neutral. Depressed adolescents showed higher activity in a cluster with its peak in the precuneus (z = 3.39, p =0.039, 713 voxels), and including parts of the posterior cingulate gyrus and intracalcarine cortex.

II. Sad processing capacity showed hypoactivity of the frontal pole in depressed adolescents.



Whole-brain; cluster-based threshholded, z>2.3; cluster-wise FWE corrected, p < 0.05

Overall Sad > Neutral. Control subjects showed higher activity in a cluster with its peak in the frontal pole (z = 4.32, p = 0.018, 763 voxels).

Behavioural data revealed no significant group differences in reaction times and accuracy rates.

Conclusion

During stimulation with a face processing task, depressed adolescents showed abberant activity of the precuneus and frontal pole during the processing of happy and sad expressions respectively.

Resting- state studies have linked the precuneus, which plays an important role in self-awareness, to dysfunctional self processing in depression. Depression is also characterized by impaired cognitive control, which has been traced back to frontoparietal hypoconnectivity.

Next steps

We aim to further look at connectivity, and to investigate the effects of Cognitive Behavioural Therapy on abberant neural activity.

fMRI Limitations

The Multiple Comparisons Problem: Although FLAME1 is relatively less sensitive to false positives, and we corrected for multiple comparisons, current research is pointing towards the use of non parametric permutation tests for fMRI analyses. [3]

Contact Nazia:

nj304@cam.ac.uk

Twitter: @naziajassim

References:

1. Hagan, C.C., et al., 2015. Neurodevelopment and ages of onset in depressive disorders. Lancet Psychiatry 366 (15):1–5.

2. Goodyer, I.M., et al., 2011. Improving mood with psychoanalytic and cognitive therapies (IMPACT): a pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with --moderate to severe unipolar depression. Trials 12:175.

3. Eklund A, Nichols TE, Knutsson H. Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. Proc Natl Acad Sci U S A. 2016 Jul 12;113(28):7900–5..