The emotional processing network at the onset of social anxiety disorder: a combined diffusion tensor imaging and functional connectivity study

Laura Muzzarelli1, Marco Tettamanti2,3, Matilde Taddei4, Marco Battaglia5,6
1 Faculty of Psychology, University Vita-Salute San Raffaele, Milano, Italy; 2 San Raffaele Hospital, Nuclear Medicine Unit, Milan, Italy; 3San Raffaele Scientific Institute, Division of Neuroscience, Milan, Italy; 4Istituto Neurologico C. Besta, Developmental Neurology Division, Milan, Italy; 5University of Toronto, Department of Psychiatry, Toronto, Canada; 6Centre for Addiction and Mental Health, Division of Child and Youth Psychiatry, Toronto, Canada

Contact: laura.muzzarelli.rodrigues@gmail.com

Results 1. DTI Analyses: FA - BOLD correlations

Correlation between white matter and amygdala response to ANGRY (orange) and NEUTRAL (blue) faces.

Involvement of several commissural, projectional, and associative tracts.

(Result confirmed by the PPI analysis. For both angry and neutral face processing, increased functional connectivity between left amygdala and distributed regions including prefrontal/prefrontal cortices, and ventral anterior cingulate cortex.)

Results 2. DCM Network Analysis and correlation with SAD indices

Following the structural and functional connectivity results, the DCM models for both angry and neutral facial expressions included 5 nodes (see picture). The final optimised DCM models were:

1. How does amygdala activity during facial emotional processing relate to structural and functional connectivity?
2. What is the effective connectivity architecture underlying emotional face processing in adolescence?
3. How does SAD and its developmental indices influence this functional architecture?

Experimental Hypotheses

Methods

Our sample is composed of 19 subjects (mean age 14.8±1.1 years; 7 girls), part of a longitudinal study on emotional processing and SAD[1],[2],[3] having the following structure:

Sample

Time Point Sample Age Sample Size Analyses
1 7-8 150 Emotion recognition task Harm Avoidance (HA) and SAD assessment
2 8-9 49 ERP (EEG) recording during an emotional processing task
3 14-15 19 fMRI and DTI measurements Psychiatric (SAD) assessment

Presence of psychiatric symptoms was assessed via the K-SADS, parent version. At age 14/15, 5 subjects (2 girls) had SAD, 5 (1 girl) had sub-threshold SAD (presence of 1-to-3 SAD symptoms), and 9 had no SAD symptoms.

1. FMRI - DTI correlational analyses

The acquisition procedures are detailed elsewhere[1],[2]. Briefly, the fMRI experiment was an implicit emotional processing task in which participants viewed face stimuli of peers showing happy, angry, and neutral expressions. Left amygdala (peak MNI: -20, -10, -20) activation to angry and neutral faces was correlated with SAD[2] and was the seed for the current analyses.

For each subject the mean % BOLD signal change from the left amygdala peak was extracted for neutral and angry faces. Two GLMs were employed to analyse the association between this BOLD response and whole-skeleton fractional anisotropy (FA), through TBSS analyses and FSL software.

Functional connectivity analyses

Psychophysiological Interaction (PPI) in SPM8 was used to assess functional connectivity (results not shown).

2. DCM Network and correlational analyses

Based on the fMRI activation, the DTI, FA-BOLD and PPI results, we tested effective connectivity through DCM Network Discovery, via the post-hoc Bayesian model selection implemented in SPM8.

Two models were created, one for anger and one for neutral processing; in both, a parametric modulator modelling the contrast of interest provided input to the left fusiform. No binlinear terms were specified, in order to focus on the attentional engagement. Significant intrinsic connection strengths were correlated with SAD, HA (age 7-8), ERP N400 amplitudes, and PPI reaction times (Spearman correlation test).

Conclusions & Outlook

1. In adolescence, amygdalar activity influences broadly distributed brain regions and white matter, mostly on commissural and projectional tracts.
2. The network underlying emotional face processing in adolescence, and particularly anger processing, involves also dorsal brain structures, including motor-related areas.
3. Angry facial expressions trigger in subjects with SAD both a hyperresponsivity of the amygdala and an inhibition of the motor responses. Such inhibition parallels the one displayed in anxiogenic contexts by both infants and primates[1],[2], suggesting a developmental and translational stability of this endophenotype.

References


The authors declare no potential conflict of interest.
Laura Muzzarelli  
MSc licensed psychologist

After completing my Master's Degree in Psychology with a specialisation in Cognitive Neurosciences, I enrolled in a Research and Clinical Training required to be part of the Italian Psychological Association. I recently completed the national psychology license exam, and I am currently applying for PhD programs across Europe. During the last years, I have had the chance to work in the fields of psychobiology and psychiatric neuroimaging, and in social/affective neuroscience, gaining therefore expertise in structural and functional neuroimaging, in cognitive and personality assessment, and in the design of scientific research and experiments. In particular, my last research experience allowed me to work with social anxiety traits and emotional perception in adolescent populations. The results of this work have been selected for poster presentation and awarded a Travel Award for the 29th ECNP Congress in Vienna. My research interests point at unraveling the complex paths to the development of psychopathology across youth, with a particular interest in its underlying brain (dys)function and in the impact of attachment relationships in this process.