PROJECT

Supervisor: Sara Poletti

Title: Gender-dependent development of depressive behavior: role of early stress and inflammation

Curriculum: _____

Link to the personal page of the University or relevant hospital site website:

https://research.hsr.it/en/divisions/neuroscience/psychiatry-and-clinical-psychobiology/sara-poletti.html

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Major depressive disorder (MDD) is the leading cause of years lost owing to disability worldwide and the third overall contributor to the burden of disease. Women are twice as likely to suffer as men and typically experience prolonged or recurrent depression more than depressed males, with a younger onset age and lower quality of life. Accumulating evidence from human and animal studies supports the existence of profound sex differences in the endocrine, behavioral aspects of the stress response, partially attributed to the impact of gonadal hormones on the neuroendocrine system throughout development. Males and females display also distinct vulnerabilities to different types of inflammatory dysregulation suggesting underlying biological differences.

Rationale and hypothesis

We hypothesize that males and females will show different immune and brain imaging profiles. Further, we expect that experiencing adverse childhood experiences will have a different impact in males and females contributing to the individual profiles. Finally, we hypothesize that independently of sex patients who experienced higher levels of early stress will show more brain and immunological abnormalities.

Objectives and specific aims

1- identify gender specific alterations in immune/inflammatory markers;

2- investigate the impact of early stress on immune/inflammatory markers into adulthood;

3- identify gender specific alterations in brain imaging profiles;

5- implement gender specific predictive models of clinical outcome based on immune/inflammatory markers and neuroimaging profiles.

Expected outcomes

Skills that the student should acquire (max. 600 characters including spaces):

• "Imaging genetics": the use of anatomical or physiological imaging technologies as phenotypic assays to evaluate genetic variation, including gene polymorphisms and gene expression

• MRI analyses to explore functional & structural networks: BOLD fMRI (SPM12), VBM, subcortical volumes (Freesurfer) and cortical thickness (CAT12), Tract-Based Spatial Statistics (TBSS; FSL) and tractography analysis of WM tracts, Dynamic Causal Modelling (DCM; SPM12), new fMRI tools for the analysis of seed-to-voxel connectivity maps, ROI-to-ROI connectivity and graph metrics, Independent Components (ICA networks), local homogeneity, intrinsic connectivity, centrality, etc.; resting state fMRI (RestPlus, CONN)

References (max. 15)

Benedetti F, Bollettini I, Radaelli D, Poletti S, Locatelli C, Falini A, Smeraldi E, Colombo C. Adverse childhood experiences influence white matter microstructure in patients with bipolar disorder. Psychol Med. 2014 Oct;44(14):3069-82.

Poletti S, de Wit H, Mazza E, Wijkhuijs AJ, Locatelli C, Aggio V, Colombo C, Benedetti F, Drexhage HA (2017) Th17 cells correlate positively to the structural and functional integrity of the brain in bipolar depression and healthy controls. Brain, Behavior and Immunity; 61:317-325.

Poletti S, Melloni E, Mazza E, Vai B, Benedetti F. Gender-specific differences in white matter microstructure in healthy adults exposed to mild stress. Stress. 2019 Sep 3:1-9.