# TNF-α Contributes to Depression in Bipolar Disease

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**INTRODUCTION:** An imbalance of the immune system towards a pro-inflammatory profile has been associated with the pathogenesis of the Bipolar Disorder (BD). Macrophages are immune cells with pleiotropic actions on tissues. Microenvironment can modulate macrophages' phenotype in a continuum of diverse interconvertible phenotypic spectrums designated in the literature for simplicity as M1 and M2. **OBJECTIVE**: To evaluate the impact of the systemic inflammatory environment of individuals with BD on the expression of M1 and M2 markers. **MATHERIALS AND METHODS**: The study included 23 subjects divided into 4 groups. BD patients in remission (n=8, BD-R); BD with depression (n=5, BD-D); BD in the maniac state (n=5, BD-M) and control subjects (n=5, CON). The human monocyte cell line U-937 was activated with PMA (phorbol 12-myristate 13-acetate) and polarization was induced with RPMI-1640 media supplemented with 10% plasma from each patient for 24 hours. Gene expression of selected M1 (IL-1β, TNF-α, CXCL9, CXCL10 and STAT1) and M2 (CCL13, TGF-β and IL-10) markers was assessed by qPCR. **RESULTS**: CON and BD-R showed similar pattern of cytokines' expression. BD-D and BD-M also had a similar pattern and showed increased IL-1β, TNF-α and TGF-β expression. CXCL9 and CXCL10 expression was decreased in BD-D with no significant difference in IL-10, CCL13 and STAT1 expression. Positives correlations between depression (HDRS scale) and IL-1β ($r^2$= 0.696, p=0.001), TNF-α ($r^2$= 0.785, p<0.001), TGF-β ($r^2$= 0.528, p=0.024) and a negative correlation with CXCL10 ($r^2$= -0.551, p=0.018) were found. When we applied a model of linear regression, only TNF-α was significant ($r^2$=0.634, t=2.426, p=0,028). **CONCLUSION**: Dysfunction of the BD immune system exerts different effects on macrophages, with modulation of inflammatory and regulatory cytokines. In our *in vitro* model, TNF-α appears to be an important factor secreted by macrophages that influence the microenvironment and might influence depression episodes.

Key-words: bipolar disorder, macrophages, TNF-α
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