DYSFUNCTIONAL RESPONSE OF MONOCYTES/MACROPHAGES IN LATE-STAGE BIPOLAR DISORDER

Bárbara Antqueviezc [1], Bruna M Ascoli [1], Mariana M Parisi [2], Giovana Bristot [1], Luiza Géa [1], Rafael Colombo [3], Flávio Kapczinski [4], Fátima Theresinha Costa Rodrigues [5] Guma, Florencia M Barbé-Tuana [2], Adriane R Rosa [1]

[1]Laboratory of Molecular Psychiatry, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS
[2]Laboratory of Molecular Biology and Bioinformatics, Department of Biochemistry, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS
[3]Laboratory of Pharmacology and Physiology, Universidade de Caxias do Sul, Caxias do Sul, RS
[4]Department of Psychiatry & Behavioral Neurosciences, Mcmaster University, Hamilton, Canada
[5]Laboratory of Biochemistry and Cellular Biology of Lipids, Department of Biochemistry, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS

Introduction: Innate immune system dysfunction has been recognized as an important element in the pathophysiology of bipolar disorder (BD). The aim of this study was to investigate a different aspect of immunity, e.g. the pattern of macrophage polarization, classic (M1) or alternative (M2), and examine how this pattern changes from early to late stages of BD.

Methods: Human monocytes purified from PBMC of patients with BD and healthy individuals were differentiated with M-CSF. Monocyte-derived macrophages (MDM) were exposed to IFN-γ plus LPS or to IL-4 to induce their polarization into the M1 or M2 phenotype, respectively and the secretion of cytokines (IL-1β, IL-6, IL-10 and TNF-α) was used as index of macrophage activity.

Results: Macrophages from BD patients in the late stage secreted lower levels of IL-1β (M1), IL-6 (M0, M1 and M2) and IL-10 (M0 and M1) compared to early stage group. Additionally, BD patients in late stage had lower secretion of IL-1β (M0 e M1), IL-6 (M0, M1 and M2), TNF-α (M0, M1 and M2) and IL-10 (M1) than healthy controls. In contrast, there were no significant differences in cytokine levels in the macrophages (M0, M1 and M2) from early BD patients compared to healthy controls.

Conclusion: Our results point to a dysfunction in the innate immune compartment of BD patients in the late stages of illness. We hypothesize that persistent microenvironmental and systemic changes that occur during the progression of the disease, might promote exhaustion of the immune system. In this regard, it is plausible to speculate that this failure of the immune system to regulate and counterbalance a peripheral inflammatory response may contribute to structural and neurocognitive changes commonly observed in the advanced stages of the illness.

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