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**Difference in proinflammatory cytokines produced by monocytes between patients with major depressive disorder and healthy controls****Hong-Xia Zhang<sup>a</sup>, Ye-Qing Xu<sup>b</sup>, Yuan-Yuan Li<sup>c</sup>, Ming-Fang Lu<sup>d</sup>, Shen-Xun Shi<sup>a</sup>, Jian-Lin Ji<sup>c,\*</sup>, Li-Wei Wang<sup>a,\*</sup>**<sup>a</sup>Department of Psychiatry, Huashan Hospital, Fudan University, Shanghai, China<sup>b</sup>Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China<sup>c</sup>Department of Psychological Medicine, Zhongshan Hospital, Fudan University, Shanghai, China<sup>d</sup>Department of Immunology, Shanghai Medical School, Fudan University, Shanghai, China

*Abbreviations:* MDD, major depressive disorder; LPS, lipopolysaccharide; TNF- $\alpha$ , tumor necrosis factor-alpha; IL-6, interleukin 6; IL-1 $\beta$ , interleukin 1 beta; PHA, phytohemagglutinin; ACTH, adrenocorticotrophic hormone; M.I.N.I., Mini International Neuropsychiatric Interview; HAMD17, 17-item Hamilton Depression Scale; LES, Life Events Scale; EDTA, ethylenediaminetetraacetic acid; PBMC, Peripheral blood mononuclear cells;

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**Abstract**

**Background:** Immune activation and suppression in patients with major depressive disorders (MDD) have been both reported in different studies. We assume that these findings may indicate innate immunological tolerance in MDD, with subclinical elevated level of proinflammatory cytokines and the decrease in innate immune response while encountering pathogens.

**Methods:** Peripheral monocytes of 50 untreated patients with MDD and 40 healthy controls were isolated and cultured, with or without 10 ng/ml lipopolysacchride (LPS) for 6 hours (6 h, LPS+/-), and with LPS for 18 hours (18, LPS+). The cell culture supernatants were collected to measure concentrations of tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin 6 (IL-6), and interleukin 1 beta (IL-1 $\beta$ ).

**Results:** The baseline concentrations of IL-6 and IL-1 $\beta$  (6 h, LPS-) were significantly higher in the MDD group than those in the control group. There was no significant difference of TNF- $\alpha$  between the two groups. The fold changes of LPS-induced secretion of IL-6 and IL-1 $\beta$  from monocytes cultured for 6 and 18 hours were all lower in the patient groups, and that was true for IL-1 $\beta$  as monocytes cultured for 18 hours.

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