Social stress and polymorphisms of *CRP* gene influence antidepressant treatment outcome in major depressive patients

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Background Major depressive disorder (MDD) is a severe disease, and it is predicted to become first leading cause of disability worldwide by 2030 according to World Health Organization. Previous studies have shown that social stress would promote the expression of inflammation-related genes like C-reactive protein (CRP), IL1B, TNFα, and IL6. These proinflammatory cytokines induce the expression of indoleamine 2,3-dioxygenase, which catalyzes the tryptophan metabolism into kynurenine. It thus causes less serotonin metabolized from tryptophan, which is a hypothesis concerning MDD. Until now, however, there is no evidence whether social stress and polymorphisms of *CRP* gene are related to the antidepressant treatment outcome.
Aims In this study, we aimed to investigate the treatment outcome by social stress, polymorphisms of *CRP* gene, and their interaction in MDD patients.
Material and Methods Sixty-six patients (aged 18-65 years old) who met the Diagnostic and Statistical Manual of Mental Disorders, 4th version (DSM-IV) for MDD. In addition, 17-item Hamilton Rating Scale for Depression (HAM-D) scores of all the patients greater than 15 were enrolled. MDD patients were randomly treated with fluoxetine or venlafaxine. HAMD scores were evaluated at baseline and week 2, 4, and 6. Also, we recruited 30 healthy controls from the community through advertisement who were diagnosed by Mini International Neuropsychiatric Interview (MINI) to make sure the past disease state. We collected 15 milliliter venous blood from the subjects, extracting the DNA by FlexiGene DNA kit (QIAGEN, Hilden, Germany), then carrying out gene sequence. We genotyped CRP rs2794520. Besides, social stress was assessed by self-reported questionnaires, social support scale (SSS) and World Health Organization Quality of life (QOL) Taiwan version. The difference between the groups was considered significant if the p value was less than 0.05 （based on a two-sided α of 0.05）.
Results The mean age of MDD patients and healthy controls were 39.7±12.9 and 34.7±11.3, respectively. There were 75.8% in MDD patients and 60.0% female in healthy controls. The demographic characteristics were not significantly different between MDD patients and healthy controls. At baseline, MDD patients had lower SSS and QOL scores than healthy controls (93.2 ± 22.1 vs. 114.6 ± 13.4, $p<0.001$; 74.3 ± 11.5 vs. 96.5 ± 9.8, $p<0.001$, respectively). After 6 weeks of antidepressant treatment, Patients with higher SSS and QOL scores had better treatment outcome ($p= 0.013$ and $p= 0.041$). Moreover, interaction of polymorphisms of CRP rs2794520 and social support was associated with antidepressant treatment outcome ($p= 0.006$).
Conclusions Remission from MDD was not just dependent on antidepressant, but social stress may play an important role. Moreover, polymorphisms of *CRP* gene interacted with the regulation of social stress modulated the antidepressant treatment outcome in MDD patients. In the future, we need more subjects to confirm these results.

Key words major depressive disorder, social stress, C-reactive protein, genetic polymorphism, treatment outcome