Associations between plasma levels of C-reactive protein and catecholamine metabolites in patients with major depression

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Dear Editor,

Inflammation plays a role in the pathophysiology of psychiatric diseases, including major depression (MD).[1] Patients with MD exhibit increased peripheral blood concentrations of C-reactive protein (CRP).[2] A recent report observed that serum IL-6 and CRP levels were positively correlated in drug-naïve MD patients.[3] Dysregulation of monoamines is also associated with the pathophysiology of MD.[4] Neuroinflammation and cytokines affect the monoamine nervous systems that are involved in the pathophysiology of MD.[5] Peripherally administered cytokine could activate a brain inflammatory response in humans that interacts with serotonin metabolism, which is associated with MD.[6] The association between inflammation and catecholamine, however, remains unknown. Therefore, we investigated the association between plasma levels of CRP and catecholamine metabolites in patients with MD to confirm the relationship between inflammation and catecholamine systems. This study included 43 first-episode, drug-naïve patients who met the Diagnostic and Statistical Manual of Mental Disorders, Fifth edition criteria for MD (male/female: 19/24, age: 44.3 ± 10.6 years) and did not have any physical diseases.[7] All participants enrolled in the study signed an informed consent document that explained the study protocol and potential risks involved. The study was approved by the Ethics Committee of the University of Occupational and Environmental Health, Kitakyushu, Japan (approval number: H25-13; 8 May 2013) and was conducted while upholding its ethical standards. We evaluated the severity of depression using the Hamilton Rating Scale for Depression (HAMD).[8] Blood samples were collected at 7.00 am, before breakfast (at least 12 h after the last medication). After overnight resting while lying down, 15 ml of venous blood was drawn with the patients in the supine position. The serum samples were quickly separated using a centrifuge (2000 *g*, 10 min, 4°C) and stored at −80°C until assay. Plasma levels of 3-methoxy-4-hydroxyphenylglycol (*MHPG*) and homovanillic acid (HVA) were measured using high-performance liquid chromatography, and that of CRP was measured using an enzyme-linked immunosorbent assay. Spearman's rank correlation was used for statistical analysis. The level of significance was set at $p < 0.05$. Plasma CRP level was not associated with plasma MHPG (rho = 0.137, $p = 0.383$) or HVA levels (rho = 0.151, $p = 0.334$). Plasma CRP level and HAMD scores (rho = 0.058, $p = 0.709$). A previous meta-analysis demonstrated that cerebrospinal fluid levels of HVA, but not MHPG, were decreased in patients with MD,[9] suggesting that the brain dopamine system might be involved in MD. Similarly, a recent review reported on the afferent modulation of the dopaminergic system and its association with MD.[10] Furthermore, inflammation-induced reduction in ventral striatal responses to hedonic reward, decreased brain dopamine levels, and decreased availability of dopamine in the striatum may lead to anhedonia, fatigue, and psychomotor retardation.[2] No association was found between plasma levels of CRP and HVA or MHPG, indicating that peripheral inflammation does not affect dopamine or noradrenaline dynamics. The results indicate that

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inflammatory does not affect catecholamine systems in peripherally in patients with MD. We could not however measure other metabolites of catecholamines including normetanephrine, and VMA. Further research using cerebrospinal fluid and measuring the rest of catecholamine metabolites, is needed to investigate the associations between inflammation and catecholamine systems in the brain with MD.

Author contributions

RY, NO, YK, and AI contributed to conception and design and were involved in the 43 clinical investigations and writing of the manuscript. All authors have read and approved the final manuscript.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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