

# Can taming inflammation help reduce aggression?

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Several psychiatric disorders, including depression, schizophrenia, bipolar disorder, Alzheimer's disease, traumatic brain injury, autism, and posttraumatic stress disorder, are associated with a dysregulated immune response and elevated levels of inflammatory biomarkers. Inflammation has long been associated with an increased risk of aggressive behavior.<sup>1,2</sup> By taming immune system dysregulation, we might be able to more effectively reduce inflammation, and thus reduce aggression, in patients with psychiatric illness.

## Inflammation and psychiatric symptoms

An overactivated immune response has been empirically correlated to the development of psychiatric symptoms. Inducing systemic inflammation has adverse effects on cognition and behavior, whereas suppressing inflammation can dramatically improve sensorium and mood. Brain regions involved in arousal and alarm are particularly susceptible to inflammation. Subcortical areas, such as the basal ganglia, and cortical circuits, such as the amygdala and anterior insula, are affected by neuroinflammation. Several modifiable factors, including a diet rich in high glycemic food, improper sleep hygiene, tobacco use, a sedentary lifestyle, obesity, and excess psychosocial stressors, can contribute to systemic inflammation and the development of psychiatric symptoms. Oral diseases, such as tooth decay, periodontitis, and gingivitis, also contribute significantly to overall inflammation.

## Anti-inflammatory agents

Using nonsteroidal anti-inflammatory drugs as augmentation to standard treatments

has shown promise in several psychiatric illnesses. For example, low-dose aspirin, 81 mg/d, has demonstrated reliable results as an adjunctive treatment for depression.<sup>3</sup> Research also has shown that the use of ibuprofen may reduce the chances of individuals seeking psychiatric care.<sup>3</sup>

Individuals who are at high risk for psychosis and schizophrenia have measurable increases in inflammatory microglial activity.<sup>4</sup> The severity of psychotic symptoms corresponds to the magnitude of the immune response; this suggests that neuroinflammation is a risk factor for psychosis, and that anti-inflammatory treatments might help prevent or ameliorate psychosis.

In a double-blind, placebo-controlled study, 70 patients diagnosed with schizophrenia who were taking an antipsychotic were randomized to adjunctive aspirin, 1,000 mg/d, or placebo.<sup>5</sup> Participants who received aspirin had significant improvement as measured by changes in Positive and Negative Syndrome Scale total score.<sup>5</sup>

## Targeting C-reactive protein

Inflammation has long been associated with impulsive aggression. C-reactive protein (CRP) is a biomarker produced in the liver in response to inflammatory triggers. In a study of 213 inpatients with schizophrenia, researchers compared 57 patients with higher levels of CRP (>1 mg/dL) with 156 patients with normal levels (<1 mg/dL).<sup>2</sup> Compared with patients with normal CRP levels, those with higher levels displayed increased aggressive behavior. Researchers found that the chance of being physically restrained during hospitalization was almost 2.5 times greater for patients with elevated CRP levels

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### Disclosure

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**In 1 study, patients with high levels of C-reactive protein displayed increased aggressive behavior**

on admission compared with those with normal CRP levels.

Statins have long been used to reduce C-reactive peptides in patients with cardiovascular conditions. The use of simvastatin has been shown to significantly reduce negative symptoms in patients with schizophrenia.<sup>6</sup>

Vitamin C also can effectively lower CRP levels. In a 2-month study, 396 participants with elevated CRP levels received vitamin C, 1,000 mg/d, vitamin E, 800 IU/d, or placebo.<sup>7</sup> Although vitamin E didn't reduce CRP levels, vitamin C reduced CRP by 25.3% compared with placebo. Vitamin C is as effective as statins in controlling this biomarker.

Several nonpharmacologic measures also can help reduce the immune system's activation of CRP, including increased physical activity, increased intake of low glycemic food and supplemental omega-3 fatty acids, improved dental hygiene, and enhanced sleep.

Using a relatively simple and inexpensive laboratory test for measuring CRP might help predict or stratify the risk of aggressive

behavior among psychiatric inpatients. For psychiatric patients with elevated inflammatory markers, the interventions described here may be useful as adjunctive treatments to help reduce aggression and injury in an inpatient setting.

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