

## Correlation of Proinflammatory Cytokines, Brain-Derived Neurotrophic Factors, Disease Severity, Depressive Symptoms, and Reduced Gray Matter Volumes in patients with Atopic Dermatitis

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### Background

Itch is a cardinal symptom of atopic dermatitis (AD). Some studies reported that cognitive-behavioral treatment and transcranial direct current stimulation could reduce itch. However, little attention has been paid to the brain mechanisms and structural changes in AD. In addition, the comorbid depression and fluctuation of itch and disease severity hinder further research.

### Aims & Objectives

To investigate the association between pro-inflammatory Cytokines, brain-derived neurotrophic factors (BDNF), depressive symptoms, and brain structural alterations (gray matter [GM] volume differences), in AD patients

### Methods

We enrolled 11 AD patients and 11 age- and sex-matched healthy subjects within 2 years. All participants underwent comprehensive assessments, including clinical assessment (Eczema Area and Severity Index [EASI]), patient report questionnaires (Quick Inventory of Depressive Symptomatology [QIDS]), serum proinflammatory cytokines or cytokine receptors (IgE, soluble interleukin-2 receptor [sIL-2R], tumor necrosis factor- $\alpha$  receptor 1 [TNFR1]), serum BDNF, and brain magnetic resonance imaging. Voxel-based morphometry was performed to analyze the GM volume difference between AD patients and healthy subjects. Correlations of the disease severity, depressive symptoms, proinflammatory cytokines, BDNF, and the GM volume difference were analyzed.

### Results

In total, 5 male and 6 female AD patients with average age ( $37.82 \pm 14.30$ ) and 8 male and 3 female healthy participants with average age ( $35.27 \pm 8.60$ ) were enrolled. Patients with AD exhibited significant decreased GM volume in bilateral middle frontal gyrus (cluster equivalent,  $k_E=201$  in right MFG,  $k_E=341$  in left MFG,  $P < .001$ ) and left temporal pole ( $k_E=155$ ,  $P < .001$ ) than healthy subjects. No brain region was larger in AD patients than healthy subjects. The GM volume was positively associated with serum BDNF in right middle frontal gyrus ( $r = 0.786$ ,  $p = 0.021$ ), but negatively associated with TNF- $\alpha$  receptor-1 ( $r = -0.714$ ,  $p = 0.047$ ) in left middle frontal gyrus

### Discussion & Conclusion

Patients with AD demonstrate significant brain GM volume reduction in bilateral middle frontal gyrus and left temporal pole. A negative correlation between GM volume and serum TNF- $\alpha$  receptor- level indicates that increased chronic proinflammatory cytokines in AD patients may be associated with decreased brain GM volume, that might further impact patients' mood, and serum BDNF may increase as a compensation to the GM reduction. Hence, a positive correlation between GM volume and serum BDNF was found.