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# Antibodies to Signaling Molecules and Receptors in Alzheimer's Disease are Associated with Psychomotor Slowing, Depression, and Poor Visuospatial Function.

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**Abstract**

**BACKGROUND:**

Alzheimer's disease (AD) is associated with several antibodies as well as signaling molecules and receptors. These may be detrimental in the presence of a disrupted blood-brain barrier (BBB).

**OBJECTIVE:**

To investigate whether the levels of antibodies toward 33 signaling molecules involved in neurotransmitter, vascular, and immune functions were associated with AD and, within the AD group; cognitive function and mood.

**METHODS:**

Antibodies in sera from patients with mild AD [(n = 91) defined as a Mini-Mental State Examination ≥ 20 or a Clinical Dementia Rating Scale≤1] and healthy controls (n = 102) were measured with enzyme-linked immunosorbent assays. Levels in AD and controls were compared by Mann-Whitney test. In the AD group, associations between antibodies and psychometric test scores were analyzed by robust regression. The false discovery threshold was set to 0.05.

**RESULTS:**

Antibodies to serotonin receptors [5-HT2AR (effect size (r) = 0.21, p = 0.004), 5-HT2CR (r = 0.25, p = 0.0005) and 5-HT7R (r = 0.21, p = 0.003)], vascular endothelial growth factor receptor 1 [VEGFR1 (r = 0.29, p < 0.001)] and immune-receptors (Stabilin-1 (r = 0.23, p = 0.001) and C5aR1 (r = 0.21, p = 0.004) were higher in AD. Psychomotor speed was associated with D1R-abs (β 0.49, p < 0.001), depression with ETAR-abs (β 0.31, p < 0.001), and visuospatial function with 5-HT1AR-abs (β 0.27, p = 0.004) despite similar antibody levels compared to controls.

**CONCLUSIONS:**

Antibody levels to VEGFR1, serotonergic receptors, and receptors in the immune system were increased in AD. Antibodies at similar levels as in controls were associated cognitive dysfunction and depression in AD.

**KEYWORDS:**

5-HT2AR; 5-HT2CR; 5-HT7R; C5aR; MADRS; Stablin-1; Trail Making A; VEGFR1; VOSP; naturally occurring antibodies