



## Documents

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### **Relationship of selective complement markers with schizophrenia**

(2022) *Journal of Neuroimmunology*, 363, art. no. 577793, .

**DOI:** 10.1016/j.jneuroim.2021.577793

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### **Abstract**

Immune system dysregulation may be involved in schizophrenia, but biomarker studies have thus far reported inconsistent findings. The relationship of plasma levels of complement markers C3 and C4, with schizophrenia, sociodemographic and clinico-psychological factors were here studied in 183 patients and 212 controls. C3 and C4 levels were significantly higher in the patients and in subjects with elevated C-reactive protein (CRP), and positively correlated with body mass index (BMI) ( $p < 0.05$ ). Schizophrenia, BMI, and CRP were significant predictors for C3 and C4 levels in multivariate analyses ( $p < 0.001$ ). In conclusion, complements C3 and C4 are potential peripheral biomarkers in schizophrenia. © 2021 Elsevier B.V.

### **Author Keywords**

C-reactive protein; Complement C3; Complement C4; Schizophrenia

### **References**

- Alexander, J.J.  
**Blood-brain barrier (BBB) and the complement landscape**  
(2018) *Mol. Immunol.*, 102, pp. 26-31.
- Birnbaum, R., Weinberger, D.R.  
**A genetics perspective on the role of the (neuro)immune system in schizophrenia**  
(2020) *Schizophr. Res.*, 217, pp. 105-113.
- Charlson, F.J., Ferrari, A.J., Santomauro, D.F.  
**Global epidemiology and burden of schizophrenia: findings from the Global Burden of Disease Study 2016**  
(2018) *Schizophr. Bull.*, 44 (6), pp. 1195-1203.
- Chen, Y., Zhao, Z., Lin, F.  
**Associations between genotype and peripheral complement proteins in first-episode psychosis: evidences from C3 and C4**  
(2021) *Front. Genet.*, 12.  
647246
- Comer, A.L., Jinadasa, T., Sriram, B.  
**Increased expression of schizophrenia-associated gene C4 leads to hypoconnectivity of prefrontal cortex and reduced social interaction**  
(2020) *PLoS Biol.*, 18 (1).

- Copenhaver, M., Yu, C.Y., Hoffman, R.P.  
**Complement components, C3 and C4, and the metabolic syndrome**  
(2019) *Curr. Diabetes Rev.*, 15 (1), pp. 44-48.
- Dean, A.G., Sullivan, K.M., Soe, M.M.  
**OpenEpi: open source epidemiologic statistics for public health, version 3.01.**  
[online] OpenEpi  
(2013),  
Available at: [Accessed 9 Sep. 2021]
- Enache, D., Nikkheslat, N., Fathalla, D.  
**Peripheral immune markers and antipsychotic non-response in psychosis**  
(2021) *Schizophr. Res.*, 230, pp. 1-8.
- Fernandes, B.S., Steiner, J., Bernstein, H.G.  
**C-reactive protein is increased in schizophrenia but is not altered by antipsychotics: meta-analysis and implications**  
(2016) *Mol. Psychiatry*, 21 (4), pp. 554-564.
- Idonije, O.B., Akinlade, K.S., Ihenyen, O.  
**Complement factors in newly diagnosed Nigerian schizophrenic patients and those on antipsychotic therapy**  
(2012) *Niger. J. Physiol. Sci.*, 27 (1), pp. 19-21.  
Retrieved from
- Kay, S.R., Fiszbein, A., Opler, L.A.  
**The positive and negative syndrome scale (PANSS) for schizophrenia**  
(1987) *Schizophr. Bull.*, 13 (2), pp. 261-276.
- Kopczynska, M., Zelek, W., Touchard, S.  
**Complement system biomarkers in first episode psychosis**  
(2019) *Schizophr. Res.*, 204, pp. 16-22.
- Laskaris, L., Zalesky, A., Weickert, C.S.  
**Investigation of peripheral complement factors across stages of psychosis**  
(2019) *Schizophr. Res.*, 204, pp. 30-37.
- Li, H., Zhang, Q., Li, N.  
**Plasma levels of Th17-related cytokines and complement C3 correlated with aggressive behavior in patients with schizophrenia**  
(2016) *Psychiatry Res.*, 246, pp. 700-706.
- Miller, B.J., Culpepper, N., Rapaport, M.H.  
**C-reactive protein levels in schizophrenia: a review and meta-analysis**  
(2014) *Clin. Schizophr. Relat. Psychoses.*, 7 (4), pp. 223-230.
- Mitchell, A.J., Vancampfort, D., Sweers, K.  
**Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders—a systematic review and meta-analysis**  
(2013) *Schizophr. Bull.*, 39 (2), pp. 306-318.
- Mongan, D., Sabherwal, S., Susai, S.R.  
**Peripheral complement proteins in schizophrenia: a systematic review and meta-analysis of serological studies**  
(2020) *Schizophr. Res.*, 222, pp. 58-72.

- Norlelawati, A.T., Kartini, A., Norsidah, K.  
**Relationship of psychological symptoms, antipsychotics and social data with psychosocial function in schizophrenia patients in Malaysia**  
(2015) *Asia Pac. Psychiatry*, 7 (1), pp. 45-53.
- Nsaiba, M.J., Lapointe, M., Mabrouk, H.  
**C3 polymorphism influences circulating levels of C3, ASP and lipids in schizophrenic patients**  
(2015) *Neurochem. Res.*, 40 (5), pp. 906-914.
- Osimo, E.F., Beck, K., Reis Marques, T.  
**Synaptic loss in schizophrenia: a meta-analysis and systematic review of synaptic protein and mRNA measures**  
(2019) *Mol. Psychiatry*, 24 (4), pp. 549-561.
- Presumey, J., Bialas, A.R., Carroll, M.C.  
**Complement system in neural synapse elimination in development and disease**  
(2017) *Adv. Immunol.*, 135, pp. 53-79.
- Santos Soria, L., Moura Gubert, C., Cereser, K.M.  
**Increased serum levels of C3 and C4 in patients with schizophrenia compared to eutymic patients with bipolar disorder and healthy**  
(2012) *Braz. J. Psychiatry*, 34 (1), pp. 119-120.  
Retrieved from
- Sekar, A., Bialas, A.R., de Rivera, H.  
**Schizophrenia risk from complex variation of complement component 4**  
(2016) *Nature*, 530 (7589), pp. 177-183.
- Sproston, N.R., Ashworth, J.J.  
**Role of C-reactive protein at sites of inflammation and infection**  
(2018) *Front. Immunol.*, 9, p. 754.
- van der Gaag, M., Hoffman, T., Remijsen, M.  
**The five-factor model of the positive and negative syndrome scale II: a ten-fold cross-validation of a revised model**  
(2006) *Schizophr. Res.*, 85 (1-3), pp. 280-287.
- Walss-Bass, C., Lokesh, G.L.R., Dyukova, E.  
**X-aptamer technology identifies C4A and ApoB in blood as potential markers for schizophrenia**  
(2019) *Mol. Neuropsychiatry*, 5 (1), pp. 52-59.
- Woo, J.J., Pouget, J.G., Zai, C.C.  
**The complement system in schizophrenia: where are we now and what's next?**  
(2020) *Mol. Psychiatry*, 25 (1), pp. 114-130.
- Yang, Y., Chung, E.K., Zhou, B.  
**Diversity in intrinsic strengths of the human complement system: serum C4 protein concentrations correlate with C4 gene size and polygenic variations, hemolytic activities, and body mass index**  
(2003) *J. Immunol.*, 171 (5), pp. 2734-2745.

• Zhang, S., Zhou, N., Liu, R.

**Association between polymorphisms of the complement 3 gene and schizophrenia  
in a Han Chinese population**

(2018) *Cell. Physiol. Biochem.*, 46 (6), pp. 2480-2486.

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**Publisher:** Elsevier B.V.

**ISSN:** 01655728

**CODEN:** JNRID

**Language of Original Document:** English

**Abbreviated Source Title:** J. Neuroimmunol.

2-s2.0-85122160905

**Document Type:** Article

**Publication Stage:** Final

**Source:** Scopus

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