VH subfamiliy usage: Identifying a biomarker of autoimmunity in schizophrenia

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Schizophrenia (SCZ) is a rather widespread neuropsychiatric illness without defined causes. Studies have implied an immunological dysfunction hypothesis for SCZ by identifying differences in lymphocyte distribution and aspects of autoimmune diseases, including autoantibodies against M1 mAChR and NMDAR in patients. To further understand how autoantibodies could play a role in pathogenesis, the cerebrospinal fluid (CSF) and serum of 5 SCZ and 8 healthy controls (HC) was analyzed for IgM, IgG, and antibodies against M1 mAChR and NMDAR using ELISAs. To evaluate changes in lymphocyte distribution and differences in gene usage in antibodies, the B cells in the peripheral blood (PB) of SCZ and HC were sequenced. There were significant differences in IgM vs. IgG concentration in both groups. Concentrations of mAChR and NMDAR were low to the point of unquantifiability. VH subfamily usage of five different families was different in the PB of HC and SCZ, with overexpression of the V4-34 subfamily in SCZ. The difference in IgM and IgG concentrations was consistent with that of serum. Low levels of mAChR and NMDAR indicate that either the CSF doesn't play a role in the transmission of autoantibodies, or the antibodies only play a role in the onset of the illness. The variation in VH family usage indicates that the heavy chains of antibodies in SCZ have a different composition than those in HC. The overexpression of V4-34 is consistent with B cell subfamily usage in autoimmune diseases such as systemic lupus erythematosis and juvenile chronic arthritis. By using different families, the antibodies of SCZ patients recognize different antigens than HC. Usage of specific V genes provides insight into B-cell maturation and selection in SCZ and verifies autoimmunity as a cause of SCZ.

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