Autoantibodies in disorders of the brain

Summary

In this dissertation, we summarized the current knowledge of autoantibodies in neuropsychiatric disorders, and searched for known and novel pathogenic neuronal autoantibodies in a broader range of brain disorders including encephalitis, epilepsy, psychotic disorders, depression, and anxiety. We also compared different methods for Glutamate decarboxylase autoantibodies (GAD-Abs) detection for the diagnosis of type 1 diabetes and epilepsy.

Chapter 1 introduced the general background of the field of neuronal autoantibodies and their related disorders. It also addressed the pitfalls in neuronal autoantibody detection and provided an overview of the research plans.

Chapter 2 reviewed the evidence in the recent literature for the role of NSAbs as well as related systemic autoantibodies in five neuropsychiatric disorders. It evaluated the techniques used, discussed how results can be interpreted and identified the research gaps.

Chapter3 reviewed the recent evidence for the occurrence of NSAbs in mood disorders with a special focus on depression. It discussed how those NSAbs could potentially be related to neuropsychiatric disorders focusing on their putative pathogenic role in depression.

Chapter 4 assessed the prevalence of NSAbs in the plasma of patients with depression or anxiety by using IHC, CBA and staining on live neurons to analyze if they were more common in patients compared to controls. We found no difference in the prevalence of known neuronal autoantibodies between depression or anxiety groups and the controls without a mental disorder. Certain novel NSAbs existed in a subgroup of patients with current anxiety or depression.

Chapter 5 investigated the prevalence of neuronal and bystander autoantibodies in the sera of psychotic disorders. We found the prevalence of neuronal autoantibodies was very low with no significant difference between healthy controls and patients with mental disorders.

Chapter 6 compared different methods (ELISA, CBA, and IHC) for the detection of GAD-Abs. Additionally; we investigated whether NSAbs rather than GAD-Abs were present in patients with suspected autoimmune brain diseases. We found serum autoantibody levels in patients with GAD related autoimmune encephalitis/epilepsy were higher than in patients with DM1/LADA although high levels of GAD65-Ab (>10000 U/mL) that could be detected by CBA and IHC existed in both groups. Therefore, the clinical relevance, despite these high levels, remains to be elucidated. Only a small portion of patients suspected of GAD-related autoimmune disorders had other neuronal autoantibodies and their clinical significance should be studied individually

Chapter 7 summarized the key findings of this thesis, discusses the limitations and outlines further research directions.

To summarize, the observation that a small subgroup of current anxiety but not psychotic disorder patients had novel NSAbs in the peripheral circulation opens the possibility that some patients are in fact autoimmune patients and thus would benefit from immunotherapy. This finding is important because the autoimmune subgroup of patients can be treated targeting the cause of the problem in contrast to traditional pharmacological approaches that treat only the symptomatology. It would, therefore, be important to replicate the current findings using robust methods and paired serum and CSF samples. The identification of novel antigens targeted by the autoantibodies will help to understand their cause-effect. Besides, a small portion of patients suspected of GAD65-Ab related disorders had other neuronal autoantibodies and their clinical significance should be studied individually.