Different autoantibody concentrations in serum and CSF in Gilles de la Tourette syndrome

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Background and aim
1. Several lines of evidence support the hypothesis of an autoimmune origin of Gilles de la Tourette syndrome (GTS) (Figure 1).
2. Accordingly, in a recent study we detected positive oligoclonal bands (OCB) in cerebral spinal fluid (CSF) in >30% of adult patients indicating an intrathecal antibody synthesis.
3. However, until today no corresponding antibodies could be identified.

Research questions
Are there any specific serum autoantibodies in GTS? Are there any specific CSF autoantibodies in GTS?

Methods
1. We included 20 adult patients with GTS (male: female=18:2, median age 36.1 years ± 14.34 SD)
2. IgG antibodies with binding capacities to central nervous system (CNS) proteins were identified with a protein macroarray representing 6,909 human brain proteins using CSF and serum from three of these patients.
3. Based on binding patterns, and overlap positivity (Figure 2) of detected autoantibodies six autoantibodies were chosen and analyzed using solid-phase ELISAs in a larger collective of patients with GTS (N=70) and compared to non-inflammatory CSF controls and blood donators.

Results: serum
1. Significant differences of autoantibody concentrations in serum were found in 3 of the 6 selected autoantibodies namely against FAM 161a, E3 ubiquitin ligase and kinesin 5B.
2. In comparison to controls, a lower concentration of serum autoantibodies against FAM 161a (p=0.049), a protein which is involved in dopaminergic signal conduction, was found in patients with GTS (Figure 3).
3. We also found lower antibody against E3 ubiquitin ligase concentrations in GTS patients (p=0.031), involved in the regulation of synaptic plasticity (Figure 3).
4. Conversely, we have found higher serum antibody against kinesin 5B concentration (p=0.021), which belongs to a group of proteins involved in intracellular transport (Figure 3).

Results: CSF
1. Significant different autoantibody concentrations were only found against pleiotrophin (PTN), a protein involved in cell differentiation and survival.
2. Compared to controls autoantibody concentrations against PTN (p=0.0001) were decreased in GTS patients.

Conclusions
1. Our results indicate that autoantibodies might play a role in the pathophysiology of GTS.
2. Main pathways involved in autoimmunity in GTS are related to cell differentiation, intracellular transport, synaptic plasticity and dopaminergic neurotransmission.