Multiscale analysis of anti-NMDA receptor autoantibody in psychosis (AutoScale)

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Psychotic disorders, encompassing schizophrenia and bipolar disorders, are major health problems worldwide. It is well-established that several converging factors are involved in these complex psychiatric disorders, among which immune status, including autoimmunity, are particularly relevant. A role for autoimmune dysfunction in psychiatric disorders, reported in schizophrenia almost a century ago, is supported by specific autoimmune responses to self-antigens identified in particular in psychotic disorder. The importance of autoimmunity in major psychosis has been strongly reinforced as a number of syndromes characterized by global encephalopathy and by more focal psychiatric symptoms was found to result from autoimmune dysfunction, caused by autoantibodies against the NMDAR. To uncover the behavioral, cellular and molecular mechanism by which NMDAR-Ab induce psychosis, we here built a complementary and synergistic consortium of clinical and basic research experts. The partners, i.e. L. Groc (France), J. Dalmau (Spain), C. Geis (Germany), P. Marquet (Canada), and M. Leboyer (France), have already strongly contributed to our current understanding of autoimmunity in brain disorders. Our main objective is to uncover how NMDAR-Ab underlie psychotic disorders in seropositive NMDAR-Ab patients, using a unique and multi-scale combination of experimental approaches.