SELECTIVE INVOLVEMENT OF INHIBITORY NEURONS IN THE PATHOGENESIS OF NEURAL INJURY IN EXPERIMENTAL ANTIPHOSPHOLIPID SYNDROME

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The antiphospholipid syndrome (APS) is characterized by central nervous system (CNS) dysfunction associated with antibodies to a complex of phospholipids and □2-glycoprotein I (□2-GPI) causing hyper-coagulation and immune mediated neurodegenerative mechanisms. Mice immunized with □2-GPI develop systemic and CNS manifestations of experimental APS (eAPS). The aim of the present study was to evaluate the pathogenic mechanisms involved, in particular direct effects of antiphospholipid antibodies (aPL) on the brain. Histological stainings for IgG binding were performed in vitro on normal brain slices and in vivo on APS and control brain slices. aPL from APS mice bind in vitro to specific brain structures, most of them white matter tracts in the limbic system. Specific accumulation of aPL-IgG in brain neuronal cells was demonstrated in vivo in APS mice. More specifically, we found that interneurons (Basket cells) in the hippocampus were intensely stained for IgG in APS mice. This staining was highly specific for the 5 ePAS brains stained compared to 5 adjuvant immunized control mice. Both in vitro and in vivo binding patterns are compatible with the neurobehavioral effects: The Basket cell interneurons are inhibitory and secrete GABA. We suggest that a loss of such neurons can account for the hyperactive behavior in eAPS mice and possibly also account for the learning and memory deficit. Furthermore, similar selective loss of inhibitory neurons in the brain may account for the increased incidence of epilepsy associated with APS in humans. Thus, the eAPS model provides a unique tool to define the anatomical, physiological, and signaling effects of the aPL in vitro and in vivo.