



Inflammatory psychosis and HERV-W

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Major psychosis such as bipolar disorder and schizophrenia are complex disorders that may involve a complex interplay of genetic and environmental factors such as infections. Successive studies showed an association between major psychosis and Human Endogenous retroviruses (HERVs). The HERVs are components of the human genome, representing 8% of human DNA. A specific type of HERVs, called HERV-W, has, through several recent studies, been associated with major psychoses. For instance, elevated transcription of HERV-W elements has been documented, and antigens of HERV-W envelope and capsid proteins have been found in blood samples from patients. Viruses and/or parasite that have been implicated in the pathology of major psychoses such as herpesviridae, influenzae, and *Toxoplasma Gondii* have been shown to activate HERV-W elements, and such activation has been associated with elevated biomarkers of systemic inflammation. New research indicates that HERV-W may be an important genetic factor interplaying with the environmental risk factor of infections and that, through this, HERV-W may be important for disease pathogenesis.

Therefore, our hypothesis is that an infectious or major inflammatory event during pregnancy, such as infections, can trigger HERV-W elements activation in embryo. Subsequent DNA modifications would cause aberrant HERV-W Env expression and might lead to an abnormal neurodevelopment, in a general context of inflammatory neurotoxicity. Particular stress conditions and/or a secondary postnatal infection with neurotropic agents such as, e.g., cytomegalovirus (CMV) or herpes simplex virus type 1 (HSV-1) would reactivate latent and/or *in-utero* modified HERV-W elements. However, further researches are needed to find out if specific treatment strategies could reduce the expression of HERV-W and if this will be associated with remission.