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Early postnatal infection with neurotropic influenza A virus: effects on gene expression and behavior in mice

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Introduction

A number of genes have been associated to the development of schizophrenia, several of which are involved in central nervous system development. It has also been suggested that exposure to viral infections during early life increases the risk for later developing schizophrenia. In this study we investigate if an early postnatal infection by influenza A/WSN/33 virus in mice can cause changes in the expression of genes, including genes associated with schizophrenia, in the brain during development and if the early life infection affect the behavior in adult mice. In addition to wild type mice, an immunodeficient strain (*Tap1-/-*) was included in the study to model the potential influence of a genetic immune dysfunction.

Methods

Mice were injected intraperitoneally with 2400 plaque forming units of the neurotropic influenza A/WSN/33 virus or vehicle on postnatal day (P) 3. Brains were sampled at postnatal day (P) 7, P13, P24, P50 and P90. Gene expression and presence of viral RNA were analyzed by real-time PCR, viral antigens were detected by immunohistochemistry. Behavioral testing was performed at 3–4 months of age.

Results

Following infection at P3, altered expression of the genes *Gcm1*, *Olig2* and *Cxcl1* was observed in both strains of mice at postnatal day (P)7. At P24 infected *Tap1-/-*, but not wild type, mice exhibited altered expression of the genes *Gcm1* and *Nrg1*. Infected *Tap1* knockout mice exhibited increased rearing activity and anxiety-like behavior, as well as deficits in working memory compared to controls. In contrast, infected wild type mice were deficient only in the long-term memory task when compared to wild type controls.

Conclusion

Early postnatal infection by influenza A virus can affect the expression of schizophrenia-associated genes during development and affect cognitive and emotional functions in adult animals. The extent of these changes was influenced by genetic variation in the host animals.