Influence of antipsychotic drugs on human endogenous retrovirus (HERV) transcription in brain cells.

Abstract: Human endogenous retroviruses (HERVs) have been associated with various neurological and neuropsychiatric disorders. Transcripts and proteins of at least three HERV groups, HERV-W, ERV9 and HERV-K(HML-2) have been detected repeatedly in brain samples or cerebrospinal fluid of patients with schizophrenia suggesting that alterations in HERV activity may play a role in etiopathogenesis. Current therapies otherwise include neuroleptics and/or antidepressants that may induce epigenetic alterations and thus influence HERV expression. To investigate the effects of these drugs on HERV transcriptional activity, HERV expression profiles of a broad range of human brain cell lines treated with valproic acid (VPA), haloperidol, risperidone, and clozapine were analyzed using a retrovirus-specific microarray and qRT-PCR. Investigation of 52 HERV subgroups revealed upregulation of several class I and class II HERV elements by VPA in a dose-dependent manner. The strongest effect was observed on HERV-W and ERV9 groups in the human glioblastoma cell lines SK-N-SH and SK-N-MC, respectively. The transcript level of HERV-K(HML-2) elements was not influenced. Transcription of HERV-W, ERV9 and HERV-K(HML-2) taxa was further quantified in postmortem brain samples of patients with schizophrenia, bipolar disorders and a healthy control group with regard to their medication. Patients with
schizophrenia showed a significantly higher HERV-W transcription associated with VPA treatment. However in case of ERV9, enhanced transcript levels could not be explained solely by VPA treatment, since a slight increase was also found in untreated patients compared to healthy controls. HERV-K(HML-2) elements appeared to be upregulated in some patients with bipolar disorders independent from medication. In conclusion, these results suggest that antipsychotic medication may contribute to increased expression of distinct HERV taxa in patients with neuropsychiatric diseases.

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