Large scale transcriptional analysis of an animal model of seizures

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Wistar Audiogenic Rat (WAR) is an animal model in which seizures are developed by acoustic stimulation that activate the quadrigeminal plate structure. The characterization of the model´s transcriptional profile can elucidate aspects regarding gene regulation related with the occurrence of seizures. The purpose of the study was to evaluate the WAR quadrigeminal plate transcriptome in post-ictal state. Two Wistar and two WAR rats were submitted to acoustic stimulation. The WAR exhibited seizures and the Wistar did not respond to the stimulus. Four days after the stimulus, the quadrigeminal plates were collected and processed to prepare the libraries. The RNA-Seq was realized in MiSeq platform (Illumina). The screened data by Cutadapt software were mapped using the Bowtie2 software. The gene counting was made at the HTseq and Features Counts and the differential expression was determined using DEseq and EdgeR softwares. The PCA was realized in R, the genes were submitted for functional annotation by GO Consortium and, finally, the results validation was performed by qPCR. Considering the value FDR ≤ 0,05 by EdgeR, 62 genes were identified differentially expressed between the WAR and the control. DEseq identified 16 genes, in which 14 genes were also recognized by EdgeR. Considering both analysis, 28 genes was upregulated and 36 downregulated in WAR. The PCA revealed a segregation between the samples of Wistar and WAR, showing that the seizure's predisposition is the main determinant of gene expression variation between these groups. The functional annotation clustered the genes in six categories of molecular functions: binding, catalytic activity, receptor, signal transducer, structural molecule and transporter. Among the 16 genes identified by DEseq, 13 were validated by qPCR. Three genes, *Gpr126*, *Gria2* (receptor category) and *Qdpr* (catalytic category) showed an interesting result regarding expression pattern and the connection of their function with the phenotype. The *Gpr126* gene was downregulated and the *Gria2* and *Qdpr* genes was upregulated in WAR animals that had seizures. These results allow us to conclude that there is a differential gene regulation related to seizure's occurrence in WAR model, which could explain the susceptibility of this strain to ictal events.