

First task

Akvilė Višniauskaitė ir Ieva Pudžiuvėlytė

3/11/2022

Introduction

This work will present data analysis from a research that studied the enhancer's at *IGF2* differential methylation association with abnormal dopamine synthesis in major psychosis.

Our samples were taken from the prefrontal cortex isolated neurons in schizophrenia and bipolar disorder.

Study analysed data from individuals diagnosed with schizophrenia, bipolar disorder and controls (29, 26 and 27 individuals, respectively). In the analysis study controlled for age, sex, post-mortem interval, genetic ancestry (determined by genotyping the same individuals).

Experiment design

The experiment design was multi-omics study with 55 cases (with schizophrenia or bipolar disorder) and 27 controls.

Objective of the research

According to authors, schizophrenia and bipolar disorder have got characteristic of periods of psychosis. The main objective of the research was to gather epigenomic profiling data to get a more accurate model of neuronal dysregulation in diseases with periods of psychosis.

Biological targets of the research

Researchers intended to look for specific patterns of DNA methylation in isolated neurons from the frontal cortex of individuals that had diseases.

- IGF2 - insulin growth factor 2 protein
- *IGF2* - IGF2 gene
- *Igf2* - enhancer of *IGF2* gene
- TH - tyrosine hydroxylase protein
- dopamine - a neuromodulatory molecule
- psychosis - an abnormal condition of the mind that results in difficulties determining what is real and what is not real

Results received

Authors found a strong association between methylation of *Igf2* and TH synthesis. TH is the bottleneck enzyme that is responsible for dopamine synthesis. If enhancer *Igf2* is hypomethylated, levels of TH are higher, which determines the higher production of dopamine. Apparently, dopamine is responsible for psychosis in the mental disorders of interest.

Additional information

Schizophrenia and bipolar disorder patients are consistently hypomethylated at *IGF2* locus when compared to controls. This locus remained significantly hypomethylated even after accounting lifestyle-related variables of smoking and anti-psychotic use.

The reaction chain of interest of the research (upward arrows show elevated expression or synthesis of the protein, product, or effect):

Hypomethylation of *Igf2* \rightarrow \uparrow IGF2 \rightarrow \uparrow TH \rightarrow \uparrow dopamine \rightarrow \uparrow psychosis

References

Pai, Shraddha, Peipei Li, Bryan Killinger, Lee Marshall, Peixin Jia, Ji Liao, Arturas Petronis, Pirooska E Szabó, and Viviane Labrie. 2019. “Differential Methylation of Enhancer at *Igf2* Is Associated with Abnormal Dopamine Synthesis in Major Psychosis.” *Nature Communications* 10 (1): 1–12.