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Effects of Three Different Classes of Antidepressants in the Proteome of a Human Oligodendrocyte Culture

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Abstract

Depression is a complex and multifactorial neuropsychiatric disorder that affect 4% of the world's population. The main hypothesis that underlies its pathophysiology is about neuronal dysfunctions, with a focus on monoamines dysregulation. However, recent studies have shown disturbances in oligodendrocytes and myelination in the pathophysiology of disease. Treatment for depression is mainly based on the use of antidepressants that modulate the levels of monoamines and their receptors, but their effects on oligodendrocytes are still scarce. Thus, the aim of this study is to investigate the proteome of a human oligodendrocyte cell line (MO3.13), treated with three different classes of antidepressants, in order to unreveal pathways and biological processes that could be implicated or associated with the pathophysiology and treatment of this disorder.

Key words: *Fluoxetine, amitriptyline, bupropion*

Introduction

Major Depressive Disorder (MDD) is a multifactorial psychiatric disease that affects around 350 million people worldwide[1]. The symptoms include depressed mood, diminished interest in almost all activities, fatigue and cognitive dysfunction. These are mainly treated with antidepressants, such as fluoxetine, amitriptyline and bupropion[2,3]. Several hypotheses have been put forward to explain the pathophysiology of MDD, mostly involving neuronal cells. However, strong evidence has been shown the involvement of oligodendrocytes (OLD), oligodendrocyte progenitor cells (OPC) and myelination in the pathophysiology of the illness[4].

Oligodendrocytes are responsible for myelination of the central nervous system and myelin is important for maintaining neuronal integrity[5]. The loss of OLD, as well as myelination impairments in prefrontal cortex and other brain's regions of MDD patients have been reported[4]. Lesions of myelinated fibers in the white matter were associated with the severity of depression and patients with severe damage to myelinated fibers had a poor response to antidepressants. These indicate that the myelinated fibers may not only participate in the pathophysiology of depression but also play a key role in the mechanism of antidepressant therapy[6]. Thus, the aim of this study is to investigate the biological processes and biochemical pathways involved in the treatment with three different classes of antidepressants in a human oligodendrocytes cell line

Results and Discussion

The concentrations of the drugs to be tested have been standardized through MTT assay, that measure the cell viability. After this, the MO.313 cells will be cultured, and subsequently treated with fluoxetine (selective serotonin reuptake inhibitor), amitriptyline (tricyclic antidepressants) and bupropion (norepinephrine-dopamine reuptake inhibitor). Cell will be harvested after 8h and their proteins will be extracted and digested. These samples will be submitted to mass spectrometry-based shotgun proteomics.. Data will be processed by Progenesis software, where the proteins will be identified and quantified. The differentially expressed proteins between treatment and vehicle (p-value <0,05) will be analysed using bioinformatics tools available online; DAVID (https://david.ncifcrf.gov), Reactome (https://reactome.org) and String (https://string-db.org).

PS: As this project has still not start, there are no results or discussion to be presented at the present moment . We are going to have results to present at the moment of the conference.

Conclusions

MDD is a leading cause of disability worldwide and how do the antidepressants modulate de proteome of human oligodendrocytes is a question that awaits further research. Proteomics allows the analysis of differentially expressed proteins, as well as the biological process and metabolic pathways altered by these drugs. Therefore, in this study, we aim to characterize the proteome of a human oligodendrocyte cell line treated with three different classes of antidepressants in order to shed light on their possible implications on the pathophysiology and treatment of this disorder.

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