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Investigation of changes in the expression of human blood plasma proteins in major depressive disorder patients associated to an effective antidepressant response

Pamela T. Carlson*, Licia C. Silva-Costa, Daniel Martins-de-Souza.

Resumo

Major depressive disorder is a complex multi-factor psychiatric disorder whose consequences can be debilitating, being one of the main worldwide causes of suicide. Its treatment is predominantly antidepressants and regular counseling and despite the treatment's effectiveness, 10-30% of the patients respond differently and present adverse reactions to it, which can lead to the a change in the medication used. Due to this, it is important to understand what differs in patient's blood plasma protein that can help identify good and bad responders to treatment. Through the analysis of differential expressed protein in good responders, it is possible to investigate which biochemical processes vary between them and therefore predict possible responses to better adapt patient's treatment.

Palavras-chave:

major depressive disorder, differential expression, proteomics

Introdução

Major depression disorder (MDD) is a long lasting or recurrent disorder which affects 4,4% of the world population, with 322 million people affected worldwide in 2015[1]. MDD patients present many symptoms such as depressed mood, loss of interest and enjoyment, and decreased energy and can be categorized as mild, moderate or severe, which, in the last case, can lead to suicide.

The main method of managing MDD is through antidepressants and regular counseling. On the other hand, 10%-30% of the treated patients exhibit treatment-resistant symptoms and difficulties in social and occupational function, decline in physical health and suicidal thoughts[2]. Therefore, it is important to investigate the mechanism that may be the bottomline behind good and bad response to treatment, which can be done by comparing the differentially expressed of proteins in the blood plasma of good and bad responders.

Resultados e Discussão

Metabolism and immune pathways proteins have been identified differentially expressed in patients who had subsequent favourable response to treatment[3]. Taken that and the article by Christoph W. Turck et al[3] into account, we decided to analyze in terms of biochemical pathways and protein interactome data presented in table 2, which corresponds to the differentially expressed proteins found differentially expressed in good and poor responders before the initiation of antidepressant treatment. In order to do the analysis, we used systems biology in silico tools such as David (https://david.ncifcrf.gov) and String (https://string-db.org/).

Activation of stress pathways can lead to depression[4]. Data found by Turck et al confirm this statement, as shown in blue in Image 1, differentially expressed. Other pathways whose differential expression of proteins was expected due to evidence of dysregulation in MDD patients and can be seen in red in Image 1 are the immune pathways[5]. On the other hand, good responders overexpressed proteins related to both intrinsic and extrinsic prothrombin activation pathways and underexpressed proteins related to serine endopeptidases inhibition and serines. These could assist in identifying good and bad responders, once a hypothrombotic state can induce depression[6] as can the presence of serine endopeptidases in the brain[7] which could, then, activate the inhibition pathways mentioned.

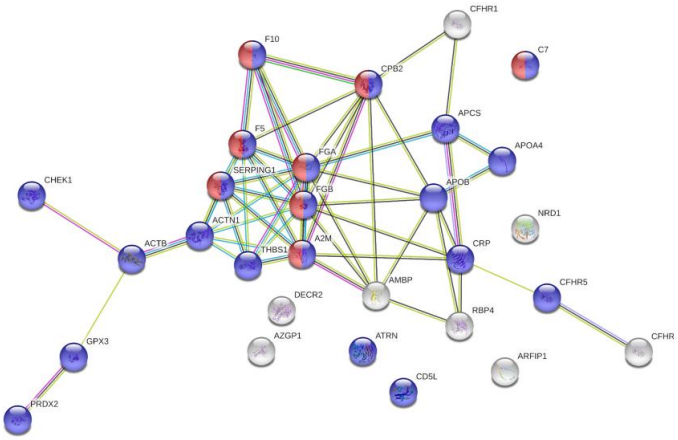

Image 1: Differentially expressed proteins in MDD good responders.

Conclusões

Differential expression of proteins in good and poor responders can lead us to a better understanding of the underlying molecular differences present in MDD patients.

Agradecimentos

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