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A computational model for genetically inherited depression

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Depression, or major depressive disorder (MDD) is one of the most disabling and prevalent disorders. It is seen in all age groups, both genders, and all races. One of the biggest problems of depression is the frequency of suicidal thought and suicide attempts among suffers of this disorder. MDD is characterized as either unipolar or bipolar. Unipolar MDD has two subtypes: melancholic which is mainly caused by genetic vulnerability and psychotic which is mainly caused by environment, specifically early life trauma. The focus of this project was to build a computational model for MDD. The purpose of this model was to highlight the changes in the brain areas of a person who suffers from MDD compared to a normal person. The type of MDD chosen for this model was melancholic unipolar. The model was constructed from information gathered from research literature related to the brain, depression, and neuroscience. The precursors for melancholic MDD are polymorphisms of alleles that code for serotonin (5-HT) receptor types, tryptophan hydroxylase, and the 5-HT transporter. Melancholic MDD is seen in people who have genetic vulnerability caused by these polymorphisms. These genetic vulnerabilities were used to show the hypoactivity of the 5-HT systems and the corresponding symptoms caused by this irregularity. Amygdala hyperactivity was also mapped to show how it causes increased cortisol secretion which resulted in hypoactivity of the neuroephinephrine (NE) system. The corresponding symptoms were also linked to these problems. This model also shows the hypoactivity of the dopamine (DA) system along with the corresponding symptoms. The physical map of this disorder is complete and a framework for the computational model is being developed. Though the model is based on published information and studies, there are gaps in our understanding of several issues. For instance, it is known that the 5-HT, NE, DA and cortisol systems are involved in the symptoms of depression. However, it is not known which system(s) trigger(s) the start of the disease in people who suffer from MDD. Also a lot of research sources do not specify whether the dysfunctions and symptoms referred to are for melancholic of psychotic MDD, so there might be some overlap between these disorders in this model. Such gaps will also be better understood as part of this research. The genome/proteome information will also be incorporated into the model in the future.