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GENETIC RESEACH: PROMISES AND PITFALLS FOR CLINICAL TREATMENT OF DEPRESSION

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The lifetime prevalence of mood disorders is estimated around 20% in the general population leading to a main cause of disability worldwide and a major public health issue.[1] The ethiology of mood disorders is still unknown, but its various phenotypes are believed to be caused by multiple genetic variants interacting in a complex way with environmental vulnerability factors. Therefore, the identification of biomarkers and environmental markers is crucial to improve our understanding and diagnosis as well as our treatments. Despite intensive and costly research for more than two decades to unravel suceptibility genes, although pathophysiological pathways of interest have been recongnized, results have not been consistant so far and not a single genetic biomarker of depression has been identified and replicated. More recent systematic genome-wide association studies (GWAS) have reported weak associations of some genetic variants in large samples, but multiple rare variants may concur to confer only part of the suceptibility to depression. Structural variations may also be considered to be promising as is the case for copy-number-variations (CNVs). Methodological issues and limitations will also be critically discussed in light of the complexity of gene-evironment interactions (epigenetic modulation of gene expression)[2] and in relation to future prospects for individualized pharmacotherapy of depressive illness.

1. Murray GJ., Lopez AD. Alternative projections of mortality by cause 1990-2020: Burden of Disease Study. Lancet, 1997; 349:1498-1504.

2. Munafo MR, Flint J. Replication and heterogeneity in gene x environment interaction studies. Int. J. Neuropsychopharmacology. 2009; 12:727-729.

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