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GENE ENVIRONMENTAL INTERACTION IN PSYCHIATRY: THE 5-HTTLPR AND COMT STORY FROM AN EVOLUTIONARY POINT OF VIEW

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The general medical model explains that there are genetic and environmental risks and protective factors in the aetiology of any complex disease. The main idea supported by this model is the existence of good and bad polymorphisms. We present a review of the literature and some examples of our own empirical studies about this issue in psychiatry; with special focus on the methodological problems of this medical model.

In relation with 5-HTTLPR we present the results of a longitudinal study of 1804 women. In this study the “LL” genotype seems to be a risk factor for post-partum depression, probably due to gene-hormone interaction after delivery. But the same genotype might be a protective factor of emotional disorder in other life-time and environmental condition.

In relation with COMT gene, we present a meta-analysis (including our own data) of 51 studies comprising 13,894 schizophrenic patients and 16,087. We found a small but significant protective

effect for heterozygosis at rs4680 (pooled OR ¼ 0.947, P¼ 0.023; pooled OR ¼ 0.813, P¼ 0.0009). Thus, the COMT functional polymorphism rs4680 contributes to schizophrenia genetic susceptibility under an over-dominant model, indicating that both too high and too low levels of dopamine (DA) signalling maybe risk factors.

In summary, both examples suggested that there are no 'bad' or 'good' genotypes in relation to common variants. The controversial results of many genetics associations' studies in psychiatry might become comprehensive under an evolutionary approach.

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