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Insights from pharmacogenetic studies of antidepressants

Laura Mandelli

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Up to 60% of depressed patients do not respond completely to antidepressants and up to 30% do not respond at all. Among the many reasons leading to non-response, such as inadequate treatments and comorbid conditions, genetic factors as likely to contribute to up to 50% of variance in antidepressant response. Environmental factors, such as chronic stressors, psychosocial adjustment and personality traits may also influence response to treatment and interact with these. The investigation of both of these types of factors has been informative in genetic aetiological studies (e.g. Caspi et al., 2003) and is increasingly employed in pharmacogenetics.

A growing number of genetic variants have been replicated in terms of association with SSRI efficacy. They include polymorphisms in the serotonin transporter gene (5-HTTLPR), tryptophan hydroxylase gene (TPH), 5HT1A and 5HT2A receptors, the G-protein beta3-subunit (GNB3), Catechol-O-methyltransferase (COMT), the noradrenaline transporter (NAT), and dystrobrevin binding protein 1 (DTNBP1). Data indicating environmental stressors and temperamental traits as moderators of the effect of such genes on response to treatment will also be presented.

In conclusion, there are genetic and environmental factors that interact in a complex manner to impact on response to treatment with antidepressants. Increased understanding of these, including clinical characteristics such as "harm avoidance," may assist the clinician in deciding the best antidepressant to prescribe for a given patient.

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Institute of Psychiatry, University of Bologna, Italy

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