CS02-01 - EUROPEAN PROGRAM FOR TREATMENT RESISTANT DEPRESSION (TRD)

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It has been estimated that 30 to 45% of adequately treated major depressive disorder (MDD) episodes in a psychiatric setting fail to achieve an adequate response. The Group for the Study of Resistant Depression (GSRD), a collaborative project between 8 centers in Europe in Belgium, France, Greece, Italy, Israel, and Austria developed a staging model that distinguishes between 'non-responders' (patients who fail to respond to one form of treatment, administered for 6-8 weeks), a condition which is now termed *"insufficient response"* by the European Medicines Agency (EMA), 'treatment resistant depression' (TRD, patients that fail to respond to two or more adequate antidepressant trials of different classes of antidepressants), and 'chronic resistant depression' (CRD, patients being treated with several antidepressants for more than 12 months). The aim of the European multicenter project performed by the GSRD, was to study methodological issues, operational criteria, genetic variables, clinical characteristics and treatment factors associated with treatment response in the largest sample published to date focusing on patients with major depressive disorder. The aim was to study methodological issues, operational criteria, genetic variables and clinical characteristics associated with TRD. The findings of the GSRD provide a set of 11 clinical variables associated with treatment response, among them comorbid anxiety disorders as well as melancholic features. The GSRD performed the until now largest candidate gene studies to investigate associations with treatment response phenotypes. It emerged that metabolism status as studied by cytochrome P450 genes (CYP1A2, CYP2C9, CYP2C19 and CYP2D6) may not be helpful to predict the rate of response and remission to antidepressants. Due to the existence of genetic vulnerability to suicidality and reported associations of COMT with suicidal behaviour, we further elucidated the impact of COMT on suicidal behaviour in a sample of TRD patients. Significant single marker and haplotypic association (rs2075507, rs737865 and rs6269) with suicide risk was found in MDD patients not responding to antidepressant treatment, but not in responders. Although there is a plethora of hints in textbooks that switching the mechanism of action should be obtained when a patient does not respond to one medication, the results of the GSRD challenge this notion by describing that staying on the same antidepressant mechanism of action for a longer time is more beneficial than switching. Taken together the results of the GSRD European multicenter project contributes to clinical and genetic characterization of the subphenotype of TRD, and, since this is an ongoing project, will provide further insights to this clinical relevant issue in the near future.

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