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PHARMACOGENETIC ASSOCIATION BETWEEN 5HTT/SLC6A4, 5HTR2A AND TPH2 GENES AND THE RESPONSE TO TIANEPTINE IN MAJOR DEPRESSIVE EPISODE

N. RAMOZ<sup>1</sup>, E. Burgess<sup>1</sup>, Y. Le Strat<sup>1</sup>, P. Gorwood<sup>1,2</sup>

<sup>1</sup>INSERM UMR894, <sup>2</sup>CMME, Hospital Sainte-Anne (Paris-Descartes), Paris, France

Introduction: Depression is the most frequent psychiatric disorder. Antidepressant drug treatment response is modulated by genetic factors. Tianeptine molecule does not inhibit serotonin reuptake. Possible targets to this treatment are the serotonin transporter (5HTT/SLC6A4), the serotonin receptor 2A (5HT2A) and, the neuronal-specific enzyme that controls brain serotonin synthesis, the tryptophan hydroxylase-2 (TPH2).

Objectives: We screened variants of candidate genes 5HTT/SLC6A4, 5HTR2A and TPH2 in 3500 outpatients treated with tianeptine for a major depressive episode (MDE) to search for an association to a positive treatment response.

Aims: The goal of this work was to study the pharmacogenetic response to tianeptine treatment in MDE.

Methods: A total of 3500 outpatients were treated with tianeptine for a MDE. The criteria for a MDE were examined by the clinicians according to the DSM-IV diagnosis and the duration of each symptom was recorded during the inclusion and at 4 to 8 weeks of treatment. The Hospital Anxiety and Depression Scale (HAD) was evaluated at the two visits. DNA was extracted from saliva sample and genotyping of single nucleotide polymorphisms (SNPs) was performed by Taqman assay.

Results: All clinical and genotype data were collected for 1855 tianeptine-treated patients. The SNP rs6354 in SLC6A4 gene was significantly associated with response to tianeptine ( $p=0.009$ ; Odds ratio=1.26; 95% confident interval=1.06-1.50). Two SNPs in 5HT2A and one in TPH2 were also associated to treatment response (rs7322347  $p=0.03$ , rs7997012  $p=0.04$  and rs7955501  $p=0.04$ ).

Conclusions: We detected a pharmacogenetic association between serotonin genes and the response to tianeptine in major depressive episode.