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INFLUENCE OF IL6-174G>C, IL6-6331T>C AND IL6R D358A A>C IL-6 GENETIC POLYMORPHISMS IN ANTIDEPRESSANT TREATMENT PHENOTYPES

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Introduction: Several studies associated Major Depressive Disorder (MDD) with an increased production of pro-inflammatory cytokines, such as interleukin 6 (IL-6). Serum IL-6 levels were found to be significantly increased in subjects with MDD and with Treatment Resistant Depression (TRD). Moreover, ketamine, a drug with fast-acting antidepressant properties, has proven to reduce IL-6 levels in rat prefrontal cortex and hippocampus. However, despite the clear influence of IL-6 in the pathophysiology of depression and in antidepressant response, studies evaluating the impact of IL-6 functional genetic polymorphisms on treatment response phenotypes are scarce.

Objectives: We aim to evaluate the role of *IL6-174G>C, IL6-6331T>C* and *IL6R D358A A>C* functional polymorphisms in antidepressant treatment phenotypes, specifically remission, relapse and TRD.

Methods: We genotyped the referred polymorphisms in a subset of 80 MDD patients followed at Hospital Magalhães Lemos, Portugal, within a period of 18 months.

Results: We found that patients carrying *IL6-174* GG genotype are more prone to develop TRD (OR=4.125; 95%CI: [1.151-14.786]; p=0.038). We also observed that patients carrying *IL6-6331* TC genotype have a higher risk of relapse (OR=3.988; 95%CI: [1.176-13.516]; p=0.022), and present a lower time to relapse, TC: 26 weeks vs. TT: 45 weeks (p=0.041, Log-rank test). No association was found between *IL6R* D358A genetic polymorphism and any of treatment phenotypes.

Conclusions: The *IL6-174G>C* and *IL6-6331T>C* polymorphisms influence antidepressant treatment response in our subset of MDD patients. These polymorphisms may possibly contribute to the elevated IL-6 levels found in patients with TRD.
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