

Influence of IL-18 Genetic Polymorphisms in Antidepressant Treatment Phenotypes

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Introduction: Recent studies suggested that immune activation and cytokines might be involved in depression. The proinflammatory cytokine interleukin-18 (IL-18) is less reported in depression but is still relevant since it is expressed in the brain and serum levels of IL-18 have been found to be increased in patients with moderate to severe depression. Therefore, it seems reasonable that IL-18 promoter SNPs may have an effect in antidepressant response phenotypes.

Objectives: We aim to evaluate the role of *IL18-607C>A* and *IL18-137G>C* promoter polymorphisms in antidepressant treatment phenotypes, specifically remission, relapse and treatment resistant depression (TRD).

Methods: We genotyped the referred polymorphisms in a subset of 80 MDD patients followed at Hospital Magalhães Lemos, Portugal, within a period of 27 months.

Results: We found that patients carrying *IL18-607 CA* or *AA* genotypes are more prone to relapse after AD treatment (OR=4.145; 95%CI: [1.038-16.555]; p=0.043) and present a lower time to relapse than patients carrying *CC* genotype (69 vs 115 weeks, p=0.019, Log-rank test). We also observed that patients carrying *IL18-137 GC* or *CC* genotypes have a higher risk of relapse (OR=3.988; 95%CI: [1.176-13.516]; p=0.022) and display relapse earlier than the ones carrying *GG* genotype (64 vs 112 weeks, p=0.006, Log-rank test). No association was found between the evaluated genetic polymorphisms and remission or TRD.

Conclusions: The *IL18-607A>C* and *IL18-137G>C* polymorphisms seems to influence relapse after antidepressant treatment in our subset of depressed patients. These polymorphisms may possibly contribute to the elevated IL-18 levels found in patients with moderate to severe depression.