to have an effect in labour analgesia. Most of the papers proved that A118G genetic polymorphisms interfere in labour epidural analgesia, and carriers of G118 allele seemed to be more sensitive to the opioid drugs (Landau et al) and require smaller dose (ED50) (Camorcia et al), even though there's no enough data to prove its interference in analgesia extent. However Sia et al (20) has shown that carriers of A118 allele are more sensitive to intravenous morphine administration. A118G polymorphism seems to influence variability in pain analgesia and side effects. However it seems to play a differential role whether the drugs are administered intravenously or via epidural route. Larger studies using validated methodology are required to fully elucidate the real effect of this polymorphism in labor pain.

Influence of common ABCB1 genetic polymorphisms in the risk of Major Depressive Disorder and antidepressant treatment phenotypes.

Santos Marlene, Carvalho Serafim, Lima Luís, Nogueira Augusto, Assis Joana Mota-Pereira Jorge, Pimentel Paulo Maia Dulce, Correira Diana, Gomes Sofia, Cru Agostinho, Medeiros Rui.

Major depressive disorder (MDD) is a highly prevalent disorder, which has been associated with an abnormal response of hypothalamus-pituitary-adrenal (HPA) axis. Reports have shown that abnormal HPA axis response can be due to an altered P-Glycoprotein (P-GP) function. This argument suggests that genetic polymorphisms in ABCB1 may have an effect HPA axis activity; however it is still not clear if this influences the risk of MDD. Moreover, there are reports that showed P-GP as responsible for the efflux of some antidepressant drugs; therefore ABCB1 genetic polymorphisms may influence treatment outcome. Our study aims to evaluate the effect of ABCB1 C1236T, G2677TA and C3435T genetic polymorphisms on MDD risk and antidepressant treatment phenotypes in a subset of Portuguese patients. DNA samples from 80 MDD patients of a 18 months-follow-up study carried at Hospital Magalhães Lemos, and 160 controls subjects were genotyped using TaqMan SNP Genotyping Assays. A significant protection for MDD males carrying T allele was observed (C1236T: OR=0.360, 95%CI:[0.140-0.950], p=0.022; C3435T: OR=0.306, 95%CI:[0.096-0.980], p=0.042; and G2677TA: OR=0.300, 95%CI:[0.100-0.870], p=0.013). Male Portuguese individuals carrying 1236T/2677T/3435T haplotype had nearly 70% less risk of developing MDD (OR=0.313, 95%CI:[0.118-0.832], p=0.016). No significant differences were observed regarding overall subjects. Regarding antidepressant treatment phenotypes, although no influence was found for each of the evaluated treatment phenotypes, specifically remission and treatment resistant depression, individuals carrying 1236TT display a shorter time to remission, and are likely to remit 7 weeks earlier that CC and CT carriers (Log rank test, p=0.045). Our results suggest that genetic variability of the ABCB1 is associated with MDD development in male Portuguese patients. The presence of 1236T/2677T/3435T haplotype affects P-GP activity and may influence HPA axis, due to an increased access of glucocorticoid into central nervous system (CNS). The observed gender-specific risk may be explained by a gender dimorphic sensitivity of the HPA-axis and reflect a gender-specific pathophysiology of depression. Regarding antidepressant treatment outcome, a putatively less active P-GP found among 1236TT genotype carriers, may lead to higher antidepressant concentrations in CNS, which explain the earlier remission.

FAS -670A>G genetic polymorphism is associated with Treatment Resistant

Santos Marlene, Carvalho Serafim, Lima Luis, Nogueira Augusto, Assis Joana, Mota-Pereira Jorge, Pimentel Paulo, Maia Dulce, Correia Diana, Gomes Sofia, Cruz Agostinho, Medeiros Rui.

Hippocampal neurogenesis has been suggested as a downstream event of the mechanism of action of antidepressants (AD) and might explain the lag time between AD administration and the therapeutic effect. Despite the widespread use of antidepressants in the context of Major Depressive Disorder (MDD), there are no reliable biomarkers of treatment response phenotypes, and a significant proportion of patients display treatment resistant depression (TRD). Fas/FasL system is one of the major pathways in apoptosis and is important to regulate cell proliferation and tumor cell growth. Recently, this pathway has been described to be involved in neurogenesis and neuroplasticity. Functional polymorphisms in the promoter region of FAS and FASL genes have been identified and are known to alter the transcriptional activity of these genes.

We aim to evaluate the role of FAS -670A>G and FASL -844T>C functional polymorphisms in antidepressant treatment response phenotypes, since they have never been addressed in the context of depression and antidepressant therapy.

We genotyped FAS -670A>G and FASL -844T>C functional polymorphisms in a subset of 80 MDD patients followed at Hospital Magalhães Lemos within a period of 18 months.

We found that patients carrying FAS -670 G allele are more prone to have poor prognosis (relapse or TRD: OR=6.200; 95%CI: [1.875-20.499]; p=0.001). We also observed that patients carrying this allele have a higher risk to develop TRD (OR=10.895; 95%CI: [1.362-87.135]; p=0.007). Moreover, multivariate analysis adjusted to potentials confounders showed that patients carrying G allele have higher risk to early relapse (HR=3.827; 95%CI: [1.072-13.659]; p=0.039). No association was found between FASL-844T>C genetic polymorphism and any treatment phenotypes.

To the best of our knowledge this is the first study to evaluate the role of FAS functional polymorphism in the outcome of antidepressant therapy. FAS -670