

Psychoneuroimmunology

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Inflammatory cytokines and glutaminergic excitotoxicity in patients with obsessive-compulsive disorder (OCD)

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Introduction In vitro studies have demonstrated possible neuroprotective effects of the following pro-inflammatory cytokines: IL-6, IL-1 β and TNF- α against glutaminergic excitotoxicity in brain through different pathways.

Objectives In the current study, we aim to correlate level of the above pro-inflammatory cytokines in serum with glutamate levels in head of caudate nucleus measured using Proton Magnetic Resonance Spectroscopy (¹H-MRS) in patients with obsessive-compulsive disorder (OCD), a neuropsychiatric illness with possible multifactorial aetiology including immunological and excitotoxic factors.

Method Thirty psychotropic-naïve patients with OCD and an equal number of gender and age-matched normal controls were recruited in the study. A detailed psychiatric assessment was carried out including sociodemographic and clinical variables. A 3T MR imaging and spectroscopy session was carried out in head of caudate nucleus. Further, absolute quantification of glutamate level was obtained using LC model. Simultaneously, 5 mL of blood sample was collected and assayed for the above pro-inflammatory cytokines (Siemens, ImmuliteTM). The level of glutamate was correlated with the cytokine levels in patients with OCD.

Results The level of Glx was significantly higher in patients with OCD as compared to controls ($P < 0.05$). The Glx level negatively correlated with two of the three pro-inflammatory cytokines: IL-6 and TNF- α ($r = -0.807$; $r = -0.838$; $P < 0.05$) while no significant correlation was demonstrated with IL-1 β .

Conclusions The findings provide preliminary evidence regarding possible neuroprotective effects of pro-inflammatory cytokines against glutaminergic excitotoxicity in patients with OCD. Further studies including patients with other psychiatric illnesses as controls are required for confirmation of the above findings.

Disclosure of interest The authors have not supplied their declaration of competing interest.

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Psychopharmacology and pharmacoeconomics

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Impact of DRD2 polymorphisms on prolactin level in risperidone-treated Thai children and adolescent with autism spectrum disorders

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Introduction A large number of studies have reported that the prolactin concentration was significantly increased in the Taq1A A1 allele carriers because several reports revealed that individuals with the DRD2 Taq1A A1 allele have a reduced density of brain D2 receptors.

Objective The main aim of this study was to identify the impact of pharmacogenetic markers associated with prolactin concentration in risperidone-treated children and adolescents with autism spectrum disorders.

Methods One hundred and forty-seven children and adolescents with autism, aged 3 to 19, received risperidone. The clinical data of patients were recorded from medical records. Prolactin levels were measured by chemiluminescence immunoassay. Three CYP2D6 single nucleotide polymorphisms (SNPs), CYP2D6*4 (1846G>A), *10 (100C>T), and *41 (2988G>A), one gene deletion (*5), and DRD2 Taq1A (rs1800497) polymorphism were genotyped by TaqMan real-time PCR.

Results The three common allelic frequencies were CYP2D6*10 (55.10%), *1 (32.65%) and *5 (6.12%), respectively. Patients were grouped according to their CYP2D6 genotypes. The DRD2 genotype frequencies were Taq1A A2A2 (38.77%), A1A2 (41.50%), and A1A1 (19.73%), respectively. There were statistically significant differences in prolactin level of patients among the three groups ($P = 0.033$). The median prolactin level in patients with DRD2 Taq1A A2A2 (17.80 ng/mL) was significantly higher than A1A2 (17.10 ng/mL) and A1A1 (12.70 ng/mL).

Conclusion DRD2 Taq1A A2A2 polymorphisms may be a critical role in an influence prolactin elevation during risperidone treatment in ASD.

Disclosure of interest The authors have not supplied their declaration of competing interest.

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Detection of CYP2D6 polymorphism using Luminex xTAG technology in autism spectrum disorder: CYP2D6 activity score and its association with risperidone levels

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Introduction The determination of the accurate CYP2D6 genotyping is essential in the clinical setting and individualization of drug therapy.

Objectives In this study, was to apply the Luminex xTAG technology to detect significant CYP2D6 polymorphisms and copy number variation, including assessment the relationship of CYP2D6 polymorphisms and risperidone plasma concentration in autism spectrum disorder children (ASD) treated with risperidone.

Methods All 84 ASD patients included in this study had been receiving risperidone at least for 1 month. The CYP2D6 genotypes were determined by luminex assay. Plasma concentrations of risperidone and 9-hydroxyrisperidone were measured using LC/MS/MS.

Results Among the 84 patients, the most common genotype was CYP2D6*1/*10 (26.19%). The most common allele was CYP2D6*10 (51.79%) and the second most allele was CYP2D6*1 (27.98%). There were 46 (55.42%) classified as EM, 33 (39.76%) as IM, and 4 (4.82%) as UM. The plasma concentration of risperidone and risperidone/9-hydroxyrisperidone ratio in the patients were significant differences among the CYP2D6 predicted phenotype group

($P=0.001$ and $P<0.0001$, respectively). Moreover, the plasma concentration of risperidone and risperidone/9-hydroxyrisperidone ratio in the patients with CYP2D6 activity score 0.5 were significantly higher than those with the CYP2D6 activity score 2.0 ($P=0.004$ and $P=0.002$, respectively).

Discussions The present study suggests that it would be ideal to identify the CYP2D6 genotype of patients before prescribing and administering risperidone. Furthermore, the use of CYP2D6 gene scoring system to determine an individual's metabolic capacity may become an essential tool for a more rational and safer drug administration.

Disclosure of interest The authors have not supplied their declaration of competing interest.

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Angiotensin II type 1 receptor blockade diminishes negative effect of chronic stress on memory via upregulation of brain-derived neurotrophic factor

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Introduction A critical need exists for progress in the characterization of targets for pro-cognitive drug discovery. We previously demonstrated that Telmisartan (TLM), an angiotensin type 1 receptor (AT1) blocker and partial agonist of peroxisome proliferator-activated receptor gamma (PPAR γ), alleviates cognitive decline in chronically stressed rats. Understanding of mechanistic background of this phenomenon is hampered by both dual binding sites of TLM and limited data on the molecular consequences of central AT1 blockade and PPAR γ activation.

Objectives To discriminate molecular effects of AT1 blockade and PPAR γ activation in stress induced memory impairment.

Aims In this study, we investigated mechanism of neuroprotection provided by TLM in chronic psychological stress.

Methods We analyzed BDNF gene expression in the hippocampus (HIP) and medial prefrontal cortex (mPFC) in chronically restrained stressed Wistar rats (2.5 h, 21 days), repeatedly treated

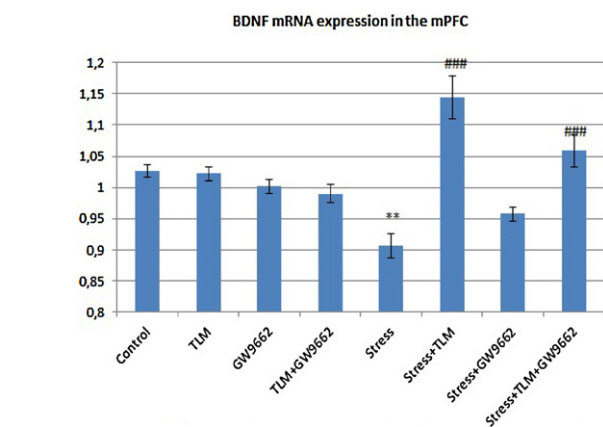


Fig. 1 Effect of chronic stress (2.5 h, 21 days), chronic TLM (1 mg/kg, 21 days), chronic GW9662 (0.5 mg/kg, 21 days) or all in combination on mRNA BDNF expression in the mPFC (BDNF/Tbp ratio). Bars represent mean \pm SEM; $n=5$; ** $P<0.01$; Control vs. Stress; ### $P<0.001$ Stress vs. Stress + TLM and Stress vs. Stress + TLM + GW9662.

with TLM (1 mg/kg), GW9662 (0.5 mg/kg) – a selective PPAR γ receptor antagonist, or both in combination. TATA box binding protein (Tbp) was an internal control for expression studies.

Results Alterations of mRNA expression of BDNF are shown on **Figs. 1 and 2**.

Conclusions AT1 receptor blockade restores cognitive functions in chronically stressed subjects, which is associated with changes in primarily cortical gene expression.

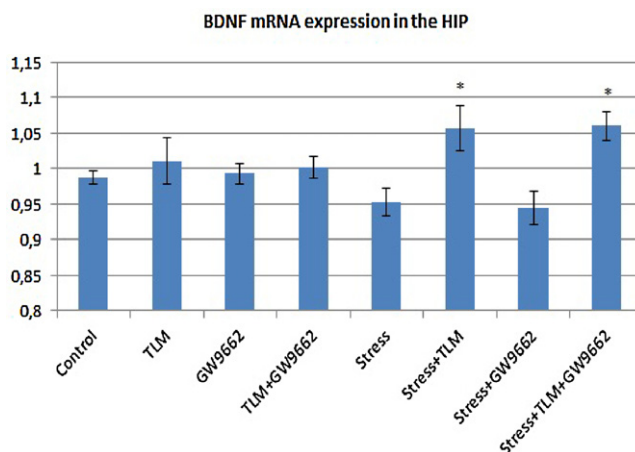


Fig. 2 Effect of chronic stress (2.5 h, 21 days), chronic TLM (1 mg/kg, 21 days), chronic GW9662 (0.5 mg/kg, 21 days) or all in combination on mRNA BDNF expression in the HIP (BDNF/Tbp ratio). Bars represent means \pm SEM; $n=5$; * $P<0.05$; Stress vs. Stress + TLM and Stress vs. Stress + TLM + GW9662.

Disclosure of interest The authors have not supplied their declaration of competing interest.

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Psychosurgery and stimulation methods (ECT, TMS, VNS, DBS)

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Neuropsychiatric consequences of deep brain stimulation surgeries in the patients affected by chronic movement disorders: A brief report

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The main surgical procedure for PD and other chronic movement disorders is deep brain stimulation. DBS has been reported to have specific consequences such as decline in verbal fluency and episodes of depression.

We designed an interventional study in 12 patients affected by Parkinson, dystonia and tic who underwent DBS surgery. Patient assessed before surgery, one month and one year after surgery. The results proved a significant improvement in SF36. The Hamilton's anxiety scale showed an overall but insignificant improvement. The mean of scores of the BDI had a great drop one