**The role of *AMBRA1, NRGN* and *TCF4* in the etiology of recurrent depressive disorder**

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**Introduction**

Recurrent depressive disorder is one of the most commonly diagnosed disease entities among psychiatric disorders. Numerous studies have demonstrated the role of genetic factors in the etiology and pathogenesis of depressive disorders.

**Aim**

The aim of this study was to investigate the role of AMBRA1, NRGN and TCF4 in the etiology and pathogenesis of recurrent depressive disorder. In particularly, aimed to assess the expression of these genes at the mRNA and protein levels in patients with recurrent depressive disorder versus healthy individuals. A further aim was to determine the relationship between the expression of these genes at the mRNA and protein levels and the severity of symptoms, age of onset and various other clinical variables in the group of patients with depressive disorder.

**Material and Methods**

A total of 260 subjects were enrolled in this study: 170 patients with the ICD-10 diagnosis of F32 or F33, and 90 healthy individuals. All the subjects were asked to complete questionnaires designed specifically for the study to collect sociodemographic data from all the subjects and, additionally, clinical data from the patients. At baseline, each patient underwent an assessment of the severity of his/her depressive symptoms using the Hamilton Rating Scale for Depression. The next step involved the collection of a single blood sample of 10 ml from each subject to assess the expression of the three genes at the mRNA and protein levels. This was done by real-time PCR. Whole blood was used as the substrate, from which cRNA was then isolated and, at a further step, converted to cDNA.

**Results**

Decreased AMBRA1, NRGN and TCF4 expression at the mRNA and protein levels was found in patients with depressive disorder versus healthy individuals. Expression did not differ significantly between the patients with the so-called early-onset depression and those with the so-called late-onset depression. Expression of the study genes was not affected by the patients' sex and age. There was no correlation between the expression of AMBRA1, NRGN and TCF4 at the mRNA and protein levels and the number of episodes, number of psychiatric hospitalisations or the severity of symptoms. Of the clinical manifestations of depression, only the duration of the illness correlated with the expression of NRGN and TCF4 at the mRNA level.

**Conclusions**

Expression of AMBRA1, NRGN and TCF4 at the mRNA and protein levels plays a role in the pathogenetic mechanism of recurrent depressive disorder. The impact of AMBRA1, NRGN and TCF4 expression at the mRNA and protein levels on the development of recurrent depressive disorder is independent of sex. The impact of AMBRA1, NRGN and TCF4 expression at the mRNA and protein levels on the development of recurrent depressive disorder is independent of the age.