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# ALLELIC VARIANTS OF PAX5 AND MEF2C-AS2 GENES ARE ASSOCIATED WITH DEPRESSION IN MESIAL TEMPORAL LOBE EPILEPSY (MTLE)

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## Introduction

Depression is one of the most frequent psychiatric comorbidity in epilepsy, worsens quality of life in these patients, and is accompanied by considerable morbidity, mortality, heightened risk of suicide, and significantly increases the healthcare costs associated with the management of the seizure disorder.

## Objective/Methods

We tested whether 14 independent SNPs previously associated with risk of major depression in individuals of European descent were also risk factors for depression associated with temporal lobe epilepsy (TLE).

Therefore, we performed a genetic association study with a 160 TLE patients. All patients had detailed medical variables analyzed and were submitted to Structured Clinical Interview for DSM-IV (SCID) for evaluating depression. All subjects were genotyped by TaqMan® SNP genotyping assays in a Real-Time PCR System.

## Results

The mean age of TLE patients was 44.5 (SD=12.4) years; 107 patients (66.9%) were females. The duration of epilepsy was 25.4 (SD=4.1) years. Depression alone was observed in 102 (63.7%). Univariate analysis showed that female sex and anxiety and mood disorders were risk factors for Depression in TLE patients (data not show). All the characteristics of the sample are represented in the Table 1.

The allele variability in the rs7044150, rs8025231, rs12065553, rs2422321, rs1475120, rs1518395, rs1656369, rs4543289, rs10514299, rs2125716, rs2179744 and rs10786831 polymorphisms were similar between the patients with and without depression, suggesting that these variants studied are not risk factors for development of depression in TLE (data not show), whereas the rs454214 and rs6476606 differ among the patients groups (Table 2).

The frequency of the G allele in the rs6476606 and of the C allele in the rs454214 was higher in patients with TLE with depression (p=0.013 and p=0.030).

After logistic regression, independent risk for Depression in TLE were female sex (O.R.=0.4; 95%CI=0.2-0.9;p=0.03), CC genotype in rs454214 (O.R.=2.4; 95%CI=1.1-5.4.0; p=0.028) and GG genotype in rs6476606 (O.R.=2.5; 95%CI=1.2-5.0.0; p=0.012) (data not show).

**Table 1. Characteristics of the sample.**

| Variable | All patients |
|---|---|
| **Gender** | |
| Female | **107 (66.9%)** |
| Male | 53 (33.1%) |
| **Age, y (SD)** | **44.50 (12.39)** |
| **Epilepsy age onset, y (SD)** | 19.07 (14.68) |
| **Epilepsy duration, y (SD)** | 25.45 (14.12) |
| **Seizure control** | |
| Controlled | **77 (48.1%)** |
| Non-controlled | 83 (51.9%) |
| **Mood Disorders** | |
| Absent | **87 (54.4%)** |
| Present | 73 (45.6%) |
| **Anxiety Disorders** | |
| Absent | **108 (67.5%)** |
| Present | 52 (32.5%) |
| **Anti-epileptic drugs** | |
| Monotherapy | **87 (54.4%)** |
| Polytherapy | 73 (45.6%) |

**Table 2.Frequencies of allelic variations in the PAX5 e MEF2C genes.**

| *Polymorphism (Gene)* | *Genotype (n)* | | | |
|---|---|---|---|---|
| **rs6476606 (PAX5)** | **AA** | **AG** | **GG** | ***p*** |
| **SCID** | | | | |
| Positive | 12 | 49 | 42 | *0.581* |
| Negative | 4 | 31 | 22 | |
| **Only Depression** | | | | |
| Yes | 10 | 35 | 17 | ***0.015**** |
| No | 6 | 45 | 47 | |
| **rs454214 (MEF2C)** | **CC** | **CT** | **TT** | ***p*** |
| **SCID** | | | | |
| Positive | 20 | 45 | 38 | ***0.009**** |
| Negative | 24 | 16 | 17 | |
| **Only Depression** | | | | |
| Yes | 11 | 31 | 20 | ***0.025**** |
| No | 33 | 30 | 35 | |

## Conclusions

The biological effect of allelic variations rs454214 (upstream of *MEF2C gene)* and rs6476606 (in an intron of *PAX5* gene) in these SNPs are unknown. However, variations in these SNP have been associated with risk for Major Depression. Our results suggest that rs6476606 GG genotype and rs454214 CC genotype might be also an independent risk factor for development of depression in TLE. If confirmed, our study might help to elucidate the common variant genetic architecture of depression in epilepsy.

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