

# FUNCTIONAL POLYMORPHISM RS73598374 OF THE ADA IS ASSOCIATED WITH ANXIETY DISORDERS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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## INTRODUCTION

Among epileptic patients, those with temporal lobe epilepsy (TLE) are especially prone to suffer from psychiatric disorders, including anxiety, whose prevalence ranges from 15 to 25%.

Adenosine is a neuromodulator thought to have great influence over the signaling pathways related to anxiety.

The functional c.22G>A polymorphism (rs73598374) of the adenosine deaminase (ADA) reduces enzymatic activity and the conversion to inosine, increasing extracellular adenosine levels.

## OBJECTIVES

To assess the prevalence of the ADA polymorphism rs73598374 and its influence on psychiatric disorders in a sample of patients with TLE.

## METHODS

Study of 169 patients with TLE undergoing clinical follow-up at a tertiary hospital in south Brazil.

DNA was extracted from patient's peripheral blood samples and stored at Hospital de Clínicas de Porto Alegre (HCPA).

TaqMan® real-time PCR was used for genotyping.

Statistical analyses were performed with the IBM® SPSS® Statistics Package v. 20, and the two-tailed Pearson chi-squared test and Fisher's exact test were used for categorical variables.

## RESULTS

The study population was composed primarily of females (65,1%), with a mean age of 44,1(±12,4). Mean age of epilepsy onset and mean epilepsy duration were 18,9 years (±14,5) and 25,2 years (±14,1) respectively.

- ▶ The majority (60,4%) of patients presented at least one psychiatric comorbidity and over a third of those (22,5%) had multiple disorders, identified by the Structured Clinical Interview for DSM-IV(SCID).

- ▶ Mood disorders (21,9%) and anxiety disorders (10,1%) were the main isolated comorbidities observed, followed by psychosis and alcohol and drug abuse

- ▶ When considered individual disorders, the frequency of CT genotype was significantly higher in patients with anxiety, being observed in 18,8% and 6,8% of patients with and without this comorbidity respectively (p= 0.03).

SCID	Frequency (%)
No diagnosis	67 (39,6)
Mood disorders	37 (21,9)
Anxiety disorders	17 (10,1)
Psychotic disorders	6 (3,6)
Alcohol and drug abuse	4 (2,4)
Multiple disorders	38 (22,5)

Figure 1. Frequency of psychiatric disorders identified by the SCID.

ADA Genotype	Anxiety disorder		Total
	No	Yes	
CC	108	43	151
CT	8	10	18
Total	116	53	169

Figure 2. Frequencies of ADA genotypes and anxiety disorder.

## CONCLUSIONS

Previous studies found that extracellular adenosine should have an anxiolytic effect, mostly through selective inhibition of excitatory synapses.

- ▶ However, there is also evidence that excessive levels of adenosine, found in deleterious conditions such as undue alcohol ingestion, sterile inflammation, tissue injury and hypoxia, could act as an anxiogenic through the activation of caspase-1 and production of IL-1  $\beta$ .
- ▶ Moreover, elevated plasma adenosine levels have been linked to a higher prevalence of anxiety among other psychiatric disorders.

Our results suggest that the ADA polymorphism rs73598374 may contribute to the presence of anxiety in patients with TLE.