ANGELMAN SYNDROME: CHARACTERISTICS OF EPILEPSY, ELECTROENCEPHALOGRAPHYC ABNORMALITIES AND CORRELATION TO GENETIC MECHANISMS (ABSTRACT) *. **THESIS. SÃO PAULO, 2001**.

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Angelman syndrome is characterized by severe mental retardation, speech disorder, stereotyped jerky movements, peculiar behavioral profile and typical facial traits. Eighty to 90% of these patients present epilepsy and suggestive electroencephalographic patterns which are used as diagnostic criteria and become important when the phenotype is not suggestive enough, as in infants. The syndrome results from distinct genetic mechanisms [deletion (75-80%), paternal uniparental disomy (1-2%), imprinting center abnormality (2-3%) and UBE3A point mutation, found in ¼ of the negative genetic cases (20-25%)], which affect the maternal chromosome 15. The preservation of a larger genic contingent is probably related to a milder clinical phenotype as observed in patients without deletion making its recognition less evident.

The aim of this study was to analyze the correlation between distinct genetic mechanisms that determine Angelman syndrome and the severity of epilepsy and electroencephalographic abnormalities in a series of 26 consecutive patients with clinical and/or genetic diagnosis.

Patients were classified according to their genetic studies in cases with deletion (n=19), disomy (n=3) and negative genetic studies (n=4). Sixty-eight EEGs were studied for the characterization of the EEG patterns, background activity and the occurrence of electrographic seizures. Epilepsy was studied through clinical history, V-EEG and file revision and occurred in 84.6% (22/26) of these patients. Suggestive EEG patterns were found in 96.1% (25/26). Prevalence of epilepsy was significantly higher in patients with deletion. Parameters indicating severity of epilepsy such as earlier onset age, higher occurrence of daily, disabling or multiple seizures, *status epilepticus* and febrile seizures presented a higher tendency of occurrence in patients with deletion. Patients with disomy did not present epilepsy and negative cases were less severe.

Suggestive electroencephalographic patterns were observed in the three groups. Delta pattern was the most frequent followed by posterior discharges. Theta pattern was observed only in patients with deletion. Prolonged, continuous or quasicontinuous bursts, as well as electrographic seizures and unspecific interictal epileptiform discharges, were predominantly observed in patients with deletion. Normal age-related background activity was more frequent in patients without chromosomic deletion.

We concluded that, although epilepsy has been observed in non-deletion patients, epilepsy was more severe in patients with deletion. This is probably due to a major involvement of genes, which decodify GABA receptors through this mechanism. In spite of the presence of epilepsy or of a less suggestive clinical phenotype and regardless the genetic mechanism involved, EEG could be used as a diagnostic criterion in patients in all groups.

KEY WORDS: Angelman syndrome, EEG, epilepsy, genetic mechanism, deletion, uniparental disomy.

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TEACHING INFANTILE NEUROLOGY IN BRAZIL: CURRENT ASPECTS, CHALLENGES AND PERSPECTIVES (ABSTRACT)*. **THESES. CAMPINAS, 2001**.

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This study intends to identify how many and which are the formation and training centers in Infantile Neurology in our country and its particularities. Besides, it tries to find out whether or not there are differences between the services which are *accredited* by the National Commission of Medical Residence and the services that are not accreditated by this Commission.

Another purpose is to find out why the Institutions that have medical residence in Neurology and in Pediatrics do not have Infantile Neurology residence even though they have the necessary conditions to offer it.

It is also about the improvement course in Infantile Neurology for non doctor professional of the health area that is taught by the Universidade Estadual de

Campinas. The expectations of the components of 2 groups in the beginning and in the end of the course will be evaluated.

In the initial part, are woven considerations about the medical teaching and its characteristics. It is presented brief report about the beginning of the medical attendance and of the foundation of the medical schools in Brazil. In aditttion to this, it is presented small history of the Neurology and of the Infantile Neurology in our country.

It is approached the teaching of Neurology in medical graduation course and it is stood out the importance of the Medical Residence courses to prepare qualified and modernized professionals in their area of performance front the new knowledge in Medicine.

At the end, the results of the researchs are presented and are woven considerations related to each researched segment.

KEY WORDS: formation and training centers in infantile neurology; medical residence in infantile neurology.

ANALYSIS OF HLA DQ, DP, DR ALLELES ASSOCIATED WITH MULTIPLE SCLEROSIS SUSCEPTIBILITY IN A POPULATION OF PATIENTS FROM THE RIO DE JANEIRO CITY (ABSTRACT) * **DISSERTATION. NITERÓI, 2002.**

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Multiple sclerosis (MS) is a chronic inflammatory disease of the human central nervous system of putatively autoimmune origin characterized by multifocal demyelination. Genetic and environmental factors are thought to be involved in the pathogenesis of MS, with the disease considered rare in tropical countries, including Brazil. Genetic studies indicate that the major histocompatibility complex (MHC)/HLA region on chromosome 6p21 contains MS-predisposing component(s). However, which gene(s) present in this region are responsible for MS susceptibility in the brazilian population is still an unsettled issue.

This study aimed to analyze the frequencies of HLA class II alleles (DQA1*0102, DQB1*0602, DPA1* 0301, DRB1*1501, DRB1*1503) expression in a group of MS patients from the Rio de Janeiro city. It was included 42 individuals (73.8% female and 26.2% male) with clinically definite MS with age range of 15 to 55 years. In relation to ethnic background, MS patients were of white/caucasian (CA) descendent (76.2%) and (23.8%) black/african-brazilian (AF) descendent. Age-matched (16 to 58 years) control healthy individuals, consisted of 53.6% (female) and 46.4% (male) with the following ethnic background: 58.3% white/caucasian descendent and 41.7% black/african-brazilian descendent. HLA typing was performed by amplification of the DNA isolated from peripheral leukocytes with Polymerase Chain Reaction (PCR) followed by SSOP hybridization.

MS patients showed a positive association for alleles DQB1*0602 (Pc=0.021; RR=2.40) and DQA1*0102 (Pc= 0.0041; RR=3.30). Likewise, increased frequencies of DQB1*0602 (45.2%) and DQA1*0102 (35.7%) endowed strong correlation of this allele combination with disease susceptibility in CA patients. DR2 haplotype frequencies among healthy individuals and MS group was low. Since both (CA, AF) ethnic groups of MS patients showed very low frequencies of DRB1*1501 and DRB1*1503 it is suggested that another DRB allele association may be conferring susceptibility to MS in this population. Finally the low frequency (RR=0.36) of DPA1*0301 allele consistently observed in our MS patients but not in the control group, indicate that such allele may rather have a protective role against MS.

In conclusion, genetic susceptibility to MS in brazilian individuals may depend upon a specific allele mosaic interacting at several loci necessary to reach a critical threshold for disease development.

KEY WORDS: multiple sclerosis, HLA, autoimmune disease, demyelination