"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

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ELECTROENCEPHALOGRAPHIC ASPECTS IN CHILDREN DIAGNOSED WITH AUTISM SPECTRUM DISORDER

PHD THESIS SUMMARY

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Content table

List of published scientific papers

1. **Capisizu A**, Sandu C, Caragea RM, Capisizu AS. A missense mutation in the MACF1 gene in a patient with autism spectrum disorder and epilepsy. *Journal of Medicine and Life*, 17(11), 1023-1029, 2024. https://doi:10.25122/jml-2024-0312. PMID:39781307; PMCID: PMC11705475.
   Journal indexing: PubMed.
2. **Capisizu, A.**, Zăgrean L, Poenaru E, Tudorache E, Bulf MA., Capisizu AS. Investigation of Electroencephalographic Aspects, Adaptive Features, and Clinical Phenotypes in a Group of Children with Autism—A Pilot Study. *Clinics and Practice*, 15(3), 50, 2025. https://doi.org/10.3390/clinpract15030050.
   Journal indexing: Scopus, ESCI (Web of Science), PubMed, PMC, Embase.
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3. **Capisizu A**, Zăgrean L, Capisizu AS. Electroencephalographic aspects and phenotypic characteristics in children with autism. *Journal of Medicine and Life*, 3(18), 246-256, 2025. doi: 10.25122/jml-2025-0053.
   Journal indexing: PubMed.
4. Anghelescu, A, Onose G, Ciobanu V, Mihalache R, Spanu A, Popescu C, Oprea M, Firan CF, **Capisizu A**. Late-onset Epilepsy in the Elderly: Difficulties of Diagnosis and Personalized Pharmacological Management, with Particularities to Covid-19 Pandemic–Systematic Review of Literature. *FARMACIA*, 70, 184-197, 2022. https://doi.org/10.31925/farmacia.2022.2.2.
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INTRODUCTION

Autism Spectrum Disorder (ASD) is a heterogeneous group of neurodevelopmental disorders, of persistent and variable severity. It is characterized by the fulfillment of the triad: deficits in social interaction, in communication and stereotyped, restrictive behavior, this symptomatology being generally observed under the age of three.

It is a condition that has seen a spectacular increase in prevalence in recent years (approximately 0.6% globally), with a diversity of clinical presentations affecting a variety of phenotypically different individuals. With an etiology still debated, considered multifactorial, of which genetic and environmental factors are the most frequently considered factors, with a pathology associated with social implications, autism has become a genuine target of research. In the absence of a sufficient number of studies addressing autism, the need for awareness and research of this condition is also observed in Romania.

In this context, a first hypothesis for the research of the doctoral thesis is related to the existence of various types of abnormalities in standard wake electroencephalographic (EEG) recordings in children with autism spectrum disorder, and the existence of associations between electroencephalographic abnormalities and personal history, clinical and neurological examination, but also of associations between clinical phenotypes, features of neurological examination and diagnostic entities of ASD.

The second hypothesis of the research is related to the existence of associations between adaptive disorders identified by assessing adaptive behavior, using the Adaptive Behavior Assessment System II (ABAS II) test, and abnormalities identified during the neurological examination.

For a comprehensive evaluation, the paper included two substudies, of which, in the first we studied the clinical-paraclinical correlations in children diagnosed with ASD evaluated electroencephalographically, and in the second substudy we investigated the correlations between the adaptive profile of children with ASD and neurological abnormalities.

I. GENERAL PART

1. Autism spectrum disorder (ASD) in children – current state of knowledge

1.1. Definition and classification of Autism spectrum disorder

Autism spectrum disorder (ASD) is a group of severe and persistent neurodevelopmental disorders defined by the association of deficits in social interaction, in communication, and stereotyped, restrictive behavior, which are apparent before the age of 3. According to the International Classification of Diseases, 10th revision (ICD-10) of Mental and Behavioral Disorders, autism is classified under the "Pervasive Developmental Disorders" chapter, which contains several categories [1].

1.2. Epidemiology of ASD

Recent epidemiological data show that autism is no longer considered a relatively rare condition. A 2022 meta-analysis, which looked at 74 studies published from 2008 to 2021, showed a worldwide prevalence of ASD of 0.6% [2,3].

1.3. Risk factors and diagnosis in ASD

ASD is a multifactorial disorder involving a multitude of genetic factors, with numerous pathological genetic variants, syndromic or non-syndromic, associated with autism in approximately 40%-80% of cases [4]. Genetic mutations in the MACF1 gene have been associated with neurodevelopmental and neurodegenerative disorders, and variants of uncertain significance (VUS) have been associated with autism spectrum disorder [5,6]. A number of conditions frequently associated with ASD have been described: psychiatric disorders (63-96%), motor disorders (51%-38%), sleep disorders (50-80%), intellectual disability (20-50%), epilepsy (12-26%) and gastrointestinal disorders (9-91%) [7].

1.4. Psychological assessment in ASD

The process of diagnosing autism involves observing and interacting with the child in a structured manner, using screening tools - specific tests and forms - in a first stage. Subsequently, children thus identified are referred to a specialist and are evaluated for diagnosis [8,9].

2. The relationship between autism, epilepsy and EEG abnormalities

2.1. Epilepsy: epidemiological data, diagnosis and therapeutic principles

Epilepsy affects approximately 50 million people worldwide, of all ages, and is considered the most common neurological disorder. The conceptual definition of epilepsy, developed by the International League Against Epilepsy (ILAE) in 2005 and further improved in 2013 and 2017 with the operational definitions, comprises three entities: 2 unprovoked (or reflex) epileptic seizures occurring more than 24 hours apart; 1 unprovoked (or reflex) epileptic seizure associated with a probability of recurrence within the next 10 years; or epileptic syndrome [10,11]. Depending on the economic and educational status, there are regional differences in the quality of life of people with epilepsy, especially in terms of access to antiepileptic medication [12].

2.2. Prevalence of epilepsy in children with autism

There is variation in the prevalence of epilepsy in children with ASD, explained by differences in study sample characteristics, sample sizes, or age of participants. Studies have shown that epilepsy is more common among individuals with autism spectrum disorder (5–46%) compared to the general population (0.5–1%) [13,14]. Epilepsy has also been shown to be associated with a higher rate of cognitive impairment [15,16].

2.3. Common pathophysiological mechanisms

The association between ASD and epilepsy, or that between ASD and electroencephalographic abnormalities, suggests common pathological mechanisms or genetic causes [17]. Phenotypic biomarkers of susceptibility to epilepsy or to EEG abnormalities in individuals with ASD have been identified, thus characterizing the “Autism-Epilepsy phenotype” [17]. Other studies have demonstrated the existence of glutamate-mediated neuronal conduction deficits, due to specific genetic mutations [15,18,19]. At preschool and school age, various imbalances between excitatory and inhibitory brain networks have been identified in patients with ASD that increase or decrease the efficiency of communication between cortical regions, representing the basis of the appearance of autism abnormalities and of epileptogenesis [20].

2.4. Electroencephalography, the method of choice for diagnosing epilepsy

Electroencephalography (EEG) is the most widely used investigation method that records brain bioelectric activity [3,21] and the paraclinical method of choice for the diagnosis of epilepsy, also having the role of identifying the type of epilepsy [3,22]. EEG is used in a variety of clinical situations: disease follow-up, monitoring response to treatment, changes in the semiology of epileptic seizures, management of critically ill patients, or in the presurgical evaluation [22], and for the pediatric population in the case of genetic syndromes, metabolic disorders, psychomotor regression and developmental disorders [22]. Due to its non-invasive and safe characteristics, EEG is used in various fields of research, such as neuroscience, regarding the capture, amplification, recording of epileptic abnormalities, inter-ictal epileptic discharges and subsequent analysis of cerebral electrical signals generated by groups of neurons [22,23]. There are several types of EEG recordings, which differ in duration, wakefulness / sleep state, or sleep deprivation, and the presence or absence of concurrent video recording. The methodology of EEG recording differs in duration, patient age, type of recording, and requires a prior accurate history [22].

2.5. Electroencephalographic abnormalities in autism

The association of electroencephalographic abnormalities in patients with autism has been demonstrated in the scientific literature, and their prevalence varies considerably, being reported between 8%–80% [3,15,24]. It is known that 25% of children with ASD who present epileptiform abnormalities end up developing epilepsy [25]. EEG abnormalities can have a negative impact on brain development, being associated with cognitive deficit and behavioral disorder [15], irritability and aggression in children with ASD, associated with persistent epileptic activity on the EEG [26]. Regarding the prevalence of epileptic-type EEG abnormalities alone in patients with autism, it varies between 28% [27] and 30% [15,28]. Sometimes, the electroencephalography can help us to differentiate an epileptic syndrome from a possible feature of autism spectrum disorder. These data suggest that routinely performed EEG can bring significant benefits to children diagnosed with ASD.

II. PERSONAL CONTRIBUTIONS

3. Electroencephalographic aspects in children diagnosed with autism spectrum disorder

3.1. Research hypotheses

Hypothesis 1: There are different types of abnormalities in standard wake electroencephalographic recordings in children with autism spectrum disorder, and there are associations between electroencephalographic abnormalities and personal history, clinical and neurological examination.

Hypothesis 2 : There are associations between clinical phenotypes, neurological examination features, and diagnostic entities of autism spectrum disorder, according to the international classification ICD-10.

Hypothesis 3 : Adaptive impairments identified by evaluating adaptive behavior through ABAS II testing are associated with abnormalities in the neurological examination and with autism spectrum disorder entities.

3.2. General purpose and objectives

The purpose of this work is to establish correlations between aspects of the wake EEG in children with ASD, aspects of the adaptive profile identified by testing with the ABAS II assessment scale, and elements from the personal history and clinical examination. To carry out the research, we set the following **general objectives**:

1. Determining aspects of the wake electroencephalography and the incidence of electroencephalographic abnormalities in children with autism spectrum disorder.

2. Determining the phenotypic profile of children with autism spectrum disorder, based on history, clinical examination, and type of autism, ass follows :

a. Characterization of the study group according to: demographic data (age and gender), pre- and peri-natal history, family history of psychiatric disorders, dysmorphic features, and neuroleptic treatment.
b. Neurological examination of the study group, as follows: cranial nerves, gait, muscle tone, fine motor skills, coordination, osteo-tendinous reflectivity.

c. Identifying the diagnosis of autism according to the ICD-10 classification.

3. Determining the correlation between identified electroencephalographic abnormalities and the phenotypic profile in children with autism spectrum disorder.

4. Determining the adaptive profile of children with autism spectrum disorder, according to the ABAS II scale.

5. Determining the relationships between the phenotypic profile and the adaptive profile according to ABAS II, in children with autism spectrum disorder.

6. Determining correlations between identified electroencephalographic abnormalities and the adaptive profile in children with autism spectrum disorder.

3.3. General research methodology

We conducted a retrospective study that included 101 patients who presented to the Pediatric Psychiatry Clinic of Titan Psychiatric Hospital "Dr. Constantin Gorgos", Bucharest, Romania, between 02.2021–04.2023. The study was approved by the Ethics Committee of Titan Psychiatric Hospital "Dr. Constantin Gorgos", Bucharest, Romania, no. 4747/02.12.2020.

For an efficient organization of the study, we divided the research into two sub-studies, as follows:

SUBSTUDY A - Electroencephalographic evaluation of children with autism spectrum disorder and clinical-paraclinical correlations, and

SUBSTUDY B - Evaluation of the adaptive profile of children with autism spectrum disorder and clinical-paraclinical correlations.

3.3.1. *Statistical analysis*

The collected data were entered into a database designed and implemented using IBM SPSS Statistics version 23. The tests were statistically significant when the *p*-value reported by the significance tests was less than 0.05. For quantitative data for which a test based on the normal distribution could be applied, a parametric test was used and the mean ± standard deviation was calculated, for quantitative data for which a test based on the normal distribution could not be applied, a non-parametric test was used, the median and the interquartile range IQR were calculated and reported, and for qualitative data, the frequency and percentage were calculated,

for testing the associations between variables, linear correlation analysis and multiple linear regression were applied, using the Chi-square (X^2) test.

4. SUBSTUDY A - Electroencephalographic evaluation of children with autism spectrum disorder and clinical-paraclinical correlations

4.1. Research hypotheses and specific research objectives

4.1.1. *Research hypotheses*

Within substudy A, we addressed **Hypothesis 1** and **Hypothesis 2** of the General Research Hypotheses.

4.1.2. *Specific objectives*

1. The determination of the phenotypic profile of children with autism spectrum disorder (ASD) was carried out by:
    - Characterization of the patient group according to demographic data
    - Characterization of the patient group according to personal history
    - Characterization of the patient group according to dysmorphic features
    - Determining the presence of neurological deficit
    - Determining the presence of neuroleptic treatment
    - Determining the diagnosis of autism according to the ICD-10 classification, by the pediatric psychiatrist
2. Determination of wake EEG abnormalities by the pediatric neurologist in children diagnosed with autism spectrum disorder.
3. Determining the correlation between identified electroencephalographic abnormalities and the phenotypic profile in children with autism spectrum disorder.

4.2. Research materials and methods

4.2.1. *Study design and study group selection*

The inclusion criteria in the study were: children aged 2 - 18 years, patients with a diagnosis of autism formulated by the attending pediatric psychiatrist, patients with a clinical neurological evaluation and wake EEG recording by the pediatric neurologist.

Exclusion criteria from the study were: patients who did not present a diagnosis or criteria for autism, patients diagnosed with autism according to the ICD-10 classification, who met diagnostic criteria for epilepsy, patients with insufficient data for the study in their medical records, patients who could not cooperate for the neurological examination, patients who could not cooperate for the EEG, and patients without signed informed consent.

4.2.2. *Methodology*

The variables that were collected and analyzed were the following:

I. **Demographic and clinical data**: age and gender of patients, presence of personal history, presence of dysmorphic features, presence of abnormalities in neurological examination, diagnosis of autism, administration of neuroleptic treatment;

II. **Paraclinical data**: presence of abnormalities in the wake EEG recording.

Defining variables:

- ***age*** groups: “toddlers” for children under 2 years of age; “early childhood” for ages 2-5 years; “middle childhood” for ages 6-11 years; “adolescence” for ages 12-18 years [29].
- ***personal history:*** pre- and perinatal history and family history [15].
- ***neurological disorders*** in the neurological examination: cranial nerve disorders, motility disorders such as involuntary movements, abnormal postures, fine motor skills disorders, muscle tone disorders such as muscle hypo- or hypertonia, spasticity, or any other movement disorders that can constitute a clinical picture of mono-, hemi-, di- or tetra-paresis, coordination deficit, osteo-tendinous hyperreflectivity, pathological cutaneous reflexes [15].

- ***EEG abnormalities:*** non-epileptic abnormalities such as paroxysmal activity or bursts of slow waves, paroxysmal activity or bursts of fast waves, generalized paroxysmal activity or asymmetric trace, and epileptic abnormalities such as epileptic discharges as spikes, spike-wave complexes or poly-spike-wave complexes, focal or generalized [15].

4.2.2.1. *Stages and techniques*

All patients included in the study underwent neurological examination [15]. All patients included in the study underwent standard wake EEG. EEG traces were interpreted by a pediatric neurologist with expertise in EEG interpretation [15,30]. Demographic, clinical, and laboratory data of the patients in the research group were collected. After collecting the data in a research database, the results obtained were analyzed and statistically interpreted.

Techniques: ***Wake EEG***

The electroencephalograms performed were wake recordings with 19 cephalic electrodes placed on a bridge-type headset, using a bipolar montage, in the international 10-20 system, with a reference system and ECG line. The recordings had the following steps: eyes open, eyes closed, tracks with the Hyperventilation and Intermittent photic stimulation procedures, lasting for 15 minutes.

4.3. Results

4.3.1. Characterization of the study group - *Distribution of patients according to the demographic data* :

- Gender distribution: 76.2% (77) male, 23.8% (24) female.
- Distribution by age group: middle childhood with 39.6% (40), followed by the adolescence group with 33.7% (34) and the early childhood group with 26.7% (27).
- 28.7% (29) had a pre- or perinatal history, 69.3% (70) had no pre- or perinatal history, and 1.9% (2) had an unknown history. 37.6% (38) presented dysmorphic features. 30.7% (31) were receiving neuroleptic treatment.
- Regarding the disorders identified during the neurological examination: 6.9% (7) presented abnormalities in the examination of the cranial nerves, 25.7% (26) presented gait disturbance, 12.8% (13) presented muscle tone deficit, 6.9% (7) presented fine motor

skills abnormalities, 2.9% (3) presented coordination deficit and 3.9% (4) presented osteo-tendinous reflectivity abnormalities.

- 11.9% (12) were diagnosed with Childhood Autism, 72.2% (73) were diagnosed with Atypical Autism, 15.9% (16) were diagnosed with Other Pervasive Developmental Disorders.

4.3.2. Associations between elements of the phenotypic profile and age groups

- For the *"adolescent" age group*, statistically significant associations were identified for the presence of dysmorphic features (X^2=10.23, p=0.006), for gait disturbance (X^2=6.65, p=0.03), for osteotendinous reflectivity deficit (X^2=8.20, p=0.01) and for neuroleptic treatment (X^2=9.15, p=0.01).
- A statistically significant association was also identified between age groups and the diagnosis of Atypical autism (X^2=23.23, p=0.001).

4.3.3. Correlations between autism diagnoses and phenotypic profile

- A statistically significant difference in *age* (expressed in months) was identified between the Childhood Autism, Atypical Autism, and Other Pervasive Developmental Disorders groups.
- A statistically significant difference (p=0.002690) was identified for negative *pre- and peri-natal history* between the Childhood Autism (41.7%) and Other Pervasive Developmental Disorders (93.8%) groups.
- Statistically significant differences were identified for *dysmorphic features*, *fine motor skills* deficit, *gait disturbance*, *muscle tone* deficit and *neuroleptic treatment* between the Childhood Autism, Atypical Autism and Other Pervasive Developmental Disorders groups.

4.3.4. Results of electroencephalographic recordings

- Distribution of patients according to the presence or absence of wake EEG *abnormalities* : 89.1% (90) patients had a normal EEG, while 10.9% (11) patients showed abnormalities. Of the patients who showed abnormalities in the EEG recording, 9 (8.91%) patients showed **non-epileptic** abnormalities, of which 5 (4.95%) patients showed bilateral slow wave bursts, one (0.99%) showed unilateral slow wave bursts, two

(1.98%) showed generalized bursts, and one (0.99%) showed fast wave bursts. Two (1.98%) patients showed **epileptic** abnormalities, such as spikes and spike-wave complexes. Of the identified **epileptic** and **non-epileptic** abnormalities: 18.1% (2) were located in the *frontal* leads, 72.7% (8) in the *central* leads, 18.1% (2) in the *temporal* leads, 36.3% (4) in the *parietal* leads, and 27.2% (3) were *generalized* [15].

4.3.5. Correlations between EEG abnormalities and phenotypic profile

- The percentage of patients with dysmorphic features was different ($p = 0.096144$) between the group with normal EEG (34.4%) and the one with abnormalities (63.6%).
- The percentage of patients with neuroleptic treatment was different ($p = 0.087894$) between the group with normal EEG (27.8%) and the one with abnormalities (54.5%).

4.4. Discussions and partial conclusions

Studies in the scientific literature have demonstrated the association of electroencephalographic abnormalities in patients with autism. The prevalence of EEG abnormalities in autism varies, being reported to be approximately 42% in studies using wake recordings and approximately 78% in studies using sleep recordings [15,27,31]. In the present study, EEG abnormalities were identified in 10.89% of all patients, 8.9% of the patients in the study presenting non-epileptic EEG abnormalities and 1.9% of the patients in the study presenting epileptic abnormalities. Santarone et al. reported an even higher prevalence of EEG abnormalities (78%) in a group of preschool children with autism, but they used sleep EEG in their study [27]. The current study considered abnormalities such as paroxysmal activity or bursts of slow waves, paroxysmal activity or bursts of fast waves, generalized paroxysmal activity, or asymmetric tracing as non-epileptic EEG abnormalities. Similarly, Santarone et al. reported non-epileptic abnormalities consisting of paroxysmal slow wave activity in 58% of subjects, paroxysmal fast wave activity in 23% of subjects, and asymmetric tracing in 21% of subjects [15,27].

Neurological deficits, and mainly motor deficits, in autism are as common and have as important a functional impact as other problems considered to be specific to autism [32]. De Jong et al. reported deficits in the cranial nerve area in 39% of patients, abnormalities of muscle tone in 87%, abnormalities of fine motor skills in 75%, coordination disorder in 58%, and abnormal osteotendinous reflexes in 23% [15,33]. In the present study, deficits were identified

on neurological examination - 6.9% (7) with abnormalities in cranial nerve examination, 25.7% (26) with gait disturbance, 12.8% (13) with muscle tone deficit, 6.9% (7) with fine motor skills deficit, 2.9% (3) with coordination deficit, and 3.9% (4) with osteotendinous reflex abnormalities [15].

Regarding the relationships of autism in relation to EEG and neurological examination brought into perspective by this study, it was highlighted how the diagnosis of Childhood autism was differentiated from other diagnoses in terms of dysmorphic features, fine motor skills deficit, gait disturbance and muscle tone deficit. In addition, the identified EEG abnormalities were similar to those of other studies that used wake EEG [15]. The scientific literature on children with autism in Romania is limited, especially in relation to data on neurological examination and epilepsy in children with autism. Budișteanu et al., investigating the clinical picture of the child with autism, identified early signs and symptoms of autism [3,15,34].

In conclusion, considering the phenotypic diversity in ASD, the approach to a patient with autism spectrum disorder should focus on identifying a clinical phenotypic profile as complete as possible, associated with an EEG screening [5], a non-invasive assessment tool alongside the neurological examination. Therefore, children with autism should be carefully examined neurologically, and those with special clinical phenotypes should be identified, in order to improve diagnosis and case management. Thus, non-invasive assessment tools provide valuable support for understanding the clinical characteristics and deficiencies of the patient with autism [15].

5. Substudy B - Evaluation of the adaptive profile of children with autism spectrum disorder and clinical-paraclinical correlations

5.1. Research hypotheses and specific research objectives

5.1.1. *Research hypotheses*

Within substudy B, we addressed **Hypothesis 1** and **Hypothesis 3** of the General Research Hypotheses.

5.1.2. *Specific objectives*

1. Determining the phenotypic profile of children with autism spectrum disorder.
2. Determining the adaptive profile of children with autism spectrum disorder, evaluating the levels of adaptive skills and behaviors by applying the ABAS II scale.
3. Determining correlations between adaptive profile and phenotypic profile.

5.2. Research materials and methods

5.2.1. *Study design and study group selection*

The study group was selected based on the same inclusion and exclusion criteria used in Substudy A.

5.2.2. *Methodology*

The variables that were collected and analyzed were the following:

I. **Demographic and clinical data:** similar to substudy A.

II. **Paraclinical data:** presence of abnormalities in the wake EEG recording, presence of adaptive impairment by ABAS II testing.

Defining variables :

- The ABAS II test yields individual scores for individual ability areas or adaptive skill areas, for three behavioral domains (conceptual, social, and practical), and the general adaptive composite score, GAC (General Adaptive Composite) [9].

Regarding data collection, neurological examination, EEG, analysis and statistical interpretation of results, the stages and working techniques were similar to Substudy A. In addition, patients in the research group were assessed using the ABAS II scale by a licensed psychologist.

Working technique: ***Adaptive Behavior Assessment System II (ABAS II) scale***

The ABAS II testing consisted of an answering questionnaire composed of a series of items. Individual scores were obtained for the *individual ability areas* or adaptive skill areas and for the *GAC score*. The scaled composite scores, for each of the skill areas, can be characterized as being on performance levels corresponding to 7 levels from “Very high” to “Very low”. For ease of statistical analysis, since the scores of the majority of patients were located at the “Lower” and

“Very low” levels, we regrouped the levels for the adaptive and GAC domains, as follows: the “Lower” and “Very low” scores fell into the “*Minimum Score*” category, and the rest of the composite scores fell into the “*Above Minimum Score*” category [9,15].

5.3. Results

5.3.1. Characterization of the study group according to ABAS II testing

Distribution of patients according to ABAS II test scores: Regarding the *GAC* score, in the group of patients: the most numerous 91.09% (92) were those with the "Very low" level, followed equally by 2.97% (3) by the "Average" level, the "Below average" level, and the "Lower" level [15].

5.3.2. Correlations between adaptive and phenotypic profiles

1. *Correlations between adaptive profile and family history*: a statistically significant association was identified between the "*Minimum Score*" level of the GAC and family history (X^2=4.04, p=0.04) [15].
2. *Correlations between the adaptive profile and elements of the neurological examination*: A series of statistically significant associations were identified: between **coordination disorder** and the "Very low" level of the GAC (X^2=9.98, p=0.01), the "*Minimum Score*" level of the GAC (X^2=4.15, p=0.04), the "*Minimum Score*" level of the conceptual domain (X^2=5.29, p=0.02), and the "*Minimum Score*" level of the social domain (X^2=7.01, p=0.008) [15].
3. *Correlations between adaptive profile and autism diagnosis*: Statistically significant differences were identified for GAC, conceptual, social, and practical scores, between the Childhood Autism, Atypical Autism, and Other Pervasive Developmental Disorders groups [15].

5.3.3. Correlations between adaptive profile and electroencephalographic abnormalities

No statistically significant differences were identified between the domains of the adaptive profile, regarding the group with normal EEG and the group with EEG abnormalities.

5.4. Discussions and partial conclusions

Autism is a neurodevelopmental disorder with significant phenotypic heterogeneity, which associates different degrees of adaptive impairment, thus resulting in the need for investigation using specific assessment tools. Studies have shown that epilepsy in autism was frequently associated with poorer adaptive levels [35,36]. In the context in which the scientific literature has demonstrated a higher incidence of epilepsy and EEG abnormalities in autism [24,27,28,30], and both autism and epilepsy have been frequently associated with a lower degree of adaptability [35], we can assume that EEG abnormalities may independently indicate poorer adaptive functioning. It has been shown that there is a correlation between lower levels of assessed adaptive skills and a higher degree of impairment in autism [37].

The results of this personal research have demonstrated a series of correlations between the adaptive and phenotypic profiles. Thus, a series of statistically significant associations were identified: between the "*Minimum Score*" level of the GAC and the family history, and between a deficit identified by the neurological examination, the ***coordination deficit,*** and low levels of the GAC and the adaptive conceptual and social domains. In addition, statistically significant differences were identified between the autism groups, depending on elements of the adaptive profile. Lopata and collaborators [38], who investigated the adaptive functioning in school-age children with high-functioning autism, reported significant deficits in the GAC and the adaptive domains. In previous studies that investigated the relationship between autism, EEG abnormalities and adaptive behavior, Romero-González et al. identified lower results, similar to the present study, when assessing adaptive functioning in children with ASD who also associated epileptic abnormalities [31].

6. Conclusions and personal contributions

Conclusions :

1. Regarding the neurological examination - the highest percentage (25.7%) was represented by patients who presented gait disturbance, and 12.8% presented muscle tone deficit. The majority of patients (72.2%) were diagnosed with Atypical autism.
2. Statistically significant associations were identified between age and phenotypic profile, between the "adolescent" age group and the presence of dysmorphic features, gait

disturbance, osteo-tendinous reflectivity deficit and administration of neuroleptic treatment.

3. Correlations between autism subtypes and phenotypic profile have been identified, as follows:
    - Statistically significant differences were identified for age, negative pre- and peri-natal history, dysmorphic features, fine motor skills deficit, gait disturbance, muscle tone deficit and neuroleptic treatment, between the Childhood Autism, Atypical Autism and Other Pervasive Developmental Disorders groups.
    - The diagnosis of Other pervasive developmental disorders was associated with negative pre- and peri-natal history.
    - Childhood autism was more frequently associated with the presence of dysmorphic features, fine motor skills deficit, gait disturbance, muscle tone deficit, and the administration of neuroleptic treatment.
4. Regarding the results of EEG recordings, in the research group, the majority (89.1%) presented normal EEG, and 10.9% presented EEG abnormalities. Of the patients who presented abnormalities in the wake EEG recordings, the majority (81.8%) presented non-epileptic abnormalities.
5. Correlations between EEG abnormalities and the phenotypic profile were determined, as follows: differences close to statistical significance limits were identified between the normal EEG and EEG with abnormalities groups, in terms of the percentage of patients with dysmorphic features and in terms of the percentage of patients with neuroleptic treatment.
6. A series of correlations between the adaptive and phenotypic profile were determined:
    - A statistically significant association was identified between the "*Minimum Score*" level of the GAC and family history.
    - Statistically significant associations were identified between **coordination deficit** and some elements of the **adaptive profile**: the "Very Low" level of the GAC, the "*Minimum Score*" level of the GAC, the "*Minimum Score*" level of the conceptual domain, and the "*Minimum Score*" level of the social domain.

- Statistically significant differences were identified for the GAC score and for the adaptive domains, between the Childhood Autism, Atypical Autism and Other Pervasive Developmental Disorders groups.
- The diagnosis of Other Pervasive Developmental Disorders was associated with ***higher scores*** for the GAC and for the adaptive domains.

7. The relationship between the adaptive profile and EEG abnormalities was also investigated, but no statistically significant differences were identified.

Personal contributions

-Evaluation of a group of children with autism by identifying correlations between electroencephalographic aspects, their phenotypic profile and their adaptive profile.

-Adding data to the scientific literature regarding the electroencephalographic study of autism in children - *chapter 4 pages 36-73*.

-Including in the research the **subtypes of autism** - *chapter 4 pages 30-44* and the **dysmorphic features**, *chapter 4 pages 30-44*, thus improving the phenotypic profile of the patient to be researched.

-**Association of testing the adaptability** of children with autism, using the ABAS II scale. The testing of the adaptive skills of children with autism, and identifying correlations between the results obtained and the electroencephalographic aspects or the phenotypic profile, represents another personal contribution of the research - *chapter 5 pages 81-99.*

• Childhood autism was more frequently associated with the presence of dysmorphic features, fine motor skills deficit, gait disturbance, muscle tone deficit and the administration of neuroleptic treatment – *chapter 4 pages 45-53*.

• Associations were identified between the adaptive profile and an element of the neurological examination, **coordination deficit** – *chapter 5 page 94*.

• The *Other Pervasive Developmental Disorders* autism subtype was associated with higher scores for GAC and for the adaptive domains – *chapter 5 pages 95-99.*

Research Limitations, Future Research Directions

One of the limitations of the research was that the study was single-centered. Other limitations of the study were related to the exclusion criteria, the number of patients included

being limited by insufficient clinical data or by the difficulties in collaborating for the investigations. In addition, the study used only wake electroencephalographic recordings, this study lacking long-term EEG recordings, of wakefulness or sleep.

In the context in which the prevalence of autism is increasing, it is necessary to continue research on autism in a prospective manner, by including as many patients as possible, in a multicentric, national manner. Also, the EEG investigation of children with autism could be improved by associating long-term, including sleep, recordings.

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