

The Combination of Mind and Brain Alteration in A Resource-Limited Country: Autism Spectrum Disorders and Epilepsy in A Child Psychiatry Unit in Dakar

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ABSTRACT

Purpose of the study: Autism spectrum disorders (ASD) and epilepsy can coexist in the same person, constituting poor bilateral prognosis factors. This study describes the sociodemographic elements of patients with ASD and studies the clinico-paraclinical aspects of their epilepsy and its evolution in 2003.

Patients and Methods: Cross-sectional and descriptive study in Child psychiatry at CHNU Fann, with analysis of the files of all patients followed between January 2004 and September 2018 for ASD with/without epilepsy. We used a standardized survey with several items.

Results: Forty -five patients with ASD collected, with an epileptic frequency of 37.8%. The main history was fetal suffering (24.4%) and parental inbreeding (22.2%). Most of the symptoms of ASD were seen before 3 years old (66.6%) and epilepsy started before 5 years (94%). Seizures were generalized (58.8%), mainly tonic-clonic (80%) or focal (35.3%), with a frequency of 2 seizures / day at 1 seizure / week. The EEG showed abnormalities in frontal areas in 60%, and Centro-parietal in 26.6%. Brain imaging and evoked auditory potential were normal respectively in 93.9%, and 87.2%. Management was multimodal for ASD (neuropsychological, psychomotor, speech therapy) and medicated for epilepsy, mainly by monotherapy (82.4%) with Valproate (58.8%), Phenobarbital (17.6). Forty percent of patients were out of school and 55.6% in primary school. Twenty-five patients were self-reliant to moderately independent, mainly the epileptics (60%). The 2023 evaluation of this cohort concerns 60% of patients with epilepsy in complete remission and behavioral and language stability under continuous management.

Conclusion: We find a statistic difference by age between epilepsy and ASD with a genetic predisposition related to parental inbreeding and a family history of ASD and epilepsy and to a lesser extent the existence of acute fetal suffering. The contribution of EEG was significant with a predilection of frontal abnormalities whose epileptic treatment appears to improve the impact in children's behavioral disorders.

Keywords

Autism, Child psychiatry, Epilepsy, Assessment at 2023, Senegal.

Introduction

Autism spectrum disorders (ASD) are a group of developmental disorders characterized by impairments in social interactions, language and communication, as well as stereotypic behaviors. Childhood autism accounts for approximately 33.3% of all ASD

cases and is usually the most severe form of ASD [1]. Epilepsies are also a heterogeneous group of neurological disorders with multiple aetiologies, with cognitive and behavioral difficulties [2]. Epilepsy is found in a greater proportion in autism spectrum disorders (ASD) [3,4]. Thus, in a review concerning studies between 1963 and 2006, Amiet et al. [5] evaluated the relative risk of occurrence of epilepsy in autism based on the intelligence quotient (2112 patients including 627 with an IQ \geq 70 and 1485 with IQ < 70) and

gender (1530 patients including 1191 boys and 339 girls). Children already diagnosed with ASD are at high risk for later development of epilepsy, particularly in the presence of intellectual disability [5-7]. The prevalence of epilepsy in people with ASD has been estimated at 8% in the absence of intellectual disability and 21.5% in people with intellectual disability [5]. Approximately 30% of people with ASD develop epilepsy as adults, and approximately 30% of people with epilepsy meet the diagnostic criteria for ASD [4-7]. More than 10 years later, the autism – epilepsy relationship is confirmed; Thus, in its 2017 meta-analysis, Strasser et al. [8] reported 57 studies, 36 of which concerned populations with ASD and 21 studies on populations of people living with epilepsy (PVE); An overall prevalence of autism of 6.3% was found among PVE compared to a prevalence varying from 0.75% to 1.1% in the general population. In this meta-analysis, the prevalence of autism varied depending on the type of epilepsy with respectively 4.7%, 19.9%, 41.9%, and 47.4% in generalized epilepsy, infantile spasms, focal seizures and Dravet syndrome [8].

In black Africa, data on this relationship are insufficient or even non-existent. The objective of our study, in the child psychiatry department of the national teaching hospital of Fann in Dakar (Senegal), were to determine the frequency of epilepsy in patients followed for autism spectrum disorders, to describe the electroclinical characteristics and to appreciate their evolution by the level of education and autonomy of the patients.

Patients and Methods

This was a cross-sectional and descriptive study of patients followed between January 2004 and September 2018 in the child psychiatry department of the Fann National teaching hospital in Dakar (Senegal). All patients included had a confirmed diagnosis of autism spectrum disorders under 18 years old of age, regardless of sex or race, and followed on day hospital. Patients diagnosed with ASD with unusable or incomplete files because they were subsequently lost to follow-up, 5 in number, were excluded from the study. The child psychiatry department welcomes patients of all disabilities, including ¼ autistic patients in day hospital with a capacity to cope of 30 intermittent places. Patients are admitted around the age of 3 and followed until the pediatric age limit before leaving the care system. Patients benefit from specialized educational education in small classes with educators assisted by support staff. At the same time, psychomotor activities, play therapy and repeated interviews with school and clinical psychologists are carried out for everyone; Depending on the indications, some patients also benefit from enhanced speech therapy. Socialization and the progressive and personalized development of autonomy, such as the acquisition of cleanliness and self-feeding, are instilled by specialized help and volunteers. Data collection was carried out using a standardized form including several items: sociodemographic factors, personal and family history, presence or absence of epilepsy and his characteristics, paraclinical explorations, electroclinical syndromes classification, chronology of epilepsy on ASD, management of epilepsy and ASD, and the evolution. The socio-economic levels of the parents were estimated on the average of monthly income according to

the parents'work. Electroencephalography (EEG) was carried out or repeated in all epileptic patients identified, from the start of their seizures, in the Department of Clinical Neurophysiology. Awake and sleep record during at least 60 minutes was carried out in all patients by following a 10/20 montage with 20 electrodes including a reference (Figure 1). Five years later, in 2023, 60% of the initial cohort was seen again for clinical evaluation.

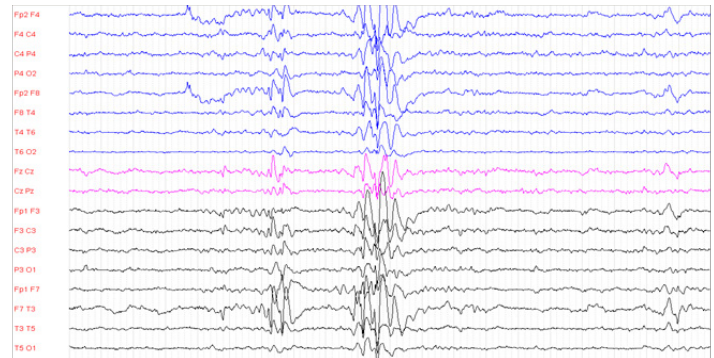


Figure 1: Illustration awake EEG of patient N Mbaye 14 years old.

Burst of diffuse spike-waves that are larger and/or sometimes isolated in the frontal regions.

Results

Forty-five patients were collected between January 2004 and September 2018 and all of our patients lived with their own families. Table 1 summarizes the sociodemographic profile of our patients and their parents.

Table 1: Socio-demographic parameters of patients.

Socio-demographic parameters				
Gender	Male		Female	
Headcount (%)	30 (66,7)		15 (33,3)	
Age	3-5 years	6-10 years	11-15 years	16-18 years
Headcount (%)	6 (13,3)	29 (64,4)	8 (17,8)	2 (4,4)
Geographical origin	Urban	Semi-urban	Rural	
Headcount (%)	17 (37,7)	20 (44,4)	8 (17,8)	
Educational attainment	Out-of-school	Primary	Secondary	University
* Parents Headcount (%)	4 (8,9)	11 (24,4)	8 (17,8)	22 (48,9)
* Enfants Headcount (%)	18 (40)	25 (55,6)	2 (4,4)	0
Socio-economic level	Low	Medium	High	
Headcount (%)	5 (11,1)	31 (68,9)	9 (20)	

Table summarizing the different socio-demographic characteristics of our patient cohort. (%): percentage.

In the antecedents, pregnancies occurred normally in 34 patients (75.5%). Acute fetal suffering (AFS) concerned 11 patients (24.4%), requiring resuscitation then hospitalization in the neonatology department for 2 patients. Table 2 summarizes the rest of the patient's background, as well as the paraclinical data. Clinically, in 30 patients (66.7%), ASD symptoms were noted before the age of 3 years, compared to 33.3% after the age of 3 years. Twenty-six patients (57.8%) had consulted less than 6 months after the onset of symptoms, four patients (8.9%)

Table 2: Comparison of clinical and paraclinical patient data: epileptics versus non-epileptics.

Modalities		Epileptics (n = 17)	Non epileptics (n = 28)	p
Age	< 5 years	16	0	0.000
	5 – 10 years	1	23	
	> 10 years	-	5	
Personal History	Prematurity	1	1	0.353
	AFS (acute fetal distress)	11	-	
	Premature rupture of membranes	1	-	
	Meningitis	1	-	
	Traumatic brain injury	2	-	
Family history	Parental inbreeding	4	12	0.004
	Epilepsy	3	2	
	Schizophrenia	-	3	
	ASD (Autism Spectrum Disorder)	-	4	
Syndromic Classification		CTSE 2 CSWS 1 Unidentified 14	Moderate ASD 7 Severe ASD 15 Uncategorized 6	
AEP (n = 39)	Normal (n= 34)	11	23	0.238
	Pathological (n= 5)	-	5	
EEG (n= 45)	Normal (n= 28)	2	26	0.000
	Pathological (n= 17)	15	2	
Cerebral Imagery (n= 33)	TDM (n= 21)	Normal	16	0.726
		Pathological	1	
	IRM (n= 12)	Normal	12	
		Pathological	-	

p: statistical probability value; CSWS: Continuous Spike-Waves on Sleep; CTSE: Centrottemporal Spike Epilepsy; ASD: Autism Spectrum Disorder; AEP: Auditory evoked potential; EEG: Electroencephalography; TDM: Brain CT scan; MRI: Magnetic resonance imaging.

Table 3: Electroclinical characteristics of persons with epilepsy (PWE).

Characteristics	Modalities		Percentage (%)
Type of seizures	Generalized seizure (n= 10)	Tonic	80
		Atonic	10
		Typical Absence	10
	Focal seizure (n= 6)	Tonic	50
		Clonic	50
Undetermined seizure (n= 1)		5,9	
Seizure Schedule	Daytime (n= 11)		64,7
	Nocturnal (n= 2)		11,8
	Mixed (n=4)		23,5
EEG Abnormalities	Frontal focus (n= 9)		60
	Centro-parietal areas (n= 4)		26,6
	Temporal focus (n= 1)		6,7
	Centro-temporal areas (n= 1)		6,7
Antiepileptic drugs	Monotherapy (n= 14)	Valproate (VPA)	58,8
		Phenobarbital (PHB)	17,6
		Carbamazepine (CBZ)	5,9
	Combination therapy (n=3)	VPA + PHB	17,6

within 6 to 12 months, and fifteen patients (33.3%) after 1 year of development. The symptoms reported were communication and behavioral disorders: difficulties or absence of interactions, restricted interests, stereotypies and/or repetitive solitary games. ASD appeared before epilepsy in 7 patients (41.2%) and after epilepsy in 6 patients (35.3%), and concomitant diagnosis in 4 patients (23.5%). Epileptic seizures had a frequency of 2 seizures daily to 1 seizure weekly. Table 3 summarizes the electro clinical characteristics of epileptics.

Only 2 brain images were abnormal with bilateral frontal cortico-subcortical atrophy and right frontal hypodensity secondary to meningitis. Pathological auditory evoked potentials (AEP) in 5 patients (12.8%) showed bilateral retro-cochlear damage, bilateral endocochlear damage, mixed hypoacusis, axonal neuropathy and isolated deafness.

Epilepsy was mostly unclassifiable (82.3%) and ASD was mainly severe (53.6%). There was a statistically significant relationship between * epilepsy and ASD for age less than 10 years, * family history of consanguinity in epilepsy and psychiatric pathologies in autistic people, and * EEG findings. All patients benefited, in the day hospital, from multidisciplinary care, associated in 10 patients (22.2%) with specialized care at home reducing their weekly travel to 1 time. Each patient has a specialized educator as a referent who evaluates them on a daily basis and prescribes

specific reinforcements in other areas, particularly speech therapy and neuropsychology, on a case-by-case basis; psychomotor skills and play therapy are daily. Evolutionarily, only 3 patients (6.7%) were autonomous. 22 patients (48.9%) rarely required help from a third person and 20 patients were dependent requiring almost constant help. In 2003, 27 patients (60%) were seen again for a 5-year evaluation, of which only 5% were still in the care circuit and were almost autonomous. Only 5 children (18.5%) still had active but stable epilepsy on monotherapy with rare occasional seizures during intercurrent ailments.

Discussion

Rare series have been carried out on epilepsy in people with ASD mainly in Europe and North America. These were most often retrospective surveys [5, 6, and 9]. To our knowledge, no study has been carried out in Africa and particularly in Senegal on this subject. This study with recruitment over 14 years made it possible to have an exhaustive cohort of 45 patients followed for ASD in a child psychiatry center specializing in child disabilities with an annual follow-up frequency of 25% of cases of suspected ASD including more of half will not ultimately meet the essential criteria of the CARS scale (Childhood Autism Rating Scale) [10] and are more related to profound emotional deficiencies and/or excess early exposure to screens (Unpublished data from local registries).

Autism should not be considered as an illness caused by a pathological parental relationship or a psychological disorder; there is a cerebral predisposition such as epilepsy, for which it shares common genetic and environmental mechanisms and risk factors [11-16]. Thus, their association is not fortuitous; epilepsy was found in autistic patients, between 10 and 12.5% according to studies by Viscidi EW et al. And Ewen JB et al. [3,9].

The frequency of epilepsy in children with ASD in our study population was 37.8% with a statistically significant association according to age (Table 2). This result is similar to those described in the literature which vary between 11 and 39% [5-8,17-20]. Almost all of our patients (94%) had an early age of onset of epileptic seizures before the age of 5 years. Unlike Viscidi et al. [9] who reported a prevalence of epilepsy of 12.5% in children aged 2 to 17 years with ASD, versus 26% in those over 13 years old. Autistic behaviors appeared in children often before the age of 3 years in certain authors [1,6,21], as in our series with 30 patients affected, or 66.7%. A male predominance as mentioned in the literature [1,5,6, and 22] was also observed in our series.

The etiology of autism remains poorly understood; genetic predisposition has been proven [12,14,23]; however other factors such as gynecological complications have been incriminated. A statistical link was found with these two factors in our series. Thus, in our study, acute fetal distress was reported in 11 patients (24.4%) requiring resuscitation and followed by hospitalization in only 2 cases, because there are neonatal crèches only in large hospital centers in Dakar. with low capacity and a cost that is not financially accessible for most parents. On the other hand, home births are still common in rural -urban areas with more

or less help from matrons who are often overwhelmed in the event of complications. The etiologies of this fetal suffering are mainly prolonged labor due to cervical dystocia or erroneous indications for vaginal delivery (circular cord, narrowed pelvis, fetal malposition , etc.) not taken due to lack of last prenatal assessment. A genetic basis with a statistically significant difference was found in 16 patients or 35.5% with parental consanguinity and a family history of ASD in respectively 4 patients, epilepsy in 5 patients, and schizophrenia in 3 patients. Christensen et al. [21] reported that the overall risk of epilepsy in younger children increases by 70% if an older sibling had ASD, and increases by 54% if an older sibling had epilepsy.

Children with ASD combined with epilepsy have a higher rate of intellectual disability and paroxysmal EEG abnormalities in the frontal lobe compared to children with ASD alone [24,25]. Paroxysmal EEG abnormalities were found in 37.8% of our patients. Hughes et al. [26] reported that up to 60% of EEG recordings from children with ASD have interictal spikes. We found a statistically significant difference between epileptic ASD and ASD isolated to the waking and sleeping EEG: the paroxysmal abnormalities were frontal (60%) and Centro -parietal (26.6%), more rarely temporal. It was the same in study of Masmoudi et al. [27]. Matsuo et al. reported frontal anomalies with a rate of 76%, Centro -parietal in 15%, occipital 6% and temporal 2% [24]. This frontal seat of predilection can reinforce autistic-like disorders [28] in particular desocialization and emotional indifference, and therefore the early detection of a frontal paroxysmal focus should guide medical treatment to improve behavioral disorders. Thus, several studies report an improvement in the basic symptoms of autism, impulsivity and aggressiveness in children with ASD and epilepsy or with ASD with paroxysmal EEG abnormalities without epileptic seizures, treated with valproic acid. [29,30]. In our case, all patients benefited from neuropsychological, psychomotor and speech therapy care in the day hospital, associated with specialized care at home in 22.2% of patients. Psychosocial care was based on the behavioral, developmental and psychoanalytic profile. Medical management concerned epileptic patients with antiepileptic drugs mainly as monotherapy (82.4%) and with sodium valproate (VPA) (58.8%). Medical management of epilepsy, integrated into global and multidisciplinary care, in patients with ASD makes it possible to improve the behavioral disorders inherent in these children [17]. This was our case with relative autonomy for the majority of patients (55.5%), mainly epileptics (60%).

Conclusion

Despite multiple studies on this subject, the nature and frequency of the association between epilepsy and ASD remain poorly understood [4,15,20,31,32]. Underlying mechanisms, common genetic and environmental risk factors have been identified [3,7,8,12]. This study made it possible to confirm the statistically significant link between ASD and epilepsy depending on age and to highlight local specificities, particularly in the risk factors for the occurrence of epilepsy in the context of ASD and vice versa; notably a pathological perinatal period such as fetal suffering as well as consanguinity and a family history of ASD or epilepsy. We also

found a significant statistical difference with a frontal topographic predilection of abnormalities in epileptics with ASD versus ASD isolated; and relative autonomy of epileptics under antiepileptic treatment, especially valproate. Thus, electroencephalography can be of interest in the early detection of epilepsy in autistic patients [28, 33, and 34]. The globally and multidisciplinary take care of epilepsy of ASD patients improves behavioral disorders. In our practice context, the systematization of electroencephalography for ASD cases could be a good contribution in the early detection of the behavioral disorders and of great help in the clinical evolution of patients, as we notice in 2023.

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