

## Electroencephalographic Assessment of Cerebral Activity in Patients with Spinal Muscular Atrophy

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### Abstract

<b>Background</b>	Spinal muscular atrophies are a group of degenerative diseases primarily affecting the anterior horn cells of the spinal cord and motor cells of cranial nerve nuclei. Even if the clinical picture is mainly dominated by the diffuse muscular atrophy, in some cases, patients may show associated, atypical clinical features. There have been a few reported cases of spinal muscular atrophy with central nervous system involvement; in particular, the association with progressive myoclonic epilepsy has been rarely described.
<b>Objectives</b>	To clarify the impact of this degenerative disease on central nervous system and specifically on cerebral activity by using electroencephalographic exam.
<b>Methods</b>	Thirty two patients with spinal muscular atrophy and 20 control subjects were included in this study. Their ages were between two months and one year. Brain CT and MRI, electroencephalography was done for all of them and cerebral activity was precisely assessed with emphasis on normal brain waves frequency and distribution.
<b>Results</b>	The frequency of brain waves recorded from patients with spinal muscular atrophy who show abnormal electroencephalography were $1.49 \pm 0.4$ and it is significantly lower than that of control subjects ( $4.11 \pm 1.1$ ). The mean frequency of brain waves recorded from patients with spinal muscular atrophy with normal electroencephalography were $4.13 \pm 1.2$ which is higher than the mean frequency of brain waves recorded from patients with abnormal electroencephalography ( $1.49 \pm 0.4$ ).
<b>Conclusion</b>	Central nervous system could be affected in patients with spinal muscular atrophy specifically cerebral activity, which might show diffuse slowing in brain waves as revealed in this study.
<b>Keywords</b>	Spinal muscular atrophy, cerebral activity, electroencephalography

**List of Abbreviation:** SMA = spinal muscular atrophy, EEG = electroencephalography, CT = computerized topography, MRI = magnetic resonance imaging, CNS = central nervous system, PML = progressive myoclonic epilepsy.

### Introduction

Spinal muscular atrophies (SMAs) are a group of degenerative diseases primarily affecting the anterior horn cells of the spinal cord and motor cells of cranial nerve nuclei<sup>(1,2)</sup>. Clinically, it is classified into three subtypes based on the age of onset and severity. Type one is the severe form with onset before the age of six months, and the patient is unable

to sit without support; type two is the intermediate form with onset before eighteen months, and the patient is unable to stand or walk without aid; and type three is the mildest form with age of onset after eighteen months, and the patient is able to stand and walk<sup>(3)</sup>.

Genes for all the three subtypes of SMA have been mapped to chromosome 5q13<sup>(4,5)</sup>. Even if the clinical picture is mainly dominated by the diffuse muscular atrophy, in some cases, patients may show associated, atypical clinical features ("SMA plus"). There have been a few reported cases of SMA with central nervous

system (CNS) involvement, in particular, the association of SMA and progressive myoclonic epilepsy (PME) has been rarely described<sup>(6,7)</sup>.

The aim of this study is to clarify the impact of this degenerative disease on CNS and specifically on cerebral activity using electroencephalography (EEG) exam to see if there is any possible influence of the disease process on cortical neurons which might contribute later on to affect cognitive function and cause behavioral changes for those individuals who complain subtle changes on cerebral functions.

### Methods

This is a cross sectional study carried out in the period from February 2012 to October 2014 in Basra Children Specialty Hospital. It includes thirty two patients with proved SMA (clinically and electrophysiologically; their ages were between two month and one year. Brain computed tomography (CT) and Magnetic resonance imaging (MRI) had been done for all of them and were normal. They were stopped using any type of medication especially sedative drugs for at least two weeks before doing EEG.

Digital EEG had been done for them using digital EEG machine (Nihon Kohden EEG 1200 J/K) according to the 10-20 International system. The measured impedances were less than 5 Kohms at all electrodes. All studies utilized both bipolar and referential montages. Initial analog signal conditioning included a 0.3-1 Hz high pass filter, a 35-70 Hz low pass filter and a 50 Hz notch filter. The digital sampling rate was 200-500 per second. EEG recordings last for 30 minutes. Activating techniques including intermittent photic stimulation were used and the record obtained during awaking and during sleep. The EEG record were re-analyzed and reviewed and background cerebral activity were assessed by calculating the frequency of brain waves and their distribution manually and by specific analysis program software (EEG examination support software:QP-150AK). According to the results patients were divided in to two groups:

1. Group A: patients with normal EEG.
2. Group B: patients with abnormal EEG .

We include twenty infants as a control group aged between one month and one year whom referred to the neurological outpatient clinic in Basra General Hospital or the Neurophysiology Outpatient Clinic in Basra Children Specialty Hospital in the same period of our research for conditions other than flaccid paralysis or suspected CNS disorders. After taking the acceptance of their parents about the aim of our further investigations, a brain imaging studies was done for them and those with completely normal results and on no medical treatment of any kind for at least the last two weeks were selected. Then we did EEG study for them using the same protocol that had been used for the patients. This study was conducted in accordance with a protocol approved by the Committee on Clinical Investigations at Basra College of Medicine and Basra Health Directorate. All patients were informed about the aim of study and their acceptance obtained. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 20 computer software. Descriptive statistics for all data of each set was expressed as mean  $\pm$  2SD. The difference in mean frequency of brain waves between groups was assessed by independent sample t-test,  $P < 0.05$  considered statistically significant.

### Results

The total number of patients included in the study were thirty two patients with SMA, fifteen of them (46.9%) were males and seventeen (53.1%) were females. Twenty control subjects age and gender- matched were also included in the study (Table 1).

**Table 1. Number of patients with spinal muscular dystrophy and control subjects**

Gender	SMA patients		Control Group	
	No	%	No	%
Male	15	46.9	10	50
Female	17	53.1	10	50
Total	32		20	

SMA = spinal muscle atrophy

Table 2 show the number of patients with SMA and have abnormal EEG pattern (group B) they were thirteen patients (40.6%), six males and seven females, and patients belongs to SMA who have normal EEG (group A) were nineteen patients (59.4%), no significant difference between males and females patients were obtained regarding their EEG findings.

**Table 2. Number and percentage of patients with normal and abnormal EEG findings**

Gender	Group A		Group B		Total
	No	%	No	%	
Male	9	47.4	6	46.2	15
Female	10	52.6	7	53.8	17
Total	19	59.4%	13	40.6%	32

The comparison in mean frequency of brain waves recorded by EEG from patients with SMA in group (A) and control subjects show no significant difference obtained and the p. value was not significant. When we compare the frequency of brain waves recorded by EEG from patients in (group B) and control subjects, the results show that the mean frequency of brain waves for patients in (group B) were (1.49±0.4) which is significantly lower than that of control subjects (4.11±1.1) as observed in table 3.

**Table 3. Frequency of brain waves in control subjects and patients with and without EEG abnormalities**

Subject	Group A		Group B	
	No	mean±SD	No	mean±SD
Patients	19	4.13±1.2	13	1.49±0.4
Controls	20	4.11±1.1	20	4.11±1.1*

\* P = 0.001

The results in table 4 showed that the mean frequency of brain waves recorded by EEG exam for patients in group (A) were (4.13±1.2) which is higher than the mean frequency of brain waves recorded form patients in group (B) (1.49± 0.4).

**Table 4. Frequency of brain waves between spinal muscle atrophy patients with abnormal and patients with normal electro-encephalogram**

Group	No.	Mean ±SD
A	13	1.49±0.4
B	19	4.13±1.2*

\*P = 0.001

### Discussion

We found that 46% of SMA patients have significant slowing in their brain activity as compared to control group and this high percentage cannot be explained by an accidental finding or an incidental condition.

When the pathology of this disease was revised; an obviously no evident pathology had been found in both corticospinal and corticobulbar tracts at autopsy<sup>(8,9)</sup>, yet this is not necessarily means a normal function of these systems or the cerebrum during their lives, specially there are only several studies investigate this issue<sup>(5,21)</sup>. So we have to revise our knowledge about the believe of the only affection of motor neurons of brain stem and spinal cord by SMA and cortical and subcortical structure have to be further investigated and analyzed functionally and structurally (either by autopsy or histologically if possible at life) for possible effect of the degenerative disease process on these organs<sup>(10,5)</sup>.

In one study by Striano *et al* there was an association between SMA and PME but it was unclear whether it was a separate conditions (genetically independent syndromes) or a variant from SMA<sup>(6,11)</sup>.

In another study by Anderson *et al*, a clear association between Duchenne muscular dystrophy, which should be purely muscle disease and brain pathology was found. Despite of the fact that Duchenne muscular dystrophy has nothing to do with our study, nevertheless, it can give an exemplary of how we have to restudy these diseases using modern tools to see how these diseases actually affect different

systems of our body and not only the targeted system of the degenerative processes<sup>(12,13)</sup>.

In conclusion, although SMA affects mainly motor neurons in bulbar and spinal cord region but CNS could be affected specifically cerebral activity, which might show diffuse slowing in brain waves as revealed in this study.

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### **Author contributions**

Dr Mohammed did the study conception and design, in addition to the EEG recording; Dr Hammady collect the cases, made the diagnosis and neurological examination. The authors share the responsibility in preparing and completing this work.

### **Conflict of interest**

There is no conflict of interest that could influence the objectivity of the research reported.

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