

# CONTINUOUS SPIKE-WAVES DURING SLOW WAVES SLEEP

## A CLINICAL AND ELECTROENCEPHALOGRAFIC STUDY IN FIFTEEN CHILDREN

ADRIANA A. F. DJABRAIAN\*, MARCUS SABRY AZAR BATISTA\*\*,  
MÁRCIA M. DE LIMA\*\*\*, DÉLRIO FAÇANHA SILVA\*\*\*

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**ABSTRACT** - We report on the clinical and EEG features of 15 patients with the syndrome of "continuous spike waves during slow wave sleep" (CSWSS). The differential diagnosis of CSWSS includes benign epilepsy of childhood with centro-temporal spikes, and Landau-Kleffner and Lennox-Gastaut syndromes. We found normal CT and MRI features in 6 cases, periventricular leukomalacia with and without diffuse brain atrophy in 4 cases and hydrocephalus in 1 case. There was no association between specific neurological findings and CSWSS. Nine of our cases had relatively focal discharges, like some cases from the literature. The occurrence of CSWSS appears to be age-related, generally between the ages of 5 to 12 years, with a strong temporal relation to the neuropsychological deterioration in its nature, severity and prognosis. We believe that this striking disorder has been overlooked and that routine sleep EEG studies on epileptic children may disclose additional cases of CSWSS.

**KEY WORDS:** electroencephalogram, sleep, epilepsy, continuous spike-wave.

### **Ponta-onda contínua do sono lento: estudo clínico e eletroencefalográfico em quinze crianças**

**RESUMO** - Relatamos as características clínicas e eletroencefalográficas de 15 pacientes com a síndrome de ponta-onda contínua do sono não-REM (POCSNR). O diagnóstico diferencial da POCSNR inclui a epilepsia benigna da infância com pontas centro-temporais e as síndromes de Landau-Kleffner e Lennox-Gastaut. Encontramos TC e RNM de crânio normais em 6 casos, leucomalácia periventricular em 4 e hidrocefalia em 1. Não houve associação de achados neurológicos específicos e a POCSNR. Nove dos nossos casos tinham descargas relativamente focais, como alguns casos da literatura. A ocorrência da POCSNR parece ser idade-dependente, geralmente entre 5 e 12 anos, com forte relação temporal à deteriorização neurocognitiva, em sua natureza, severidade e prognóstico. Acreditamos que esta síndrome tem sido pouco diagnosticada e que a realização rotineira de EEG em sono em crianças epiléticas possa revelar novos casos de POCSNR.

**PALAVRAS-CHAVE:** eletroencefalograma, sono, epilepsia, ponta-onda contínua.

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The epilepsy with continuous spike-waves during slow wave sleep (ECSWSS) was first described by Patry et al. (1971) under the title "subclinical electrical status epilepticus" induced by sleep in children. Nowadays it is defined as "continuous spike waves during slow wave sleep"(CSWSS)<sup>1</sup>. This entity is characterized by spike-and-wave complexes (SWC) that occurs most continuously (>85%) during slow or non-rapid-eye movement (NREM) sleep. The close relationship between CSWSS and Landau-Kleffner syndrome (LKS), as well as with the benign childhood epilepsy with centrotemporal spikes (BECTS), is suggested by several reports<sup>2-12</sup>.

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Dr. Marcus A. S. Batista. - Rua Olavo Bilac 3381/502 - 64001-600 Teresina PI - Brasil.



Table 1. Clinical and EEG characteristics of 15 patients with continuous spike waves during slow wave sleep (CSWSS).

N	Age (y)	Age at CSWSS	Sex	Seizures	Encephalopathy (etiology)	CT/MRI	Electroencephalogram	
							BA/ Awake	NREM (SWC>85%)
1	6	4	M	PMS/ CPS (SE 6y)	no	N	N/ N	Focal SWC
2	5	4	M	Sleep seizures Atypical absence (SE 5y)	no	N	N/ N	Focal SWC
3	8	8	M	PMS/ (SE 4y)	no	N	N/ left fronto-temporal spikes	Focal SWC
4	6	5	M	PMS/ Atypical absence (SE 5 y)	Hypoxic-ischemic	Brain atrophy	Slow/ multifocal	Focal SWC
5	11	4	M	PMS	Hypoxic-ischemic	N	Slow/ multifocal	Focal SWC
6	14	12	F	PMS	Hypoxic-ischemic	Brain atrophy	Slow/ multifocal	Focal SWC
7	9	7	F	PMS/ (SE 2y)	Hypoxic-ischemic	-	-	Focal SWC
8	12	10	F	PMS/ (SE 1y)	Hypoxic-ischemic	-	Slow/ left fronto-temporal spikes	Focal SWC
9	7	7	F	Sleep seizures	no	N	N/ central spikes	Focal SWC
10	8	4	F	PMS/ (SE 3y)	Myelomeningocele	Hydrocephaly	Slow/ multifocal	Diffuse SWC
11	8	2	F	PMS	Congenital rubella	N	-	Diffuse SWC
12	9	7	F	PMS	no	N	N/ multifocal	Diffuse SWC
13	9	7	F	PMS	Hypoxic-ischemic	Brain atrophy	-	Diffuse SWC
14	10	6	M	PMS	Hypoxic-ischemic	-	Slow/ multifocal	Diffuse SWC
15	12	6	M	PMS	Hypoxic-ischemic	Brain atrophy	Slow/ multifocal	Diffuse SWC

M, male; F, female; y, year old; PMS, partial motor seizure; CPS, complex partial seizures; SE, status epilepticus; SWC, spike-wave complex; N, normal; CT, computerized tomography; MRI, magnetic resonance imaging; BA, base activity; NREM, non-REM sleep.

damage). His development was abnormal with marked motor deficit. MRI showed periventricular leukomalacia with brain atrophy. At the age of 3 an awake and sleep EEG was carried out for about 30 minutes, displaying slow BA with rare spikes over the left frontal and parietal regions. Further EEGs, done at 4, 5 and 7 year-old disclosed multifocal discharges of spikes and SWC that markedly increased during NREM sleep, but without continuous spikes (<50%). At 8 year-old, after 4 months seizure-free, another EEG was performed for 60 minutes and showed nearly continuous generalized

activity during NREM sleep. At age 9, an overnight EEG still showed the characteristic of CSWSS (Fig 1). In 1997, at 13 year-old and already seizure-free, another EEG was carried out disclosing only bilateral temporal discharges, without the CSWSS.

## DISCUSSION

The CSWSS is primarily an EEG diagnosis and secondarily a clinical one. The main diagnostic criterion is the occurrence of SWC nearly continuously during the NREM sleep but not during the awake state or REM sleep and must involve at least 85% of NREM sleep<sup>1</sup>. CSWSS occurs with a male to female ratio of 2:1. Onset appears to be age-related, occurring between the ages of 5 to 12 years<sup>5,12,15,16</sup>. In our patients we first recorded the CSWSS between the ages of 4 and 13 (mean 6.2). Seven of them were male and the others were female.

The differential diagnosis of CSWSS includes BECTS, LKS and Lennox-Gastaut syndrome (LGS). In the first condition, there is an intense sleep activation of interictal abnormalities, however, it never reaches the 85% threshold required for the diagnosis of CSWSS<sup>1,12</sup>. In LKS there is activation of paroxysmal abnormalities during sleep onset and during each REM period, a distinguishing feature of CSWSS<sup>12</sup>. In LGS the SWC index is about 60% during the NREM sleep.

There is no specific association of neurological findings with CSWSS. Eight out of 18 patients reported by Tassinari et al. had "encephalopathy" before the onset of the CSWSS, like 10 of our 15 patients<sup>21</sup>. Specific etiologies have not been completely defined but include mainly birth asphyxia, like 7 of our 15 patients, as well as meningitis, encephalopathy of unknown origin, congenital cytomegalovirus infection and cryptogenic category<sup>1,8,12,16</sup>.

With regard to neuroimage studies (CT and MRI) in 12 patients, we found normal features in 6 cases, periventricular leukomalacia with and without diffuse brain atrophy in 4 cases and hydrocephalus in 1 case.

Regarding EEG findings, in 6 of our 15 cases the distribution of the activity was generalized SWC discharges without any clinical manifestations during NREM sleep and were completely suppressed during REM sleep and wakefulness state. However, cases have been described with discharges relatively focal in distribution, like 9 of our 15 cases, or characterized by nearly continuous diffuse bisynchronous sharp waves and not SWC, a controversy that the literature has called generalized SWC<sup>1,11-14,16-18</sup>. These features support the assumption that the pathophysiological background of CSWSS may be associated to the reticular system, giving rise to paroxysmal bilateral synchronous SW, suggesting that CSWSS pattern is of a focal, rather than a generalized nature<sup>1</sup>.

The basic electrophysiological mechanisms involved in CSWSS are not known and some questions are unanswered as the link to sleep activities, functional and structural consequences on the developing brain. According to some authors, the secondary bilateral synchrony (SBS) was suggested to be the pathophysiology of CSWSS, with statistical analysis of SW activity such as coherence and phase analysis in addition to the clinical-EEG study<sup>1,15,19</sup>. In this case, the corpus callosum may play a role in the generation of the SBS in CSWSS<sup>19</sup>.

A study of electrophysiology of CSWSS in LKS, with EEG, intracarotid amobarbital and methohexital suppression tests, registered the SWC arising unilaterally, despite the apparent bilaterality and widespread distribution, what was later correlated with electrocorticographic recording<sup>21</sup>.

There is no specific anti-epileptic treatment for this disorder because clinical seizures have not posed a management problem and have responded to a variety of drugs, like our 15 cases. On the other hand, the EEG abnormality is generally refractory. Few reports concerning treatment of CSWSS are found in the literature. Patry et al. reported nitrazepan to be effective in improving the EEG pattern but not the clinical manifestations<sup>17</sup>. Yasuhara et al. showed that clonazepan gradually improved the clinical features and EEG pattern in five patients<sup>22</sup>. Nitrazepan and clobazam have

apparently abolished the characteristic SWC activity and improved neuropsychological function<sup>3,4,8,18</sup>. In our opinion it may have been a coincidental remission.

There is a strong temporal correlation between the onset of CSWSS and the neuropsychological deterioration in its nature, severity and prognosis. This probably depend on many factors, including the location of the main epileptic focus, the duration of the CSWSS and the state of maturation of the concerned brain areas at onset. All of our 15 cases had disorders such as short attention, hyperactive behavior, speech disturbance, spatial disorientation and intellectual deterioration. Besides the severe neuropsychological disorders, the partial seizures had the usual favorable prognosis.

We believe that this distressing disorder has been overlooked and that the routine EEG sleep studies on epileptic children may disclose additional cases of CSWSS.

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