

## Hemispheric Assymetry of Abnormal Focal EEG Findings

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### ABSTRACT

Left and right cerebral hemispheres are morphologically similar, although they are functionally different. Focal EEG abnormalities should appear with an equal frequency in both of them, but the literature has reported a left predominance. We presented the first Latin American study on lateralization of focal EEG abnormalities. **Method:** We retrospectively studied 10,408 EEGs from April 2001 to April 2010. They were separated by age and gender to estimate the frequency of left-sided versus right-sided focal abnormalities (discharges or slow waves). Associated clinical features were also accessed. **Results:** Discharges were more prevalent in left cerebral hemisphere, in temporal lobe, and a stronger lateralization was found among adults. Right-sided discharges occurred more in frontal lobe. Slow waves were also more prevalent in the left cerebral hemisphere and among adults. Among left-sided slow waves group, women were more prevalent. Contrarily, men were more observed among right-sided slow waves EEGs. Left-sided slow waves were more prevalent in temporal and parietal lobes. Contrarily, right-sided slow waves occurred more in frontal and occipital lobes. Epilepsy was the most frequent disease among the patients with focal discharges in both cerebral hemispheres. Right-sided slow waves were more associated to epilepsy, and left-sided slow waves were more associated to headache. **Conclusion:** There were significant differences between cerebral hemispheres on focal EEG abnormalities, considering lateralization, gender, age and clinical features. These results suggest a neurofunctional asymmetry between cerebral hemispheres which may be explained by different specificities, as well as by cerebral neuroplasticity.

**Keywords:** lateralization, interictal EEG, spikes, sharp waves, slow waves.

### RESUMO

#### *Assimetria hemisférica de anormalidades eletrencefalográficas focais*

Embora sejam morfológicamente semelhantes, os hemisférios cerebrais apresentam diferenças funcionais geneticamente determinadas. Ainda assim, anormalidades eletrencefalográficas focais deveriam ocorrer simetricamente numa população geral, embora a literatura tenha referido um predomínio à esquerda. Nosso objetivo é relatar o primeiro estudo latino-americano sobre uma grande série de EEGs, no intuito de observar se há lateralização de anormalidades focais. **Método:** Foram estudados retrospectivamente 10.408 EEGs, realizados de abril de 2001 a abril de 2010, os quais foram classificados de acordo com a presença de anormalidades focais específicas (descargas) e inespecíficas (ondas lentas focais). Os EEGs foram divididos de acordo com o gênero e a idade, e foram analisados achados clínicos associados. **Resultados:** As descargas foram mais prevalentes no hemisfério cerebral esquerdo, no lobo temporal, observando-se uma lateralização mais forte entre os adultos. À direita, elas prevaleceram no lobo frontal. Ondas lentas focais prevaleceram também à esquerda e no lobo temporal, especialmente entre os adultos. Entre os que apresentaram ondas lentas à esquerda, observou-se maior prevalência entre as mulheres. Os homens prevaleceram entre os que apresentaram ondas lentas à direita. À esquerda, ondas lentas prevaleceram nos lobos temporal e parietal. À direita, nos lobos frontal e occipital. Epilepsia foi o achado clínico mais associado à presença de descargas em ambos os hemisférios cerebrais. Ondas lentas à direita foram mais associadas a epilepsia, enquanto que, à esquerda, elas foram mais associadas a cefaleia. **Conclusão:** Houve diferenças entre os hemisférios cerebrais quanto à lateralização das anormalidades focais, assim como entre os gêneros, faixas etárias analisadas e quadro clínico associado.

**Unitermos:** lateralização, eletrencefalograma, atividade epileptiforme, ondas lentas.

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Left and right cerebral hemispheres have a well documented functional asymmetry, even being morphologically similar.<sup>1</sup> Genetically determined events probably lead to anatomical differences that result in functional specializations, although the human brain plasticity can also override them in order to preserve higher cognitive functions.<sup>29</sup> Nevertheless, because of cytoarchitectural similarities, it might be expected that the focal electroencephalographic (EEG) findings should appear with an equal frequency in each cerebral hemisphere. Contrarily, the literature has reported a predominance of left focal (epileptiform or not) EEG abnormalities in adults.<sup>6,8,12,17,23,27</sup> Nevertheless, some different results may occur in children.<sup>9</sup> The aim of our study was to find out if there is an asymmetry for focal EEG abnormalities in a retrospective study of a series of EEGs. Presumably, half of focal abnormalities (specific and non-specific) should have a right brain origin. The other half should be recorded from left hemisphere, as both of them are equally exposed to injuries and genetic disorders in a general population. We also did not expected differences in focal abnormalities considering gender, age, brain localization and associated clinical features.

## METHOD

We retrospectively examined EEG recording of 10,408 patients (aged 1-94 years) refereed to Santa Vitória EEG laboratory, in Campina Grande, state of Paraíba, Brazil, from April, 2001 to April, 2010. The records were scalp surface routine EEG, EEG following sleep deprivation and they were done with a 20-channel Med 420 Meditron EEG-recorder. Twenty-one electrodes were used according to the International 10-20 system. We analyzed only one EEG of each patient. EEGs lasted 20 to 30 minutes and included hyperventilation and photic stimulation. Bipolar longitudinal, transverse, referential and average montages were used. The EEGs were reported and reviewed by a board-certified neurologist and neurophysiologist. We classified the recordings according to the presence of unilateral focal abnormalities. Clear unilateral focal discharges were considered to be 'specific abnormal pattern' (SAP), including sharp waves, spikes, polyspikes and sharp wave complexes. Discharges that were generalized with a lateralized component were excluded. Focal unilateral slow waves were considered to be 'non-specific abnormal pattern' (NSAP), including intermittent, continuous or rhythmic slow waves. We excluded bilateral SAP and NSAP as well as benign epileptiform transients of sleep, 6 s/wave, 14 and 6 positive spikes and wicket spikes. The EEGs were separated according to the gender and localization of the focal abnormality. Because of possible different proportions of diseases across the ages we

examined 3 age-groups: children (C), age <13 years; young (Y), age 13-18 years and adults (A), age > 18 years. We also analyzed clinical features associated to the EEG requests. Data were tabulated in Statistical Package for Social Sciences (SPSS 13.0). They were divided in left and right brain hemisphere EEG focal abnormalities according to the age and gender. We used chi-squared tests. They were considered to be significant at 0.05. This research was approved by the Ethical Committee on Research of the State University of Paraíba (CEP-UEPB, CAAE – 0356.0.133.000-07).

## RESULTS

### General analysis

Out of 10,408 EEGs recorded, only 1,411 met the inclusion criteria (Table 1). Focal abnormalities were more prevalent in the left cerebral hemisphere.

Left-sided predominance of focal abnormalities was significant only among adults, when compared to teenagers and children ( $p < 0.001$ ).

### Discharges analysis

Left-sided discharges were more prevalent than right-sided ( $p < 0.001$ ), Table 1.

Left-sided discharges were more prevalent in all ages but a stronger left lateralization was found among adults, when compared to teenagers and children ( $p < 0.05$ ).

Focal discharges were observed in 212/625 (33.9%) of men and 239/786 (30.5%) of women. This difference was not significant.

### According to the localization

Focal discharges were more prevalent in temporal lobe (Table 2). Left-sided discharges occurred more in temporal and parietal lobes ( $p < 0.05$ ). Contrarily, right-sided discharges were more observed in frontal lobe ( $p < 0.05$ ).

### Slow waves analysis

*According to the lateralization:*

Slow waves were more prevalent in the left cerebral hemisphere, compared to the right ( $p < 0.05$ ), Table 1.

Left-sided slow waves were more prevalent among adults, when compared to teenagers and children ( $p < 0.05$ ).

Women were more frequent in left-sided slow waves group, while men were more observed in right-sided slow waves group ( $p < 0.001$ ).

**Table 1.** EEG focal abnormalities, according to the age and gender.

		FD			SW			Total
		C	Y	A	C	Y	A	
<b>LH</b>	Men	68	12	49	39	40	156	364
	Women	33	28	88	44	39	315	547
<b>RH</b>	Men	52	6	26	43	42	92	261
	Women	32	15	49	42	13	88	239
<b>Total</b>		185	61	212	168	134	651	1,411

FD = focal discharges; SW = focal slow waves; LBH = left brain hemisphere; RBH = right brain hemisphere; C=children; Y =teenagers; A = adults.  $p<0.001$ .

*According to the localization*

Focal slow waves were more prevalent in temporal lobe (Table 2). Left-sided slow waves occurred more in temporal and parietal lobes ( $p<0.001$ ). Contrarily, right-sided slow waves were more observed in frontal and occipital lobes ( $p<0.001$ ).

**Table 2.** EEG findings according to cerebral localization.

	FD			SW		
	LH	RH	MULTI	LH	RH	MULTI
Frontal	8	15		8	64	
Temporal	163	100	67	539	93	236
Parietal	26	9		6	0	
Occipital	31	32		0	14	
<b>Total</b>	228	156	67	553	171	236

FD = focal discharges; SW = focal slow waves; LH = left hemisphere; RH = right hemisphere; MULTI: multilobar findings.  $p<0.001$ .

*Clinical features*

Epilepsy was the most frequent disease associated with focal discharges in both cerebral hemispheres ( $p<0.05$ ), Table 3.

**Table 3.** Clinical features associated to focal EEG abnormalities.

	FD	SW	TOTAL
Epilepsy	399	386	785
Headache	17	393	410
Behavioural Change	15	-	15
Syncope	10	-	10
Stroke	-	58	58
Head Trauma	-	45	45
Cerebral Tumor	-	10	10
Aneurism	-	3	3
Other	17	58	75
<b>Total</b>	458	953	1,411

$p<0.001$ .

Among 633 patients with left-sided slow waves, headache was referred by 334 (52.7%) and 231 (36.5%) referred epilepsy. Among 320 patients with right-sided slow waves, 155 (48.4%) referred epilepsy and 59 (18.4%) complaint of headache.

In resume, epilepsy was the most frequent clinical association with right-sided slow waves, and headache was more referred by the patients with left-sided slow waves ( $p<0.001$ ).

**DISCUSSION**

**Summary**

We present the first Latin American analysis of lateralization of focal EEG abnormalities series so far, to our knowledge. It still seems to be impossible to answer to a question: does functional hemispheric lateralization result in or come from structural brain asymmetry? Genetically determined anatomic details may determine specific functions. Nevertheless, human brain dynamic plasticity can override those basic principles in order to preserve higher cognitive functions.<sup>29</sup>

Thereby, this discussion is far from a definitive conclusion at all. Our sample comprised epileptic patients and patients with other neurological or clinical disorders. We improved specificity of our results by eliminating EEGs with bilateral focal abnormalities. We also analyzed the results according to the age, gender and associated clinical complaints. In general, focal abnormalities were more prevalent in the left temporal hemisphere (64.6%). This result is similar to other in the literature.<sup>6,12,22,23</sup>

**Discharges analysis**

A strong left predominance was observed for focal discharges, i.e. 271/451 (60.1%) vs. 180/451 (39.9%). Earlier reports have confirmed this tendency,<sup>6,9,22</sup> although it has been suggested that this preponderance may result from different cerebral networks related to left and right

handedness<sup>17</sup>. Left-sided discharges were more prevalent in temporal lobe, similarly to other report.<sup>20</sup>

Left-sided discharges occurred more in temporal and parietal lobes, and right-sided discharges were more prevalent in frontal lobe. We shall speculate if left temporoparietal zone is more epileptogenic than the right because of the presence of more complex left neuronal networks, related to language and other important cognitive functions. Other research observed a posterior prevalence of right-sided discharges and slow waves in posterior regions.<sup>16,18</sup>

In our series, left-sided discharges were more prevalent in all ages with a stronger lateralization among adults. Other reports displayed similar results. Doherty et al. reviewed 1,579 pediatric EEG interpretations for evidence of hemispheric favoring of focal discharges.<sup>9</sup> They concluded that focal discharges displayed a discrete age-related favoring: left predominance of discharges only occurred upon 5 years-old children. Loddenkemper et al. pointed that left-sided lateralization of interictal findings also increased with age.<sup>23</sup> Age-related increase of left-sided discharges may be related to the maturation of cerebral tissue, probably reflecting the formation of more complex networks in the left cerebral hemisphere. Besides, a more prolonged exposition of the brain to potential injuries may also explain age-related increase of lateralized focal EEG findings, which reflects epileptic and non-epileptic neural tissue abnormalities.

### Slow waves analysis

A stronger left lateralization was found among adults in our series, similarly to other reports.<sup>12,23</sup> Nevertheless, Doherty et al. (2002) found that focal slowing occurred symmetrically<sup>6</sup>. Interestingly, slow waves were less frequent and more symmetric among children. Other similar reports are missing, but we speculate if children's cerebral tissue is more protected from lesions and epileptic phenomena because of a stronger activity of neuroplasticity and the presence of more redundant areas.<sup>12</sup>

Left-sided focal slow waves were more prevalent in temporal and parietal lobes and right-sided slow waves occurred more in frontal and occipital lobes, similarly to discharges distribution. It has been suggested that slow waves may sometimes represent incomplete sharp waves.<sup>23</sup> Other reports observed a central-posterior predominance of right-sided slow waves.<sup>16,18</sup>

We also speculate if 'central' left cerebral hemisphere is more likely to present injuries and epileptic phenomena than the right homonymous region. The same speculation may be applied to the 'polar' regions of the right hemisphere. Those differences may result from functional specificities. In other words, regions with more complex functions, as cognitive and language processes (as observed in left

temporal and parietal lobes) may be more affected by injuries or developmental alterations than more 'silent' regions (like the left frontal lobe). Besides, the right cerebral hemisphere play a special role on attention processes, which may lead to more complex frontal-occipital networks, when compared to the left. Consequently, those regions may be more affected by injuries and development alterations than the homonymous left regions. Other studies are missing to confirm these findings and speculations.

Women were more frequent in left-sided slow waves group, while men were more observed in right-sided slow waves group. This has not been pointed before, to our knowledge. We speculate if there could be more redundant networks in women's right hemisphere and in men's left hemisphere, which could play a protective role.<sup>12</sup> This difference may also play a role on different male-female cognitive and motor abilities. Other researches are needed to confirm those findings.

### Clinical features

As predictable, epilepsy was the most frequent clinical feature among all the patients with focal discharges. The value of interictal EEG in the diagnosis of epilepsy has already been reported: abnormal EEGs with discharges may occur in 42 to 69%.<sup>5,26</sup> Among the patients with focal slow waves, headache was the most frequent complaint. Interestingly, there was a significant difference between the patients with left and right-sided focal slow waves: left-sided slow waves were more related to headache, and right-sided, to epilepsy.

Headache is one of the most frequent complaints that lead to EEG, yet TC and MRI scans are preferable. Interestingly, right-sided slow waves were more associated to epilepsy, instead of left-sided. We speculate if some of the right-sided slow waves may correspond to 'incomplete discharges' as previously suggested.<sup>23</sup> If this is true, maybe the left cerebral hemisphere is more likely to exhibit more 'well-formed sharp waves' than the right. Other studies are needed to confirm those findings.

### Final discussion

Hemispheric lateralization of functional and anatomic aspects has already been established.<sup>2,14</sup> They result from specific hemispherical functional abilities, such as language, psychiatric, memory and other cognitive processes and the consequent different arrangement of cytoarchitecture and neurotransmission. Differences between left and right hemispheres, as well as differences between men and women have been pointed by recent researches.<sup>1,2,4,19,21</sup> Handedness seems to be related to representation of body space<sup>15</sup> and to creativity.<sup>28</sup>

There is also a hemispheric asymmetry on hypnosis susceptibility.<sup>25</sup> Prenatal testosterone levels may play a role on language lateralization processing.<sup>24</sup>

All these differences may lead to or come from different cytoarchitectural left-right brain arrangements and may be related to the presence and absence of specific redundant areas, which are less likely to present symptoms. This is probably the best hypothesis to explain the left predominance of abnormal EEG findings in a general population.<sup>12</sup> It has also been suggested that the presence of language function in the left hemisphere (in the majority of right-handed people) would lead affected patients to the attention of a physician earlier.<sup>6</sup> Contrarily, right-sided 'silent' lesions may cause a delay in diagnosis an EEG detection of brain diseases. However, it might be expected that a more prolonged time for diagnosis would also result in greater damage of brains tissues in right-sided lesions, which would lead to more extensive and obvious focal EEG findings in a general population, especially when a long-term research is done.<sup>12</sup>

Other explanation is that left cerebral hemisphere matures later than the right<sup>13</sup> being more exposed to potentially harmful agents during developmental processes. Left cerebral hemisphere has also more sophisticated and complex functions which result in more complicated neuronal networks. Consequently, left cerebral hemisphere is more vulnerable to injuries.<sup>13</sup> As a consequence, for instance, cerebral palsy is more related to left cerebral hemisphere injuries.<sup>21</sup> This also seems to be a reasonable explanation for left-predominance of focal EEG findings.

There have also been described left-right differences on GABA, dopamine and choline acetyltransferase expression on the human brain, resulting on a greater neuronal excitability in the left hemisphere<sup>5,13,26</sup> as well as a predominance of left-sided brain tumors likelihood to provoke seizures related to tumors.<sup>10</sup>

Defazio et al. reported side-related differences on the efficacy of antiepileptic drugs to prevent secondarily generalized tonic-clonic seizures in patients with complex partial seizures.<sup>7</sup> All these reports reinforce the discrepancies between left and right hemisphere, and the consequent lateralization of EEG focal findings (which may result from epileptic and non-epileptic injuries).

A possible referral bias has been pointed by other reports because of a selection of patients with left-sided epileptic focus, as the EEGs were recorded in epilepsy center services.<sup>23</sup> We virtually eliminated this bias, because our EEG service is a general one and the patients are referred for many other clinical or neurological diseases.

We conclude that focal abnormalities (discharges and slow waves) were more prevalent in left cerebral hemisphere. A stronger left-sided lateralization was observed among adults, when compared to teenagers and children.

Focal discharges were more prevalent in temporal lobe. Left-sided discharges occurred more in temporal and parietal lobes and right-sided discharges were more observed in frontal lobe. Women were more observed among left-sided slow waves group, while men were more prevalent among right-sided slow waves EEGs.

Focal slow waves were more prevalent in temporal lobe. Left-sided slow waves occurred more in temporal and parietal lobes and right-sided slow waves were more observed in frontal and occipital lobes.

The most prevalent clinical feature associated to focal discharges was epilepsy, in both cerebral hemispheres. Headache was the most frequent clinical complaint associated to focal slow waves. Epilepsy was the most frequent clinical association with right-sided slow waves, and left-sided, to headache.

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