# Congenital Bilateral Perisylvian Syndrome: Familial Occurrence, Clinical and Psycholinguistic Aspects Correlated with MRI

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Key words
- epilepsy
- polymicrogyria
- malformations of cortical development
- congenital bilateral perisylvian syndrome
- dyslexia
- specific language impairment

## Abstract

**Objective:** Congenital bilateral perisylvian syndrome (CBPS) is frequently caused by polymicrogyria (PMG). The aim of this study was to correlate the clinical and psycholinguistic aspects with neuroradiological data of patients with CBPS.

**Methods:** Thirty-one patients were studied. We performed a clinical investigation of the patients and their families, including MRI scanning, neuropsychological tests and language evaluation.

**Results:** The statistical analysis showed that: a) prenatal events are associated with the non-familial type of PMG; b) diffuse PMG is associated with pseudobulbar signs, as opposed to BPPP; c) motor deficit is associated with diffuse PMG; d) epilepsy is equally present in patients with both familial or non-familial PMG, but is more frequently seen in patients with diffuse PMG; e) dyslexia and SLI can be a feature of both the diffuse or BPPP, and either familial or sporadic cases of PMG.

**Conclusions:** The severity of clinical manifestations in CBPS is correlated with the extent of cortical involvement. Most patients with CBPS have a history of speech delay or language difficulties and no epilepsy. Dyslexia can be found in patients with PMG.

## Introduction

Polymicrogyria (PMG) is characterized by an excess of small gyri, shallow sulci and abnormal cortical lamination [2–4,21,27]. Congenital bilateral perisylvian syndrome (CBPS) is a neurological disorder characterized by the presence of polymicrogyric cortex distributed around the Sylvian fissure. Clinically, patients may present with pseudobulbar palsy of the oropharyngoglossal region, epilepsy, and variable degrees of cognitive deficits and language disorders [14,19]. Other types of PMG selectively affect different cortical areas [3,9,15,25,31]. Although most cases of CBPS are sporadic, several families have been reported with a pattern consistent mainly with X-linked inheritance [13]. In these families, clinical manifestations are extremely variable and male patients tend to be affected more often and more severely. In the pediatric population, CBPS has different manifestations than in adults [12,14]. The characterization of patients with PMG offers an opportunity to assess the impact of anatomic abnormalities on cognitive function. The aim of this study was to correlate the clinical features, psycholinguistic aspects and neuroradiological data of patients with CBPS.

## Patients and Methods

### Ascertainment of patients and their families

We performed a detailed clinical investigation of 31 patients and their families. Family histories were obtained and pedigrees were constructed. Twenty-two patients, belonging to six unrelated kindreds, had a familial recurrence of PMG.

The criteria for diagnosis included a clinical presentation of pseudobulbar palsy, epilepsy and/or language disorder without hearing deficits, mental retardation or oral motor/structural abnormalities, and PMG on imaging studies. We systematically interviewed patients and their family members according to a standard detailed questionnaire, emphasizing the family history of problems with phonation and delayed speech,

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Bibliography
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motor development and occurrence of prenatal events during the first two trimesters of the pregnancy.

Particular attention was paid to the seizure history, age at onset, type, frequency and response to treatment. A diagnosis of epilepsy was defined by at least two recurrent unprovoked seizures based on family descriptions, and using the International League against Epilepsy classification [11]. All patients were examined by clinical neurologists.

Informed consent was obtained in accordance with human study protocols approved by the Medical School Ethics Committee of our university hospital.

The neuropsychological assessment included the Wechsler Intelligence Scale for Children-III (WISC-III) [36], Wechsler Preschool and Primary Scale of Intelligence (WPPSI) [38] or Wechsler Adult Intelligence Scale - Revised (WAIS-R) [37].

A language evaluation was performed by two child speech therapists (EPMO and SRVH). Spontaneous language and free conversation were evaluated according to a semi-structured protocol that characterized the following aspects of language: phonologic, syntactic, semantic, pragmatic and lexical. In addition, some aspects of reading and writing were assessed. The following tests and protocols used were: Yavas Protocol [39], Peabody Picture Vocabulary Test – revised (PPVT), Brazilian Standardization by Capovilla and Capovilla [7], Phonological Awareness Test and Scholar Performance Test [30]. The diagnosis of specific language impairment (SLI) was applied when language evaluation showed deficits in comprehension, production, and use of language that is not in keeping with a child's mental age [26] and performance IQ was > 70. Dyslexia was applied when the evaluation showed an unexpected difficulty in reading in children and adults who otherwise possessed the intelligence, motivation, and schooling considered necessary for accurate and fluent reading [29].

### Magnetic resonance imaging studies

Magnetic resonance imaging (MRI) scans were performed in a 2-T scanner (Elscint Prestige®), and included $T_1$- and $T_2$-weighted images in three orthogonal planes, as well as thin coronal $T_1$ inversion recovery (IR) images.

MRI acquisition parameters were: (i) sagittal $T_1$ spin echo, 6 mm thick, flip angle = 180°; repetition time (TR) = 430, echo time (TE) = 12, matrix 200 × 350, field of view (FOV) = 25 × 25 cm; (ii) coronal images, perpendicular to long axis of hippocampus, defined by the sagittal images; (ii.a) $T_2$-weighted "fast spin echo" (FSE), 4 mm thick, flip angle = 120°; TR = 4800, TE = 129, matrix 252 × 320, FOV = 18 × 18 cm; (ii.b) $T_1$-weighted IR, 3 mm thick, flip angle = 200°; TR = 2800, TE = 14, inversion time (TI) = 840, matrix 130 × 256, FOV = 16 × 18 cm; (iii) axial images parallel to the long axis of the hippocampus; (iii.a) $T_1$-weighted gradient echo, 3 mm thick, flip angle = 70°, TR = 200, TE = 5, matrix 180 × 232, FOV = 22 × 22 cm; (iii.b) $T_2$-weighted FSE, 4 mm thick, flip angle = 120°, TR = 6800, TE = 129, matrix 252 × 328, FOV = 21 × 23 cm; (iv) $T_1$-weighted 3D gradient echo, acquired in the sagittal plane (1 mm thick, flip angle = 35°, TR = 22, TE = 9, matrix 256 × 220, FOV = 23 × 25 cm). MRI visual analyses were performed using multiplanar reconstruction on an OMNIPRO® workstation.

We used three criteria to identify our patients with PMG: abnormal gyral pattern, increased cortical thickness and irregularity of the cortical white matter junction [1, 22].

Patients were divided into two groups according to the presence or absence of family history. Patients were also divided into two groups according to neuroimaging findings [22]: (a) diffuse polymicrogyria around the entire extent of the sylvian fissure (PS PMG = perisylvian polymicrogyria), including its extension posteriorly to the parietooccipital regions, and (b) polymicrogyria restricted to the posterior aspects of the parietooccipital regions (BPPP = bilateral posterior perisylvian polymicrogyria), without any cortical abnormality at the anterior two thirds of the sylvian fissure.

### Statistical analysis

Statistical analysis was performed using Fisher's exact test, with a level of significance of 0.05.

## Results

**Table 1, 2** list pertinent data from the 31 patients with the diagnosis of CBPS. Some of our patients have been presented elsewhere [13, 14, 22]. These patients have been followed up for almost 10 years. Computed tomography was performed in only one individual (II-9, **Table 1** – family 2) who was unable to undergo an MRI because of a metallic femur prothesis. She was included because she is the mother of three affected patients. Bilateral sylvian fissure cortex involvement (**Fig. 1**) and a variable extent of involvement of the adjacent lobes were present in 14 patients. BPPP was observed in 15 patients (**Fig. 2**). The last patient had normal cortex of the sylvian fissure, but was included because he had dyslexia and was the father of the two children with dyslexia and PMG. The inclusion of a patient with normal neuroimaging has been previously justified [13]. The diagnosis of dyslexia was also present in nine other patients whose MRI confirmed PMG. In addition, as pointed out above, one patient with normal neuroimaging study did not undergo an MRI because of a metallic femur prothesis. These two patients with normal neuroimaging findings may have a mild cortical abnormality not yet detected by current neuroimaging techniques [13].

Twenty-two patients belonged to six unrelated kindreds with no parental consanguineity; in one family, dizygotic male twins were both affected (**Fig. 3**). Nine patients were isolated cases (**Table 2**).

Nine patients were female. Age, at the time of study, ranged from five years to 65 years (mean age of 20 years).

Prenatal events were: hypertension, twin pregnancy, vaginal bleeding or drug addiction. Labor and delivery were normal and full term for all patients with the exception of the twins (II-1 and II-2, family 4, **Table 1**) who were born prematurely at 30 weeks gestation.

Seizures were reported in six of the 31 patients: all had diffuse bilateral PMG around the Sylvian fissures. All patients had generalized tonic-clonic seizures. Patients 2 and 8 (**Table 2**) had also other seizure patterns: partial complex and infantile spasms. Of the six patients with seizures, two were controlled with antiepileptic drugs and four had remained seizure-free during the last five years and were not on anticonvulsants. The median age at onset of epilepsy was 4.3 (range: eight months to 13 years).

Neurological examinations revealed in 17 patients pseudobulbar signs like oromotor incoordination with inability to isolate the tongue from the mandible on lateral tongue movements or to protrude it. Hemiparesis was present in three patients, tetraparesis in one and microcephaly in two patients. Delayed motor

**Table 1** Characteristics of the six families with CBPS.

| Family | Pt | Age (years) | Gender | Language Dev. | Prenatal events | PIQ/VIQ | Language skill | Seizure: age/type | Neurological examination | MRI/CT |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | I–2 | 65 | F | normal | – | 102/83 | normal | | normal | PS PMG |
| | II–3 | 42 | F | normal | – | 93/80 | dyslexia | | normal | BPPP |
| | II–4 | 39 | M | delay | – | 79/NO | SLI | 13 yr/GTC/SF | pseudobulbar palsy + left hemiparesis | PS PMG |
| | II–6 | 35 | F | normal | – | 105/91 | normal | | normal | BPPP |
| | III–1 | 19 | M | delay | hypertension | 74/57 | SLI | | pseudobulbar palsy | PS PMG |
| | III–2 | 16 | M | delay | – | 95/97 | dyslexia | | normal | BPPP |
| | III–3 | 9 | M | delay | – | 97/93 | dyslexia | | normal | BPPP |
| 2 | II–9 | 44 | F | normal | – | 87/73 | dyslexia | | pseudobulbar palsy | normal (CT) |
| | II–12 | 39 | M | delay | – | 109/82 | normal | | pseudobulbar palsy | PS PMG |
| | II–13 | 37 | M | delay | – | 121/83 | dyslexia | | pseudobulbar palsy | PS PMG |
| | III–4 | 19 | M | delay | – | 123/101 | normal | | normal | BPPP |
| | III–5 | 16 | M | delay | – | 82/84 | dyslexia | | pseudobulbar palsy | BPPP + ACC |
| | III–6 | 9 | F | delay | – | 112/87 | SLI | | pseudobulbar palsy | BPPP |
| 3 | III–10 | 12 | M | delay | – | 84/66 | SLI | | normal | BPPP |
| | III–11 | 6 | M | delay | – | 90/59 | SLI | | pseudobulbar palsy | BPPP |
| 4 | II–1 | 15 | M | delay | twin pregnancy | 73/47 | SLI | 6 yr/GTC/SF | pseudobulbar palsy | PS PMG |
| | II–2 | 15 | M | delay | twin pregnancy | 104/109 | normal | | normal | BPPP |
| 5 | II–4 | 43 | M | normal | – | 116/95 | dyslexia | | normal | normal |
| | III–4 | 9 | F | delay | – | 113/105 | dyslexia | | normal | BPPP |
| | III–6 | 7 | M | delay | – | 89/98 | dyslexia | 4 yr/GTC/Con | pseudobulbar palsy + right hemiparesis | PS PMG |
| 6 | III–2 | 35 | F | normal | – | ND/ND | normal | | normal | BPPP |
| | IV–1 | 6 | F | delay | – | 90/ND | SLI | | normal | BPPP |

Pt = patient; PIQ = performance IQ; VIQ = verbal IQ; MRI = magnetic resonance imaging; CT = computed tomography; M = male; F = female; NO = not obtained; ND = not done; – = absent; GTC = generalized tonic-clonic; PS = perisylvian; PMG = polymicrogyria; BPPP = bilateral posterior parietal polymicrogyria; SLI = specific language impairment; ACC = agenesis of corpus callosum; SF = seizure free; Con = controlled with antiepileptic drug

**Table 2** Characteristics of the 9 patients with sporadic PMG.

| Pt/age, y/sex | Language Dev. | Prenatal events | PIQ/VIQ | Language skill | Seizure: age/type | Seizure frequency | Neurologic examination | MRI |
|---|---|---|---|---|---|---|---|---|
| 1/14/M | delay | – | 79/67 | SLI | none | | pseudobulbar palsy | PS PMG |
| 2/10/M | delay | – | 110/54 | SLI | 8mo/CP,GTC | seizure-free | pseudobulbar palsy | PS PMG |
| 3/13/M | delay | – | 78/59 | SLI | none | | pseudobulbar palsy | PS PMG |
| 4/10/M | delay | vaginal bleeding | 79/64 | SLI | none | | pseudobulbar palsy | PS PMG |
| 5/8/M | delay | hypertension | 79/61 | SLI | none | | normal | BPPP |
| 6/15/M | delay | vaginal bleeding | ND | ND | none | | pseudobulbar palsy + microcephaly | PS PMG |
| 7/12/M | delay | hypertension | 110/99 | dyslexia | none | | normal | BPPP |
| 8/5/F | delay | – | ND | ND | 9 mo/IS,GTC | controlled with AED | pseudobulbar palsy + tetraparesis + microcephaly | PS PMG |
| 9/8/M | delay | drug addiction | 86/71 | SLI | 18 mo/GTC | seizure-free | pseudobulbar palsy + left hemiparesis | PS PMG + HA |

IS = infantile spasms; CP = complex partial; GTC = generalized tonic-clonic; NO = not obtained; ND = not done; - = absent; Schiz = schizencephaly; PS = perisylvian; PMG = polymicrogyria; BPPP = bilateral posterior parietal polymicrogyria; SLI = specific language impairment; mo = months; HA = hippocampal atrophy; AED = antiepileptic drug

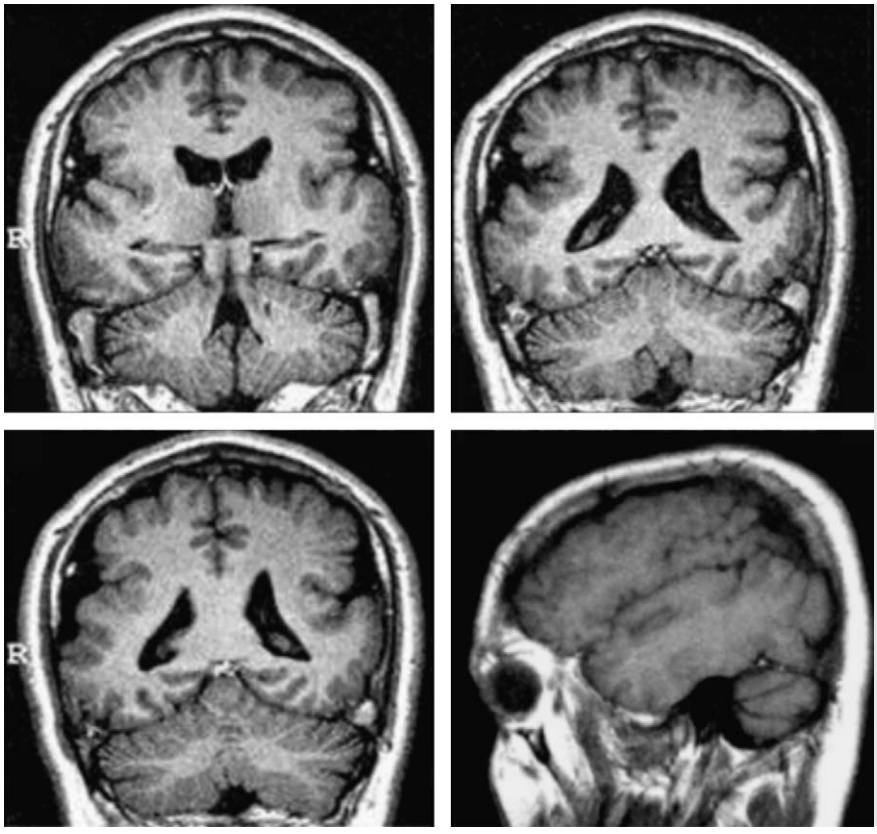

**Fig. 1** Patient II-4 (family 1). Coronal $T_1$-inversion recovery and sagittal $T_1$-weighted (bottom right) images showing diffuse polymicrogyria around the sylvian fissure.

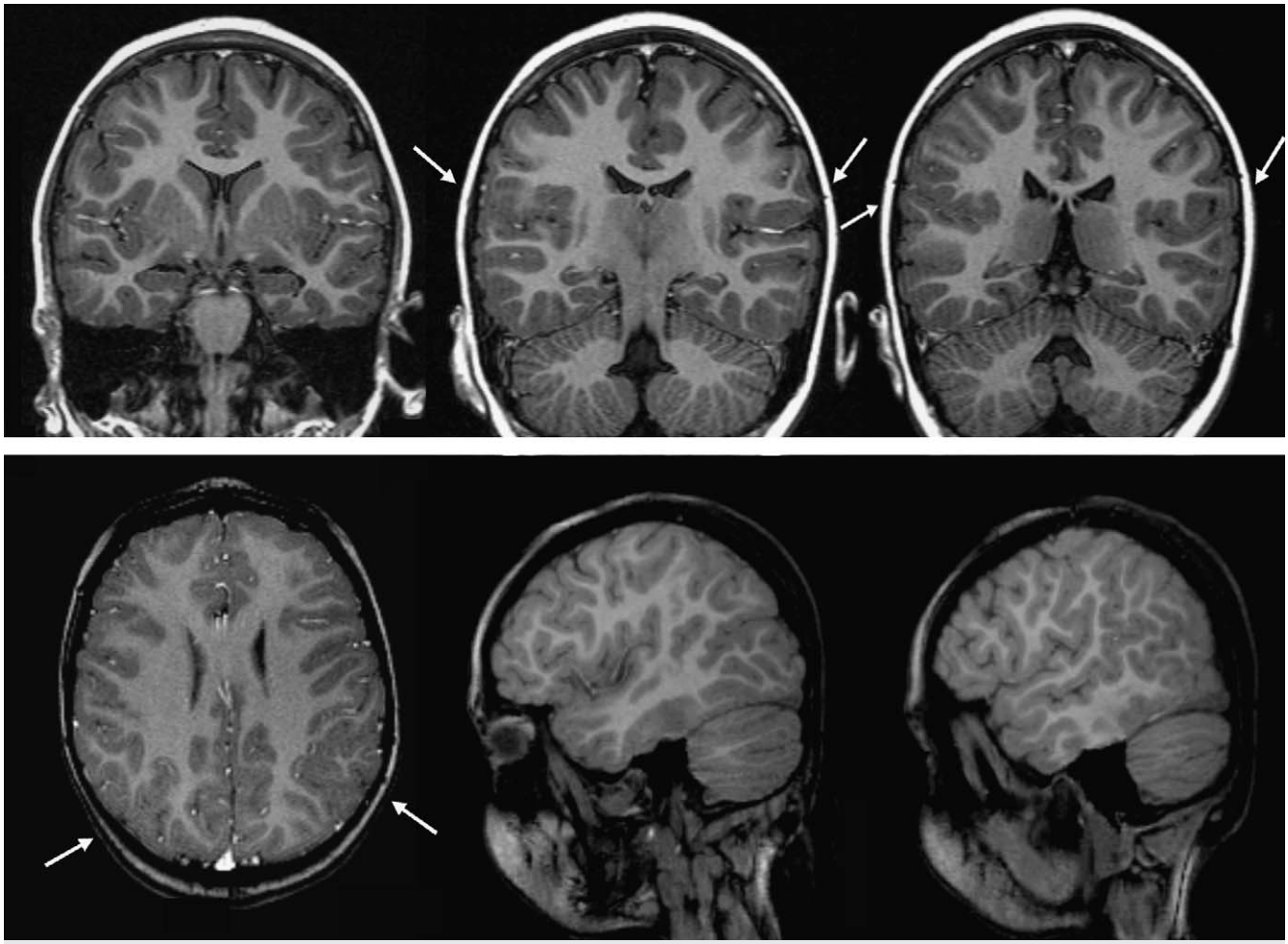

**Fig. 2** Patient IV-1 (family 6). Coronal $T_1$-inversion recovery images (top row) and axial and sagittal $T_1$-weighted images (bottom row) showing bilateral posterior PMG (arrows). Note that the anterior aspect of the sylvian fissure is spared (top left).

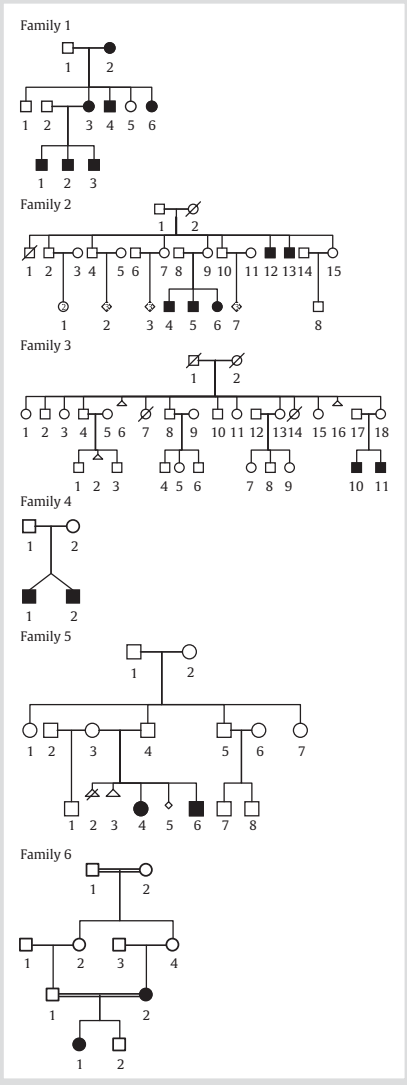


**Fig. 3** The figure shows the pedigrees of the six families.

**Table 3** Clinical presentation of familial cases versus sporadic cases of PMG.

| Characteristics | Familial PMG (n = 22) | Sporadic cases of PMG (n = 9) | Statistical analysis |
|---|---|---|---|
| prenatal events | | | |
| present | 3 | 5 | p = 0.027 |
| absent | 19 | 4 | |
| epilepsy | | | |
| present | 3 | 3 | p = 0.320 |
| absent | 19 | 6 | |
| language skill | | | |
| SLI | 7 | 6 | p = 0.088 |
| dyslexia | 9 | 1 | |
| pseudobulbar signs | | | |
| present | 10 | 7 | p = 0.131 |
| absent | 12 | 2 | |
| motor deficit other than PBS | | | |
| present | 2 | 2 | p = 0.559 |
| absent | 20 | 7 | |

PMG = polymicrogyria; PBS = pseudobulbar sign

**Table 4** Clinical presentation regarding localization of PMG.

| Characteristics | Diffuse PMG (n = 14) | BPPP (n = 15) | Statistical analysis |
|---|---|---|---|
| prenatal events | | | |
| present | 5 | 3 | p = 0.427 |
| absent | 9 | 12 | |
| epilepsy | | | |
| present | 6 | 0 | p = 0.006 |
| absent | 8 | 15 | |
| language skill | | | |
| SLI | 8 | 5 | p = 0.182 |
| dyslexia | 2 | 6 | |
| pseudobulbar signs | | | |
| present | 13 | 3 | p = 0.0001 |
| absent | 1 | 12 | |
| motor deficit other than PBS | | | |
| present | 4 | 0 | p = 0.042 |
| absent | 10 | 15 | |

PMG = polymicrogyria; BPPP = bilateral posterior parietal polymicrogyria; PBS = pseudobulbar sign

milestones with axial hypotonia were reported in only five of the 31 patients, whereas language development was delayed in 25 patients.

Language testing revealed 13 patients had specific language impairment; normal examination in six patients; and dyslexia in 10 patients. Two of the 31 patients have not yet been evaluated. In all patients evaluated, the comprehension of language was more advanced than expressive speech.

Neuropsychological assessment in 29 of the 31 patients revealed that a global cognitive deficit was not present in most of the patients.

The statistical analysis showed that (**Table 3, 4**): a) prenatal events are associated with the non-familial type of PMG (0.012); b) diffuse PMG is associated with pseudobulbar signs, as opposed to BPPP ($p < 0.001$); c) motor deficit is associated with diffuse PMG ($p = 0.042$); d) epilepsy is equally present in patients with both familial or non-familial PMG ($p = 0.346$), but is more frequently seen in patients with diffuse PMG ($p = 0.016$); e) dyslexia and SLI can be a feature of both the diffuse or BPPP ($p = 0.387$), and either familial or sporadic cases of PMG ($p = 0.210$).

## Discussion

This study presents a large cohort of patients with CBPS seen at a single medical center. The long-term follow-up of our patients allowed us to diagnose dyslexia in several patients who have had the previous diagnosis of SLI [14]. This is a new finding since a clear relationship of PMG and dyslexia had only been suggested in previous studies [14,24]. Our study is different from others because most researches addressing CBPS patients were conducted in epilepsy clinics; by contrast, our patients were accessed through the Child Neurology Outpatient Clinic, allowing the recruiting of many children with language delay, changing significantly the group of patients studied. In addition, we systematically and prospectively interview our patients and their family members according to a standard detailed questionnaire. Another point that makes our study unique in the literature is that all patients underwent a detailed language evaluation which allowed us to detect subtle clinical manifestations. Our data clearly show that when subtle manifestations are found in patients with CBPS, the possibility of familial recurrence has to

be investigated thoroughly and the matter discussed in detail with the family members seeking counselling.

### Prenatal events were associated with the non-familial type of PMG

PMG is a brain dysgenesis with a complex nosology. It is currently classified under malformations due to abnormal cortical organization (including late neuronal migration), perhaps due to vascular injuries [3,33]. The high incidence of bilateral lesions in the perisylvian region has been used as evidence for fetal hypotension and ischemic cortical damage as the underlying factor [34], but toxic and inflammatory damage cannot be ruled out [32]. In this study, prenatal events were associated with the non-familial type of PMG. Such prenatal events, particularly hypertension, in the sporadic patients, may have lead to vascular injury during cortical organization, thus causing PMG.

Although major prenatal events can be associated with several cases of the familial form of PMG, it is more often associated with the isolated cases of PMG. This is in keeping with other studies that show that PMG is frequently associated with prenatal events and a major prenatal event in an already genetically predisposed individual (familial PMG) may result in a more diffuse lesion and, consequently, a more severe phenotype [23,24]. The higher incidence of prenatal events in the sporadic patients does not automatically mean that they are responsible for the PMG.

Apart from the theories of pathogenesis from fetal injuries, a genetic contribution to the development of PMG in some patients is supported by reports of familial cases, which suggests that gene mutations may cause this brain anomaly [5,6,8,13]. We present six families, therefore our data reinforce the genetic contribution to the occurrence of PMG. These cortical regions in specific syndromes suggest that underlying genetic factors may influence cortical development in a topologically specific manner [10].

### Diffuse PMG was associated with pseudobulbar signs and motor deficit

In 60% of the patients, feeding difficulties in the perinatal period, as well as swallowing and sucking problems were reported. Speech delay was found in 91% of the cases. An explanation is that our inclusion criteria included patients and family members with speech delay or abnormal language skills. Pseudobulbar signs characterized by difficulties with palatal and tongue movements, with variable limited protrusion and lateral movements were found in 56% of our patients. Our data indicate that the extent of cortical involvement is very important in the determination of patients' neurological signs, as pseudobulbar signs were associated with diffuse PMG at the Sylvian fissure, and mild speech difficulties were associated with localized PMG at the posterior parietal region. Our data showed that motor deficit is associated with diffuse PMG as well. Patients with posterior parietal cortical involvement tended to present with milder clinical signs, as observed previously [14,22].

### Epilepsy is equally present in patients with both familial or non-familial PMG, but is more frequently seen in patients with diffuse PMG

There was no patient with refractory epilepsy in our series, as previously described by other authors [16,18,20]. Only 19% of our patients had seizures. It seems that there is no correlation between the type of epilepsy and the location of the cortical involvement [12], but our data showed that there is a positive correlation between epilepsy and the extent of cortical involvement.

### Dyslexia and SLI can be a feature of both the diffuse or BPPP, and either familial or sporadic cases of PMG

Perisylvian PMG has been associated with SLI and developmental dyslexia [14,24]. One theory assumes that dyslexia is caused by deficits of the magnocellular system that is responsible for processing fast sensory information and projects mostly to the parietal cortex. According to this theory, dyslexia could be caused by a specific parietal dysfunction [17]. To date, most individuals with dyslexia have not shown cortical lesions on brain MRI. We found patients with dyslexia and PMG extending from the Sylvian fissure to the posterior parietal regions, and in patients with isolated PMG at the posterior parietal regions. Therefore, the anatomic findings of our study are relevant to understanding the factors involved in the etiology of dyslexia. In addition, psychological assessment showed that global cognitive deficit was not present in most of the patients, although they usually presented with lower verbal IQ than performance IQ scores.

### Mode of inheritance

In this study, the analysis of the pedigrees showed that the mode of inheritance in familial perisylvian polymicrogyria appears to be genetically heterogeneous, as previously described [13]. Two different loci have been already identified for the X-linked form of the perisylvian syndrome [28,35].

We believe that the sporadic occurrence does not automatically mean that these cases are acquired, but that sporadic cases can also be caused by de-novo mutations.

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## References

1 *Barkovich AJ*, *Hevner R*, *Guerrini R*. Syndromes of bilateral symmetrical polymicrogyria. Am J Neuroradiol 1999; 20: 1814–1821
2 *Barkovich AJ*, *Kjos BO*. Schizencephaly: correlation of clinical findings with MR characteristics. Am J Neuroradiol 1992; 13: 85–94
3 *Barkovich AJ*, *Kuzniecky RI*, *Jackson GD et al*. A developmental and genetic classification for malformations of cortical development. Neurology 2005; 65: 1873–1887
4 *Barth PG*. Disorder of neuronal migration. Can J Neurol Sci 1987; 14: 1–16
5 *Bartolomei F*, *Gavaret M*, *Dravet C et al*. Familial epilepsy with unilateral and bilateral malformations of cortical development. Epilepsia 1999; 40: 47–51
6 *Borgatti R*, *Triulzi F*, *Zucca C et al*. Bilateral perisylvian polymicrogyria in three generations. Neurology 1999; 52: 1910–1913
7 *Capovilla AGS*, *Capovilla FC*. Phonologic awareness test. In: Capovilla AGS, Capovilla FC, eds. Problemas de Leitura e Escrita. São Paulo, Memnon; 2003
8 *Caraballo RH*, *Cersosimo RO*, *Mazza E et al*. Focal polymicrogyria in mother and son. Brain Dev 2000; 22: 336–339
9 *Chang BS*, *Piao X*, *Bodell A et al*. Bilateral frontoparietal polymicrogyria: clinical and radiological features in 10 families with linkage to chromosome 16. Ann Neurol 2003; 53: 596–606
10 *Chang BS*, *Piao X*, *Giannini C et al*. Bilateral generalized polymicrogyria (BGP). A distinct syndrome of cortical malformation. Neurology 2004; 62: 1722–1728

11 *Commission on classification terminology of the International League Against Epilepsy*. Proposal for classification of epilepsies and epileptic syndromes. Epilepsia 1985; 26: 268–278
12 *Gropman AL*, *Barkovich AJ*, *Vezina LG et al*. Pediatric congenital bilateral perisylvian syndrome: clinical and MRI features in 12 patients. Neuropediatrics 1997; 28: 198–203
13 *Guerreiro MM*, *Andermann E*, *Guerrini R et al*. Familial perisylvian polymicrogyria: a new familial syndrome of cortical maldevelopment. Ann Neurol 2000; 48: 39–48
14 *Guerreiro MM*, *Hage SRV*, *Guimarães CA et al*. Developmental language disorder associated with polymicrogyria. Neurology 2002; 59: 245–250
15 *Guerrini R*, *Barkovich J*, *Sztriha L et al*. Bilateral frontal polymicrogyria. A newly recognized brain malformation syndrome. Neurology 2000; 54: 909–913
16 *Guerrini R*. Genetic malformation of the cerebral cortex and epilepsy. Epilepsia 2005; 46: 32
17 *Jaskowski P*, *Rusiak P*. Posterior parietal cortex and developmental dyslexia. Acta Neurobiol Exp 2005; 65: 79–94
18 *Kobayashi E*, *Bagshaw AP*, *Jansen A et al*. Intrinsic epileptogenicity in polymicrogyric cortex suggested by EEG-fMRI BOLD responses. Neurology 2005; 64: 1263–1266
19 *Kuzniecky R*, *Andermann F*, *Guerrini R*, *the CBPS Multicenter Collaborative Study*. Congenital bilateral perisylvian syndrome: study of 31 patients. Lancet 1993; 341: 608–612
20 *Kuzniecky R*, *Andermann F*, *Guerrini R*. The epileptic spectrum in the congenital bilateral perisylvian syndrome. Neurology 1994; 44: 379–385
21 *MacBride MC*, *Kemper L*. Pathogenesis of four-layered macrogyric cortex in man. Acta Neuropathol (Berl.) 1982; 57: 93–98
22 *Montenegro MA*, *Guerreiro MM*, *Lopes-Cendes I et al*. Bilateral posterior parietal polymicrogyria: a mild form of congenital bilateral perisylvian syndrome. Epilepsia 2001; 42: 845–849
23 *Montenegro MA*, *Guerreiro MM*, *Lopes-Cendes I et al*. Interrelationship of genetics and prenatal injury in the genesis of malformations of cortical development. Arch Neurology 2002; 59: 1147–1153
24 *Oliveira EPM*, *Hage SRV*, *Guimarães CA et al*. Reading impairment associated with polymicrogyria. Brain Dev 2007 [in press]
25 *Piao X*, *Basel-Vanagaite L*, *Straussberg R et al*. An autosomal recessive form of bilateral frontoparietal polymicrogyria maps to chromosome 16q12.2-21. Am J Hum Genet 2002; 70: 1028–1033
26 *Rapin I*. Understanding childhood language disorders. Curr Opin Pediatr 1998; 10: 561–566
27 *Robain O*. Introduction to the pathology of cerebral cortical dysplasia. In: Guerrini R, Andermann F, Canapicchi R, Roger J, Zifkin BG, Pfanner P, eds. Dysplasia of Cerebral Cortex and Epilepsy. Philadelphia, Lippincott-Raven Publishers; 1996; 1–9
28 *Roll P*, *Rudolf G*, *Pereira S et al*. SRPX2 mutations in disorders of language cortex and cognition. Hum Mol Genet 2006; 15: 1195–1207
29 *Shaywitz SE*. Dyslexia. New Engl J Med 1998; 338: 307–312
30 *Stein LM*. TDE – School performance test. São Paulo, Casa do psicólogo; 1994
31 *Sztriha L*, *Nork M*. Bilateral symmetrical fronto parietal polymicrogyria. Eur J Paediatr Neurol 2002; 6: 229–232
32 *Toti P*, *Felice C De*, *Palmeri MLD et al*. Inflammatory pathogenesis of cortical polymicrogyria: an autopsy study. Pediatr Res 1998; 44: 291–296
33 *Bogaert P Van*, *David P*, *Gillain CA et al*. Perisylvian dysgenesis: clinical, EEG, MRI and glucose metabolism features in 10 patients. Brain 1998; 121: 2229–2238
34 *Bogaert P Van*, *Donner C*, *David P et al*. Congenital bilateral perisylvian syndrome in a monozygotic twin with intra-uterine death of the cotwin. Dev Med Child Neurol 1996; 38: 166–171
35 *Villard L*, *Nguyen K*, *Cardoso C et al*. A locus for bilateral perisylvian polymicrogyria maps to Xq28. Am J Hum Genet 2002; 70: 1003–1008
36 *Wechsler D*. WISC III: Wechsler Intelligence Scale for Children – Manual. 3th ed, 1981. Adapted in a Brazilian sample, 1st edn. Vera Lúcia Marques de Figueiredo. Casa do Psicólogo, São Paulo; 2002
37 *Wechsler D*. Wechsler Adult Intelligence Scale – Revised. San Antonio. Tx: The Psychological Corporartion; 1981
38 *Wechsler D*. Wechsler Preschool and Primary Scale of Intelligence – Revised. San Antonio. Tx: The Psychological Corporartion; 1989
39 *Yavas M*, *Hernandorena CLM*, *Lamprecht RR*. Phonologic assessment of children: re-education and therapy. Porto Alegre: Artes Médicas; 1992