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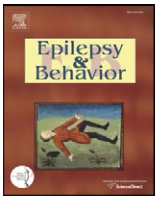

Atypical hemispheric asymmetries for the processing of phonological features in children with rolandic epilepsy

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ABSTRACT

We assessed language lateralization in 177 healthy 4- to 11-year-old children and adults and atypical asymmetries associated with unilateral epileptic foci in 18 children with benign epilepsy with centrotemporal spikes (BECTS). Dichotic listening results revealed two indices of immature functional asymmetry when the focus was left-sided (BECTS-L). First, children with BECTS-L did not show left hemisphere dominance for the processing of place of articulation, which was recorded in children with BECTS-R and control children. On the contrary, healthy children exhibited a gradual increase in left hemisphere dominance for place processing during childhood, which is consistent with the shift from global to finer-grained acoustic analysis predicted by the Developmental Weighting Shift model. Second, children with BECTS-L showed atypical left hemisphere involvement in the processing of the voiced value (+V), associated with a long acoustic event in French stop consonants, whereas right hemisphere dominance increased with age for +V processing in healthy children. BECTS-L, therefore, interferes with the development of left hemisphere dominance for specific phonological mechanisms.

1. Introduction

Benign epilepsy with centrotemporal spikes (BECTS), also known as rolandic epilepsy, is the most common form of focal idiopathic epilepsy of childhood. It is not correlated with any lesion and may be genetically determined [1]. Rare facial sensorimotor simple seizures, without alteration of consciousness, are reported between 3 and 13 years of age [2–4]. However, centrotemporal paroxysmal discharges frequently occur in the interictal period. The rolandic spikes are unilateral in 60% of cases [5,6]. The prognosis is good and the EEG normalizes by puberty [7]. The absence of neurological and intellectual deficits is considered a prerequisite for diagnosis of BECTS, and medical treatment is not necessary or restricted to small doses of valproate or carbamazepine. Therefore, psychosocial and cognitive consequences are limited in this syndrome, which offers the opportunity to assess the specific impact of subclinical epileptic activity on cognitive mechanisms.

Although the IQ of children with BECTS ranges generally within the limits of normality [8–10], it is statistically lower than in controls [11,12], even in patients who do not receive treatment [13], and 72.7% of them exhibit a deficit in at least one subtest [14]. Additionally, school difficulties are frequently reported in these patients [15,16], and they often present with specific cognitive deficits for selective attention [12,17–21], sustained attention [17,20,22], attention control and executive functions [12–14,17,22–27], short-term memory [12,13], learning [22,28], visual–spatial processing [12,19,21,29,30], visual–motor coordination [12,13,31], fine motor skills [19,22], or language [27,32–35], especially in reading [21,36–38], fluency [12,22,33,39], and phonological awareness [40].

The temporal relationship between larger number of spikes during interictal periods and neuropsychological disturbances is consistent with the occurrence of transitory cognitive impairment (TCI) directly triggered by subclinical paroxysmal activity [41,42]. Repeated subclinical epileptic activity is also suspected of inducing cerebral

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immaturity [43], resulting in enduring cognitive impairment and in atypical organization of functional hemispheric dominance if the epileptic activity is restricted to one hemisphere.

Although some studies have failed to report a relationship between lateralization of the spike focus in BECTS and specific cognitive deficits [3,13,38,44], others have provided evidence of such an association [20,45–47], which suggests a specific impact of subclinical epileptic activity on cognitive mechanisms. The anomalously large number of ambidextrous and left-handed children among patients with BECTS suggests that this syndrome may be associated with perturbations in the development of hemispheric lateralization [32]. Some studies have shown that verbal and nonverbal tasks are disturbed differently according to the side of the epileptic discharges [48–50]. For verbal processing, some authors have not reported differences associated with the lateralization of epileptic discharges [12], but others have described greater difficulties in linguistic tasks for children with a left-sided epileptic focus (BECTS-L) [10,37,47,48]. Additionally, some authors have pointed out the absence of typical left hemisphere (LH) dominance for linguistic processes in children with BECTS-L [20,29,45,46,51]. However, very few studies have precisely addressed atypical hemispheric organization for speech processing in BECTS [14,36,52], and a fine-grained investigation of hemispheric asymmetry for specific phonological features is lacking.

Dichotic listening is a useful method for assessing hemispheric asymmetry for language. Each ear is simultaneously supplied with a different speech stimulus, and the recall of information reveals a right-ear advantage (REA) in a majority of right-handers, provided that stop consonants are used [53–57]. As contralateral projections in the auditory system provide better transmission and take precedence over ipsilateral projections, the REA is assumed to reflect a dominance of LH areas in this process [58–61]. Speech is known to be processed preferentially by the LH in most right-handers, and dichotic listening offers a noninvasive procedure to quickly and validly estimate hemisphere dominance for language in presurgical candidates [62]. Dichotic listening has been successfully used to point out the decrease in functional hemispheric dominance in children with lateralized, but not benign, epilepsy [63]. Consequently, this task shows promise in the assessment of functional brain asymmetry in children with BECTS.

Researchers, however, have reported a lower REA in healthy subjects when the competing stimuli differ by voicing rather than by place of articulation [57,64,65], which suggests a lesser LH lateralization for voicing than for place processing. This is in line with the accumulated evidence for significant involvement of the RH in voicing processing, from studies on language acquisition [66] and neuropsychological investigations [67]. For instance, aphasic patients whose RH is spared are more efficient in the processing of voicing than place of articulation contrasts [68–70]. Additionally, event-related potentials (ERPs) have been recorded in healthy subjects who listened to a series of stop consonants with varying voice onset times (VOTs). ERPs from the LH varied linearly (low-level processing) with the VOT, whereas ERPs from the RH varied categorically [71,72], which suggests the role of RH areas in the categorical processing of voicing cues.

The involvement of the RH in voicing processing is not in line with the strong version of the linguistic hypothesis, whereby speech, whatever its acoustic content, triggers a specific processing mode most favorably associated with the LH. It is better accounted for by the auditory hypothesis, which suggests that some cerebral areas of the RH may be proficient in the processing of the acoustic cues of voicing. According to the asymmetric sampling in time model (AST), the temporal resolution of the analysis conducted by cerebral structures may differ between hemispheres, and the relative importance of LH and RH in speech processing may be governed by the presence of short versus long acoustic events, respectively. LH areas may preferentially extract information from short integration windows, whereas RH areas may extract information from larger ones [73]. Consequently, the rapid acoustic cues associated with place of articulation may be better processed by the LH. On the contrary, the longer integration windows used by RH areas may favor the energy envelope of syllables, prosodic phenomena, and frequency modulated sounds with slow rates of change or long duration [74]. A RH advantage has been reported for the detection of long (but not short) frequency transitions [75]. Additionally, fMRI data have revealed stronger activation in the dorsal bank of the *right* superior temporal sulcus for long segment duration [76].

Additional arguments in favor of this interpretation have recently been provided by the results of dichotic listening tasks involving pairs of words starting with stop consonants that differed in voicing. French and English are opposites with respect to the phonetic implementation of voicing contrasts in terms of long versus short VOTs. In English, the difference between voiceless and voiced stops is realized by long versus short positive VOT, respectively [77], whereas it is realized in French by the opposition of short (almost null) positive versus long negative VOT (i.e., a periodic low-frequency sound typically spanning some 100 ms before the release of the burst, for initial voiced stops). In accordance with the AST assumption, the lowest REA has been reported in dichotic listening when English voiceless stops (long positive VOT) are presented to the left ear [79]. The duration of acoustic cues of voicing seems to play a crucial role in the involvement of each hemisphere, as a decrease in REA has been observed when a French voiced stop (long negative VOT) was played to the left ear [64]. Additionally, voiced stops were more frequently reported among blend responses (i.e., erroneous responses combining the place of articulation of one of the consonants with the voicing value of the other) when a French voiced consonant was presented to the left ear.

Consequently, in the assessment of hemispheric asymmetry for speech processing with a dichotic listening task, caution is required regarding the acoustic characteristics of the stimuli. To our knowledge, four studies have used dichotic listening to assess hemispheric asymmetry in children with BECTS. They showed a decreased REA in children with BECTS-L as well as BECTS-R [36,52,79], except in one study in which all four patients exhibiting a LEA, among 20 patients, had a left-sided epileptic focus [14]. However, the authors did not take into account the type of phonological features and the corresponding acoustic cues, which may partly explain those inconsistent data. Consequently, the major purpose of our research is to investigate the impact of lateralized BECTS on the organization of functional hemispheric asymmetry. Given the importance of the duration of acoustic cues for hemispheric specialization in stop consonant processing, it is necessary to disentangle the influence of epileptic discharges and the role of the phonetic features in the stimulus pairs provided in a specific language. Before conducting such an investigation, it is also necessary to assess the developmental trajectory of the REA for word pairs opposed by voicing or place of articulation in healthy children matched for native language with the patients. The lack of appropriate standards of linguistic performance in healthy children is assumed to contribute to the paucity of knowledge of the effects of epileptic discharges on language processing [49].

Our aim is twofold: (1) we conducted a developmental investigation of the REA associated with place of articulation and voicing processing in healthy 4- to 18-year-old controls, and (2) we assessed REA in children with a left- or right-sided epileptic focus in BECTS, to elucidate some consequences of subclinical epileptic discharges on the pattern of functional organization of language.

2. Methods

2.1. Participants

The epilepsy group comprised 18 children, who were right-handed [80] and native French speakers. All met the ILAE criteria for BECTS, and the subclinical spikes were predominant in one cerebral hemisphere without contralateral shifting and secondary generalization, as attested by EEG recordings (last record during the previous 3 months). These sites were unchanged through the last two EEGs. The focus was predominant in the LH of 9 children (BECTS-L), 4 boys and 5 girls (mean age = 9 years 3 months, SD = 1 year 11 months). They were matched for age with a group of 9 children whose epileptic focus was predominant in the RH (BECTS-R), 7 boys and 2 girls (mean age = 9 years 1 month, SD = 19 months). Their histories included neither prenatal cerebral injury nor neurological defects. Moreover, clinical features were in accordance with EEG findings. Demographic and clinical data are summarized in Table 1. The patients had experienced rare clinical seizures: mean = 2.6 (SD = 1.8) for the BECTS-L group, and mean = 3.2 (SD = 1.6) for the BECTS-R group. The mean age at onset of seizures was 7 years 1 month (SD = 3 years) in BECTS-L and 5 years 8 months (SD = 1 year 7 months) in BECTS-R. No child in the sample was mentally retarded, and the main neuropsychological data are summarized in Table 2. Children were examined by a neuropediatrician or neurologist and by a neuropsychologist. They were free from behavioral and psychiatric problems. However, one of the children with BECTS-L was dyslexic and another had attention-deficit/hyperactivity disorder (ADHD). Among the patients with BECTS-R, two had specific language impairment (SLI), patient 12 had ADHD, patient 11 also had ADHD but was being treated with methylphenidate, and another patient had attention problems. Every child attended regular classes in school, but one patient with BECTS-L and two patients with BECTS-R had repeated a year at school. Nine patients (4 BECTS-L and 5 BECTS-R) were being treated with small doses of valproate (in combination with ethosuximide in one BECTS-L case); two patients with BECTS-R were being treated with methylphenidate. Three patients with BECTS-L and three patients with BECTS-R were receiving treatment to reduce interictal activity: in the BECTS-L group, one child was taking clobazam, one sulthiame, and another ethosuximide, and in the BECTS-R group, three patients were taking clobazam.

The control group comprised 54 children. Each patient was matched with three controls for age and sex. They were selected from the group tested in the developmental section of our study. A total of 177 healthy subjects participated in the experiment. All were right-handed and native French speakers. They were divided into eight age groups: 4–5 years ($n = 9$, 4 girls); 5–6 years ($n = 10$, 5 girls); 6–7 years ($n = 30$, 18 girls); 7–8 years ($n = 28$, 16 girls); 8–9 years ($n = 28$, 13 girls); 9–10 years ($n = 27$, 18 girls); 10–11 years ($n = 21$, 14 girls); adults ($n = 24$, mean age = 25 years 3 months, 17 girls). The children were recruited from elementary schools. Their teachers confirmed that they had not had particular difficulty at school and they had not repeated a year. Adult participants were undergraduates, and their results were previously reported [64].

Hearing of all participants was tested by determining ascending and descending thresholds for each ear individually for pure tones of 250, 500, 750, 1000, 2000, 4000, 6000, and 8000 Hz. No participant had interear threshold differences greater than 10 dB. The absolute hearing threshold for each ear was found to be below 20 dB, except in very few speakers whose threshold was higher for specific frequencies (typically, 6000–8000 Hz). Adults were rewarded with bonus course credits, and written informed consent was obtained from the children's parents before the study.

2.2. Stimuli and procedure

Fifteen pairs of rhyming CVC French words differing only in the first consonant (/p, b, t, d, k, g/) were used. The vowel was always /a/. In the V condition, the initial consonants of the words of each pair differed only in voicing; in the P condition, they differed in place of articulation; and in the VP condition, they differed in both voicing and place. The test words starting with a voiceless stop had a much higher lexical frequency than their voiced counterparts, which reflects the higher frequency of voiceless stops at the beginning of French words. More information about those characteristics and the acoustic details of the stimuli can be found elsewhere [64, p. 135]. Each member of a word pair was presented to the left and the right ears equally. The dichotic material was presented in four runs of 36 trials each (total = 144 trials), which were punctuated by rests. Temporal alignment between the right and left channels was set at the first period of the large-amplitude vocalic portion of the syllables (for similar alignment in Finnish, i.e., another language in which prevoicing also occurs in voiced consonants, see [81]). The subjects reported that they could hear only one single word, as in the English Fused Dichotic Word Test (FDWT) [82], which has the advantage of being almost not influenced by attention manipulations [83]. Both syllables were matched for peak intensity. The signals were played through Beyerdynamic DT 770 Pro headphones. Testing took place in a soundproof booth for adults and in a quiet room at school for children. The experiment was run with the Praat program.

The participants did not know that the syllables within dichotic pairs were not alike and they were simply informed that the signal was slightly altered. They were required to "focus on the center of their head" to identify the word and immediately report it aloud. At the start of the experiment, they heard the list of stimuli in binaural

Table 1
Demographic and clinical data of the patients diagnosed with BECTS included in the study.

Case	Age at evaluation (years;months)	Sex	Side of EEG focus	Age at Onset (years;months)	Number of seizures	AED/other treatment	Neuropsychological disorder	Years repeated at school
01	7;3	M	Left	4;6	Unknown	VPA + CLB[a]	–	–
02	11;5	F	Left	5	2	VPA	Delay in language acquisition + dyslexia	–
03	10;5	M	Left	2	5	VPA	–	–
04	10;4	F	Left	7	5	SLT	–	–
05	10;7	M	Left	9;10	1	None	–	–
06	6;0	F	Left	nr	Unknown	None	–	–
07	12;4	F	Left	12	1	None	ADHD	1
08	9;5	F	Left	6;5	3	VPA + ESM	–	–
09	10;8	M	Left	10	1	None	–	–
10	10;4	M	Right	4;6	Unknown	VPA	SLI	1
11	8;11	M	Right	6;6	3 or 4	VPA + MPH	SLI + ADHD	1
12	8;3	M	Right	5;10	1	None	ADHD	–
13	11;3	M	Right	3;6	3 or 4	CLB	–	–
14	8;1	M	Right	3	Unknown	CLB	–	–
15	11;1	M	Right	7;3	Unknown	MPH	Attention disorder	–
16	7;4	F	Right	7;2	2	VPA + CLB	–	–
17	7;0	F	Right	6;10	Unknown	VPA	–	–
18	9;3	M	Right	6;2	5	VPA	–	–

[a] CLB, clobazam; ESM, ethosuximide; MPH, methylphenidate; SLT, sulthiame; VPA, valproate; SLI, specific language impairment.

Table 2
Neuropsychological data of patients diagnosed with BECTS included in the study.

Case	Side of EEG focus	Verbal index			Nonverbal index		WISC-IV Working Memory Index (WMI)	WISC-IV Processing Speed (PS)
		EVIP[a]	WISC-III Verbal IQ	WISC-IV Verbal Comprehension index (VCI)	WISC-III Nonverbal IQ	WISC-IV Perceptual Reasoning index (PRI)		
01	L			112		92	91	73
02	L		95		114			
03	L			120		94	133	115
04	L			84		90	103	73
05	L			101		104	94	93
06	L			122		116	94	131
07	L			79		88	82	103
08	L			110		92	91	76
09	L			110		90	109	96
10	R		76		79			
11	R			49		96	62	66
12	R			88		71	82	96
13	R			132		128	103	88
14	R	116				Matrices[b] = 50–75th percentiles		
15	R			98		77	79	81
16	R			122		99	94	88
17	R			Vocabulary[c] = 9 (−0.33 SD, 37th percentile)		Matrices[c] = 12 (+0.66 SD, 75th percentile)		
18	R			116		128	97	103

[a] French version of the Peabody Picture Vocabulary Test—Revised.

[b] Matrices: Raven's Matrices subtest.

[c] Subtests of WISC-IV.

presentation to become familiar with the words, and they were invited to recall each word aloud. In this practice list, the experimental stimuli were mixed with all the other words, which shared the same rhyme but differed in the initial consonant, to allow the participants to hear the stimuli, but also their lexical competitors.

2.3. Data analysis

For each participant, the number of correct CVC recalled from the right and left ears was determined in the three conditions, and the λ value was calculated for each condition as

$$\lambda = \ln\left(\frac{R+1}{L+1}\right),$$

where ln is the natural logarithm, R is the number of responses to the right ear, and L is the number of responses to the left ear [84]. It is considered to be particularly reliable and does not depend on overall accuracy [85–87]. A positive λ indicates a REA, a negative λ a LEA.

A significance level of $P<0.05$ was adopted throughout. With respect to healthy participants, an analysis of variance with repeated measures was conducted on the λ coefficient, with age (4–5, 5–6, 6–7, 7–8, 8–9, 9–10, 10–11 years and adults) as the between-subject factor, and condition (V, P) as the within-subject factor. Post hoc differences were computed using Scheffe's test, a very conservative procedure that can be used despite unequal sample sizes. The VP condition was not integrated into this analysis, as a specific phenomenon was observed in this condition: many blend responses were made by combining the place of articulation of one word with the voicing value of the other word. Consequently, the REA was computed on fewer accurate responses and it could not be directly compared with the REA observed in the V and P conditions. Subsequent analyses of blend errors have been conducted to appreciate the involvement of each hemisphere in the VP condition. We evaluated whether the voicing value (+V or –V) of the response was taken from the stimulus played to the right or to the left ear. In addition, some participants consistently reported the same member of a pair regardless of ear of presentation. The pairs for which all the responses given by a participant reflected such a stimulus dominance effect are considered an obstacle to an accurate measurement of auditory asymmetries [88]. They were therefore discarded [82,89].

The λ values for REA were compared between patients with BECTS-L, those with BECTS-R, and control children, separately in conditions V and P, using the Mann–Whitney U test. Additionally, the Wilcoxon test was used to evaluate the condition effect (V vs L) in each group and to test if the percentage of blend responses beginning with a +V consonant was higher when this voicing value had been extracted from the left or the right ear.

3. Results

As illustrated in Fig. 1, the REA was higher when the two words differed by place of articulation than by voicing, $F(1, 169)=93.99$, $P<0.0001$, $\eta^2=0.36$, and it progressively increased with age, $F(7, 169)=2.61$, $P<0.014$, $\eta^2=0.10$. The proportion of children exhibiting a LEA sharply decreased in the youngest groups of children. A LEA was indeed recorded in 33% of the 4- to 5-year-olds, whereas it

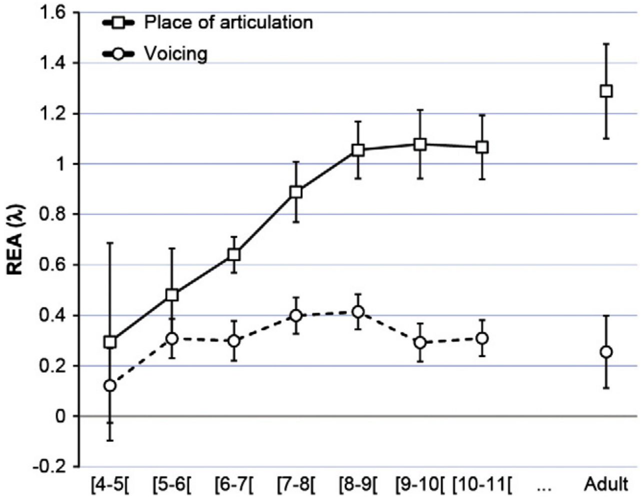

Fig. 1. Mean right-ear advantage (REA), calculated as the lambda value in healthy participants, when the two words differed in voicing or in place of articulation. Vertical bars represent SE.

was observed in only 11% of the 5- to 6-year-olds and in 6% of the 6- to 7-year-olds.

A significant Condition × Age interaction, $F(7, 169)=3.59$, $P<0.0012$, $\eta^2=0.13$, was due to the increase in REA with age in the P condition, $F(7, 169)=3.92$, $P<0.0006$, $\eta^2=0.11$, but not in the V condition, $F(7, 169)<1$. A higher REA was recorded in the P condition than in the V condition, except in the 4- to 6-year-olds. From 6 to 7 years of age, children exhibited a higher REA in the P than in the V condition, and the size of this difference progressively increased according to η^2 values: $F(1, 29)=10.47$, $P<0.003$, $\eta^2=0.25$ in 6- to 7-year-olds; $F(1, 27)=19.38$, $P<0.0002$, $\eta^2=.42$, in 7- to 8 year-olds; $F(1, 27)=29.56$, $P<0.0001$, $\eta^2=0.52$ in 8- to 9 year-olds; $F(1, 26)=31.12$, $P<0.0001$, $\eta^2=0.54$ in 9- to 10-year-olds; $F(1, 20)=32.97$, $P<0.0001$, $\eta^2=0.62$ in 10- to 11-year-olds; and $F(1, 23)=42.46$, $P<0.0001$, $\eta^2=0.65$ in adults.

The analysis of blend responses revealed that the participants frequently combined the voicing value of one word with the place of articulation of the other, as illustrated in Fig. 2, and such responses preserved the voiced value (+V) more frequently than the voiceless value (−V), $F(1, 169)=235.82$, $P<0.0001$, $\eta^2=0.58$. The difference between +V and –V consonants word-initially in blend responses varied with age, $F(7, 169)=5.49$, $P<0.0001$, $\eta^2=0.19$, with better preservation of +V in blend responses from 6 to 7 years of age. Additionally, blend responses beginning with a voiced consonant were more numerous when +V was extracted from the left ear than from the right ear, $F(1, 169)=71.69$, $P<0.0001$, $\eta^2=0.30$ (Fig. 3). This effect of the ear on the preservation of +V in blend responses interacted with age, $F(7, 169)=3.26$, $P<0.003$, $\eta^2=0.12$, because it was significant in each age group, except in 4- to 5-year-old children. On the contrary, the ear of presentation of –V did not affect the percentage of blend responses beginning with a voiceless consonant, $F(1, 169)<1$, and did not interact with age.

With respect to the patients, the REA in the P condition was lower in children with BECTS-L than in children with BECTS-R, $z=-2.34$, $P=0.019$ (Fig. 4). Additionally, the REA was higher in the control group than in the BECTS-L group, $z=-3.40$, $P<0.0007$, but did not differ from the REA of children with BECTS-R in this condition, $z=-0.14$, $P=0.89$. On the contrary, there was no statistically significant difference in REA in the V condition between the two groups of patients, $z=-0.09$, $P=0.93$, and the REA of the control group did not differ from the REA of children with BECTS-L, $z=-0.56$, $P=0.57$, or children with BECTS-R, $z=-0.44$, $P=0.66$. As illustrated in Fig. 4, children with BECTS-R exhibited a higher REA in the P condition than in the V condition, $z=2.52$, $P=0.0117$, like control children, $z=6.14$, $P<0.0001$, whereas REA did not differ between these two conditions in children with BECTS-L, $z=0.42$, $P=0.67$.

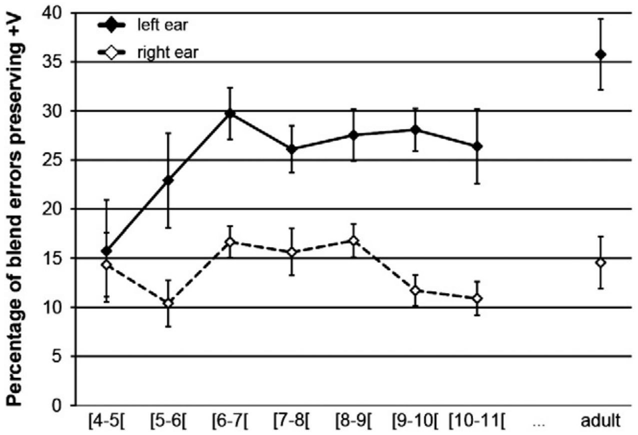

Fig. 3. Percentage of blend errors preserving the voiced (+V) feature, when +V was presented to the left ear or to the right ear. Vertical bars represent SE.

Finally, analyses conducted on the blend responses that preserved +V showed that this voicing value was more frequently extracted from the left ear in control children, $z=5.03$, $P<0.0001$, and in children with BECTS-R, $z=2.67$, $P<0.008$, but not in children with BECTS-L, $z=1.86$, $P=0.063$. This atypical absence of difference in children with BECTS-L reflected anomalously frequent extraction of +V from the right ear in this group. Indeed, controls and children with BECTS-L made respectively 27.8 and 27.2% blend errors preserving +V when +V was played to the left ear, whereas they respectively made 14.7 and 21.8% blend errors preserving +V when +V was played to the right ear.

4. Discussion

Our study combined a developmental investigation of the REA associated with place of articulation and voicing processing in dichotic listening with the evaluation of the impact of lateralized spikes in BECTS on hemispheric asymmetry for the perception of these phonological features.

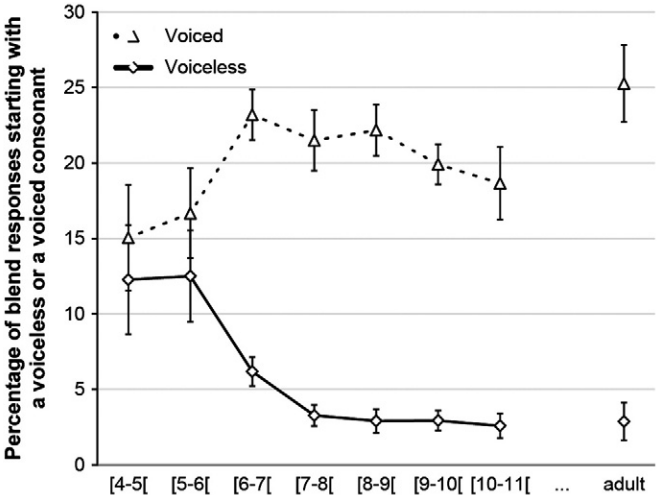

Fig. 2. Percentage of blend errors combining the place of articulation of one word with the voicing value (voiced or voiceless) of the other. Vertical bars represent SE.

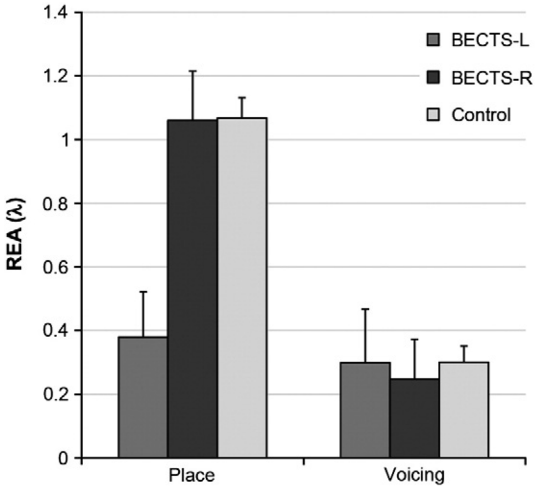

Fig. 4. Mean right-ear advantage (REA) when the words differed by place of articulation or voicing in the two groups of patients and the controls. Vertical bars represent SE.

4.1. Developmental trajectories of right ear advantage for place and voicing

Regarding healthy subjects, we observed a reliable REA from 5 to 6 years of age, whereas it was not systematic in 4- to 5-year-olds. Emergence of REA at 5 is consistent with the recording of LH dominance for dichotic listening in similar age groups [82,85–94] and its absence in a 4-year-old group [91]. Therefore, by using words and a fused dichotic procedure, the LH dominance for speech processing can be efficiently assessed from 5 years of age. In younger children, other procedures should be used (see, e.g., [95] for experimental devices not requiring overt verbal responses and explicit identification of phonemes).

Additionally, the increase in REA with age provides a new argument for the gradual process of functional hemispheric lateralization during the first decade [96], with a sharp rise between 4 years and 8–9 years and a gradual increase until adolescence. This replicates the REA enhancement previously observed between 4 years 2 months and 7 years 7 months [97] and the less systematic REA recorded in 9-year-olds compared with adults [98]. However, incompatible results have been reported in studies that failed to show any change in REA with age, for instance, from 6 to 12 years [99] and from 5 to 11 years [90]. One possible explanation for the difficulty in observing a clear development of REA during childhood in the latter two studies could be the nonlexical status of the stimuli presented to children, as words engage LH areas more strongly than nonlexical speech stimuli [100–102]. Moreover, our study showed that REA magnitude varies with the type of phonological feature, a factor that was not systematically taken into account in previous studies.

One of the main results of our study is the variation in children's REA magnitude according to the type of phonological feature manipulated in dichotic pairs, an effect that was previously reported in adults [57,64,65]. Although the increase in REA with age is significant on the whole, it is due only to the enhancement of LH dominance for dichotic words differing by place of articulation. Clearly, such a difference in REA suggests that specific mechanisms are entailed by the perception of different speech-related cues. The difference in functional hemispheric asymmetry for place of articulation and voicing is not statistically significant in 4- to 6-year-old children, but it starts at about 6–7 years, with a gradual increase until adulthood. Although a clear REA is already observed as soon as 5 years of age, the difference in REA for place and voicing emerges slightly later. It can be noted that the most salient part of the rise in LH dominance for place of articulation is concomitant with a crucial period for learning to read and the acquisition of automatisms regarding grapheme–phoneme correspondence. This change occurs at a period when children are also known to improve their metaphonological skills [103] and exhibit refined organization of phonological knowledge at the phonemic [104] and subphonemic [105] levels. The strong requirements of reading acquisition in terms of phonological organization may entail growing specialization of the cerebral substrates of subphonemic aspects, resulting in the observed increase in REA for one specific kind of phonological feature. The frequently reported weaker REA [106,107] and the reduced involvement of the LH in phonemic categorization in dyslexic persons [108] are consistent with this idea.

In our study, the difference in REA for place and voicing increased throughout childhood. The reported gradual increase in the magnitude of LH dominance for place processing until late childhood is in line with the long developmental progression of other phonological processes, such as boundary precision in phoneme identification increasing beyond 9 years [109,110], the consistency in phonemic contrast categorization increasing beyond 12 years [111], and the sensitivity to some acoustic parameters increasing from 3 years of age toward adulthood [112,113].

The developmental pattern allows specifying that the setting up of the difference in REA for place and voicing processing is not due to any change in the symmetric involvement of both hemispheres in voicing processing, but rather to the gradual deepening of the LH dominance in place processing. We propose interpreting the increasing role of the LH in place processing as a cerebral correlate of important developmental changes regarding attention given to acoustic cues for this phonological feature. According to the Developmental Weighting Shift (DWS) theory [114,115], children start out processing speech globally. By gaining linguistic experience, they are assumed to become more analytical and to rely on finer-grained phonetic information, which results in weighting more heavily smaller acoustical cues. In the case of prevocalic stop consonant processing (as in our experiment), formant transitions are supposed to provide the initial perceptual cues for young children [116, but see 117 for alternative accounts]. Such dynamic spectral information reflects the influence of both consonants and vowels. Subsequently, children are supposed to gradually differentiate shorter-duration segments [115]. Place identification undergoes modification beyond the 11-year-old level, with increasing weight given to short-time spectral characteristics at stimulus onset [118]. This process requires the integration of properties extracted from a short time window spanning the region of rapid spectral change between the noise burst and vowel onset [119]. In adults, brief stimuli with a voicing interval as short as 10 ms provide cues to place of articulation [120].Younger children have been shown to process short informative cues less efficiently [116,118,121]. Therefore, the minimum window size seems to narrow with age. The increased ability to integrate information within short intervals is consistent with the enhancement in REA with age that we observed for place of articulation. Indeed, according to the AST model, LH areas may preferentially extract information from short temporal windows, whereas RH areas may extract information from larger ones [73], by analogy with hemispheric asymmetries for local versus global visual structure processing [122–124].

Therefore, an association can be inferred between increased recruitment of LH areas with age in dichotic processing of place of articulation and greater reliance on small acoustic cues to process speech with age. Various factors may contribute to the specific impact of this phenomenon on place processing. One reason could be the difficulty in finding invariant acoustic cues for perception of place of articulation across vowel contexts and, consequently, the necessity to refine speech processing regarding this component to increase lexical knowledge. Although a generalized psychoacoustic mechanism is used by humans and monkeys for VOT and manner of articulation processing, the development of human-specific mechanisms has been shown to be triggered by the lack of invariance in the acoustic cues related to place of articulation [125].

4.2. Early involvement of the right hemisphere in voicing processing

The findings on the low REA associated with voicing in adults and children contribute to the growing body of evidence supporting the specific involvement of the RH in the processing of this feature [57,64–72]. However, two changes were recorded for voicing during childhood.

First, we observed the development of a strong dominance of voiced consonants in blend errors. It contrasts with the opposed dominance observed in English [78,126]. In English, the dominance of voiceless stops has been attributed to a temporally salient acoustic cue (long VOT) in these consonants. In French, the dominance of voiced stops cannot be attributed to lexical frequency effects [64]. The minimal effect of nonsensory variables on this dominance suggests that it may be considered as a bottom-up factor [127]. Because of the occurrence of the low-frequency signal during closure (voice bar), CVCs starting with a voiced stop begin earlier than CVCs starting with a voiceless stop. The higher salience of the voiced value in French may be induced by this temporal acoustic superiority [64]. The present results suggest that the sensitivity to such temporal differences increases during childhood, with a dramatic improvement by 6–7 years of age, a period when refined phonological processes are required for learning to read.

Second, the pairing of voiced and unvoiced consonants in the VL condition resulted in more blend errors starting with a voiced stop if the voiced value was extracted from the left ear rather than from the right ear. This asymmetry did not show in the 4- to 5-year-olds, but it was significant from 5 to 6 years, with additional increase in the magnitude of this effect until adulthood. This late developmental progression provides new evidence for the strengthening of hemispheric specialization in the processing of specific subphonemic aspects during childhood. Analogous developmental effects were reported on the modulating impact of voicing features on ear advantage in 5- to 8-year-old children recruited in western Norway [128]. In reference to the AST model [73,74], better processing of the French voiced value in stops when played to the left ear can be attributed to the preference of the RH for extracting information from large integration windows, fitting with long acoustic cues [75,76]. The present data show that this hemispheric specialization proceeds from a long developmental progression.

Therefore, the developmental section of this research reveals important changes in hemispheric asymmetries for the processing of subphonemic details of speech during childhood. Taken together, the results indicate the need to improve our understanding of the developmental trajectories of these phenomena in healthy children before assessing their disturbance in children with epilepsy. Additionally, the onset of BECTS classically occurs during the period when these functional hemispheric asymmetries are in progress, and it could interfere with this maturational process.

4.3. Lateralized epileptic focus in BECTS and hemispheric asymmetry for speech processing

The most significant outcome of this study concerns the finding that benign idiopathic epilepsy of childhood with lateralized subclinical spikes disturbs the typical hemispheric asymmetries in phonological processing.

As far as place of articulation is concerned, children with BECTS-L exhibited a lower REA than both controls and children with BECTS-R. BECTS-L indeed entails an REA that is as low for place as for voicing processing. This suggests that, in the absence of obvious lesions and seizures, left-lateralized subclinical epileptic discharges may alter the LH dominance for subtle aspects of phonological processes. This is in line with indices of bilateral organization of language function in children with BECTS-L, as compared with controls and children with BECTS-R [29,32,33]. However, to our knowledge, except in one case [14], previous dichotic experiments involving children with BECTS failed to provide evidence for a selective impact of lateralized discharges [36,52,79]. In the present study, we showed that atypical asymmetry in dichotic listening performed by children with BECTS has to be assessed for specific and fine-grained aspects of phonology. Thus, our data further support the role of the side of the epileptic discharges and provide additional evidence for the reduced specialization of the epileptic hemisphere in this benign pathology. They therefore support the "lesion effect pattern" in the case of subclinical discharges, modulated by the side of the epileptic focus.

More precisely, by independently assessing REA for place and voicing, our study provides two lines of evidence for disturbance in the development of hemispheric specialization in the phonological domain. On the one hand, the anomalously low involvement of LH areas in place processing suggests that children with BECTS-L do not shift from an immature and global phonological strategy (probably centered on dynamic spectral cues in formant transitions) to a more analytical strategy extracting small acoustic aspects from the region of rapid spectral change between the noise burst and vowel onset [115,119]. In other words, by selectively impairing left-lateralized areas, a left-sided focus in BECTS may disturb typical development of fine-grained phonological processes. Immaturity in functional cerebral organization subserving speech processing is consistent with frequently observed language deficit in children with BECTS [12,21,22,27,32–40], and particularly with verbal impairments selectively associated with BECTS-L [10,37,47,48].

On the other hand, the LH of children with BECTS-L exhibited surprising proficiency in +V processing, according to the frequent blend errors in which +V was preserved when it was extracted from the right ear. On the contrary, the developmental section of our study provided evidence for an increase in RH involvement in +V processing between 4–5 years and adulthood. That is why the high preservation of +V presented to the right ear (i.e., LH) is surprising in patients with BECTS-L. This result suggests that the LH not only fails to develop abilities in the processing of fine details to identify place of articulation, but additionally handles acoustic cues that are classically better processed by RH areas (i.e., long voice bar in French +V). Although the side of the diagnosed focus may not be considered absolute and definitive during the active phase of the BECTS, our results provide new evidence for the specific impact of side of focus on hemispheric functional lateralization in language processing.

In our study, some of the patients had additional disorders or received medical treatments, which may have an impact on performance and on the development of hemispheric specialization. First, ADHD may reduce the REA in dichotic listening, as it has been shown to do so, for example, in unmedicated adults with ADHD [129]. However, this decrease in LH specialization was eliminated in experiments requiring focused attention. Consequently, this hemispheric difference has been interpreted to be due to management of available resources rather than to inherent incapacity of LH areas in speech processing. In our experiment, it was possible to adapt the testing conditions to attention difficulties of participants. Indeed, three rests punctuated the test, and a pair of stimuli was played only when the experimenter triggered the new item by clicking the mouse. These characteristics were designed to stop testing if the participant's behavior gave cues of inattention. Moreover, in our experiment, the numbers of unmedicated patients with ADHD in the groups were equal: one was in the BECTS-L group and the other in the BECTS-R group. A third patient with ADHD was recruited in the BECTS-R group, but he was treated (methylphenidate). Additionally, although ADHD could reduce the REA in some studies, it can be seen in Fig. 5 that the REA in our experiment was not strictly determined by this attention disorder, as patients 7 and 12 did not have the smallest REA among our patients.

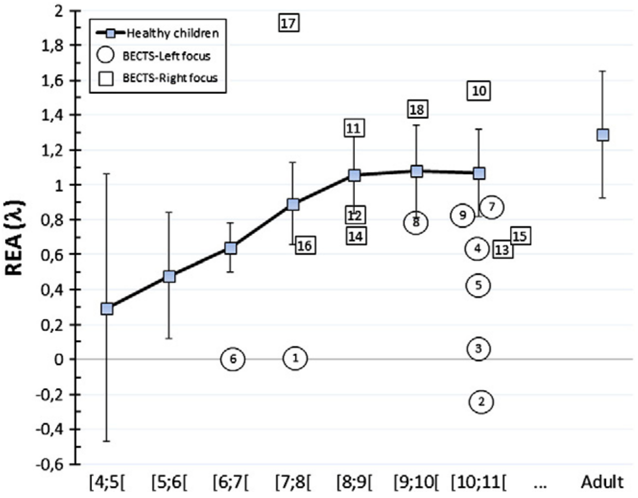

Fig. 5. Mean right-ear advantage (REA) when the words differed by place of articulation in each patient and in children with typical development. Vertical bars represent 95% confidence intervals.

Second, two patients with BECTS-R were diagnosed with SLI. Although a reduced REA could be assumed to occur in children with important language deficiencies, the responses of these two patients with SLI did not reflect such a decrease in LH dominance (Fig. 5). Consequently, it cannot be said that the SLI of these patients with BECTS-R was a determinant factor in the reduced REA associated with BECTS-R in our study.

Third, many patients in our sample were taking AEDs. Some treatments (namely, clobazam, ethosuximide, and sulthiame) are considered effective in suppressing interictal epileptiform discharges. Thus, they may diminish the negative impact of BECTS on cognition and reduce the risk of disruption in hemispheric functional asymmetries. However, the proportions of patients who received one of these three AEDs were balanced across groups: three children with BECTS-L (patients 01, 04, 08) and three children with BECTS-R (patients 13, 14, 16). Nevertheless, there were differences in the treatment of patients in our study, leading to modulation of the conclusion, although the location of these six patients in Fig. 5 does not suggest any direct relationship between preservation of the REA and treatments assumed to suppress interictal spikes.

As our experiment was not designed to investigate a direct link between hemispheric dominance and epileptic discharges, it is not possible to infer the etiology of atypical hemispheric asymmetry in BECTS. It could be the result of transitory impairment concomitant with the occurrence of epileptic discharges [41,42]. The repetition of paroxysmal activity and specific inhibition occurring mainly in the same cortical area may also produce chronic effects in the immature brain, resulting in enduring cognitive impairment [43,45]. The mechanism by which repeated subclinical spikes may modify functional hemispheric asymmetry is still undecided. To obtain the restricted diffusion of paroxysmal activity, neuron hyperpolarization is known to occur in the neighboring cortical areas, resulting in "specific surround inhibition," which could disturb cerebral functioning [130]. In addition, the slow wave following the spike is sometimes considered a source of transitory cognitive impairment [131].

The negative impact of BECTS-L on hemispheric specialization in place of articulation processing, which probably reflects disturbance in the development of fine-grained phonological processes, addressed the issue of indications for medical treatment in benign epilepsy of childhood. With respect to treatments designed to suppress interictal EEG abnormalities, several factors may be taken into account. First, neuropsychological assessment may reveal if the cognitive deficiencies observed in a patient with BECTS result from developmental learning disabilities (SLI or dyslexia) or ADHD rather than benign epilepsy. Treatment is indicated if sudden regression occurs in cognitive abilities, which is very different from cognitive deficiencies related to developmental learning pathologies (SLI, dyslexia, etc.). Additionally, the association of abundant spikes with an early onset of epilepsy or with a progressive decrease in cognitive abilities with age is an appropriate indication to consider stopping seizures and reducing interictal discharges. Progressive decrease in cognitive abilities can be diagnosed only if the initial neuropsychological investigation was conducted as early as possible in the patient with BECTS, because it provides the basis for assessment of further atypical cognitive development. Designing experiments such as our dichotic listening task may contribute to enrichment of the neuropsychological assessment of young patients with epilepsy, mainly regarding cerebral functional organization.

To sum up, both sets of results converge to demonstrate that LH areas of children with BECTS-L are fundamentally impaired in developing specialization in fine acoustic detail extraction from short integration windows. Both the previous developmental investigation in this study and the DWS model provide accurate contexts to illuminate the indices of atypical functional asymmetry observed in children with BECTS-L regarding speech processing. Conclusions should be modulated in light of the small number of patients assessed in this study. However, the reduced involvement of the LH in place of articulation processing and its atypical role in the voiced value of French stop consonants in children with BECTS-L highlight specific alterations of functional cerebral specialization by subclinical epileptic activity itself, despite the "benign" aspect of the electrophysiological pathology.

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