Temporal Lobe Impairment in West Syndrome: Event-Related Potential Evidence

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Objective: This study investigates auditory processing in infants with West syndrome (WS) using event-related potentials (ERPs).

Methods: ERPs were measured in 25 infants with mainly symptomatic WS (age range = 3–10 months) and 26 healthy term infants (age range = 3–9 months) using an auditory novelty oddball paradigm. The ERP recordings were made during wakefulness and repeated in stage II sleep.

Results: The obligatory components (P150, N250, P350) and novelty response components (P300, Nc) were recordable during both sleep and wakefulness in patients and controls. All ERP latencies decreased with age in controls but not in the WS group (age $\times$ group interaction, $F = 22.3$, $p < 0.0001$). These ERP latency alterations were not affected by pharmacological treatment for WS.

Interpretation: This study demonstrated a persistently altered ERP signature in patients with a recent history of infantile spasms. The prolongation of auditory obligatory and novelty ERPs in WS patients indicates a severe failure of temporal lobe maturation during infancy. It remains to be investigated whether this predicts long-term cognitive impairments characteristic for this epileptic encephalopathy.

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Epilepsies of childhood have a strikingly high incidence of behavioral, psychiatric and cognitive disorders.[1–4] West syndrome (WS), which affects about 1 in 3,000 live births, is the commonest severe epilepsy syndrome.[5,6] It presents at 4 to 6 months of age with epileptic spasms (infantile spasms [IS]), characteristic electroencephalographic (EEG) changes, and psychomotor regression.[7] The two-fifths of children with WS who have lesions[8] are more likely to experience seizure intractability[9] and marked cognitive and social impairment.[10] The epilepsy in this subgroup of symptomatic WS patients is a significant determinant of outcome.

Prospective studies of children with perinatal brain injury and with tuberous sclerosis found that those who developed WS regressed in visual and cognitive abilities.[11,12] These observations are consistent with epileptiform activity impairing long-term cognitive and neurological function beyond that observed from the underlying brain lesions alone. The pathophysiological basis of the term *epileptic encephalopathy*[13–15] remains unclear, however. Preliminary evidence would suggest dynamic effects of epilepsy on the connection architecture of the developing brain bilaterally. First, prompt removal of focal epileptogenic lesions, which controls seizures, can normalize contralateral EEG abnormalities[16] and promote development.[17–20] Second, a prolonged schedule of anticonvulsant weaning is typically required following successful lesion excision to maintain seizure freedom.[20] This led us to hypothesize that

epileptogenesis interferes with the normal remodeling of the connection architecture of the developing brain bilaterally.

Mid-infancy, the peak onset of WS, is a critical period for temporal lobe development.[17,21–25] We therefore reasoned that the effects of WS on the infant brain will be prominent for temporal lobe function. Here we used auditory event-related potentials (ERPs) to measure temporal lobe function with a time resolution in the order of milliseconds.[26] Specifically, obligatory ERP responses to simple tone stimuli allow us to make inferences on the maturation of the auditory cortex,[27,28] whereas ERPs to rare environmental sounds elicit prominent novelty ERPs in temporal, frontal, and parietal association cortex.[29] ERP data were utilized to evaluate differences in temporal lobe maturation between symptomatic WS patients and healthy control infants during the first year of life.

Subjects and Methods

Subjects

The study was approved by the ethics committee of the University College London Institute of Child Health and Great Ormond Street Hospital, London (GOSH). Parental informed consent was obtained prior to participation as a control or as a patient. Neonatal hearing tests were all normal.

Controls

Controls were recruited from the community and university staff. All showed age-appropriate development and no congenital hearing impairment, chronic otitis media, or other significant health problems as obtained by parental interview. They also had a normal neurological and structured developmental examination that screened for fine motor, vision, gross motor, hearing and speech, and social behavior impairments.[30] Formal psychometric testing was not performed.

Patients

Cases were recruited prospectively and consecutively over 4 years (2002–2006) from GOSH. The entry criteria were a diagnosis of WS based on clinical and EEG features and informed parental consent. The study did not interfere with patients' normal clinical management. Clinical investigations were brain neuroimaging (predominantly magnetic resonance imaging [MRI]) and neurometabolic investigation of blood, urine, and cerebrospinal fluid. The brain MRI scan was inspected and reported by neuroradiologists at GOSH. For statistical analysis, scans were classified as either normal or not normal. Treatment was initiated after video-EEG confirmation of a diagnosis of WS. Parents were counseled on WS by their neurologist, and received information regarding the first-line therapies for infantile spasms. The therapeutic agent was agreed between neurologist and parents.

Experiments

The study intervention was a pseudorandomized oddball auditory stimulus paradigm comprising a 1,000Hz sinusoidal pure tone standard stimulus (80%), a 2,000Hz "deviant" (10%), and novel environmental sounds (10%). The latter consisted of musical instruments, animal calls, machine sounds, and white noise sounds. Each stimulus lasted 200 milliseconds, including 10-millisecond rise and fall times. Stimulus onset asynchrony was 700 milliseconds. The paradigm is described in more detail elsewhere.[31]

Data Acquisition

Scalp EEG was recorded in an electrically shielded sound-attenuated chamber using Ag/AgCl electrodes in the international 10/20 montage. Gentle scalp abrasion with commercial gel minimized impedance to <10 kΩ, and adhesive paste affixed the electrodes. An electrode at the right external canthus and another in the left infraorbital area detected horizontal and vertical eye movement artifacts.

The experiments occurred around midday, with the infant on its mother's knee, having just been fed. An experiment during wakefulness was followed by a repeat during natural sleep. Two blocks of the same auditory paradigm were presented in each state, with different novelty sounds in each. Computer software (Presentation; Neurobehavioral Systems, Albany, NY) delivered auditory stimuli to the infant via speakers located 30cm from each ear. Sound intensity was adjusted to be comfortable for infants (about 60dB SPL).

EEG data were acquired in continuous mode with a Neuroscan recording system (Neuroscan, El Paso, TX). The EEG signal was digitized at a sampling of 500Hz, amplified (band pass = 0.15–100Hz), and stored at 32-bit resolution for offline analysis. The data were analyzed without additional offline filtering. The abnormality of the background EEG during the ERP recording session in stage II non–rapid eye movement (NREM) sleep was classified as either moderate, severe, or hypsarrhythmic. Moderate abnormality showed excess slow activity of similar amplitude to the ongoing activity, present for <50% of the recording, with definite evidence of age–appropriate activity. Severe abnormality was established by continuous excess of slow activity and/or absence of age-appropriate rhythmic activity and frequent epileptiform features. Hypsarrhythmia was defined as the presence of diffuse, high-amplitude, nonsynchronous slow-wave theta and delta activity with loss of normal background features, with the pattern being continuous when awake and fragmented in sleep. Asymmetry in the hypsarrhythmic pattern was permitted in the presence of structural lesions.

Data Processing

Data analysis was performed offline using Neuroscan Edit software. Preprocessing was performed offline to reject artifacts and to extract ERPs. Epochs exceeding ±300 μV in stage II sleep were automatically rejected. EEG segments contaminated by physical (eye blinks, eye movement, head movement, sucking, or excessive muscle activity) and electronic artifacts were rejected by visual assessment. Stage II NREM sleep as defined by the following EEG criteria: the presence of sleep spindles, K-complexes, and high-amplitude slow delta activity.[32–36] The arithmetic average locked to the epoch −100 to +800 milliseconds with respect to the presentation of each stimulus

(standards, deviants, and novels) was computed to yield the respective ERP responses. The ERP components were isolated by referencing the data from the recording electrodes offline to the average potential of the mastoid (M1 and M2) electrodes.[37] Following this demonstration of ERP components, the average all scalp electrodes was used as the reference for performing amplitude and latency measurements.

The ERPs for each block were extracted from the responses to standards, deviants, and novels. The data for the second block of experiments were inspected visually to establish replication of the components identified in the first block. A participant had valid data if the specific component was clearly visible across multiple neighboring electrodes and was demonstrated in both experiment blocks of the 2 arousal states. The statistical analysis described below was performed on the ERP components isolated in the first block of experiments for participants with valid data.

ERPs

SIGNAL-TO-NOISE RATIO AND STIMULUS SET SIZE. The study design incorporated a minimum number of stimulus repetitions required to identify the novelty ERP robustly. This was based on typical ERP amplitudes reported in sleeping infants, and the estimated mean EEG background amplitude in stage II sleep. A novelty ERP signal of amplitude ±15 μV and a mean background amplitude of ±75 μV results in a signal-to-noise ratio (SNR) of 0.2. Due to SNR scaling as a function of the square-root of the number of stimuli, we required a minimum of 100 novelty stimulus repetitions to achieve an SNR of 2.[38] The basic stimulus block comprised 1,050 stimuli (100 novel stimuli, 100 deviants, and 850 standards). Evaluation of the performance of the paradigm revealed that technically satisfactory obligatory and novelty responses could be measured distinctly from the background.

ERP MEASUREMENT. The component peak amplitude and latency were measured manually from the prestimulus baseline The obligatory ERP response (also known as the N1-T-complex), produced by repetition of the standard,[28] occurs over the temporal regions after 100 to 300 milliseconds in children.[39] The components of the obligatory response were recognized: P150, N250, and P350. The mismatch negativity (MMN) was defined as the largest negative deflection exceeding the average baseline voltage by 1.0μV at 80 to 300 milliseconds after stimulus onset in the difference between the response to the deviant stimuli and the standards immediately preceding. This had to be present at any 2 of the 4 electrodes F3, F4, C3, and C4. The novelty response is maximal at the frontocentral electrodes.[40–43] We measured the novelty P300, which was the largest positive deflection between 200 and 450 milliseconds, and the Nc response (sometimes termed *N450*), a negative slow wave occurring immediately after the novelty P3 at 400 to 700 milliseconds poststimulus. The novelty P300 was measured at M1, M2, P7, P8, C3, C4, and Cz electrodes; the novelty Nc at F3, F4, F7, F8, and Fz electrodes.

Statistical Analysis

Statistical analyses were performed using SPSS v16 (SPSS, Chicago, IL) package. Repeated measures analysis of variance was used to compare the amplitudes and latencies of WS patients with control subjects. This utilized the measurements over the electrodes that showed the largest amplitude of the waveform. These were C3, C4, F3, and F4 for each obligatory component; M1 and M2 for the novelty P300; and Fz and Cz for the novelty Nc. Fisher exact chi-square test (1-tailed) was used post hoc to verify whether a better yield of ERP components occurred with less severe background EEG abnormality. The existence of a relationship between ERP components and clinical factors was tested using logistic regression. The clinical factors tested were: development before seizure onset (normal, abnormal), brain MRI abnormality (present, absent), EEG background abnormality (moderate, severe), and focal epileptiform activity (present, absent). The criterion for statistical evidence was $p < 0.05$.

Results

Demographics

The 25 WS patients (10 female, 15 male,) had a median age of onset of infantile spasms of 4 months old (range = 3–9 months). The age distribution at onset of infantile spasms was 3 to 4 months (n = 13), 5 to 8 months (n = 10), and 9 months (n = 2). Their ERP testing was performed at a median age of 8 months (range = 3–10 months). The median lag to ERP testing from the onset of infantile spasms was 3 months (range = 2 weeks to 13 months). There was no difference in patient demographic characteristics by sex. None of the patients showed normal developmental ability on clinical assessment.

The 26 controls (13 female, 13 male) who were recruited to the ERP study had a median age at ERP recording of 7 months (range = 3–9 months). The breakdown of ages at ERP recording (controls, patients) was: 3 to 4 months (n = 5, n = 5), 5 to 8 months (n = 10, n = 9), and 9 months (n = 11, n = 11). There was no statistical difference in the demographic characteristics of the control and patient groups at the time of ERP recording.

Drug Treatment

FOR INFANTILE SPASMS. Treatment for infantile spasms was initiated at a median lag of 4 weeks (range = 2–20 weeks). Seventeen patients were treated with steroids. Fifteen were treated with vigabatrin, of whom 7 did not subsequently receive steroids. Of the 6 patients who had experienced no further IS following the initiation of treatment, control had been achieved on the first agent in 4 cases (3 steroids, 1 vigabatrin). The cessation of spasms occurred within 2 weeks of initial treatment.

FOR OTHER SEIZURES. Ten patients were treated for other seizures prior to referral to our center.

EEG

The EEG recording was possible in 23 patients during both wakefulness and sleep, whereas in 1 patient it was only possible during wakefulness and in another patient only during sleep. The EEG background was severely abnormal in 12 patients during wakefulness (including hypsarrhythmia in 1), and in 16 patients during sleep (including hypsarrhythmia in 4). Focal discharges over temporal leads or multifocal discharges involving the temporal lobe were present in 15 patients (EEG details available upon request).

MRI

The brain MRI scans were classified into 5 groups: normal (n = 8), malformations of cortical development (n = 8), tuberous sclerosis (n = 3), hypoxic–ischemic changes (n = 3), or delayed myelination without cortical abnormality (n = 3; Table 1).

ERP Components

IDENTIFICATION OF OBLIGATORY COMPONENTS. The presence of clearly defined ERP components (Fig 1) was used as a measure of normal auditory cortex maturation.[28,37] Patients were more likely than controls to fail to show the full triadic obligatory response component structure ($p < 0.001$ for all components: P150, N250, P350) for each arousal state (Table 2).

MMN. The MMN was evaluated as part of this study, using the 2,000Hz deviant stimulus presented at a 10% probability. This large frequency deviance was expected to elicit an MMN on the basis of previous work in infants.[44] However, the criterion for reliability of an ERP component in this study (demonstrability in both blocks of both states) was not fulfilled for the MMN in any patient and was met by only 2 control subjects.

NOVELTY COMPONENTS. The novelty components were detected in both blocks during sleep in most control subjects (96%, 25 of 26) and in a proportion of WS infants (60%, 15 of 25). During wakefulness, novelty ERPs were present in both blocks in 88% (23 of 26) of control subjects and in 44% (11 of 25) of WS patients.

ERP Components and the EEG Background

All controls had normal EEGs. Patients showed a graded relationship between the severity of the abnormality of the EEG background and the presence of obligatory and novelty ERP components for both sleep and wakefulness. Considering the obligatory and novelty responses, full ERP component structure manifested less with severe as compared to moderate background EEG abnormality in both states. (Fisher exact test, $p = 0.004$). This reflects the following details: the proportion of patients with severe background EEG abnormality compared to moderate background EEG abnormality showing all obligatory ERP components was 4 of 16 versus 7 of 8 during sleep (Fisher exact test, $p = 0.025$) and 2 of 12 versus 9 of 10 during wakefulness ($p = 0.001$) . The proportion showing all novelty ERP components was 9 of 16 versus 8 of 8 during sleep ($p = 0.033$) and 4 of 12 versus 8 of 10 during wakefulness ($p = 0.038$).

Group Comparisons

OBLIGATORY COMPONENTS. The obligatory ERP response (P150, N250, P350) showed an age-dependent shortening of the latency of all components in controls (see Fig 1), which was not seen in patients (Table 3). The obligatory response latencies were prolonged in WS compared to controls during both wakefulness and sleep (Fig 2, Table 4).

NOVELTY COMPONENTS. The novelty ERP response (P300, Nc) showed an age-dependent shortening of the latency in healthy infants (Fig 3). This was statistically significant for the novelty P300 (see Table 3). The group comparison of novelty ERPs (Fig 4) evidenced a latency prolongation in WS patients (sleep and wake data collapsed: $F = 6.74$, $p = 0.012$ for P300 latency; $F = 4.76$, $p = 0.037$ for Nc latency). The data are shown separately for each arousal state in Table 4.

The obligatory and novelty ERP latencies shortened with age in controls but not WS patients (for sleep and wake data collapsed: age $\times$ group interaction, $F = 22.3$, $p < 0.0001$). ERP amplitudes did not show group differences, with 1 exception. There was a trend toward a larger Nc amplitude in WS patients ($F = 3.97$, $p = 0.05$ for sleep and wake data collapsed).

MMN. The majority of study subjects did not fulfil the criterion for a reliable MMN, precluding group statistical comparison between controls and patients.

Relationship between Demographic and Clinical Factors

Logistic regression failed to find a relationship between age, gender, or clinical factors and the presence of ERP components in WS patients.

Unilateral Epileptogenic Lesions, Bilateral Effects

The observation was made of 2 cases of unilateral right-sided lesions that involved the temporoparietal junction,

TABLE 1. Patient Clinical Characteristics

Patient	Sex	Age at IS Onset, mo	Normal Development before IS Onset	Any Other Seizures Before IS Onset?	Magnetic Resonance Imaging	Medication Received	Spasm Cessation prior to ERP Recording	Age at ERP in days (mo)	Lag time to ERP, mo
1	F	6.5	+	−	Normal	VGB, VPA, STER	−	318 (10.5)	4
2	F	4	−	−	Delayed myelination	STER	+	319 (10.5)	6.5
3	F	4.5	−	−	Microcephaly	VGB	−	174 (5.5)	1
4	F	7	−	+	Tuberous sclerosis	VGB	−	304 (10.0)	3
5	F	6	+	−	Normal	STER	+	279 (9.0)	3.0
6	F	3	−	−	Aicardi syndrome	PHB, VPA	−	121 (4.0)	1
7	F	6	−	−	Right middle cerebral territory infarct	VGB, STER	−	301 (10.0)	5.0
8	F	3.5	−	−	Lissencephaly (Miller–Dieker syndrome)	VGB, STER	−	122 (4.0)	0.5
9	F	3	−	+	Left hemimegalencephaly	VGB, STER, VPA	−	288 (9.5)	6.5
10	F	4	−	−	Bilateral IVH; periventricular leukomalacia	VGB	+	214 (7.0)	3
11	M	3.5	−	−	Left perisylvian polymicrogyria	VGB, STER	−	238 (7.5)	4.0
12	M	3.5	+	−	Right parietal cortical dysplasia	VGB, VPA, CLB	+	160 (5.0)	1.5
13	M	6	+	+	Normal	PHB, STER	−	200 (6.5)	0.5
14	M	3	+	−	Normal	CMZ, VGB, STER	−	172 (5.5)	2.5
15	M	5	+	−	Normal	ACTH	+	198 (6.5)	1.5
16	M	10	−	+	Normal	PHB, STER	−	420 (14.0)	4
17	M	5	−	+	Tuberous sclerosis	VPA, VGB	−	295 (9.5)	4.5
18	M	3	+	+	Delay of myelination	PHB, STER	+	109 (3.6)	0.5
19	M	9.5	−	−	Tuberous sclerosis	VGB, STER, TOP	−	369 (12.0)	2.5
20	M	3	−	+	Normal	PHB, STER	−	90 (3.0)	0.5

TABLE 1: Continued

Patient	Sex	Age at IS Onset, mo	Normal Development before IS Onset	Any Other Seizures Before IS Onset?	Magnetic Resonance Imaging	Medication Received	Spasm Cessation prior to ERP Recording	Age at ERP in days (mo)	Lag time to ERP, mo
21	M	3	–	+	Hypoxic ischemic injury	PHB, VGB, STER	–	276 (9.0)	6
22	M	5	–	–	Delay of myelination, absent corpus callosum	VGB, STER	–	199 (6.5)	1.5
23	M	6	–	+	Hypoxic ischemic injury	PHB, STER	–	255 (8.5)	2.5
24	M	3.5	–	+	Hypoxic ischemic injury	PHB, VGB	–	123 (4.0)	0.5
25	M	4	+	–	Normal	VGB, STER	–	395 (13)	9

The postnatal age in days is corrected for gestation. The lag time to ERP is the difference between age at IS onset and the age at ERP.
ACTH = adrenocorticotropic hormone; CLB = clobazam; CMZ = carbamazepine; ERP = event-related potential; F = female; IS = infantile spasms; M = male; PHB = phenobarbital; STER = steroids; TOP = topiramate; VGB = vigabatrin; VPA = valproate.

in which the contralateral auditory novelty ERP response was abolished (data available upon request). In contrast, unilateral lesions in other regions did not abolish the contralateral novelty response.

Discussion

This study probed alterations of temporal lobe function in patients with a history of WS using auditory ERPs to frequent sounds (obligatory ERPs) and rare novel sounds (novelty ERPs). The obligatory ERP responses (P150, N250, P350) are presumed to be generated within auditory cortex, whereas temporoparietal and frontal association cortex are the sources of the novelty responses (P300, Nc).[29] These ERP signatures of basic (acoustic) and higher order (novelty) auditory processing were detectable in all healthy control infants and in a smaller proportion of WS patients. Notably, patients' ERPs failed to show the full complement of age-appropriate components and had prolonged peak latencies. A limitation of this study is that MMN, which is generated in the superior temporal plane in response to deviant sounds,[45] could not be elicited reliably.

To our knowledge, this is the first study demonstrating robust ERP latency prolongation in patients with WS. This appears to be due to the failure of ERP components in WS patients to show the expected rapid age-dependent latency reduction during the first 2 years of life.[27,46] The findings in WS are in keeping with the observation of prolonged ERP latencies in heterogeneous groups of children with other severe epilepsies.[47–49] The finding in WS of ERP impairment across the hierarchy of auditory processing could potentially underlie the language deficits recognized in these patients.[50]

We cannot rule out the possibility that anti-epilepsy drug (AED) treatment influenced ERP latencies in the absence of pretreatment ERP recordings. As patients had been treated for WS, it is inferred that treatment did not normalize auditory ERPs. Nevertheless, we failed to find ERP differences between WS patients on AED treatment and those without, as well as between those treated with steroids compared to vigabatrin. There are no published data on the effect on ERPs of typical treatment doses of the anticonvulsants used for WS. There is, however, some limited evidence to suggest that the findings in the present study are probably not primarily treatment-induced. First, steroid treatment (using adrenocorticotropic hormone and corticotropin-releasing hormone at low dose) did not alter ERP latencies in healthy adult controls.[51,52] Second, in other severe epilepsies therapeutic doses of other anticonvulsants did not alter ERP latencies.[47,53] We did not identify clear ERP differences in relation to clinical factors such as development before
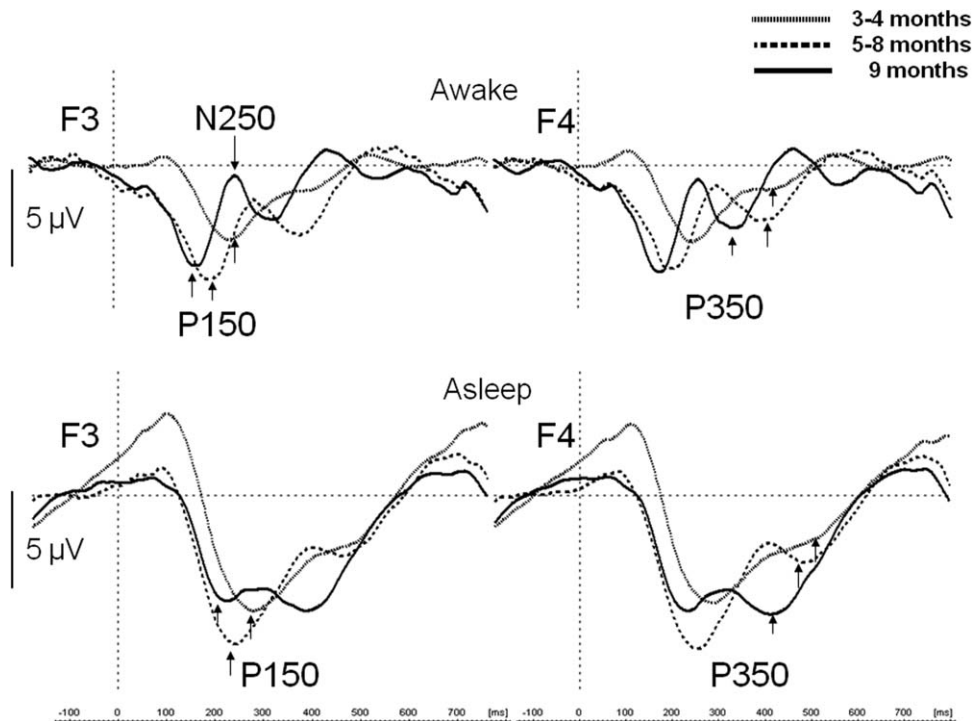
FIGURE 1: The obligatory event-related potential morphology in 3 age groups of healthy control infants during wakefulness and sleep at frontal electrodes F3 and F4. Note shortening of P150 latency with emergence of N250 and P350 with increasing age.

seizure onset, the presence of brain MRI abnormality, EEG background abnormality, and focal epileptiform activity, albeit limited by small sample size.

TABLE 2. Identification of Obligatory ERP Components

ERP Component	Awake	Asleep
P150		
Controls	26/26 (100%)	26/26 (100%)
Patients	12/25 (48%)	12/25 (48%)
p, chi-square test	<0.0001	<0.0001
N250		
Controls	22/26 (84%)	20/26 (77%)
Patients	8/25 (32%)	5/25 (25%)
p, chi-square test	<0.001	<0.0001
P350		
Controls	22/26 (84%)	20/26 (77%)
Patients	8/25 (32%)	6/25 (23%)
p, chi-square test	<0.001	<0.001

In each arousal state, patients were less likely than controls to show all 3 components.
ERP = event-related potential.

The ERP data are consistent with a qualitative difference in temporal lobe maturation between the WS group and controls. The former showed less integrity of ERP component structure, with a lower probability for generating all obligatory components, and did not show evidence of the marked age-related latency reduction found in control infants. The integrity of ERP component structure was poorer, with more severe EEG background abnormality and fewer ERP components being isolated. The higher amplitude of the background EEG was not, however, a sufficient explanation for WS patients' ERP findings. First, if their background EEG merely rendered ERPs less identifiable, then patients' ERP amplitude ought to be diminished. However, the ERP amplitude did not differ between patients and controls. Second, the novelty ERPs' detectability would be expected to deteriorate during sleep given the more abnormal and higher amplitude background EEG during sleep in WS patients. This was found not to be the case. For these reasons, we do not assume that the ERP findings in WS simply represent the consequence of reduced signal-to-noise ratio given the high-amplitude background EEG in this group.

The inference that the developmental patterning of the temporal lobe connections differs between controls and patients is supported by our ERP findings in cases of right hemispheric lesion. Our observation of bilateral

TABLE 3. Shortening of ERP Latencies during Sleep with Age						
ERP Component		Patients			Controls	
	n	R	p	n	R	p
Obligatory						
P150	12			26		
Right (F4)		0.382	0.05		−0.473	<0.0001
Left (F3)		0.379	0.06		−0.519	<0.0001
N250	5			20		
Right (F4)		−0.330	0.25		−0.525	<0.0001
Left (F3)		−0.280	0.33		−0.506	<0.0001
P350	6			20		
Right (F4)		−0.180	0.52		−0.546	<0.0001
Left (F3)		−0.189	0.50		−0.512	<0.0001
Novelty						
P300	15			25		
Right (M2)		−0.255	0.15		−0.529	<0.0001
Left (M1)		−0.058	0.75		−0.432	0.001
Nc	15	0.010	0.96	25	−0.467	0.002

The Pearson correlation coefficient (R) between ERP latency and age (in days) is shown. Controls showed a shortening of all ERP latencies with age, which was not reproduced in the West syndrome group.
ERP = event-related potential.

ERP alteration in cases with unilateral epileptogenic structural lesions of the right temporal lobe hints at a degree of interhemispheric dependence of brain func-

tional maturation. The suggestion of earlier maturation of the right cerebral hemisphere in infancy[54] could mean that it reaches its peak density of synaptic connections
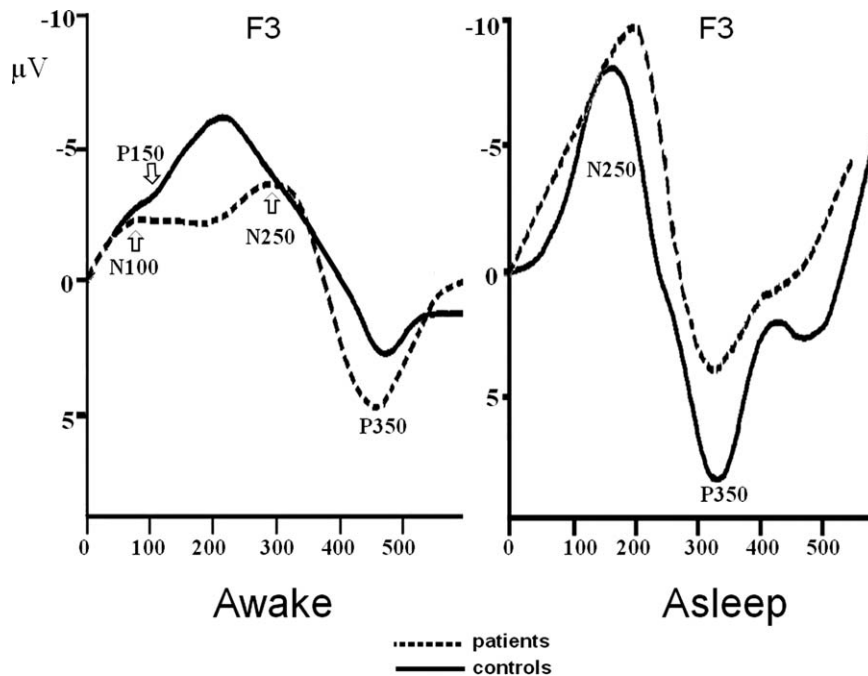

FIGURE 2: Group mean obligatory event-related potentials at electrode F3 in sleep for controls and patients.

TABLE 4. ERP Group Statistics for Controls and Patients with West Syndrome

ERP Component	West Syndrome, Mean ± SD		Controls, Mean ± SD		p	
	Sleep	Awake	Sleep	Awake	Sleep	Awake
Obligate response[a]						
P150 latency	394 (87)	298 (95)	262 (44)	207 (38)	<0.001[b]	<0.001[b]
P150 amplitude	11.0 (7.7)	4.4 (13)	7.8 (5.4)	4.7 (2.0)	0.183	0.218
N250 latency	321 (95)	363 (118)	267 (33)	284 (47)	0.008[b]	<0.001[b]
N250 amplitude	−21.4 (16.6)	−16.8 (6.5)	−22.0 (7.3)	−18.1 (8.5)	0.689	0.299
P350 latency	616 (219)	513 (160)	462 (60)	386 (52)	0.017[b]	0.018[b]
P350 amplitude	5.9 (4.0)	3.2 (2.7)	5.3 (3.1)	3.2 (2.9)	0.608	0.429
Novelty response[c]						
Novelty P300 latency	692 (152)	950 (193)	585 (91)	729 (74)	<0.001[b]	<0.001[b]
Novelty P300 amplitude	19.6 (18.7)	7.7 (3.6)	14.2 (5.6)	6.5 (4.1)	0.378	0.343
Novelty Nc latency	772 (233)	837 (130)	665 (102)	791 (76)	0.280	0.037[b]
Novelty Nc amplitude	−13.4 (12.6)	−4.8 (3.6)	−9.5 (7.6)	−3.8 (4.7)	0.015[b]	0.453

The analysis is based on those subjects showing the particular component. Latencies are in milliseconds and amplitudes are in microvolts.
[a]For obligatory response, see Table 2.
[b]Significant difference.
[c]For the novelty response, the number of subjects for patients and controls was 25 and 15 respectively in sleep and 23 and 11 respectively awake, for both the novelty P300 and novelty Nc.
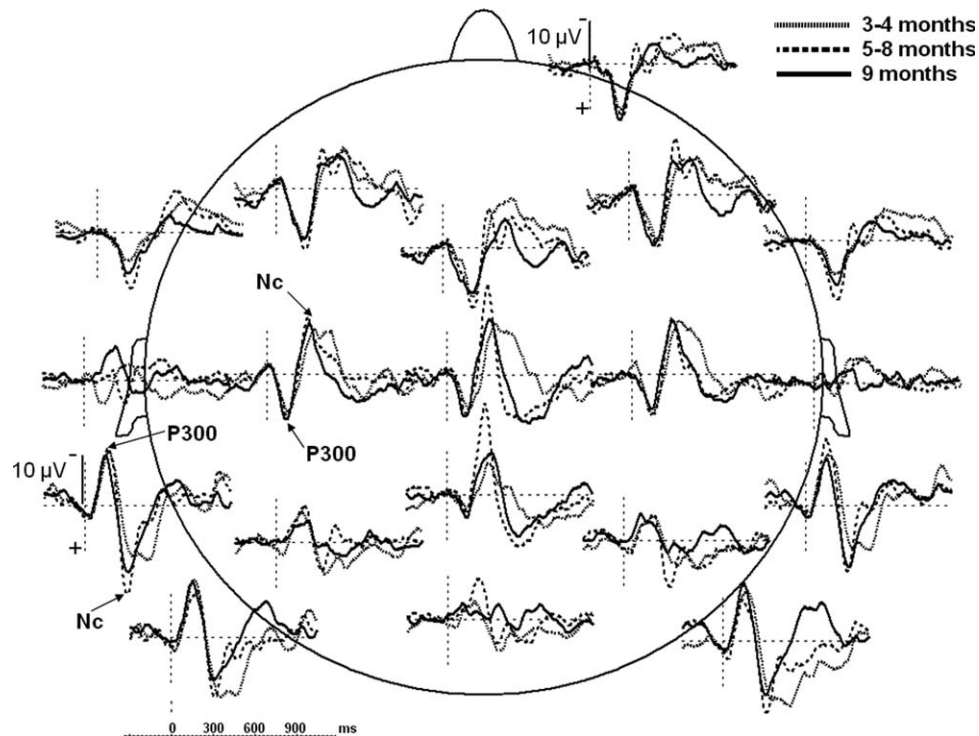ERP = event-related potential; SD = standard deviation.

FIGURE 3: Novelty event-related potential responses in 3 age groups of healthy control infants during sleep. Note inversion of P300 and Nc over temporal leads (labeled on the left side).
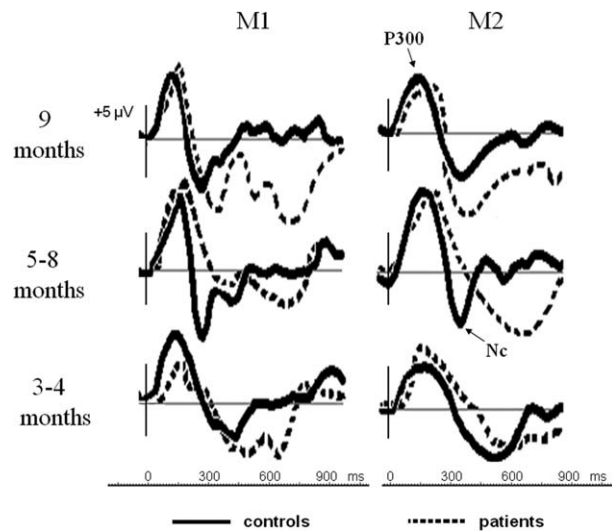
FIGURE 4: The group average novelty event-related potential response in sleep at the mastoid electrodes in controls and patients, showing delayed P300 and Nc components. Note that the Nc and P300 are shown as the phase reversals from their original frontal polarity.

first. We presume that such connections might facilitate a functional effect at a distance or *diaschisis* upon the maturation of cortical networks in the contralateral hemisphere to account for our observations with right temporal lobe lesions. The diaschisis phenomenon has been proposed to account for the finding that focal cortical resection around the epileptogenic lesion, or hemispheric disconnection, can restore the contralateral hemisphere's functional and hemodynamic maturation.[16,55–57] It will be important to determine whether impairments in interhemispheric temporal lobe connectivity impact on the development of verbal skills, as has been reported for cohorts of children with perinatal pathology.[58,59]

In conclusion, an impairment of temporal lobe maturation is a likely sequela of WS. This is proposed to reflect defective neuroplasticity associated with WS. Further study should establish the predictive value of ERP findings for cognitive and language development in affected children. New treatments that specifically modulate neuroplasticity promise improved future outcomes in WS,[60] and the use of auditory ERPs may permit monitoring of temporal lobe maturation following such treatments.

Authorship

K.W. and T.F. are joint first authors.

Potential Conflicts of Interest

Nothing to report.

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