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Origin and dynamics of epileptic activity in a symptomatic case of Panayiotopoulos syndrome: Correlation with clinical manifestations

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HIGHLIGHTS

- Panayiotopoulos syndrome (PS) is a frequent childhood epileptic syndrome with typical clinical features but unknown localisation of the epileptogenic area.
- We describe the first symptomatic case of PS where both clinical and EEG features converge to demonstrate that an epileptic focus in the inferior parietal lobe can originate the epileptic syndrome.
- Fast spread of epileptic activity through physiological networks involved in eye-movement control, gastrointestinal autonomic control and consciousness can explain the diversity of clinical manifestations in PS.

ABSTRACT

Objective: The aim of the study was to demonstrate the dynamics and structure of the epileptic network and provide a tentative correlation with the clinical manifestations, in a symptomatic case of Panayiotopoulos syndrome (PS).
Methods: JP, 5-year-old girl. Gestational period and developmental milestones were normal. At age 4 years, two episodes of recurrent vomiting, tonic eye deviation and consciousness impairment lasting for about 30 min occurred. Multifocal spikes were apparent over frontal areas in the EEG and MRI demonstrated an inferior parietal lobe (IPL) lesion.
Results: A long-term 35-channel scalp EEG was obtained, which was processed with a Blind Source Separation algorithm. The most significant components with a dipolar field were submitted to source analysis and the recovered generators used to build the nodes of a brain network associated with each spike type. Analysis of information flow supported epileptic propagation from the left parietal lobe to both frontal and temporal lobes around spike peak. The good spatial overlap with physiological networks controlling eye movements, autonomic functions and consciousness, provides a tentative explanation to the diverse clinical manifestations of PS.
Conclusions: Spreading patterns of epileptic activity form an extended network in PS.
Significance: An epileptic focus in an IPL can reproduce both neurophysiological and clinical features of PS.

1. Introduction

The Panayiotopoulos syndrome (PS) is one of the most recently described and prevalent benign epilepsy syndromes of childhood. Despite the significant effort devoted to elucidate its clinical (Panayiotopoulos, 2002), neurophysiological (Caraballo et al., 2007) and neuropsychological aspects (Specchio et al., 2010a), several problems remain that prevent a deeper insight into the aetiology of the syndrome: the multifocal interracial spike activity present in most cases precluded the unambiguous identification of a common epileptogenic area; the peculiar combination of ictal autonomic manifestations, eye deviation and long-lasting impairment of consciousness, typical of the condition, has not allowed the determination of the precise locus of the epileptogenic zone on clinical grounds; It remains uncertain whether a single, yet unknown, cortical focus is responsible for the stereotyped seizure manifestations or these can be produced by foci in diverse areas.

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The few neurophysiological recordings of ictal events in the literature have also failed to provide focal EEG patterns with clear clues to their origin (reviewed in Specchio et al., 2010b).

Despite the close morphological similarities of the interictal spikes in PS with the ones of rolandic epilepsy, the localisation information of each type is very different, with rolandic spikes showing stable dipolar fields with consistent generators within the primary somato-sensory area (Leal et al., 2007) and PS spikes demonstrating variable scalp topographies and significant spread of epileptic activity (Leal et al., 2008; Yoshinaga et al., 2010; Kokkinos et al., 2010).

Clues to the localisation of the epileptogenic area in PS could potentially be obtained from the analysis of the few reported symptomatic cases. Nevertheless, the analysis of such cases failed to provide a consistent hypothesis and has led the authors to postulate a fortuitous coincidence between the epileptic syndrome and the structural abnormalities (Panayiotopoulos, 2002; Yalçin et al., 2009). In none of the reported cases was a source analysis of the EEG epileptic activity performed, nor any type of processing besides visual evaluation.

We report on a patient with important clues to the source of epileptic activity in PS.

2. Methods and patient data

2.1. Patient data

JP, 5-year-old girl. In the gestational period, the mother was continuously medicated with warfarin. Vaginal delivery occurred at the 37th week and the birth weight was 2160 kg. The neonatal period was complicated with sepsis and transient insulin-dependent diabetes (up to the 53rd day of life) but developmental milestones were reached at appropriate age. In the first 3 years, three renal urinary infections were reported, with associated febrile seizures.

At the age of 4 years, a night event occurred lasting about 30 min with vomiting, conjugate and sustained eye deviation upward and to the left side, with unresponsiveness. After regaining consciousness, there was a transient period of confusion and somnolence but ultimately she recovered completely. She was investigated at the emergency department of a local hospital and discharged after normal blood and serum parameters and also a normal head CT were obtained.

Five months later, a similar nocturnal event was reported. An EEG revealed multifocal spike activity. A 1.5-T MRI scan demonstrated a cortical lesion in the left inferior parietal lobe (IPL), with imaging features compatible with cortical dysplasia (Fig. 1b).

A long-duration (24 h) video-EEG monitoring could not record seizure events, but abundant interictal spikes were noticed, occurring independently over the central area of the right hemisphere and the frontal area of the left one (Fig. 1a).

The cognitive development was evaluated with the Portuguese version of the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R). The neurological examination was normal. No genetic analyses were performed.

2.2. EEG acquisition and processing

The EEG signal during the 24-h video-EEG monitoring was collected with 35 gold disc electrodes glued with Colodium to the scalp positions (Fp1/2, F3/4, C3/4, P3/4, O1/2, F7/8, T7/8, P7/8, Fz, Cz, Pz, F11/12, FT9/10, TP9/10, P11/12, FC5/6, FC1/2, CP5/6 and CP1/2). The sampling rate was 1000 Hz, the high- and low-pass filters were set at 0.5 and 70 Hz and the electrode impedances remained below 5 kΩ. A Micromed EEG recording system was used for data acquisition, controlled by the SystemPlus software. The EEG data were exported to the Scan 4.3.1 software (Compumedics NeuroScan, Charlotte, NC, USA), where the trace was visually inspected by an experienced clinical neurophysiologist (AL), to identify spikes with independent topology. For each of the two recognised classes of spike topology, an amplitude threshold was applied at the channel with maximum spike amplitude to automatically detect spikes of this class and insert a trigger at each detection. The triggers were then used to epoch the EEG with a window of −200 to +500 ms, which were then concatenated. The final result was a continuous EEG file containing all the detected spikes for each topology class.

The concatenated EEG record for each spike class was then imported to the EEGLAB 10.1 software (Delorme and Makeig, 2004) and decomposed using the Infomax (Bell and Sejnowski, 1995) independent component analysis (ICA) algorithm. The ICA spatial components were fitted with a dipole solution (using the standard boundary element method (BEM) (Montreal Neurological Institute model) included in EEGLAB) and only the ones with a residual variance (RV) lower than 10% were retained. These were then ordered by their relative contribution to the spike signal in the time range from −50 to +50 ms around the peak. The dipole solutions associated with the four ICA components with the largest contribution to each spike type were obtained with the CURRY 6 software (Neuroscan, Charlotte, NC, USA), using the sLORETA algorithm (Pascual-Marqui, 2002) in a standard BEM model of the head (Fig. 2a and c).

Spectral analysis of the ICA components activity around the spike peak was done using the event-related spectral perturbation method (ERSP) (Makeig, 1993) as well as the inter-trial coherence (ITC) method (Tallon-Baudry et al., 1996), both implemented in the EEGLAB software. Statistical significance of the changes was obtained through a bootstrap procedure comparing changes in the ERSP with the spectral distribution in the prestimulus period.

The functional connectivity analysis was performed in the averaged time course of the four ICA components with the largest contribution to the spike of each class, using the point of maximum score in the sLORETA inverse solution as the node of each component. We used the adaptive direct transfer function (ADTF) (Wilke et al., 2008) as a dynamical measure of information flow between the ICA component nodes, as implemented in the e-connectome software (He et al., 2011). The average amount of information flow in the band 4–30 Hz was calculated and statistical significance was obtained using a permutation test with phase randomisation.

3. Results

3.1. Electro-clinical data

Our clinical case exhibits the main features of PS, with rare, predominantly autonomic seizures, long-lasting impairment of consciousness, sustained conjugate eye deviation and multifocal interictal spikes in a normal background EEG. The WPPSI-R test revealed a verbal IQ of 107 (score 68%), a performance IQ of 101 (score 53%) and a full-scale IQ of 103 (score 58%). These results support an average cognitive development.

3.2. Dynamics of epileptic activity

The EEG revealed a normal background rhythm and multifocal spikes with consistent maxima over the frontal lobes of both hemispheres (Fig. 1a). No spikes could be identified in the left parietal–occipital electrodes, near the scalp projection of the cortical lesion. The mapping of the scalp potential at different times through the rising phase of the spikes revealed a changing topographical con-