Clinical Neurophysiology 121 (2010) 145–152

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Interhemispheric asymmetry in EEG photic driving coherence in childhood autism

V.V. Lazarev [a,*], A. Pontes [a], A.A. Mitrofanov [b], L.C. deAzevedo [a]

[a] Laboratory of Neurobiology and Clinical Neurophysiology, Fernandes Figueira Institute, Oswaldo Cruz Foundation, Ministry of Health, Rio de Janeiro, Brazil
[b] Moscow Scientific Research Institute of Psychiatry, Moscow, Russia

ARTICLE INFO

Article history:
Accepted 15 October 2009
Available online 1 December 2009

Keywords:
Autism
Children
EEG photic driving
Coherence
Left hemisphere
Right hemisphere

ABSTRACT

Objective: Examination of the EEG photic driving coherence during intermittent photic stimulation in autistic patients with relatively intact verbal and intellectual functions in order to enhance the likely latent interhemispheric asymmetry in neural connectivity.
Methods: Fourteen autistic boys, aged 6–14 years, free of drug treatment, with I.Q. 91.4 ± 22.8, and 19 normally developing boys were subject to stimulation of 12 fixed frequencies of 3–27 Hz. The number of high coherent connections (HCC) (coherence >0.6–0.8) was estimated among 7 leads in each hemisphere.
Results: In contrast to the spectral characteristics showing the right hemisphere deficit in the photic driving reactivity, the number of HCC differentiated the groups only in the left hemisphere where it was higher in autistics at the EEG frequencies corresponding to those of stimulation at 6–27 Hz without asymmetry at other frequencies, the left-side prevalence increasing with frequency. No asymmetry was observed in the resting state.
Conclusions: Spectral and coherence characteristics of the EEG photic driving show different aspects of latent abnormal interhemispheric asymmetry in autistics: the right hemisphere "hyporeactivity" and potential "hyperconectivity" of likely compensatory nature in the left hemisphere.
Significance: The EEG photic driving can reveal functional topographic alterations not present in the spontaneous EEG.

1. Introduction

The resonance-like EEG photic driving response to the intermittent photic stimulation (IPS) is utilized as a functional test in order to enhance the manifestation of latent normal or abnormal neurophysiological mechanisms not present in the spontaneous EEG of the resting state (Takahashi, 1987). This rhythmic activity is time-locked to the stimulus at a frequency identical or harmonically related to that of the stimulus. In clinical practice, its utilization is very often limited to ascertaining the presence of a photoparoxysmal response in so called 'photosensitive epilepsy'. However, characteristics of non-paroxysmal driving responses to IPS may serve as additional EEG signs of cerebral pathology not always present in the resting EEG in various types of neuropsychiatric diseases (Scheuler, 1983). Among them are partial epilepsy (Beydoun et al., 1998) and functional and mild endogenous disorders which usually are not evident in EEG diagnostics, such as headache (Gronseth and Greenberg, 1995) and schizophrenia (Jin et al., 2000). In these pathologies, the topographic peculiarities of the photic driving demonstrated a promising potential for revealing subtle functional disturbances in regional reactivity (Jin et al., 2000). IPS can emphasize the functional interhemispheric asymmetry (Hirota et al., 2001) and regional functional alterations through asymmetric driving effects (Scheuler, 1983; Beydoun et al., 1998).

Our research in children has shown that the topography and amplitude of the EEG photic driving spectral peaks at various IPS frequencies and their harmonics may be a quite sensitive tool for assessing the functional brain maturation and its pathological alterations (Lazarev et al., 2001, 2008). In patients with partial epilepsy, the reduced driving generalization reflected a likely delay in brain maturation together with the effects of antiepileptic drug therapy (Lazarev et al., 2006). The topographic characteristics of the photic driving proved to be sensitive enough to reveal right hemisphere reactivity deficit at the alpha and beta frequencies in autistic boys with relatively intact verbal and intellectual functions who did not show such alteration in the spontaneous EEG of the resting state (Lazarev et al., 2004a, 2009).

In reference to autistic patients, the literature usually describes general non-specific EEG changes, such as some prevalence of slow

* Corresponding author. Address: Fernandes Figueira Institute, Laboratory of Neurobiology and Clinical Neurophysiology, Av. Rui Barbosa, 716, Rio de Janeiro, 22250-020, Brazil. Tel.: +55 21 2554 1955; fax: +55 21 2554 1805.
E-mail addresses: vlad.v@iname.com, vladimir@iff.fiocruz.br (V.V. Lazarev).

1388-2457/$36.00 © 2009 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.clinph.2009.10.010

bioelectrical activity, alpha-rhythm suppression and rhythmic disorganization (Small, 1987; Bashina et al., 1994; Murias et al., 2007; Chan et al., 2007; Coben et al., 2008) and/or excess of high frequency oscillations (Murias et al., 2007; Orekhova et al., 2007). The interhemispheric asymmetry was frequently described in terms of relatively lower activation of the left hemisphere (Dawson et al., 1982; Cantor et al., 1986; Harrison et al., 1998) probably due to language problems inherent to most autistic patients.

The right hemisphere alterations in the spontaneous EEG of autistic children were only recently described as reduced beta activity and excessive theta power in posterior regions (Coben et al., 2008). An abnormal spectral power decrease in the right temporal areas was revealed during sustained visual attention in younger autistics (Stroganova et al., 2007). Some right hemisphere alterations in autistic patients were also detected by event-related potential techniques (Kujala et al., 2005; Senju et al., 2005). In neuroimaging studies, certain abnormalities in the right hemisphere have been noted in the high-functioning forms of autism (McKelvey et al., 1995; Waiter et al., 2005). These findings are in accordance with recent neuropsychological data which emphasize a crucial role of right hemisphere dysfunction in the development of some basic features of the autistic spectrum (Ozonoff and Miller, 1996; Siegal et al., 1996; Sabbagh, 1999) including impairments in social interaction, communication and imagination which constitute the classical autistic triad (Wing, 1997).

The above-mentioned capacity of the driving spectral characteristics to detect subtle alterations in the functional interhemispheric asymmetry in autistics (Lazarev et al., 2009) encouraged us to test in the same patients other topographic manifestations of the EEG photic driving such as the coherence of the rhythmic oscillations evoked by IPS in different brain areas (Miranda de Sa et al., 2001). An increase of the EEG coherence at the stimulation frequency among the leads showing the driving spectral peaks was to be expected. In the literature, the EEG coherence is the well known indicator of functional relationships between brain regions (Livanov, 1977; French and Beaumont, 1984). Some authors observed abnormal coherence – excessive or reduced – in various brain areas of autistic patients at different frequencies of spontaneous EEG (Cantor et al., 1986; Murias et al., 2007; Coben et al., 2008), including an asymmetry in intrahemispheric connections (Murias et al., 2007). The coherence of the EEG oscillations induced by IPS permitted to reveal latent features of cerebral functional connections not apparent in the resting state, such as gender-based differences in the interhemispheric relationships in normal subjects (Wada et al., 1996) or aberrant functional organization in schizophrenia (Wada et al., 1998) and Alzheimer's disease (Kikuchi et al., 2002). These findings prompted us to test the capacity of the EEG coherence to detect some peculiarities of the photic driving generalization in the left and right hemispheres in addition to those of the spectral characteristics (Lazarev et al., 2009) in the aforementioned group of autistic patients and thus to reveal more complete patterns of likely alterations in hemispheric activation not explicit in the spontaneous EEG.

2. Methods

Fourteen autistic boys aged 6–14 years (mean ± SD: 9.7 ± 2.2) were diagnosed in the Neurology Division of the Fernandes Figueira Institute (Rio de Janeiro) according to the DSM-IV criteria (Filipek et al., 1999). All of them had a classical autistic triad of impairments in social interaction, communication and imagination (Wing, 1997), with relatively intact verbal functions and without severe or moderate mental retardation (I.Q. levels: average from 90 to 109 in 7 patients, below average in 4 patients and above average in 3 patients; verbal, performance and total I.Q. levels: 91.2 ± 27.5, 94.3 ± 20.4 and 91.4 ± 22.8, respectively) (Wechsler, 1991). They did not have epileptic symptoms and neurologic abnormalities other than those directly related to autism. The computerized helicoidal tomography of the brain was normal for all cases. The patients were free of drug treatment. The control group consisted of 19 boys, aged 6–16 years (10.1 ± 3.46), without a history of neurologic, psychiatric or drug related disorders and with normal academic achievement. None of the patients and controls was overtly left-handed. The Ethics Committee of the Fernandes Figueira Institute approved this research and the subjects or persons responsible gave informed consent to participate in the study.

The EEG was recorded by a Nihon Kohden machine EEG-4418 at 14 scalp points (International 10/20 System, see Fig. 1) with unilateral references to the corresponding earlobes and with simultaneous registration of EOG, during 2–3 min of initial resting state before stimulation (background) and during white flicker IPS of 12 fixed frequencies of 3, 4, 5, 6, 8, 10, 12, 15, 18, 21, 24 and 27 Hz, 25-s duration each, with 30-s periods between stimulation runs. For each IPS frequency and for the background EEG, one EEG fragment of 25-s duration was digitized on-line at the sampling frequency of 256 Hz. The portions of some of these fragments containing excessive eye or muscle movements (total duration less than 7-s) were removed prior to further analysis. The recording characteristics were: 0.3-s time constant and 70-Hz high frequency filter. Photic stimulator was Nihon Kohden 4418 K – LS-701B – a xenon lamp with flash duration of less than 20 μs. The lamp was positioned at a distance of 25 cm from the eyes, with dim surrounding light. The subjects were awake with eyes closed throughout the experiment.

The EEG was analyzed with computerized system «Brainsys» (Neurometrics, Moscow, Russia). The duration of EEG epochs submitted to spectral analysis and calculation of coherence (Fourier transform) was 1 s. This provided a frequency resolution of 1 Hz. Auto-power spectrum and cross-power spectrum estimates were obtained by averaging of sample spectra of disjoint EEG epochs, with normalized standard error of 0.20 for the EEG fragment of 25-s duration (Bendat and Piersol, 2000). The complex coherence function was calculated as a normalized cross-power spectrum (Zaveri et al., 1999). The results were presented in individual or group average topographic maps of high coherent connections (HCC) among all the leads with the coefficient of coherence (CC) – the square root of the computed magnitude squared coherence exceeding a certain threshold. The CC was interpreted as an analogue of the frequency indexed correlation coefficient (Jenkins and Watts, 1968).

It was hypothesized that the extent of the photic driving topographic generalization will correlate with the total number of HCC. Such a number based on a certain fixed CC threshold varied greatly in different individuals, so that in some of them it could be close to either 0 or 100%. In such cases, the interhemispheric asymmetry in the number of HCC was not reliable. Therefore, we tried to emphasize the peculiarities of the HCC topographic distribution by considering the 20 most HCC in each individual at each EEG frequency corresponding to that of the stimulation. In some rare cases when the 20th and the 21st CCs values (ranged from the maximum) were equal, the 19 most HCC were considered. The total number of the *intra*hemispheric HCC was evaluated for each hemisphere.

A more adequate comparison between the groups was based on a fixed CC threshold for HCC common to both groups. For each IPS frequency, such a threshold was calculated as averaged over individual CC thresholds of all control subjects and autistic patients. In this approach, the general level of coherence in each individual could be characterized by the total number of HCC. The number of HCC was also averaged over all IPS frequencies corresponding to each of the four standard frequency bands, i.e. for 5 frequencies in the beta (15, 18, 21, 24 and 27 Hz), 3 in the alpha (8, 10 and