BRAIN RESEARCH 1594 (2015) 305–309

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Brain Research

Research Report

Reduction of epileptic spike-wave activity in WAG/Rij rats fostered by Wistar dams

*Evgenia Sitnikova**, *Elizaveta M. Rutskova*, *Vladimir V. Raevsky*

Institute of the Higher Nervous Activity and Neurophysiology of Russian Academy of Sciences, Butlerova str., 5A, Moscow 117485, Russia

ARTICLE INFO

Article history:
Accepted 29 October 2014
Available online 6 November 2014

Keywords:
WAG/Rij rats
Absence epilepsy
Spike-wave discharges
Development

ABSTRACT

In WAG/Rij rat genetic model of absence epilepsy, the first spike-wave discharges (EEG hallmark of absence epilepsy) are known to appear after puberty, and their incidence increases with age. WAG/Rij rats are known to have a genetic predisposition to absence epilepsy, and further development of epilepsy might be influenced by epigenetic factors. This preliminary study examined the effect of early postnatal factors on the incidence of epileptic spike-wave discharges in adulthood. The newborn WAG/Rij rats were fostered by Wistar dams (from birth throughout the weaning age), and their EEG was examined continuously from 5 to 13 months of age. It was found that the number and duration of absence seizures was reduced in WAG/Rij rats adopted by Wistar dams as compared with the age-matched control WAG/Rij rats nursed by their own mothers. These data indicate that natural (epigenetic) factors, such as maternal care during suckling period, affect development of seizure activity in genetically prone subjects. It is suggested that improvement of primarily care-giving environment in subjects with genetic predisposition to absence epilepsy is a way to reduce epileptic activity in later life.

1. Introduction

Absence epilepsy is idiopathic generalized epilepsy, characterizing by a strong genetic predisposition and age-related onset (Panayiotopoulos, 2005; Nordli, 2005). Typical absence seizures are predominantly spontaneous, and they are accompanied by spike-wave discharges (SWD) in the electroencephalogram (EEG). In genetic model of absence epilepsy, WAG/Rij rats, SWD are known to appear spontaneously, and the number and duration of SWD gradually increases with age (van Luijtelaar and Coenen, 1986; Coenen and van Luijtelaar, 1987). In particular, young adults WAG/Rij rats (2–3 months old) express only immature forms of SWD, whereas fully blown EEG seizures can be recorded at about 6 months of age and older (Coenen and van Luijtelaar, 1987; 2003; van Luijtelaar and Bikbaev, 2007). The number and duration of SWD in WAG/Rij rats was found to increase from 2 to 6 months of age (Klein et al., 2004), and percent time in SWD significantly increased from 2 to 4 month of age with a tendency to further increase at 6 months of age. Previously we indicated (Sitnikova, 2011) that in Moscow's population of WAG/Rij rats (IHNA RAS, Russia) matured seizure activity appeared at the age of 8–9 months that is later in comparison to what was found in

*Corresponding author. Fax: +7 499 743 00 56.
E-mail addresses: jenia-s@mail.ru (E. Sitnikova), li-za-za@yandex.com (E.M. Rutskova), vraevsky@mail.ru (V.V. Raevsky).

http://dx.doi.org/10.1016/j.brainres.2014.10.067
0006-8993/

the original breeding colony of WAG/Rij rats (see above). In the present study we examined the influence of the environment, i.e., epigenetic factor, on the incidence of genetically predetermined absence epilepsy in WAG/Rij rats.

There is a strong inherited component of absence epilepsy in WAG/Rij rats, as it was demonstrated in cross breeding studies, whereas some parameters of SWD could be arisen from maternal effect (Peeters et al., 1990; 1992). Some experimental evidences were collected showing that absence epilepsy in WAG/Rij rats is governed by epigenetic factors. For example, Schridde et al. (2006) indicated that neonatal handling and maternal deprivation in WAG/Rij rats resulted to a pronounced decrease of epileptic discharges later in life. Our previous experiments (Sitnikova, 2011) demonstrated that whisker trimming during the first 3 postnatal weeks in WAG/Rij rats led to significant increase of seizure activity at adult ages. Moreover, oral administration of anti-absence drug ethosuximide in WAG/Rij rats prior to the development of SWD suppressed epileptic activity up to 90 days after cessation of treatment (Blumenfeld et al., 2008).

It is well known that maternal care during early postnatal life is important for the emotional and cognitive development of the offspring (i.e., McGowan et al., 2011). Despite the fact that the quality of maternal care is proved to impact on the offspring's learning abilities, memory and neuroplasticity, its role in epileptogenesis is less obvious Slamberová et al., 2010, 2011). Maternal deprivation and brief handling in Wistar rats during 2–10 postnatal days was found to promote vulnerability to limbic epilepsy (Salzberg et al., 2007; Kumar et al., 2011). Cross-fostering studies in Mongolian gerbils (Kaplan, 1981) indicated that seizure-prone gerbils fostered to nonseizure-prone parents exhibited delayed onset of seizure activity, whereas seizure-prone gerbils fostered to seizure-prone parents did not. Taken into account that WAG/Rij female rats with genetic predisposition to absence epilepsy characterized by a poorer maternal care in comparison to non-epileptic Wistar rats (Dobryakova et al., 2008) and also our unpublished data indicating that WAG/Rij dams exhibited "specific strategy" of maternal behavior, which was significantly distinguished from that in Wistar dams, we hypothesized that "specific" maternal behavior in WAG/Rij female rats might negatively affect early affect brain development in their offspring and, therefore, promote absence seizures later in life. In the present paper we performed the first step to investigate this hypothesis and examined development of epileptic spike-wave activity in WAG/Rij rats fostered by Wistar.

2. Results

Epileptic activity was analyzed in EEG in two groups of WAG/Rij male rats (Fig. 1). The first control group consisted of 9 rats nursed by their mothers and the second group—6 rats fostered by Wistar dams. The body weight in rat pups was examined daily from the postnatal day 2 to day 21, and it was found that the body weight of fostered rats (experimental group) did not differ from the controls, suggesting that the adopted pups were nursed well.

SWD were recognized in EEG as generalized spike-wave complexes in the fronto-parietal cortical area (Fig. 2B). Immature SWD (Fig. 2A) represented short trains of sharp waves with occasional spikes and were less generalized. Fig. 2 demonstrates changes of the waveform of SWD in a control WAG/Rij rat between 6 and 12 months of age, where the spike

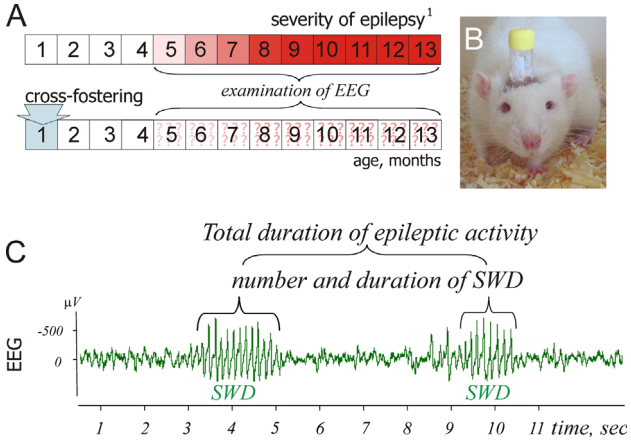

Fig. 1 – Details of experimental design and EEG data analysis. (A) The scheme of experiment. (B) Photo of WAG/Rij rat taken next day after the stereotactic operation (implantation of epidural EEG electrodes) at the home cage. (C) An example of frontal EEG with spike-wave discharges (SWD), indicating measurable characteristics of discharges that were statistically analyzed. Severity of absence epilepsy in WAG/Rij rats is known to be increased during late ontogenesis (Coenen and van Luijtelaar, 1987; 2003; Klein et al., 2004; van Luijtelaar & Bikbaev, 2007), and in WAG/Rij rat colony at our institution, significant increase of the number and duration of SWD was found in a period from 5 to 8 months of age (Sitnikova, 2011).

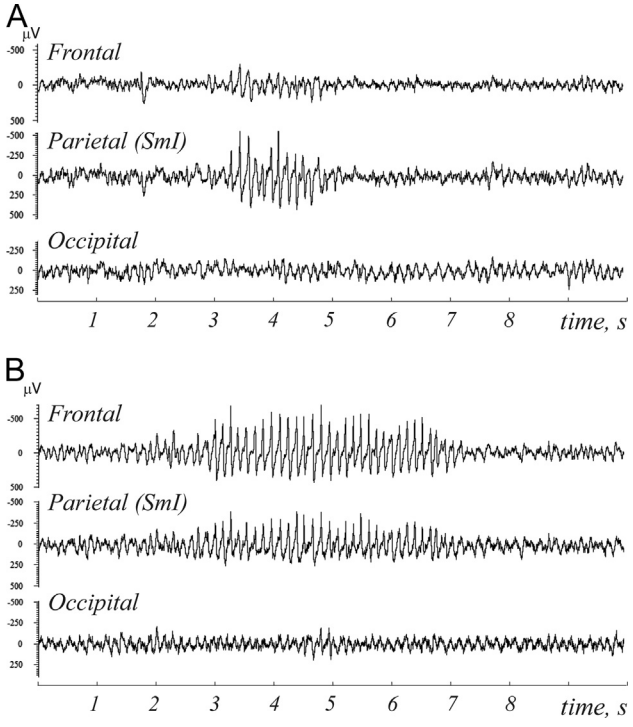

Fig. 2 – Spike-wave discharges in EEG as recorded in a control WAG/Rij rat at different ages. The parietal electrode was placed over the primary somatosensory cortex (SmI).