



Spontaneous absence-like activity in Wistar rats: Behavioral and electrographic characteristics and the effects of antiepileptic drugs

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ABSTRACT. Current investigation describes the behavioral and electrographic characteristics of spontaneous absence-like seizures identified in Wistar rats (referred to here as FMUSP-rats, after the Faculty of Medicine, University of São Paulo, São Paulo State, Brazil), and characterized by spike-wave discharges (SWDs) in the neocortex and the hippocampus. After consanguineous crossing directed to an increased incidence of seizures, the latter were observed in almost all F9 offspring. FMUSP-rat seizures are expressed as immobility and concomitant SWDs, oscillating between 7.5 and 12 Hz in the frontoparietal cortex and the hippocampus. Behaviorally, they are mainly associated with clonic movements of the eyes, rostrum and vibrissae, the latter ranging between 1 and 70 seconds and occur at a rate of up to 229 per hour. Systemic injections of ethosuximide (0, 25, 50, 100, 250 mg kg⁻¹) and of diazepam (15 mg kg⁻¹) increased the latency for the first seizure and reduced both the hourly incidence of SWD bursts and their mean duration. Carbamazepine (30 mg kg⁻¹) injections increased both the incidence and duration of the SWDs, leaving the latency for the first seizure unchanged. Comparisons between FMUSP-rats and well-established genetic models of absence seizures data indicated that the animals described herein might contribute towards studies on the neurological condition under analysis.

Keywords: absence, epilepsy, epileptic FMUSP rats, antiepileptic drugs.

Atividade epiléptica espontânea tipo ausência em Ratos Wistar: características eletrográficas e comportamentais e os efeitos de drogas antiepilépticas

RESUMO. Neste estudo, descrevemos aspectos eletrográficos e comportamentais de atividade semelhante às crises de ausência identificadas em ratos Wistar (ratos FMUSP - Faculdade de Medicina da Universidade de São Paulo, Estado de São Paulo, Brasil), que são caracterizadas por descargas em forma de espícula-onda no neocórtex e no hipocampo em 100% dos ratos da geração F9 resultante de cruzamentos consanguíneos. As crises se manifestaram com imobilidade comportamental associada com atividade eletrográfica em forma de espícula-onda oscilando entre 7,5 e 12 Hz no córtex frontoparietal e no hipocampo. Também foram observados comportamentos associados como clonias oculares, rostrais e de vibrissa que duravam de 1 a 70 segundos podendo ocorrer a uma taxa de até 229 eventos por hora. Injeção sistêmica de etosuximida (0, 25, 50, 100 e 250 mg kg⁻¹) and of diazepam (15 mg kg⁻¹) aumentaram a latência para a primeira crise e reduziram tanto a incidência quanto a duração das crises. Injeções de Carbamazepina (30 mg kg⁻¹) aumentaram tanto a incidência quanto a duração das crises sem interferir na latência. Comparações feitas entre os ratos epiléticos FMUSP com os modelos genéticos de epilepsia bem estabelecidos na atualidade indicaram que o modelo aqui descrito pode contribuir para um melhor entendimento dos mecanismos relacionados a esta condição neurológica.

Palavras-chave: ausência, epilepsia, ratos FMUSP epiléticos, drogas antiepilépticas.

Introduction

Absence seizures are one of the most common types of seizures experienced by patients with idiopathic generalized epilepsies, occurring in a number of different syndromes, including childhood absence epilepsy, juvenile absence epilepsy and juvenile myoclonic epilepsy (ILAE, 1989). Absence seizures are

characterized by recurrent non-convulsive episodes with loss of awareness and responsiveness, and are commonly accompanied by minor motor manifestations, but without loss of postural tone. EEG recording during absence seizures shows bihemispheric, synchronous, generalized spike-and-wave discharges (SWDs) at approximately 3 cycles per second, which start and end abruptly on an

otherwise normal background EEG (JONES et al., 2011).

Nearly one hundred models of spontaneous and experimental epilepsy have been studied over the past three decades (LÖSCHER, 1997). This research effort reveals the need for and importance of valid animal models of human epilepsy that would present clinical and pharmacological characteristics similar to human seizures (KORNETSKY, 1977). This is particularly the case of absence seizures, in which spike-wave complexes, pathognomonic expressions of absence seizures (*petit mal* epilepsy), are either produced spontaneously or induced in rodents and primates through the injection of penicillin, pentylenetetrazol, gamma-hydroxybutyrate and GABAergic agonists (SNEAD, 1994, 1998). Absence seizures are behaviorally expressed as immobility and clonic movements of the limbs, face, eyes and rostrum. A number of available models of this condition allows in-depth studies of their manifestations and mechanisms. However, neither the specific lesions that determine absence seizures nor all of their manifestations have been found in any experimental model so far (NIEDERMEYER, 1996).

The occurrence of pathological rhythmic cortical potential in rodents was first described in 1958 (LIBOUBAN; OSVALDO-CRUZ, 1958). In the past 30 years, many types of spontaneous or pharmacologically induced animal “absence-like” epilepsy have been reported (HOSFORD et al., 1995; MAXSON et al., 1983; NOEBELS; SIDMAN, 1979; SERIKAWA et al., 1987; VAN LUIJTELAAR; COENEN, 1986; VERGNES et al., 1982, 1986), with cortical spike-and-wave discharge, associated with various behavioral phenomena, as common denominator. A presumably new type of spontaneous epilepsy, resembling human absence seizures, was identified in a fraction of Wistar rats used in our laboratory. It is characterized by SWDs oscillating at 6-12 Hz in the neocortex and the hippocampus. The above serendipitous observations prompted us to select from them a highly characteristic strain of epileptic rats (referred to here as FMUSP-rats, after the Faculty of Medicine, University of São Paulo, São Paulo State, Brazil). Current paper describes the behavioral and electrographic characteristics of these seizures and investigates the effects of three different anti-epileptic drugs on these manifestations.

Material and methods

Animals and selection procedures

All procedures used in current study were approved by two committees for Ethics in Animal Research

(UNIFESP, protocol n. 1255/00 and CAPPesq-HC-USP, protocol n. 197/00). The rats used in the initial observations that led to the discovery of the spontaneous absence-like activity were obtained from the regular stock of the vivarium of the Faculty of Medicine, University of São Paulo, São Paulo State, Brazil. Most animals derived from second or third generation of animals obtained directly from the Wistar Institute.

The rats were reared and maintained at our laboratory for genetic selection experiments. Animals were housed in individual cages in an isolated room at a constant temperature of 22°C, with 12h photoperiod (light period from 7:00 a.m. to 7:00 p.m.) and free access to food and filtered water.

The crosses were carried out to the F9 generation, by consanguineous crosses between rats that showed spike-wave activities at each generation. Criteria for inclusion in the breeding procedures included the presence of SWDs in neocortical areas and in the hippocampus of adult rats (2-3 months old). All rats between F7 and F9 showed epileptiform electrical activity in neocortical leads. Rats coming directly from the vivarium with no apparent EEG abnormalities during a 4h long recording session were used as controls. The “epileptic” FMUSP-rats examined in this study descend, from the fifth generation onwards, from the consanguineous crossing of rats that manifested spike-wave activity.

Surgery

Forty spontaneously epileptic F9 FMUSP-rats of both sexes (between 230 and 400 g bw) were implanted, under general anesthesia (4 mg kg⁻¹ of diazepam and 100 mg kg⁻¹ of ketamine, ip), with bipolar nickel-chrome electrodes (200 µm in diameter, isolated except at the end cross section) over the neocortical area A₃ (AP = -1.5; L = 3.0) A10 (M₁-M₂ – AP = 3.0; L = 2.5) (KRIEG, 1946; PAXINOS; WATSON, 1997; ZILLES, 1992) and in the CA₁ (AP = -3.0; L = 1.5; H = -3.0) or CA₃ (AP = -3.3; L = 2.5; H = -3.8) hippocampus fields (Figure 1A and B), following stereotaxic coordinates derived from Paxinos and Watson (1997). Electrodes were also bilaterally implanted in the trapezius muscles, in the muscle pad that moves the vibrissae and in the lateral epicanthus of each eye, in order to record head, rostrum/vibrissae and eye movements, respectively.

Experiment 1:

Behavioral and electrographic recordings in experimentally naïve FMUSP-rats.

Numerous recording sessions were carried out in 20 chronically implanted, freely moving FMUSP-rats

for descriptive and exploratory purposes. Recording sessions started at least seven days after electrode implantation. The rats were placed in the recording environment (a wire mesh cage, 20 x 30 x 40 cm, placed in an acoustically and thermally isolated room) 2 hours before the experiments. Experiments were initiated at varying day hours (from 9:00 a.m. to 14:00 p.m. of the light phase of the cycle), except for the experiments on drug effects, which started at 10:00h. Typical recording sessions were 2 to 4 hours long, during which the rats were continuously observed for behavioral changes, which were annotated directly and contingently in the recording media. In the case of five animals, 24h long recording sessions started at 7:00h.

Digital and 'on-paper' electrographic recordings were taken on a 21 channel Nihon-Kohden electroencephalograph (Neurofax EEG 4400) locked to a personal computer. The recording parameters included a calibration pulse of 50 μ V, time constants of 0.3 s (for the EEG) and 0.001 s (for the EMG), low-pass filters of 30 Hz (EEG leads) and 120 Hz (EMG leads) and a 60 Hz notch filter for all recordings. Recordings were inspected off-line to detect and count the duration, frequency and latency of the seizure bursts, as well as to indicate the behavioral state before, during and after these seizures. The behavioral catalogue comprised attentive wakefulness

(presence of exploratory and/or locomotive behavior, associated with desynchronized cortical EEG and theta activity in the hippocampus leads, as well as intense EMGraphic and EOGraphic activities), relaxed wakefulness (presence of grooming behavior or immobility, associated with low EMGraphic and EOGraphic activities, desynchronized cortical EEG in the absence of hippocampus theta rhythm), and the three phases of slow-wave sleep, pre-paradoxical sleep and paradoxical sleep (presence of resting postures), associated with the classical electrographic sleep signs (GOTTESMANN, 1998; TIMO-IARIA et al., 1970; VALLE et al., 1992). For the spectral (FFT) analysis and other measurements, at least 10 epochs (2 s each) per animal of the EEG tracings were selected from stable and homogeneous periods of ictal and of interictal events. The routine used for FFT analysis was based on MatLab (The Mathworks, Inc. Version 5.3), developed in our laboratory.

Upon the termination of all experiments and observations, each animal was killed by an overdose of the anesthetic. After perfusion with saline solution and formalin 4%, the brain was removed and cut (Vibratome, at 50 μ m thickness) for Nissl staining to determine the correct location of the electrodes (Figure 1A and 1B).

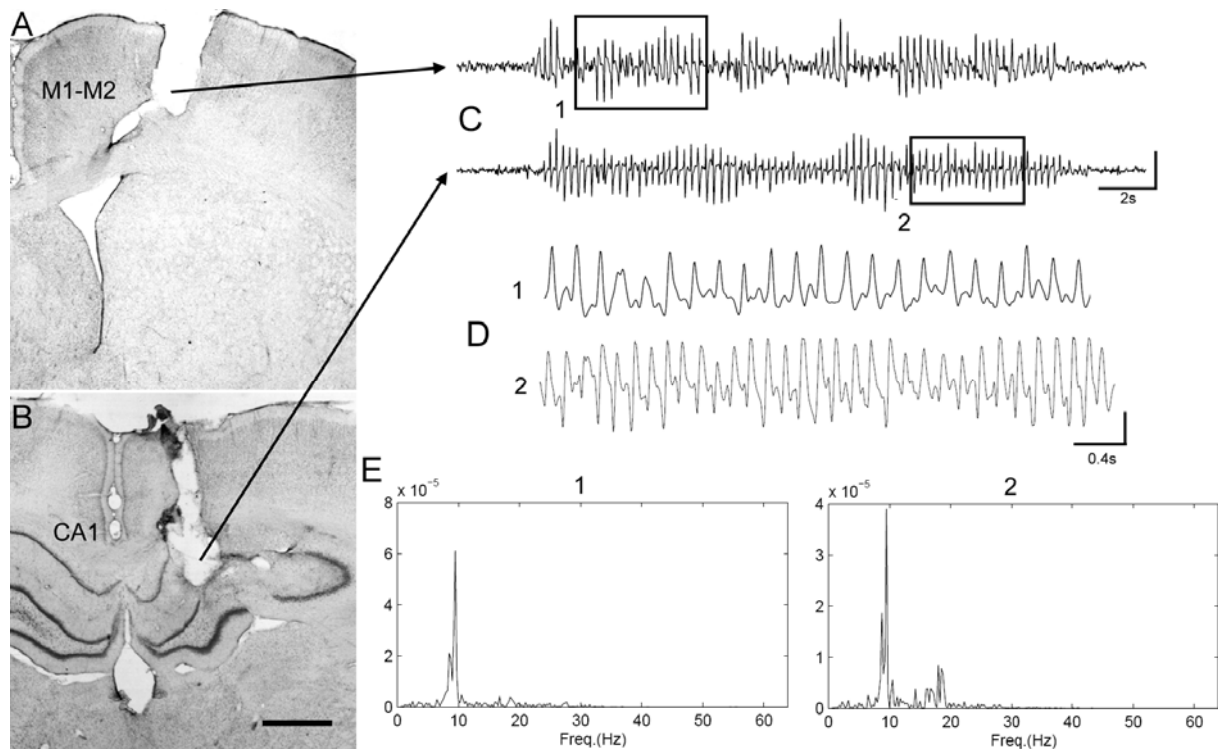


Figure 1. Photomicrographs (A and B) of Nissl-stained (thionin) frontal sections of the rat brain, showing the recording sites examined. A: primary/secondary motor cortex (M1-M2). B: CA1 field of the hippocampus (CA1). Scale bar = 1 mm. C and D) Spike-wave bursts characteristic of FMUSP-rats, occurring simultaneously in A10 (upper tracing) and in CA1 (lower tracing). Vertical calibration bar: 100 μ V. E) Frequency spectra (FFT) of 10 pooled epochs (2 s each) per animal of the A10 (1) and CA1 (2) EEG.

Experiment 2:

The effects of antiepileptic drugs.

The acute effects of systemic (ip) injections of ethosuximide (ETX), diazepam (DZP) and carbamazepine (CBZ) were examined in 20 F9 FMUSP-rats. ETX (25, 50, 100, 250 mg kg⁻¹) or saline (pyrogen-free NaCl 0.9% solution) injections were carried out in 10 rats immediately before the beginning of a 4h long recording session. Doses were retrieved from assays which indicated the anti-seizure effects of these drugs (MARESCAUX et al., 1992), and our emphasis on the study of ETX treatment came from its efficacy in rat models of absence seizures and in child epilepsy treatment (MARES, 1998; POSNER et al., 2005). All animals received all treatments (with at least 7-day intervals), distributed according to a Latin square design. Another group of 10 experimentally naïve FMUSP-rats received DZP (15 mg kg⁻¹), CBZ (30 mg kg⁻¹) or their vehicles (pyrogen-free NaCl 0.9% solution for both drugs); all animals received all treatments with at least 7-day intervals, also distributed according to a Latin square design. DPZ and CBZ doses were derived from studies which indicated their effectiveness in reducing (DZP) (COENEN; VAN LUIJTELAAR, 1989) or increasing (CBZ) (PERUCCA et al., 1998) absence-like seizures in rats. All experiments were performed between 9.00 and 2.00 p.m. All drugs were supplied by Sigma, Inc. Data on drug effects were analyzed by one-way ANOVA procedures, followed by tukey's post hoc test; data were expressed as mean \pm SEM; $p < 0.05$ was adopted as the significance criterion in all procedures.

Results

Experiment 1: Behavioral and electrographic recordings in experimentally naïve FMUSP-rats.

The general behavior (sleep-waking activities and postures) and size/weight at adult age of the 40 FMUSP-rats studied were not noticeably different from that of control animals. Non-systematic observations by those who were in charge of their daily maintenance (ANDRÉ et al., 1999), indicated that F5-F9 FMUSP-rats tended to be more aggressive to handling and less fertile than control animals. It was also interesting to note that, between F5 and F9, the animals apparently developed an increased resistance to the anesthetic used (ketamine), usually requiring double or triple doses to achieve a proper anesthetic level for surgery.

Although behaviorally undistinguishable from control animals, the 40 FMUSP-rats studied here showed EEGraphic recordings permeated by frequent bursts (127.7 ± 9.3 seizures per hour, minimum of 43

and maximum of 229 bouts h⁻¹) of neocortical and hippocampus SWDs (Figure 1C and D), with a duration of 1-76 seconds (8.7 ± 0.13 s) for each seizure. The spikes that compose the bursts varied between 5.5 and 12 Hz and 50-250 μ V (peak-to-peak) in amplitude, while waves ranged between 20 and 100 μ V and 6.5 Hz (Figure 1E).

The above-mentioned bursts appeared first in the cortex or hippocampus in the same rat, without a clear preference (Figure 2A and B). The bursts of spike-wave activity usually occurred concomitantly with hypotonic EMG activity and suggested behavioral arrest (Figure 2A), without any noticeable postural changes. The animals remained motionless during the electrophysiological seizures. Eye, rostrum (Figure 2A and B) and vibrissae/facial clonic movements were occasionally observed during these arrest periods. It is interesting to note that some clonic movements occurred at the end of or preceding the SWDs in the neocortical areas.

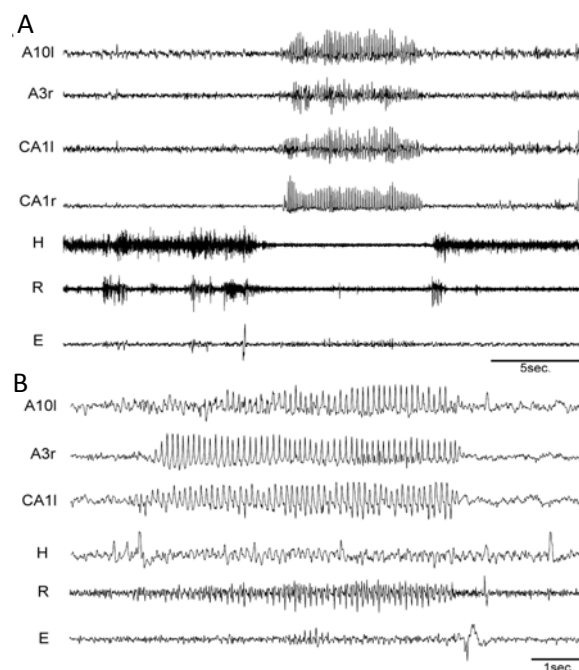


Figure 2. Spike-wave bursts during seizures in a FMUSP-rat, in the cortical A10 (l, left) and A3 (r, right); and in CA1 (l, left) and CA1(r, right). H, R and E: head, rostrum/vibrissae and eye movements, respectively. Vertical calibration bar: 100 μ V. (A): Spike-wave burst interrupting an active wakefulness period. Note the sudden decrease in EMG activity, preceding the onset of the electrographic seizure. (B): Spike-wave episode beginning in the left CA1 area, and accompanied by rhythmic movements of the rostrum.

Figure 2B shows the waxing of seizure activity amplitude in the A10 (motor cortex, but note its absence in the A3 and hippocampus leads), possibly associated with a waxing of the rhythmic, clonic EMG activity in the rostrum (but not in the neck or eye

leads). During these recordings, an unequal distribution of seizures over the different periods of the day, as well as differential associations with sleep-waking states were observed. These differences will be detailed in a separate paper.

Experiment 2: The effects of antiepileptic drugs in FMUSP rats.

Systemic injections of ETX resulted in a dose-related anti-seizure effect. Latency for the first seizure was significantly increased after the three higher doses (from 22 ± 4 minutes after vehicle injection to 230 ± 18 minutes after the 200 mg kg^{-1} dose, Figure 3) and the same doses also significantly reduced both the hourly incidence of SWD bouts (from 104.3 ± 7.3 in vehicle-treated animals to 12.5 ± 6.9 in animals treated with the higher ETX dose, after the delayed first episode) and their mean duration (from 6.7 ± 0.10 s in vehicle-treated animals to 3.5 ± 0.9 s in animals treated with the 200 mg kg^{-1} dose).

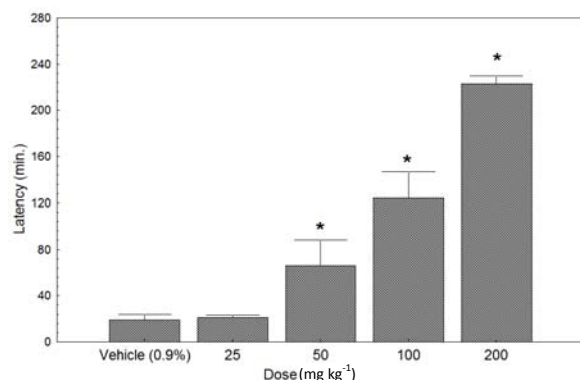


Figure 3. Effects of ethosuximide (ETX) injections on latency of the first seizure episode in FMUSP-rats. (*) $p < 0.05$ as compared to vehicle-treated animals.

DZP injections evoked a prompt and significant reduction in seizure incidences (between 94.3 ± 6.1 in vehicle-treated animals and 18.3 ± 3.6 in DZP-treated animals) and their mean duration (between 9.5 ± 1.30 s in vehicle-treated animals and 4.5 ± 0.4 s in DZP-treated animals); DZP injections also significantly postponed the first spike-wave bout to 54 ± 5 min after the start of the recording session when compared to the first burst latency in vehicle-treated animals (21 ± 2.9 min.). CBZ injections, on the other hand, increased both incidence and duration of the spike-wave discharges but the latency for the first seizure remained unchanged when compared to vehicle-injected animals.

Discussion

Current study describes the behavioral and electrographic characteristics of spontaneous absence-like seizures identified in Wistar rats (FMUSP-rats) characterized by SWDs in the neocortex and the hippocampus, concomitant with a general behavioral arrest (resembling freezing) and with clonic movements of the eyes or rostrum/vibrissae. These behavioral and electrophysiological attributes are characteristic of absence seizures in human (FUTATSUGI; RIVIELLO JR., 1998; STERIADE, 1990; WILLIAMS, 1953) and non-human primates (FUTATSUGI; RIVIELLO, 1998; STERIADE, 1990; TENNEY et al., 2004), but the frequency of the spike-wave complex in the FMUSP-rats (5.5 to 12 Hz) is much higher than those commonly observed in humans (3 Hz, see Niedermeyer, 1996). Arrest behavior and seizures electrophysiologically resembling the primate absence seizures have been extensively described in rodents. One of the most studied models of spontaneous epilepsy in rats, the WAG/Rij (Wistar Albino Glaxo rat of Rijswijk) (VAN LUIJTELLAR; COENEN, 1986; COENEN et al., 1992), shows “absence”-like seizures expressed as 7-9 Hz SWDs during quiet wakefulness and synchronized sleep. Another extensively examined model of spontaneous epilepsy is the GAERS rat (Genetic Absence Epilepsy Rats from Strasbourg) (MARESCAUX et al., 1992) presenting seizures with high voltage (250-800 μV) 7-10 Hz discharges lasting 0.5 to 7.5 seconds. Such discharges are recorded from neocortical areas, mainly frontoparietal, and thalamic nuclei during quiet wakefulness and synchronized sleep (VERGNES et al., 1982, 1986; DANOBER et al., 1998).

However, abnormal hippocampus activity was not found during seizures in WAG/Rij (COENEN et al., 1992) or in GAERS rats (DANOBER et al., 1998) but were consistently present in the FMUSP-rats. The above suggests that important differences in the neural mechanisms underlying these seizures may exist between these well-known models and the one described herein. Although no spike-waves were recorded from the hippocampus in GAERS, glutamate content in the animals hippocampus area was very high, or rather, almost three times as much as that found in normal rats. In addition, despite the lack of electrophysiological epileptogenic potentials in the hippocampus of GAERS, as has been consistently found, a large increase in local glucose utilization in the dorsal hippocampus (+36%), in the ventral hippocampus (+37%) and in the dentate gyrus, occurred in these animals (NEHLIG et al.,

1991), suggesting a certain degree of mobilization of the hippocampus in absence seizures in this strain of rats. It is thus possible that hippocampus neurochemical abnormalities similar to that of GAERS may also be present in FMUSP-rats and they may be intense enough to be translated into important electrical abnormalities.

The study of the neuropeptide-Y expression in dentate gyrus granule cells in stargazer mutant mice (CHAFETZ et al., 1995) revealed that it was concentrated in mossy fibers following spike-wave seizures, and considered as a reflection of the gene induction triggered by synchronous bursting. Current study clearly demonstrates that SWDs are present in the hippocampus of a rodent although this assumption was challenged (KANDEL et al., 1996) following the analysis of single/multi-unit recordings from the sensorimotor cortex, the ventrolateral thalamus and the hippocampal CA₁ and CA₃ fields. While such recordings show a strong correlation between the unit recordings and the spike component of the SWDs in the cortex and thalamus, no correlation was found in the hippocampus. Another demonstration of the lack of hippocampal activation during absence seizures induced by GABA is that $\alpha 1$ and $\alpha 4$ subunits mRNA expression appear in the thalamic relay nuclei but not in the hippocampus (BANERJEE et al., 1991).

It is interesting to note that seizure-related hippocampus activity (SWDs) has been observed in rodents. Noda's epileptic rats (NER) show high voltage 7-9 Hz polyspikes and diffuse spike-wave complexes, mainly in cortical and hippocampus EEG (NODA et al., 1998). In the SER (Spontaneous Epileptic Rats) model the 5-7 Hz (mostly 6 Hz) spike and wave complex, synchronously in the cerebral cortex and hippocampus, is accompanied by an absence-like seizure (SERIKAWA et al., 1987). In the AY-9944 model (CORTEZ et al., 2001) SWDs of similar morphology and varying amplitudes were recorded from bipolar electrodes in the cortex, thalamus and hippocampus between 5 and 6 Hz.

Spike-wave discharges in the FMUSP-rats may start much earlier in the hippocampus than in neocortical areas. Since the lack of SWDs in the hippocampus in absence seizures has been considered a defining characteristic of this kind of epilepsy in rodents (COENEN; VAN LUIJTELLAR, 1989; DANOBER et al., 1998; KANDEL et al., 1996), these potentials define a specific kind of spontaneous epilepsy in our rats. The existence of reciprocal, cortico-thalamic volleys is one of the most generally accepted explanations

for the cortical spike-wave activity in the above-mentioned rat models of absence seizures and in humans (SARKISIAN, 2001; URE; PERASSOLO, 2000). It is conceivable that hippocampus-directed rhythmic activity, originated in pattern generators located in extra-cortical and extra-hippocampus areas may be operating in FMUSP-rats. In support of this possibility, the motor manifestations of the FMUSP-rat seizures was shown to precede, in some events, the appearance of cortical and/or hippocampus electrical abnormalities, further suggesting the involvement of an extra-prosencephalic generator in the origin of the described seizures.

The profile of the FMUSP-rat responses to seizure-affecting drugs may further characterize the "absence-like" nature of their seizures. Ethosuximide is a voltage-dependent T-type Ca⁺² channel blocker, or rather, the anticonvulsant of choice in the treatment of absence epilepsy (COULTER et al., 1989; MACDONALD; MCLEAN, 1986; MANNING et al., 2003). In current experiments, injections of this drug increased, in a dose-related fashion, the latency for the first seizure and reduced both the incidence and duration of SWDs. It has also been shown to inhibit absence-like seizures in a number of rodent models (COENEN; VAN LUIJTELAAR, 1989; MARES, 1998; MARESCAUX et al., 1992) in the dose range used in current experiments. Furthermore, this drug failed to affect other types of seizure (GUERRINI; PARMEGGIANI, 2006). DZP injection also increased the latency and reduced the incidence/duration of FMUSP-rat seizures. Benzodiazepines have reduced the severity of absence and myoclonic seizures in humans (MELDRUM; ROGAWSKI, 2007) and suppressed pentylenetetrazol-induced seizures (MARES; SLAMBEROVÁ, 2006) as well as those in GAERS and other rodent models (COENEN; VAN LUIJTELLAR, 1989; DANOBER et al., 1998; COENEN; VAN LUIJTELAAR, 2003) by acting on GABA_A receptors. These data may suggest that a common neurochemical mechanism was affected in the human absence condition, in these other rodent models and in FMUSP-rats.

On the other hand, carbamazepine injections increased the incidence and duration of the spike-wave. CBZ is an iminostilbene that slows the recovery of voltage-activated Na⁺ channels and exacerbates SWDs in absence seizures while it suppresses complex and simple partial seizures as well as tonic-clonic generalized seizures in humans (SCHUMACHER et al., 1998) and in rodent models such as the GAERS (DANOBER et al.,

1998). The similarity between FMUSP-rat responses to these treatments and the absence of related primate and rodent models, indicate their predictive value in studies of anti-absence drugs and their potential as subjects in experimental studies on this subject. High-voltage 7-12 Hz rhythmic spikes or SWDs are frequently detected in several strains of rats, including WAG/Rij, GAERS, Long-Evans, Brown Norway and Fischer-344 (JANDÓ et al., 1995; KAPLAN, 1985; POLACK; CHARPIER, 2006; SHAW, 2004, 2007; WILLOUGHBY; MCKENZIE, 1992). As observed in almost all F9 offspring of the FMUSP-rats, consanguineous crossing may be successfully directed to an increased incidence of seizures, suggesting that these abnormalities may be genetically transmitted.

The importance of genetic factors in idiopathic generalized epilepsies, including absence epilepsy, has been repeatedly demonstrated (CRUNELLI; LERESCHE, 2002; LENNOX; JOLLY, 1954; NOEBELS; SIDMAN, 1979; PURANAM; MCNAMARA, 1999; SARKISIAN, 2001; WILLIAMS, 1953;), and “face validity” of rodent models of this condition have been suggested on the basis of its inherited nature, in addition to the electroencephalographic, behavioral and pharmacological aspects (COENEN; VAN LUIJTELAAR, 2003).

Conclusion

Comparing earlier established genetic models of absence seizures data with FMUSP-rats revealed that the animals described herein, easily found and selected from the healthy and current Wistar rats stock available, might contribute towards neurobiological studies within this neurological condition. The seizures of the FMUSP-rats described in this paper may also relate to atypical absence-like seizures, mostly due to hippocampus involvement.

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developed as part of the Ph.D. thesis of the first authors.

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