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Spontaneous spike-wave discharges in rat neocortex and their relation to behaviour

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Abstract. A certain proportion of laboratory rats of various strains show spontaneous nonconvulsive ECoG seizures in the form of bursts of spike-and-wave discharges (SWD). Since in the majority of behavioural experiments the EEG is not controlled, the experimenter is usually unaware of this fact. The purpose of the present work was to find out whether the SWD trait is related to the rats behavioural performance in selected test situations. The experiment was performed on two groups of male Wistar rats, outbreds, aged six (group 6M, n = 17) and 24 months (group 24M, n = 14). First, in both groups the following forms of behaviour were assessed: (1) seeking water reward in an 8-arm radial maze, (2) exploration of a new object, (3) inhibition of a locomotor response (passive avoidance), and (4) paw-lick response to a thermal stimulus (54.5^{o}C) applied to the feet before and after intermittent footshock. The rats were then implanted with intrabrain electrodes and the level of SWD activity was assessed. Rats of the 24M group, compared with those of the 6M one, showed a significantly shorter exploratory response to a new object and diminished responsiveness to heat. The groups did not differ, however, in passive avoidance and radial maze performance. The analysis of 3-h ECoG sections revealed SWD bursts in 73% and nearly 93% of rats from groups 6M and 24M, respectively. The groups did not differ in the number of bursts or in the total duration of SWD activity. A correlation analysis of pooled data from both groups revealed that the exploration time of a new object was significantly (negatively) correlated with the number of SWD episodes. The total duration of SWD activity, and the number of perseveration errors in the radial maze, was significantly (positively) correlated with the total duration of SWD activity. The results suggest that SWD rats are behaviourally impaired in some test situations.

Key words: spike-wave discharges, age, behaviour, rat

INTRODUCTION

In a certain proportion of laboratory rats of different strains, bursts of spike and wave discharges (SWD), reminiscent of human petit-mal epilepsy, occur spontaneously in the ECoG (see Coenen et al. 1992, and Marescaux et al. 1992 for reviews). Behavioural manifestations of SWDs are minimal (immobile posture, fixed staring, vibrisse twitching) and usually pass unnoticed during casual observation. It has been established that the propensity for SWD generation is a hereditary trait with a dominant pattern of inheritance (Peeters et al. 1990). Although strains homogenous in respect to the SWD trait have been bred out in some laboratories, in a majority of studies heterogenous rat populations are being used and, if EEGs are not performed, the experimenter is unaware of the EEG pathology in a proportion of the subjects under study. The rats with SWD bursts (SWD rats) differ from those with normal EEG patterns (nonSWD rats) in the activity of some neurotransmitter systems (Poumain et al. 1992, Spreafico et al. 1993, Luhman et al. 1995, Sadamatsu et al. 1995, Ekonomou et al. 1998), metabolic activity in some brain regions (Nehlig et al. 1998), and certain sleep parameters (Gandolfo et al. 1990). It cannot be excluded that these features as well as the occurrence of SWD itself, have behavioural consequences. In that case, in experiments with behavioural endpoints performed on rat populations heterogenous in respect to the SWD trait, this heterogeneity may result in an increased within-group variability in performance of some tasks and, owing to that, obscure the effect of the factors under study in statistical comparisons.

The existing literature concerning the relationship between the SWD trait and behaviour is somewhat ambiguous. In a comparative study of rat lines homogenous in respect to the SWD trait, SWD rats were found unimpaired in learning and performance of simple tasks (Marescaux et al. 1992). In another study on SWD and non SWD rats selected from the same stock, however, the SWD animals appeared deficient in spatial alternation and passive avoidance learning (Aporti et al. 1986).

In the SWD rats, the occurrence of SWD bursts and the burst duration increase as the animal gets older (Aldinio et al. 1985, Aporti et al. 1986, Vergnes et al. 1986, Buzsaki et al. 1988). It has been suggested that this increase may be due to age-related atrophy of basal forebrain cholinergic structures, the activity of which suppresses the SWD pacemaker neurones in the reticular nucleus of the thalamus. The age-related cholinergic atrophy is also regarded as the likely cause of behavioural impairments in old animals (Buzsaki et al. 1988, Gage et al. 1988). Thus, if a correlation between SWD parameters and at least some behavioural measures were found in old rats, it might be explained by the fact that in these animals both increased SWD activity and behavioural impairments have a common cause: a decreased cholinergic output. However, in most experimental studies with behavioural endpoints 3-6 mo old rats have been used, i.e, before the age-related neurodegeneration is likely to occur. Therefore, if a correlation between SWD activity and behavioural measures were found in young animals, it might rather support a casual relationship between the inborn SWD determinants, (neurochemical and/or structural), and behavioural alterations.

In the present experiment we tried to identify the differences in behaviour of young adult (6 month) and old (24 month) rats in selected test situations and to look for correlations between behavioural measures and SWD parameters within each age group. We hoped that the results would throw some light on the relationship between the SWD activity and behaviour.

In our earlier studies (Piasecka et al. 1989) SWD bursts were found in about 50% of the Wistar rats (outbreed stock) from our breeding farm, tested at the age of about 6 months. We expected that in both the adult (6 month old) and in the old (24 month old) groups, the proportion of SWD and nonSWD rats would be similar to that found in the preliminary studies quoted earlier and that this would enable us to make reliable comparisons between the SWD and nonSWD rats within each age groups.

METHODS

Animals

Two groups of Wistar rats, males, from the Imp:DAK stock (outbreds) were used for the experiment. One group consisted of 6 month old rats (Group 6M, $n = 17$); the second comprised 24 month old animals (Group 24M, $n = 14$). During the experiment the rats were housed in single rat cages in standard laboratory conditions (humidity: 50-60%, temperature: 21-23°C, 12/12 h dark/light cycle with light on at 0600 h). The access to dry food (Murigran pellets) was unlimited. During a part of the experimental period, the access to water was restricted to 5 min per day.

Behavioural investigations. Test situations and testing procedures

In the behavioural part of the experiment four tests were performed in the following sequence: radial maze, response to novelty, passive avoidance and hot-plate test. A one-week interval between successive tests was adopted. The first three tests were carried out to evaluate mnemonic processess. Two of them , the radial maze and the passive avoidance tests, are frequently used in studies of age effects on memory. The fourth test was used to assess the magnitude of the stress response induced by a noxious stimulus. It is known that the responsiveness to stressful stimuli declines with age (Nyakas et al. 1990).

All behavioural tests were performed between 8.00 and 12.00 h in a 3 x 4 x 2.2 m room with chalk-white walls and ceiling and no windows, separated from sources of the laboratory noise except for the ventilators. The temperature and humidity in that room were the same as in the animal room, and it was lighted with a 40 W white bulb located 2.0 m above floor level. During tests the equipment (eg. the maze) was located in the centre of the room, right below the bulb. Small objects (pieces of dark cotton, paintings) were hung on the walls to serve as spatial cues.

RADIAL MAZE

The radial maze was built of stainless steel foil, and consisted of a circular platform (diam: 40 cm) from which eight arms (12.5 cm wide, 15.5 cm high and 30 cm long), opened at the top, protruded perpendicularly. The inside of the arms was painted white. The floor of the maze was made of stainless steel bars 0.5 cm in diameter with 1 cm distance between neighbouring bars. A small, 0.2 ml container protruded from the back wall of each arm, 2 cm above the floor level. The maze rested on a 80 cm high base.

Tests in the radial maze were performed in two consecutive five-day stages: adaptation and training, separated by a two-day (Saturday and Sunday) interval. One trial a day was performed with each rat during each stage. On each day of the adaptation stage, the rat was placed in the centre of the platform and left in the maze for 5 min. The containers located at the end of each arm were empty. The number of arms visited and the number of repeated entries (revisits) were noted. After a 5 min stay in the maze the rat was immediately transferred to its home cage.

Two days before the beginning and during the training, the accessibility of water in home cages was limited to 5 min a day. Thus, each daily trial was preceded by a period of water deprivation lasting nearly 24 h. Before the trial, each arm of the maze was supplied with 0.2 ml of water. At the onset of each trial, the rat was placed on the platform facing one of the arms (the same on each trial). The trial ended immediately after the water had been drunk from all containers or 5 min had elapsed. The total number of arm entries, the number of arms omitted (omission errors), and the number of reentries into visited arms (perseveration errors) were noted. After the trial the rat was transferred to the home cage and allowed to drink water from an open container for 5 min.

RESPONSE TO NOVELTY

Testing the response to novelty began on the third day after the radial maze test. The testing equipment consisted of an open field 65 x 45 cm limited by 30 cm high walls made of plywood, a stopwatch, and two pairs of small objects (boxes and tubes). The objects belonging to a given pair did not differ between themselves. A shortened version of the procedure described by Ennaceur and Delacour (1988) was adopted. During the first three days of the test each rat was allowed to freely explore the open field for 5 min a day. On the fourth day an object (object *A*) of one of the two pairs was placed near one of the walls in the central position and then the rat was placed inside facing the opposite wall. The total duration of exploring the object (sniffing from a distance not less than 2-3 cm, climbing the object) during a 3 min period was measured. The rat was then transferred to an expectation cage for one min. The old object (object *A*) was removed, a twin object (object *a*) was placed in one corner of the field and a new object (object *B*) from the second pair in the opposite corner. Then the rat was put in the open field for 3 additional min during which the cumulated time of exploration was measured separately for object *a* and object *B*.

PASSIVE AVOIDANCE

The test apparatus consisted of a transparent box (65 x 34 x 34 cm) with a floor made of stainless steel bars connected in parallel with a source of DC electric impulses. The current intensity, pulse duration and frequency were controlled. An elevation (platform), 15 cm high, 17 cm long and 6 cm wide, made of hard cardboard, was fastened to the floor in a central position. The test consisted of seven trials: Trials 1, 2 and 3 were performed at 30 min intervals. In trials 1 and 2, the rat was placed on the platform and after stepping down it was left on the floor for 10 s and then transferred to its home cage. On trial 3, immediately after stepping off the platform electric foot shocks (4.5 mA pulses of 20 ms duration applied at 2/s frequency) were applied for 10 s before transferring the rat to its home cage. Trials 4, 5, 6 and 7 were performed on the first, second, fourth and seventh days, respectively, after the foot shock. These trials were performed in the same way as trials 1 and 2. In all trials the time the rat stayed on the platform was measured; 180 s was accepted as the upper limit (if the rat did not stepped down during this time limit, it was removed from the platform and transferred to its home cage).

HOT-PLATE

The test equipment consisted of a hot-plate and a shock chamber. The hot-plate was a square box (35 x 35 x 35 cm) made of copper foil and filled with water. The water temperature was kept constant at 54.5 (± 0.2)°C. A plastic, translucent cylinder (280 mm diameter, 250 mm height) with a top cover formed an enclosure preventing the rat from stepping off the plate. The shock chamber was a tight (100 x 200 x 400 mm) box equipped with a metal grid floor which could be electrified. Three trials were performed: one preshock trial (trial 1) and two postshock trials (trials 2 and 3). Each trial consisted of placing the rat on the hot-plate within the enclosure where it remained until it had performed the expected response - licking the hind foot, or 60 s had elapsed. Then it was removed from the enclosure, which ended the trial. Right after trial 1 the rat was transferred into the shock chamber where it received a train of electric foot shocks for 1 min (square 10 ms pulses of 4.5 mA intensity, applied at frequency of 0.5 Hz). Trial 2 was performed several seconds after the shocking. Trial 3 was performed 24 h after trial 2. The latencies of the paw-lick response in trials 1, 2 and 3 were measured and denoted as L1, L2 and L3, respectively.

Electrophysiological investigations

SURGERY

After completion of the behavioural tests all rats underwent neurosurgical operation. The surgery was performed under barbiturate anaesthesia (pentobarbital sodium, 50 mg/kg, i.p.). Monopolar electrodes (stainless steel screws of 1.0 mm diam) were implanted epidurally over the parietal cortex (3.0 mm posteriorly to Bregma and 3.0 mm laterally from the midline). An identical screw was implanted over the cerebellum, and a silver plate of 3.0 mm in diameter was placed on the nasal bone. These served as a reference electrode and as a ground, respectively.

ELECTROPHYSIOLOGICAL TESTING

Two to three weeks after the surgery 3 h ECoGs were made for each rat. For the recording, the animal was transferred from its home cage and placed in an opaque plastic container (30 x 30 x 40 cm). ECoG was made with an 8-channel electroencephalograph. The electrodes were connected to the electroencephalograph with low--weight, low-noise shielded cables enabling the animal to move freely within the cage. The low and high filters were set at 1 Hz and 35 Hz, respectively. Before the recording, the rats were adapted to the recording conditions 1h a day, for two successive days. In all cases the recording started at about 0900 h, Fifteen minutes after placing the animal in the recording cage.

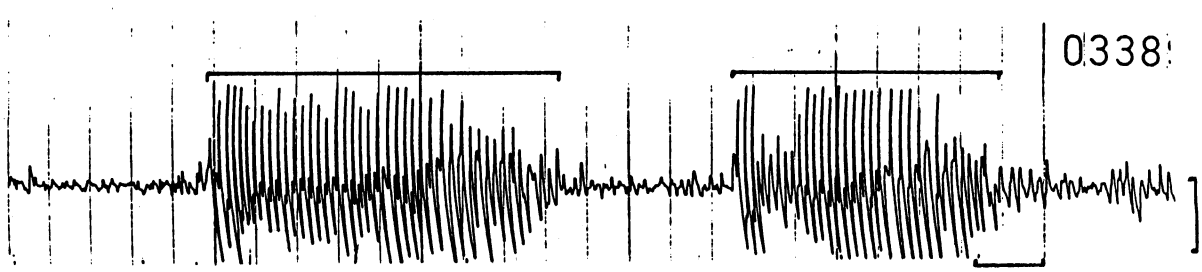

Fig. 1. An ECoG section (frontoparietal cortex, monopolar derivation) of a SWD rat. Callibration: vertical, 100 μV; horizontal, 1.0 s.

The obtained 3 h ECoGs were analysed visually. The analysis consisted in counting the number and duration of SWD episodes in successive recording hours (Fig 1).

Statistics

Statistical comparisons were performed using a one--way (parametric or nonparametric) or, when justified, a two-way repeated measures ANOVA. Multiple comparisons were performed with the use of the Dunn test or Tukey test (Winer 1961). In order to assess the relationship between the electrophysiological and behavioural measures, a correlation analysis was performed. Differences were regarded as significant when the null hypothesis probability was less than 5%.

RESULTS

Effect of age on the behavioural performance

RADIAL MAZE PERFORMANCE

Adaptation

The groups were compared in respect to the global number of visited arms and the number of repeated entries (revisits) during the successive 5 min daily trials. A two way ANOVA (Groups x Days) was used. In each case only the effect of Days was significant (number of entries: $F_{1,29}$ = 30.37, $P<0.0001$, repeated entries: $F_{1,29}$ = 19.69, $P<0.0001$); during the first day of adaptation the values of both measurements were significantly higher than those during the remaining four days (data not shown).

Training

Generally, the groups did not differ between themselves in respect to the trial duration. In both groups, the trial duration shortened on successive days (effect of Days: $F_{1,29}$ = 6.57, $P<0.02$). The effects of Groups and the Groups x Days interaction were not significant. In the case of the total number of entries, only the effect of Days was significant ($F_{1,29}$ = 16.58, $P<0.001$); on the first day, the total number of entries was significantly lower than on the remaining days).

In the case of the omission errors, only the effect of Days was significant ($F_{1,42}$ = 40.25, $P<0.001$); in all groups, on the first day, the number of omission errors was significantly higher than on the remaining days. As to perseveration errors, neither of the main effects nor the interaction were significant (Fig. 2).

Response to novelty

The measurement of the exploration time was characterized by a large between subject variability. Generally, the rats spent more time exploring the object presented alone during the first trial (object *A*) than exploring the twin object (object *a*) presented jointly with a new object (object *B*) in the second trial. A two-way ANOVA (Groups x Measurements) confirmed the significance of the Measurements factor ($F_{1,29}$ = 35.70, $P<0.001$) but the effect of Groups was insignificant. The Groups x Measurements interaction was significant ($F_{1,29}$ = 4.54, $P<0.05$). Subsequent comparisons revealed difference between groups in the first trial ($F_{1,87}$ = 8.80, $P<0.005$; rats of the 24M group spent significantly less time exploring object *A* then rats of the 6M group. In the second trial no difference between groups was found in the exploration time of object *a* or object *B*. In that trial rats of the 6M group, unlike rats of the 24M group, explored ob-

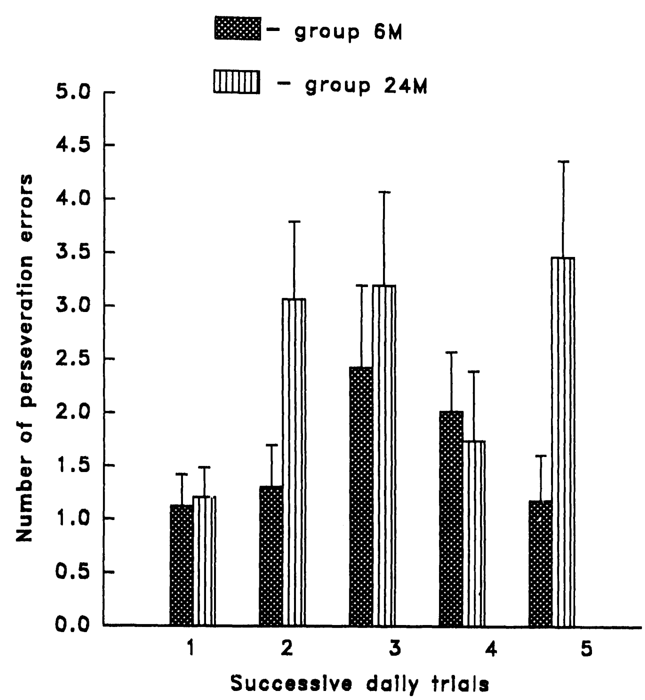

Fig. 2. Perseveration errors made by 6 month old (group 6M, $n = 17$) and 24 month old (group 24M, $n = 14$) rats during training in the 8-arm radial maze. The bars denote mean error numbers and SEM.

ject *B* longer than object *a* but this difference did not reach statistical significance (Fig. 3).

Passive avoidance

In the rats of both groups, step-down latency decreased gradually in the first three trials (before the foot shock) and increased gradually in the remaining trials (after the foot shock). A two-way ANOVA (Groups x Trials) showed a highly significant effect of Trials ($F_{1,29}$ = 30.61, $P<0.0001$), but the Groups effect and the Groups x Trials interaction were not significant (Fig. 4).

Hot-plate behaviour

Two rats from group 6M and two from group 24 M were excluded from the analysis because they did not show the paw-lick response within the 60 s limit in any of the three trials. First, the groups were compared in respect to the L1 direct value. For rats of group 24M the L1 value was significantly higher than in rats of the 6M group ($F_{1,25}$ = 12.87, $P<0.005$). In the rats of both groups, application of foot shock resulted in an increase in the paw-lick latency. The increase was most pronounced immediately after the foot shock (L2) and considerably reduced 24 h later (L3). The groups did not differ in the L2 and L3 values (Fig. 5).

Relationship between the SWD activity and age

SWD bursts occurred in 24 (82.7%) out of 29 rats (two animals of the 6M group died after the surgery). In four rats from group 6M (26.6%) and one from group 24M (7.1%), SWD bursts were not observed. In the remaining animals, the number of SWD bursts noted in the 3 h EEG sections varied from 11 to 343 in group 6M and from 22 to 390 in group 24 M. Significant differences were found only in the burst duration (U= 53, $P<0.05$, Mann-Whitney test, two-tailed); in group 24M the bursts were significantly longer (mean = 6.47 ±2.57 s) than in the 6M group (mean =3.46 ± 3.32 s).

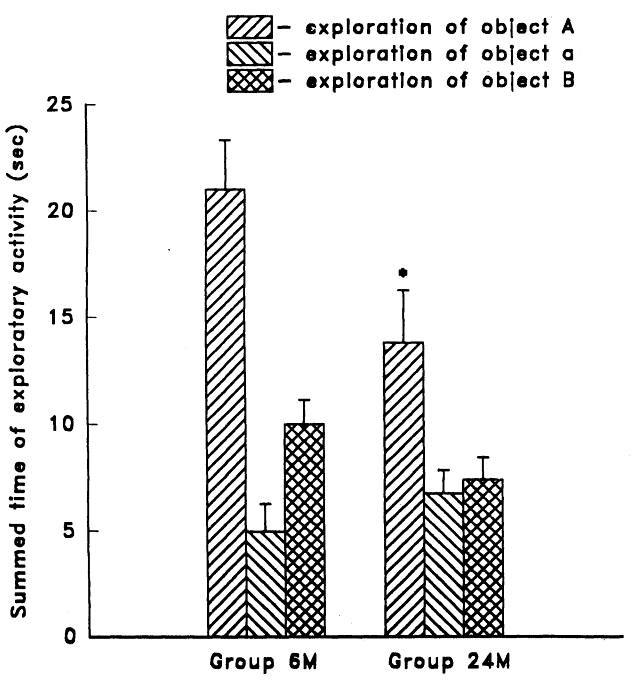

Fig. 3. Effect of age on exploration time. Six month old (group 6M, n = 17) and 24 month old (group 24M, n = 14) rats were placed in an open field where they were presented with an object (object *A*) for 5 min and then, after one min spent outside the test apparatus, with two objects: a twin of object *A* (object *a*) and a new object (object *B*) for another 5 min. The bars represent means and SEM of the time spent on exploring the objects. * - $P<0.05$ compared to the corresponding measure in group 6M.

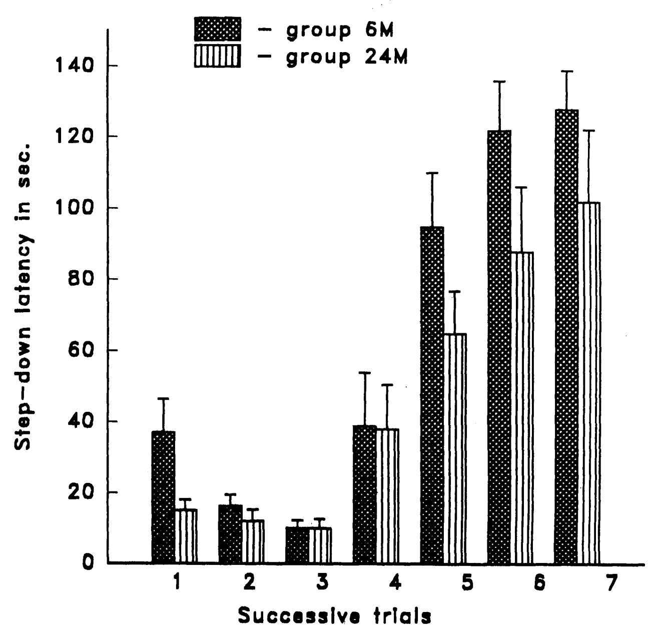

Fig. 4. Step-down passive avoidance learning in 6 month old (group 6M, n = 17) and 24 month old (group 24M, n = 14) rats. Trials 1, 2 and 3 were performed at 24 h intervals. The step-down response was punished by a 10 s foot shock only in trial 3. Trials 4, 5, 6 and 7 were performed 24 h, 48 h, 4 days and 7 days after trial 3, respectively. The maximum step-down latency was 180 s. The bars represent group means and SEM.

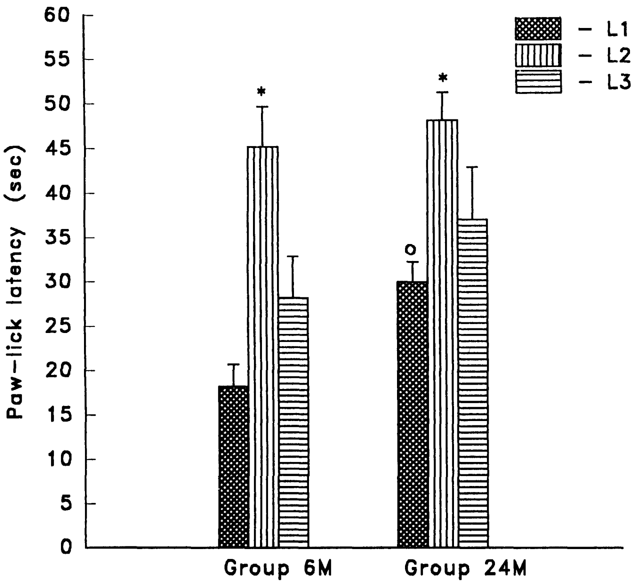

Fig 5. A comparison of the latency of the paw-lick response to a thermal stimulus (54. 5°C) in 6 month old (group 6M, n = 15) and 24 month old (group 24M, n = 12) rats. L1: paw-lick latency in trial 1 performed before a 2 min intermittent foot shock. L2: paw-lick latency in trial 2 performed several seconds after the foot shock. L3: paw-lick latency in trial 3 performed 24 h after the foot shock. * P<0.05 compared to trial 1 in the same group, ^{O} P<0.05 compared to the same trial in group 6M.

TABLE I

Correlations between the behavioural and EEG data

	No. of SWD episodes	Total SWD duration
Total SWD duration	**0.972****	
Resp. to novelty. Exploration time on A	**-0.439***	**-0.474****
Response to novelty. Exploration time: a/A (%)	0.250	0.265
Radial maze: adaptation No of entries on day 1	0.074	0.069
Radial maze: adaptation No of entries on day 5	-0.276	-0.243
Radial maze: training. Total number of perseveration errors	0.273	0.333
Radial maze: training. Perseveration errors on day 1	0.009	0.039
Radial maze: training. Perseveration errors on day 5	0.424	**0.484****
Passive avoidance. Step-down latency on day 1	-0.059	-0.070
Passive avoidance. Step-down latency on day 4	0.019	0.061
Passive avoidance. Step-down latency on day 7	0.166	0.140
Hot plate L1	0.284	0.271
Hot plate L2/L1	-0.174	-0.184
Hot plate L3/L1	-0.142	-0.109

Legend: Numbers in rows - Spearman rank-order correlation coefficient values. *- P<0.01, ** - P<0.001

Relation between the SWD activity and behaviour

In order to estimate the association between SWD activity and behaviour, Spearman rank correlation coefficient (Siegel 1956) was computed. The computations were performed for each group separately and after combining them into one group.

In no group did the separate computations reveal a significant correlation between any of the behavioural measures and the number of SWD episodes or the total duration of SWD activity. In each of the groups, however, the correlation between the number of perseveration errors made on day 5 of the maze training and number of SWD bursts as well as total duration of SWD activity approached the level of significance.

After combining the groups, the computations revealed a significant negative correlation between the exploration time of a new object in trial 1 of the novelty test and the number of SWD episodes (n = 29, r = - 0.44, P<0.05) and the total duration of SWD activity (r = - 0.47, P<0.01). Of the measurements made during the radial maze test, only the number of perseveration errors made on day 5 of training was positively correlated with the total duration of SWD activity (r = 0.48, P<0.01). No correlation between the SWD and the behavioural measures made during the passive avoidance and the hot-plate tests were found (Table I).

DISCUSSION

The behavioural as well as the electrophysiological results of the present study were somewhat surprising.

The behavioural differences between groups 6 M and 24 M were rather small and concerned only the response to novelty (exploration time shorter in old rats) and sensitivity to the thermal stimulus (lower in old rats). Contrary to expectations based on the literature (Aporti et al. 1986, Gage et al. 1988, Stone et al. 1989, Zanotti et al. 1989, Abdulla et al. 1995, Frick et al. 1995, Geinisman et al. 1995, Winocur and Gagon 1998), the groups did not differ statistically in passive avoidance learning and radial maze behaviour, mainly because of the high variability of individual scores within both age groups.

The individual EEG data from the SWD rats of each group were also extremely variable. The only significant difference was the longer duration of the SWD episodes in the 24M group.

Owing to the larger-than-expected proportion of the SWD rats in each age group, the intended comparisons between SWD and non SWD rats within each group could not be done. Therefore, it was not possible to obtain results which would be directly comparable with those from the Aporti et al. (1986) study. These authors found that SWD rats scored lower on spatial alternation and passive avoidance learning, which might suggest impaired short- and long-term memory in these animals. In the present work, a relation between SWD and behaviour is suggested by the correlation between SWD parameters and the number of perseveration errors in the radial maze and duration of the response to novelty. The *r* values were significant only after the two age groups had been combined into one. It should be mentioned, however, that in case of perseveration errors, the values were close to the level of statistical significance in the 6M as well as the 24M group. Thus, it is quite likely that the results of the separate analyses were negative simply because the groups were not large enough.

The positive correlation between SWD measures and perseveration errors at the end of training in the radial maze conforms with the spatial alternation impairment found in SWD rats by the Aporti et al. 1986. In that study, however, the SWD rats showed also a passive avoidance deficit, whereas in the present study no correlation between any of the SWD parameters and the passive avoidance performance was found. At present we do not know the reasons of this inconsistency. The negative correlation between SWD measures and exploration time of a new object might suggest that an increase in SWD activity goes along with an exaggerated neophobia.

According to some authors (Colier and Coleman 1991) neophobia, like deficits in solving spatial problems, develops with age and is positively related to age-related atrophy of some brain structures. It is rather unlikely, however, that in some rats of the 6M group the age-related atrophic changes were more advanced than in rats of the 24M group. Therefore, the correlations cannot be explained exclusively in terms of the effects of age-related neurodegeneration on SWD activity on one hand and behaviour on the other. The inherited brain anomaly determining the propensity for SWD generation should also be taken under consideration.

According to the literature, when compared with the non SWD rats, the SWD rats show abnormalities in the GABAergic (Lin et al. 1993, Spreafico et al. 1993), glutamatergic (Poumain et al. 1992), adenosinergic (Ekonomou et al. 1998), and peptidergic (Sadamatsu et al. 1995) systems. It is not unreasonable to assume that these alterations are more pronounced in rats with a high rather than low level of SWD activity, which might account for the correlations found in the present study. Unfortunately, we are not aware of any literature which might support the above conjecture. In the neurochemical studies cited above as well as in those concerning SWD activity and behaviour (Aporti et al. 1986, Vergnes et al. 1991), the variability of the SWD measures was not taken into account and comparisons were made between groups of SWD and nonSWD rats only .

Another possibility worth considering while looking for the causes of the SWD-behaviour relationship, is the detrimental effect of SWD seizures on perceptual, cognitive and motoric functions suggested by some reports from electrophysiological (Inue et al. 1991) and behavioural (van Luijtelaar et al. 1991, Drinkenburg et al. 1996) studies. It has been suggested that SWD seizure might induce amnesia, comparable to that induced by a mild electroconvulsive shock (van Luijtelaar et al. 1991). It is likely, then, that the occurrence of SWD bursts during trials or during intertrial intervals may disrupt learning and performance of some tasks. However, the bursts appear usually when the animal is relaxed (Drinkenburg et al. 1991, Gralewicz et al. 1994). In many test situations the tasks require a level of arousal incompatible with the SWD activity. An occasional occurrence of SWD bursts, however, seems quite likely in a rat performing a nonstressful task in a well known experimental setting. Of the four tests performed in the present study, the response to novelty and radial maze tests were certainly less stressful than the remaining two (passive avoidance and hot plate tests) and it was only the results of these two tests which were correlated with the SWD activity.

To sum up, the results obtained in the present study show that the level of the spontaneous SWD activity characterizing a given animal may be associated with the rats behavioural performance in some test situations. Whatever the background of the SWD-behaviour relationship might be, its existence should be taken into account when selecting animals for experiments with behavioural endpoints.

The purpose of many animal studies (pharmacological or toxicological) is to obtain information which may be extrapolated to the general human population. It seems obvious that rat populations characterized by a marked proportion of subjects with SWD activity are not appropriate for this purpose; the prevalence of absence epilepsy in the human population is estimated to be about 0.03% (Sander 1996), whereas in rat samples used for behavioural studies the proportion of subjects with SWD may exceed 50%. It should also be emphasized that SWD activity is a product of a specific neural substrate which remains under the influence of unspecific systems controlling the level of arousal (Snead 1995). This means that any interventions, pharmacological or neurosurgical, exerting a direct or indirect effect on the functional state of these systems may also affect the level of SWD activity. It is quite likely that in SWD rats the behavioural consequences of such interventions might not be the same as in nonSWD rats. Therefore, the use of rats free of the SWD trait is recommended in all works except those intended to study this specific form of brain pathology.

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