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0014-4754/91/100990-09$1.50 + 0.20/0

Genetic and environmental influences on reactive and spontaneous locomotor activities in rats

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Abstract. Paired groups of rats (derived from divergent, selective breeding or living in divergent environmental conditions) were compared with regard to locomotor activities. Intrapair differences were found to vary non-systematically, depending upon whether the rats were initially exposed to a test-environment with or without a slight environmental modification (reactive activities), or were allowed to habituate extensively to the environment (spontaneous activity). Since the behavioral patterns were found to represent distinct entities, this pointed to the necessity of differentiating clearly between spontaneous and reactive activities and indicated, once again, that both genetic and environmental influences are important in these behaviors and must be taken into account. Accepting and controlling for these variables makes it possible to use the factor of individual differences in laboratory animal behavior to advantage.
Key words. Locomotor activity; RHA vs RLA rats; SHR vs WKY rats; Fawn hooded rats; Wistar rats; individual housing; selective breeding; spontaneous activity; reactive activity.

Individuality is an accepted characteristic of human beings; that is, it is accepted that each individual's physiological and behavioral responses are different, depending upon his or her genetic background and prior experience. Even in domestic animals (e.g. dogs, cows, etc.) the importance of both genetic and environmental influences is appreciated and accepted. In contrast, where laboratory animals are concerned, scientific communications of otherwise high quality often contain such sentences as 'normal rats were used' or 'studies were carried out in albino mice'– ignoring, in particular, the potential importance that the genetic background of the subjects used could have for the experiments in question [5, 13]. This is especially true for pharmacological and toxicological studies on laboratory animals, in which it has been demonstrated on many occasions that the action of any drug clearly depends upon the animals's genetic background, age, sex and previous experience, as well as upon the time of day and other environmental considerations.

As most animal studies aim to improve our understanding of physiological and pathophysiological processes in humans, we feel that individuality in animals should be accepted and accounted for. In other words, such factors as 'genetic predisposition', 'transcultural differences' and 'life events' should also be recognized in studies on experimental animals. The advantage of animal studies, of course, as compared to human studies, is that one can profit from the shorter generation-time involved, as well as take advantage of being able to control the genetic and environmental circumstances. Furthermore, the additional knowledge gained about genetic and environmental influences on an animal's physiology and/or behavior could help to clarify further the enormous influence of these factors in humans. Keeping these goals in mind, the present review will be devoted to a description of several aspects of locomotor activity in rats, a behavioral parameter which has been extensively studied in this laboratory for several years.

Terminology

The determination of locomotor activity is probably one of the most frequent behavioral measurements in experimental animals, as sophisticated equipment is not a necessary prerequisite. In addition, locomotor activity has proven to be very susceptible to the influence of drugs as well as to genetic and environmental manipulations. However, in behavioral studies, and especially those concerned with locomotor behavior, superficial, and often misleading, terminologies are frequently encountered. 'Activity' or 'locomotor activity' in experimental animals, or 'differences in activity' between distinct groups of animals, have frequently been reported without any detailed information on the nature of the behavioral act. In order to avoid these linguistic problems, we would propose that non-specific terms such as 'activity' or 'locomotor activity' should always be properly defined and used, if at all, with much reservation.

We would define the term 'locomotor activity' as the sum of all horizontal movements of an animal's body from its present position to an adjacent area of its surroundings. Distinct types of locomotor activity can be differentiated,

with the main distinction being made between reactive and spontaneous locomotor activity. The amount of movement depends upon both the external environment and the animal's own internal state, and locomotor activity should be viewed as an overall result of the existing situational conflict. On the one hand, in a novel environment, an animal requires a certain activity in order to get to know where it is (exploration). This activity is largely determined by the animal's state of motivation and arousal. The environment, on the other hand, with its potential threats, induces fear and thus promotes inactivity. Combined with the animal's genetic background and/or previous experiences, both of which would be expected to contribute to its emotional state, these factors determine the level of 'reactive' locomotor activity. The term 'spontaneous' locomotor activity defines those movements which remain after an animal has been extensively habituated to the test-environment. As we have systematically compared both reactive and spontaneous locomotor activity between genetically distinct groups of rats, and between groups differing with regard to post-weaning environment, these definitions will become clearer in the following sections.

Description of the rats used in the present studies

Our individually- and group-housed rats were derived from a local Wistar strain (Ibm: RoRo; Roche-Füllinsdorf, Basel) with housing conditions as the sole variable. Rearing conditions, previously described in detail[23], can be briefly summarized as follows: pregnant females, supplied a few days before parturition, were kept with one animal per cage. After female siblings had been removed between the 15th and the 19th day after birth, the 19-day-old male rats were divided (split-litter design) into two groups. Individually-housed rats (also called 'isolated rats') were kept in 26 × 20 × 14 cm macrolon cages, and social or group-housed rats lived in triads (42 × 26 × 14 cm macrolon cages). Visual contact between isolated rats was prevented, but isolated and group-housed rats were kept in the same animal room.

Using shuttlebox performance as the selection criterion, the Swiss line of Roman high avoidance rats (RHA/Verh) was selected and bred on the basis of rapid acquisition of a two-way, active conditioned avoidance response, whereas the Roman low avoidance rat line (RLA/Verh) was selected and bred on the basis of the failure to acquire that response. The two lines, acquired in 1972 from the University of Birmingham (GB), are outbred, care being taken to avoid common ancestors in each pair going back two generations. For detailed information relating to these two rat lines, see the reviews by Driscoll et al.[12,14], whose laboratory also supplied the adult RHA/Verh and RLA/Verh rats used in these studies.

In 1963, Okamoto and Aoki[51] reported the selection of inbred Wistar-Kyoto rats (WKY) from which a strain of spontaneously hypertensive rats (SHR) was finally produced, using the animal's blood pressure as the selection criterion. SHR develop hypertension at a rate of 100%. Trippodo and Frohlich[65] feel justified in affirming that the SHR is indeed an excellent laboratory model of essential hypertension. As different lines of SHR and WKY are now simultaneously being bred worldwide, it is important to state that the adult SHR (SHR/KyoNIbm) and WKY (WKY/NIbm) rats used in our studies were bred in, and obtained from, a local breeding station (Roche-Füllinsdorf, Basel).

With regard to the origin of the Fawn-hooded (FH) rats, it has been summarized by Tobach et al.[64], that the FH-line 'appeared as a mutant from unplanned crosses of various populations of laboratory rats of unknown genealogy' carried out some 20 years ago at the University of Michigan by the psychologist E. L. Walker. Tobach et al. added that the colony was maintained there and that Walker believed that his stock of FH rats resulted from crosses among 'German brown' rats brought from Germany and Albino rats brought from Lashley's laboratory in Chicago. According to Magro et al.[43] '... FH appeared from crosses between colonies of Long-Evans, Wistar and brown rats'. FH rats develop hypertension spontaneously[40,58], show severe proteinurea, and were observed to die prematurely at the age of 10–15 months[39]. In addition, and among other deviations, this strain manifests a platelet serotonin storage deficiency[66]. At least to our knowledge, other than the anecdotal 'unusual docility', described by Bellin and Sorrentino[2], no systematic behavioral data have been thus far collected on these rats. Our FH rats were derived from a stock generously supplied by Dr T. Tschopp (Hoffmann LaRoche, Basel, Switzerland) and were subsequently compared to ancestral Wistar rats, after being raised in our laboratory (as were our individually- and group-housed Wistar rats).

Housing conditions

Only male rats were used in most of the studies and, unless otherwise stated (e.g. individual housing), all rats were housed in groups of three or six animals per macrolon cage (42 × 26 × 14 cm, 55 × 36 × 20 cm, respectively). Prior to behavioral testing rats were adapted to the light cycle (L12:D12). Food (Nafag 890) and tap water were provided ad libitum, and the room-temperature remained stable at 25 °C.

Reactive locomotor activity

Reactive locomotor activity represents the sum of horizontal movements exhibited by an animal when it is newly placed in a novel environment. The level of reactive locomotor activity, together with other parameters (e.g. defecation, stress-hormone levels), is frequently taken as an indicator of the animal's emotionality. A high number of crossings is interpreted as a sign of a low emotional response; it is considered to be an orienting reaction not inhibited by fear. Important points to be taken into consideration are:

1) The longer an animal is exposed to a novel environment, the more will its locomotor activity progressively diminish, leading, after this 'intra-trial habituation' and complete familiarization with the surroundings, to pure spontaneous activity (see below). Comparably, during repetitive exposures to the same (novel) environment, the orienting reaction (and the fear) will vanish, and this 'inter-trial habituation' leads even sooner to spontaneous activity.
2) Reactive locomotor activity is situation-dependent, varying with the environment's complexity and its fear-inducing aspects. For example, increased complexity, as in a maze, increases the time needed before complete familiarization is achieved. In addition, reactive locomotor activity will correlate negatively with the illumination of the test-environment, thus reflecting the situation's aversiveness.
3) Manipulations prior to behavioral testing may influence subsequent performance. Thus, any stress prior to testing should be avoided (e.g. transportation, unsuitable handling etc.) and naive animals should, of course, be used.
4) In a forced exploration paradigm the animal is placed by an observer in the test environment and is thus forced to inhabit it. On the other hand, in a free exploration paradigm, the animal can enter the novel environment starting from a familiar place (e.g. the home cage). It can choose when, or if at all, to enter the experimental surroundings. These two paradigms have different influences on the conflict between the need to explore and the innate fear of novelty, and will therefore cause different behavioral responses.
Unless otherwise stated, all our studies were carried out during the middle of the dark-phase of the L12:D12 lighting cycle, when the rats were most alert. The rats had been transported several hours previously from the animal room to the observation room, avoiding any unnecessary stress. A pale, red light was used to illuminate the observation area. 'Forced exploration' was always determined, with trials being started by removing the rat from its home cage and immediately placing it in the novel environment. All group comparisons were carried out with age-matched rats, and animals of the different groups were always tested in a counterbalanced order.

The three types of testing areas were:
1) Macrolon cages of larger dimensions than the home-cage, as a novel environment. The floor was covered with sawdust, and two lines painted onto the metallic cover 'divided' the cage into four equally sized quadrangles. Reactive locomotor activity was the sum of all passages from one cage-quadrangle to the next. As these macrolon cages were also used for the manual assessment of spontaneous locomotor activity, the cages were equipped with food- and water-reservoirs.
2) A wooden box (56 × 66 cm), with its floor divided into nine equal squares, as a simple openfield. The field was bordered by 12-cm side walls and illuminated by a 100 W reddish lamp suspended 80 cm above the center.

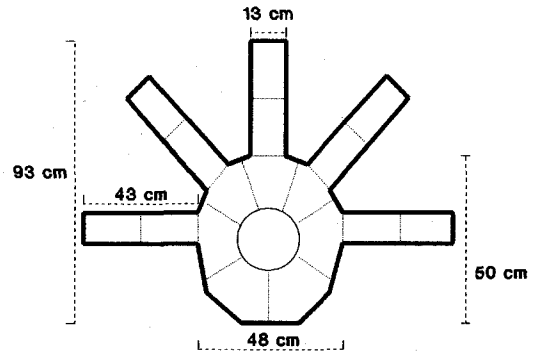

Figure 1. Schematic representation of the complex openfield.

3) A complex openfield consisting of a round, open area (diameter 50 cm) with five adjacent arms (43 cm long, 13 cm diameter), all perpendicularly positioned on one half of the open area. The entire configuration, shown in figure 1, was bordered by 20-cm side walls and regularly illuminated by a reddish lamp. The open area was divided into eight equally sized segmental sectors plus one central area, and all five alleys were divided into two squares each (comparable in size to the nine sectors of the open area).
The testing procedure consisted, initially, of registering the inter-square crossings for periods of 10 and 20 min. To gain insight into possible time-of-day effects and time × group interactions, the number of inter-quadrangular crossings (15-min trials) in a macrolon cage was determined starting at different time-points within the light or dark phase.
Finally, as described previously[23], four consecutive, simple openfield trials (each lasting 20 min) were carried out within one single dark phase at 135-min intervals. Between trials, rats were put into their home cage. The openfield was unaltered for trials I, II and III, but before trial IV, three different objects were put into the openfield in order to observe the animals response to slight environmental modifications.

Spontaneous locomotor activity
Spontaneous activity is that part of activity remaining after the animal has completely habituated to its external world. It is most frequently determined when investigators are interested in the temporal organization of activity throughout the day. Such long-term, continuous registration obviously requires some form of automatization, such as photobeam interruptions, electrically-monitored tilt- or vibration-cages, or video recordings with subsequent computer-evaluation. Some of these methods (depending on the number, position or sensitivity of the detector-units), however, do not distinguish between different body movements. As a general rule, and to minimize the number of reactive behavioral items that are included in spontaneous activity, continuous

registration should last for more than just one day/night cycle and should be started only after an extensive period of adaptation to the environment and the equipment (e.g., after one whole cycle). When spontaneous activity is no longer mixed up with reactive activity, consecutive 24-h periods should produce similar activity levels and activity patterns.

In our testing, we used photobeam interruptions or current changes in resonant circuits. Registration lasted for several days and spontaneous activity was only calculated after 24 h of adaptation. In addition, some limited manual recordings (at four different time-points throughout the day/night cycle) were carried out. For these, animals had been accustomed to the macrolon cages for 24 h before their interquadrangle passages were measured.

Results

Individually- vs group-housed Wistar rats (fig. 2)

A) *Reactive locomotor activity:* Individually-housed rats, when compared to group-housed controls, generally show, among other behavioral alterations, a higher locomotor reactivity in the openfield test[11,16,19,68]. This hyperreactivity has, upon occasion, been preceded by an initial hypoactivity[7]. We also found a pronounced locomotor hyperreactivity after individual housing[22,23,26] which, together with the attenuated defecation seen during, and the lower plasma-corticosterone levels measured after, the 10-min openfield-trial, indicated an attenuated emotionality after long-term isolation[27]. Analysis of the intra-trial distribution for crossings revealed a clear-cut time effect (intra-trial habituation) but no significant time × housing interaction, thus pointing to a comparable habituation-rate in both individually- and group-housed rats. Ontogenetically, the significantly increased number of crossings was already present after 5 weeks of differential housing (8-week-old animals), with no dramatic increase in this effect after a further 2–10 weeks of isolation[23]. In the complex openfield, reactive locomotor activity in both individually- and group-housed rats increased with the number of accessible arms (increasing complexity). In general, the activity of individually-housed rats tended to exceed that of group-housed controls most dramatically in simple configurations; however, this difference tended to decrease, or disappeared, when all five arms were made accessible. In line with this finding, another study has shown that differences in activity between differentially housed groups of rats were no longer found when they were tested in an even more complex environment, i.e. an enclosed maze consisting of six hexagonal alleys[67].

In order to test whether the housing effect in simpler configurations was dependent upon the time of day, locomotor activity was assessed in macrolon cages, in parallel experiments starting at either L + 3, L + 6, L + 9, D + 3, D + 6 or D + 9. Passages between the four cage-quadrangles were counted over 15 min. Two-way analysis of variance revealed significant housing and time of day effects, but no significant time × housing interaction[21]. Intertrial habituation, within the dark phase, was tested for as follows: after 12 weeks of differential housing, 4 consecutive openfield-trials (trials I to IV; each lasting 20 min) were carried out. Individually-housed rats exceeded group-housed controls in the number of crossings during trials I, II and III. In trial IV, after three different objects had been placed in the openfield, group-housed rats, but not individually-housed rats, showed a renewed increase in locomotor activity. Their number of crossings in this trial equalled those observed upon initial exposure in trial I[23]. Further analysis of this particular locomotor response in trial IV (a ratio of trial IV/trial I was calculated), indicated that at an age of 4 or 6 weeks (with differential housing for 1 or 3 weeks) neither individually- nor group-housed rats displayed a fully restored locomotor activity. At any of the four later ages (5, 7, 9 and 12 weeks of differential housing), however, the mean number of crossings in trial IV was, only for group-housed rats, similar to that exhibited in the initial trial I[23].

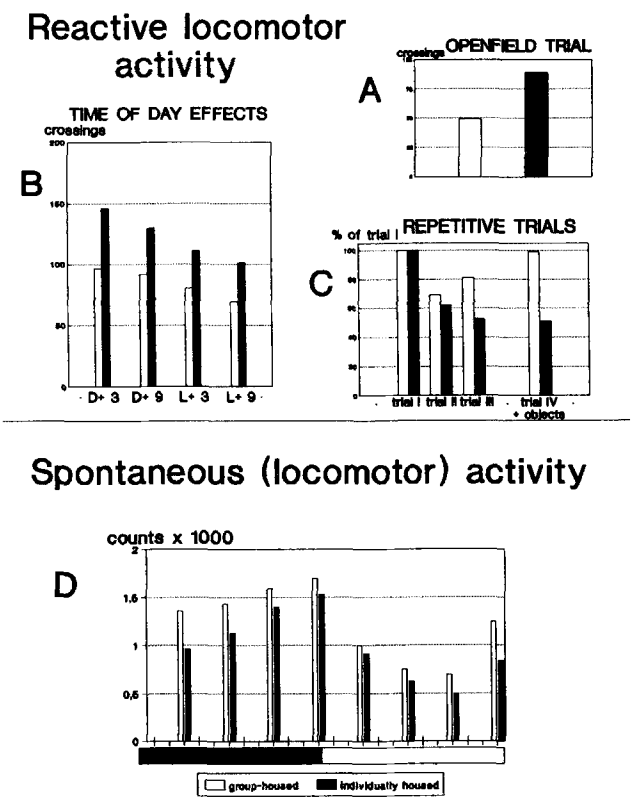

Figure 2. Comparison between individually- and group-housed Wistar rats.

A Rectangular openfield (10-min trials; middle dark-phase).

B Time of day effects (macrolon cages D + 3, D + 9, L + 3, L + 9).

C Repeated openfield trials at 135-min intervals (in trial IV, 3 different objects were present).

D Spontaneous (locomotor) activity (automatic registrations) over 24 h.

B) *Spontaneous (locomotor) activity:* Dalrymple-Alford and Benton[7], in their 24-h registration of 'spontaneous activity', found no significant housing effect, but a housing × time interaction. Their analysis of the simple main effect of housing condition at each successive hour revealed that individually-housed rats were significantly more active than group-housed rats during seven of the first 14 hours, and that no further significant intergroup differences could be established for hours 15–24. Such data clearly indicate that individually-housed rats are hyperreactive during the first hours of registration, but are no longer different from group-housed controls at later time-points (when spontaneous activity is actually recorded). Using female rats, Syme[63] did not find any housing effect when measuring spontaneous activity on activity platforms.

We used the sum of lightbeam interruptions (per 3-h period) as a measure of spontaneous activity, and our registrations lasted for 84 h. During the first day, absolute numbers were not significantly different between the two groups of rats (9 weeks of differential housing). However, for individually-housed, but not for group-housed rats, a more than 20% higher overall activity was found during this first day as compared to any of the subsequent 24-h periods. It is concluded that during the initial day, reactive locomotor activity (already known to be higher in individually-housed rats) was still superimposed onto spontaneous activity. Between the 25th and the 84th hour of registration, individually-housed rats were marginally less active than group-housed controls during both the light and the dark phase (− 12% and − 17%, respectively). There was no apparent difference in periodicity. Similar results to those described here after 9 weeks were obtained after 5, 7 or 12 weeks of differential housing, and a two-way analysis of variance revealed a clear-cut housing effect ($p < 0.005$), but no age effect[25]. In another study, individually- and group-housed rats (after 7 weeks of differential housing) were placed into large macrolon cages and, after an adaptation for 24 h, spontaneous locomotor activity was manually assessed at L + 3, L + 6, L + 9, D + 3, D + 6 and D + 9. Two-way analysis of variance revealed a significant time of day effect ($p < 0.001$), but neither the housing effect nor the housing × time interaction was significant[21]. Such a finding was not completely consistent with the results obtained with automatic registrations, and it is highly probable that short-term manual recordings (only 5–25 crossings per 15 min) are not sensitive enough to assess 10–20% intergroup differences, unless larger numbers of rats per group are used.

In summary, individual housing for 5 or more weeks increased reactive locomotor activity in simple environments. This effect was consistently observed at several time-points within the light/dark cycle. Upon repeated testing in an openfield, adult group-housed, but not individually-housed rats, responded to an environmental modification with a renewed increase in locomotor activity. Finally, individual housing induced, at most, a marginal reduction in spontaneous (locomotor) activity.

RHA/Verh vs RLA/Verh rats (fig. 3)

A) *Reactive locomotor activity:* A higher locomotor activity for RHA/Verh rats, as compared to RLA/Verh rats, has been described several times in studies of openfield, Y-maze or complex maze behavior[1,8,15,44,45,50]. During our 10-min openfield trials, RHA/Verh rats consistently made more crossings when compared to RLA/Verh rats[22,24]. Together with the dissimilar defecation-rate during these tests (RHA/Verh < RLA/Verh) and the differing post-trial plasma stress-hormone levels (RHA/Verh < RLA/Verh) such findings pointed toward a marked interline difference in emotionality (RHA/Verh < RLA/Verh)[27]. Similar differences were observed for intercompartment passages in a non-electrified shuttlebox or during short-term automatic registrations (animal activity monitors). In the latter experiment, RHA/Verh rats showed a significantly higher activity during the entire 60 min; the parallel curves for the Roman rat lines pointed, in addition, to comparable habituation rates. In the complex openfield (20-min trials in which all five arms were accessible) RHA/Verh exceeded RLA/Verh rats in the total number of crossings by 60%, and comparable differences were observed in both the center area (+ 65%) and the alleys (+ 52%). Mean latencies for initially entering the five arms were 8, 25, 45, 73 and 153 s for RHA/Verh, and 24, 76, 110, 156 und 260 s for RLA/Verh rats, respectively.

Differences in reactive locomotor activity in both the light or the dark phase have previously been described for a complex tunnel labyrinth[1]. In a similar experiment, RHA/Verh and RLA/Verh rats were placed into large macrolon cages and passages from one cage-quadrangle to the next were recorded during 15 min. Starting at 4 different time-points (L + 3, L + 9, D + 3, D + 9), two parallel curves were obtained. A two-way analysis of variance revealed, in addition to the interline difference, clear-cut day/night variations, but there was no significant time × rat line interaction[30].

The percentage of decrease between consecutive trials implied an equal habituation rate in the two Roman rat lines. In trial IV, however, when three objects were put into the openfield, RLA/Verh rats reacted with an increase in their number of crossings and the overall number was indistinguishable from that registered during trial I (the pattern thus resembled that previously described for group-housed Wistar rats). In RHA/Verh rats, on the other hand, this environmental modification in trial IV did not affect locomotor activity, and the number of crossings in this final trial remained at the (habituated) level exhibited during trial III. During trial IV, we also compared the number, and latencies, of contacts with the objects, between the two rat lines. For the RHA/Verh rats a mean of 15.7 ±4.2 contacts, and for RLA/Verh a mean of 20.0 ±4.0 contacts, were observed during the

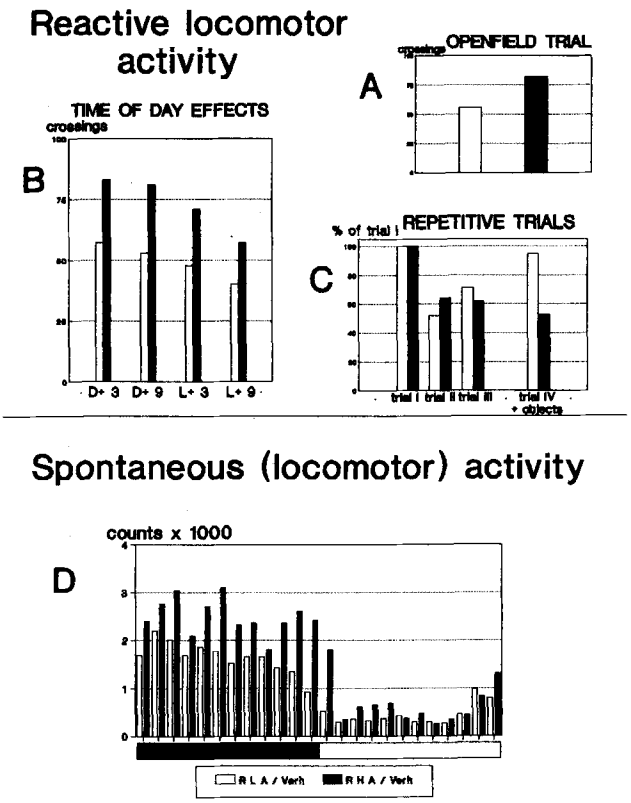

Figure 3. Comparison between Roman high- (RHA/Verh) and Roman low avoidance (RLA/Verh) rats.
A Rectangular openfield (10-min trials; middle dark-phase).
B Time of day effects (macrolon cages D + 3, D + 9, L + 3, L + 9).
C Repeated openfield trials at 135-min intervals (in trial IV, 3 different objects were present).
D Spontaneous (locomotor) activity (automatic registrations) over 24 h.

20-min session (mean ± SD; Student's t-test; $t = 2.22$; $2p < 0.05$). Relative to the number of crossings, the frequency of contacts was comparable (23.3 vs 21.8% for RHA/Verh and RLA/Verh, respectively). Mean latencies for approaching the first, second and third object, respectively, were 11.1, 32.2 and 66.1 s for RLA/Verh rats, and 8.3, 25.6 and 78.3 s for RHA/Verh rats. Such data indicate that the discovery of the objects, and the relative frequency of object-contact, differed only slightly between the two Roman lines. It may be concluded, therefore, that it was not the quantity of object-contacts which was responsible for the dissimilar response-rate. Instead, we propose (once again) that the RHA/Verh and RLA/Verh rat lines must have acquired divergent assessments of their surroundings during the preceding trials.

B) *Spontaneous (locomotor) activity:* Automatic registration of spontaneous activity revealed that RHA/Verh rats exceeded RLA/Verh rats at all 12 time-points within the dark phase and at 8 of the 12 points within the light phase. A steady interline difference in both the dark phase (+ 52%) and the light phase (+ 51%) was observed. No indications for clear-cut interline differences in periodicity were obtained. In addition, after a 24-h habituation to large macrolon cages, interquadrangle passages were recorded for 15 min at L + 3, L + 9, D + 3, D + 9. RHA/Verh rats were hyperactive at all four time-points and a two-way analysis of variance revealed a significant interline difference ($p < 0.001$) but no time of day, or time × rat line interaction [30].

In summary, RHA/Verh rats exceed RLA/Verh rats in both reactive and spontaneous locomotor activity at different time points within the light/dark cycle. Upon repeated testing in an openfield, RLA/Verh rats, but not their RHA/Verh counterparts, responded to an environmental modification with a renewed increase in locomotor activity.

SHR vs WKY rats (fig. 4)

A) *Reactive locomotor activity:* Locomotor reactivity has previously been compared between SHR and WKY rats in several laboratories. Pappas et al. [55] found SHR rats to be more active than normotensive controls in an openfield test. According to Rosecrans and Adams [56], SHR rats showed reduced activity upon initial testing in an openfield, but were hyperactive in subsequent exposures. Knardahl and Sagvolden [37], using a free-exploration paradigm, found SHR to be less active during an initial trial. Upon repeated testing, however (one 15-min trial per day), SHR rats became much more active than the

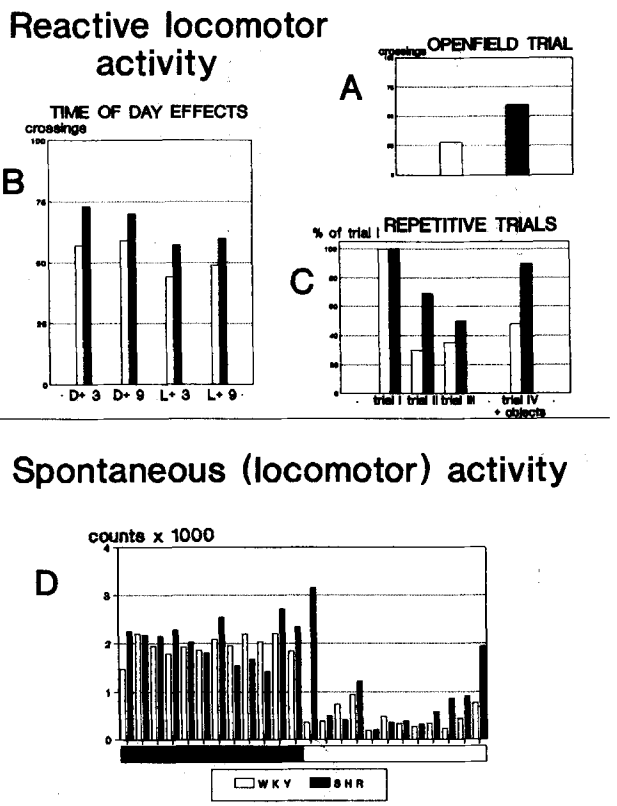

Figure 4. Comparison between spontaneously hypertensive (SHR) and Wistar-Kyoto (WKY) rats.
A Rectangular openfield (10-min trials; middle dark-phase).
B Time of day effects (macrolon cages D + 3, D + 9, L + 3, L + 9).
C Repeated openfield trials at 135-min intervals (in trial IV, 3 different objects were present).
D Spontaneous (locomotor) activity (automatic registrations) over 24 h.

normotensive controls. These results have been confirmed by Moser et al.[49]. In our 10-min openfield trials[20,22], as well as in the elevated plus maze[20], a higher number of crossings and arm entries, respectively, was observed for SHR. Locomotor hyperreactivity was, once again, accompanied by an attenuated defecation rate during exposure, and lower post trial plasma corticosterone concentrations[22], indicating that SHR are less emotional than WKY rats[27]. In the complex openfield, with all five arms accessible, SHR were more active than WKY rats in both the central area (+ 42%), and in the alleys (+ 33%).

Kraeuchi et al.[38] have reported on consistently higher levels of ambulation for SHR in an openfield, irrespective of whether they were tested in the light or the dark phase. In our studies, using large macrolon cages as a novel environment, SHR exceeded WKY rats by 30, 22, 28 and 19% at L + 3, L + 9, D + 3, D + 9, respectively. A two-way analysis of variance revealed significant strain and time of day effects, but no significant time × strain interaction. During repeated trials in the rectangular openfield, during the dark phase, SHR exceeded WKY rats in the number of crossings during all trials. Locomotor activities declined to 49% for SHR, and to 35% for WKY rats, by trial III, these results being in line with previous reports[35,37,38,56]. In response to the three objects in trial IV, SHR reacted more and re-attained 90% of the number of crossings of trial I. The WKY rats' crossing-activity increased to only 48%, however, remaining comparable to the 35% they exhibited in trial III.

B) *Spontaneous (locomotor) activity:* Kraeuchi et al.[38] started their interstrain comparison after 1 day of adaptation to the registration-environment. Clear-cut day/night variations were present in both strains and, according to those authors, SHR showed an elevated spontaneous activity mainly during the light phase (most marked at the end of the phase), with the two strains not differing significantly in overall 24-h activity counts. When the levels of activity were continuously monitored for 24 h in the home cage, McCarty and Kopin[47] also found no difference in the amount or pattern of total activity between SHR and WKY rats. Such results were in contrast to 60-min registrations (SHR > WKY), thus providing further evidence against the interpretation of short-term registrations as 'spontaneous activity'. Besides an increased number of crossings for SHR in the openfield, Moser et al.[49], in their free exploration paradigm, observed no interstrain difference for the number of crossings within the homecage (at least when the rats had habituated to the experimental procedure). Using automatic registration, our own studies have revealed only a slight, non-significant difference (SHR > WKY; 13%) in spontaneous activity. In line with Kraeuchi et al.[38], our data hinted at a higher activity for SHR between L + 9 and L + 12. Furthermore, after a 24-h habituation to large macrolon cages (manual registration) the mean number of interquadrangle passages at L + 6 and D + 6 were comparable between the two strains and a clear time of day effect was obvious. In summary, SHR exceed WKY rats in reactive locomotor activity, and they are more sensitive to the slight openfield modification introduced in trial IV. There is virtually no significant difference between the strains in spontaneous activity.

FH vs Wistar rats (fig. 5)

A) *Reactive locomotor activity:* In our standard openfield, FH rats were significantly less active than the Wistar rats. No studies in the complex openfield, or repeated testings within the dark phase, have been carried out so far.

B) *Spontaneous (locomotor) activity:* For our comparison between FH and Wistar rats for spontaneous activity we used changes in capacities of a resonance circuit, installed beneath the cage, for the assessment of activity. Registrations lasted for 60 h. Mean 24-h activity-counts were quite comparable (27,300 vs 29,800 counts for Wistar and FH, respectively). For both groups of rats mean counts per 24 h differed by less than 6% over successive days. When food intake and water consumption were measured concomitantly, however, it became apparent that FH rats, as compared to the Wistar strain, were slightly hyperphagic (+ 13%), and seemingly polydipsic

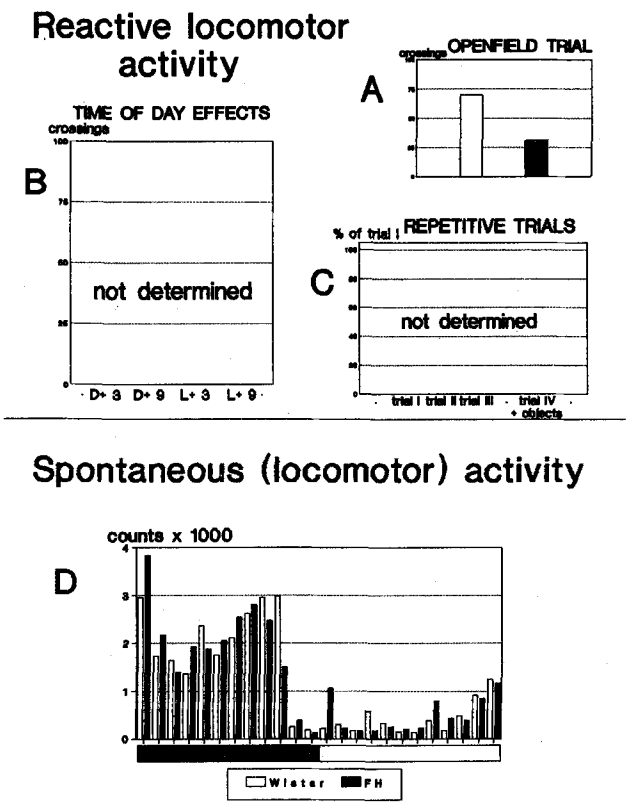

Figure 5. Comparison between Fawn-hooded (FH) and Wistar rats.
A Rectangular openfield (10-min trials; middle dark-phase).
D Spontaneous (locomotor) activity (automatic registrations) over 24 h.

(+ 53%). As the polydipsia and/or hyperphagia may have negatively influenced our registrations for spontaneous activity, the present results have to be considered in this context until more appropriate determinations (e.g. manual recordings) have been performed.

In summary, FH rats exhibited an attenuated reactive locomotor activity when compared to (ancestral) Wistar rats. Only a slight intergroup difference in spontaneous activity could be established. However, such data might have been negatively influenced by the relative polydipsia and hyperphagia observed for FH rats.

Discussion

Any observation on a behavioral, intrapair difference between genetically differing groups of rats does not automatically implicate that the selection criterion and the behavioral parameter are tightly linked. For example, by including additional groups of rats, it has been demonstrated for SHR rats that hypertension and hyperactivity are independent variables[9]. Hendley et al.[36] used a genetic approach, crossing SHR males with WKY females. After inbreeding the F_1-progenies, no correlation between locomotor activity and blood-pressure was observed in the F_2-generation. Such observations led the authors to conclude that different genetic factors are involved in the transmission of the hypertensive and the hyperactive trait[36]. No such studies have been conducted for the Roman rat lines discussed in this review. However, at least with regard to reactive locomotor activity and avoidance behavior, some preliminary comparisons between six genetically differing groups of rats did not point to a correlation between openfield behavior and avoidance performance[29]. In addition, SHR, RHA/Verh and individually-housed Wistar rats were all shown to be hyperactive, as compared to their respective counterparts, but there were no comparable similarities in avoidance-behavior or blood pressure found[27]. Furthermore, other laboratories have been able to select rats on the basis of avoidance behavior without producing any concurrent differences in locomotor activity[4, 59].

We stated in the introduction section that a 'normal' rat does not exist. It is becoming increasingly apparent that genetic variations among experimental animals, intergroup, interstock and interindividual, should be more frequently considered. For example, Glick et al.[31] compared spontaneous rotational behavior among Sprague-Dawley-derived rats from different breeders and observed clear intergroup differences. Such interstock (intrastrain) variations would indicate that various Sprague-Dawley sublines exist, depending upon where they are purchased. Self-evidently, such an observation (which is, by the way, not restricted to the Sprague-Dawley strain) might explain why different laboratories, supposedly all working with identical rat strains, often produce dissimilar results.

Though the present studies were concerned with genetically and environmentally induced intergroup differences, this does not imply that interindividual variations within these groups are ignored. By strictly controlling for breeding and environmental conditions, however, the importance of previous 'life-events' in causing unexpected, and perhaps undesirable, intergroup differences is limited. For most scientists this would at least imply that if experimental conditions are standardized to the greatest possible extent, and they are aware of the animals' genetic background and/or sensitivity toward environmental manipulations, their results will become more reliable. For those with a more profound interest in behavioral mechanisms, interindividual and intragroup variability are fundamental, and can be actively profited from.

An individual's reaction is also moment-specific, depending upon its initial state. For example, Dickinson et al. found variable drug effects after injections of alpha$_2$-adrenergic antagonists[10]. When a treated rat was placed in a novel environment for the first time, no drug effects were apparent. However, after extensive adaptation to the test-surrounding, a similar drug concentration induced a clearcut locomotor stimulation. Such observations clearly demonstrate that a drug can or cannot induce behavioral effects, depending upon the animal's current status (in the present example, the level of novelty and habituation). Other parameters which can effectively influence a drug's action are age and time of day, both in animals and humans, and an animal's position within its social group.

Recognizing the individuality of responses in experiments might even be advantageous. Clinical experience indicates that antidepressants relieve depressive symptomatology in patients. Similar doses, however, when given to healthy controls, induce fatigue but do not affect mood. This indicates that a drug's action can depend upon the subject's state of mind. Such observations in humans should have some direct implications for animal studies. Pointing to the crucial differences between normal animals and people on the one hand and depressed patients on the other, File and Tucker[17] questioned the usefulness of screening for potentially effective drugs by looking at the behavior of 'normal' rats. We would thereby propose that genetically and environmentally manipulated groups of rats offer some promising starting populations for studying deviating behavioral patterns and psychopathological states.

Returning to the present studies, marked differences in locomotor activities were observed within all of the rat group-pairings. Since the intrapairing differences were observed at different time-points within the day in all four cases, it is unlikely that the differences were solely caused by different rhythmicities. Reactive locomotor activity differed comparably within all four group-pairings, indicating that this parameter was comparably influenced by both genetic and environmental manipula-

tions. However, only between the Roman rat lines were the differences for reactive locomotor activity paralleled by comparable differences for spontaneous activity. This clearly indicates that spontaneous and reactive locomotor activity are distinct behavioral entities, and that the terminology for describing an animal's locomotor activity needs to be more precise than that which has been used all too often in the past.

When looking at the locomotor responses to a slight modification of the environment (in 'trial IV' of the present studies), clear differences were seen which were not directly related to reactive or spontaneous activity. One initially hyperactive group (SHR) reacted with an almost complete restoration of activity, whereas the comparably hyperactive RHA/Verh and individually-housed Wistar rats did not react to the three objects. We assume, therefore, that the enhanced locomotion displayed during the previous trials was not equally explorative in all three (hyperactive) groups. SHR and RHA/Verh or individually-housed Wistar rats probably absorbed dissimilar information from the environmental cues. As RHA/Verh and isolated Wistar rats showed no reaction to the slight modification, we conclude that these two groups of rats, as compared to their respective counterparts, build up a less precise knowledge of their test-environments.

Numerous studies have supported the important role of the nigrostriatal dopaminergic system in motor activity, both in rats and mice, and often in genetic comparisons between groups of the same [14, 34, 35, 41, 52, 60–62, 69]. Certain relationships between the number of striatal dopaminergic receptors and aspects of locomotor activity have sometimes been proposed. For example, Helmeste reported on parallel interstrain differences for both spontaneous activity and the density of striatal D_2-receptors, this being based on a comparison between F344 and Buffalo rats [33, 34]. Unfortunately, this is another case in which the term 'spontaneous activity' was erroneously used, since activity was measured during only 60 min after the rats had been placed in the novel environment. Indeed, such data indicate that the number of striatal ^{3}H-spiroperidol binding sites correlates, if at all, with reactive locomotor activity. Along similar lines, Overstreet et al., comparing their genetically differing strains of rats (Flinders sensitive (FSL) vs Flinders resistant line (FRL)), also found a relationship between locomotor activity (FSL < FRL) and striatal ^{3}H-spiroperidol binding (FSL < FRL) [53, 54].

For SHR, relative to WKY rats, a higher number of striatal D_2-receptors was found in some [3, 6, 41] but not all [18] studies. It must be noted that locomotor activity (SHR > WKY) and receptor binding (SHR = WKY) were concomitantly determined only in the last study. For individually-housed rats, Del Rio's group found a locomotor hyperactivity [19] and an increased ^{3}H-spiroperidol binding [32]. In our own studies on the two Roman rat lines (separate comparisons for both males and females) B_{max}- and K_d-values for striatal ^{3}H-spiroperidol binding did not differ [28]. In the light of behavioral observations, such data do not support an absolute relation between striatal D_2-binding and reactive or spontaneous (locomotor) activity. Some other observations similarly fail to indicate a strict relationship between these two parameters. While comparing D_2-binding at different time-points within the light/dark cycle, Watanabe et al. [68] failed to establish significant circadian variations, although marked day/night differences for both reactive and spontaneous activity are known to exist. For diabetic rats (alloxan- or streptozotocin-induced diabetes) locomotor activity in an openfield was found to be lower than in untreated controls [57] (and our own, unpublished, observations). However, an increased number of binding sites has been described for these rats [42]. Similarly, spontaneously diabetic Wistar BB rats exhibited an attenuated reactive and spontaneous locomotor activity [48] as compared to non-diabetic controls, but no differences in striatal ^{3}H-spiroperidol binding were found (Z. Merali, personal communication). All of these findings together would appear to preclude drawing any definitive conclusions regarding the role of striatal ^{3}H-spiroperidol binding in an individual's or strain's locomotor capacities.

In summary, the present studies clearly indicate that genetically and environmentally induced differences in locomotor activities exist, and that they are not uniform for reactive locomotor activity, spontaneous (locomotor) activity or reaction to slight environmental modifications. These three behavioral patterns are, therefore, not interdependent, but represent distinct entities.

Acknowledgments. The authors wish to thank M. L. Sfoggia and B. Poux for their technical assistance and Dr P. Driscoll for his suggestions and criticisms. One of the authors (C. G.) has been partly supported by the 'Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung'.

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0014-4754/91/100998-11$1.50 + 0.20/0

Heritable variation for aggression as a reflection of individual coping strategies

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Abstract. Evidence is presented in rodents, that individual differences in aggression reflect heritable, fundamentally different, but equally valuable *alternative* strategies to cope with environmental demands. Generally, aggressive individuals show an active response to aversive situations. In a social setting, they react with flight or escape when defeated; in non-social situations, they react with active avoidance of controllable shocks and with sustained activity during an uncontrollable task. In contrast, non-aggressive individuals generally adopt a passive strategy. In social and non-social aversive situations, they react with immobility and withdrawal.

A main aspect of these two alternative strategies is that individuals with an active strategy easily develop routines (intrinsically determined behaviour), and consequently do not react (properly) to 'minor' changes in their environment, whereas in passively reacting animals it is just the other way around (extrinsically determined behaviour).

It has become clear that active and passive behavioural strategies represent two different, but equivalent, coping styles. The coping style of the aggressive males is aimed at the removal of themselves from the source of stress or at removal of the stress source itself (i.e. active manipulation). Non-aggressive individuals seem to aim at the reduction of the emotional impact of the stress (i.e. passive confrontation). The success of both coping styles depends upon the variability or stability of the environment. The fact that aggressive males develop routines may contribute to a fast execution of their anticipatory responses, which is necessary for an effective manipulation of events. However, this is only of advantage in predictable (stable) situations, but is maladaptive (e.g. expressed by the development of stress pathologies) when the animal is confronted with the unexpected (variable situations). The flexible behaviour of non-aggressive individuals, depending strongly upon external stimuli, will be of advantage under changing conditions.

Studies on wild house mice living under natural conditions show how active and passive coping functions in nature, and how the two types have been brought about by natural selection.

Key words. House mouse; rat; wild mice; aggression; individual differences; genetic variation; selection; Y-chromosome; behavioural strategies; routine formation; active coping; passive coping; natural population.

Introduction

The most commonly used definition of aggression is the delivery of noxious or potentially harmful stimuli to another animal to gain some advantage[48, 100]. The gain can be thought of as achieving and/or maintaining hierarchical ascendency and priority in the access to food, nesting material, shelter, mates and territory. Harm refers to any physical and emotional consequence to which a recipient shows an aversion[71]. As there are many types of aggres-