Social housing of rats: Life-span effects on reaction time, exploration, weight, and longevity

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Social Housing of Rats: Life-Span Effects On Reaction Time, Exploration, Weight, and Longevity[1]

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Sprague-Dawley rats were housed throughout their lives either in group cages or singly in standard laboratory cages. Locomotor activity was observed at selected ages and, in addition, operant conditioning procedures were used with an extensively trained subset of the animals to study reaction time and fixed ratio responding. The major effect of prolonged isolation was to induce timidity and inactivity during open field and emergence tests. Responding by isolates was depressed relative to socially-housed animals at 13 and 19 months of age although the higher levels of the social animals progressively declined during tests at 19 and 25 months. By comparison, neither housing condition nor age (7 to 25 months) systematically influenced the well-practiced operant responses (response rates, postreinforcement pauses, reaction times, foreperiod responses). A serendipitous finding was that isolated animals tended to die at earlier ages, an outcome that may be related to the fact that isolates also tended to weigh more throughout the experiment.

The environment in which a laboratory rat is housed can have important behavioral effects [3]. Animals housed singly in small cages (a "deprived" environment) differ from those reared with other animals in large cages (an "enriched" environment). Isolated animals eat and weigh more [8], drink greater amounts of a morphine solution [2], are less active in emergence [14] and open field [1] tests (but see also [5]), and have greater difficulty learning mazes [9; 15] and solving problems [11]. These and other findings have suggested that isolation induces behavioral and physiological abnormalities [10], or, alternatively, that social housing has beneficial effects on development [4].

Studies of isolated and social environments have emphasized the early part of the rat's life span, typically from weaning to 3-6 months of age. We did locate two experiments which extended the inquiry to the older rodent. Doty [6] housed rats from Month 10 to Month 22 either in groups in an enriched environment or individually in standard cages. The socially-housed animals performed better on two of three avoidance tasks. More recently, Warren et al. [19] found that socially-housed mice, living from Day 600 to Day 750 in a complex environment, were superior to isolated animals on two of four learning tasks but not on an activity test.

In this paper, we report a life-span study of the effects of housing. Rats born in our laboratory lived their entire lives either alone in small cages or as members of a same-sexed group inhabiting a large cage. The research focused on behavioral processes hypothesized to change with advancing age, specifically locomotor activity and reaction time. Although the animal literature is not completely consistent, a number of studies, mainly following cross-sectional designs, have found age-correlated decreases in these behaviors (see Elias [7] for a review of studies with rats).

METHOD

Subjects and Housing

Thirty-eight albino (Sprague-Dawley) rats, born in the laboratory, were the offspring of four females, purchased pregnant (Holtzman Co., Madison, WI). The mothers and pups lived in standard double-sized laboratory cages containing nesting material. On Day 15, members of two litters were randomly assigned to the Social Condition (males = 9; females = 12) and moved with their mothers to the large cages described below. Animals were weaned and segregated by sex on Day 25. The offspring of the remaining two mothers (males = 10, females = 7) were assigned to the Isolated Condition and lived singly in standard laboratory cages from Day 25 on. At the time of weaning, subjects in the two conditions were comparable from the standpoint of their weights and apparent health.

The two group cages, 97 × 76 × 43 cm, had hardwood floors and wire cloth sides and tops. Attached to one wall were water bottles and food hoppers (providing Wayne Lab Blox). Shredded corn cobs covered the floor to a depth of 3.5 cm. The individual cages were standard rack-suspended stainless steel units (Wahmann), 25 × 18 × 18 cm, each with a wire cloth floor, and a food hopper and water bottle mounted on the front. Additional food pellets were scattered on the floors of both types of cages which were located in a continuously illuminated vivarium also used to house other animals. Cages were cleaned and animals weighed weekly.

Procedure

Emergence and Open Field Tests. All surviving animals were

observed for four consecutive days at 13, 19, and 25 months. Those in the reaction time condition (see below) were still food deprived; others were under the usual condition of freely-available food.

Emergence tests were conducted in a quiet laboratory office. The animal was carried to the test room in the emergence box: a wooden chamber, 22 × 13 × 13 cm, with a removable front and a perforated fiberboard top. The box was placed on the edge of a bare desk with the opening facing the center. The experimenter then opened the front and recorded emergence time (all four paws on the table top). When the test was over (maximum = 5 min), the animal was carried in the box to a second room for the independent open field test.

The open field was a fiberboard table top, 112 × 76 cm, partitioned into 12 squares (3 × 4) by thin wooden strips, 1.5 cm high. Each test lasted 16 min. The animal was placed in a middle square and the number of squares entered (all four paws) was recorded. The emergence box and the open field top were washed with a disinfectant solution before the next animal was tested.

Reaction Time. Twelve animals, 3 males and 3 females randomly selected from each housing condition, were observed for periods of 6–8 wks beginning at 7, 13, 19 and 25 months. For these periods, the animals were deprived to 80% of their free-feeding weights, and the animals from the social condition were maintained in individual cages. This schedule allowed at least four months of free feeding before start of the next deprivation period.

Reaction times were measured using standard operant chambers (Grason-Stadler). The dipper delivered 0.1 ml of sweetened milk through an opening on one wall, and the lever and two stimulus lamps were positioned above. Suspended from the ceiling at the other end of the chamber was a beaded light-pull chain, attached to a microswitch. White noise from the speaker and the sound of the exhaust fan produced a masking noise (70 dB).

Operant sessions usually lasted about 45 min and continued until 50 trials were completed (not counting 10 warmup trials and those aborted by foreperiod responses). Under the self-paced procedure, the rat initiated each reaction time trial by pulling the chain ten times (fixed ratio 10). Reaction times to a pure tone (5000-Hz, 80 dB, produced by an Eico tone generator) were measured using the method developed by Stebbins and Lanson [e.g. 17]. The rat held down the lever in response to the ready signal (illumination of the stimulus lamps) and initiated a variable foreperiod (1.0, 1.5, or 2.0 sec). The time between onset of the tone, and release of the lever (measured to the nearest 50 msec) constituted the reaction time for that trial. Times shorter than 1000 msec were reinforced whereas all other responses were not. Performances also were observed when the trials were experimenter-paced in which case the pull chain was removed and an interval of 10 sec intervened between the end of one trial and the beginning of the next. With both procedures, a foreperiod response aborted the trial (the session was continued until the requisite 50 trials had been completed).

Observations were continued until performances were stable, and, at a minimum, for 10 subject-paced sessions, 4 experimenter-paced sessions, and 4 final subject-paced sessions. Before the 7-month set of observations, about 30 sessions were required to train the animals to perform properly. During subsequent observations, preliminary training was given as needed (usually 10 to 15 sessions).

Cause of Death. Our original intention was not to intervene regardless of health status. But as the study progressed we found it necessary to sacrifice 14 of the animals for humane reasons.
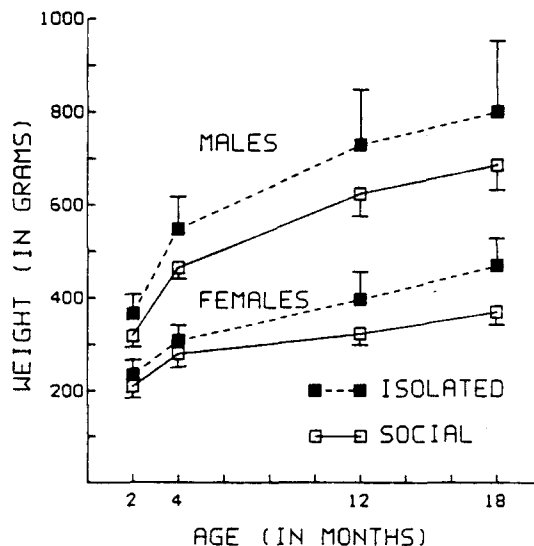

Figure 1. Mean weight of socially-housed and isolated male and female rats at 2, 4, 12, and 18 months of age. Standard deviations are represented by the bars. Only animals that lived at least 18 months were included in the analysis.

Ten developed major tumors that became severely ulcerated (Social = 7; Isolated = 3). Five others that were not sacrificed developed similar ulcerating tumors, but died before the planned sacrifice date. The other four sacrificed animals manifested contagious inner ear disease (Social = 2; Isolates = 0), or were found moribund (Social = 1; Isolate = 1). Thus, except for the animals with inner ear disease, sacrificed animals would have died at or near the point of intervention, and we believe that the need to sacrifice animals for humane reasons did not bias the results. For the remaining animals, the cause of death was unknown. Most often, the animal simply was found dead during the daily inspection. The behavioral data reported below were collected from animals which, to all appearances, were in good health.

RESULTS

Body Weight and Longevity

The social animals weighed less than the isolates throughout the study. Figure 1 summarizes weights at 2, 4, 12, and 18 months of age (too few animals survived beyond that point to continue the analysis). Data include the reaction time animals (after 4–5 months of free feeding their weights were comparable to nondeprived animals), but exclude six animals that did not survive to 18 months and one reaction time animal whose feeding was restricted at the 12- and 18-month points (Social = 19; Isolated = 12). Also, the last data points are based on the heaviest weights attained by each animal between 13 and 18 months (this was because some of the animals, mostly males regardless of housing, showed decreases in weight during this period; see below). Body weights were subjected to a 2 × 2 × 4 repeated-measures analysis of variance with type of housing and sex as between-group factors and age (2, 4, 12, and 18 months) as the repeated measure. The analysis confirmed that socially-housed animals weighed less than isolates across the four age comparisons and that differences were magnified as the animals grew older: housing, $F(1,27) = 16.26$, $p < .001$; housing × age, $F(3,81) = 8.45$, $p < .001$. Other reliable effects, also apparent in Figure 1, reflected the heavier weights of the males, sex, $F(1,27)$
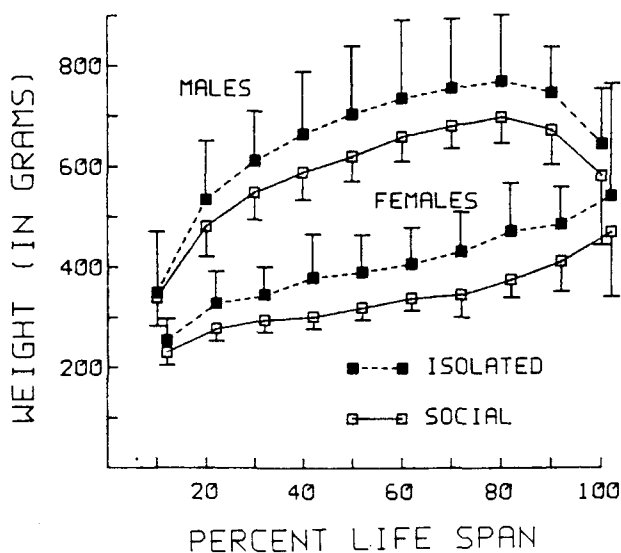
Figure 2. Mean weight of socially-housed and isolated male and female rats as a function of percentage life span. Standard deviations are represented by the bars. Only animals that were never food deprived (i.e., did not serve in the reaction time condition) and that lived at least one year were included in the analysis.

$= 164.40, p < .001$; weight increases with age, $F(3,81) = 472.05$, $p < .001$; and the interaction of age with sex, $F(3,81) = 65.70$, $p < .001$.

A different way of characterizing developmental changes is to express weight relative to each animal's life span (percentage life span). This analysis excluded three animals that did not survive the first year and those that had been food deprived (Social = 15; Isolates = 11). The data, summarized in Figure 2, were subjected to a repeated-measure analysis of variance with percentage life span (10% intervals) as the repeated measure.
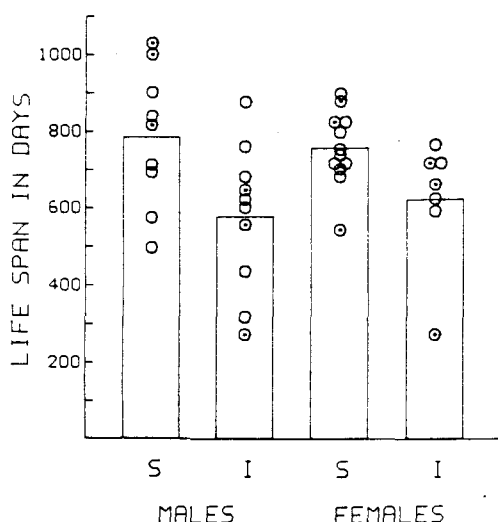
The results paralleled those of the previous analysis in showing the general effect of housing on body weight: housing, $F(1,22) = 5.94, p < .025$. Also reliable were changes associated with age, sex, and the interaction of age with sex: age, $F(9,198) = 55.10$, $p < .001$; sex, $F(1,22) = 86.77$, $p < .001$; age × sex, $F(9,198) = 11.94, p < .001$. Figure 2 indicates tendencies for the males to decrease in weight prior to death. Of the 13 males, 9 lost weight from the 80% point on, a pattern present under both housing conditions. By comparison the females continued to gain until they died.

The condition under which the animals were housed influenced longevity as well as body weight. Figure 3 shows the number of days of life for all animals, identified as to housing condition, sex, and exposure to the reaction time procedure (the latter factor did not appear to systematically influence longevity and was not considered further). Although animal-to-animal variation was considerable, socially-housed males and females lived longer, on the average, than their isolated counterparts: housing, $F(1,34) = 10.62, p < .01$; sex, ns; sex × housing, ns. The outcome was similar when the three isolated animals that lived less than one year were excluded from the analysis: housing, $F(1,31) = 5.64$, $p < .025$; sex, ns, sex × housing, ns.

Emergence and Open Field Tests

Figure 4 shows that socially-housed animals were more likely to leave the emergence box than isolated animals. All subjects were included: a preliminary analysis did not reveal systematic differences as a function of the state of deprivation under which the reaction time animals were observed. Differences as a function of housing were quite marked during the 13-month tests when the social animals emerged on at least three of the four tests (mean = 3.1 emergences) by comparison with the isolated animals who usually did not respond (mean = 0.6): housing, $F(1,30) = 33.37, p < .001$; sex, ns; housing × sex, ns. The pattern was similar at 19 months: housing, $F(1,20) = 8.23$, $p < .01$; sex, ns; housing × sex, ns. The social females, however, decreased somewhat relative to the earlier tests. Also apparent in Figure 4 are declines in the performances of socially-housed animals with increasing age (of the 9 animals observed at 25 months of age, 7 were below their 13-month scores).

Figure 3. Mean life span of socially-housed (S) and isolated (I) male and female rats. Individual animals are shown by the circles; those containing a dot designate animals serving in the operant portion of the study (and were food deprived for parts of their lives). Included are two animals, both socially-housed females, which had to be sacrificed at 715 days because of inner ear disease.
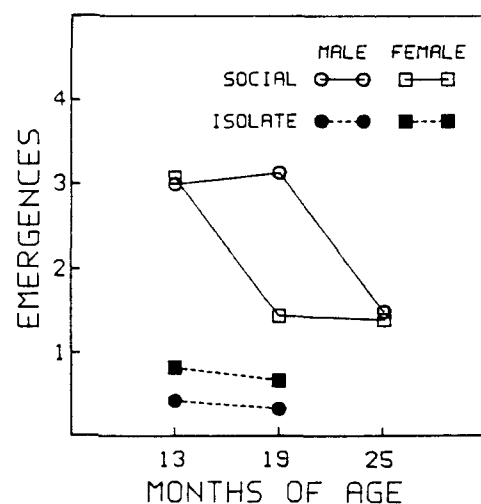

Figure 4. Mean number of emergences by socially-housed and isolated male and female rats. Tests were conducted on four consecutive days when animals were 13 months (Social, n = 21; Isolates, n = 13), 19 months (Social, n = 18; Isolates, n = 6), and 25 months (Social, n = 9) of age.
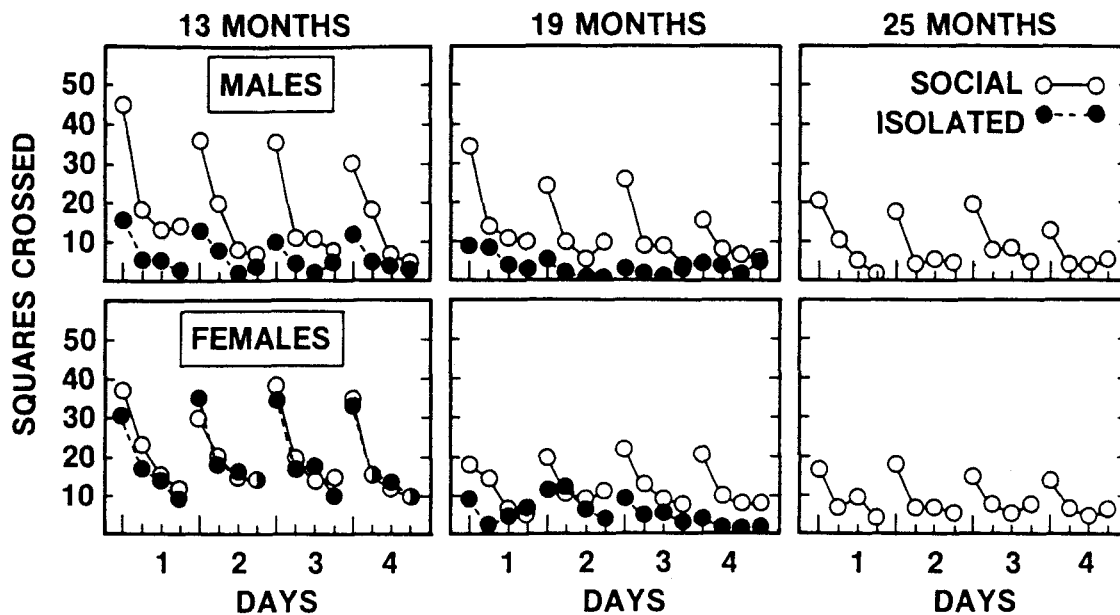
Figure 5. Mean number of square crossed by socially-housed and isolated male rats (top panels) and female rats (bottom panels). Tests were conducted on four consecutive days when animals were 13 months (Social, n = 21; Isolates, n = 13), 19 months (Social, n = 18; Isolates, n = 6) and 25 months (social, n = 9) of age. Data from each session are grouped in 4-min blocks.

Open field activity also varied as a function of age and housing. These results are summarized in Figure 5 as numbers of squares crossed on each test day, grouped in 4-min blocks. At 13 months, social animals crossed more squares, but this difference was largely due to the depressed performances of the isolated males. This result was confirmed by a repeated measures analysis with the four test sessions and the four 4-min blocks within each session as the repeated measures: housing, $F(1,30)$ = 8.20, $p<.01$; sex, $F(1,30) = 11.40$ $p<.01$; housing $\times$ sex, $F(1,30) = 4.73$, $p<.05$. Other findings at 13 months were that activity decreased between and within sessions: between sessions, $F(3,90) = 3.18$, $p<.05$; within sessions, $F(3,90) = 134.26$, $p<.001$. By 19 months, sex differences were absent and isolated males as well as females were less active than socially housed animals: housing, $F(1,20) = 5.84, p<.05$; sex, ns; housing $\times$ sex, ns. During these tests, activity continued to decline within but not between sessions: within sessions, $F(3,60) = 19.77, p<.001$; between sessions, $F(3,60) = 2.43, p<.05$. As with the emergence measure, most of the social animals declined in activity from 13 to 25 months (7 of 9 animals had lower scores).

Reaction Time and Operant Chain Pulling

Figure 6 summarizes a single-subject analysis [see 16] of reaction times. The open and closed circles in the top of the panels give each animal's characteristic reaction time (median of 200 reaction time trials) during the last four sessions in the self- and experimenter-paced conditions. The open and closed bars in the lower part of the panels show the proportion of trials when foreperiod responses occurred during these sessions.

The results provided no evidence of systematic differences in reaction times as a function of the housing or age variables, even in the cases of animals observed when more than 2 yrs old. Additionally, there was no indication that self-pacing of trials influenced performances. Although individual differences in reaction times were substantial, within-subject performances were orderly. The data shown in Figure 6 were collected when

session-to-session measures were stable, and times were similar under the self- and experimenter-paced procedures. Moreover, the relative ordering of the animals was consistent as the animals aged (7-13 months: r = + .76; 13-19 months: r = + .60). Also apparent in Figure 6 are substantial numbers of foreperiod responses, for some sessions on one-half or more of the trials. These anticipatory responses were unrelated to age, housing, or pacing, but were correlated with reaction time (r = − .58).

Other operant conditioning data included the rate of fixed ratio chain pulling (self-paced procedure), and the duration of pausing following delivery of the reinforcer (the post-reinforcement pause, sometimes seen as a measure of motivation to perform the upcoming ratio). These findings paralleled those for reaction times and foreperiod responses: systematic effects, either as a function of age or housing condition, were absent.

DISCUSSION

The environments in which the rats were housed had selective behavioral effects, in that locomotor activity (emergence and open field tests) was markedly influenced whereas reaction times to an auditory stimulus and associated operant responding were not. With regard to the activity measures, some researchers have concluded that isolation leads to abnormal activity levels [13], as well as undue aggressivity [10]. Our results indicated, to the contrary, that prolonged isolation was associated with timidity and inactivity (see [4], for a critical review of research on this question). Patterns of decreased activity, seen in the younger isolated animals, also appeared among the older socially-housed animals. Given the repeated testing entailed by the study's longitudinal design, the conclusion that these latter changes were a consequence of advancing age is somewhat problematic. Such a conclusion would, however, be consistent with the results of cross-sectional studies which controlled for testing effects [e.g., 7].
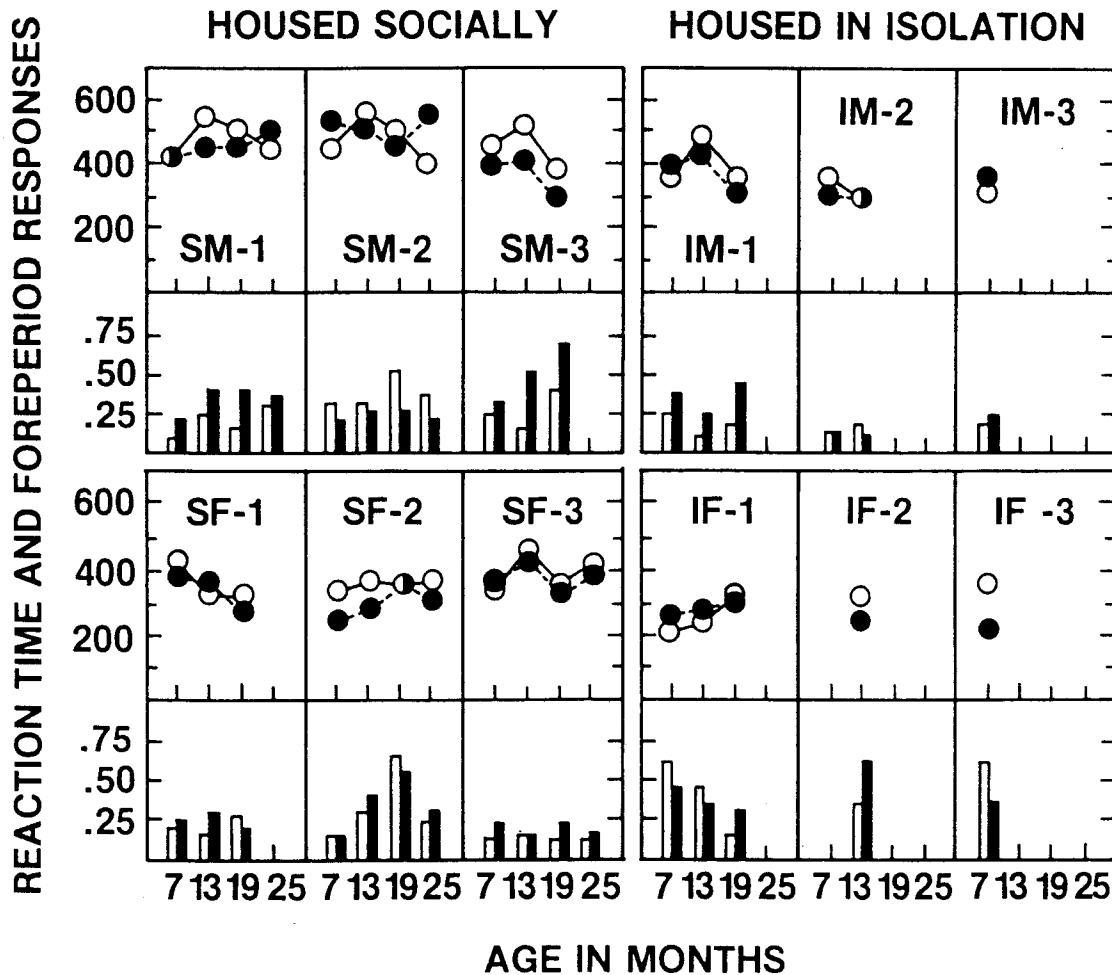
Figure 6. Each panel shows median reaction times (circles) and percentage of foreperiod responses (bars) for an individual animal serving in the reaction time part of the experiment. Data are based on the last 200 trials under the self-paced (open symbols) and experimenter-paced (closed symbols) conditions. Observations required periods of 4-6 weeks and were conducted when the rats were 7, 13, 19, and 25 months of age. Missing data points indicate that the animal had died, or, in the case of IF-2 at 7 months, that data were not collected.

Other studies also have found that isolation inhibits emergence [1] and open field responding [12]. But as noted above, there is a body of literature indicating the contrary finding that isolation leads to increased activity. In an effort to reconcile the contradiction, Dalrymple-Alford and Benton [5] suggested that isolation-induced hyperactivity can only appear after initial emotional reactions have dissipated, and that differences in results were due to the brief durations of the tests. In support of their hypothesis they presented data showing that isolated rats explored less than socially-housed rats at the start of two 5-day test series, but more as the tests progressed.

The present findings of decreased open field activity by isolates even when tests were prolonged (16 min/day for 4 days) may have been a consequence of the duration of exposure to the housing conditions. The animals had lived in the environments for a year or longer at the time of the tests, whereas other results are from animals no more than 3-4 months old [e.g., 5]. Another difference pertains to handling. Our animals were handled regularly (at the time of weekly weighing in addition to that required by the tests), and, regardless of housing condition, they appeared to us to be docile and unaggressive. In this regard, Hatch et al. [10] characterized the isolated rat as "a nervous, aggressive, intractable animal," but also noted that handling may attenuate abnormalities associated with

"isolation stress." Our findings are in agreement to the extent that regular handling reduced emotional reactions to the human experimenters. But handling did not offset the depressed activity that accompanied prolonged isolation.

The operant procedures provided extensive information about the capabilities of individual animals. Nevertheless, no evidence was forthcoming that reaction times or other aspects of performances varied as a function of housing or age. Our procedures appeared to provide a fair measure of speed of responding. With rare exception, animals met the reinforcement criterion (lever release within 1000 msec), and times were within the published ranges of distributions reported by Stebbins and Lanson [e.g., 17] for auditory stimuli (our modal values tended to be longer). Further, the absence of consistent effects cannot be attributed simply to the unreliability of the measures. Individual reaction times were stable across consecutive sessions, as well as between the self- and experimenter-paced procedures. Also noteworthy was that the relative ordering of the animals' times did not change much over intervals of six months or longer.

Complicating interpretations of operant performances are the substantial numbers of foreperiod responses observed throughout the study. Most likely, they were due to the absence of explicit negative contingencies (by comparison, in Stebbins

and Lanson [17] foreperiod responses delayed onset of the next trial by 2 min). We omitted such contingencies in favor of a procedure allowing collection of data about inhibitory processes (as indexed by different rates of foreperiod responses; however, age and housing differences were not observed). Various other arguments can be adduced for and against procedures which do not penalize foreperiod responses. Certainly, the occurrence of such responses on some trials implied weakening of control by the imperative stimulus. On the other hand, procedures which suppress foreperiod responses may have the undesirable consequence of slowing reaction times.

The finding that reaction times did not change with age is curious, given the well-known changes in human reaction times. Possibly significant was the longitudinal design which excluded the cohort effects inherent within the cross-sectional designs of most human studies. Furthermore, the older human's motivation to perform may not be optimal, whereas our rats were observed under controlled conditions of heightened motivation. Perhaps most critical is that reaction times of older adults usually are measured during a single brief session. By comparison, the study of rats necessitated extensive training on a task requiring perceptual-motor coordination (chain pulling) and psychomotor speed (rapid release of a lever). To the extent that age-related psychomotor declines are due to lack of practice, the present procedures may have inadvertently developed and maintained these capacities as the animals aged.

The finding that socially-housed rats tended to live longer than isolates also surprised us and, apparently, has not been reported before. The restricted sample size as well as difficulties in specifying the critical differences between the two environments suggest caution in viewing this result. One interpretation is that the life-extending variable was the enriched stimulation provided by cage mates. Alternatively, extended social isolation may be a source of stress with associated life-limiting effects. Also to be considered are other differences: the large cages in which the social animals were housed provided special opportunities for exploration and exercise (e.g., climbing the mesh walls and burrowing in the bedding material on the floor).

Of interest are the lesser weights of the socially-housed animals. Fiala et al. [8] showed that socially-housed rats eat less than isolates even though food is continuously available, and it is known that restricted food intake increases longevity [18]. Thus, longevity differences may have been mediated by differences in food intake, although the results do not reveal whether differences were due to overeating by the isolates (Fiala et al. suggested that "isolates may simply eat to relieve the boredom of their situation") or undereating by the social animals. In either case, a special feature of the present results is that these weight differences were behaviorally-mediated, this by comparison with procedures which manipulated weight by restricting available food.

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